

Sustainable Nanoscience: Modeling Liquids in Confinement and Nanoplastics

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“What helps a lot is just to enjoy the science and to see what the science can bring.”

Emmanuelle Charpentier

Publications

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3. University of Debrecen, Debrecen (Hungary), June 27-30, **2022**: Visit to the working group of Prof. Oldamur Hollóczki. Holding a talk on the packing effects of liquids confined in nanoporous materials.
4. Congress on Ionic Liquids (COIL-9), Lyon (France), April 24-28, **2023**: Talk on the coordination behavior of ionic liquids in the confinement of carbon nanotubes.
5. European Molecular Liquids Group (EMLG) Conference, Bordeaux (France), September 5-7, **2023**: Presentation of a poster on the CONAN program and a talk discussing the functionalities of CONAN, as well as discussing the coordination behavior of an ionic liquid in confinement.
6. JungesChemieForum (JCF), Bonn (Germany), July 2, **2024**: Talk on the effects of confinement of nanoporous materials on the behavior of confined liquids.
7. Gordon Research Conference (GRC), Newry, Maine (USA), August 4-9, **2024**: Presentation of a poster highlighting the functionalities of the program CONAN.
8. University of California San Diego (UCSD), San Diego (USA), January - April, **2025**: Guest stay in the working group of Prof. Francesco Paesani.

Abstract

As the global demand for electric power surges and the transition away from fossil fuels continues, developing optimized energy storage systems has become increasingly important. The optimization of electrode materials and electrolytes is central to maximizing storage efficiency. In this context, nanoporous materials, such as porous carbons, carbon nanotubes and metal-organic frameworks have gained significant attention. The geometry of their porous networks governs the structure and dynamics of the confined electrolytes and is fundamental to consider for further optimizations of electrode-electrolyte systems.

At the same time, nanoplastics have become ubiquitous in the environment over the past decades. The particles primarily arise from tire abrasion, mechanical wear of textiles and degradation of macroplastics improperly disposed of. While the long term toxicological impacts on human health are not yet fully understood, recent studies show that nanoplastics can cross various biological barriers and have been found in the digestive tract, blood and even the brain. These findings underscore the need for further studies in this area and to establish new methods that provide further insight into how nanoplastics behave on a molecular level.

Although the two topics do appear unrelated at first glance, both cover areas of *nanoscience* in which understanding the behavior of matter at an atomic resolution is key. This thesis relies on computational methods to model these systems and novel analysis methods and modeling approaches to advance the research in both fields are presented.

The first part focuses on modeling liquids within nanoporous materials using molecular dynamics simulations. The liquids studied include ionic liquids, salt-in-ionic liquid mixtures, and water, while the nanoporous materials comprise carbon nanotubes of differing size and the metal-organic framework ZIF-8. In order to resolve the structure and dynamics of liquids of these highly anisotropic, solid-liquid systems, a main part of this thesis covers the development of a new analysis program, CONAN. It is an open-source software that focuses on the analysis of confinement effects impacting the structure and dynamics of confined liquids. Using CONAN, the structural features of ionic liquids and salt-in-ionic liquids in the confinement of sub-nanometer carbon nanotubes and the metal-organic framework ZIF-8 are analyzed relying on novel analysis tools. Furthermore, structural and dynamical properties of water in confinement of single, isolated carbon nanotubes and vertically aligned carbon nanotube arrays are discussed.

Secondly, this thesis explores various methods for folding individual polymer strands into nanoplastic particles. The goal of this task lies in capturing the variability of nanoplastics found in the environment in terms of their structure and composition and to generate sets of relevant conformations. As these plastics consist of multiple, interwoven polymer strands which can fold into a myriad of possible

conformers, a complete scan of the conformational space is computationally unfeasible. Instead, sets of nanoplastic structures are generated, evaluated, and provided as datasets for further research. In addition, nanoplastics readily aggregate with surrounding colloidal matter and organic molecules. This includes other pollutants such as antibiotics, which are increasingly prevalent in the environment. In this context, the adsorption of the antibiotic onto various types of nanoplastics is studied, and relevant nanoplastics and nanoplastic–tetracycline aggregate conformations are discussed. Furthermore, a novel approach for nanoplastic folding is presented that significantly expands the diversity of accessible nanoplastic structures.

Contents

Publications	v
Abstract	vii
1 From Philosophy to Nanoscience	1
1.1 Computational chemistry	3
1.1.1 Theoretical background	3
1.2 Density functional theory	4
1.2.1 Exchange-correlation functionals	5
1.2.2 Basis sets	6
1.3 Semiempirical models	7
1.4 Molecular dynamics	7
1.5 Force fields	10
1.6 MB-pol potential	12
1.7 Periodic boundary conditions	13
1.8 Thermodynamic ensembles in molecular dynamics	14
2 Modeling and Analysis of Molecular Systems	17
2.1 Liquids	17
2.2 Materials	20
2.2.1 Carbon allotropes	20
2.2.2 Metal organic framework	22
2.2.3 Nanoplastic particles	23
2.3 Calculating properties from simulations	24
2.3.1 Molecular and structure recognition	26
2.4 Analysis options	28
2.4.1 Static properties	29
2.4.2 Dynamic properties	31
3 CONAN- Novel Tool to Create and Analyze Liquids in Confined Space	33
4 Coordination Behavior of a Confined Ionic Liquid in Carbon Nanotubes from Molecular Dynamics Simulations	37

5	Influence of Internal Interfaces on the Structure and Dynamics of IL-Based Electrolytes Confined in a Metal–Organic Framework	41
6	Carbon polarization and carbon nanotube stacking impacts the behavior of water in nanoconfinement	45
7	The adsorption of drugs on nanoplastics has severe biological impact	49
8	Building Nanoplastic Models for Molecular Calculations	53
9	Nanoplastics can build themselves	57
10	Summary	61
	Acknowledgements	65
A	Appendix: CONAN - Novel Tool to Create and Analyze Liquids in Confined Space	67
B	Appendix: Coordination Behavior of a Confined Ionic Liquid in Carbon Nanotubes from Molecular Dynamics Simulations	79
C	Appendix: Influence of Internal Interfaces on the Structure and Dynamics of IL-Based Electrolytes Confined in a Metal–Organic Framework	93
D	Appendix: Carbon polarization and carbon nanotube stacking impacts the behavior of water in nanoconfinement	107
E	Appendix: The adsorption of drugs on nanoplastics has severe biological impact	121
F	Appendix: Building Nanoplastic Models for Molecular Calculations	141
G	Appendix: Nanoplastics can build themselves	155
	Bibliography	163
	List of Figures	179
	List of Acronyms	181

From Philosophy to Nanoscience

SINCE ancient times, humans have sought to understand and manipulate the materials around them, driven both by curiosity and the need to create tools with specific, tailored properties. Material science and chemical processes, although not yet considered as such, were already important back then. Around 500 BC, the philosophers Leucippus and Democritus from ancient Greece were devoted to the question of how matter is built. They concluded that all matter must be composed of indivisible, smallest units, which they named “atomos”, meaning “indivisible” in Greek language. It laid the foundation for the atomic concept, even if the conclusion was drawn from a purely philosophical perspective. A systematic approach to describing matter did, however, not emerge until the Age of Enlightenment, starting in the 17th century. Experimental evidence and reasoning became the basis of explaining natural phenomena and establishing physical concepts. Based on this methodology, it was Lavoisier to first recognize oxygen as a chemical element and to describe its role in combustion reactions. Further, his work, and works from other researchers at the time, lead to the discovery of the law of mass conservation. His experimental work and data-based reasoning earned him his reputation as the “father of modern chemistry”. Building on this foundation, it took until the 19th century to further consolidate the atomic view on matter. In 1803, Dalton came to the conclusion that elements consist of atoms of the same type, while chemical compounds consist of different types of atoms, which come in fixed compositions. Avogadro could show in 1811 that two ideal gases with the same volume and temperature contain the same number of particles, introducing the connection between the amount or weight of a substance and the number of particles it contains. Then, in 1869, Mendeleev and Meyer independently constructed the periodic table of elements. The logical arrangement of elements allowed for the prediction of yet undiscovered elements and even forecasted their physical and chemical properties.

The discovery of the electron by Thomson in 1897 changed the view on the most fundamental particles again. It took the work of Rutherford¹² and Bohr¹³ in 1911 and 1913, respectively, to introduce a new atomic model, with a tiny, positively charged nucleus in the center surrounded by a cloud of electrons. Bohr was the first to introduce quantization into the atomic model by describing the movement of electrons in discrete orbitals, accounting for some quantum effects. When an electron jumps from one orbit to another, the transition is accompanied by the absorption or emission of quantized electromagnetic radiation. The quantum mechanical description of matter was continuously developed further by Planck, Dirac, Fermi, Einstein, Schrödinger, Heisenberg, de Broglie^{14–21} and

others.

With the newly developed theoretical framework to accurately describe matter on an atomic and electronic level, including chemical bonding and intermolecular interactions, the conceptual basis for a new scientific discipline was laid: *nanoscience*. The beginning of nanoscience is often attributed to Feynman, who delivered a famous lecture “There’s plenty of room at the bottom” in 1959.²² In his lecture, he envisioned that many devices could be miniaturized and materials be customized on an atomic level. Nanoporous compounds such as activated carbons, zeolites and clays were already known at that time, but it took until the 1980s, for the first experimental breakthroughs to be made in synthesizing new nanomaterials. The discovery of fullerenes in 1985 by Kroto, Curl and Smalley,²³ who were awarded the Nobel Prize in Chemistry in 1996, marked the beginning of modern nanoscience. The discovery of carbon nanotubes (CNTs) by Iijima in 1991 further fueled the research on nanomaterials, followed by the first synthesis of graphene by Geim and Novoselov in 2004,²⁴ who were awarded the Nobel Prize in Physics in 2010 for their work. Besides carbon based materials, other porous, tunable nanomaterials were developed in the last decades. Metal-organic frameworks (MOFs) were synthesized for the first time by Yaghi in 1995.²⁵ They are highly porous compounds consisting of inorganic metal clusters and organic linkers, building a three-dimensional network. Yaghi, Kitagawa and Robson were awarded the Nobel Prize in Chemistry for their work on MOFs in 2025.²⁶ CNTs and MOFs have in common that they allow for a high degree of tunability of their porous structure, i.e., pore size.^a

Parallel to this development, the 20th century was transformed by the invention and widespread use of synthetic polymers. Starting with Bakelite in 1907, many different polymers were developed and found their way into everyday life. Much of this progress can be attributed to the works of Staudinger, who was awarded the Nobel Prize in Chemistry in 1953 for his work on macromolecules.²⁷ Ziegler and Natta were also awarded the Nobel Prize in Chemistry in 1963,²⁸ for their work on polymerization catalysts, which enabled the synthesis of polymers of high molecular weight with specific properties at low cost. With this development, plastics became ubiquitous in modern life due to their durability and versatility. However, in recent times, it has become clear that the widespread use of plastics causes environmental problems. The accumulation of plastic waste in the environment, especially in the oceans, has become a major concern. The degradation of plastics is slow and leads to the formation of micro- and nanoplastics (MNPs) over time. The environmental impact of these particles and their toxicological effects on living organisms are not yet fully understood. At the nanoscale, polymer fragments behave fundamentally differently compared to macroplastics, and the interaction between nanoplastics (NPs) and biological systems is an active field of research. Recent studies show that they do impact ecosystems and human health.^{29–33}

Despite the progress in understanding and manipulating nanomaterials, their interaction with the environment requires insights at an atomic level that are difficult to obtain experimentally. This task has driven the rise of computational chemistry as an important part of modern material science. By solving the fundamental equations of quantum mechanics (QM) and classical physics, computational models allow for the prediction of molecular properties and reaction mechanisms, as well as the simulation of dynamic processes.

This thesis builds upon these theoretical foundations to investigate structural and energetic properties of nanomaterials. The following sections in this chapter provide an overview of the computational methods employed and their theoretical background. The materials investigated are presented in

^a Details for these materials are given in Section 2.2.

Chapter 2, together with an introduction to novel analysis tools developed to study them. Chapter 3–Chapter 6 present research contributions on the behavior of liquids confined in nanoporous materials. Chapter 7–Chapter 9 focus on the molecular structure of NPs and their interactions with other molecules. Finally, Chapter 10 summarizes the key findings and gives an outlook on future research directions in this field.

1.1 Computational chemistry

1.1.1 Theoretical background

The description of molecular systems through the use of computer models is an ever-growing field in chemistry and material science. Historically, in the latter half of the 19th century, multiple microscopic phenomena were observed, e.g., the emission spectra of atoms, which could not be explained using Newtonian mechanics. First attempts to describe these phenomena were made by Planck in 1900, introducing the quantization of energy levels and the Planck's constant h .¹⁵ He showed that any harmonically oscillating system can only absorb and emit energy in discrete quantities, based on multiples n of h and connected to the frequency ν of the oscillation:

$$E = nh\nu, \quad n = 1, 2, 3, \dots \quad (1.1)$$

This theoretical framework was further developed by de Broglie, who introduced the concept of electron waves.²¹ He argued that electrons positioned around the nucleus of an atom could be understood as standing waves. Based on this introduction, all matter could be described as waves, laying the groundwork for the wave-particle duality concept. Developed by Schrödinger in 1926, the time-dependent Schrödinger equation¹⁹ provides a mathematical framework to describe the behavior of quantum mechanical systems as a function of time t :

$$i\hbar \frac{\partial}{\partial t} |\Psi(t)\rangle = \hat{H} |\Psi(t)\rangle \quad (1.2)$$

Here, the Hamilton operator $\hat{H}$ is applied to the wavefunction $\Psi(t)$ of the system, and the result shows the time evolution of the wavefunction. i is the imaginary unit, $\hbar$ the reduced Planck constant and $\frac{\partial}{\partial t}$ the partial derivative with respect to the time t . The probability of finding a particle at a given position r is described using a probability density:

$$P(r, t) = |\Psi(r, t)|^2 \quad (1.3)$$

When considering stationary states only, the time independent Schrödinger equation can be formulated:

$$\hat{H} |\Psi\rangle = E |\Psi\rangle \quad (1.4)$$

Here, the Hamilton operator is applied to the wavefunction of the system, resulting in the total energy E as its eigenvalue. Analytical solutions to the Schrödinger equation exist only for simple systems, such as the hydrogen atom, or theoretical models like the particle in a box. For realistic systems, approximations are required to estimate the solution by an iterative numerical approach.

The Hamilton operator describes the total energy contributions of a quantum chemical system,

consisting of kinetic and potential energy terms for electrons and nuclei:

$$\hat{H} = \hat{T}_e + \hat{T}_n + \hat{V}_{ee} + \hat{V}_{nn} + \hat{V}_{en} \quad (1.5)$$

$\hat{T}_e$ and $\hat{T}_n$ describe the kinetic energy of electrons and nuclei, respectively. The potential energy contributions are described through the electron-electron repulsion $\hat{V}_{ee}$, the nucleus-nucleus repulsion $\hat{V}_{nn}$ and the electron-nucleus attraction $\hat{V}_{en}$.

For the computation of molecular systems, the full Hamiltonian is often simplified using the Born-Oppenheimer approximation,³⁴ which is the basis for most electronic structure methods. By assuming that the wave functions of the nuclei and electrons can be treated separately, the nuclei are treated as fixed point charges. This is based on the fact that nuclei are much heavier than electrons, and therefore move much slower. One can envision this approximation as the electrons moving in a static potential created by the fixed nuclei. With the nuclear positions being constant, the electronic Hamiltonian $\hat{H}_{el}$ that acts on the electronic coordinates is

$$\hat{H}_{el} = \hat{T}_e + \hat{V}_{ee} + \hat{V}_{en}, \quad (1.6)$$

as the nuclear kinetic operator $\hat{T}_n$ is neglected and the nucleus–nucleus repulsion V_{nn} is a constant for the given nuclear geometry.

The electronic Schrödinger equation can then be used to obtain the electronic energy E_{el} at fixed nuclear positions $\mathbf{R}$, which defines the potential energy surface (PES) on which the nuclei move. The total energy E_{tot} on the potential energy surface is calculated using

$$E_{tot}(\mathbf{R}) = E_{el}(\mathbf{R}) + V_{nn}(\mathbf{R}). \quad (1.7)$$

A central challenge in solving the Schrödinger equation for multi-electron systems lies in accurately describing the electron-electron repulsion term $\hat{V}_{ee}$. Here, the motion of each electron is influenced by the presence and motion of all other electrons, leading to a complex many-body problem. To approximate the solution to the Schrödinger equation, multiple *ab-initio* methods have been developed. They split into two main categories, wavefunction theory and density functional theory (DFT). As no wavefunction-based methods are used in this work, only DFT is briefly discussed in Section 1.2.

1.2 Density functional theory

The fundamental concept of DFT is to describe a quantum-mechanical system through its electron density $\rho(\mathbf{r})$ rather than the complex many-body wavefunction $\Psi(\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N)$. While $\mathbf{r}$ denotes the three-dimensional spatial coordinates, $\mathbf{r}_i$ represents the coordinates of the i -th electron, with N being the total number of electrons in the system. While Thomas and Fermi were the first to propose a model based on the electron density in the late 1920s,^{17,35} it was the work of Hohenberg and Kohn in 1964 that laid the formal foundation for modern DFT with two central theorems.³⁶ The first theorem establishes that the ground state density uniquely determines the system's potential and thereby all other ground state properties. The second theorem introduces the concept of a universal energy functional $E[\rho(\mathbf{r})]$, which yields the ground state energy when minimized with the correct ground state density. However, the theorems only prove the existence of this functional, not its exact form. In particular, the kinetic energy term and the electron–electron exchange–correlation energy are difficult

to express as explicit functionals of the electron density. Nevertheless, the theorems gave a prospect of a significant reduction in computational cost compared to wavefunction-based methods, as the energy functional depends on three spatial coordinates instead of $3N$ coordinates for a wavefunction of N electrons. In 1965, Kohn and Sham introduced the Kohn-Sham equations, marking a major step forward in making DFT a practical method.³⁷ They introduced the idea of mapping the interacting many-electron system onto a fictitious system of non-interacting electrons moving in an effective potential. This approach allows the total energy functional to be approximated as

$$E[\rho(\mathbf{r})] = T_s[\rho(\mathbf{r})] + \int V_{\text{ext}}(\mathbf{r})\rho(\mathbf{r})d\mathbf{r} + E_H[\rho(\mathbf{r})] + E_{xc}[\rho(\mathbf{r})], \quad (1.8)$$

where $T_s[\rho(\mathbf{r})]$ describes the kinetic energy of non-interacting electrons with density $\rho(\mathbf{r})$, and the external potential, $V_{\text{ext}}(\mathbf{r})$, accounts for the interaction between the electrons and the nuclei.

The Hartree energy $E_H[\rho(\mathbf{r})]$ describes the classical electrostatic repulsion between electrons. All complex many-body effects that are difficult to capture, as well as correction terms, are summarized in the exchange-correlation functional $E_{xc}[\rho(\mathbf{r})]$. This term accounts for the difference between the exact and non-interacting kinetic energy, non-classical electron-electron exchange effects, and correlation contributions. The practicality of the approach and the ability to systematically improve $E_{xc}[\rho(\mathbf{r})]$ to enhance accuracy (see Section 1.2.1), drove the widespread adoption of DFT in computational chemistry.

1.2.1 Exchange-correlation functionals

The need to improve the exchange-correlation term to achieve higher chemical accuracy led to the development of various classes of functionals. These functionals are grouped into different rungs on “Jacob’s Ladder”, which categorizes them based on their complexity and accuracy.³⁸

Local density approximation One of the simplest approximations is the local density approximation (LDA).³⁷ The LDA assumes that the exchange-correlation energy at each point in space depends only on the local electron density $\rho(\mathbf{r})$ at that point. It is expressed as:

$$E_{xc}^{\text{LDA}}[\rho(\mathbf{r})] = \int \rho(\mathbf{r})\epsilon_{xc}^{\text{uni}}(\rho(\mathbf{r}))d\mathbf{r} \quad (1.9)$$

Here, $\epsilon_{xc}^{\text{uni}}(\rho(\mathbf{r}))$ is the exchange-correlation energy per particle of a homogeneous electron gas with density $\rho(\mathbf{r})$. This approach is efficient and works well for systems with slowly varying spatial electron densities, such as metals. A major drawback is that the approach does not account for density variations in space, often overestimating correlation effects while underestimating exchange effects. Consequently, the LDA is often not suitable for systems with strong inhomogeneities in the electron density, such as molecular systems.

Generalized gradient approximation To better account for the spatial variation of the electron density, the generalized gradient approximation (GGA) was developed.^{39–41} Its form depends not only

on the local density but also on its gradient:

$$E_{xc}^{GGA}[\rho(\mathbf{r})] = \int \rho(\mathbf{r}) \epsilon_{xc}^{uni}(\rho(\mathbf{r}), \nabla \rho(\mathbf{r})) d\mathbf{r} \quad (1.10)$$

This approach can significantly improve the description of inhomogeneous systems. Common functionals such as PBE⁴² and BP86^{40,43} belong to this family. Meta-GGAs (mGGAs) further extend the GGA by including higher-order derivatives of the electron density. Despite these advances, these local and semi-local approximations are still prone to systematic errors, such as the self interaction error and the inability to capture long-range dispersion effects.

Hybrid functionals Introduced by Becke in 1993,⁴⁴ hybrid functionals represent a significant advancement in density functional theory. By incorporating a fraction of exact Hartree-Fock (HF) exchange into the GGA or meta-GGA framework, they reduce the self-interaction error inherent in pure DFT functionals, leading to improved accuracy. A prominent example is the Becke-3-LYP (B3LYP) functional, which constructs the exchange-correlation energy by mixing 20% exact HF exchange with 80% local spin density approximation (LSDA) exchange, supplemented by the Becke 88 (B88) gradient correction.⁴⁰ Other widely used hybrid functionals are, e.g., PBE0,⁴⁵ where 25% of exact HF exchange is combined with 75% of Perdew-Burke-Ernzerhof (PBE) exchange, along with the full PBE correlation energy:

$$E_{xc}^{PBE0} = 0.25E_x^{HF} + 0.75E_x^{PBE} + E_c^{PBE} \quad (1.11)$$

Dispersion corrections A general shortcoming of mean field theory methods is their inability to accurately describe long-range electron correlation, resulting in a lack of London dispersion forces. To address this, additive dispersion corrections are often used. In this work, the D3 dispersion correction with Becke–Johnson damping [D3(BJ)] is utilized during geometry optimizations.^{46,47} It adds an atom-pairwise potential to the DFT potential, improving the description of non-covalent interactions at minor computational cost.

1.2.2 Basis sets

To solve the Kohn-Sham equations computationally, the molecular orbitals (and thus the electron density) must be represented mathematically. This is achieved by constructing the molecular orbitals ψ_i as linear combinations of a set of atomic orbitals ϕ_j , called basis functions. This approach is known as the linear combination of atomic orbitals (LCAO) method:

$$\psi_i = \sum_j c_{ij} \phi_j \quad (1.12)$$

The running parameters j and i denote the number of basis functions and molecular orbitals, respectively. The set of the functions $\{\phi_j\}$ represents the basis set. The coefficients c_{ij} are determined by minimizing the total energy. Ideally, a complete basis set (infinite number of functions) would be used to reach the basis set limit, but in practice, a finite set must be chosen to keep calculations feasible. Most quantum chemical codes rely on simple Gaussian-type orbitals (GTOs) as basis functions because they allow for efficient integration. They are used to approximate Slater-type orbitals (STOs), which

are computationally more difficult to handle due to the cusp at $r = 0$. The GTOs are centered around the atom nuclei. Minimal basis sets use the minimum number of functions required to describe all occupied orbitals of the atoms. For example, STO- n G (e.g., STO-3G) approximate a single STO using n GTOs. This makes them computationally efficient, but they often lack the flexibility to accurately describe molecular properties. Valence electrons are involved in chemical bonding and reactivity, and often require a more flexible description. Split-valence basis sets (e.g., Pople’s 6-31G*)⁴⁸ try to address this by using multiple functions for valence orbitals, while keeping the minimal approach for core electrons. Core orbitals are thus described with one set of functions and valence orbitals with two or more sets (double- ζ , triple- ζ , etc.). This allows the valence electron density to adjust more flexibly to the chemical environment.

In this work, the “def2” family of basis sets developed by the Ahlrichs group is primarily used.⁴⁹ The basis sets cover nearly the entire periodic table and are designed to minimize basis set superposition error (BSSE).⁵⁰ Common examples include the split-valence def2-SV(P) (Split Valence Polarization) for quick estimates and the triple- ζ def2-TZVP (Triple Zeta Valence Polarization) for accurate energies and geometries.

1.3 Semiempirical models

Semiempirical methods aim to simplify high-level *ab initio* methods, offering a compromise between computational efficiency and accuracy.^{51–55} Derived from first-principles theories such as HF and DFT, they introduce approximations, particularly regarding the two-electron interactions, which are computationally the most expensive part of standard QM calculations. Empirical parameters are introduced, which are fitted against experimental data or high-level quantum chemical reference values to account for the approximations made.

In the works presented here, the GFN2-xTB (Geometry, Frequency, Non-covalent interaction eXtended Tight Binding) method is employed.⁵⁵ In this model, only valence electrons are treated explicitly using a minimal basis set of atom-centered Gaussian functions to estimate STOs, while core electrons are modeled by effective potentials. To accurately describe non-covalent interactions, such as hydrogen bonding and dispersion forces, the model includes anisotropic second-order density fluctuation effects.

1.4 Molecular dynamics

The quantum-mechanical methods discussed in the previous sections are important tools for determining static properties of molecules and materials by solving the time-independent Schrödinger equation. The access to the electronic structure enables, for example, the calculation of energy minima on the PES, yielding optimized molecular geometries. Transition states of chemical reactions, or the prediction of reaction enthalpies and reaction barriers can be calculated. However, these methods describe *static* configurations, specific points on the PES that are searched for.

In many cases, not only the static properties of a molecular system and its equilibrium configurations are of interest, but also the system’s *dynamic* behavior. A time-dependent evolution of a system provides valuable insight into chemical reaction mechanisms, conformational changes of molecules, the diffusion of molecules and other dynamical properties, or vibrational spectra.^{56–60}

Also, some static quantities within molecular systems are not directly time-dependent, but require a large number of system configurations for a robust statistical evaluation. Examples include liquids, in which the local structure around a molecule fluctuates over time and is not strictly defined as it is in solids. To generate such a set of configurations, molecular dynamics (MD) simulations are an important tool.

In the MD formalism, the time evolution of a molecular system containing N atoms is described by repeatedly solving Newton's second law of motion,⁶¹ which connects the change in the momentum of an atom to the force exerted on it:

$$\mathbf{F}_i(\mathbf{x}_i(t), \mathbf{v}_i(t), t) = \frac{d\mathbf{p}_i(t)}{dt}, \quad i = 1, \dots, N \quad (1.13)$$

The position, velocity and momentum of atom i are denoted by $\mathbf{x}_i(t)$, $\mathbf{v}_i(t)$ and $\mathbf{p}_i(t)$, respectively. The momentum is defined as $\mathbf{p}_i(t) = m_i \cdot \mathbf{v}_i(t)$ and combines the mass m_i and velocity of a given particle. All quantities in Eq. (1.13) are functions of time t . The equation can be rearranged as:

$$\mathbf{F}_i = m_i \cdot \frac{d\mathbf{v}_i(t)}{dt} = m_i \cdot \mathbf{a}_i, \quad i = 1, \dots, N \quad (1.14)$$

Here, $\mathbf{a}_i$ describes the acceleration of atom i . The force acting on atom can also be expressed as the negative gradient of the systems potential energy U_{pot} , following the equation:

$$\mathbf{F}_i = -\nabla_{\mathbf{x}_i} U_{\text{pot}}(\mathbf{x}_1, \dots, \mathbf{x}_N) \quad (1.15)$$

The potential energy depends on all particle positions $\mathbf{x}_i$ within the system and describes all intramolecular and intermolecular atomic interactions.

The total energy (U_{tot}) of a molecular system is defined as the sum of its kinetic (U_{kin}) and potential (U_{pot}) contributions,

$$U_{\text{tot}} = U_{\text{kin}} + U_{\text{pot}}, \quad (1.16)$$

where the kinetic energy represents the sum of the kinetic energies of all atoms present in the system, covering vibrational and translational motions:

$$U_{\text{kin}} = \sum_{i=1}^N \frac{1}{2} m_i \mathbf{v}_i(t)^2 \quad (1.17)$$

The potential energy U_{pot} of each atom is computed using a potential energy function or force field, with specifics discussed in the next sections.

The time integration of the system is achieved by solving the equation of motion using small, discrete time steps Δt , typically in the order of femtoseconds. The choice of the time step is important, as it has to be small enough to accurately describe fast motions, such as bond vibrations, but large enough to allow for the simulation of relevant time scales with reasonable computational effort.^a

For each time step, the forces $\mathbf{F}_i$ acting on each atom are calculated based on their current positions. Using Eq. (1.14), the acceleration $\mathbf{a}_i$ of each atom is computed, and the positions and velocities are updated. This is done using established integration algorithms from the Verlet⁶² or Velocity-Verlet

^a The studies presented in this work rely on simulations using time steps of 0.5 fs to 1 fs, depending on the system investigated and the model used.

family of algorithms.⁶³ The Verlet algorithm in its original form is given by:

$$\mathbf{x}_i(t + \Delta t) = 2\mathbf{x}_i(t) - \mathbf{x}_i(t - \Delta t) + \mathbf{a}_i(t)\Delta t^2 \quad (1.18)$$

Here, the new position $\mathbf{x}_i(t + \Delta t)$ is calculated based on the current position $\mathbf{x}_i(t)$, the previous position $\mathbf{x}_i(t - \Delta t)$, and the current acceleration $\mathbf{a}_i(t)$. The velocity is not explicitly calculated in this formulation, but can be estimated as:

$$\mathbf{v}_i(t) = \frac{\mathbf{x}_i(t + \Delta t) - \mathbf{x}_i(t - \Delta t)}{2\Delta t} \quad (1.19)$$

The velocity calculation is thus always lagging behind by one time step. With the Velocity-Verlet variation, the velocities are also updated explicitly, ensuring a simultaneous update of positions and velocities:

$$\mathbf{v}_i(t + \Delta t) = \mathbf{v}_i(t) + \frac{\mathbf{a}_i(t) + \mathbf{a}_i(t + \Delta t)}{2}\Delta t \quad (1.20)$$

By iterating through this process over a large number of time steps, a MD trajectory is generated, providing a time-resolved picture of the studied system. A trajectory file contains the positions of all atoms at each saved time step. Depending on the file format, it can also include the atomic velocities and other system information. Typically, simulations require either long simulation times or multiple independent replicas to adequately sample the configurational space of a system. The number of time steps that need to be calculated to gain a robust set of configurations varies between several hundred thousand to multiple millions, depending on the system and the properties of interest.

A trajectory of the system is generated by saving every n^{th} computed time step, resulting in a series of configurations forming the set. The frequency of saving frames is a compromise between having a sufficiently large number of configurations to capture the systems behavior, while keeping the size of the trajectory file manageable. It also depends on the properties of interest, as some require a high temporal resolution, e.g., for the computation of short-lived dynamical properties or the computation of vibrational spectra. Other system properties, such as average structural motifs, are best evaluated with a large time gap between saved configurations to avoid structural correlations.

The computational feasibility of running MD simulations in relation to the system size and the number of time steps strongly depends on the method used to compute U_{pot} . A prominent but costly option is *ab initio* MD, which estimates the potential energy and the resulting forces at each simulated time step through electronic structure calculations^a (Section 1.2).

Feasible systems sizes are in a range of 100 – 1000 atoms modeling 0.1 – 1 ns, even when relying on small basis sets and low-cost functionals. The systems covered in this work, e.g., modeling liquids in CNTs or modeling NPs, require systems containing multiple thousand of atoms and simulation times of multiple ns. This is accomplished by relying on methods which try to estimate the PES by further approximations.

^a Often, *ab initio* MD simulations are performed using DFT with GGA-type functionals, e.g., PBE, and small basis set for sufficient computational speed.

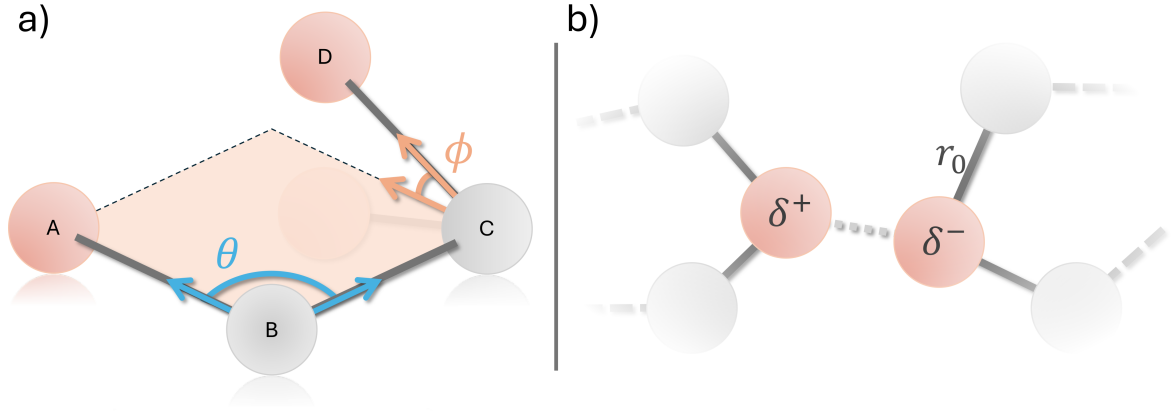


Figure 1.1: a) Scheme of four atoms connected by bonds to form a chain. θ describes the angle between the bonds B-A and B-C. ϕ describes the dihedral angle between the planes created by ABC and BCD. b) Scheme of two molecules, with two atoms highlighted in light-red interacting through non-bonded interactions. The respective atoms are assigned partial charges δ^+ and δ^- to model electrostatic interactions. r_0 describes the equilibrium distance between two bonded atoms.

1.5 Force fields

Force field (FF)-based MD simulations, as the name suggests, rely on classical force fields (FFs) and empirical parametrization to approximate U_{pot} . Atoms are modeled as classical point particles, with intra- and intermolecular interactions described by a set of fixed parameters. This allows for the modeling of large systems, containing tens of thousands of atoms, over long time scales. Coarse-grained methods group multiple atoms, functional groups or even entire molecules into larger particles, further reducing the computational cost. Usually, chemical reactions are not considered with this approach, however several reactive force fields do exist.^{64–66} Rather, the focus lies on describing the structural and dynamic properties of materials. In this thesis, all MD simulations were carried out at an atomistic resolution.

Using a set of parameters to model the bonded and non-bonded interactions, the potential energy function is given as:

$$U_{\text{pot}} = U_{\text{bonds}} + U_{\text{angles}} + U_{\text{dihedrals}} + U_{\text{nonbonded}} \quad (1.21)$$

The individual contributions are calculated depending on the FF used. A common approach is to describe the bond and angle terms (U_{bonds} and U_{angles}) using harmonic potentials. Figure 1.1a depicts a scheme of four atoms connected by bonds, forming a line. θ describes the angle between atoms A, B and C, while ϕ is the dihedral angle between atoms A, B, C and D. At the example of the OPLS-AA^{67,68} force field,^a intramolecular interactions are calculated by:

$$U_{\text{bonds}} = \sum_{\text{bonds}} k_r (r - r_0)^2 \quad (1.22)$$

$$U_{\text{angles}} = \sum_{\text{angles}} k_\theta (\theta - \theta_0)^2 \quad (1.23)$$

^a The OPLS-AA force field was employed for multiple works presented here.

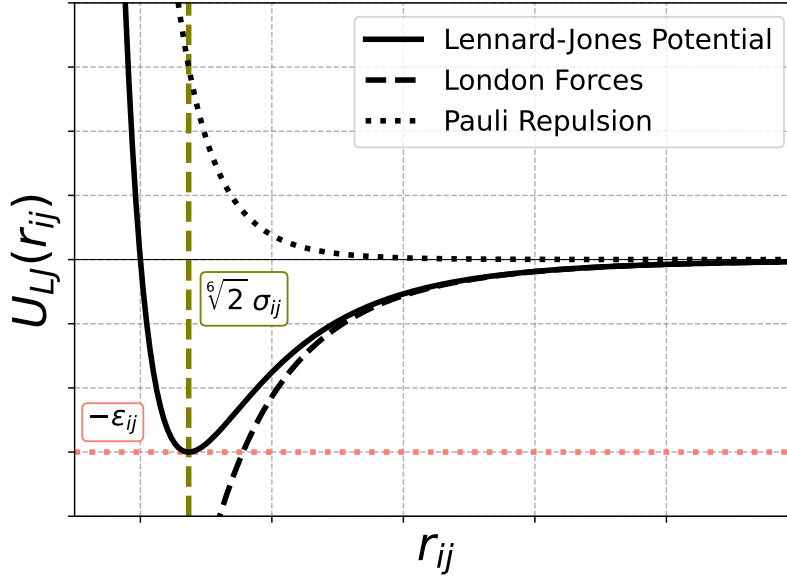


Figure 1.2: The figure depicts a LJ potential $U_{\text{LJ}}(r_{ij})$ in relation to the radial distance r_{ij} between two atoms i and j . The well depth is described by $-\epsilon_{ij}$, the position of the minima by $\sqrt[6]{2}\sigma_{\text{LJ}}$. The contributions from the Pauli repulsion and London forces terms are depicted in dotted, and dashed lines, respectively.

$$U_{\text{dihedrals}} = \sum_{\text{dihedrals}} \frac{1}{2} [V_1(1 + \cos(\phi - \phi_1)) + V_2(1 - \cos(2\phi - \phi_2)) + V_3(1 + \cos(3\phi - \phi_3)) + V_4(1 - \cos(4\phi - \phi_4))] \quad (1.24)$$

The force constants k_r and k_θ define the stiffness of the bonds and angles, respectively, while r_0 is the equilibrium bond length and θ_0 the equilibrium bond angle. V_i and ϕ_i are the Fourier coefficients and phase shifts for the dihedral angle potential. Non-bonded interactions $U_{\text{nonbonded}}$ are described using a Lennard-Jones (LJ) potential to account for van der Waals (vdW) interactions. The LJ potential consists of an attractive term, which models the London dispersion forces, using:

$$U_{\text{disp}}(r_{ij}) = -\frac{C}{r_{ij}^6} \quad (1.25)$$

Here, C is a term depending on the ionization energies and polarizabilities of the interacting atoms, while r_{ij} is the distance between the atoms i and j . At short distances, a repulsive term ensures that atoms do not collapse into each other, modeling Pauli repulsion. For practical reasons, this term is often modeled using a r^{-12} dependence, as it is the square of the attractive term and therefore computationally easily available. The complete (12-6)-LJ potential is given by

$$U_{\text{LJ}}(r_{ij}) = \frac{C}{r_{ij}^{12}} - \frac{C}{r_{ij}^6}, \quad (1.26)$$

or in its more common form:

$$U_{\text{LJ}}(r_{ij}) = 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right], \quad (1.27)$$

where ϵ_{ij} describes the depth of the potential well, σ_{ij} the distance at which the crosses the zero point between atoms i and j .

In addition to the LJ term, fixed partial charges q_i are assigned to each atom, and electrostatic interactions are modeled using Coulomb's law (see Figure 1.1b). This results in the total non-bonded interaction energy:

$$U_{\text{nonbonded}} = \sum_{i < j} \left(\frac{A_{ij}}{r_{ij}^{12}} - \frac{C_{ij}}{r_{ij}^6} + \frac{q_i q_j e^2}{4\pi\epsilon_0 r_{ij}} \right) \quad (1.28)$$

A_{ij} and C_{ij} are the FF parameters to adjust the LJ potential. r_{ij} is the distance between atoms i and j , while q_i and q_j are the partial charges assigned to the respective atoms. e is the elementary charge and ϵ_0 the vacuum permittivity.

The parameters of a FF are normally derived from a combination of experimental data and theoretical calculations. A FF is usually not generic, but optimized for specific classes of molecules or materials. Examples of classical force fields employed in studies presented in this thesis are optimized for ionic liquids (ILs),^{69,70} water,^{71–73} carbons^{74,75} and hydrocarbons for NP research.^{76–78} To run the MD simulations, multiple software packages were used.^{79–82}

1.6 MB–pol potential

The data-driven many-body potential for water, MB–pol, developed by Francesco Paesani and co-workers,^{83–89} is a subclass of potential energy functions, trained to accurately predict the behavior of water across different phases and environments on a molecular level. It is based on the many body expansion, describing the energy of a system of N water molecules by:

$$E_N(1, \dots, N) = \sum_{i=1}^N V^{\text{1B}}(i) + \sum_{i < j}^N V^{\text{2B}}(i, j) + \sum_{i < j < k}^N V^{\text{3B}}(i, j, k) + V_{\text{pol}}(1, \dots, N) \quad (1.29)$$

The 1-body, 2-body and 3-body terms are expressed as V^{1B} , V^{2B} , and V^{3B} , respectively. V_{pol} describes many-body polarization effects. The intramolecular 1-body term V^{1B} represents the distortion energy of a single water molecule from its equilibrium geometry. It is fitted to high-level *ab initio* data and accurately captures the vibrational properties of water. Geometry-dependent atomic partial charges and polarizabilities are calculated. The 2-body term V^{2B} describes the interaction between pairs of water molecules, including electrostatics and dispersion:

$$V^{\text{2B}} = V_{\text{elec}}^{\text{2B}} + V_{\text{disp}}^{\text{2B}} + V_{\text{ML}}^{\text{2B}} \quad (1.30)$$

The electrostatic term $V_{\text{elec}}^{\text{2B}}$ models the Coulomb interactions between partial charges on different water molecules. The dispersion term $V_{\text{disp}}^{\text{2B}}$ accounts for London dispersion forces using a damped $1/r^6$ term.

$V_{\text{ML}}^{2\text{B}}$ is a machine-learned correction term, represented by a permutationally invariant polynomial (PIP), fitted to high-level *ab initio* data and accounting for short-range quantum mechanical effects, such as exchange-repulsion and charge transfer. The 3-body term $V^{3\text{B}}$ is solely represented by fitted machine-learned PIP terms, $V_{\text{ML}}^{3\text{B}}$. Beyond the $V^{3\text{B}}$ term, higher-order many-body interactions ($n > 3$) are implicitly captured through polarization effects. However, it is possible to also explicitly include 4-body terms $V^{4\text{B}}$, using the same approach as for the 3-body term.

To describe the decay of interactions with increasing distance between water molecules, switching functions are applied to the 2-body and 3-body terms. Beyond a set cutoff distance, the contributions smoothly go to zero. For 2-body interactions, for O–O distances larger than 6.5 Å, the contributions are switched off. The same is true for 3-body interactions, whenever the distance between any two oxygen atoms in the trimer exceeds 4.5 Å.

With this approach, all essential physical interactions are captured, representing all relevant many-body effects for all water molecules without reliance on experimental parameterization. The MB-pol potential has been tested extensively against experimental data and has shown to predict the properties of water very accurately in gas- and condensed phases. This includes vibrational spectra,^{90,91} thermodynamic and dynamical properties,^{87,92} as well as reproducing the phase diagram of water over a wide range.^{86,93}

MBX⁹⁴ is the standalone program package to employ the MB-pol potential in MD simulations, but it is also interfaced with popular MD engines, such as LAMMPS⁹⁵.

1.7 Periodic boundary conditions

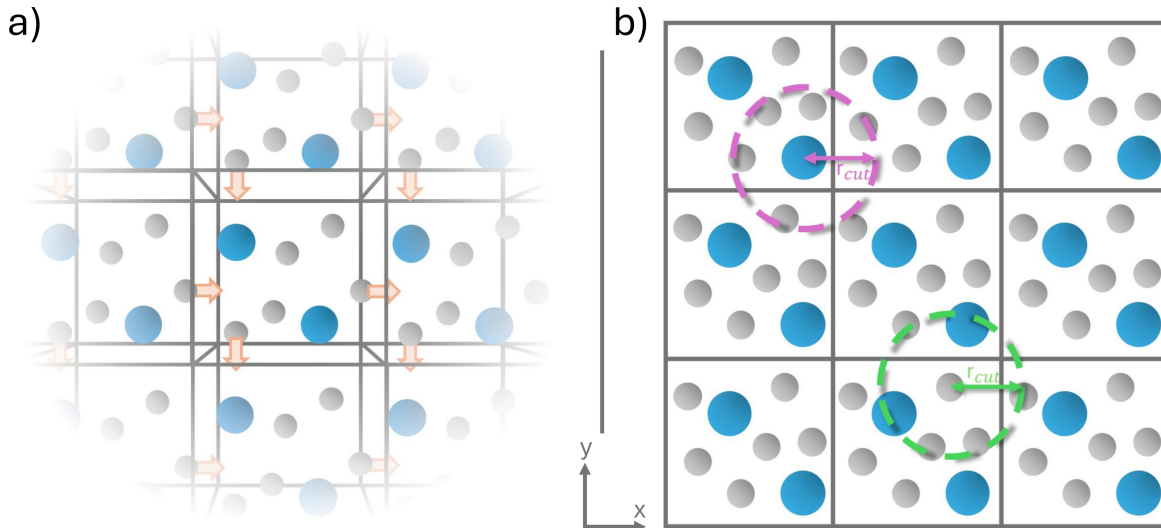


Figure 1.3: a) Scheme depicting a simulation box positioned in the center, with periodic images surrounding it in x and y direction. The orange arrows indicate layer crossing of an atom from one periodic box to another. b) 2D depiction of a similar simulation box. The green and purple, dashed circles mark the radial cutoff distance with respect to the central atom.

In real materials, particles interact with an effectively infinite environment. Simulations, however, are restricted to a finite number of atoms, limited by the box size. This limitation introduces artificial

boundary effects, as atoms located at the edge of the simulation box can collide with the simulation box wall, affecting the system's behavior and introducing artifacts, even in amorphous systems with no long-range order. Thus, to accurately model the behavior of bulk systems like liquids or solids, simulations must account for length scales beyond the finite simulation box.

To address this problem, periodic boundary condition (PBC) are used. The goal is to enable the calculation of macroscopic properties of bulk systems while using minimal system sizes. For a proper implementation of PBC, the simulation box must be able to tile space in all three dimensions without gaps. By creating mirror images of the box along all dimensions, an infinite system is approximated. A scheme is depicted in Fig. 1.3a, showing a two dimensional simulation box with surrounding periodic images in x and y direction. When a particle leaves the simulation box on one side, it re-enters from the opposite side, conserving the total number of particles. To avoid artifacts from interactions between a particle and its periodic images, the simulation box must be sufficiently large. This is showcased in Fig. 1.3b, where the radial cutoff distance r_{cut} for nonbonded interactions is marked with dashed circles. To ensure that each atom within the system interacts with only one image of any other atom and does not interact with its own periodic image, r_{cut} must satisfy $2r_{\text{cut}} < d_{\text{box}}^{\text{min}}$, with $d_{\text{box}}^{\text{min}}$ as the minimal simulation box dimension.

PBC were included for all MD simulations presented in this thesis.

1.8 Thermodynamic ensembles in molecular dynamics

An MD simulation generates a series of configurations of the system studied, connected through their time evolution. These configurations can be related to macroscopic thermodynamic properties using the principles of statistical mechanics. By computing ensemble averages over the generated configurations, various thermodynamic properties of the system can be derived. The thermodynamic ensembles are classified based on the constraints imposed on the system and its interaction with the environment. Common ensembles used in MD simulations include:

- microcanonical ensemble (NVE): constant number of particles (N), volume (V) and total energy (E)
- canonical ensemble (NVT): constant number of particles (N), volume (V) and temperature (T)
- grand canonical ensemble (μVT): constant chemical potential (μ), volume (V) and temperature (T)
- isothermal-isobaric ensemble (NpT): constant number of particles (N), pressure (p) and temperature (T)

Often, systems are modeled as a thermodynamically closed system, where the number of particles remains constant. An exception is the grand canonical ensemble, which allows for particle exchange with a reservoir at a constant chemical potential.

By default, MD simulations follow the microcanonical ensemble. However, for many applications and for the comparison to experimental data, it is desirable to control the temperature or pressure of the system. This is achieved using thermostats and barostats, which modify the equations of motion to maintain the desired temperature or pressure. The Nosé-Hoover thermostat^{96–98} represents a common choice for temperature control. In this approach a heat bath is simulated, which exchanges energy with

the system to maintain a constant temperature. Barostats, on the other side, allow for fluctuations in the simulation box volume to maintain a constant pressure. Variables are coupled to particle velocities and simulation box dimensions, enabling the box to expand or contract. In the MD-simulations presented in the following chapters, the isothermal-isobaric ensemble is used to equilibrate the studied systems. The canonical ensemble is used in the production runs, enabling temperature control at a fixed system size.

Modeling and Analysis of Molecular Systems

With the theoretical background laid out, the focus shifts to nanomaterials and nanoporous environments. In the following subsections, the liquids and solids investigated in this work are presented. Then, the methods and programs designed to extract relevant structural and dynamic properties from the simulations are presented.

2.1 Liquids

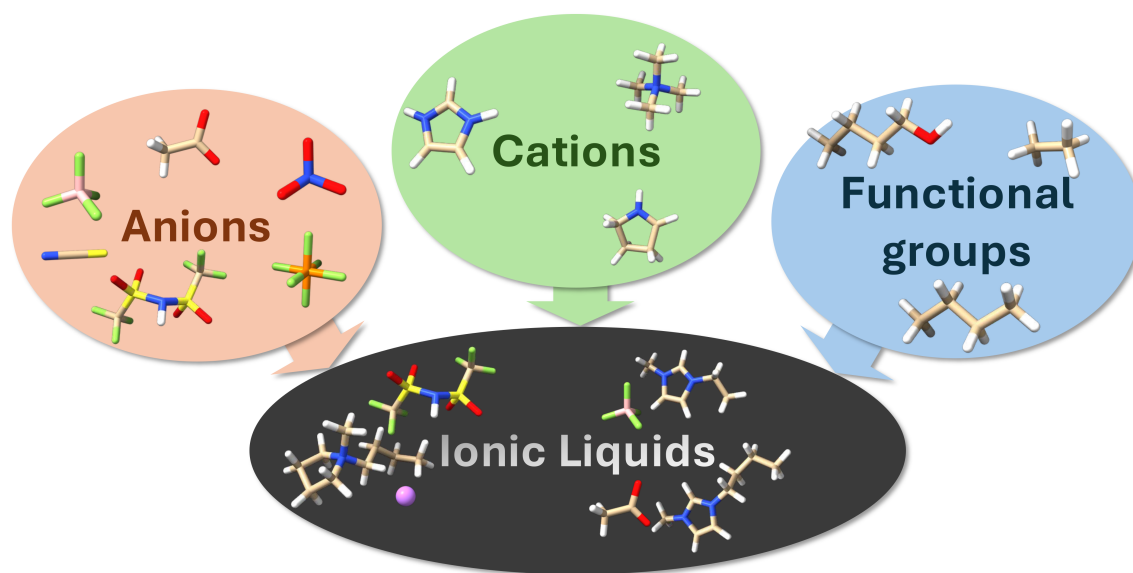


Figure 2.1: Ionic liquids (black) are a combination of anions (red) and cations (green) with functional groups attached (blue). Shown are exemplary cations, anions and functional groups utilized. The shown ILs and composites $[\text{C}_4\text{C}_1\text{Im}][\text{OAc}]$,^{57,99–101} $[\text{C}_2\text{C}_1\text{Im}][\text{BF}_4]$ and $[\text{Pyr}_{14}][\text{NTf}_2]/\text{Li}[\text{NTf}_2]$ ^{102–104} were modeled in the studies presented in this thesis.^{1–3} (color code: hydrogen = white; nitrogen = blue; fluor = green; sulfur = yellow; carbon = beige; oxygen = red; phosphorous = orange; lithium = purple; boron = salmon).

Ionic liquids ILs are a versatile class of materials,^{105–109} defined as salts that remain in a liquid state at temperatures below 100°C,¹¹⁰ some even at room temperature (room temperature ionic liquids (RTILs)),¹¹¹ consisting solely of ions without any additional solvent.¹¹² Cations are generally organic, bulky and asymmetric, preventing the formation of a stable crystal lattice and thus preventing early solidification. Furthermore, the hydrophobic nature of many cations leads to the formation of distinct polar and non-polar domains within the bulk liquid, resulting in a micro-heterogeneous structure.^{113–115} The anion is either organic or inorganic and often smaller in size. Referred to as “designer solvents”, ILs exhibit a high structural diversity, and their properties can be fine-tuned for specific applications by adjusting the chemical composition of the anion and cation, including their functionalization and combination.¹¹⁶ Depicted in Figure 2.1 are commonly used cations, comprising imidazolium (Im^+), pyrrolidinium (Pyr^+) and ammonium (NH_4^+) based groups, while typical anions include tetrafluoroborate (BF_4^-), hexafluorophosphate (PF_6^-), bis(trifluoromethylsulfonyl)imide (NTf_2^-) or acetate (OAc^-). The shown ILs butyl-methyl-imidazolium acetate ($[\text{C}_4\text{C}_1\text{Im}][\text{OAc}]$), ethyl-methyl-imidazolium tetrafluoroborate ($[\text{C}_2\text{C}_1\text{Im}][\text{BF}_4]$) and pyrrolidinium bis(trifluoromethylsulfonyl)imide together with the salt lithium bis(trifluoromethylsulfonyl)imide at various concentrations ($[\text{Pyr}_{14}][\text{NTf}_2]/\text{Li}[\text{NTf}_2]$),^a were modeled in the works presented in this thesis.^{1–3} In general, ILs are characterized by high thermal stability, negligible vapor pressure, and a wide electrochemical stability window (ESW).¹¹⁷ These properties make them ideal candidates for energy storage applications, particularly in electric double-layer capacitors (EDLCs) where they are used as electrolytes.^{117,118} Small amounts of additives like water or organic solvents can be intentionally used to tune the performance of ILs.^{119,120} Water is often introduced accidentally, as many ILs are hygroscopic and absorb moisture from the environment. At very low concentrations, water can enhance the viscosity and ionic conductivity of ILs.^{8,121–123} At higher concentrations, it however also reduces the ESW.¹²⁴ Adding salts to the IL can mitigate this effect, as the salt ions do interact strongly with water molecules, reducing the amount of free water in the IL.¹²⁵ In the confinement of nanopores, ILs exhibit unique behaviors that differ significantly from their bulk properties, both structurally and dynamically.¹²⁶ Strong ion-ion correlations lead to complex structural arrangements, such as an alternative cation-anion ordering in confinement with a lowered coordination as well as layering effects at the carbon interface. On one hand, the characteristics of ILs in the confinement of CNTs in the sub- and low nanometer regime is investigated.^{1,2} Further, salt-in-ionic liquids (SiILs), are studied in the confinement of the zeolitic imidazolate framework (ZIF)-8³ and CNTs.

Water Water is arguably the most important liquid on Earth, both due to its abundance and as the fundamental basis of life. Although its molecular structure is simple, water exhibits complex and anomalous behavior compared to other liquids.¹²⁷ Examples include its high surface tension and density anomaly (the density decreases upon freezing). This anomalous behavior is also evident in its phase diagram, where, in addition to the gas and liquid phases, there are 20 described and characterized phases of ice.¹²⁸ These chemical and physical properties are closely linked to strong intermolecular interactions. In bulk water, extensive dynamic hydrogen bond (HB) networks form. Together with the molecule’s polar nature, these networks are key to many of its properties. The HB network is highly dynamic, with short-lived water clusters forming and breaking in the order of picoseconds.¹²⁹ Due to its importance and complexity, water is the most thoroughly studied liquid in both experimental and computational research. This applies to direct studies of water under various

^a The IL was modeled with and without added salt at various concentrations in the confinement of the MOF ZIF-8.³

conditions, as well as its frequent use as a solvent, for example, in biomolecular systems.

Despite extensive studies, there are ongoing debates in the scientific community regarding the correct description of water, such as the coordination and its structure and dynamics at solid interfaces.^{130–132}

Additionally, it is experimentally known that water shows anomalous behavior under extreme confinement,¹³³ such as an increased flow rate in CNTs.^{134–136} The extreme spatial limitations significantly alters the waters' HB network, as well as its structural and dynamic properties.^{137–139}

An accurate description of water at a molecular level using theoretical approaches is challenging. The peculiar characteristics of water are not fully captured by conventional classical FF models, especially when considering a wide range of temperatures or pressures using the same model. Capturing phase transitions and complex behavior under extreme conditions (such as nanoconfinement) remains difficult. Consequently, most classical water models are optimized for specific temperature or pressure ranges, or to reproduce certain thermodynamical properties well, leading to the development of numerous water models over the years.

The simplest classical models are the 3-site models, where each water molecule is represented by three interaction sites corresponding to the atoms, with fixed partial charges and masses. In most models, the molecules are treated as rigid entities, matching experimental findings of the molecule's geometry (angle and bond terms). Multiple classical water models have been developed and improved over the years, like the well-known SPC¹⁴⁰ model or its successor the SPC/E model,⁷¹ which includes updated partial charges for the oxygen and hydrogen atoms and an additional average polarization correction term. These models are still widely used today, as the simplicity of these approaches makes them highly computationally efficient and effective at ambient conditions for many applications.

In more complex models, additional dummy interaction sites are included. In 4-site models (e.g., TIP4P⁷²), an additional dummy site is added near the oxygen atom along the bisector of the two O–H bonds. The dummy site bears no mass, but the negative partial charge of the oxygen atom. This way, the electrostatic distribution around a water molecule is captured more accurately. 5-site models (e.g., TIP5P¹⁴¹) incorporate two additional dummy sites to explicitly represent the lone electron pairs of the oxygen atom. Together with the two hydrogen atoms, this arrangement reproduces a tetrahedral coordination geometry with the oxygen atom at its center. 6-site models incorporate the approaches from both 4- and 5-site models. Flexible models, such as SPC/Fw¹⁴² or TIP4P/2005f⁷³, also consider dynamic bond lengths and angles, allowing for vibrational modes of the water molecules. Also, special models have also been developed for a detailed description of ice phases, such as the TIP4P/Ice model¹⁴³. Generally, the computational cost of these models increase with the number of interaction sites considered, as well as with including flexibility. However, these computational models are still significantly less demanding than any *ab initio* approach and allow for the simulation of large systems over long time scales with reasonable accuracy.

More recently, many-body potentials have been developed to better capture the complex interaction between a water molecule and its local surroundings. As presented in Section 1.6, MB-pol is a very sophisticated water model, accurately capturing many properties of water across different phases and conditions. This is especially important when studying water under extreme conditions, such as nanoconfinement, where its molecular behavior deviates significantly from bulk water.

In Chapter 6, water is modeled in the confinement of CNTs of different sizes to identify how nanoconfinement impacts the water's structure and dynamics using the MB-pol potential, TIP4P and TIP4P/2005f. Chapter 7 deals with studying the behavior of NPs interacting with antibiotics in an aqueous environment,⁵ where the SPC/E model for water was used.

2.2 Materials

2.2.1 Carbon allotropes

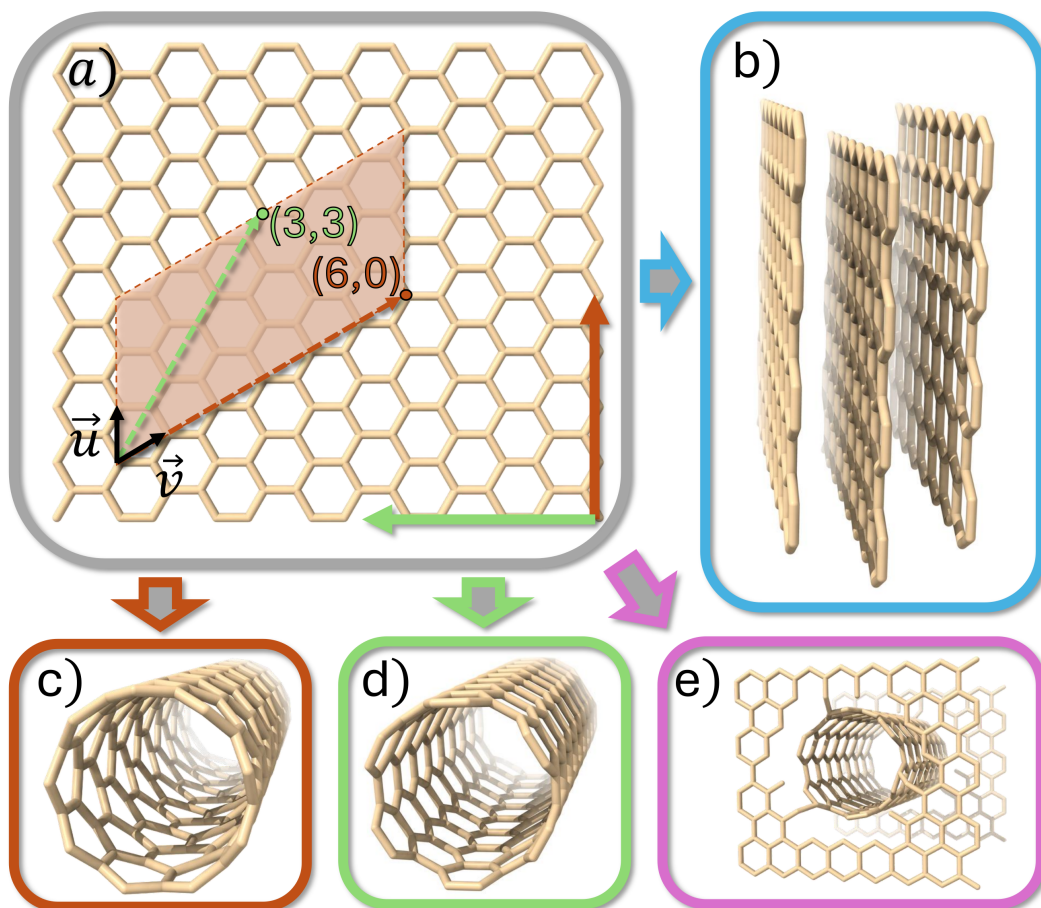


Figure 2.2: Depicted are different carbon structures: a) A Graphene sheet, b) A Graphite consisting of three ABA-stacked graphene sheets. When rolling up the graphene sheet shown in a) along the arrows (green/red), either a (9,0) CNT in zigzag configuration (red, c)), or a (6,6) CNT in armchair configuration (green, d)) is formed. e) A pore structure as a combination of two graphene sheets attached to a CNT. All structures were generated using CONAN¹ and visualized using ChimeraX^{144–146}. The carbon structures are shown in bond depiction, colored in beige.

Carbon materials come in a rich variety of allotropes, each with distinct structures and properties. The basis for this diversity lies in the basic properties of carbon atoms. Each atom comes with four valence electrons, allowing for covalent bonding with up to four neighboring atoms. Additionally, the carbon atom can assume different hybridization states (sp^3 , sp^2 , sp), leading to a wide range of bonding configurations and structures. In diamonds, for example, the carbon atoms are fully sp^3 -hybridized, and each atom forms four covalent bonds with adjacent carbon atoms in a tetrahedral shape and a three-dimensional crystal lattice is formed. sp^2 -hybridized carbon forms three bonds and is characteristic for graphitic structures. Lastly, sp -hybridized carbons allow for the formation of triple bonds, and are found in, e.g., linear carbon chains. The type of hybridization generally determines the

structure and properties of the respective carbon material, ranging from one dimensional structures, such as CNTs, over two-dimensional graphene sheets to three-dimensional allotropes. Both amorphous and highly crystalline forms can be synthesized. The carbon materials relevant in the context of this work are presented in more detail in the following.

Graphite & graphene Graphite is a naturally occurring mineral form of carbon, consisting of stacked layers of graphene (see Figure 2.2b). In a graphene layer (see Figure 2.2a), each carbon atom is sp^2 -hybridized and bonded to three neighboring carbon atoms, creating a two-dimensional honeycomb structure. Each bond is separated by an in-plane angle of 120° , resulting in a highly symmetric structure, with a bond length of approximately 1.42 Å. The double bonds originating from the sp^2 -hybridized carbons are fully delocalized in the structural plane. In graphite, individual graphene layers are held together by vdW forces with an interlayer distance of 3.35 Å, allowing for exfoliation in one direction. Graphite comes in two stacking configurations, namely alpha (hexagonal) graphite with an ABA stacking and beta (rhombohedral) graphite with an ABC stacking sequence. In the more common ABA stacking, every second layer is aligned, while the layer in between is shifted by a C–C bond length (see Figure 2.2b). This layered structure gives graphite its characteristic properties, such as high electrical and thermal conductivity along the planes, but low conductivity perpendicular to them. Graphite and graphene are widely used in various applications, e.g., as transistors, for water filtration or in EDLCs.¹⁴⁷ In this work, graphene mostly poses as planar carbon interfaces for the study of a liquids behavior at the interface and their usage as building blocks to construct pores (see Figure 2.2e). Next to the pristine carbon structures, doped and functionalized graphene structures have emerged to further tune the properties of graphene for specific applications.^{148,149}

Carbon nanotubes CNTs can be understood as rolled up graphene sheets, with their configuration determined through the basis vectors $\vec{u}$ and $\vec{v}$ (see Figure 2.2). The direction in which a graphene sheet is rolled up is described by the two vectors, from which the chiral vector $\vec{C}_h$ is constructed (two examples for $\vec{C}_h$ are shown as dashed arrows (green/red) in Figure 2.2a)

$$\vec{C}_h = m\vec{v} + n\vec{u}, \quad (2.1)$$

with n and m being integers defining the chirality and diameter of the CNT. For $m = 0$, the CNT assumes a zigzag configuration (see Figure 2.2c), if $m = n$ the CNT is in armchair configuration (see Figure 2.2d). For all other cases, with $m \neq n$ and $m \neq 0$, the resulting (m,n) CNT is chiral, and its enantiomeric counterpart is obtained by switching m and n . CNTs either come as single-walled CNTs (SWCNTs), consisting of a single graphene sheet rolled up into a tube, or as multi-walled CNTs (MWCNTs), where multiple concentric graphene sheets are rolled up.^a CNTs show various highly desirable properties, though often only at a microscopic scale. Along the tubular axis, they are highly conductive, both electrically and thermally, and exhibit a high tensile strength, making them suitable for a wide range of applications. However, all properties are highly depending on the chirality and diameter of a given CNT. In contrast to graphene, CNTs can be either metallic or semiconducting, depending on their chirality, but only along the tube axis. Armchair CNTs are always metallic, while zigzag and chiral CNTs can be either semiconducting or metallic, depending on m and n . In the context of this work, CNTs are used as model systems to study liquids under extreme confinement. With their

^a In the context of this work, only SWCNTs are studied and simply referred to as CNTs in the following.

idealized geometries and the tunability of the CNT diameter, CNTs allow for systematic studies of confinement effects as well as their size dependency on the structure and dynamics of confined liquids.

CNTs are predominantly synthesized using chemical vapor deposition (CVD) methods.¹⁵⁰ Starting from a substrate (e.g., MgO or Al₂O₃), metal nanoparticles (e.g. Fe, Ni, Co), functioning as catalysts, are introduced to the substrates surface. Then, a carbon based gas (e.g. C₂H₄ or CH₄) is injected. At very high temperatures, the gas decomposes at the catalysts surface, while the carbon atoms moves to the nanoparticles edges, where the CNT forms.

Vertically aligned carbon nanotube arrays Vertically aligned carbon nanotube arrays (VANTAs), also referred to as CNT forests, as the name suggests, are structures consisting of vertically aligned CNTs. The tubes are in parallel arrangement to one another, while the individual tubes are stacked and held together purely by vdW interactions. Structurally, this yields a highly anisotropic system, and the thermal and electrical conductivity is very high along the aligned tubular axes. VANTAs are also synthesized using CVD, with deliberate care that the catalytic seeds are in close proximity to one another. This way crowding effects prohibit the CNTs to grow in any other direction than vertically upwards, resulting in the parallel alignment. Potential applications of VANTAs are diverse, as the high electrical and thermal conductivity are characteristics sought after in many applications. In addition, the very high porosity and tunability make them very interesting compounds for the use as electrode materials and for filtration membranes.

2.2.2 Metal organic framework

Another class of nanoporous materials are MOFs, hybrid materials consisting of metal ions or clusters connected by organic ligands, often referred to as *linkers*. The metal centers act as the nodes of the scaffold, while the organic linkers connect them into a periodic network. A key concept in MOF chemistry is the secondary building unit (SBU), a minimal building block containing the metal center and its immediate coordination environment. The extended framework is constructed by repeating these SBUs in three dimensions. Depending on the choice of metal nodes (e.g., Zn, Cu, Zr) and organic linkers (typically carboxylates, imidazoles, or other nitrogen/oxygen-rich heterocycles), the resulting structure, pore size, and chemical properties can be tuned. While 1D and 2D structures exist, this work focuses on 3D crystalline MOFs, which generally exhibit exceptionally high surface areas and porosity.

Beyond their static porosity, the choice of ligands can introduce flexibility into the framework. Some MOFs exhibit dynamic behaviors such as “breathing modes”, where the pore structure reversibly deforms upon adsorption or desorption of guest molecules. This tunability and structural diversity make MOFs promising candidates for applications including hydrogen and methane storage, carbon dioxide capture, use as an electrocatalyst in the oxygen reduction reaction, and use in electrochemical energy storage.^{151–153} ZIFs are a widely studied subclass of MOFs and are structural isomorphs of zeolites. In ZIFs, tetrahedrally coordinated metal ions are linked by imidazoles. The M–Im–M bond angle between the metal center M and the imidazole units Im is approximately 145°, closely resembling the Si–O–Si angle in zeolites. In addition to the porous network, ZIFs exhibit a high thermal stability and chemical resistance.¹⁵⁵ ZIF-8 is a prominent and widely studied ZIF, composed of zinc ions which are tetrahedrally coordinated by four 2-methylimidazolate linkers (see Figure 2.3 top). These form the SBU of the ZIF-8 structure, which, when interconnected, form the 3D porous network.

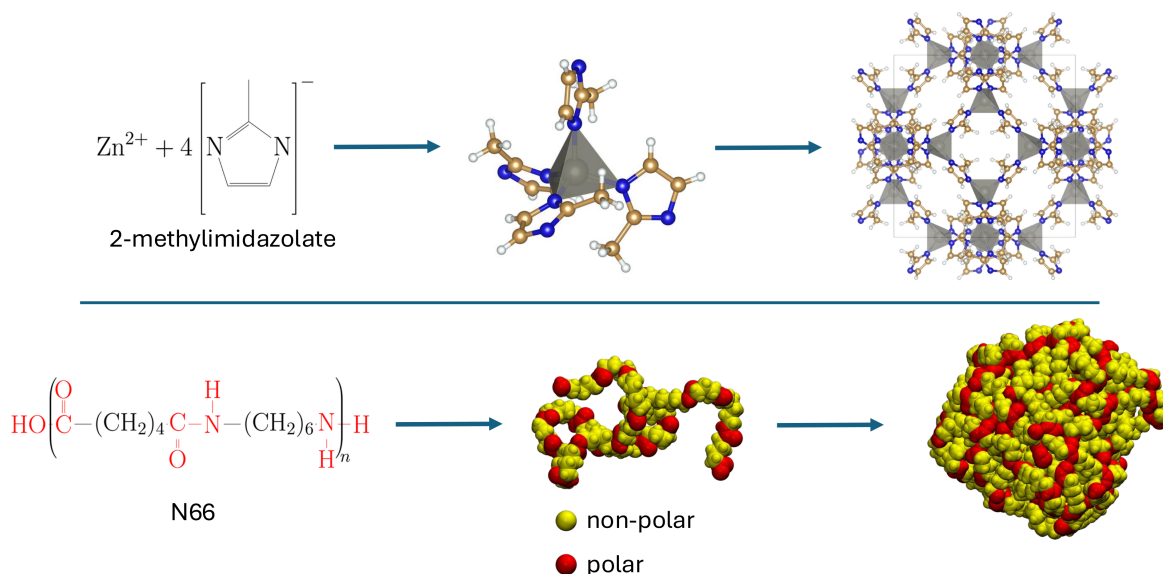


Figure 2.3: Top: Pathway from individual building blocks to ZIF-8 structures. ZIF-8 consists of zinc cations (Zn^{2+}) and 2-methylimidazolate units. Its SBU consists of a single metal cation in the center, tetrahedrally coordinated by four imidazolate units. From these SBUs, the porous MOF structure is built. (color code: hydrogen = white; carbon = beige; nitrogen = blue; zinc = gray (shown as tetrahedrons to highlight the tetrahedral coordination)). Bottom: From the skeletal formula of nylon 6,6 (N66) to polymer chains of finite length to the formation of a N66 NP. The polar groups in the polymer structure are highlighted in red color. Nonpolar regions in the polymers are shown in yellow (black in the skeletal formula). The figures were generated using vmd and VESTA.¹⁵⁴

2.2.3 Nanoplastic particles

Plastics are solid materials consisting of aggregated polymer chains. Starting from monomer units, long polymer chains are formed through polymerization reactions. This can either result in linear chains, branched structures or cross-linked networks, depending on the polymerization method and monomers used. To tune the plastic's properties, additives are mixed with the polymer matrix, such as plasticizers, stabilizers or colorants, and, if desired, a vulcanization process introduces additional cross links between the polymer chains to increase the material's mechanical strength.

Plastics have found their way into everyday life due to their low manufacturing costs, versatility and chemical inertness. Commonly used plastics include polyethylene (PE), polypropylene (PP), polyvinyl chloride (PVC), polystyrene (PS), polyethylene terephthalate (PET) and nylon 6,6 (N66). Often using Ziegler-Natta catalysts,^{156,157} the polymerization is realized, for example, by:



The arrangement of polymer chains within a plastic can be amorphous, semi-crystalline or crystalline, depending on the polymer type and processing conditions. The driving force for polymer packing are intermolecular forces, with vdW interactions as the main driving force for non-polar polymers, such as PE or PP. N66, on the other hand, exhibits strong hydrogen bonding between the polymer chains, resulting in an extensive HB network.

The worldwide production of plastics has been increasing steadily over the last decades, reaching over 400 million tons in 2022.¹⁵⁸ The overall recycling rate of 9%¹⁵⁹ is generally low, and inadequate waste management has led to a significant accumulation of plastic waste in the environment. NPs are a type of MNP, only comprising the smallest particles with diameters ranging from 1 nm to 1 μm .¹⁶⁰ These particles are predominantly originating from the abrasion of tires, the mechanical wear of clothing or the breakdown of larger plastic debris in the environment through degradation processes. NPs are also intentionally manufactured. In recent years, it has become clear that these particles have become ubiquitous in the environment, and have been found along the food chain, in the air and in water. Consequently, NPs are unintentionally consumed by humans, raising concerns about their potential health effects.^{29–33} Studies have shown that NPs can cross biological barriers and accumulate in organs.¹⁶¹ For an assessment of the potential health risks, it is crucial to characterize NPs based on their structure, size and chemical composition. NPs found in the environment cover a wide range of sizes and chemical composition. This is especially true for the surface, as weathering leads to possible surface oxidation and functionalization. Additionally, plastics potentially interact with other colloidal organic or inorganic matter forming agglomerates.^{162,163}

As NP research using computational approaches is still in its infancy, models and workflows that allow for the generation of stable, pristine NPs with a defined size and chemical composition are developed. These plastic particles are the basis for further research into the behavior of NP on a molecular level, such as their interaction with biomolecules.

Simulated annealing An established way to generate NP conformers is the simulated annealing (SA) approach using classical MD simulations.³³ Multiple polymer chains of well-defined length are created and randomly placed within a simulation box. It is taken care that the simulation box size is chosen large enough to avoid self interaction of the individual polymer chains with their periodic image. In an initial simulation run, the system is heated to very high temperatures, often higher than the polymers physical degradation point,^a before a gradual cooling of the system to low temperatures. While doing this, the mobility of the polymer chains is tracked and T_{start} , defined as the temperature where the chains form a single aggregate, and T_{end} , where the polymer chain's mobility is restricted to such a degree, that major conformational changes are suppressed, are identified. T_{start} and T_{end} highly depend on the type of plastic and therefore have to be defined individually. In a subsequent step, new simulation boxes are constructed containing dispersed polymer chains. The number of individual simulations with differing starting configurations determine the number of NP structures produced. A temperature protocol $T_{\text{start}} \rightarrow T_{\text{end}}$ is set, where the polymer chains agglomerate and form a NP particle. Theoretically, an infinitely slow cooling rate would yield the most stable structure, i.e., the global minimum on the PES would be found, however this is computationally not feasible and in practice, a compromise between computational cost and stability of the resulting NP has to be found. This makes the SA approach a stochastic method, where an ensemble of NP conformations are needed for further analysis.

2.3 Calculating properties from simulations

In MD, the first step is the computational modeling of the system of interest, i.e., performing a simulation and producing a trajectory. Extracting relevant properties from the generated trajectories

^a The used classical FFs do not allow for bond breaking, the polymers do not thermally degrade.

is however key to gain insight into the system. Tools to visualize trajectories, such as VMD^{164,165}, ChimeraX^{144–146} or PyMOL¹⁶⁶ are valuable to gain a first insight and visual impression of the system. In addition, various analysis tools exist to calculate structural and dynamic properties, such as Travis^{167,168}, MDAnalysis^{169,170} or MakroLyzer¹¹, just to name a few. For the systems presented here, most readily available analysis options are not directly applicable. The anisotropic nature of the confinement does not allow for a simple averaging over all molecules within the system, as is often done for bulk systems, prohibiting the use of most established analysis tools.

Instead, molecules located at the interface or within the confinement of a pore show fundamentally

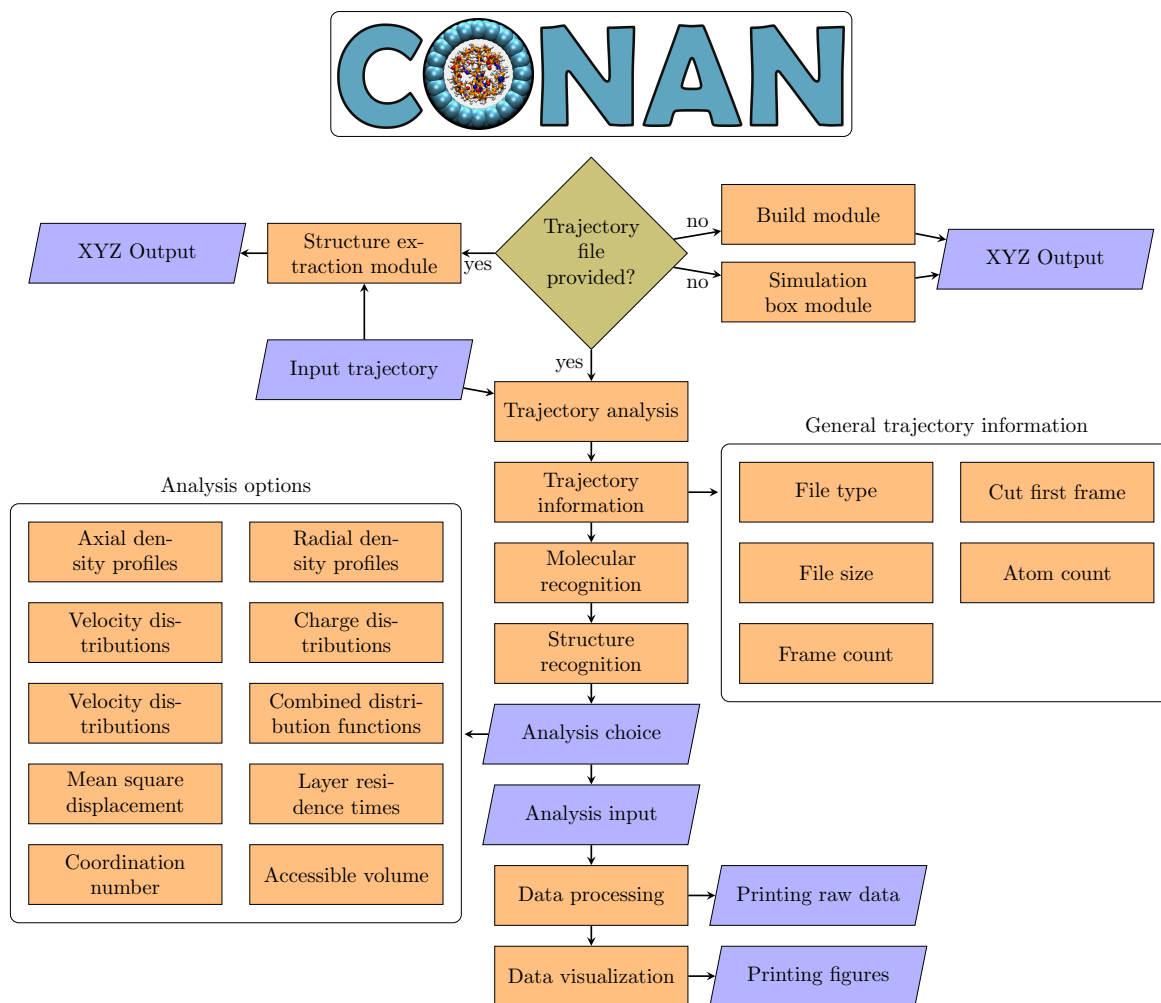


Figure 2.4: Schematic depicting a simplified flowchart of CONAN. Processing steps are shown as orange rectangles, input and output, either user input or files, are shown as blue parallelograms and conditional branches as green diamonds. Detailed information regarding the analysis options are discussed in Section 2.4.^a

different behavior compared to those in bulk systems. Consequently, customized analysis tools allowing for the study of these systems are required. With the aim of generalizing the analysis code to also be applicable for a broader field of studies, a new analysis code CONAN^{1,2} (**C**onfinement **A**nalyzer)

^a This work does not include a discussion on the coordination number analysis, as this is part of other people's work.

was developed in recent years as integral contribution to this thesis. The terminal based code is written in Python, relies on many standard libraries^a and is openly available.^{177,178} A simplified flowchart of CONAN is depicted in Figure 2.4. The focus of the code is on the analysis of liquids confined in porous materials, offering multiple analysis options, which will be discussed in detail in the following sections. Another option is to build carbon structures, as is shown in Figure 2.2, where all depicted structures were produced using CONAN.^b Other functionalities of the code include setting up simulation boxes comprising carbon nanostructures and liquids, as well as tools to cut out structures from trajectories, e.g., for visualization purposes. Generally, the code is designed modular, allowing for easy additions of further analysis modules, while ensuring that functions from other parts of the code can be easily reused.

2.3.1 Molecular and structure recognition

A fundamental aspect of generalizing the analysis code to work for a wide range of systems is to ensure that the code does correctly and reliably identify the molecules and structures within a trajectory. While some topology files do provide insight into which atoms belong to which molecule, this is not the case for all file formats. Additionally, no bonding information between atoms is provided. For structures, it is also desirable to identify substructures, such as the CNTs within a pore structure. To achieve this, a set of functions was developed to identify molecules and structures, and provide further structural information, e.g., the center of mass (COM) of molecules or the center axis of a CNT.

For all steps along the workflow, PBC are considered to ensure correct distance calculations, which is crucial for the identification of bonds between atoms in neighboring periodic images.

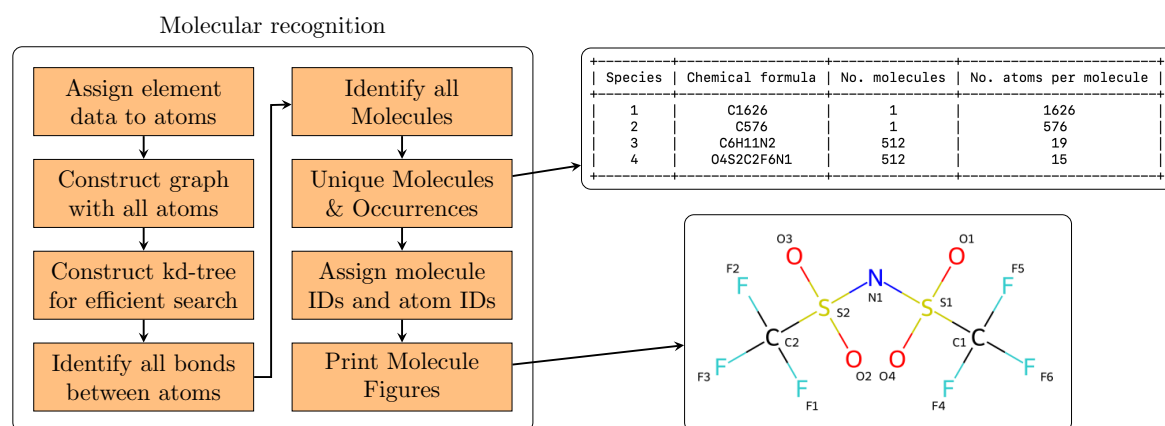


Figure 2.5: Flowchart of the molecular recognition in CONAN. The shown table and depiction of $[\text{NTf}_2]^-$ are exemplary outputs from CONAN.

Molecular recognition Identifying all molecules within a given system is achieved in a multi-step process using graph theory. The flowchart for the molecular recognition is shown in Figure 2.5. First,

^a NumPy¹⁷¹, pandas¹⁷², MDAnalysis^{169,170}, SciPy¹⁷³, RDKit¹⁷⁴, Matplotlib¹⁷⁵ and networkx¹⁷⁶.

^b New versions of CONAN have introduced additional features, such as nitrogen doping of various kind, functionalization or introducing defects into carbon structures. This however goes beyond the scope of this thesis and will not be discussed in detail.

all atomic coordinates are extracted from the first frame in a provided trajectory file. All atoms within the system are represented as nodes within a graph, each atom labeled with its element type and assigned the respective covalent radius.¹⁷⁹ The maximum possible covalent radius $r_{\text{cut}}^{\text{max}}$ within the system is identified as the largest combination of covalent radii of two atoms a and b found

$$r_{\text{cut}}^{\text{max}} = 1.15(r_{\text{cov},a} + r_{\text{cov},b}) \quad (2.3)$$

The tolerance factor of 1.15 accounts for variations in bond length due to vibrational modes and was found to work very reliably. Based on $r_{\text{cut}}^{\text{max}}$, the atomic coordinates are structured into a k - d -tree data structure,¹⁸⁰ allowing for efficient neighbor searching. This way, candidate bonds between atoms i and j are identified. Using a similar approach as before, however using the specific elemental covalent radii of atoms i and j , the cutoff radius is determined as

$$r_{\text{cut}} = 1.15(r_{\text{cov},i} + r_{\text{cov},j}), \quad (2.4)$$

where $r_{\text{cov},i}$ and $r_{\text{cov},j}$ are the covalent radii of atoms i and j . A bond between two atoms is assumed if their interatomic distance d_{ij} is smaller than the cutoff radius r_{cut} . With all bonds identified, edges are created between the nodes representing the atoms within the graph. Each molecule is then identified as a connected component within the graph. The bonding information further allows identifying which molecules are of the same species, by comparing their bonding patterns. This way, unique molecules and their count within the system are identified. Each atom is assigned a molecule ID, but also an atomic ID, representing its position within the molecule. The atomic ID is important to distinguish between atoms of the same element type within the molecule, and an atomic ID set for a given atom is the same across all molecules of the same species. This allows for a detailed analysis of individual atoms, or groups of atoms of a given molecule kind. For convenience, figures depicting schematics of the molecules are printed, together with the atomic IDs. Additionally, a table is printed providing an overview of all molecules found, including their count and their chemical composition (see Figure 2.5).

Structure recognition A flowchart of how the structure recognition is achieved is shown in Figure 2.6. Flexible structures need to be defined manually by the user after the molecular recognition step. Alternatively, the automatic identification of immobile structures is achieved by also considering the second frame of the trajectory file. By comparing the two frames, all molecules with immobile atoms are automatically identified. For all structures, general information like the number of atoms, element types and bonding patterns are stored. Carbon structures are usually modeled extending infinitely in one or more directions (PBC), and their orientation and periodic extend are stored as well. When a porous structure is found, the code automatically checks if substructures can be identified (CNTs/graphene sheets).

For CNTs, the center axes and tube radii are calculated, and their chirality determined (zigzag/armchair). The calculation of the center axis is achieved in three different ways, depending on the CNT. Often, CNTs are modeled as pristine and immobile structures, oriented in one of the main axes of the simulation box. This makes the calculation of the center axis trivial, as one can simply calculate the COM to determine the center of the CNT in the two directions perpendicular to its main axis. The extend of the center axis is determined by identifying the minimal and maximal coordinate of all carbon atoms along the main axis direction. For flexible, finite CNTs, a more elaborate approach is

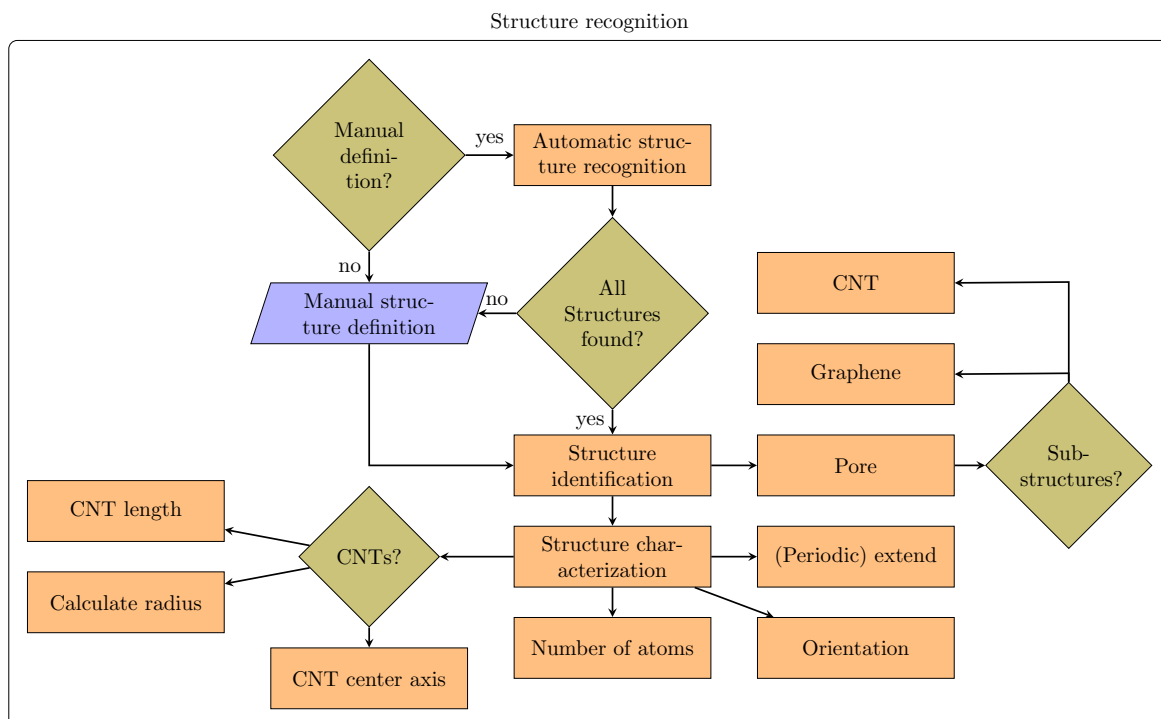


Figure 2.6: Flowchart of the structure recognition in CONAN. For immobile structures, the identification can be done automatically. Flexible structures are user defined. After the identification, the structure characterization is automated. Processing steps are shown as orange rectangles, input and output, either user input or files, are shown as blue parallelograms and conditional branches as green diamonds.

required. First, the open ends of the CNTs are identified and all terminal carbons are identified. They are split into two groups, based on a maximum distance criterion, each representing an open end of the NP. The COM of each group is calculated, defined as $\vec{p}_1$ and $\vec{p}_2$. In case of infinite CNTs, the center axis is calculated by isolating atoms forming one ring of the CNT. The COM of these atoms is calculated, and set as $\vec{p}_1$. Using the periodicity of the CNT, the periodic image of $\vec{p}_1$ constitutes $\vec{p}_2$. Finally, the center axis $\vec{z}$ is then defined as the vector between $\vec{p}_1$ and $\vec{p}_2$. With the center axis at hand, the radius of a CNT is calculated as the average radial distance of the carbon atoms to $\vec{z}$, while the length of the CNT, l_{CNT} , is simply $|\vec{z}|$.

2.4 Analysis options

With all basic information about the system gathered, the analysis of structural and dynamical characteristics of the confined liquid can be performed. All analysis features presented here are structured into separate modules, allowing for easy extensions and modifications. The modules are divided into three parts: (i) user input and gathering system information, (ii) analysis of the trajectory and processing of the desired property, and (iii) output of the results (see Figure 2.7). In this structured way, all modules can use the same functions of the backbone code, unifying the analysis process and allowing for modules to build on one another.

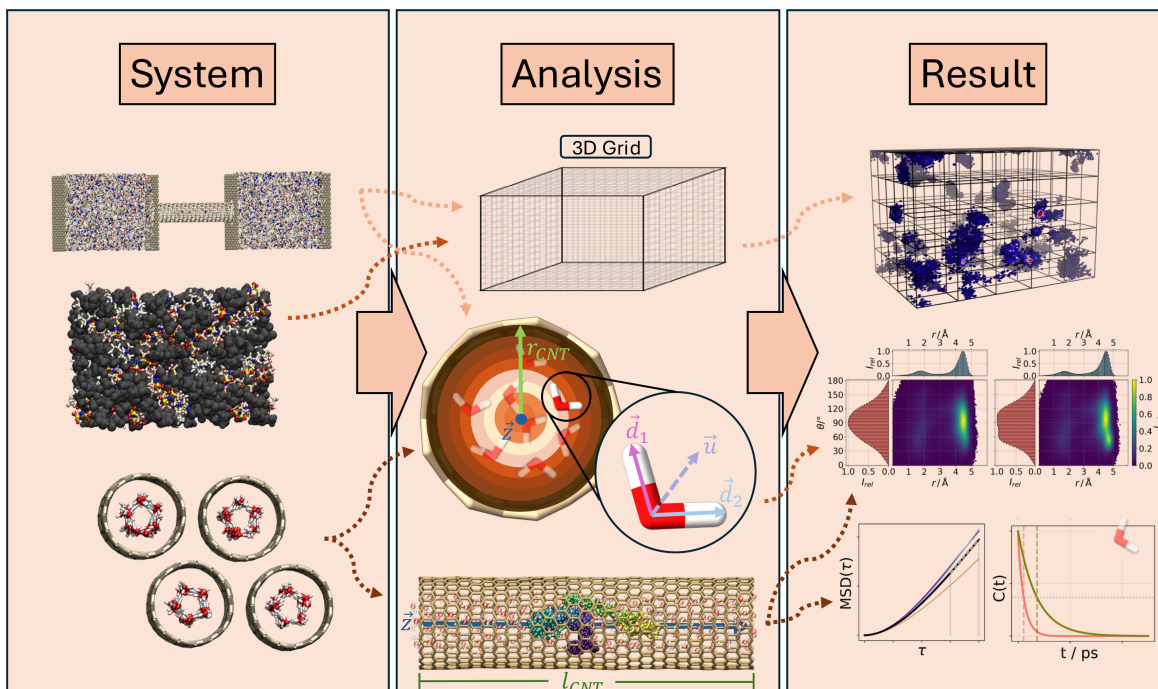


Figure 2.7: **System:** Overview of the systems studied:^{1,3,4} $[\text{C}_4\text{C}_1\text{Im}][\text{OAc}]$ in the confinement of a pristine (12,0) CNT (top); $[\text{Pyr}_{14}][\text{NTf}_2]/\text{Li}[\text{NTf}_2]$ in the confinement of the MOF ZIF-8 (center); Water in the confinement of (15,0) CNT VANTAs (bottom). **Analysis:** 3D grid, which can be adjusted to a system of choice to perform analyses for each grid point individually (top); Front view of a CNT with the radius r_{CNT} filled with water, with radial layers from the center axis $\vec{z}$ up the CNT wall. An exemplary water molecule is shown with the bond vectors $\vec{d}_1$ and $\vec{d}_2$, while $\vec{u}$ is their bisector (center); Side view of a CNT of length l_{CNT} filled with water. The movement of an exemplary water molecule over time is depicted with a viridis color code (bottom). **Result:** 3D density distribution of Li^+ ions in the confinement of ZIF-8 (top); Combined distribution functions relating the angular and radial distributions of CNT confined water (center); Mean square displacements and radial layer residence times computed for water confined in CNTs (bottom). (All structures were visualized using ChimeraX, vmd and PyMOL. The depicted molecules follow an atomic color code: hydrogen = white; oxygen = red; nitrogen = blue; carbon = beige. The atoms belonging to the MOF ZIF-8 framework are shown in darkgray.)

2.4.1 Static properties

Density distributions As the systems investigated comprise interfaces between liquids and solids, their anisotropic nature needs to be considered. In the most primitive form, the simulation box is divided into two-dimensional slices along the orientation of the interface, or pore axis. Within each slice and for each frame, the density is calculated counting all atoms present including a weighting based on their mass. Additionally, a 3D grid-based approach was developed, where the simulation box is divided along all three main axes. For each grid cell, the density is calculated individually. This way, complex porous networks present in, e.g., MOFs, can be analyzed.

Average filling and accessible volume within CNTs The average filling of liquids within CNTs is calculated by first identifying the space in the simulation box, which represents the pore volume of the CNT. For immobile CNTs it is sufficient to simply take the known pore position from the

initial frame and the CNT radius to capture the volume in the simulation box representing the space within the pore. For flexible CNTs, a different approach is needed. As described in the structure recognition part (Section 2.3.1), the start and end point of the CNT center axis are identified as $\vec{p}_1$ and $\vec{p}_2$. Using these two points and the radius of the CNT r_{CNT} , a cylinder is constructed representing the pore volume of the CNT. For each time step, all atoms at position $\vec{x}$ are identified which are within the cylinder, using the conditions:

$$(\vec{x} - \vec{p}_1) \cdot (\vec{p}_2 - \vec{p}_1) \geq 0 \quad (2.5)$$

$$(\vec{x} - \vec{p}_2) \cdot (\vec{p}_2 - \vec{p}_1) \leq 0 \quad (2.6)$$

$$\frac{|(\vec{x} - \vec{p}_1) \times (\vec{p}_2 - \vec{p}_1)|}{|\vec{p}_2 - \vec{p}_1|} \leq r_{\text{CNT}} \quad (2.7)$$

PBC are considered to ensure that atoms are identified correctly, even when the CNT crosses periodic boundaries. The average filling is calculated by simply counting the total mass of all atoms within the CNT over all frames and dividing it by the pore volume and the number of frames considered. As the calculation is done for all time steps, the pore filling can also be resolved as a function of time, allowing for further interpretation, e.g., to capture filling and emptying processes. The CNT's length l_{CNT} is calculated as the distance between $\vec{p}_1$ and $\vec{p}_2$.

For stationary CNTs, the accessible volume can be calculated. Throughout the analysis the maximal radial distance from the center axis, r_{max} , considering all confined atoms, is identified, allowing to calculate the accessible volume V_{acc} by:

$$V_{\text{acc}} = \pi \cdot (r_{\text{max}})^2 \cdot l_{\text{CNT}} \quad (2.8)$$

Density profiles within CNTs With the confined atoms identified and center axis of the CNT known, the basis is set for further analysis. Using the cylindrical approximation of the CNT, the pore volume is divided into radial increments with the central axis as their origin (see Figure 2.7). The number of increments is freely adjustable and realized by dividing the CNT radius into n slices of equal length.^a The volume of each increment V_{cyl}^n is calculated by:

$$V_{\text{cyl}}^n = \pi \cdot (r_{\Delta}^n)^2 \cdot l_{\text{CNT}} \quad (2.9)$$

$$V_{\Delta}^n = V_{\text{cyl}}^n - V_{\text{cyl}}^{n-1} = \pi \cdot l_{\text{CNT}} \cdot ((r_{\Delta}^n)^2 - (r_{\Delta}^{n-1})^2) \quad (2.10)$$

where r_{Δ}^n is the radius of the n -th increment. With the volume of each increment known, the density within each increment can be calculated by counting the total mass m_{total}^n or charge q_{total}^n of all atoms located within the increment over all frames (N_{FR}) considered. The density ρ_{Δ}^n and charge density $\rho(q)_{\Delta}^n$ within each increment is then calculated by:

$$\rho_{\Delta}^n = \frac{m_{\text{total}}^n}{V_{\Delta}^n \cdot N_{\text{FR}}} \quad (2.11)$$

$$\rho(q)_{\Delta}^n = \frac{q_{\text{total}}^n}{V_{\Delta}^n \cdot N_{\text{FR}}} \quad (2.12)$$

^a Radial increments are of equal radial width, but do not have the same volume. The volume increases for larger displacements from the center.

From these relations, radial density profiles are constructed, providing insight into layering effects of the liquid within the confinement.

Angular distributions The preferred orientation of confined molecules with respect to their radial position in the confinement of a CNT and in relation to other molecules in the immediate surrounding is a defining property. Especially at the interface, molecules tend to align in specific orientations to optimize their interactions with the confining material. To capture this effect, angular distribution functions can be calculated. Two user defined vectors are used to calculate the angle of choice, θ . Five vector options are provided (see Figure 2.7):

- The center axis $\vec{z}$ of the CNT.
- The radial vector $\vec{r}$ from the CNT center axis to the COM of the molecule or an atom of choice.
- A vector defined between two atoms within the molecule, $\vec{d}$.
- The bisector $\vec{u}$ between two vectors $\vec{d}_1$ and $\vec{d}_2$ defined within the molecule.
- Provided vectors in the trajectory file, e.g., dipole moments.

During the analysis, the COM radial distance r to the CNT center axis is calculated for each molecule and for each time step. Based on the radial distance, each molecule is assigned to a given layer. Then, for each molecule, the angle θ between the two user defined vectors is calculated and stored in a histogram, depending on the radial layer. In post processing, the histograms are visualized as angular distribution functions and contour plots. The angular and radial distributions are shown on the x and y axis, respectively, while a color scheme depicts the occurrence of θ within a radial layer.

2.4.2 Dynamic properties

Mean square displacement The mean square displacement (MSD) is a measure to characterize the movement of molecules over time. It is defined as the average of the squared displacement of their respective COM. For a bulk liquid without external forces acting on it, the molecular movement can be described as Brownian motion. Averaged over all particles of a given species, it provides insight into the mobility and diffusion characteristics of the species within the system. The maximum correlation depth $\tau_{\max}$ describes the maximum time interval observed. The MSD is calculated as:

$$\text{MSD}(\tau) = \langle |x(t + \tau) - x(t)|^2 \rangle, \quad (2.13)$$

where $x(t)$ represents the position of the particle at time t . In practice, the MSD is calculated with each time step t as a starting point, and the displacement after a time interval τ is calculated. The average is taken over all particles N of the same kind for all time steps, which significantly increases the statistical robustness.

The diffusion coefficient D is directly related to the MSD through the Einstein relation:

$$D = \frac{\text{MSD}(\tau)}{2d\tau}; \quad d = 1, 2, 3 \quad (2.14)$$

The dimensionality of the system is represented by d . In practice, the diffusion coefficient is extracted from the slope of the MSD curve in the linear regime in post processing.

Layer residence times Layer residence times $\tau_{l,c}$ describe the average time a molecule remains within a user defined radial layer l in the confinement of one or multiple CNTs or a pore, c . To calculate the residence time, functions from previously described analysis methods are exploited to define the CNTs center axis. The radial distance is calculated for each molecule at each time step and assigned to a radial layer l . The survival correlation function $C_{l,c}(t, t^*)$ for each layer and CNT is expressed as:

$$C_{l,c}(t, t^*) = \frac{N_{l,c}(t, t^*)}{D_{l,c}(t^*)} \quad (2.15)$$

Here, t represents the lag time (correlation depth), while t^* is a user defined tolerance time interval, which allows for transient departures of molecules from the layer. If a molecule re-enters the layer quicker than t^* , it is considered as a continuous residence. $D_{l,c}(t^*)$ is the total number of molecules present in the layer at a given starting time, and $N_{l,c}(t, t^*)$ is the number of those molecules that remained in the same layer over the lag time t (neglecting transient departures). Both quantities are computed for all possible starting times in the trajectory and averaged to improve statistics. In post processing, the residence time $\tau_{l,c}$ is then calculated from the survival correlation function by assuming an exponential decay:

$$C_{l,c}(t, t^*) = e^{-t/\tau_{l,c}} \quad (2.16)$$

$$\tau_{l,c} = -\frac{t}{\ln(C_{l,c}(t, t^*))} \quad (2.17)$$

When the correlation drops below $1/e$, the residence time is extracted. Additionally, throughout the simulation, the number of atoms present in every layer and time step is stored.

CONAN- Novel Tool to Create and Analyze Liquids in Confined Space

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Own contributions

- Writing the python code CONAN. This includes the core structure of the program, trajectory processing, molecular recognition, structure generation and trajectory analysis tools.
- Running all MD simulations and analyzing all trajectories with the newly developed tools.
- Writing the paper.

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THIS chapter deals with the capability of the CONAN code and its applicability to build and analyze anisotropic systems. The behavior of the IL 1-butyl-3-methylimidazolium acetate ($[\text{C}_4\text{C}_1\text{Im}][\text{OAc}]$) in pristine CNTs of different sizes in the low- to sub-nanometer range is investigated. Using FF-based MD simulations, structural properties of the confined IL are evaluated. Using CONAN, all carbon structures are generated and the simulation boxes set up.

Generally, the density of the IL is reduced in the confinement of a given CNT compared to its bulk phase, an effect which is most pronounced for the smallest nanotube considered ((12,0) CNT) and diminishes with increasing pore diameter. For the smallest CNT system studied ((n , 0) CNT with $n = 12, 14$), two additional effects come into play. For both, but especially for the smallest studied CNT, slow filling kinetics are observed during equilibration. Since the pores are filled from both sides simultaneously, it is additionally possible that ions of the same kind meet in the center of the pore, a scenario which was observed in both systems. The extreme confinement limits the spatial freedom of the confined ions to such a degree that the arrangement of the ions relative to each other is fixed once they enter the pore, i.e., it is not possible for confined ions to swap positions. While this is partly an artifact from the simulation setup, it also illustrates a realistic scenario for ions in pore networks of nanoporous materials, where the order in which the ions enter fixes their arrangement in the pore. This is consistent with experimental observations by Futamura et al.,¹⁸¹ who report a partial breakdown of the Coulombic ordering, i.e., the alternating arrangement of cations and anions, of ILs in sub-nanometer carbon nanopores.

Radial density distributions further highlight the distinct structuring of the ions in dependence to the CNT diameter. In the smallest CNT, the ions are confined to the pores' central axis, forming a single-file chain. In the (14,0) CNT based pore, the ions are shifted toward the carbon wall, a structure best described as a helical arrangement that spirals around the central axis, optimizing ion-wall and ion-ion interactions.

With a comparatively larger volume within the (16,0) CNT, the ions have more spatial freedom and assume a tubular arrangement where two ions reside next to each other at the same axial coordinate, with both ions radially displaced from the CNTs' central axis. The ions assume a similar structure confined in the (18,0) CNT, but the density profile is less distinct compared to the one obtained for the (16,0) CNT system, due to the increased volume accompanied by a less strict order. In the (20,0) CNT system a second IL layer emerges in the center of the tube. By only considering contributions from individual atoms, further insight is gained regarding the orientation of the molecules. A comparison of the density distributions of oxygen in the confinement of (16,0) and (18,0) CNTs shows, that the orientation of the carboxylate group changes. While it is oriented towards the carbon wall in the smaller CNT, with both oxygen atoms in the same distance toward the carbon wall, the density distribution is split in the confinement of the (18,0) CNT, describing an orientation where the carboxylate group stands perpendicular to the carbon wall.

Additionally, radial charge density profiles were calculated by considering the fixed partial charges assigned to each atom. Although small in magnitude, with maximal charges of $|0.01|e$, oscillating distributions emerge, which are more complex than the individual mass density profiles and show that the molecules are not only highly restricted to their radial position in the confinement, but also assume in a preferred orientation toward the CNT wall, leading to the observed charge layering stemming from the assigned partial charges.

In summary, it can be stated that the packing behavior of the IL depends heavily on the size of the confinement, while the overall density is reduced compared to the bulk, especially in the smallest CNTs.

The structure of the IL ranges from single-file chains to tubular arrangements up to the formation of multiple layers. In addition to the radial position, the orientation of the ions toward the interface changes in different confinement environments. The use of CONAN was the foundation for all of the carbon structures that were examined and all of the results that were presented.

Coordination Behavior of a Confined Ionic Liquid in Carbon Nanotubes from Molecular Dynamics Simulations

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Own contributions

- Running of MD simulations
- Participating in analyzing the trajectories.
- Writing the introduction, method section and parts of the discussion.

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IN addition to pristine ILs, the doping of ILs with salts, often referred to as SiILs, is an approach to tune the properties of an IL. The cation is usually an alkali metal, while the anion is generally chosen to be the same as the IL anion. In this context, the structural behavior of the IL 1-ethyl-3-methylimidazolium tetrafluoroborate ($[\text{C}_2\text{C}_1\text{Im}][\text{BF}_4]$) and its mixture with 25 mol% NaBF_4 in the confinement of sub-nanometer CNTs are investigated. The conducted classical MD simulations comprise pores with CNTs with radii of approximately 5 Å to 8 Å. Additionally, the influence of reduced charges on the ions, a simple model to mimic charge transfer effects, is studied using the approach of Stuchebrukhov et al.,¹⁸² where the charge scaling factor is defined as the inverse of the square root of the dielectric constant of the IL.

Special care was taken to fill the CNTs only from one side during equilibration, and a Coulombic ordering, i.e., a single-file chain with alternating cation-anion arrangement observed in the smallest studied CNT. The computed radial density profiles are consistent with the trends discussed in Chapter 3, where the step-wise increase in tube radius shows a formation of a single-file chain, a tubular arrangement and ultimately the formation of a second radial layer. Interestingly, the second, central radial layer forming in the (12,12) CNT is solely comprised of $[\text{C}_2\text{C}_1\text{Im}]^+$ ions, while the BF_4^- anions in their immediate surrounding always reside in the outer, tubular layer. The addition of salt does not impact the structure of ions in the confinement, as the Na^+ ions overwhelmingly do not enter the CNTs. An exception to this was observed in one case, where a cluster consisting of two Na^+ ions and two BF_4^- ions entered the (10,10) CNT, and stayed inside the confinement for the remainder of the simulation time.

In bulk, the Na^+ ion forms stable clusters with the surrounding anions in mixtures of ILs and sodium-based salts, and moves as a single entity with its solvation shell.¹⁸³ This makes it bulky, resulting in poor transport properties¹⁸⁴ and prohibiting the easy transfer into the extreme confinement of a CNT. Conversely, upon entering the confinement, the Na^+ ions need to shed parts of their solvation shell, and this de-solvation is energetically unfavorable. To elucidate the energetic barrier which would need to be overcome for a sodium cation to partially shed its solvation shell and enter the confined space, additional MD simulations were carried out for each pore, respectively, to calculate free energy profiles for Na^+ . A radial spring potential is set in place to pull a sodium cation from the bulk phase into the confinement of a given CNT, up to the CNT's center of mass. The equilibrium distance is adjusted in incremental steps of 0.25 Å, covering a total of 40 Å. The energy profiles show that there is a significant energy barrier for the sodium cation to move from the bulk phase into the confinement of a pore, while the height of the barrier depends on the pore size. Interestingly, the free energy decreases as the ion moves deeper into the confinement, further away from the open ends of the pore, and the position directly at the entrance is the most unfavorable. To further elucidate the structural characteristics of the confined Na^+ ions, a new analysis tool was introduced to CONAN to compute coordination numbers.^a By adjusting a three dimensional grid to the simulation box, the local dependency of coordination for a given ion is calculated for the anisotropic systems. It shows that the coordination number is reduced for the confined ions compared to the bulk. The trend of reduced coordination is also present for ions residing near the graphene interface. In addition, referring to the Na^+ ion, the coordination numbers in relation to the coordination distance (the distance between the sodium cation in the center in relation to the surrounding anions) shows that the average distance toward surrounding ions decreases in confinement. While on average 4.5 anions surround the Na^+ ion

^a The coordination number analysis tool was developed by a coworker, and is therefore not discussed in detail in Section 2.4 of this thesis.

at a cutoff distance of 5 Å in the bulk phase, in the confinement of the (10,10) CNT this number is reduced to 3.5. In this altered coordination state, two anions of the solvation shell come particularly close to the sodium cation.

Atomic radial velocity distributions were calculated for all confined atoms and for all pores, respectively. They show that the dynamics are generally slightly increased upon scaling ion charges. Further, the velocity distributions show an increased velocity for atoms which are displaced the most from the tube's center, indicating a rotational motion of the confined molecules around the CNT axis.

The investigation adds to the findings from in Chapter 3 regarding IL ion structuring within CNT confinement and also demonstrates that Na⁺ ions prefer to remain in the bulk. The formation of stable solvation shells in bulk creates a significant energy barrier that needs to be overcome for Na⁺ ions to enter the confinement, as this requires a partial de-solvation. In general, ion coordination decreases near the interface and within the confinement. During the project the functionalities of CONAN were further expanded.

Influence of Internal Interfaces on the Structure and Dynamics of IL-Based Electrolytes Confined in a Metal–Organic Framework

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Own contributions

- Running all MD simulations.
- Analyzing the trajectories.
- Writing the theoretical part of method section and parts of the discussion.

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IN addition to carbon based structures, MOFs are another class of nanoporous materials. Their porous network is highly symmetrical and the pore size and shape depends on the individual MOF of choice. In the context of Chapter 4, the behavior of SiIL in nanoporous confinement is further discussed, focusing on lithium salts in combination with ILs confined in a MOF (ZIF-8; see Figure 2.7, central depiction in the system column).

While the high ESW and low volatility of lithium based SiILs make them promising electrolytes, the formation of large Li-clusters accompanied by poor vehicular transport properties of Li^+ ^{185,186} prevents their use in batteries and EDLCs. To address these limitations, hybrid solid-state electrolytes have emerged as an alternative. In these composites, an electrolyte is confined inside a nanoporous solid material, e.g. MOFs. The solid serves as a structural element and also, as discussed in the two previous chapters, drives the IL or SiIL into a frustrated packing. In this state, the confined ions assume a structure altered from bulk behavior, accompanied by a reduced coordination and reduced Coulombic ordering. Next to the restricted spatial freedom of the ions are competing ion-wall interactions at the solid-liquid interface.

In a collaborative study, the structure and dynamics of Li^+ in various SiILs confined by ZIF-8 were investigated in connection to how interactions of the SiILs with the inner surface of the MOF dictates the ions behavior.

Parts of this work are done experimentally,^a and cover the study using various SiILs. The computational work focuses on the description of the structure and dynamics of $[\text{Pyr}_{14}][\text{NTf}_2]/\text{Li}[\text{NTf}_2]$ in the confinement of ZIF-8 at varying salt concentrations and temperatures using classical MD simulations. In the confinement, ion–ion interactions and the interplay between ions and the ZIF-8 framework govern the liquids' behavior.

Multiple radial distribution functions (RDFs) were computed to resolve the average coordination the liquid species assume in the confinement. These show, that the NTf_2^- anions^b prefer to reside near to the zinc atoms of the MOF framework. On the other hand, the lithium cations position themselves near the imidazolate-based linker units, while the Pyr_{14}^+ reside close to the methyl group of the linkers. Thus, the confined cations are in competition to coordinate with the imidazolate-based linkers of ZIF-8. These findings are supported by NMR spectra, and Raman spectra further resolve that varying the IL cation also impacts the Li^+ dynamic behavior. Connected by the competition to coordinate with the organic linkers, stronger interaction of an IL cation with the ZIF-8 framework was found to reduce the coordination of the Li^+ with the framework, resulting in increased local Li^+ dynamics.

The properties of the lithium ion dynamics is further elucidated by calculating MSDs for the ionic species at different temperatures in the MOF and in the bulk phase. In line with observations in Chapter 3 and Chapter 4, Li^+ ions, coordinated by NTf_2^- anions, are the slowest species in bulk. In contrast, while the transport is generally decreased for all species in ZIF-8 confinement, Li^+ is the fastest species in confinement. This can be rationalized when considering the change in ion coordination in confinement. In bulk, the transport mechanism of Li-cluster is a vehicular transport. However, the confinement within a given pore not only alters the immediate coordination, but it also prohibits a pore-to-pore passage for Li-anion clusters. Therefore, in confinement, the transport of Li^+ changes to a ligand exchange mechanism, where the Li^+ changes ligands upon moving from one pore to another. This effect is supported by the computed MSDs, and by the calculated 3D density profiles

^a The experimental work was conducted by the collaborators in this project. See Chapter C for more information on how the experiments were conducted.

^b NTf_2^- anions are referred to as TFSA anions in the publication.

using CONAN. Additionally, visualizations of the MD trajectories show this is indeed a ligand exchange mechanism at play.

These findings show that the coordination environment and dynamics of the ions of the SiIL, particularly of the Li^+ ions, change in confinement of ZIF-8. Importantly, the choice of IL cation influences the dynamics of the alkali metal, and the transport mechanism of Li^+ changes from a vehicular transport in the bulk phase to a ligand exchange mechanism in confinement.

Carbon polarization and carbon nanotube stacking impacts the behavior of water in nanoconfinement

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Own contributions

- Conceptualizing the scope of the paper.
- Running all MD simulations and partially analyzing the trajectories.
- Writing the introduction, method section, most of the discussion as well as the conclusion.

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THIS chapter is devoted to the behavior of water confined in CNTs. In this context, individual, isolated CNTs filled with water are modeled, and also VANTAs, in order to understand whether interactions between water in adjacent CNTs impact the structural and dynamic properties of the confined water. The MB-pol water model (see Section 1.6) is utilized and compared to the TIP4P/2005f water model (see Section 2.1). In addition, polarization effects of the CNT carbon atoms are taken into account to monitor changes in the behavior of the confined water. Compared to the studies of ILs confined in CNTs (see Chapter 3 and Chapter 4), two central changes are made to the simulation setup. Instead of relying on immobile carbon structures, the CNTs are modeled as fully flexible entities. The modeling of a reservoir from which the water molecules can enter the confinement (and into which they can leave the CNT) is omitted in the simulation production runs. Instead, the CNTs are filled in an initial simulation step and subsequently modeled as infinite structures, creating a closed system in which water permanently remains confined. This setup offers the distinct advantage that all molecules reside in the confined environment over the whole simulation time, allowing for better statistics but more importantly also allowing for a serious reduction of the required system size and thereby the computational effort. Additionally, dynamic properties of the confined water are better captured, as no exchange of molecules with a reservoir takes place and no ordering effects at the CNTs' open ends occurs. The analysis of these systems required a significant expansion of CONAN to account for the flexibility on CNTs and maintain the validity of previously written code (see Section 2.4). Additionally, analysis methods are developed to investigate molecular orientations as a function of radial position within CNTs, as well as to calculate dynamic properties, namely diffusion coefficients extracted from MSD calculations and layer residence times (Section 2.4.2).

Three CNTs in zigzag configuration are studied (($n,0$) CNT with $n=10, 15, 20$). In the smallest tube, with a radius r_{CNT} of approximately 4 Å, the water molecules form a single-file chain along the CNTs' central axis. The water molecules form HBs with their two adjacent neighbors, resulting in a one-dimensional HB network. One O–H bond of each water molecule is approximately oriented along the direction of the tube axis, while the other one is dangling and roughly oriented radially in direction of the tube wall. Within the (15,0) CNT, water molecules arrange in pentagonal rings, stacked along the tube axis. Each water molecule participates in in-plane hydrogen bonding in the formed pentagon, while out-of-plane HBs interconnect the pentagons, although these come with less favorable angles. In the largest studied CNT ((20,0) CNT), water molecules arrange are less ordered, forming a dynamic network of HBs, while two distinct radial layers of water molecules emerge. These effects are described in the combined distribution functions of radial positions and angular orientations, but are also visible in water infrared (IR) spectra, where a distinct splitting of the O–H stretching modes ($\omega > 3200 \text{ cm}^{-1}$) is observed for the (10,0) and (15,0) CNTs, while a broader band without distinct features is seen for the largest tube studied. The ice-like, highly ordered nature of water in the (10,0) and (15,0) CNTs is underlined by distinct peaks in the librational region of the IR spectra ($\omega \approx 100\text{--}1000 \text{ m}^{-1}$), showcasing that some librational modes are favored, while others are suppressed.

Structurally, minor deviations are observed when comparing the systems with and without considering carbon polarization effects. This is the case when comparing the results for single CNTs to those obtained modeling VANTAs, as well as when comparing the results from both water models. An exception to this is the angular distribution of water molecules confined in (20,0) CNTs, where the inclusion of carbon polarization effects leads to a change in the preferential orientation of water molecules at the carbon interface. Without considering polarization, water molecules at the interface

tend to orient with one O–H bond roughly parallel to the CNT wall (with a slight tilt toward the wall), while the other bond is oriented more towards the tube center. When carbon polarization is accounted for, a second preferred orientation emerges, where one O–H bond points directly towards the CNT wall, while the other bond is oriented more towards the tube center.

With respect to the dynamics of the confined water, especially the systems comprising (20,0) CNTs are analyzed in detail. Large differences are observed when comparing the dynamics of water confined in isolated CNTs compared to water confined in VANTAs. Intermittent hydrogen bond lifetimes, a measure of the longevity of HBs, are decreased by approximately 20–25% when comparing water confined in isolated CNTs or VANTAs. This indicates that CNT stacking and the presence of water in adjacent CNTs destabilizes the HB network within a given tube. Further, layer residence times are computed for water confined in (20,0) CNTs, where two radial water layers form. It provides an estimate of how long water molecules reside in a given radial layer before moving to the other one. A decrease of approximately 20% is observed in VANTAs, further highlighting that the presence of adjacent tubes filled with water makes the water molecules more dynamic.

This underlines the various forces that are at play and need consideration at such nanoscale. Considering carbon polarization effects and modeling stacked CNTs (VANTAs) was shown to only have minimal impact the water structure, especially for the smallest CNTs considered. However, it does also show that those effects are important to consider for a good description of the water orientation at the solid–liquid interface as well as for the water dynamics.

The adsorption of drugs on nanoplastics has severe biological impact

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Note: This publication is based on the master thesis “Adsorption of Tetracycline on Nanoplastics”.¹⁸⁷ However, all calculations were redone with slightly differing setup, new MD simulations were included, all analyses were redone, and numerous new analyses were performed for this publication, making it entirely novel. For this reason, the publication is included in this cumulative work.

Own contributions

- Running all MD simulations and geometry optimizations.
- Participating in the analysis of the trajectories and optimized NP geometries.
- Partially curating and visualizing the results
- Contributions to the writing of the manuscript.

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WITH the ever increasing demand of plastics and consequently also its accumulation in the environment (discussed in Section 2.2.3), studies on MNPs and their interaction with biological matter have become increasingly important. It has been shown that MNPs interact with various biologically active substances and especially NPs are toxicologically worrying, as it has been shown that they can cross many tissues in the human body, including the blood-brain barrier.^{161,188} This chapter focuses on the theoretical approach to model the interaction of pristine NPs with an exemplary antibiotic, tetracycline (TC), to gain a deeper understanding of the aggregation process and interaction characteristics. Stable, pristine NP structures are generated, and two pathways are explored for generating TC@NP aggregates. Four different plastics are studied, namely N66, polyethylene (PE), polypropylene (PP) and polystyrene (PS),^a using the SA approach (see Section 2.2.3) for particle folding. For each type of plastic, 50 structures were generated to obtain robust sets of conformations. In the first approach for generating TC@NP aggregates, similar to the initial folding of pristine NPs, polymer chains are folded together with the antibiotic through SA, allowing for a high degree of structural freedom when the aggregate is formed. In the second approach, a pre-folded NP is used instead (the energetically most stable conformation in the NP set generated for each type) and the TC is attached to various positions on the NP surface. Then, the newly formed aggregate is relaxed in a short MD run at low temperatures. This approach skips the computationally demanding folding of the NP together with TC, but allows for a drastically less exploration of the configurational space. For each NP, a total of 104 aggregates are generated following both approaches, which are further geometry optimized considering implicit solvation. Interaction and sorption energies between the NP and TC are calculated for the optimized structures.

Overall, the approach which relies on the SA ansatz to produce TC@NP aggregate is shown to be superior. On average, energetically low-lying aggregate structures are produced and larger interactions energies between the NP and the antibiotic obtained. Furthermore, this approach allows for greater variability in the generated structures. In the final aggregates, the antibiotic stays not only on the surface of the NP, but also positions itself inside it, completely embedded between the polymer chains. These observations are highly depending on the type of plastic and can be rationalized in this regard. For N66, polymer strand interactions and the interactions between polymer chains and TC are mostly governed by polar interactions, and an extensive HB network forms throughout the particle. On the other side, intermolecular interactions in non-polar NPs are driven by dispersion forces, which are much weaker and favor different interaction sites of the TC, impacting its preferred radial position and orientation. This is quantified by the relation of the center of mass distance between the NP and TC (r_{com}), divided by the radius of gyration (r_{gyr}) of the plastic: $r_{\text{com}}/r_{\text{gyr}}$. It gives an estimate regarding the position of the antibiotic, where a smaller value indicates that the TC is more embedded into the plastic. The average r_{com} to r_{gyr} ratios are lower for all plastic types when folding the NP together with TC, highlighting that the second approach, where the TC is attached to various surface positions, is insufficient to generate relevant sets of configurations. However, these results also show that a certain dynamic of the polymer chains at ambient conditions is required for a formation of such aggregates, where the TC is fully embedded in the NP. Therefore, two additional MD simulations over 50 ns are modeled for each type of plastic, placing a TC@NP aggregate together with 32000 water molecules at ambient conditions to study the dynamics of the NP and the antibiotic. For each type of plastic, considering all structures which are in a range of 20 kcal mol⁻¹ with respect to the

^a The modeled PP NP is built from isotactic polymer chains, while the PS NP is made of atactic polymer chains. Both tacticities are the most common for their respective plastic types.

energetically best found TC@NP aggregate, the structures with the highest and lowest r_{com} to r_{gyr} ratio were chosen for modeling. The dynamics of polymer strands are governed by intermolecular polymer chain interactions, but also by steric hindrance, which is a factor for PP and especially PS, where the bulky methyl/phenyl groups hinder large conformational rearrangements. Consequently, during the MD simulation runs, the mobility of individual polymer chains are found to depend highly on the NP studied. Radial diffusion of the antibiotic during the MD simulations is observed, but the assumed radial positions are found to depend on the initial position of the TC, demonstrating the complexity of the adsorption mechanisms and the timescales that must be considered. However, the fact that the TC was found to be mobile within NPs and on their surface, and staying aggregated throughout the simulation (except for one case for PS, where the TC briefly detaches during equilibration before being re-adsorbed) demonstrates the validity of the approach of generating TC@NP aggregates. In terms of adsorption energies, the affinity of the TC to interact with NPs depends on the type of plastic: N66 > PS > PP > PE. Furthermore, the findings of the study are supported by experimental work. In a cell culture experiment, a 40–50% reduction TC-induced marker expressions in both human and mouse cell lines was reported when NPs were added.

This underlines the validity of the theoretical approach to describe NP-TC interactions through theoretical modeling. While TC was found to aggregate on all NPs studied, the interaction energy and type of sorption is individual for each plastic.

Building Nanoplastic Models for Molecular Calculations

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Own contributions

- Participating in analyzing the trajectories and NP geometries.
- Partially curating raw data, setup of the NP database.
- Participating in the visualization of results and creation of schematics.

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As was presented in Chapter 7, a robust set of conformations is key in describing the structure of NPs and for continuous works, e.g., to describe their interactions with other matter. To address this need, this chapter deals with the exploration of refining the SA approach by establishing a systematic workflow to generate energetically stable NP structures. It further deals with the exploration of structure descriptors to assess the quality of the produced conformations. As in Chapter 7, the widely used plastics PE, PP, PS and N66 were studied, and after the initial SA runs, the produced NPs are further geometrically optimized. Single point DFT calculations are done on the optimized structures, using various functionals^a and composite methods.^b This way, the quality of the FF and the workflow is assessed and it allows for a detailed energetic evaluation of the produced NPs. Additionally, the structural features of the produced sets of NPs are investigated. Finally, all generated structures are provided in an open database which is freely accessible.¹⁹³

The first thing considered for optimization is the simulation time required during the SA run to generate low-energy NP structures. As discussed in Section 2.2.3, the simulation time, and thereby the cooling rate $T_{\text{start}} \rightarrow T_{\text{end}}$, is a compromise between the computational feasibility and the required length to yield low energy conformations. Using 50 replica simulations for stochastic robustness, the cooling protocol was run for 20 ns and 50 ns, respectively. The 50 ns runs yield energetically more stable NP structures on average, demonstrating that a slower cooling rate is important for finding better conformations. A comparison of the FF-based relative energies of all produced NPs (related to the energetically best conformer found) to DFT energies show a reasonable to very good agreement, depending on the type of NP, underlining the validity of the SA approach based on a simple FF for conformer generation.

All plastics are also structurally evaluated. At these sizes, with NPs coming in diameters of 3-5 nm, two opposing effects are at play. For large plastics, i.e., macromolecules with polymer chains in bulk, the intra- and intermolecular interactions are the driving force in polymer chain structuring, often leading to the formation of crystalline or semi-crystalline phases, depending on the type of plastic and polymer tacticity, which defines the stereochemical arrangement of the side groups along the polymer backbone. However, considering the small size of the produced NPs in the low nanometer range, surface effects are also important to consider. For particles of these sizes, the surface-to-volume ratio is considerable, and the high relative surface area causes a significant part of the polymer chains to be imperfectly embedded with stabilizing polymer–polymer interactions reduced. Accordingly, the driving force towards a minimal surface area cause NPs to assume a spherical shape. This stands in contrast to the formation of well-ordered polymer strands and crystalline phases, which form the internal structure and govern the shape of the particle according to their alignment. This conflict is particularly evident for PE, where the low energy conformations all show a fairly high degree of structuring and their overall shape becomes increasingly less spherical over the course of the SA protocol. This trend is monitored by tracking the percentage of *gauche* conformations in the C–C–C dihedral angles of the backbone as well as an order parameter, which quantifies the crystallinity of a given NP.¹¹ For the energetically lowest conformation found, a significant shift occurs after approximately 35 ns of simulation, time, where a drastic trend towards dihedrals in *trans* conformation occurs, accompanied by a drastic increase in the NP internal ordering. The governing structure

^a The functionals B3LYP,⁴⁴ BP86,^{40,43} PBE,⁴² PBE0,⁴⁵ ω B97X-D3¹⁸⁹ together with the def2-SV(P)⁴⁹ basis set and the def2-MTZVP/J auxiliary basis set for Coulomb fitting and the D3 dispersion correction with Becke–Johnson damping^{46,47} were used.

^b The composite methods PBEh-3c¹⁹⁰ and r²SCAN-3c^{191,192} were used.

descriptor in the formation of stable PE NPs is therefore the formation of well-aligned polymer chains. This trend is not observed for PP and PS, which can be rationalized by the side groups which impacts the preferred alignment of polymer chains, and the *gauche* ratio increases over the course of the SA runs. The relevant NPs conformers assume a more spherical shape compared to the PE counterpart. In case of N66, the number of HB was found to steadily increase over the simulation time, while the *gauche* dihedral angle ratio and the order parameter were found to be stationary for the largest part of the simulation time after the first a few ns. This shows, that the main driving force of the structure formation within a given N66 NP is the formation of a HB network.

Overall, the quality of the NP structures produced using the SA method was verified. The degree of order within a NP, and consequently its shape is ultimately a compromise between two opposing driving forces, namely surface effects and optimal polymer chain alignment. This rationalized the different shapes and characteristics of the individual plastics. All NP conformers are available in an open database.

Nanoplastics can build themselves

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Own contributions

- Conceptualizing and leading the project
- Partly running the MD simulations and participating in their analysis.
- Writing the introductory part, parts of the discussion, and the conclusion.

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WHILE the SA ansatz, together with the described workflow in Chapter 7 and Chapter 8, has proven to give robust results for generating sets of NP conformations, the MD simulations require significant computational effort. In addition, the SA method is subject to a limitation to generate sets of NPs with different conformations: As described in Section 1.5, for classical MD simulations using ordinary FFs, bonds are rigidly defined when running a simulation. Thus, when generating NPs, the number of polymer strands and their respective length, i.e., the number of monomer units, must be defined *a priori*. Rerunning calculations with differing starting configurations therefore yields NPs consisting of identical polymer strands, differing only in their conformation. However, chemical intuition suggests that NPs, also those with the same total number of monomer units, should consist of differing numbers of polymer strands of differing length. This becomes particularly clear when considering that they often result from degradation processes rather than controlled synthesis (see Section 2.2.3). In this context, the ratio between the number of monomer units building an NP (N_{mono}) and the number of end-group pairs (N_{chain}) is important to consider. End-groups within a particle introduce steric effects and, depending on the type of plastic, may also contain functional groups that participate in hydrogen bonding. Therefore, they influence the structure in a given NP, and their abundance is an important factor. To accurately capture the structural heterogeneity of NPs of the same size, it is reasonable to assume that considering multiple, diverse compositions of a respective NP in terms of the number of polymer strands and their individual length, next to a proper polymer chain folding, is important.

To address the described limitation, a novel approach was developed and validated for N66 NPs, where NPs are solely defined by their total number of monomer units. Generating NPs is realized in a three step procedure.

First, N66 monomer units are placed randomly inside a simulation box. Terminal atoms of the monomers which would split off during polymerization (OH group and an H atom) are treated as “naked atoms”. They only serve as placeholders and bear no partial charge nor interact with any other atom belonging to a terminal group. LJ interactions between the terminal carbon atom on one side and the terminal nitrogen atom on the opposite side (the atoms which form a peptide bond during polymerization) are deactivated. During the initial run, the dispersed monomers assemble into a single aggregate, driven by intermolecular monomer–monomer interactions, dominated by the formation of an extensive HB network. The terminal carbon and nitrogen atom are allowed to come into close proximity, as the “naked atoms” can overlap, however do not interact with each other at this point.

In the second step, peptide bonds are formed by activating LJ interactions between the terminal nitrogen and carbon atoms. These bonds are not explicitly expressed through the FF, but instead modeled through a scaling of the LJ interactions, modeling a C–N bond. The LJ parameters of surrounding atoms are scaled as such that a *trans* configuration of the backbone is enforced. After the polymerization run, excess “naked atoms” are removed wherever a new peptide bond was formed.

In the final simulation step, the formed NP structure is relaxed at 300 K, where the newly formed peptide bonds are explicitly modeled through the FF. Any special scaling factors used in previous simulations are discarded, and the ordinary LJ parameters from the FF are used. All generated NP structures are further geometrically optimized to allow direct comparison with the structures generated in Chapter 8, which are taken as reference.^a A special feature of this workflow is that the polymerization step also allows for the formation of polymer loops. Therefore, one needs to distinguish between polymer “chains” and polymer “rings” (where multiple monomers form a loop and

^a The reference NPs structures, taken from Chapter 8, are built from eleven polymer strands, each consisting of nine monomer units. Thus, the total number of monomer units in a reference NP is 99.

no end-groups are present), which are collectively described as polymer “strands” in the publication. Three different sets of 50 NP structures are generated, comprising 70, 99 and 130 monomer units. In a second series of simulations, the use of dimers as the smallest initial building blocks was investigated to elucidate the relationship between the size of the initial unit and the number of polymer rings formed, again producing sets of 50 NP structures each. On average, the number of polymer rings, as well as the total number of polymer strands formed, decreased when longer initial building blocks were used.

The newly generated NP structures all come with smaller $N_{\text{chain}}/N_{\text{mono}}$ ratios compared to the N66 reference structures taken from Chapter 8, showing a tendency towards less, and thus on average longer, polymer chains. However it also shows that many strands formed are short, comprising just a few monomers, while others are very long (>40 monomer units). The Herfindahl Index (HHI)¹⁹⁴ was used to quantify the lengths distribution of the polymer strands forming an NPs. On average, it shows that strands are becoming longer, while also showing that a complete monopolization of one dominant strand does not occur. Rather, it is a mixture of strands of different lengths that compose a plastic. Further, the HHI shows that using more monomers to aggregate into a single NP, i.e., building a larger particle, makes it further unlikely that few dominating polymer chains will form.

To compare NPs with varying numbers of monomers and end-groups, the total energy (E_{tot}) is approximated as a sum of an end-group energy contribution ($E_{\text{chain}} \cdot N_{\text{chain}}$) and monomer energy contributions ($E_{\text{mono}} \cdot N_{\text{mono}}$). Normalized by N_{mono} , E_{tot} is expressed by the linear relation:

$$\frac{E_{\text{tot}}}{N_{\text{mono}}} = E_{\text{chain}} \cdot \frac{N_{\text{chain}}}{N_{\text{mono}}} + E_{\text{mono}} \quad (9.1)$$

A linear regression was fitted using all newly generated NPs with and without considering the reference structures (N=300/N=401). The corrected energy term, E_{cor} , obtained by removing the linear dependency for each individual NP E_{tot} term, allows for a direct comparison, and the new structures are found to be energetically similar compared to the reference structures. The lowest E_{cor} value is found for a newly generated NP, however, there is also a considerably larger spread of E_{cor} energies across the newly generated NPs compared to the references.

Structural parameters, like the number of HBs formed, the radius of gyration or the anisotropy factor, reveal, that the newly produced NPs are structurally very similar to the reference NPs, while the *gauche* ratio of the dihedral angles of the polymer backbone is smaller for the newly generated NPs.

Generally, the applicability of the approach to produce NP conformations of good quality is underlined, while considerably reducing the computational effort compared to the SA approach. Further, the structures produced come with differing $N_{\text{chain}}/N_{\text{mono}}$ ratios, showcasing that the approach covers a broader landscape of NP structures.

Summary

THE first part of this thesis focused on computational studies of ionic liquids (ILs) and water, confined in carbon nanotubes (CNTs) and the metal-organic framework (MOF) ZIF-8. To model these complex liquid-solid interfaces, both classical and many-body based molecular dynamics (MD) simulations were carried out. The main focus lied on characterizing the behavior of confined liquids, primarily governed by the pore size and shape of, as well as the interfacial interactions with the confining materials.

A major part of this thesis evolved around the development and application of the analysis code CONAN (*Confinement Analyzer*), which was explicitly developed for the study of anisotropic systems. Section 2.3 described the general architecture of CONAN, while Section 2.4 presented the theoretical background of the implemented analysis tools. All tools were made openly accessible alongside a provided manual,^{177,178} ensuring the reproducibility of the presented results. The code is designed to process various trajectory data types and comes with a molecular recognition and automatic structure evaluation to ensure a wide applicability. Furthermore, its modular fashion allows for a straightforward implementation of new analysis tools building on existing functions of the main part of the code.

Using the tools provided by CONAN, the drastic changes to the structural arrangement of ions of the ILs 1-butyl-3-methylimidazolium acetate ($[C_4C_1Im][OAc]$) and 1-ethyl-3-methylimidazolium tetrafluoroborate ($[C_2C_1Im][BF_4]$) and its mixture with 25 mol% $NaBF_4$ within sub-nanometer CNTs were discussed in Chapter 3 and Chapter 4. The arrangement of ions was found to be highly dependent on the size of the CNTs, which dictate the structural features of the liquid phase. Radial mass and charge density profiles with respect to the CNT axis, as well as axial density profiles along the dimensions of the simulation box provided insights into the arrangement of ions in confinement. In the smallest studied CNTs, ions were forced to assume a chain-like arrangement along the CNT's central axis, while for slightly larger CNTs with radii of approximately 5.5–7 Å, a tubular arrangement of the ions was observed. In the largest examined pores ((20,0) CNT and (12,12) CNT), a second radial layer was formed. In addition, the coordination number of each ion was determined as a function of distance with respect to surrounding ions and their distance to the pore wall. The coordination number was calculated both for the bulk liquid and liquid in confinement and demonstrated a vast decrease of ion coordination in confinement, due to the limited available space. Generally, a clear reduction in density and ion coordination in confinement was observed for all studied liquids. In bulk of the salt-in-ionic liquid (SiIL) $[C_2C_1Im]_{0.75}[BF_4]/Na_{0.25}[BF_4]$, Na^+ cations were found to form

large clusters with surrounding anions. Furthermore, free energy curves calculated for the Na^+ cation revealed that a significant energetic barrier needs to be overcome for the ion to enter the confinement of the studied (10,10) CNT, stemming from a partial desolvation of the cation.

In Chapter 5, confined IL-based electrolytes in MOF structures were discussed, which are promising composites for hybrid solid-state electrolytes. The collaborative study was devoted to the analysis of SiILs in the confinement of zeolitic imidazolate framework (ZIF)-8.

The computational studies focused on studying $[\text{Py}_{14}][\text{NTf}_2]_{0.67}/[\text{Li}][\text{NTf}_2]_{0.33}$ in detail. Complemented by experimental studies, it was demonstrated that while Li^+ ions in the SiIL come with the slowest relative transport properties in bulk, the transport mechanism changes from a vehicular to a ligand-exchange mechanism in confinement, making Li^+ cations the most dynamic species within the ZIF-8 framework moving independently. This was shown by calculating the mean square displacement (MSD) of all ions and three dimensional density distributions discussed in Section 2.4.1. Experimental findings further showed that the interactions of the IL cation with the ZIF-8 framework impacts the Li^+ transport. Overall, the interplay between the ions and the MOF impacts the ion-ion interactions, while fine-tuning the competitive coordination of the IL cation and Li^+ towards the framework was identified as a pathway for improving transport limitations.

The characteristics of confined water in CNTs and vertically aligned carbon nanotube array (VANTA) were discussed in Chapter 6. For the setup of the simulation boxes and especially for the later analysis, CONAN was significantly expanded to handle multiple, flexible CNTs simultaneously and to calculate dynamic properties such as the MSD and layer residence times (see Section 2.4.2). Furthermore, a novel analysis tool provided insight into the orientation of the water molecules with respect to the interface. The MB-pol model was utilized for a detailed description of water (see Section 1.6). While it has been shown to be a very precise model in bulk, it was the first time this model was applied to water in the extreme confinement of sub-nanometer CNTs. The accuracy of the model was validated by the very good agreement between the computed infrared spectra and experimental references.

In differently sized CNTs considered, water molecules either form a single-file arrangement with a one-dimensional HB network, pentagonal rings stacked along the CNT axis, or more complex structures with two radial layers and less strict ordering. For water confined in (10,0) CNT or (15,0) CNT, the O-H bond stretching modes were drastically altered. While some O-H bonds were well aligned in the hydrogen-bond network, other O-H bonds were dangling, oriented towards the interface signaled by high frequency components in the infrared spectra. Ultimately, it was shown that the hydrogen bond network governed the structural arrangement within the confinement. In less extremely confined environments, where water molecules have more structural freedom, polarization effects proved to play an increasingly important role.

Changes in the orientation of water within the largest considered CNT were observed when accounting for carbon polarization, with water molecules oriented more toward the carbon wall. Additionally, modeling VANTAs instead of single, isolated CNTs was found to make confined water more dynamic, with reduced intermittent HB life times and layer residence times, underlining the impact of stacking effects when considering multiple CNTs. Both the stacking effects, as well as the carbon polarization were found to be crucial to consider for accurately describing the orientation of water at the CNTs interface, and capture its dynamics.

To summarize, the novel analysis tools presented for evaluating dynamic and structural properties in CONAN have been shown to be very effective in studying anisotropic systems. In addition, CONAN provides a platform for developments. Further analysis options such as reorientation times of individual molecules, or their degree of confinement,^{195,196} would be valuable future additions to the code. It

is therefore advantageous to continue developing CONAN and expanding its functionality. Given the evaluation tools already available and the ever-improving possibilities for modeling molecular systems, studying the behavior of electrolytes at interfaces and in nanoporous materials under applied electric fields is another promising research direction. This involves not only the molecular structuring under a constant applied field, but also the molecules' dynamic behavior during charging and discharging cycles in order to understand and optimize the interplay between electrolyte and electrode, maximizing the capacity of electric devices such as batteries or electric double-layer capacitor (EDLC). Additionally, functionalization or doping the carbon based nanoporous materials has been shown to impact the behavior of the confined liquid and poses as promising options for further advancements.

The second part of this thesis was devoted to research on nanoplastic (NP). Chapter 7 focused on pathways for generating stable NPs and NP aggregates. Using MD simulations and semiempirical methods, the structure and behavior of NPs and their interactions with the antibiotic tetracycline (TC) were investigated for the four plastics polyethylene (PE), polypropylene (PP), polystyrene (PS) and nylon 6,6 (N66). In a first step, NP particles were folded from individual polymer strands, using simulated annealing. To form the NP–TC aggregates, two pathways were compared: a complete refolding of the plastic particle together with the drug, and the placement of the antibiotic on the surface of a prefolded NP at various positions. It was shown, that a complete refolding yielded energetically more stable aggregates, as the larger configurational freedom allowed for TC to assume favorable positions embedded between the polymer chains. Competing forces were at play when the particles formed. Plastic–plastic interactions between the polymer chains govern the shape and alignment of the strands, while the antibiotic–plastic interactions compensate for a disruption to this polymer chain alignment upon embedding. Depending on the type of plastic, the governing intermolecular forces which ultimately determined the shape of the NP and positioning of the antibiotic were either van der Waals interactions (PE, PP, PS), or the formation of hydrogen-bond networks (N66). Steric hindrances introduced by side groups were also found to play a crucial role, as they limited the translational freedom of polymer strands with respect to one another. MD simulation showed, that the movement of the antibiotic on the surface of a given NP was, depending on the plastic type, rather dynamic. The antibiotic stayed attached, but mobile on the NPs when modeling the NP–TC aggregates in explicit aqueous solvation, which confirmed the affinity of the TC to interact with the nanoplastics. Together with the calculated adsorption energies, MD simulations indicate that the sorption mechanism is reversible, and the affinity of plastic–drug interactions highly depend of the type of plastic. Experimental findings supported these results, showing that these interactions potentially impact human health, as TC-induced marker expressions showed a reduction of up to 50% in human and mouse cells in the presence of nanoplastics.

In Chapter 8, the polymer folding using simulated annealing was further optimized. NPs were generated through temperature protocols of changing cooling rate, highlighting that slower cooling rates of 50 ns were necessary for generating energetically low-lying NP structures, as a slower cooling allowed for the exploration of a comparatively larger configurational space. The approach proved reliable in forming stable nanoparticles, yielding a large variety of stable conformers coming in vastly different conformations and shape. The quality of the approach was validated for all considered plastic types by further structural optimization and evaluation using density functional theory, ultimately supporting the validity of the simulated annealing approach for conformational search.

The overall shape of the nanoplastics was found to depend to competing effects. To minimize the surface-to-volume ratio, polymer strands tend to aggregate into spherical shapes for a minimal

surface area of the particle. This stands in contrast to the energetically favorable formation of parallel, well-aligned strands forming crystalline phases within the internal structure of a NP. This was demonstrated in detail for PE, where the structural evolution over time was observed during the polymer folding in the simulated annealing simulations. It was found that the polymer chains assume an increasingly aligned arrangement over time, increasing the order of strands with respect to each other, while the overall NP shape increasingly deviates from a spherical shape. For N66 in contrast, the formation of the hydrogen bond network between the amide moieties was found to influence the internal polymer structure most substantially.

Further progress in generating NPs was presented in Chapter 9. While it was established that the SA method can be utilized to reliably generate large sets of NP structures, the approach is computationally expensive and restricted in the sense, that the lengths and number of polymer chains forming NPs are predetermined.

These limitations were addressed by the development of a novel approach. Instead of using a defined number of polymer strands of set lengths, simulations were started from individual monomers. In an initial step monomers aggregated, forming a single particle, which was then followed by a polymerization of the monomers resulting in the formation of interwoven polymer strands. The structuring is governed by monomer–monomer interactions and avoids much of the steric hindrance which is particularly present for interwoven, long polymer strands. The set of NPs produced using the new ansatz showed a varying number of polymer strands of differing lengths, highlighting their structural diversity. Additionally, the approach allowed for the formation of polymer rings, where the monomer units form a loop during polymerization.

The novel approach is computationally efficient and offers a great structural variability, while many of the generated NPs were low energy, underlining the quality of the produced geometries. However, although the initial aggregation of individual monomers ensures that the forming polymers were in a reasonable configuration relative to each other after the polymerization step, it can be assumed that a combination of the new approach with a subsequent simulated annealing step would further advance the description of NPs through theoretical models.

As a prospect, further progress in modeling NPs could be achieved by also considering functionalization of NP surfaces. A significant portion of NP particles found in the environment originates from degradation processes and it can be assumed that at least parts of their surfaces are functionalized. Thus, a vital next step toward generating sets of NP structures with a reasonably rich in diversity would be the addition of functional groups. This would further advance the description of NPs at a molecular level, facilitating the assessment of their environmental and toxicological impacts. Based on that, further studies are needed to better understand interactions between plastics and other matter, ultimately allowing for a more accurate risk assessment of the increasing concentration of NPs in the environment.

Overall, the two parts of this thesis presented contributions that significantly advanced the description of nanomaterials, both analytically and conceptually. These findings paved the way for further, detailed research efforts in studying the characteristics of nanoconfined liquids and nanoplastics.

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Appendix: CONAN - Novel Tool to Create and Analyze Liquids in Confined Space

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Own contributions

- Writing the python code CONAN. This includes the core structure of the program, trajectory processing, molecular recognition, structure generation and trajectory analysis tools.
- Running all MD simulations and analyzing all trajectories with the newly developed tools.
- Writing the paper.

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CONAN—Novel Tool to Create and Analyze Liquids in Confined Space

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ABSTRACT: Modeling of complex liquids at solid surfaces and in confinement is gaining attention due to an increase in computer power and advancement of simulation techniques. Therefore, tools to set up structures and for analysis are needed. In this paper, we present CONAN—a Python code designed to facilitate the study of liquids interacting with solid structures, such as walls or pores. Among other things, the program provides the option to generate a variety of different structures, including carbon walls and nanotubes and their boron nitride analogs, as well as the ability to analyze various structural properties of confined and interfacial liquids. In the case of the ionic liquid 1-butyl-3-methylimidazolium acetate in carbon nanotubes of different sizes, we demonstrate the abilities of our tool. The average density within the confinement highly depends on the carbon nanotube size, and it is generally lower than the density of the bulk liquid. The arrangement of the individual species within the tube also depends on size, with radial layers forming within the tubular confinement. The density is largely increased in the respective layers, while it is drastically reduced between the layers.

1. INTRODUCTION

Carbon materials have been extensively studied, with idealized structures such as pristine carbon walls and carbon nanotubes (CNTs)^{1–13} as well as complex porous structures.^{14–16} It has been observed that liquids in confinement and at interfaces behave significantly different than in bulk. For example, changes in the packing and the rearrangement dynamics within the liquid can be observed.^{3,11,16–20}

Ionic liquids (ILs), in combination with carbon materials, are of particular interest because they are attractive for the use in various electrochemical devices,^{21–25} especially high-performance electrical double-layer capacitors (EDLCs).^{17,26} ILs consist solely of ions and remain in the liquid state at room temperature. In these electrochemical systems, e.g., an IL in porous carbons, the confinement changes the physical and electrochemical properties, leading to a unique behavior. Furthermore, the capacitance of the electrode is dramatically enhanced when the pore size of the carbon material matches that of the ions.^{15,17,27} The underlying effects of this phenomena are not yet fully understood. Yet, it is known that the adjustment of ILs and nanoporous carbon materials has the potential to significantly improve the performance of EDLCs.^{28,29} Observing the molecular level ordering and analyzing the corresponding characteristics of a liquid inside sub-nanometer confinement is experimentally challenging, and support from theoretical studies are desirable. This in turn requires the availability of simple-to-use and comprehensive

software tools. Our novel software CONAN presented herein allows us to study liquids at the interface of solid structures, which are either walls or pores and which are modeled at an atomistic resolution. CONAN can generate a variety of different carbon and boron nitride structures and combine them with any liquid bulk system in order to create input simulation boxes for simulations. More importantly, it provides a set of analysis tools to evaluate trajectories with respect to the properties of liquids in confinement. Hereby, some functions and analysis options are already known from literature (e.g., the nanostructure build plugin in VMD³⁰), or they have been described in previous works.^{1,3,6,7,14,31–36} Further some novel functions of CONAN are also provided. Since it is desirable to have all the above-described functions available in one software tool, CONAN was developed as a publicly accessible software^{37,38} and is written in Python.³⁹ The program accesses some Python libraries and packages to optimize its performance. MDAnalysis^{40,41} is used to some extent to read trajectories and NumPy,⁴² PANDAS,⁴³ SciPy,⁴⁴ and NETWORKX⁴⁵ are used for faster calculation performances. The MATPLO-

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LIB,⁴⁶ RDKit,⁴⁷ and PRETTYTABLE⁴⁸ packages are used to visualize the results, draw the identified molecules, and tabulate information regarding the investigated system and analysis results, respectively.

This article is structured into three main parts. First, the methodology needed for the production of solid structures, the setting up of a simulation box, and the respective analysis options are presented in Section 2. Second and third, to illustrate exemplary features of our software, a case study of 1-butyl-3-methylimidazolium acetate ($[\text{C}_4\text{C}_1\text{Im}][\text{OAc}]$) within a set of differently sized carbon pores is presented with computational details given in Section 3 and results shown in Section 4.

2. METHODOLOGY

2.1. Structure Generator. The automatic generation of graphene, boron nitride, and related structures is an important step toward being able to study the systems without having to write a software tool each time or manually fixing the structures. Other than CONAN, there are other published plugins and programs that are able to produce a variety of different crystalline structures, such as structures of cellulose,⁵⁰ carbon walls, nanotubes, the corresponding boron nitride analogues³⁰ and more.^{51–53} Programs such as GOPY⁵⁴ and CoNTUB^{55,56} allow for the functionalization of carbon walls and the merging of different CNTs. Still, the combination of a CNT and a graphene sheet has to be done manually so far to obtain structures as in Figure 1g–j—a feature that is now available in CONAN. Furthermore, it is also possible to dope all carbon structures with graphitic nitrogen, as well as to adjust units and bond lengths on the fly while generating the structures.

For all the carbon structures, the default value for the carbon–carbon distance is adjusted to $r_{\text{C-C}} = 142$ pm,⁵⁷ and for the boron nitride structures, the boron–nitrogen distance is set to $r_{\text{B-N}} = 144.6$ pm.⁵⁸ For the production of wall structures (e.g., Figure 1a–d), the desired dimensions are chosen by the user in x - and y -directions. Because it is important for subsequent simulations that periodic boundary conditions (PBC) are fulfilled in all the directions, the size is tuned accordingly. To this end, the program automatically produces structures that satisfy the PBC while being as close as possible to the given input. The box dimensions that need to be selected to fit the PBC are provided by CONAN. Additionally, it is possible to produce multiple, stacked layers. The stacking of the carbon sheets is carried out in a way that by shifting each consecutive layer, an ABA layering is obtained with the default interlayer distance of $r_{\text{L-L}} = 335$ pm.⁵⁷ In the case of the boron nitride analogue, successive layers are not shifted. Instead, the ABA layering is obtained by exchanging the positions of the boron and nitrogen atoms in consecutive layers, while the interlayer distance is set to $r_{\text{L-L}}^{\text{BN}} = 333$ pm.⁵⁸ CNTs and boron nitride nanotubes (Figure 1e,f) can be generated either in armchair or in zigzag conformation, while the length and the diameter of a tube is freely adjustable. The construction of a tube is done in such a way, that the PBCs are satisfied with respect to the direction of orientation. The given input length of the tube is thus adjusted slightly, similar to the one discussed for the carbon layers. The diameter of a (n,n) nanotube (armchair), or $(n,0)$ nanotube (zigzag) is defined via n , which is the number of atoms that build the circumference. Pore structures are constructed by merging walls and a nanotube of choice via two ways. One possibility is to produce

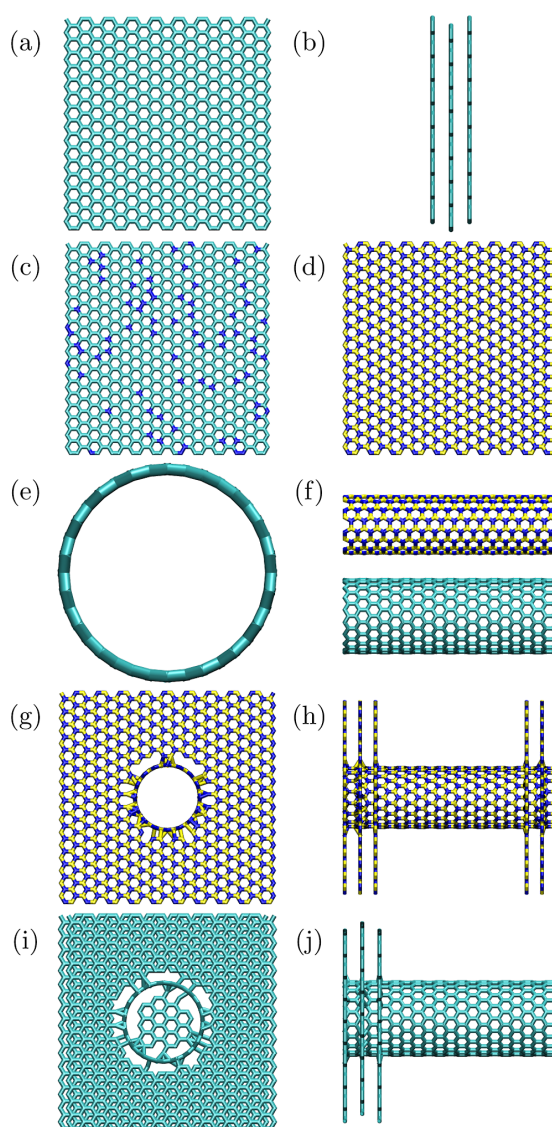


Figure 1. Variety of structures generated using CONAN. All the structures were visualized in bond representation using VMD.^{30,49} (a) Front view of a carbon wall. (b) Side view of multiple carbon layers, stacked in an ABA fashion. (c) Front view of a doped carbon wall with 10% graphitic nitrogen. (d) Front view of a boron nitride wall. (e) Front view of a (18,0) CNT. (f) Side view of a (8,8) boron nitride nanotube and a (18,0) CNT. (g) Front view of a boron nitride pore. (h) Side view of a boron nitride pore. (i) Front view of a closed carbon pore. (j) Side view of a closed carbon pore.

open-pore structures, where walls are attached to each open end of a given tube, while the atoms of the wall which cover openings are discarded (Figure 1g,h). The other option is to attach a wall on one side, while the other open end of the tube is closed (Figure 1i,j). The output file of a structure is given in xyz-format, either in units of Ångström, Bohr, or arbitrary units set by the user. All structures can be combined with any bulk liquids using CONAN to set up the desired system.

2.2. Snapshots of a Given Trajectory. Herein, all snapshots were visualized using the rendering plugin of VMD.^{30,49} With the aid of CONAN, one can cut out individual frames from a given trajectory file. It also allows to identify, characterize, and cut out a pore structure from a given frame adding the nanotubes center point. Extracting only the nanotube from the pore structure (Figure 2) is also

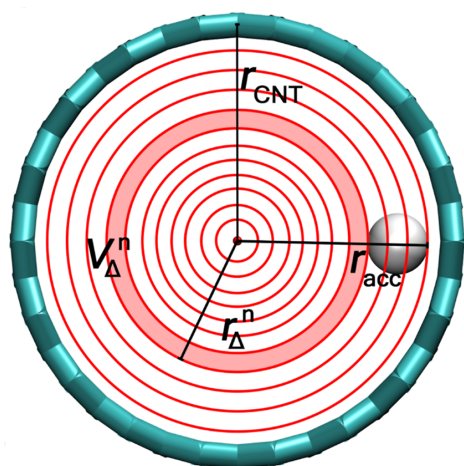


Figure 2. Front view of a (18,0) CNT with its center axis highlighted by the red dot in the center. Each increment describes the area between two red circles, which are the increment borders. The most displaced atom, in this case a hydrogen, is depicted with its van der Waals radius. r_{acc} describes the distance between the center point and the displaced atom, including its van der Waals radius. The figure was visualized using VMD,^{30,49} employing the bond model for the CNT (cyan) and the van der Waals radius model for the hydrogen atom (white).

possible. Additionally, one can extract the nanotube including the liquid that is confined within it, either atom- or molecule-wise. The molecule-wise extraction always considers complete molecules, even those that are only partially within the CNT. In the atom-wise extraction, only those atoms are considered that are within the confinement, without taking bonds into account.

2.3. Trajectory Analysis. There are established programs (such as TRAVIS^{59,60} or MDANALYSIS^{40,41}) that offer features for reading and analyzing trajectories. However, the available analysis options are typically designed for investigating bulk liquids and are often not applicable to anisotropic systems, such as liquids in confined environments. CONAN, on the other hand, is designed for the analysis of trajectories of anisotropic systems consisting of solid and liquid. A tool to identify all molecules and structures is implemented, allowing for an analysis to be performed individually for each molecular species. PBCs are thereby taken into account. In addition, the atoms in each unique molecule are labeled and images of the individual structures are generated. This makes it possible to perform each analysis exclusively for certain atoms of a molecule. The molecule recognition relies on one single frame of the trajectory; this automatically excludes the analysis of chemical reactions. Solid structures within the system are recognized by additionally analyzing a consecutive frame and labeling molecules as solids if they display no movement. The

solid structures therefore have to be kept frozen in position over the course of the simulation.

2.3.1. Radial Density Profiles. CONAN provides the option of computing radial density profiles. Thereby the space around the center axis of a tube is divided into n distinct radial increments as shown in Figure 2 by red circles, up to the wall of the nanotube ($r_{\Delta}^{\text{max}} = r_{\text{CNT}}$). The volume of the n th increment (V_{Δ}^n) is computed by simplifying the tube to be a cylinder, using the length of the CNT (l_{CNT}) as its height and the following equations

$$V_{\text{cyl}}^n = \pi \cdot (r_{\Delta}^n)^2 \cdot l_{\text{CNT}} \quad (1)$$

$$V_{\Delta}^n = V_{\text{cyl}}^n - V_{\text{cyl}}^{n-1} = \pi \cdot l_{\text{CNT}} \cdot ((r_{\Delta}^n)^2 - (r_{\Delta}^{n-1})^2) \quad (2)$$

V_{cyl}^n is the volume of a cylinder of length l_{CNT} and the radius of the n th increment (r_{Δ}^n). V_{cyl}^{n-1} is the volume of the cylinder of the same length and the radius of the next smaller increment r_{Δ}^{n-1} . While scanning the whole trajectory, each atom inside the tube is identified, weighed by either its element mass or its partial charge, and the distance to the center axis (d_{rad}) is calculated. The identified atom is then assigned to the appropriate increment according to $r_{\Delta}^n < d_{\text{rad}} < r_{\Delta}^{n+1}$. After completing the scan, the average mass/charge density of the liquid ($\rho_{\Delta}^n / \rho(q)_{\Delta}^n$) in each increment is determined. This is achieved by dividing the total mass (m_{total}^n)/charge (q_{total}^n) obtained within a specific increment by the volume of that increment and the number of analyzed time steps (TS), using the following equations

$$\rho_{\Delta}^n = \frac{m_{\text{total}}^n}{V_{\Delta}^n \cdot \text{TS}} \quad (3)$$

$$\rho(q)_{\Delta}^n = \frac{q_{\text{total}}^n}{V_{\Delta}^n \cdot \text{TS}} \quad (4)$$

To refine the computed results, they can be normalized by dividing d_{rad} by the radius of the CNT (r_{CNT}). Additionally, mirroring the results is an option provided to illustrate the relationship between the obtained results and the image of a CNT. It is also possible to display the results in the form of a contour plot. An example is given in the Supporting Information, where the radial density of the IL within the confinement is shown for system 18.

2.3.2. Accessible Volume. The accessible volume inside a pore is characterized as the space that can be occupied by the atoms in the confinement. This is determined by scanning each frame of the trajectory to find the atom inside the confinement that is situated furthest with respect to its center axis, that is, closest to the wall of the tube. The accessible radius (r_{acc}) is then calculated by adding either one of the two options, the van der Waals radius⁶¹ or the covalent radius⁶² of the given element to the position of the atom. The accessible volume is computed using eq 1, where r_{Δ}^n is substituted by r_{acc} as the radius. The calculated accessible volume can be subsequently used to compute the axial density profile, which is discussed in the next section. If the analysis is performed only for a particular type of molecule, then the accessible radius will also be calculated only for that species in the system. When conducting this analysis, CONAN also provides the xyz-structure of the CNT, including the most displaced atom, as depicted in Figure 2.

2.3.3. Axial Density Profile. Another option is the calculation of an axial density profile along the entire

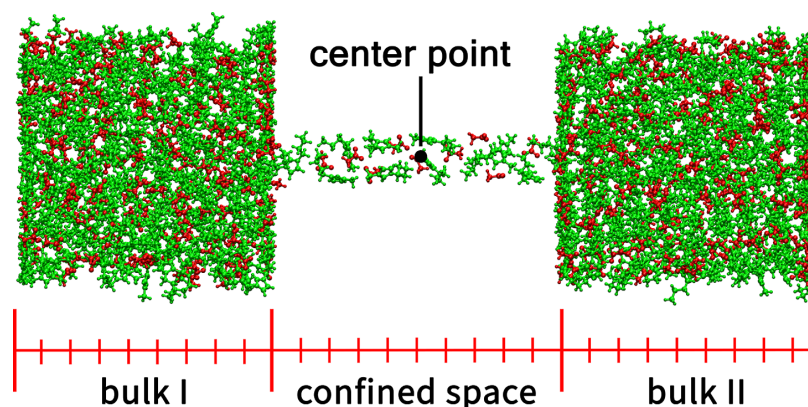


Figure 3. Side view of the simulation box with the incrementation areas depicted. The system was visualized using VMD,^{30,49} using a ball-and-stick model for the ions (anion: red, cation: green). The carbon walls and pores are not depicted.

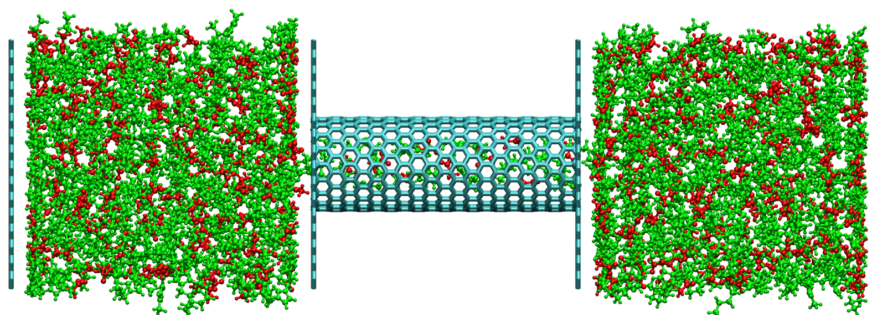


Figure 4. Exemplary system of two bulk phases with a (18,0) CNT in the center. The carbon walls on either sides act as pistons, applying 1 bar of pressure on the liquid. The IL is shown in a ball-and-stick model (anion: red, cation: green), while the carbon structures are shown with a bond model (blue). The system was visualized using VMD.^{30,49}

simulation box, including the bulk phases. To correctly compute the density inside the tube structure, the center axis must be oriented along the z axis in the simulation box. The volume of the CNT is calculated either using the accessible radius r_{acc} which is computed on the fly (Section 2.3.2) during the analysis, or using the CNT's radius r_{CNT} . The radius of the CNT is defined as the distance between a carbon atom of the CNT and the center axis (Figure 2). The number of increments and therefore the respective volumes can be freely adjusted. As the volume of the respective increments in bulk and in confined space differ, multiple regions are defined in the simulation box (Figure 3). The number of increments subdivides the confined space and the bulk phases independently to ensure that an increment does not cover an area that is partially in the bulk and partially in the confined space. The entire trajectory is scanned and all atoms are sorted into a respective increment, weighed by its element mass. All obtained total increment masses are then divided by the number of frames used for the analysis and the respective increment volume to obtain the density profile.

The results can be further processed using CONAN. The binning within the pore can be increased by mirroring the obtained densities at the center point of the pore and calculate the average. In addition, the center of the pore can be set as origin on the axis.

3. COMPUTATIONAL DETAILS

3.1. Simulation Box. The simulation boxes (see Figure 4) were built employing CONAN, combining the previously produced carbon structures (see Section 2.1) with two reservoirs of the IL $[\text{C}_4\text{C}_1\text{Im}][\text{OAc}]$, each comprising 200 ion pairs. When the simulation box is built, a distance criterium assures that the individual pieces which are to be combined (e.g., pore and bulk) are merged with a space of 300 pm in between to avoid initial hotspots. The exact workflow is described in the Supporting Information.

3.2. Molecular Dynamics Simulations. Classical MD simulations of the pure IL $[\text{C}_4\text{C}_1\text{Im}][\text{OAc}]$ were carried out in order to study the behavior of the liquid in confined space of differently sized CNTs. A bulk simulation of the IL serves as a reference system. The IL was modeled using the atomistic CL&P force field,^{63,64} which has the same functional form as the OPLS-aa force field.⁶⁵ Electrostatic interactions are computed using the Ewald summation formalism, while the Lennard–Jones interaction potential was implemented to model interatomic interactions using Lorentz–Berthelot mixing rules up to the cutoff distance set to 12 Å. In case of the carbon structures, the potential parameters of Cole and Klein⁶⁶ were used. Unity charges of 1.0e were chosen for each ion. All simulations were carried out using the Metalwalls code⁶⁷ with the TS set to 1 fs. The bulk simulation was equilibrated for 2 ns in an NpT ensemble at 400 K, using a

cubic box containing 250 ion pairs of the IL before starting the subsequent production run of 10 ns in a canonical ensemble. The obtained density of the reference system $\rho_0 = 0.973 \text{ g/cm}^3$ is in close proximity to the experimental results, with a deviation below 2%.⁶⁸

For the simulations of the IL in confinement, two IL bulk boxes were merged with two carbon walls and different carbon pore structures as described in Section 3.1. Each system comprises a total of 400 ion pairs of the IL, two outer carbon walls, and the respective pore structure composed of a CNT with a carbon wall on each open end. As for the bulk system, a temperature of 400 K was adjusted. All carbon structures were kept rigid in the simulation. After the construction of the system (workflow in Supporting Information) and a preequilibration, the systems were further equilibrated for 1 ns in an $Np(z)T$ ensemble, where PBCs were applied in x - and y -directions, while the carbon walls on each side of the box posed as pistons, acting on the liquid with a force of 1 bar. After a final equilibration phase of 1 ns in a canonical ensemble, the production run of 10 ns was set, saving every 250th TS.

The carbon walls employed in the presented systems consist of 576 atoms and extend up to 3834 pm in x direction and 3935.2 pm in y direction with PBC applied in both. The employed pore structures composed of CNTs of different sizes are listed in Table 1. In case of the pores with a (16,0) CNT,

Table 1. For Each System, the Number of Atoms of the Implemented Pore, the Respective Employed CNT, Its Radius r_{CNT} , Its Length l_{CNT} and Its Volume V_{CNT} are Listed

system	no. atoms	CNT	r_{CNT} [pm]	l_{CNT} [pm]	V_{CNT} [10^6 pm^3]
12	1540	(12,0)	470	4130	2866
14	1600	(14,0)	548	4127	3894
16a	1654	(16,0)	626	4125	5078
16b	1782	(16,0)	626	4978	6128
16c	1974	(16,0)	626	6258	7704
18	1698	(18,0)	705	4123	6438
20	1750	(20,0)	783	4122	7939

three different systems were set up using CNTs of different length to check if the set lengths of approximately 4000 pm in z direction are sufficient to describe the confined space inside a CNT. Additionally, the input Metalwalls files are provided in the Supporting Information for total reproducibility.

4. CASE STUDY: IL INSIDE A PORE

4.1. Radial Density Profiles. **4.1.1. Mass Density.** Radial density profiles were calculated for each system to gain insight into the packing of the IL within differently sized nanopores, depicted in Figure 5. In case of the three systems with pores comprising a (16,0) CNT, only 16a is shown, because differences between the three CNTs of different length are negligible, see Supporting Information. Besides the overall density distributions for the IL (black), the individual contributions from the anion (red) and cation (blue) are depicted with the distances (d_{rad}) being normalized by the radius of the respective CNT (r_{CNT}). The obtained densities ρ are divided by the bulk density of the reference system ρ_0 and mirrored with respect to the CNT center. This is done to visualize the connection between the snapshots of the respective CNTs filled with IL and the obtained density profiles of Figure 5. Unsurprisingly, the larger contribution to

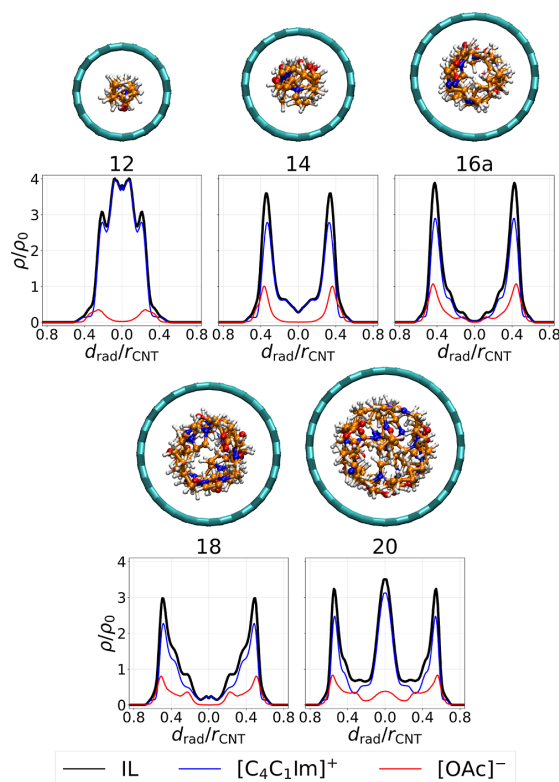


Figure 5. Radial mass density distributions of the IL inside the pores of systems 12, 14, 16a, 18, and 20. The overall density profile is shown in black, the individual contributions from the cation in blue, and from the anion in red. Above the respective plots: CNTs of the respective pores in a bond model (blue), the ions in a ball-and-stick representation (color code: carbon = orange, hydrogen = white, nitrogen = dark blue, oxygen = red). Please note, $1.0 d_{\text{rad}}/r_{\text{CNT}}$ marks the location of the CNT atoms.

the density profiles of the IL comes from the cation, because the molecular mass of the cation is larger compared to that of the acetate. Please note that over the course of the simulation, the number of the cations and anions inside the confinement may vary. Thus, especially for the smallest pore structures, the individual contributions change with respect to the filling of the pore. The shape of the individual ion density profiles is not affected.

In system 12, the $[\text{C}_4\text{C}_1\text{Im}]^+$ density profile shows that the cations are located at the CNTs center axis. The maxima at $|0.075| d_{\text{rad}}/r_{\text{CNT}}$ indicate just a minor shift toward the carbon wall. The nanotube and cation size therefore almost perfectly match, allowing only for minor adjustment in the cations radial position. The second set of maxima at $|0.215| d_{\text{rad}}/r_{\text{CNT}}$ also indicate that the rotational freedom of the cation with respect to the wall of the CNT is hindered and a certain orientation toward the wall of the CNT is preferred. The density profile of the $[\text{OAc}]^-$ anion shows a more pronounced shift toward the carbon interface, with distinct maxima at $|0.255| d_{\text{rad}}/r_{\text{CNT}}$ while the density at the center is close to 0. Due to its smaller size, the anion has greater freedom to move within the confined space, enabling it to minimize the distance to the

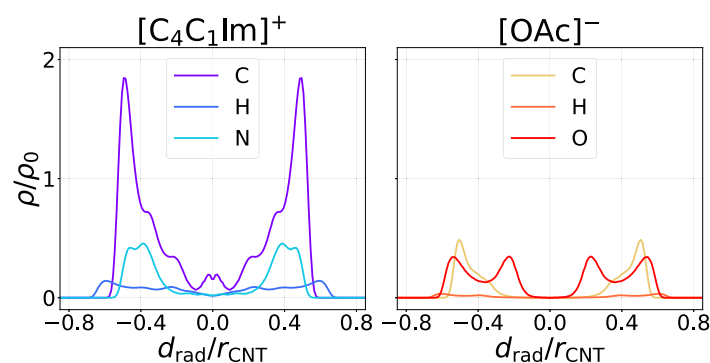


Figure 6. Radial mass density distributions of the elements in the individual ions inside the pore of system 18. In the case of the cation, the distribution for carbon is shown in purple, for hydrogen in blue, and for nitrogen in cyan. For the anion, the distribution for carbon is shown in yellow, for hydrogen in orange, and for oxygen in red.

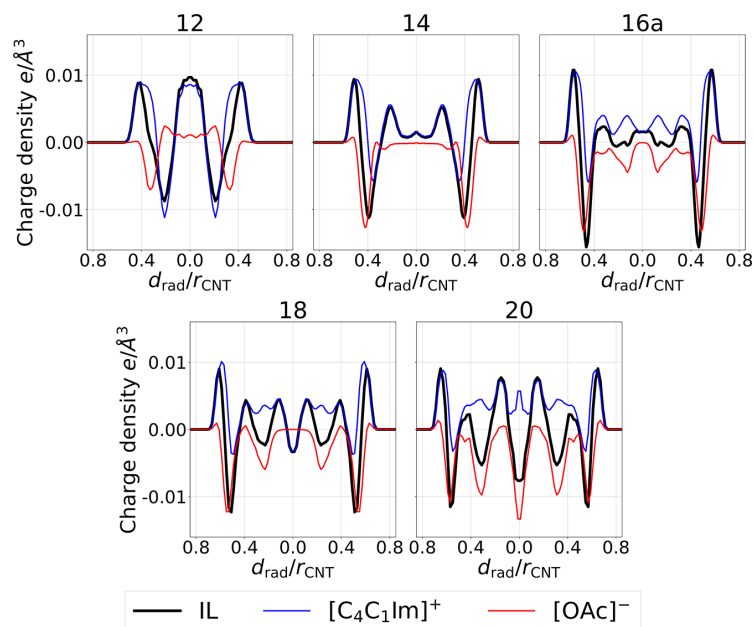


Figure 7. Radial charge density distributions of the IL inside the pores of systems 12, 14, 16a, 18, and 20. The overall density profile is shown in black, the individual contributions from the cation in blue, and from the anion in red.

interface and thereby, maximize its interaction with the CNT wall.

The density in the center of the CNT is quadrupled compared to the bulk density, and quickly decays to values below 10% of the reference density for values $>0.455|d_{\text{rad}}/r_{\text{CNT}}|$, which corresponds to a distance of 214 pm from the center.

With increasing pore size, the packing of the IL within the pore changes to a tubular shape, which was also observed in other studies.^{69,70} A tubular shape means that the ions are shifted from the center to maximize the liquid–wall interactions, resulting in an increased density at the interface, while the density in the center is drastically decreased. The distances between the maxima in the density profiles correspond to the diameter of the tubular IL packing. In case of system 14, this amounts to 378 pm (system 16a: 532

pm; system 18: 698 pm; system 20: 853 pm). Interestingly, in the case of system 18, the tubular arrangement of the IL gets an additional central contribution, that is, an increased density arises around the center axis compared to the smaller systems. This effect is especially present for the $[\text{OAc}]^-$ density profile, where four distinct maxima at $|0.225|$ and $|0.505|d_{\text{rad}}/r_{\text{CNT}}$ are present. This indicates the emergence of a second radial layer inside the confinement. These observations are supported by the largest investigated system, system 20, where an additional maximum in the density profile is present at the center. It indicates the formation of a chain of IL species positioned in the center of the CNT, composing the second radial layer inside the confinement. The species in the center of the pore do not come into direct contact with the pore wall and presumably have different characteristics regarding diffusivity and conformation with regard to their counterparts directly at

the interface. Several previous works showed that species in the center of a given pore diffuse faster compared to species at the interface of the carbon structure.^{16,71,72} In the future, CONAN will also provide the possibility to study dynamic properties, such as diffusion, of the liquid to gain further insight into its behavior in confinement.

For a more precise determination regarding the positioning of the respective ions in the confinement, it is also possible to calculate the contributions of the individual atoms from each molecule. In the example of system 18, Figure 6 shows the individual contributions of the elements of the cation and the anion, respectively.

Based on the individual contributions, it can now be seen that, especially in the case of the cation, the largest $|d_{\text{rad}}/r_{\text{CNT}}|$ values in the density distribution of the respective ions can be attributed to the hydrogen atoms. In addition, the comparison between the distribution of the carbon atoms and that of the oxygen atoms from the anion is interesting. While the density profile of the oxygen splits and marks two preferred positions (0.25 and 0.55 $|d_{\text{rad}}/r_{\text{CNT}}|$) from the central axis, this is not the case for carbon with one maximum at 0.5 $|d_{\text{rad}}/r_{\text{CNT}}|$. It therefore becomes clear that there are not yet two different layers in system 18. The double peak of the oxygen distribution can therefore be explained by the fact that the anion is no longer oriented exclusively toward the pore wall, but that the carboxylate group also assumes a conformation perpendicular to the pore wall, in which an oxygen atom points toward the center axis.

4.1.2. Charge Density. The systems presented here have been modeled with standard force fields, therefore each atom of the ions has been assigned a fixed partial charge. The charges attributed to each atom are listed in Table S1 in the Supporting Information. In the case of the acetate anion, the oxygen atoms in particular are partially negatively charged, whereas the hydrogen atoms are partially positively charged. The carbon atom of the carboxylate group also carries a positive partial charge. In the cation, the positive charge is localized on the nitrogen and hydrogen atoms, while the carbon atoms bear partial negative charges. The charge density distribution functions therefore contain information about the accumulation of charges.

Radial charge density profiles were calculated for each system and are depicted in Figure 7. The charge density for the largest respective $|d_{\text{rad}}/r_{\text{CNT}}|$ values is positive for all systems, highlighting that the atoms closest to the pore walls are hydrogen atoms. Thereby, the curves of the IL and the cation are almost on top of each other, indicating the predominant contribution at these maximum distances stem from the cation. In the case of the anion, the charge density is also positive for the largest $|d_{\text{rad}}/r_{\text{CNT}}|$ values, which can be attributed to the hydrogen atoms of the methyl group. Nevertheless, the charge density drops to negative values for smaller $|d_{\text{rad}}/r_{\text{CNT}}|$ values, which can be assigned to the oxygen atoms of the carbonyl group and thus describes their positions within the pore. Therefore, the preferred position of the anion in the smallest systems, as already described in the radial density profile, is close to the pore wall and offset from the pore center. For increasing pore diameters, a second radial layer of the anion is formed within the confinement (system 16a and 18) and in system 20, even a third layer is observed, exactly in the center of the pore. It is also striking that the radial charge density distribution of each system behaves in an oscillating manner, with the outermost values always being positive as previously

stated. The number of oscillations thereby depends on the size of the pore, with the ordering becoming increasingly more complex for larger radii. The number of oscillations exceeds the number of anions and cations arranged side by side, which means that the orientation of the individual ions and their partial charges causes and amplifies these oscillating charge distributions. This assumption is further supported when looking at the charge densities of the individual ions. Here, too, the alternating course of the charge density can be clearly seen, which indicates a certain preferred positioning of the ions within the confined space.

4.2. Accessible Volume. The accessible radius and volume of each pore were computed for all systems and are listed in Table 2. For all investigated pores, the accessible

Table 2. The Obtained Accessible Radii r_{acc} , Calculated Employing the Respective Elements van der Waals Radii, and the Deviation Δr , Which is Defined as $1 - r_{\text{acc}}/r_{\text{CNT}}$ and Describes the Percentage the Accessible Radius is Smaller Compared to r_{CNT} ^a are listed

system	r_{acc} [pm]	Δr [%]	V_{acc} [10 ⁶ pm ³]	ΔV [%]	ρ_{acc} [g/cm ³]	$\Delta\rho$ [%]
12	380	19.15	1874	34.6	0.394	59.5
14	462	15.54	2767	28.9	0.516	47.0
16a	539	13.90	3765	25.9	0.647	33.5
16b	540	13.85	4560	25.6	0.643	33.9
16c	547	12.65	5882	23.7	0.657	32.5
18	617	12.36	4931	23.3	0.644	33.8
20	702	10.43	6382	19.6	0.692	28.9

^aThe accessible volumes V_{acc} and the densities of the IL ρ_{acc} are also listed (see Figure 2). ΔV describes the percentage by which the volume is reduced, comparing V_{acc} to V_{CNT} ($1 - V_{\text{acc}}/V_{\text{CNT}}$). $\Delta\rho$ is defined by $1 - \rho_{\text{acc}}/\rho_0$ ($\rho_0 = 0.973$ g/cm³) and describes the percentage to which the density is decreased with respect to the reference bulk system.

radius r_{acc} is 80–90 pm smaller than the respective r_{CNT} . From visual observation of the most displaced atoms, it becomes apparent that the identified atoms are embedded in a hexagon of the carbons honeycomb structure, minimizing the ion–wall distance (see Figure S4 in the Supporting Information, showing the most displaced atom in system 14). For the pores in systems 16a–c, the obtained accessible radii differ slightly with r_{acc} being 8 pm larger in system 16c, where the pore is composed of the longest CNT, compared to system 16a with the shortest CNT. The deviation arises from the increased volume for the longer pore structures, leading to a higher amount of species in confinement and more sampling. Nonetheless, the difference is below 1.5%, therefore deviations are minor. $\Delta\rho$ is defined by $1 - \rho_{\text{acc}}/\rho_0$ and describes the percentage of the density that is reduced inside the respective confinement (Table 2). The results show a large decrease in density within all CNTs, with the effect becoming more drastic for smaller radii. In the (12,0) CNT, a reduction of the density of about 60% is achieved. This drops to about 30% for the larger CNTs studied, which is still significant. To evaluate the results, it should be mentioned that in the two smallest systems, anion and cation cannot exchange places, because the confinement restricts it. Thus, parts of the density decrease are due to the fact that ions of the same type can be adjacent inside the confinement, repelling each other and creating small gaps in between them. The arrangement of the ions within the CNTs is also described in detail in the next chapter. For the

systems 16a–c, 18, and 20, the rearrangement of the ions within the confinement is possible, but nevertheless significant reductions in density are observed. In the comparison of the three systems, 16a–c, it is also clear that despite better sampling for the longer pores, $\Delta\rho$ changes only slightly, with a maximum difference of 1.4%.

The occupancy of a given pore describes the proportion of the volume of the CNT (V_{CNT}) that can be accessed by the IL and is defined as $V_{\text{acc}}/V_{\text{CNT}}$. The results for the different systems, including systems 16b and 16c are plotted against the accessible radius r_{acc} of the respective CNT and are depicted in Figure 8. It is apparent that the occupancy increases steadily

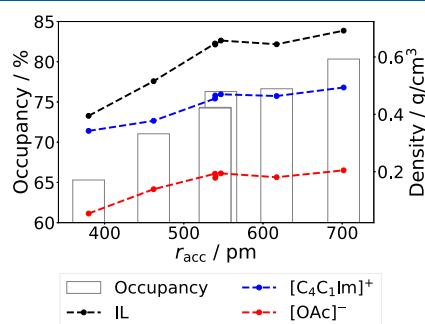


Figure 8. Occupancies ($V_{\text{acc}}/V_{\text{CNT}}$) and average densities of the IL inside the pore structures of different size, plotted against the accessible radius r_{acc} . The occupancies are shown as bars. The overall densities of the IL are depicted as a black graph, the contribution from the cation in blue, and from the anion in red.

for larger tube radii and highlights that the choice of the radius for the computation of the pore volume (r_{acc} or r_{CNT}) is crucial when calculating the density, especially for the smallest CNTs. Figure 8 also illustrates the computed average densities of the confined IL for CNTs of varying accessible radii. Smaller tube radii are accompanied by a significant reduction in average density, particularly for the two smallest pores. It is important to emphasize here again, that rearrangement of ions within these smallest pores is not possible, resulting in small cavities within the confined space. Therefore, the arrangement and filling of the pore are both critical points to consider when doing such an analysis.

4.3. Axial Density Profile. Besides the radial densities of the IL inside a pore structure, axial density profiles of the liquid were computed along the pore axis for all systems (Figure 9). A comparison between the systems 16a–c is provided in the Supporting Information. In every system, between roughly |2100| and |6500| pm, the two bulk reservoirs of the IL show the typical density oscillations described in literature.^{1,7,32} In the center of the respective IL reservoirs (|4300| pm), the oscillation of the density profile is hardly to no longer present, which shows that the imposed structuring of the IL at the interface has little influence on the structure in the respective reservoirs center. The density profile of system 12 shows that the center of the pore is filled with an anion surrounded by two cations. The mobility of the ions in the confinement appears to be small, since the density profile indicates defined areas in which the respective ion permanently resides. The open ends of the pore are occupied by additional cations that reside at a distance from the cations inside the pore. Gaps are present in between the adjacent cations, indicated by the minima in the

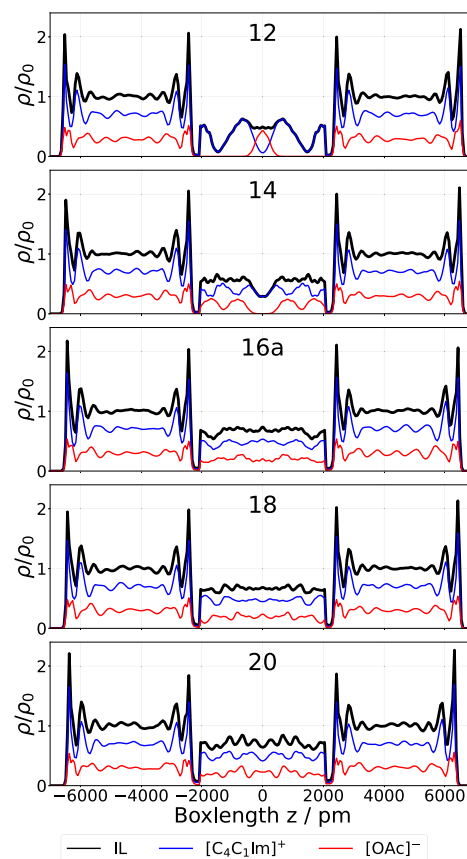


Figure 9. Axial density profiles of the liquid in systems 12, 14, 16a, 18, and 20 along the z -axis of the respective simulation boxes. The overall density of the IL is shown in black, the individual contributions from the cation in blue, and from the anion in red.

density plot at around |1500| pm. This shows that automatic filling of the smallest pores (systems 12 and 14) during the simulation does not necessarily lead to an alternating packing of anions and cations within the confinement, because the rearrangement of the species is not possible. If the alternating arrangement is to be enforced, it is recommended to fill a pore from only one side, or do it manually.

For the IL confined in the (14,0) CNT, the alternating arrangement of the different species within the pore is also clearly visible from the respective density profiles. But with two cations being adjacent in the center of the pore. Comparable to system 12, this also results in a gap within the pore between the ions of the same species, indicated by the reduced density of the individual ions at 0 pm, see Figure 9. Regarding the density profile of system 16a and supported by the visual inspection of the corresponding trajectory, it is apparent that the rearrangement of ions within the confined space is possible for pores of these and larger sizes. The oscillation of the density profiles within the confinement is also significantly weakened. This applies to the overall density profile of the IL as well as to the contributions of the individual species, suggesting a different ordering and movement of the species within the confinement. The cross-section inside the CNT is thereby sufficiently large to allow for an anion and a cation to

reside next to each other. Very similar results were also obtained for system 18. As shown in the analysis on radial densities, the IL has a very similar tubular packing within the pore. Again, the oscillating density profile is apparent in the (20,0) CNT regarding the IL and the individual contributions of the ions. This can be attributed to the presence of an additional central channel within the pore (as depicted in Figure 5), characterized by an alternating arrangement of anions and cations.

5. CONCLUSIONS

We presented a novel program for the purpose of investigating liquids in confinement. To showcase the options CONAN provides, a case study of 1-butyl-3-methylimidazolium acetate [C_4C_1Im][OAc] in well-defined pores of different size was conducted. Throughout this work, a workflow is described how to employ CONAN regarding the production of structures, the setup of solid–liquid systems of interest and the implemented analysis tools provided when studying liquids in confinement. Among other things, the program offers the possibility to calculate radial mass and charge densities of a fluid within nanotubes. In addition, the accessible volume of a tube can be determined, and an axial density can be calculated along a simulation box. Based on the generated data, further conclusions can be drawn, such as the calculation of the occupancy within a tube and the average density of a liquid in the confinement.

The case study of the IL shows that the liquid undergoes large changes in confinement compared to the bulk, with the change in density and packing being highly dependent on the pore size. When pore and ion size match, the ionic species align in a chain-like arrangement inside the pore, where the exchange of position between species is not possible. The structure of the IL changes to a tubular arrangement for larger pore sizes. The density of the IL is thereby increased at the IL–carbon interface, where the ionic species are shifted from the center to the carbon wall. This is accompanied by a decrease in density in the center of the pore, at least until the pore size is sufficiently large to allow for a second radial layer inside the confinement. It was also shown, that the overall density of the IL inside the confined structures is decreased, with the effect diminishing for increasing pore sizes.

In the future, the program will be extended to provide additional options to study MD trajectories. It is planned to extend the program with respect to the analysis of the coordination environment of a confined liquid and the calculation of diffusion properties. It is also planned to extend the structure building tool to other structures and materials.

■ ASSOCIATED CONTENT

Data Availability Statement

The code of METALWALLS is open source and freely available. The same is valid for CONAN, with the program being provided on our GitHub channel including example trajectories.

■ Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.jcim.3c01075>.

Example radial density contour plot of system 18, partial charges of the applied force field, exemplary figures of the most displaced atom from the accessible volume analysis of system 14, radial charge and mass density

profiles of systems 16a–c, and axial mass density profiles of systems 16a–c (PDF)

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Notes

The authors declare no competing financial interest.

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Appendix: Coordination Behavior of a Confined Ionic Liquid in Carbon Nanotubes from Molecular Dynamics Simulations

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Own contributions

- Running of MD simulations
- Participating in analyzing the trajectories.
- Writing the introduction, method section and parts of the discussion.

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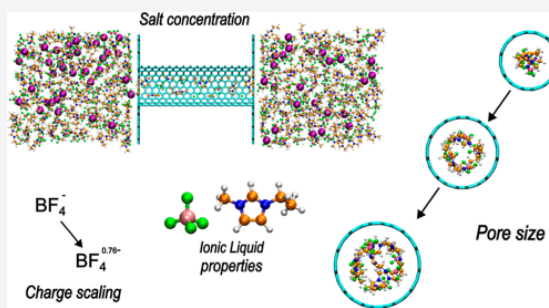
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ABSTRACT: To understand the behavior of ionic liquids (ILs) at carbon material, i.e., carbon nanotube (CNT)-containing pores, we simulated different systems and analyzed their structural in particular their coordination behavior as well as their velocity distribution. The extension of our analysis tool CONAN presented here allowed us to study the coordination behavior as a function of the distance to the carbon material. Our systems were composed of three different CNTs combined with either the neat IL 1-ethyl-3-methylimidazolium tetrafluoroborate or with their NaBF_4 salt mixtures. We investigated the impact of the force field charge scaling. As previously detected, the neat IL assumed radial layers within the confinement, with the radial density distribution depending strongly on the pore size. For the salt mixtures, the sodium cation remained in the bulk and was observed only once inside a tube. In all systems, the ions showed an overall decreased coordination behavior for regions in the bulk phase close to the carbon pore and within the confinement. The coordination number was always reduced with scaled charges. For charge scaling, higher dynamics was observed also in confinement. Interestingly, the average velocity of the atoms near the surface inside the confined space was higher than that in the center of the pore.



1 INTRODUCTION

Liquids at surfaces and in confined spaces behave significantly differently from their bulk phase, with the resulting physical properties being highly dependent on the type of liquid and solid.^{1–7} This is particularly important for energy devices where the liquid is in contact with an electrode. At the molecular level, these property changes result from liquid–electrode interactions and an imposed change in liquid–liquid interactions near the surface.^{5,6} Water,^{8–10} water-based electrolytes,^{11–13} ionic liquids (ILs),^{6,14–21} and other electrolytes^{22–24} are often studied in combination with solids such as carbon materials,^{2,9,15,16,22,23,25,26} transition-metal oxides,¹¹ metal–organic frameworks,^{20,27,28} or metal surfaces.^{12,29} ILs have several favorable properties as electrolyte materials, such as low volatility, a wide electrochemical window, and high thermal and chemical stability. However, the viscosities of most ILs are high at room temperature, accompanied by a slow diffusion of ions, and thus neat ILs usually have a relatively low ionic conductivity at ambient conditions.⁷ There are examples, where adding salt in high concentration leads to better ion transport despite the fact of a possible higher associated viscosity.^{30–33}

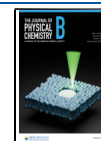
The study of the properties of such liquids at liquid–solid interfaces is of particular interest in the field of electrochemistry, with the aim of developing new types of energy storage systems and enhancing the desired properties by combining liquids and solids in a sophisticated way. For example, new electric double layer capacitors (EDLCs)^{25,34,35} with a higher energy density than conventional capacitors are sought, which are composed of carbon materials as electrodes in combination with ILs. Energy storage in these systems is based on the electrostatic attraction of charged particles, which allows rapid charging and discharging, but at the cost of a low energy density compared to conventional batteries.³⁶ The key to their energy storage capability is the formation of a Helmholtz double layer,³⁷ a concept central to describing how EDLCs work. When a voltage is applied, a double layer of charges forms at the interface between the electrode material

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and the electrolyte. This bilayer consists of two parts: one layer forms on the surface of the electrode, which carries an excess charge due to the applied voltage. The other one is the layer of ions adsorbed on the electrode surface (Helmholtz layer), which compensates for the excess charge. The Gouy–Chapman^{38,39} theory extends on this double layer concept. Instead of a distinct layer in the electrolyte, it proposes the existence of a diffuse layer that extends beyond a molecular layer and penetrates deeper into the bulk phase. The associated decrease in the potential is described as an exponential decay. Further developments to this effect were proposed by Stern⁴⁰ and later by Grahame,⁴¹ who proposed a combination of both theories. In the case of ILs and IL salt mixtures as electrolytes, there is an additional effect called overscreening.^{36,42–45} As the excess charge of the electrode is overcompensated by the first layer in the electrolyte, a second layer of counterions is formed behind the first layer. This resorting of the IL is not limited to two layers and can extend a few nm into the bulk at strong applied fields.³⁶

For the electrodes of EDLCs, porous carbon material is of particular interest because it provides a large surface area and thus a large interface with the liquid. The liquid also enters the porous carbon network, where the effect of the confined space on the properties of the liquid is highly dependent on the pore size in which it resides. It has been observed that the capacitance is greatly increased for systems where the pore size of the carbon electrode matches the size of the ions.^{18,26,46,47} Understanding the underlying effect of this phenomenon is key to the improvement of such EDLCs. However, the experimental observation of the molecular arrangement in such systems, especially within confinement, is challenging, and their computational modeling contributes to the knowledge of the governing effects at the molecular level.

The first step is to understand the behavior of ILs in a confined space without an applied field to the necessary depth to be able to draw precise conclusions for the next steps. New tools are helpful to analyze such anisotropic liquid–solid systems. CONAN,^{48–50} a program developed by our group that allows the generation of carbon structures, the setup of the simulation box, and the analysis of the simulation trajectory data, was created for this purpose. Besides the established analysis methods from our previous publication,⁴⁸ new features have been added to the code to analyze the coordination and velocity of ions in the liquid with respect to their distance from the solid structure.

In this work, we study the effect of confinement on the coordination behavior and dynamics of neat $[\text{C}_2\text{C}_1\text{Im}][\text{BF}_4]$ and its salt mixture with 25 mol % NaBF_4 in pores of three different sizes using classical molecular dynamics simulations at an atomistic resolution. In the case of the electrode material, a carbon pore is constructed by using a carbon nanotube (CNT) and adding a graphene sheet to each open end of the CNT. The pores were constructed using CONAN. The computational details together with the implementation of the coordination number (CN) and the velocity analyses are provided in Section 2 of this work. The results are presented and discussed in Section 3 with concluding remarks in Section 4.

2 METHODS

2.1 Computational Details All classical MD simulations of the neat IL $[\text{C}_2\text{C}_1\text{Im}][\text{BF}_4]$ and the IL salt mixture (25 molar fraction of NaBF_4) were conducted with the LAMMPS

program package⁵¹ using the OPLS-AA force field.^{52,53} The specific atomic partial charges are listed in Table S2 in the Supporting Information. For the $[\text{C}_2\text{C}_1\text{Im}]^+$ -cation and the BF_4^- -anion the refined CL&P parameters^{54,55} for ILs were used, while the parameters of Cole & Klein were utilized for the carbon pore.⁵⁶ Both the construction of the simulation boxes and the equilibration procedure are discussed in the Supporting Information. All simulations were carried out at a temperature of 350 K in a canonical ensemble, using a time step of 1 fs.

The Lennard-Jones potential and pairwise Coulombic interactions were computed up to a distance of 12 Å, with tail corrections applied to the Coulombic part for larger distances. A particle–particle–particle-mesh solver for long-range interactions up to an accuracy of 1.0×10^{-5} kcal mol⁻¹ Å⁻¹ was implemented.

Each system consists of a bulk phase containing 512 ion pairs and a carbon pore structure generated using CONAN.⁴⁸ The structures are pristine and consist of a CNT with a radius in the nanometer regime and carbon walls attached to both open ends. The studied pores were constructed with CNTs in an armchair configuration of three different sizes. The radius of the respective pores is defined by the number of carbon rings n building the circumference of (n, n) CNTs and is listed in Table 1 together with the pores radii (r_{CNT}), length (l_{CNT}), and the number of carbon atoms each pore is composed of.

Table 1. Features of the Investigated Pores

notation	(n, n)	$N_{\text{atoms}}^{\text{pore}}$	$N_{\text{atoms}}^{\text{CNT}}$	r_{CNT}	l_{CNT}
8	(8, 8)	1548	544	5.44	40.55
10	(10, 10)	1668	680	6.79	40.56
12	(12, 12)	1752	816	8.15	40.57

^a $N_{\text{atoms}}^{\text{pore}}$: total number of carbon atoms of each pore; (n, n) : used CNT; $N_{\text{atoms}}^{\text{CNT}}$: number of carbon atoms including the radius of the respective CNT: r_{CNT} and the length l_{CNT} , both given in Å.

The simulation box dimensions in x and y directions (x : 38.34 Å; y : 39.352 Å) are adjusted to fit the carbon sheets, modeling an infinite carbon surface through periodic boundary conditions. The carbon pore is kept rigid over the whole production run. With the modeled systems, detailed in Table 2, three CNTs of different size are investigated, together with either the neat IL (N) or IL salt mixture (S). For instance, N_{10}

Table 2. Notation and Composition of the Investigated Systems; mol % : Salt Mole Fraction; Pore: the Used Pore; l_{box}^z : Box Length in z -Direction of the Box

notation	mol	pore	$l_{\text{box}}^z/\text{Å}$
N_8	0	8	137.266
N_{10}	0	10	135.955
N_{12}	0	12	135.041
S_8	25	8	121.820
S_{10}	25	10	120.475
S_{12}	25	12	119.957
N_8^{sc}	0	8	145.762
$\text{N}_{10}^{\text{sc}}$	0	10	144.452
$\text{N}_{12}^{\text{sc}}$	0	12	144.520
S_8^{sc}	25	8	130.257
$\text{S}_{10}^{\text{sc}}$	25	10	128.981
$\text{S}_{12}^{\text{sc}}$	25	12	128.919

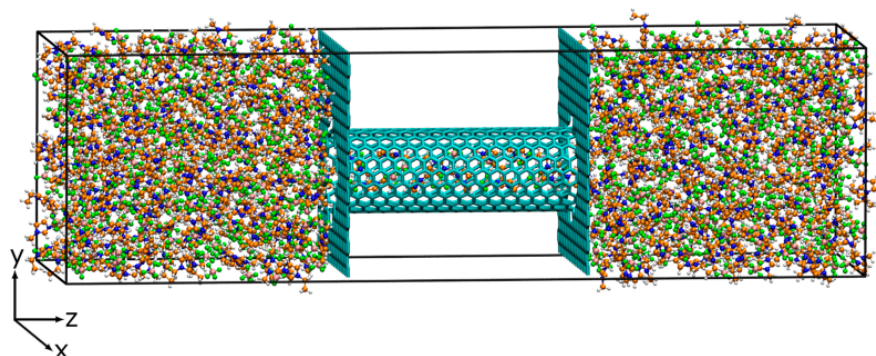


Figure 1. Ball-and-stick illustration of system N_{10} . Color code for the atoms; carbon: orange; nitrogen: blue; hydrogen: white; boron: pink; and fluorine: green. Carbon material: cyan and in a bond depiction; all was visualized using VMD.^{57,58}

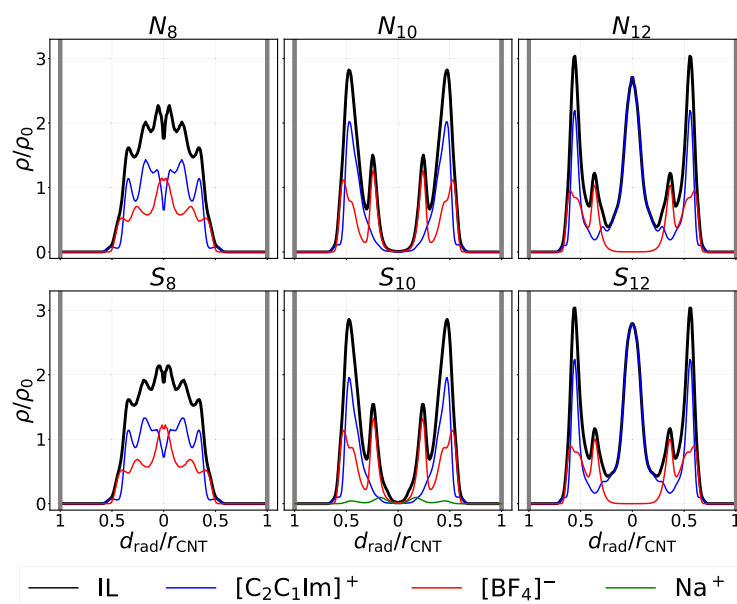


Figure 2. Radial mass density profiles for N_8 to N_{12} (upper panels) and S_8 to S_{12} (lower panels) of total and ionic contribution. Black: complete IL; blue: $[C_2C_1Im]^+$ cation; red: $[BF_4]^-$ anion; green: Na^+ cation (only visible in case of S_{10}). The vertical lines represent the pore wall.

(Figure 1) is a system that contains neat IL and features pore 10. The mixtures, e.g., S_8 , were set up by exchanging 25% of the $[C_2C_1Im]^+$ cations by Na^+ to obtain the desired 25% molar fraction of $NaBF_4$. This approach investigates the effect of the salt concentration on system properties.

In the first set of simulations, unit charges were used for the individual ions. In a second set, charges were scaled according to Stuchebrukhov and Leontyev.⁵⁹ The scaling factor is defined as the square root of the inverse of the dielectric constant ϵ_{el} . With the dielectric constant of the IL of 1.742,⁶⁰ the scaling factor of 0.76 was derived.

$$q^{sc} = \frac{q}{\sqrt{\epsilon_{el}}} = \frac{q}{\sqrt{1.742}} \approx 0.76 \cdot q \quad (1)$$

All systems with scaled charges are denoted by sc. During the first production run of the simulation (50 ns), every 1000th time step was saved. A second production run (10 ns) after the

first, saving every 250th time step, was run to compute the velocity distributions.

In order to explore the free energy landscape of a Na^+ -ion in our systems, we performed umbrella sampling for all of the pores. For this purpose, we set a radial spring potential that pulls a Na^+ -ion in 0.25 Å steps from an initial distance of 40 Å to the center of mass of the pore. The spring constant was set to 10 kcal mol⁻¹ Å⁻². After the production runs described previously, leaving all other modeling parameters unchanged, the Na^+ -ion was moved to the starting position over 0.25 ns. The start positions were determined by using the x and y coordinates of the end position (COM of a pore) and adding 40 Å to the z -coordinate. With the described approach of the radial spring potential in combination with the initial position, the energy profile depends mainly on the z -coordinate, but especially for the inside of the pore, also allows the cation to assume a radial position that is more favorable than on the central axis of the pore. For each increment studied, the Na^+ -

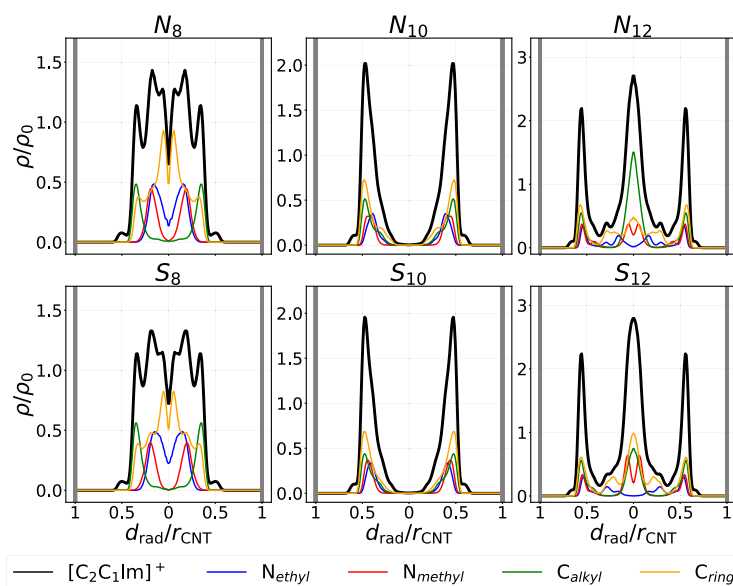


Figure 3. Radial mass density profiles for N_8 to N_{12} (upper panels) and S_8 to S_{12} (lower panels) of total $[C_2C_1Im]^+$ cation and its atomic contributions. Blue: N_{ethyl} ; red: N_{methyl} ; green: carbon atoms of ethyl and methyl group; orange: carbon atoms of the imidazolium ring. The vertical lines represent the pore wall.

ion was positioned for a time of 0.1 ns before every 100th time step was stored for subsequent analysis for a further 0.1 ns. This results in 1000 data points for each of the 161 positions studied. The free energy curves generated from the collected data were obtained using the WHAM software.⁶¹

2.2 CN Analysis To access the CN in confined space, a different approach from the number integral of the radial distribution function must be chosen because the immediate environment of a molecule depends on its position with respect to the porous carbon. Here, CN is obtained in the following way. First, a three-dimensional grid is adjusted to the simulation box with the incrementation chosen by the user. Next, the CN is computed by calculating the distances between the centers of mass of all molecules and counting how many particles are within a user-specified coordination distance. A distinction between the different types of molecules is made by default. The results are stored in Gaussian cube file format and can be visualized by appropriate visualization programs (VMD,^{57,58} PyMol⁶²). CONAN also provides the option to calculate the CN with respect to the distance to the nearest surface. This is done separately for molecules in the bulk and in the pore. The results are plotted as a heatmap. Averaging over the entire bulk or confined space is also an option.

To validate our approach, the CNs of the anions around the cations $[C_2C_1Im]^+$ in systems N_8 – N_{12} and S_8 – S_{12} were calculated for a selected bulk part and compared to the number integral. The number integral was calculated with Travis.^{63,64} The results are shown in the Supporting Information in Figure S13. It can be seen that both approaches yield the same results. Additionally, a short description for the usage of the new module is provided in the Supporting Information.

2.3 Velocity Distributions Because charge scaling usually affects the dynamical behavior more than the structural one,⁶⁵ we implemented the option to analyze the velocity of species in the pore structures into CONAN in the form of

radial velocity distributions. Similarly, as for the radial density profiles,⁴⁸ the space around the center axis of the pore is divided into distinct radial increments. The velocity of each atom within the pore is calculated and sorted into the according increments. After the entire trajectory is processed, the velocities assigned are averaged by taking the sum of all entries and dividing by the total number of entries for each grid point.

3 RESULTS AND DISCUSSION

3.1 Radial Density Analysis **3.1.1 Mass Density** Radial mass density profiles (Figure 2) reflect the preferential radial positions of each species and give insights into the arrangement of the IL perpendicular to the pore axis. The x -axis distances are normalized in that radial distances (d_{rad}) are divided by the radius of the CNT (r_{CNT}), and the values at the y -axis are densities normalized to the reference density ρ_0 ($\rho_0(352\text{ K}) = 1.244\text{ kg m}^{-3}$).⁶⁶ We show density profiles of the individual ions together with the overall density profile (black curve in Figure 2). Further, for the $[C_2C_1Im]^+$ cation, the density profiles of specific atoms are plotted in Figure 3.

The $[C_2C_1Im]^+$ cation contributes most to the overall density profile because it possesses the highest molecular mass. For the smallest pore N_8 , all ions are mainly located near the center axis with three distinct maxima (see the upper left panel in Figure 2). The proximity to the center suggests that the size of the ions roughly matches the size of the CNT, leading to very limited space for perpendicular movements to the central axis. The density at the center axis is roughly twice as large as in the bulk but decays quickly and reaches 0 at $0.6\ d_{rad}/r_{CNT}$. While the cation density profile (blue curve) consists of two maxima, one at $0.3\ d_{rad}/r_{CNT}$ and one at $0.2\ d_{rad}/r_{CNT}$, the anion density profile also exhibits three maxima. One is located at the center, one at $0.3\ d_{rad}/r_{CNT}$, and one at $0.4\ d_{rad}/r_{CNT}$. Such close-lying maxima indicate that the rotation of the

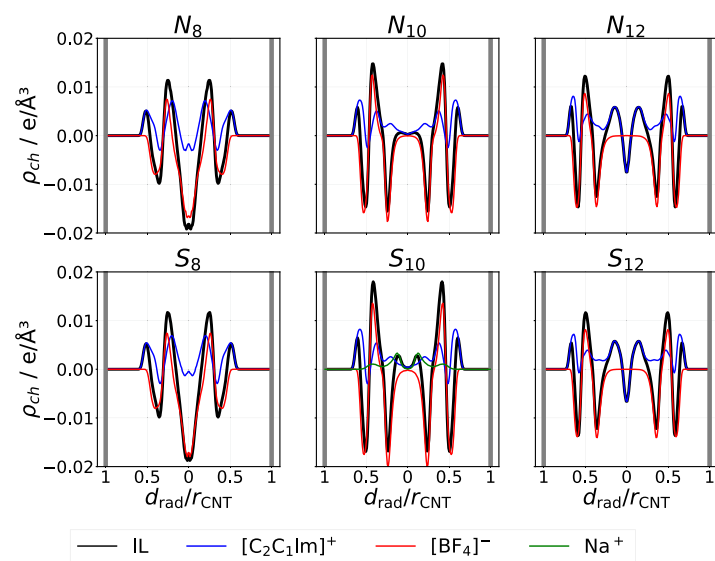


Figure 4. Radial charge density profiles of the systems N_8 – N_{12} (above) and S_8 – S_{12} (below). Black: combined charge density profile; red: BF_4^- anions; blue: $[C_2C_1Im]^+$ cations. For system S_{10} also, a profile for the Na^+ ions is given in green. The vertical lines represent the pore wall.

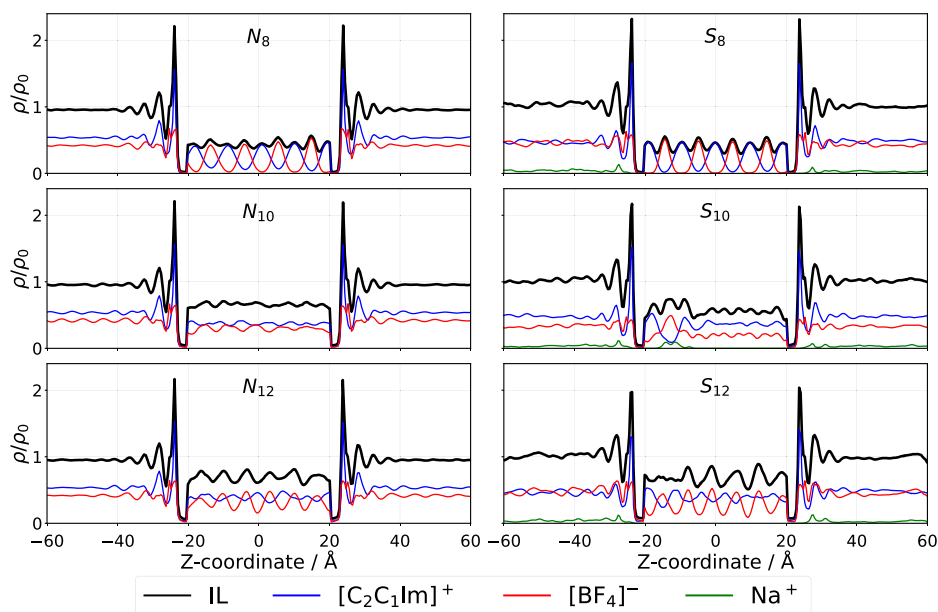


Figure 5. Axial mass density profiles of the systems N_8 – N_{12} and S_8 – S_{12} . A combined charge density profile (black curve) is shown alongside a profile for BF_4^- (red curve) and $[C_2C_1Im]^+$ (blue curve). The centers of the pore structures are placed at 0 Å. The bulk is cut off at z distances larger than 60 Å from the center to make the comparison easier.

ions is hindered and that a specific orientation toward the walls is preferred. This is also supported by the mass density profiles of the cation, see Figure 3, where the carbon atoms in the ring and the alkyl groups show well-defined maxima. A similar behavior was found in an earlier study of the IL $[C_4C_1Im][OAc]$ in a (12,0) CNT.⁴⁸

In contrast, the ions within the pore of system N_{10} form a tubular void around the central axis. The cations occupy one

specific radial position at $0.5 d_{rad}/r_{CNT}$, while the anions can be found in two different radial positions ($0.2 d_{rad}/r_{CNT}$ and $0.5 d_{rad}/r_{CNT}$). Due to fewer local maxima, it can be assumed that both anions and cations have significantly more rotational freedom compared to those in system N_8 .

In N_{12} , two distinct layers are formed. One layer is present at the center axis and exclusively consists of cations. These cations are arranged in a chain along the center axis. The

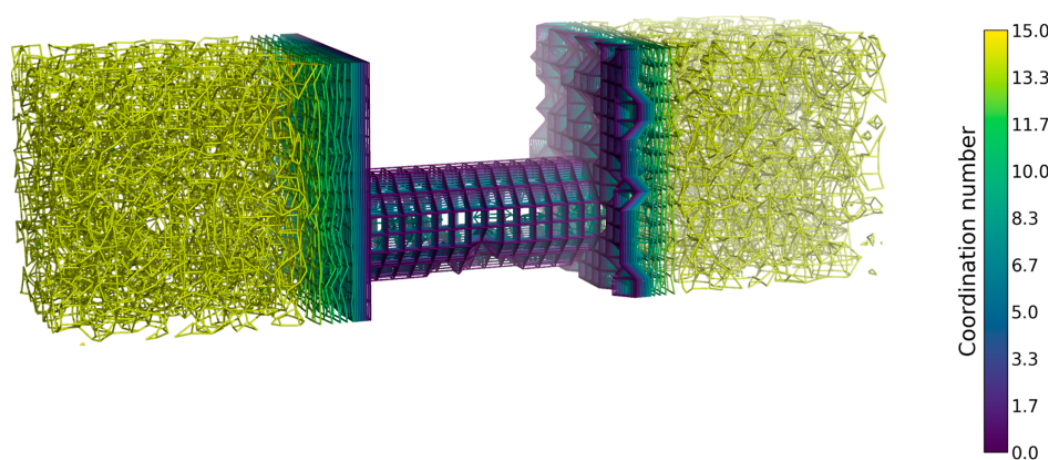


Figure 6. Three-dimensional contour plot of system N_{12} . The CN at a distance of 10 Å with the cation as reference molecule and the anion as observable is depicted in color code. For the analysis, a $15 \times 15 \times 50$ ($x \times y \times z$) grid was adjusted to the simulation box. The 3-dimensional contour plot was generated using PyMol.⁶²

second layer shows a maximum at $0.6 d_{\text{rad}}/r_{\text{CNT}}$ and forms a tubular shape. Both cations and anions contribute to the outer layer. However, the anions in this layer are slightly closer to the carbon wall with a radial density maximum at $0.6 d_{\text{rad}}/r_{\text{CNT}}$ than the cations. A second density maximum of the anions in between the outer and inner layers is found at $0.4 d_{\text{rad}}/r_{\text{CNT}}$.

When comparing the neat IL systems to those containing salt, it can be observed that the presence of the Na^+ -ions leaves the radial positions of the ions mostly unchanged. This is not the case when comparing to the charged scaled simulations; see Figure S5 in the Supporting Information. Differences to the nonscaled simulations are especially apparent for the systems containing pore 12. Both N_{12}^{sc} and S_{12}^{sc} exhibit lower maxima and higher minima compared to N_{12} and S_{12} , indicating more mobility. Interestingly, these differences are almost opposite for the smallest pore system, again indicating the constraints on the ions due to the small pore size.

3.1.2 Charge Density Radial charge densities (ρ_{ch}) indicate the radial positions that accumulate charges inside the pore. Charge density profiles can thus give a clearer picture of the ordering of the species. While the boron atom of the anion carries a positive partial charge, the fluorine atoms are partially negatively charged. For the cation, the carbon atoms bear negative partial charges, and the hydrogen and nitrogen atoms are positively charged. Figure 4 depicts the charge density profiles for N_8 – N_{12} (above) and S_8 – S_{12} (below). As for the mass densities, we provide a combined charge density profile as well as profiles for each ion.

In contrast to the mass densities, the anions contribute more to the charge density profiles than do the cations. As only the boron atom of the BF_4^- -anions carries a positive partial charge, its radial position is reflected in the positive values of the density profile. For all systems, the boron atom never occupies the center, but it is found at only one radial position, and this is shifted to larger $d_{\text{rad}}/r_{\text{CNT}}$ values with larger pores. Indicated by the two negative peaks in Figure 4 (red lines), the fluorine atoms are located at two distinct distances due to the geometry of the anion.

The charge density for all tube sizes is positive when the value of $d_{\text{rad}}/r_{\text{CNT}}$ is the largest. Keeping the density profile for

the $[\text{C}_2\text{C Im}]^+$ -cations in mind, it is clear that the position of the cations is responsible for the positive charge density. Since the nitrogen atoms are identified in radial positions below $0.5 d_{\text{rad}}/r_{\text{CNT}}$ in the radial mass density profiles, this positive contribution can be assigned to the hydrogen atoms. Interestingly, an effect due to scaling of charges on the charge density profiles is absent in all the systems, besides a decrease in the overall charge density (Figure S6 in the Supporting Information).

3.2 Axial Mass Density Axial mass density profiles of all systems are listed in Figure 5. Again, we depict the complete density profiles and the individual ion contributions. The densities are normalized to the reference density ρ_0 of the neat IL. A three-dimensional contour plot of the density distribution within the system is shown in the Supporting Information in Figure S8.

For system N_8 (upper left panel of Figure 5), the most striking feature is the alternating chain of cations and anions inside the pore. Due to the small space in this confinement, an alternating chain ordering almost like that in a solid is enforced for the ions. The larger tube sizes lack this strict ordering. In all systems, the bulk regions show the typical density oscillations near the carbon walls, which decrease in magnitude further away from the wall.^{67–69} Regarding the salt-containing systems, as mentioned before, the Na^+ ions are always located outside the tube, except for the S_{10} system. From visual inspection of the pore 8 trajectories, we observe that the Na^+ ions never penetrated the pore during the filling process. For all larger systems, the ions enter the pore during the filling process but exited them during the equilibration run. This may be explained by the different coordination behavior of Na^+ - and $[\text{C}_2\text{C Im}]^+$ -cations.

When comparing the systems comprising the smallest pore 8 to the larger ones, it can be seen that the observed ordering of N_8 as well as S_8 is also to some degree present in the larger pores, especially in the salt-containing systems S_{10} and S_{12} . This indicates that even if the Na^+ -ions remain outside the tube, they affect the ordering of ions inside the tube, possibly due to the increased viscosity of the IL salt mixture in bulk. An

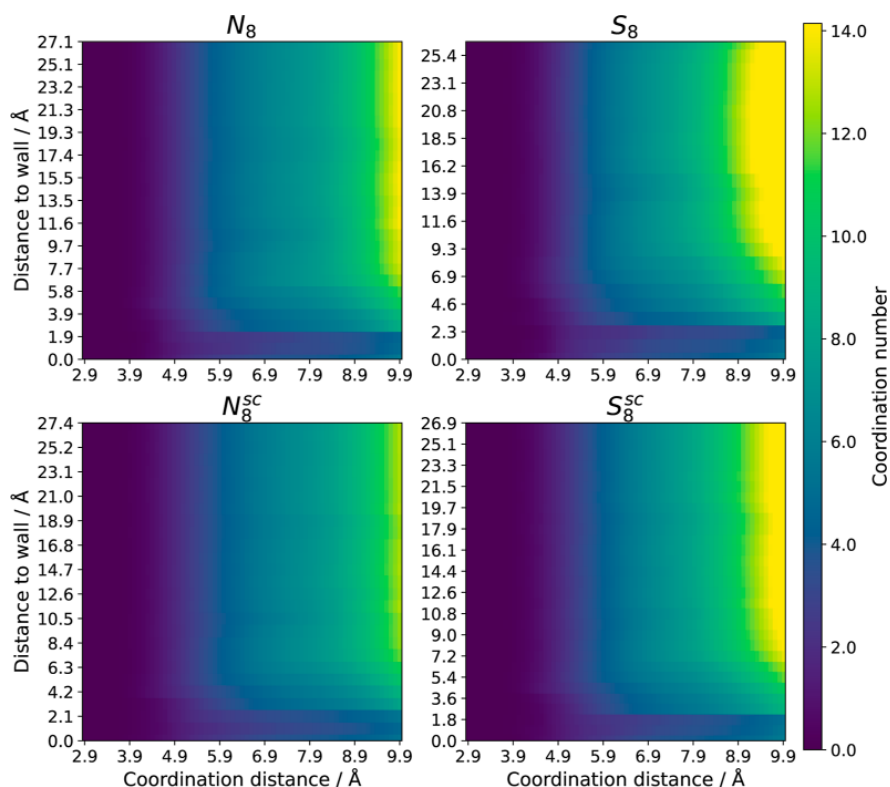


Figure 7. Heatmap of the CN at different coordination distances in relation to the distance to the wall for systems N_8 (above left), S_8 (above right), N_8^{sc} (below left), and S_8^{sc} (below right). $[C_2C\text{Im}]^+$ -cation: reference molecule; BF_4^- -anion: observable.

increased viscosity upon salt addition for ILs is also observed experimentally.⁷⁰

While the IL in systems N_8 – N_{12} reach a more or less uniform density for large distances away from the carbon structures, this is to a much lesser extent the case for systems S_8 – S_{12} . In these systems, the density distribution shows small but significant oscillations within the bulk. These density fluctuations inside and outside the pore for systems S_8 – S_{12} indicate that the Na^+ ions increase the viscosity of the IL as inferred above and amplify the layering effect perpendicular to the carbon surface further into the bulk.

The same effect is visible when comparing the systems S_8 – S_{12} to S_8^{sc} – S_{12}^{sc} (Figure S7 in the Supporting Information). The aforementioned oscillating density is largely diminished for the charge-scaled systems, indicating an increased dynamics of the ions inside the pores due to reduced Coulombic attraction at reduced charges. This is consistent with the decreased dynamics for similar IL salt mixtures in the literature.^{71–74}

3.3 Coordination Number In order to illustrate the general trends of the CN in the complete system, a 3D contour plot of the N_{12} system is exhibited in Figure 6. The CN was calculated for a maximum distance between the reference molecule and the observable of 7.72 Å. This corresponds to the distance at the first RDF minimum of the pure IL in bulk describing the first solvation shell. The shown CNs reflect exclusively the number of BF_4^- -anions coordinating to $[C_2C\text{Im}]^+$ -cations. The average CN of an ion in the bulk of the liquid is around 7 as also reported in literature^{75,76} and

decreases with increasing proximity to the pore wall. The transition from bulk to wall for all systems with pore size 8 is illustrated in Figure 7. The plots for the other systems are Figures S10 and S11 in the Supporting Information.

The heatmaps show two general trends: First, systems with scaled charges have overall lower CNs (compare the upper panels with lower panels in Figure 7). Second, for coordination distances larger than the first solvation shell, systems that contain salt generally have higher CNs than the neat IL systems (compare the yellow area on the left panels with right panels in Figure 7). The first point is in agreement with the observations for the density profiles where the charge scaling results in a reduced density. The second feature is based on the fact that for distances larger than the first solvation shell, ions of the same charge are increasingly present. Na^+ ions need considerably less space than the $[C_2C\text{Im}]^+$ -cation, which leads to an overall higher ion density within the salt system. The space saved is partly taken up by the BF_4^- -anions, which explains the higher CNs at distances larger than 7.72 Å.

For systems containing pore 10 (S10 in the Supporting Information) or 12 (S11 in the Supporting Information) it is also noticeable that the CN rises faster than expected for distances close to the wall from 0 to 2 Å. This is due to the small number of molecules located directly at the pore opening. For distances smaller than 2 Å, only molecules located at the pore opening are accounted for. These molecules naturally have a larger CN than molecules directly at the wall since their coordination sphere is not cut off by the

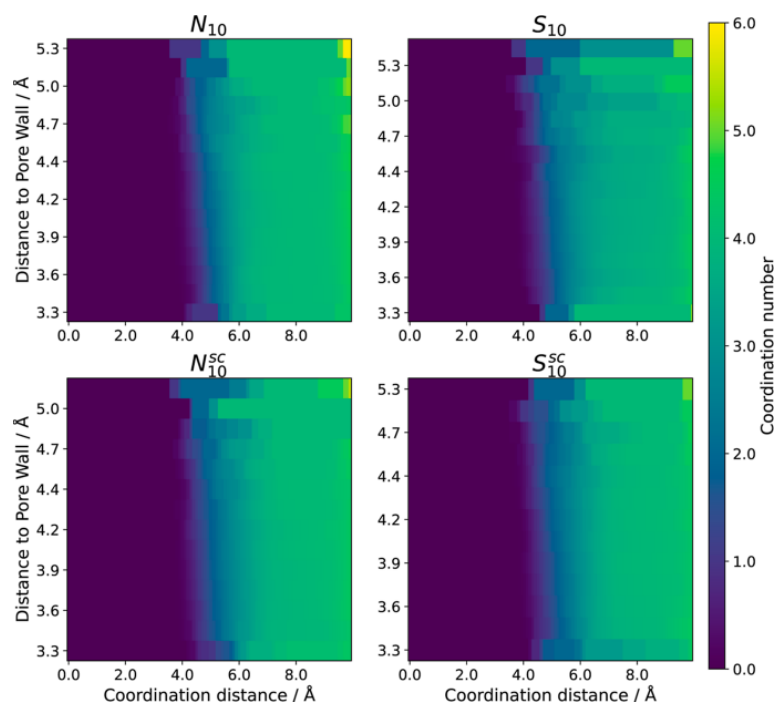


Figure 8. Cutoff of heatmap for pore 10 see Supporting Information Figure S10. $[C_2C\text{Im}]^-$ -cation: reference molecule; BF_4^- anion: observable. Different coordination distances are given in relation to the distance to the pore wall for systems N_{10} , S_{10} , N_{10}^{sc} , and S_{10}^{sc} .

wall. For distances larger than 2 Å, the average CN also includes molecules that are not directly located at the pore, and the calculated CN is therefore lower. This effect is almost absent for the smallest pore since there are not many molecules in the tube and thus the CN of molecules at the pore opening and at the wall is not significantly different.

In Figure 8 a cutoff of the heatmap for pore 10, see Supporting Information Figure S10, is presented. For the systems N_{10} and N_{10}^{sc} , the trend that the CN is smaller for the same coordination distances when scaling the charges is apparent. This is especially present in the region between 4 and 6 Å. Such a trend is not observed when comparing the systems S_{10} and S_{10}^{sc} . For all systems, noise can be seen to varying degrees for the largest distances from the pore wall. This can be explained by the radial density profiles that show a density close to 0 in the center of the pore, resulting in poor sampling in these regions. In system S_{10} , this effect is particularly pronounced because the Na^+ -cations are inside the pore, which causes the $[C_2C\text{Im}]^-$ -anions to be slightly further away from the central axis of the pore, see Figure 3. A broader minimum for system S_{10} (compared to that of N_{10}) is apparent. When a $[C_2C\text{Im}]^-$ -cation is located in the center of the pore, there is a tendency toward a lower CN for the same coordination distance compared to regions closer to the wall as the anions are overwhelmingly located at larger distances near the pore wall. However, conclusions should only be drawn cautiously in this regard as the radial position of the cation is extremely rare and sampling is correspondingly poor.

3.4 Free Energy Curves Figure 9 shows calculated free energy curves for the Na^+ -ion in the bulk and within confinement for systems S_8 – S_{12} . The region within the

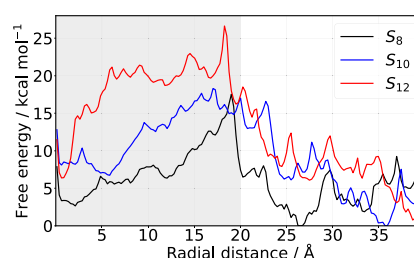


Figure 9. Free energy profiles for a Na^+ -ion in bulk and the respective pores in systems S_8 – S_{12} for radial distances of the Na^+ -ion to the center of the pore between 0 and 40 Å. The gray area describes the region within the confinement of the respective pore.

confinement is highlighted in gray. In Figure 9, the free energy is plotted against the distance of the Na^+ -ion from the center of mass of the respective pore. The comparison between this distance and the distance in the z -direction shows that the two values hardly differ (comparison in the Supporting Information). This means that the position of the Na^+ -ion varies almost exclusively in the z -direction from the starting point during umbrella sampling. The region within the bulk (at a distance >20 Å) shows that the free energy of the Na^+ -ion is subject to considerable fluctuations. These originate from the layering of the IL imposed by the surface, as discussed in Section 3.2. However, it also shows that these values should be interpreted only qualitatively and with care. A future study will provide better converged PMF curves. For all systems, a barrier of 15–25 kcal mol^{-1} must be overcome upon entering the pore. Especially for the systems S_8 and S_{12} , a strong increase of the free energy curve at the pore openings is observed. Inside

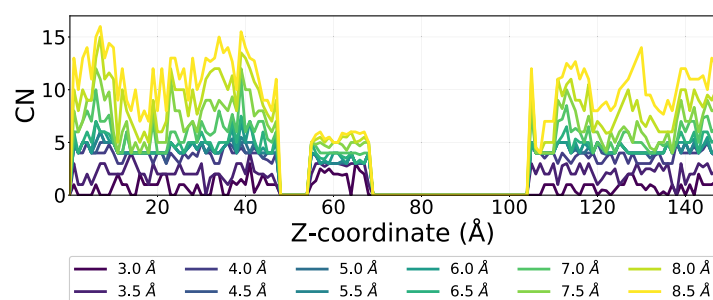


Figure 10. $\text{Na}^+ - \text{BF}_4^-$ CNs along the z -coordinate of the simulation box of system S_{10} for increasing maximal coordination distances (3.0–8.5 Å). The Na^+ ion was set as the reference species and the center of mass of the BF_4^- -anion as the observable.

the confinement, all free energy curves decrease for increasingly smaller distances, although they are on average higher than those in the bulk. This finding infers that if a Na^+ -ion were to enter the confinement, it would be trapped inside. In the previous simulations, Na^+ -ions were observed only within the confinement in system S_{10} , which is certainly due to sampling issues. For the systems S_8 and S_{12} , the energy barrier to enter the respective pores was not overcome during equilibration. However, in system S_{10} , the Na^+ -ions observed inside the pore entered the confinement during the filling process. Throughout the equilibration and production runs, the barrier at the pore opening was not overcome to leave the confinement, keeping the Na^+ -ions in a metastable state. It should be noted that in the simulations of the S_{10} system, two Na^+ -ions are present inside the pore close to each other. Due to the energetic effects of the proximity of two cations with respect to a shared coordination environment, it is conceivable that the free energy landscape would look somewhat different in this case. However, the main finding of the analysis is that, especially at the pore openings, a large energetic barrier must be overcome for the Na^+ -ion to enter and leave the confinement. As said before, these results should be taken with care, and additional simulations with better sampling must be carried out in the future.

3.5 Sodium Cation Coordination Turning now to the Na^+ -ion coordination behavior in confinement, the CNs for different maximal coordinate distances (3.0–8.5 Å) of the Na^+ -ions as reference species and BF_4^- -anions as observable are shown in Figure 10 for system S_{10} as this was the exception with Na^+ -ions being inside the CNT.

From all plots within the figure, it is apparent that the regions along the z -coordinate of the simulation box from approximately 0 to 45 Å and 100 to 147 Å are the regions where the Na^+ cation resides in the bulk. The region from approximately 50 to 70 Å describes the Na^+ cation in the confinement of pore 10. A comparison between the progression of the graphs in the bulk area and within the confinement zone clearly shows that CN increases significantly faster within the bulk, especially for larger coordination distances. This is expected since the confined space inside the pore means that less BF_4^- can reside in the radial vicinity of Na^+ , limited by the pore walls. However, the confined space not only causes the decrease of surrounding species but potentially also has an influence on the arrangement of ions within the first solvation shell. For this purpose, the average CN of Na^+ and BF_4^- in the bulk (black) region and inside the pore (blue) was calculated and plotted against the coordina-

tion distance (Figure 11). For the smallest coordination distances, CN_{ave} increases faster for the region inside the pore,

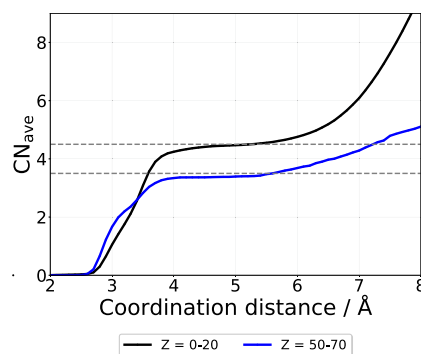


Figure 11. Average CN CN_{ave} of the Na^+ cation as reference species and BF_4^- as observable in system S_{10} . The CN was averaged in two regions. Between 0 and 20 Å (black), in the bulk of the IL–salt mixture, and between 50 and 70 Å (blue), where the Na^+ cation is in the confinement of the pore (see Figure 10). The two horizontal lines in the plot are shown at $\text{CN}_{\text{ave}} = 3.5$ and $\text{CN}_{\text{ave}} = 4.5$.

with CN_{ave} being almost 2.0, while in the bulk CN_{ave} is about 1.0 at a distance of 3.0 Å. However, CN_{ave} increases significantly faster for increasing coordination distance within the bulk, and the plots intersect at a coordination distance of about 3.3 Å and a CN_{ave} value of 2.5. Between 3.8 and 5.2 Å, both plots reach a plateau region where CN_{ave} changes very little. This region can be considered as the outer limit of the first solvation layer. CN_{ave} thus describes the average number of BF_4^- -anions directly coordinating to the Na^+ -ions. In the bulk the value is about 4.5, and in the confinement the value is lower at about 3.5. This provides also a possible explanation for the lack of Na^+ -ions inside the CNT.

For larger distances, above 5 Å, CN_{ave} increases again for both systems. However, the curve diverges as CN_{ave} increases significantly faster in the bulk than in the confinement. It can therefore be determined that the coordination between Na^+ and BF_4^- changes within the confinement. While there are statistically already two BF_4^- ions at a maximum coordination distance of 3 Å to Na^+ inside the pore, the average CN is lower in the bulk at this distance. Nevertheless, within the first solvation shell, there are on average 4.5 BF_4^- ions in the bulk, in the confinement there are only 3.5.

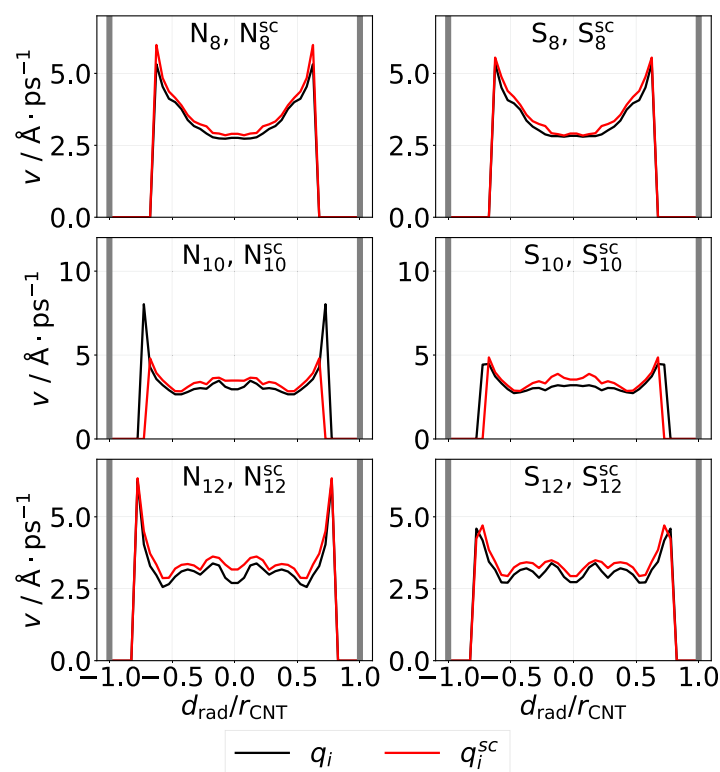


Figure 12. Radial velocity distributions of all investigated systems. The plots for the simulations with unity charges (q_i) are shown in black, with scaled charges (q_i^{SC}) in red. The velocity v is given in units of $\text{\AA} \cdot \text{ps}^{-1}$. The distances from the center axis of the pore d_{rad} are normalized using the respective pore radius r_{CNT} . The vertical bars represent the pore wall.

3.6 Radial Velocity Distributions In Figure 12 the radial velocity distributions of all systems are depicted. Overall, the velocities increase upon scaling the force field charges (depicted in red) compared to unity charges (black). This increase is only small but present in all systems. The distribution functions for the individual pores are very similar for the neat (N) and salt (S) systems. However, it is striking that for three of the six systems examined, the maximum $d_{\text{rad}}/r_{\text{CNT}}$ values are larger for the nonscaled systems. This is surprising since the carbon atoms of the pore are not charged and no polarization effects are explicitly taken into account; the interactions between bulk and liquid in the simulations are therefore governed by van der Waals interactions. Nevertheless, there seems to be a tendency that shows that in extreme cases, the ions can move a little further away from the center axis when using unity charges, being positioned a little closer to the pore wall. Please note that in this analysis, an average velocity is determined from all the velocities calculated for each bin. In extreme cases close to the pore wall, the rarity of finding an atom at a certain radial distance from the center axis of the pore is not directly apparent from the graphs. However, it can be seen from the radial density distributions (Figure 2) that the density tends toward zero at the largest values for $d_{\text{rad}}/r_{\text{CNT}}$ of the velocity distribution function. These atom positions are therefore extremely rare.

Importantly, in addition to smaller fluctuations closer to the pore center, the velocity increases for larger $d_{\text{rad}}/r_{\text{CNT}}$ values, independent of the chosen system. This suggests that the ions

within the confinement have some rotational freedom with respect to the center axis of the pore. This is in line with the increase in velocity for larger values of $d_{\text{rad}}/r_{\text{CNT}}$ since during a rotational motion of a cluster of ions, the most displaced species have to move the fastest so that the relative distances between the species of the cluster do not change. The velocity of the individual species thus depends much more on the arrangement of the ions in the pore than on the interaction with the pore wall.

4 CONCLUSIONS

MD simulations were carried out to investigate the structural arrangement of the IL $[\text{C}_2\text{C}_1\text{Im}][\text{BF}_4]$ and its 25 mol % NaBF_4 salt mixture in confined space. The examined systems consisted of a porous carbon structure combined with a bulk phase of the studied liquids.

In most simulations, the sodium ions remained outside the confinement. Interestingly, even when the Na^+ ions were absent from the tube, the salt still had a visible effect on the ordering of the IL ions along the tube axis. While only the smallest pore size exhibited an alternating mass ordering along the tube axis in the case of the neat IL, a tubular arrangement was observed in the larger systems. In the largest pore, the ions formed two different layers, a tubular layer close to the pore wall and a chain of ions in the center. Notably, the central layer almost exclusively consisted of cations.

When focusing on the salt containing systems, the oscillating ordering of the ions was also observed for larger tube sizes.

These oscillating density profiles in the larger pore sizes vanished when scaled point charges were used, reflecting the increased dynamics inside the confinement imposed by the reduced Coulomb interactions between the ions. Furthermore, if Na^+ ions were residing inside the pore, their coordination behavior with the BF_4^- ions was drastically changed, obviously with fewer species in the first solvation shell than in the bulk. Scaling of the force field charges increased the average velocities of the ions within the confined space. Surprisingly, in some cases, ions in nonscaled systems moved further away from the pore center. An increase in velocity toward the pore wall suggests a velocity dependence on ion arrangement rather than pore wall interactions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.jpcb.3c08493>.

Description of setup and equilibration process of the investigated systems; atomic parameters used for the analyses; partial charges of the applied force field; radial mass density and charge density profiles of systems $\text{N}_8^{\text{sc}}-\text{N}_{12}^{\text{sc}}$ and $\text{S}_8^{\text{sc}}-\text{S}_{12}^{\text{sc}}$; axial density profiles of systems $\text{N}_8^{\text{sc}}-\text{N}_{12}^{\text{sc}}$ and $\text{S}_8^{\text{sc}}-\text{S}_{12}^{\text{sc}}$; three-dimensional contour density plot of system N_{12} ; three-dimensional CN contour plot of system N_{12} and discussion on the correct application of the CN analysis; $[\text{C}_2\text{C Im}]^+ - \text{BF}_4^-$ CN heatmap of all systems containing pore 10 or 12; $\text{Na}^+ - \text{BF}_4^-$ CN heatmap of systems S_8-S_{12} and $\text{S}_8^{\text{sc}}-\text{S}_{12}^{\text{sc}}$; and validation of the CN analysis (PDF)

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Notes

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Appendix: Influence of Internal Interfaces on the Structure and Dynamics of IL-Based Electrolytes Confined in a Metal–Organic Framework

Janis Hessling,^a Leonard Dick,^b Sophia Keil,^a Vahideh Alizadeh,^{bcd} Michael Ryan Hansen,^b Barbara Kirchner^b, Monika Schönhoff^a

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Own contributions

- Running all MD simulations.
- Analyzing the trajectories.
- Writing the theoretical part of method section and parts of the discussion.

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Influence of Internal Interfaces on the Structure and Dynamics of IL-Based Electrolytes Confined in a Metal–Organic Framework

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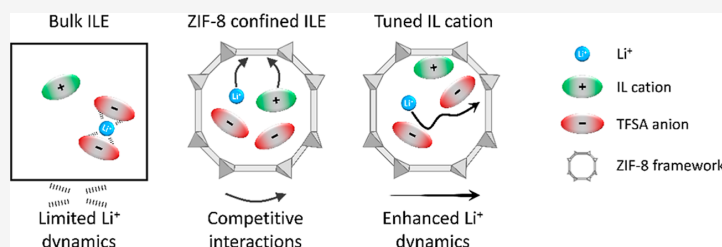
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ABSTRACT: Hybrid solid-state electrolytes, which combine ionic liquids with metal–organic frameworks, offer a promising approach to enhancing the safety and energy density of next-generation batteries. A thorough understanding of the interplay between the solid and liquid phases in hybrid solid-state electrolytes is crucial for optimizing their performance as battery electrolytes. This study investigates how interactions between different ionic liquid-based electrolytes and the metal–organic framework ZIF-8 influence the coordination and dynamics of Li^+ in confinement. To this end, we examine five different ionic liquids, varying the chemical nature of the cation. Raman spectroscopy, supported by 2D solid-state NMR and simulations, are used to elucidate Li^+ coordination and ion-wall interactions. The impact of these interactions on local Li^+ dynamics and charge transport in the ionic liquid-ZIF-8 hybrid system is investigated using ^7Li spin relaxation, impedance spectroscopy, and simulations. The results reveal a competitive interaction between Li^+ and the ionic liquid cation with the ZIF-8 framework, which can be fine-tuned by modifying the molecular structure of the ionic liquid cation. As a consequence, local Li^+ dynamics is enhanced, depending on the ionic liquid cation. The beneficial interactions in the confined system can even make Li^+ the fastest diffusing species, in contrast to bulk electrolyte, where Li^+ transport is limited by strong Li-anion clusters. Thus, blocking Li^+ -framework interactions through other competitive interactions might be an effective strategy to enhance Li^+ dynamics and increase Li conductivity in a hybrid solid-state electrolyte. Although confinement within the ZIF-8 model system leads to an overall decrease in conductivity, this study provides valuable insights into the design of hybrid electrolytes for next-generation battery applications.

INTRODUCTION

The demand for energy storage technologies, especially lithium-ion batteries, has constantly grown in recent years¹ and is also predicted to increase even more in the next years.² This increasing demand highlights significant limitations of the current battery generation. Especially the flammability and volatility of commonly used organic electrolytes, in combination with the high energy density of modern lithium-ion batteries, gives rise to severe safety risks.^{3–6} Among other approaches, solid-state electrolytes^{7–12} and ionic liquids (ILs)^{13–16} are widely discussed in the literature as potential alternative electrolytes. Solid-state electrolytes are nonflammable and in theory could have a higher energy density than organic electrolytes, due to enabling the use of lithium metal anodes.^{9–12} However, they either suffer from poor ionic conductivities at room temperature (polymer solid-state electrolytes) or face the challenge of maintaining good solid–solid interfacial contact

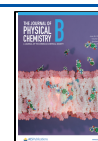
between the electrode and electrolyte (inorganic solid-state electrolytes), which if not maintained can lead to a high interfacial resistance.^{9–11} ILs on the other hand are promising electrolyte components due to their low volatility and flammability and high electrochemical stability, making them potential candidates for high-voltage battery systems.^{13–16} However, IL-based electrolytes suffer from high viscosities and low conductivities, due to strong Coulomb interactions. In particular, for mixtures of ILs with Li salt, poor Li^+ transport properties are caused by unfavorable Li-anion clusters.^{17–21} Due

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to a vehicular transport mechanism of Lithium in these net negatively charged Li-anion clusters, Li^+ transference numbers have even been reported to exhibit a negative sign, reflecting Li^+ migration in the wrong direction.^{20–23} These drawbacks of solid-state electrolytes and ILs prevent their widespread application as battery electrolytes.

Hybrid solid-state electrolytes, involving the confinement of liquids within solid matrices, represent a new class of electrolytes that hold significant promise and may help overcome the problems of the previously mentioned classes of electrolytes.^{24–28} These materials aim to use the advantages of both solid and liquid electrolytes, combining the high ionic conductivity of liquids with the structural stability of solids. For several cases of ILs confined in silica or nanotubes, even faster ion dynamics, compared to the bulk, were demonstrated experimentally^{29,30} as well as in simulations.^{31–35} These enhanced dynamics were attributed to the frustration of the IL self-organization at the nanoscale³⁰ which can be seen in reduced Coulomb interactions of the IL-ions with each other near the solid–liquid interface.³⁵ A strong confinement of ILs can even lead to a so-called “superionic state”, where the Coulombic ordering, i.e. ions are surrounded by an ion shell of alternating charge, is replaced by a block-wise alternating structure of equally charged ion pairs.^{36–39} To achieve and control such altered structural and physicochemical properties of confined liquids, an understanding of the interplay between the solid and liquid phases in hybrid solid-state electrolytes is crucial and can finally allow for optimizing their performance as battery electrolytes.^{25,40–44}

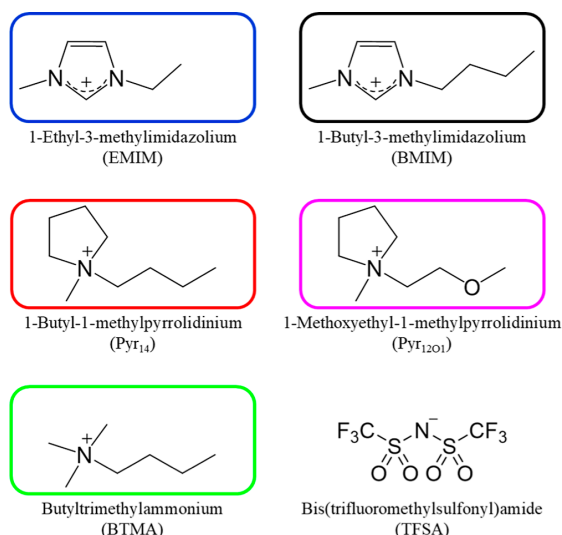
Among the various hybrid materials, those involving a confinement within metal–organic frameworks (MOFs) have shown particular promise,^{45–51} for example a sufficient conductivity for application in battery cells.⁵¹ MOFs, with their highly tunable structures and large surface areas, provide an ideal platform for hosting ILs. Furthermore, ILs also have highly customizable properties and are even referred to as “designer solvents”.⁵² This high degree of tunability of both components could allow the precise engineering of hybrid materials to achieve the desired electrochemical properties.^{53,54} For example, the confinement of an IL-based electrolyte in MOF-525(Cu) led to similar conductivities as the bulk electrolyte, while the Li^+ transference number was improved.⁴⁹ Furthermore, an analysis of the spatial distribution of IL ions within the MOF pores as a function of loading by Park et al. shows that repulsive anion–anion and cation–cation electrostatic interactions contribute to the upper limit of loading.⁴³ Notably, the loading of the MOF by ILs is known to affect the conductivity^{45,47,55–57} and therefore the performance as an electrolyte. However, to accurately assess the ionic conductivity within the MOF pores, any excess IL on the external surface should be avoided, as these “nanowetted interfaces” can significantly contribute to the overall conductivity.^{49,53,57,58} Generally, the complex interplay of the mutual interaction of anions, cations, and internal surfaces is expected to impact ion dynamics and transport in IL/MOF hybrid electrolytes, however, systematic studies which combine experimental and computational findings^{57,59} are still rare.

Recently, we investigated an ionic liquid-based electrolyte (ILE), namely 1-butyl-1-methylpyrrolidinium bis-(trifluoromethylsulfonyl)amide-based mixtures with Li salts, $\text{Pyr}_{14}\text{TFSA}_{(1-x)}\text{LiTFSA}_x$ in different nanoporous materials and found beneficially enhanced local Li^+ dynamics particularly in the MOF ZIF-8, but not in the nanopores of the porous material SBA-15.⁶⁰ While the local Li^+ coordination environment as well

as its local dynamics in SBA nanopores were very similar to the properties in bulk, it was particularly the confinement in ZIF-8, which altered the Li^+ coordination environment, causing a disruption of Li-anion clusters, thereby leading to an enhancement of the local Li^+ dynamics. The results point at a strong involvement of an interaction between the IL cation and the pore walls rather than a size effect of ZIF-8 pores.⁶⁰ The nature of such beneficial interactions and the role of the three ionic constituents, however, still remains to be understood.

Therefore, this study focuses on investigating how the interactions between different IL-based electrolytes (ILE) and the MOF ZIF-8 influence the coordination and dynamics of Li^+ ions in confinement. To this end, we study five different ionic liquids, varying the chemical nature of the cation, and employing varying fractions of Li salt. The structures of the IL cations are shown in Scheme 1. They are selected to represent a variation of

Scheme 1. IL Cations and IL Anion Investigated in This Study^a



^aThe color code introduced here for the different cations is used in all graphs throughout the paper.

Lewis acidity as well as van der Waals forces. The influence of the confinement and type of IL cation is analyzed by Raman spectroscopy, aided by 2D solid-state NMR experiments and MD simulations of structural parameters. Finally, the influence of the respective interactions on the local Li^+ dynamics as well as the charge transport in the IL-ZIF-8 hybrid system is elucidated by ^7Li spin relaxation, impedance spectroscopy and MD simulations. The emerging structural picture involves a competitive interaction of Li^+ and IL cation with the ZIF-8 wall, which can be fine-tuned by the molecular structure of the IL cation. As a consequence, enhanced local Li^+ mobility is occurring, depending on the IL cation. The beneficial interactions in the confined system even render Li^+ to be the fastest diffusing species, as opposed to the bulk ILE, where Li^+ transport is limited by strong Li-anion clusters. Thus, though confinement causes an overall decrease in conductivity, tuning the interactions in confinement has a beneficial effect on Li transference.

MATERIALS AND METHODS

Materials. The metal organic framework ZIF-8 (Basolite Z1200) was obtained from Sigma-Aldrich. 1-Butyl-1-methylpyrrolidinium bis(trifluoromethylsulfonyl)amide (Pyr₁₄TFSA, 99.5%), Butyltrimethylammonium bis(trifluoromethylsulfonyl)amide (BTMATFSA, 99%), 1-Ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)amide (EMIMTFSA, 99.5%) and 1-Butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)amide (BMIMTFSA, 99.5%) were obtained from IOLITEC. 1-Methoxyethyl-1-methylpyrrolidinium bis(trifluoromethylsulfonyl)amide (Pyr₁₂₀₁TFSA, 99.9%) was obtained from Solvionic. Lithium bis(trifluoromethylsulfonyl)amide (LiTFSA, 99.95%) was obtained from Sigma-Aldrich. All chemicals were used without further purification. In order to remove adsorbed gases, and especially water, the ILEs and the Li salt were dried at 100 °C and 10^{−7} bar for at least 12 h. ZIF-8 was activated at 100 °C and 10^{−7} bar for at least 24 h. All chemicals and samples were stored and prepared in an argon-filled glovebox (GS GLOVEBOX Systemtechnik, H₂O and O₂ < 5 ppm).

Preparation of Electrolyte Confined in Porous Materials. The electrolytes were prepared by mixing the ILEs with the Li salt at specific molar ratios, creating a concentration series of ILEs with a composition IL_(1−x)LiTFSA_x. Pyr₁₄TFSA-LiTFSA, BTMATFSA-LiTFSA, EMIMTFSA-LiTFSA, BMIMTFSA-LiTFSA and Pyr₁₂₀₁TFSA-LiTFSA are denoted as Pyr₁₄⁺ ILE *x*, BTMA⁺ ILE *x*, EMIM⁺ ILE *x*, BMIM⁺ ILE *x* and Pyr₁₂₀₁⁺ ILE *x* (in mol %), respectively. The electrolytes were confined in ZIF-8 through capillary action,^{45,46,48,61} by mixing the ZIF-8 with the electrolytes at a specific mass ratio using a mortar and pestle. The mixtures of the electrolytes with ZIF-8 were heated at 200 °C and 10^{−7} bar for 24 h, to allow the diffusion of the electrolytes into the pores of ZIF-8. It is important that no excess ILE remained on the outer ZIF-8 surface, as such excess ILE can, for example, cause apparent conductivities which are larger than the intrinsic conductivities of the hybrid electrolyte.^{55,57} Given the relatively large particle size of ZIF-8 (5 μm), a differential scanning calorimetry (DSC)-based method can be applied to accurately assess the maximum pore filling where no excess ILE is present in the interparticular voids.⁶⁰ This method leverages the fact that the solid–liquid phase transition of the nanoconfined electrolyte is suppressed within the small pores of ZIF-8, but not in the interparticular space.^{45,46,48,62} Using this approach by comparing DSC traces of varying amounts of ILE mixed with ZIF-8, the maximum filling of ZIF-8 was determined by a Pyr₁₄TFSA-based electrolyte in our previous publication to be around 50% of the theoretical pore volume.⁶⁰ This is in the same range as the filling with alcohols reported by Cousin Saint Remi et al.,⁶³ but less than reported by Fujie for EMIMTFSA in ZIF-8, where a small particle size might enhance the accessibility of inner pores.⁴⁶ For the electrolytes in this study we prepared samples with (50 ± 5)% pore filling for the Pyr₁₄⁺, BTMA⁺ and Pyr₁₂₀₁⁺-based electrolytes. For the BMIM⁺ and EMIM⁺-based electrolytes we realized that heating the corresponding amounts of IL and ZIF-8 led to a fraction of IL condensing at the vial wall, therefore we determined the actual pore filling degree by weighing, which resulted in (40 ± 5)%. Finally, the samples were filled into 5 mm NMR tubes and sealed.

Raman Spectroscopy. Raman studies were performed on a Bruker MultiRAM spectrometer (Rheinstetten) with a laser wavelength of 1064 nm and power of 263 mW. Raman spectra were recorded with a resolution of 0.5 cm^{−1} in a range of 30–

3600 cm^{−1} on sealed samples in NMR tubes at ambient temperature. The spectra were baseline corrected and normalized to the integral of the Raman band region from 383 to 435 cm^{−1}, 676 to 704 cm^{−1} or 730 to 765 cm^{−1}, respectively. Spectral decomposition was performed by fits with Voigt profiles in OPUS (Bruker, Rheinstetten) (75% Lorentz for the region from 676 to 704 cm^{−1} and 60% Lorentz for the region from 383 to 435 cm^{−1} and 730 to 765 cm^{−1}). Free parameters were peak intensity, position and width for each band.

NMR Spectroscopy and Spin Relaxation. NMR spin relaxation measurements were performed with 400 MHz spectrometers (AVANCE NEO, Bruker or AVANCE III HD, Bruker) with a broad band probe head (BBO, Bruker). The temperature was calibrated with a PT100 thermocouple in a NMR tube filled with glycol. For ⁷Li temperature dependent spin relaxation measurements an inversion recovery pulse sequence was used, obtaining the spin–lattice relaxation time *T*₁ from eq 1⁶⁴

$$M_z = M_0 \left[1 - 2 \exp\left(-\frac{\tau_{ev}}{T_1}\right) \right] \quad (1)$$

where *M_z* is the magnetization in the *z* direction and *τ_{ev}* is the evolution time. With the assumption of one random isotropic motional mode with a correlation time *τ_c*, the Bloembergen, Purcell and Pound (BPP) model⁶⁵ can be used to describe the temperature dependent spin–lattice relaxation rate *R*₁ at the Larmor frequency *ω*₀ using eq 2.⁶⁶

$$R_1 = \frac{1}{T_1} = A_{\text{quad}} \cdot \left(\frac{\tau_c}{1 + \omega_0^2 \tau_c^2} + \frac{4\tau_c}{1 + 4\omega_0^2 \tau_c^2} \right) \quad (2)$$

Here *A_{quad}* is a prefactor that describes the local interactions of the quadrupole moment with the electric field gradient, since in the case of ⁷Li, quadrupolar interactions are the dominant relaxation mechanism. Under the assumption of an Arrhenius behavior of the local motions, the correlation time *τ_c* can be described by eq 3

$$\tau_c = \tau_0 \cdot \exp\left(\frac{E_a}{RT}\right) \quad (3)$$

where *τ*₀ is the inverse attempt frequency and *E_a* the activation energy of the local motion.

The direct excitation ¹H magic-angle spinning (MAS) and 2D ¹H–¹H double-quantum single-quantum (DQ-SQ) MAS NMR correlation experiments were conducted at a Bruker AVANCE NEO spectrometer at a magnetic field density of *B*₀ = 11.74 T (*ν*₀^{1H} = 500.39 MHz) using a commercial Bruker 2.5 mm HFX probe. For DQ excitation and reconversion, the Back-to-Back (BaBa) recoupling scheme with a xy16 phase cycle was used.^{67,68} A total of 1024 increments were used with a *t*₁-increment of 4*τ_R* = 124 μs. The ¹³C{¹H-decoupled} MAS NMR experiments were performed on a Bruker DSX 500 spectrometer with *B*₀ = 11.75 T using a Bruker 4.0 mm HFX probe.

For the 2D ¹³C{¹H} HETCOR MAS NMR spectrum, a Bruker AVANCE III spectrometer operating at 11.74 T (*ν*₀^{1H} = 300.13 MHz) and a Bruker 4 mm HX probe were used. These experiments employed frequency-switched Lee–Goldburg (FSLG) for ¹H–¹H homonuclear decoupling during *t*₁ followed by a short cross-polarization (CP) time of 0.5 ms utilizing LG-CP conditions⁶⁹ to suppress ¹H–¹H spin diffusion. Here, a ramp was applied on the ¹³C channel and experimentally optimized Hartmann–Hahn matching nutation frequencies of *ν*_{CP}^{1H} = 79.1

kHz and $\nu_{\text{CP}}^{13\text{C}} = 66.7$ kHz were used. Further experimental parameters for all measurements are given in Table S1 in Supporting Information.

Impedance Spectroscopy. For impedance measurements the powdery samples of the confined electrolytes in ZIF-8 were pressed with 2 GPa into pellets (ca. 1 mm thick and 5.0 mm in diameter). An approximately 100 nm thick gold layer was then deposited onto the pellet surface using a sputter coater (BALTEC SCD 055, BALTEC preparation, Niesgrau) and a suitable mask. The samples were dried at 200 °C and 10^{-7} bar for 24 h. Impedance measurements were performed with a Novocontrol Alpha-A High Performance Frequency Analyzer (Montabaur) equipped with a BDS 1200 sample holder. The pressed pellets were sandwiched between two electrodes and placed in a cryostat filled with nitrogen gas. The impedance was determined in the frequency range of 0.01 to 10^7 Hz, applying an alternating voltage of 10 mV. The temperature range was between 293.15 and 433.15 K. The resistance of the sample was then determined in a Nyquist plot by fitting a model equivalent circuit, of a parallel connected constant phase element and an Ohmic resistance, to the data where data points due to polarization effects were removed. The dc conductivity (σ_{dc}) was calculated by multiplying the inverse resistance with the cell constant d/A , where the electrode distance d and area A are determined with a micrometer (Mitutoyo, QuantuMike, precision ± 0.001 mm).

Conductivity measurements of the bulk electrolytes were performed in a temperature range between 313.15 and 373.15 K in a Microcell HC measuring stand (rhd instruments, Darmstadt). The cell was filled and sealed in the glovebox under argon atmosphere, experiments were performed in the frequency range of $1\text{--}10^7$ Hz, applying an alternating voltage of 10 mV. The cell constant was calibrated using a standard (KCl) solution. The dc conductivity (σ_{dc}) was determined by plotting the real part of the conductivity against the frequency and extracting σ_{dc} from the dc-plateau.

Computational Details. Bulk electrolyte systems with 200 ion pairs of Pyr₁₄TFSA–LiTFSA at salt concentrations of 15 mol %, 33 mol %, and 50 mol % (see Table S3) were studied by MD simulations. In addition, confined systems consisting of 72 ion pairs of (Pyr₁₄TFSA)_{0.67}–LiTFSA_{0.33} in a ZIF-8 structure were simulated at three different temperatures (300, 450, and 600 K). The simulated ZIF-8 structure has 24 pores, each filled with three ion pairs, which is the maximum possible number. The TFSA anion exists in two conformers, cis and trans, and their molar ratios were considered from the beginning in preparing all simulation inputs. These cis and trans molar ratios were derived from experimental Raman data (Figure S1; Table S2) of the Raman band region from 383 to 435 cm^{-1} .⁷⁰

The molecular dynamics simulations were performed with the LAMMPS program package.⁷¹ The input files were built using the packmol⁷² and the fftool⁷³ packages. The Li cations were represented by the Aqvist force field,⁷⁴ Pyr₁₄ cations and TFSA anions by the CL&P^{75,76} model, and for ZIF-8 the AMBER model of Zheng et al. was used.⁷⁷ A cutoff of 12 Å was applied for nonbonded interactions and the particle–particle particle-mesh method was applied to evaluate long-range electrostatic energies with the accuracy of 10^{-5} kcal/mol. Each confined system, after an energy minimization step with a tolerance of 10^{-4} kcal/mol for the energy term and 10^{-6} kcal/mol/Å for the force term, was equilibrated for 5 ns within the NVT ensemble. The Nose–Hoover thermostat was used to control the temperature during all NVT simulations.

Subsequent production runs of 50 ns were performed for each system. Each calculation was run three times, using different initial velocity seeds to ensure the distinctiveness of each run. The numbers 12,345, 29,383, and 15,455 were used as seed values for the random number generator. The bulk simulations were done similarly, however the equilibration was initiated in an NVT ensemble for 1 ns, before switching to an NPT ensemble for 3 ns to adjust the density of the electrolyte. The production runs ran over a length of 30 ns. Details of the simulated systems are given in Table S3.

The trajectory analysis of each system was conducted using TRAVIS^{78,79} and CONAN^{80,81} and the results were averaged over the three replica simulations in the case of the confined systems to ensure statistical confidence. The visualization of the simulation box was done in VMD,⁸² shown in Figure S2.

RESULTS AND DISCUSSION

Interplay of ILE and ZIF-8 Framework. The internal interface may play an important role in understanding the impact of ZIF-8 on the Li⁺ mobility. To investigate the interactions of the different electrolytes with the ZIF-8 framework, as a first step the impact of the ILE filling on the ZIF-8 framework was analyzed by Raman spectroscopy. In Figure 1a the Raman spectra of the imidazole ring puckering mode of ZIF-8, occurring in the spectral region between 676 and 704 cm^{-1} , are shown for ZIF-8 with different ILEs incorporated. The Raman spectra for all ILE with other Li salt fractions are displayed in Figure S3.

The band at 686 cm^{-1} can be assigned to the imidazole ring puckering mode of the ZIF-8 framework.^{83,84} Upon confinement of the ILE the position is shifted to higher wavenumbers with an order of the magnitude of the shift $\text{Pyr}_{14}^+ > \text{BTMA}^+ > \text{Pyr}_{1201}^+ > \text{EMIM}^+, \text{BMIM}^+$. By fitting the Raman spectra with Voigt profiles the peak positions were determined and are displayed against the molar fraction of the respective IL cation in Figure 1b. Similar shifts are also present for the $\nu(\text{Zn–N})$ mode of ZIF-8 upon confinement of ILE (Figures S4 and S5). Since the IL fraction, $1 - x$, represents the fraction of the IL cation in relation to the total number of cations, there is a clear linear correlation between the molar fraction of the respective IL cation and the shift. In analogy to our prior study⁶⁰ we attribute this effect to interactions of the IL cation with the ZIF-8 framework due to van der Waals forces.

The average structural arrangement of the Pyr₁₄⁺-based electrolyte within the ZIF-8 framework is discussed by analyzing radial distribution functions obtained by MD simulations (Figure 2). Figure 2a shows the environment of the zinc cation of the ZIF-8 framework. The oxygen atoms of the TFSA anion seem to exclusively coordinate to the zinc cation, with Li⁺ in the second coordination shell most likely coordinating to TFSA[−]. The immediate environment of the methylimidazole anion of the ZIF-8 framework was analyzed with the center of ring (COR) (Figure 2b) and the hydrogen atoms of the methyl group (Figure 2c) set as reference points. This indicates a possible competitive coordination of the Li cation and the Pyr₁₄ cation to the methylimidazole anion. While Li⁺ preferentially coordinates with COR close to methylimidazole, possibly promoted by cation– π interactions, Pyr₁₄⁺ preferentially coordinates near the methyl group. The coordination to the methyl group is hereby favored with the hydrogen atoms of the alkyl chains and hydrogen atoms of the ring of Pyr₁₄⁺, possibly promoted through nonpolar interactions, which were already mentioned in literature for ZIF-8 systems.^{85,86}

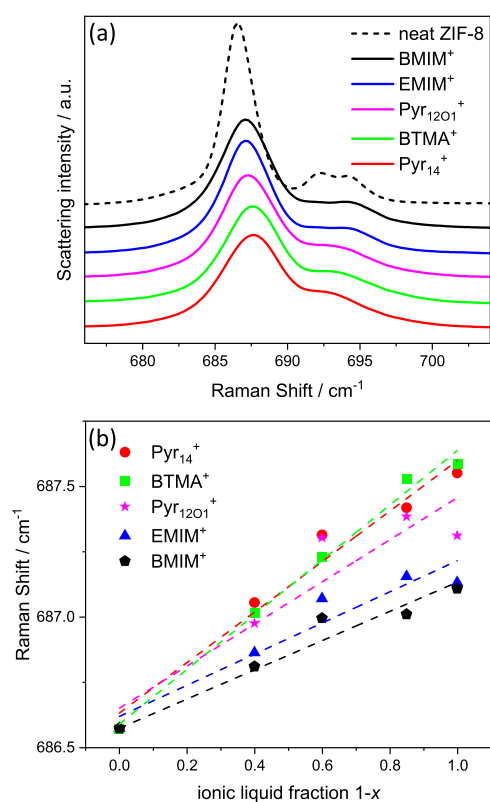


Figure 1. (a) Raman spectra of the imidazole ring puckering mode of ZIF-8 with different confined ILs (no Li salt), in the spectral region between 676 and 704 cm^{-1} . (b) Raman shift of the imidazole ring puckering mode of the ZIF-8 framework in dependence on the ionic liquid fraction in salt- in ionic liquid, $1 - x$, extracted from Figures 1a and S3.

To further demonstrate the distinct interaction between the IL cation and the ZIF-8 framework, we used solid-state NMR

spectroscopy, exemplarily employing the BTMA⁺-based electrolyte. The assignment of the respective ^1H and ^{13}C MAS NMR spectra is shown in the Supporting Information (Figure S6 and accompanying text). The 2D ^1H – ^1H DQ-SQ NMR spectra in Figure 3a,b show cross-peaks owing from the intramolecular proton species in each the BTMA⁺ and the imidazole species, as well as intermolecular cross-peaks evidencing the interaction of BTMA⁺ with the 5-Me protons and the aromatic protons of the imidazole molecules in the ZIF-8 framework at: ($\delta_{\text{SQ}}/\text{ppm}$, $\delta_{\text{DQ}}/\text{ppm}$) = (0.34, 7.2), (0.70, 7.6), (0.91, 7.8), (2.35, 9.1), (2.7, 9.4) and (6.7, 9.1). While cross-correlations are usually observed in pairs (i.e., for each signal at ($\delta_{\text{SQ},1}/\text{ppm}$, $\delta_{\text{SQ},1} + \delta_{\text{SQ},2}/\text{ppm}$), there should also be a signal at ($\delta_{\text{SQ},2}/\text{ppm}$, $\delta_{\text{SQ},1} + \delta_{\text{SQ},2}/\text{ppm}$)), it is not possible to clearly identify the presence of any cross-correlation signals at $\delta_{\text{SQ}}/\text{ppm} = 1.92$ or 6.83 assigned to the imidazole species. This is attributed to the markedly larger line width of the cross and autocorrelation peaks as well as t_1 -noise obfuscating all potential cross-peaks expected at these positions in the spectrum. Nevertheless, the peak observed at (6.7, 9.1) ppm is slightly asymmetric and more closely shifted to the expected position of a I2/B5 cross-correlation signal rather than a I2/I1 autocorrelation signal. This is interpreted to imply that both I2/B5 and I2/I1 correlation peaks are present, albeit poorly resolved.

An additional 2D $^{13}\text{C}\{^1\text{H}\}$ HETCOR MAS NMR spectrum was also acquired to prove the intermolecular ^1H – ^{13}C interaction between BTMA⁺ and the ZIF-8 framework and is shown in the Supporting Information (Figure S7). In conclusion, the solid-state NMR data confirms the close contact of IL cation protons to the imidazole of the ZIF-8 wall already noted in the radial distribution function analysis in Figure 3.

While all three constituents of the ILE are found in close contact with the ZIF-8 framework, it is interesting to note that it is only the interaction of the IL cation with ZIF-8, which affects the Raman shifts of the bands in Figure 1. The slope of the linear increase, shown in Figure 1b, is notably different for the different IL-based electrolytes. This suggests that the interactions of the IL cation with the ZIF-8 framework vary for different IL cations, presumably in the order of the strength of the Raman shift. Here, the Lewis acidity of the IL cation might be a governing factor, as

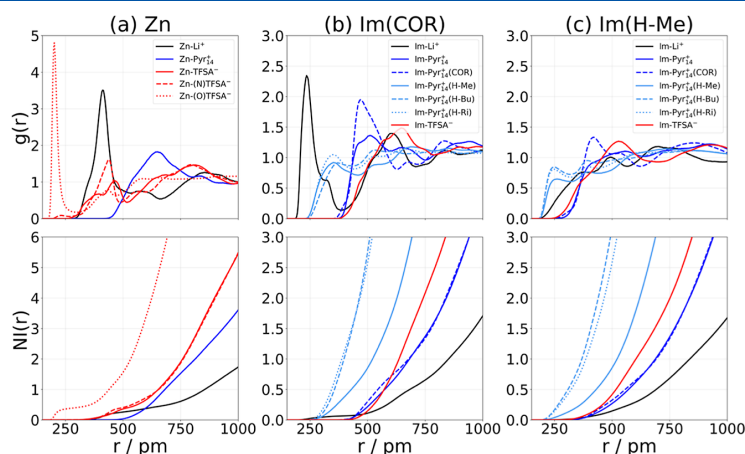


Figure 2. Radial distribution functions of the zinc atoms (a) and methylimidazole units (b,c) of the ZIF-8 structure with respect to the ionic species of the Pyr₁₄⁺-based electrolyte at 300 K and a Li salt fraction of $x = 0.33$ inside the MOF. In case of the methylimidazole units, the center of ring (COR) (b) and the hydrogen atoms of the methyl group were set as reference points (c), respectively.

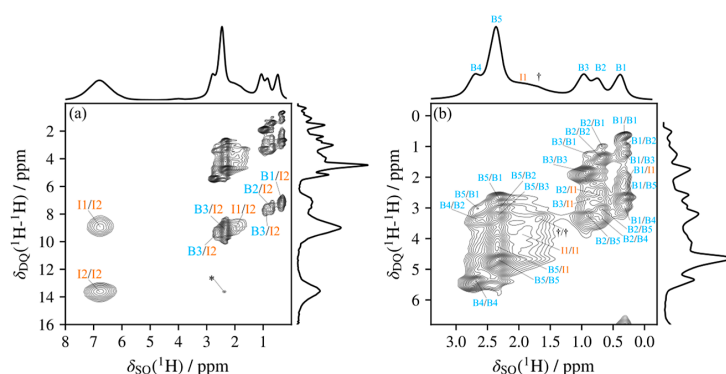


Figure 3. (a) 2D ^1H – ^1H DQ-SQ MAS NMR spectra of the BTMA $^+$ -based electrolyte confined in ZIF-8 with a Li salt fraction of $x = 0.4$ (DQ recoupling times: $\tau_{\text{exc}} = \tau_{\text{rec}} = 6 \tau_{\text{MAS}}$). Signals along the diagonal dashed line indicate autocorrelation signals. (b) Aliphatic region of (a). The assignment scheme and 1D NMR ^1H and ^{13}C MAS NMR spectra used for this assignment are given in Figure S6. The asterisk (*) indicates a spectral artifact owing to t_1 -noise and another signal, which has no definitive assignment and only shows a single autocorrelation signal, is indicated by a dagger (†).

the Raman shifts qualitatively agree with the polarity parameter $E_{\text{T}}(30)$ of the respective IL derived from solvatochromic studies,^{87–89} as shown in the Supporting Information (Table S5). Notably, the shifts are not very high (ca. 1 cm^{-1} for the imidazole ring puckering mode and ca. 2 cm^{-1} for the $\nu(\text{Zn–N})$ mode), such that these differences should rather be considered qualitatively. Nevertheless, with these results it can be shown that different confined IL-based electrolytes have different effects on the ZIF-8 framework, leading to different internal interfaces (see Figure 2).

Influence of Confinement on Li $^+$ Coordination Structure. The structure of the Li $^+$ coordination environment plays an important role for the mobility of Li $^+$. To investigate the effect of different confined electrolytes on this structure, we analyzed the Raman bands of the TFSA $^-$ anion to highlight its role in Li $^+$ coordination. Figure 4 shows the Raman spectra of

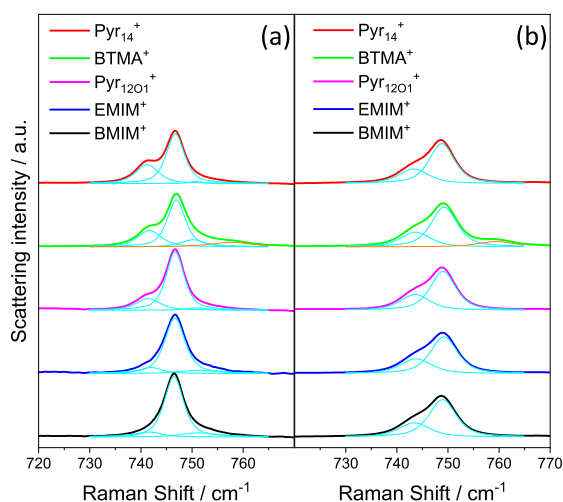


Figure 4. Raman spectra of different IL-based electrolytes confined in ZIF-8 (a) and in bulk (b). Exemplary spectra of the IL with a Li fraction $x = 0.4$, in the spectral region between 720 and 770 cm^{-1} . Cyan lines are TFSA $^-$ signals and orange lines at high wavenumber are BTMA $^+$ signals, all obtained by deconvolution using Voigt profiles.

the different confined ILE in ZIF-8 (a) and in the bulk (b) for the spectral region between 720 and 770 cm^{-1} with a Li salt fraction of $x = 0.4$. The Raman spectra for the other Li salt fractions are shown in Figures S8 + S9.

The band at 742 cm^{-1} can be assigned to the “free” TFSA $^-$ (solvent separated ion pair),^{90,91} which is not coordinated to Li $^+$. The bands at 748 cm^{-1} and 755 cm^{-1} can be assigned, respectively, to TFSA $^-$ coordinated to just one Li cation (contact ion pair) and TFSA $^-$ coordinated to more than one Li cation (aggregates).^{90,91} For the bulk electrolytes no difference in the Raman spectra can be seen, whereas for electrolytes confined in ZIF-8, the band at 742 cm^{-1} notably decreases in the order of Pyr $_{14}^+$ > BTMA $^+$ > Pyr $_{1201}^+$ > EMIM $^+$ > BMIM $^+$.

For all IL-based electrolytes the Raman shift of the “free” TFSA $^-$ is shifted to lower wavenumbers upon confinement in ZIF-8 (Figure S11). This indicates reduced interactions of TFSA $^-$ with its local environment, as already shown for Pyr $_{14}^+$ -based ILE in our previous study.⁶⁰ From the deconvoluted spectra in Figure 4 the integrals of the “free” TFSA $^-$ (A_{f}) and the coordinated species (A_{c} , including both, “contact ion pair” and “aggregate” species) can be determined. A plot of $A_{\text{c}}/(A_{\text{c}} + A_{\text{f}})$ against the Li salt fraction x , which is given in Figure 5b, reveals the coordination number n of Li $^+$, according to

$$\frac{A_{\text{c}}}{A_{\text{c}} + A_{\text{f}}} = \frac{Snx}{(Snx - nx + 1)} \approx nx \quad (4)$$

The equation simplifies with the assumption of a molar Raman scattering coefficient ratio of $S = s_{\text{c}}/s_{\text{f}} = 1$ (s_{f} : “free” TFSA $^-$, s_{c} : Li $^+$ -coordinated TFSA $^-$).⁹²

We showed already earlier for Pyr $_{14}^+$ -based ILE, that the confinement in ZIF-8 affects the coordination number.⁶⁰ The radial distribution function of the Li $^+$ cation and the TFSA $^-$ anion, shown in Figure 5a for $x = 0.33$, confirms the weaker coordination of Li $^+$ by TFSA $^-$ in confinement. As can be seen, the number integral is reduced upon confinement in ZIF-8. This is in qualitative agreement with the slight reduction of the experimentally derived coordination number in the Pyr $_{14}^+$ -based electrolyte (compare Figures 5b + S10) at a low Li salt fraction.

For the other cations the plot of $A_{\text{c}}/(A_{\text{c}} + A_{\text{f}})$ against the Li salt fraction x in Figure 5b shows a distinct dependence on the IL cation, which does not occur in the bulk (Figure S10), where the coordination number is almost the same for the different IL-

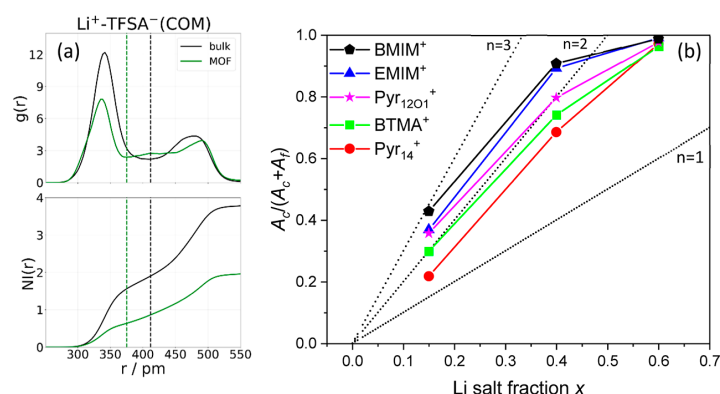


Figure 5. (a) Radial distribution function of the Li cation and the TFSA anion of the Pyr $_{14}^+$ -based electrolyte at 300 K and a Li salt fraction of $x = 0.33$ for bulk ILE and ILE confined in MOF, respectively. The distances (r) of the first maximum and minimum and number integral at the first minimum are listed in Table S4. (b) $A_c/(A_c + A_l)$ against x for different IL-based electrolytes confined in ZIF-8. Colored lines are guides to the eye. Black dotted lines represent the expectation for a given stoichiometry n .

based electrolytes. The average coordination number for electrolytes in confinement is $n = 1.7$ for Pyr $_{14}^+$, $n = 1.9$ for BTMA $^+$, $n = 2.1$ for Pyr $_{1201}^+$, $n = 2.3$ for EMIM $^+$ and $n = 2.4$ for BMIM $^+$. In dependence on the structure of the IL cation it thus follows the same trend as the magnitude of the imidazole Raman shift (Figure 1). Therefore, we see a direct correlation between the strength of the interaction of the IL cation and the ZIF-8 framework with the stoichiometry of Li-TFSA coordination. A strong interaction of the IL cation with the ZIF-8 framework (see Pyr $_{14}^+$) is correlated with a weaker Li-anion coordination, while the weakest IL cation interaction with the ZIF-8 wall (see BMIM $^+$) is associated with a larger coordination number of Li $^+$ to anions. For an understanding of these features, the strong correlation of cation and anion in ILs, which is for example documented by the low ionicity values of ILs, needs to be taken into account. As both constituents, IL cation and Li $^+$, exhibit significant interaction with the wall (see Figure 2), a stronger interaction of the IL cation with the wall would reduce the role of IL cation–anion interactions and allow a more pronounced Li-anion coordination, as observed by the larger Li $^+$ coordination number for weakly wall-interacting IL cations.

We expect that the subtle competition of interactions has an influence on Li dynamics, which we analyze in the next section.

Influence of Confinement on Local Li $^+$ Dynamics. To investigate the local Li $^+$ dynamics, temperature dependent spin–lattice relaxation time (T_1) measurements were performed. In Figure 6 the ^7Li relaxation rates (R_1) are shown for the different IL-based electrolytes at 40% Li salt content (a) in the bulk and (b) confined in ZIF-8. Corresponding data for other Li salt fractions is shown in Figure S12.

Upon confinement of all electrolytes in ZIF-8 the maxima of R_1 ($R_{1,\text{max}}$) are shifted to significantly lower temperatures. In the framework of the BPP model (see eq 2), which assumes a single motional correlation time τ_c , the maximum of R_1 occurs at $\omega_0\tau_{c,\text{max}} = 0.616$, where ω_0 is the Larmor frequency.⁶⁶ Thus, with a constant Larmor frequency, the shift of the maximum to lower temperature reflects the fact that $\tau_{c,\text{max}}$ is already reached at lower temperature. This indicates much faster local Li $^+$ dynamics for all confined electrolytes. In addition, the value of $R_{1,\text{max}}$ increases by a factor of about two. Since $R_{1,\text{max}}$ is mainly dependent on the quadrupolar coupling constant and the local symmetry,⁶⁶ a strong change of the local Li $^+$ environment upon confinement

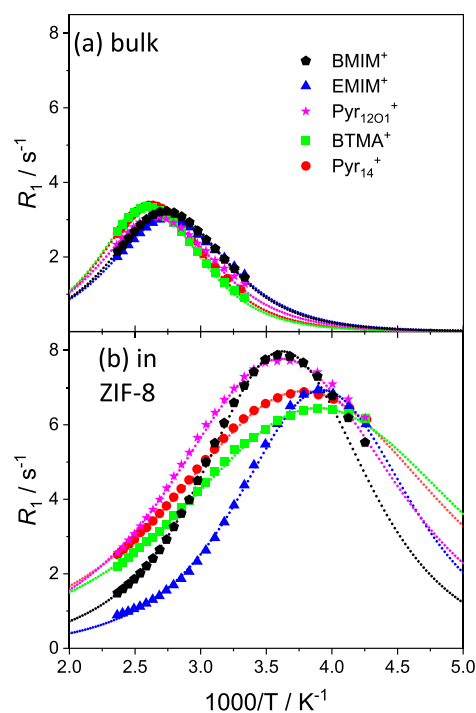


Figure 6. Temperature dependent ^7Li spin–lattice relaxation rates of different IL-based electrolytes in bulk (a) and confined in ZIF-8 (b). Exemplary data for the Li fraction $x = 0.4$. Dotted lines are fits obtained from the BPP-model.

can be concluded. For a quantitative analysis of the relaxation data the BPP model is employed (see the detailed description in Supporting Information, with eqs S1 to S4 and Figure S13). The results for (a) the local motion correlation time τ_c at 298 K and (b) its activation energy E_a are given in Figure 7 for the bulk electrolytes and the electrolytes confined in ZIF-8.

For all electrolytes, τ_c and E_a decrease upon confinement, thus showing faster local dynamics of Li $^+$ as well as lower activation energies of the local motion in confinement. The results for A_{quad}

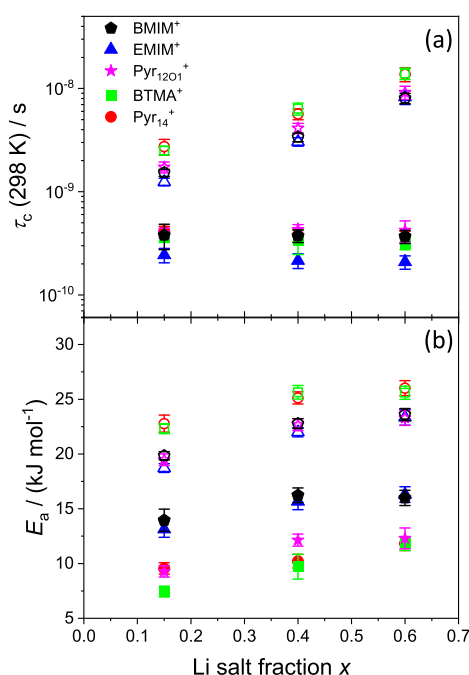


Figure 7. Values of the correlation time τ_c at 298 K (a) and the activation energy E_a (b) of ^7Li for different IL-based electrolytes in bulk (empty symbols) and confined in ZIF-8 (filled symbols) obtained by the BPP model.

are given in Figure S14a. Here, all IL-based electrolytes show a higher prefactor A_{quad} upon confinement in ZIF-8, indicating a more asymmetric local environment for Li^+ , which is consistent with the slightly reduced coordination by TFSA anions, as concluded from the Raman spectra. The asymmetry is most enhanced for those electrolytes with IL cations only weakly interacting with the ZIF-8 wall (e.g., BMIM⁺). This finding could reflect a larger fraction of Li^+ ions at the ZIF-8 wall, where their coordination environment would be more asymmetric, exhibiting a mixed imidazole and TFSA coordination.

As can be seen in Figure 7, the type of IL, the Li salt concentration and the confinement in ZIF-8 have distinct effects on the Li^+ dynamics. In order to focus solely on the effect of confinement on the Li^+ dynamics in each ILE, a correlation time ratio r_τ and an activation energy deviation $E_{a\text{-bulk}}$ are defined as

$$r_\tau = \frac{\tau_c^{\text{ZIF}}}{\tau_c^{\text{bulk}}} \quad (5)$$

and

$$E_{a\text{-bulk}} = E_a^{\text{ZIF}} - E_a^{\text{bulk}} \quad (6)$$

The values for (a) r_τ and (b) $E_{a\text{-bulk}}$ are shown in Figure 8. The dotted lines are guides to the eye and represent the respective values of the bulk. A prefactor ratio r_A was also calculated in analogy to eq 5 and is shown in Figure S14b.

For each electrolyte confined in ZIF-8 r_τ is much lower than one, indicating faster local Li^+ dynamics. This dynamic enhancement of Li^+ becomes even more pronounced at higher Li salt concentrations. Despite showing indications of a trend in

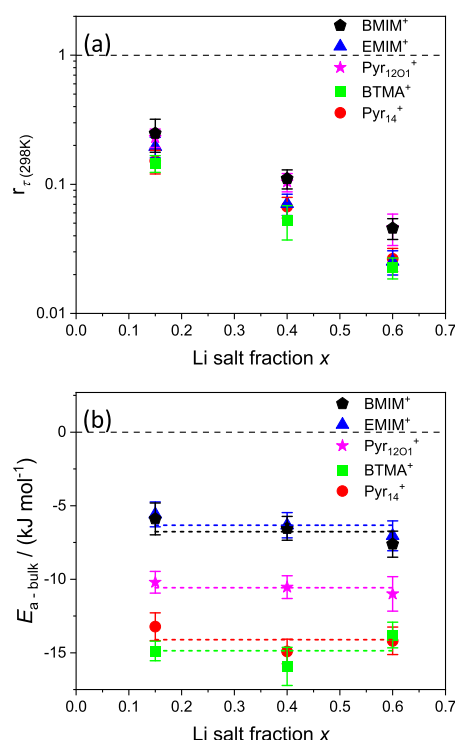


Figure 8. Contrast between bulk and confined behavior as described by the correlation time ratio at 298 K (a) and the activation energy difference (b). The dotted lines are guides to the eye, dashed lines at a value of 1 and 0, resp., represent the respective values of the bulk.

dependence on the type of IL cation, the values of the different electrolytes are mostly within error.

However, for the activation energy change $E_{a\text{-bulk}}$ a clear trend is visible. $E_{a\text{-bulk}}$ is lower than 0 for all electrolytes, suggesting weaker local interactions of Li^+ . Those electrolytes with the strongest interactions of the IL cation with the ZIF-8 framework (Pyr₁₄⁺ and BTMA⁺-based) cause the strongest reduction of E_a , and thus enhancement of Li^+ dynamics upon confinement. This correlation between IL cation–framework interactions and the Li^+ dynamics is remarkable. A possible explanation for this behavior is the competitive coordination of the Li^+ cation and the IL cation to the methylimidazole anion of the framework. The radial distribution functions in Figure 2 showed that the preferential location of Li^+ is near the pore wall, either directly coordinating to the COR of the methylimidazole anion of ZIF-8 or in the second coordination shell around the zinc cation of ZIF-8, presumably coordinated to TFSA⁻. A stronger coordination of the IL cation with the methylimidazole anion could then lead to a shift of the coordination environment of Li^+ toward a more favorable coordination in the second coordination shell.

Although the influence of the IL cation–framework interactions on the Li^+ dynamics cannot be fully explained yet, it is also consistent with the coordination number n of Li^+ determined by the Raman measurements, where a larger $E_{a\text{-bulk}}$ would be expected for higher n .

Influence of Confinement on Ion Transport. Next, we turn to impedance spectroscopy and analyze how far the different IL cations influence the long-range charge transport.

Here, the movement of ions over several pores is tracked. An analysis of the temperature-dependent impedance spectra is given in [Supporting Information](#), demonstrating the validity of time–temperature superposition and Summerfield scaling, i.e. the invariance of the number density of charge carriers with temperature (see [Supporting Information](#), [Figures S15 and S16](#) and accompanying text).

In [Figure 9](#) the dc conductivities of the different IL-based electrolytes confined in ZIF-8 are shown and compared to the bulk conductivities of the respective electrolytes.

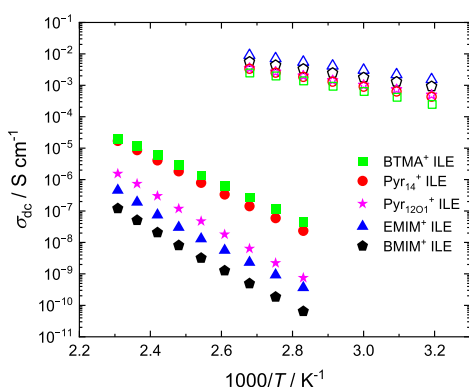


Figure 9. Dc conductivity of different IL-based electrolytes in bulk (empty symbols) and confined in ZIF-8 (filled symbols) for the Li fraction $x = 0.4$.

The bulk conductivities are much higher than the conductivities of the hybrid electrolyte. While another MOF containing Li, but no IL, showed excellent conductivity,⁵¹ ion transport in ZIF-8 is most likely hindered, due to the strong confinement in pores with extremely small pore aperture diameters (3.4 Å),⁹³ which reduces the rate of transitions of ions to adjacent pores. This is also reflected in the higher activation energies of the hybrid electrolytes compared to the respective values of the bulk electrolytes, see Arrhenius fits in [Figure S17](#) and resulting values in [Table S6](#). In comparison, in the MOF HKUST-1 a somewhat larger conductivity of 3 μS/m was found at full coverage with ILE, and it was strongly dependent on the Li addition, and on the degree of pore filling.⁵⁷

Remarkably, however, the conductivity differs by more than 2 orders of magnitude between the various hybrid electrolytes. Such a difference cannot be observed when comparing values of the bulk electrolytes with each other. We note here that the absolute values of conductivity have to be taken with care, since they might be affected by slightly different degrees of pore filling.^{45,47,57} A reduced degree of filling might either result in lower conductivities,^{45,47} or even higher conductivities.⁵⁷ Nevertheless it is interesting to note that the dc conductivity of the hybrid electrolytes follows a similar trend in relation to the IL cation–framework interactions, as described above for the local Li⁺ dynamics. For the electrolytes where the interactions of the IL cation with the ZIF-8 framework caused the strongest Raman shift, the highest conductivities are observed. In the following we build the interpretation on the discussion of the activation energy deviation E_{a-bulk} , which should not be affected by pore filling issues. The deviation E_{a-bulk} is defined here in analogy to [eq 6](#) for the activation energy of conductivity and calculated from the respective values of E_a in [Table S6](#). The

results are given in [Table 1](#) and represent again a clear trend of a more beneficial transport in case of BTMA⁺ and Pyr₁₄⁺-based

Table 1. Activation Energy Deviation E_{a-bulk} of the dc Conductivity for Different IL-Based Electrolytes for the Li Fraction $x = 0.4$

electrolyte	BTMA ⁺	Pyr ₁₄ ⁺	Pyr ₁₂₀₁ ⁺	EMIM ⁺	BMIM ⁺
$E_{a-bulk}/\text{kJ mol}^{-1}$	62	72	91	90	93

confined ILE as opposed to other IL cations. The interpretation is more complex in this case, as the partial conductivities of all ions in the sample contribute to the overall conductivity.

[Figure 10](#) shows a comparison between the mean square displacement (MSD) of the ionic species of the Pyr₁₄⁺-based electrolyte at a Li salt fraction of $x = 0.33$ in bulk at 300 K (a) and confined in ZIF-8 at 300 K (b) and 600 K (c), with respect to the correlation time τ . At 300 K (b), the dynamics of the ions are slow, and the MSD does not exceed the pore size, therefore not reflecting the long-range diffusive behavior of the ions, even after 50 ns of simulation time. Simulations at an elevated temperature were included to characterize the transport mechanism of the species within the confinement, see [Figure 10c](#).

As can be seen in [Figure 10a](#), Pyr₁₄⁺ is the fastest diffusing species in the bulk, followed by TFSA[−] and then Li⁺ as the slowest species. This order is in agreement with experimentally derived diffusion coefficients of ILE from PFG-NMR^{94,95} and can be explained by the formation of Li-TFSA clusters, which reduce the dynamics of TFSA[−] and especially of Li⁺. For higher Li salt fractions, the TFSA[−] displacements even approach the ones of Li⁺ ([Figure S18](#)), due to a higher share of TFSA anions being present in Li-TFSA clusters. In contrast to this, [Figure 10b](#) shows that in confinement Li⁺ is the fastest species, followed by Pyr₁₄⁺ and then TFSA[−]. In the 300 K simulation, the MSD in the diffusive regime is smaller than the pore diameter, and during the simulated time interval τ the ions primarily rattle around their initial positions. However, in the simulation at 600 K, the MSD exhibits a short ballistic regime ($\tau < 1$ ns) from 0 to approximately 4 Å², reflecting ion mobility within a single ZIF-8 cage. This is followed by a diffusive regime, with MSD(τ) showing an almost linear trend, describing the ion movement between pores. [Figure S21](#) depicts a three-dimensional occurrence of Li⁺ positions within the ZIF-8 structure at 600 K, to visualize the Li⁺ transfer between adjacent pores. The slight flattening of the slope of the respective MSDs between $\tau = 3$ –9 indicates a transition from subdiffusive to diffusive behavior of the ions. The difference between the displacement of Li⁺ and the other ionic species is increased for higher temperatures. A comparison for all studied temperatures is shown in [Figure S19](#). For the ZIF-8 system modeled at 600 K, diffusion coefficients were derived from the MSDs as described in [Figure S20/ Table S7](#) and accompanying text in the [Supporting Information](#). The ideal transference number for Li⁺ was calculated from the diffusion coefficients, which results in a value of $t_{+}^{\text{ideal}} = 0.23 \pm 0.08$.

The larger MSD of Li⁺ indicates that Li⁺ is not predominantly moving together with counterions in a larger complex, but there is independent Li⁺ transport through the pores. Two videos presented in [SI](#) exemplarily show the ligand exchange between anion and Li⁺ ion, which allows Li⁺ displacement in space without significant anion displacement, thus rationalizing the findings of the MSD on a local length scale. Therefore, the mechanism of Li⁺ transport is a ligand exchange as suggested for

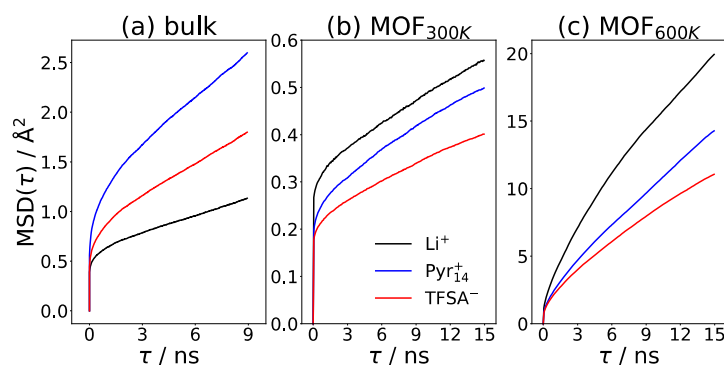


Figure 10. Mean square displacement of the ionic species of the Pyr_{14}^+ -based electrolyte with a Li salt fraction of $x = 0.33$ in bulk at 300 K (a), and within the confinement of the ZIF-8 structure at 300 K (b) and at 600 K (c).

similar systems,⁵⁷ rather than a vehicular transport in Li-anion clusters as observed in bulk.^{20,21} Interestingly, a similar inversion of the order of diffusion coefficients of the different species has also been observed in ILE in HKUST-1, where Li is also the fastest species.⁵⁷ The authors attributed this to a pore blocking of the large IL ions, while Li^+ ions can diffuse via a ligand exchange. We believe that our data for ZIF-8 reflect a similar mechanism, where the pore-to-pore passage is not possible for Li-anion clusters, which are the transport-relevant species in bulk ILE, but a ligand exchange is required for Li ions to transfer to an adjacent pore.

Notably, the MSDs do not converge against a limit, and at high temperature (see Figure 10c) the simulations cover a distance far larger than the pore size. This is evidence that the displacements observed here are not restricted to one pore, and all ionic species are able to undergo long-range transport over different pores.

The transition of the Li^+ transport mechanism from vehicular Li-anion transport to uncorrelated motion of Li^+ as the fastest species could explain the large difference in conductivity for confined ILE with different IL cations. As the fastest species in ZIF-8 pores the influence of Li^+ transport on the overall conductivity should be dominant. Indeed, the electrolytes with the lowest activation energy enhancement for the local dynamics (Figure 8b; BTMA^+ and Pyr_{14}^+) exhibit the highest conductivities in confinement (Figure 9).

CONCLUSION

We were able to show that the interactions between IL cation and MOF framework can have significant impact on the Li^+ ion dynamics, and on ionic transport. MD simulations showed complex interactions of the IL-based electrolytes with the ZIF-8 framework, where IL cation and Li^+ are in competition to coordinate to the methylimidazole anion of the framework. Li^+ coordinates preferentially to the imidazole ring, and the IL cation to the methyl group (see Figure 2b,c). The anion TFSA^- is found close to the Zn^{2+} cation of the pore wall, with Li^+ in the second coordination shell (Figure 2a).

Raman studies elucidated different coordination behaviors of the IL to the MOF in dependence on the IL cation employed. The structure of the cation gave rise to a change in Li^+ coordination environments, local Li^+ dynamics and conductivities. A trend was visible where a stronger Raman shift of the methylimidazole ring puckering mode induced by the IL cation correlated with lower Li^+ coordination numbers to TFSA^- ,

enhanced local Li dynamics and higher total conductivities of the hybrid electrolytes. The balance of the competitive coordination of IL cation and Li^+ to the framework is decisive for these improved properties. A stronger coordination of the IL cation to the framework could modify the dominating coordination environment of the Li^+ ions, with consequences for the dynamic behavior of Li^+ . We showed that in confinement the Li^+ ions move independently of their counterions as the fastest species (Figure 10), via a ligand exchange mechanism as already discussed for similar systems in the literature.^{47,57} This is in contrast to the transport mechanism in bulk, which is dominated by vehicular Li-anion transport.^{20,21} This structural Li^+ transport involves the breakup of Li-anion clusters and also explains the comparatively lower activation energy of conductivity in combination with the lowest activation energies of the local Li^+ motion for those IL cations strongly interacting with the walls.

Overall, the confinement of IL in ZIF-8 causes reduced long-range charge transport, but a strong interaction of the IL cation to the framework is beneficial in terms of enhancing local Li^+ dynamics by subtle changes of the respective ion–ion interactions. A breakup of Li-anion clusters, by interactions of the IL-ions with the MOF framework, is a desired property in the hybrid electrolytes to enhance Li^+ dynamics. Too strong interactions of Li^+ itself with the rigid framework could however have negative effects on the Li^+ dynamics. Blocking these Li^+ -framework interactions by other competitive interactions might be an effective strategy to enhance Li-dynamics and increase Li conductivity in a MOF. While ZIF-8 serves as a model system in the present work, other MOFs with larger pore sizes and further tailored interactions might provide similarly positive impacts on the local Li-dynamics as ZIF-8, while reducing overall transport limitations.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.jpcb.5c01702>.

Details of experimental and computational methods, further Raman spectra and their deconvolution procedure and coordination number analysis, MAS SS NMR spectra, ^7Li spin relaxation analysis in BPP model, T -dependent conductivity spectra and their scaling, mean square displacements and diffusion coefficients from simulations, visualization of Li occurrence (PDF)

Visualization of Li⁺ transport by ligand exchange (MP4)
(MP4)

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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Notes

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Appendix: Carbon polarization and carbon nanotube stacking impacts the behavior of water in nanoconfinement

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Own contributions

- Conceptualizing the scope of the paper.
- Running all MD simulations and partially analyzing the trajectories.
- Writing the introduction, method section, most of the discussion as well as the conclusion.

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Carbon Polarization and Carbon Nanotube Stacking Impacts the Behavior of Water in Nanoconfinement

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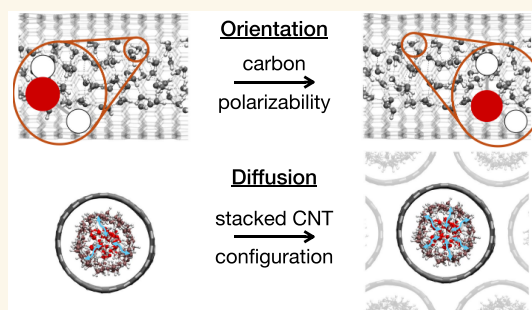
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ABSTRACT: The structural and dynamical properties of water confined in subnanometer, single-walled carbon nanotubes (CNTs) are investigated using molecular dynamics simulations. With radii ranging from 4 to 8 Å, we assess confinement-size effects using fully flexible CNTs with explicit carbon polarizability and the MB-pol water model. Density distributions reveal, that single-file water chains form in the narrow (10,0) CNT, pentagonal ring structures form in the intermediate (15,0) CNT, and a two-layer arrangement forms in the wider (20,0) CNT. Angular distributions show that the influence of carbon polarization on water orientation grows with CNT diameter, accompanied by a pronounced tilt of water molecules toward the CNT wall. Comparisons with the TIP4P/2005f model indicate that while this classical model captures structural trends, MB-pol affords a deeper description of interfacial water behavior by enabling direct simulations of infrared spectra from dipole trajectories and consistently accounting for polarization effects. Finally, simulations of vertically aligned CNT arrays demonstrate that intertube interactions significantly impact water dynamics: in stacked (20,0) configurations, intermittent hydrogen-bond lifetimes decrease by 20–25% and layer residence times drop by up to 20% relative to isolated CNTs. These findings illustrate the complex relationship between water structure and dynamics in relation to the size of the confinement and show that carbon polarizability and explicitly considering multiple CNTs are important factors to consider in modeling confined water.

KEYWORDS: nanoconfined water single-walled carbon nanotubes carbon nanotube stacking carbon polarizability MB-pol hydrogen-bond dynamics infrared spectroscopy



INTRODUCTION

Confinement significantly alters both the structural arrangement and diffusive properties of water, as demonstrated in numerous experimental^{1–4} and theoretical studies,^{5–13} many of which rely on molecular dynamics (MD) simulations. These changes are governed by steric constraints imposed by the confining geometry and size, as well as by the altered formation and reorganization of hydrogen-bond networks.¹¹ As a result, the behavior of water under confinement fundamentally differs from its bulk-phase behavior. Several studies have reported phase transitions and the formation of nanoice phases when water is confined at the nanoscale.^{14–21} These transitions are highly dependent on the structure and geometry of the confining substrate.

The present study focuses exclusively on the confinement of water within single walled carbon nanotubes (SWCNTs), which will hereafter be referred to simply as CNTs. CNT membranes and other nanoporous carbon materials are of technological interest in applications such as desalination membranes^{22–26} and energy storage devices.^{27–30} Beyond isolated CNTs, we also consider arrays of vertically aligned carbon nanotubes

(VANTAs).³¹ The stacking of multiple CNTs of the same kind yields a highly anisotropic system, and collective confinement effects between water in adjacent pores are conceivable. Experimental studies on VANTAs have demonstrated exceptionally fast water transport.^{32,33}

Numerous reviews^{9,34,35} describe the considerable progress made in understanding the behavior of water confined inside CNTs. Nevertheless, several common simplifications in modeling CNT–water systems leave room for improvement. One frequent assumption is to treat CNTs as perfectly rigid, nonpolar materials fixed in space during simulations. While computationally efficient and easy to implement, this approach may influence how water packs inside the pore and its diffusivity. Chemical intuition suggests that polarization effects at the

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108

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CS Nano 2026 20 1304–1315

CNT/water interface could influence the arrangement of the polar water molecules. Indeed, studies have shown that polarized or charged surfaces significantly impact the structure of interfacial water.^{36–42} Furthermore, coupling between the confined water and the longitudinal phonon modes of a flexible CNT may affect water's diffusive behavior. In fact, CNT wall flexibility has been reported to reduce interfacial friction and enhance flow, leading to greater water mobility.^{43–46} In addition to structural arrangement and dynamics, confinement also impacts the chemical behavior of water. For instance, it was recently shown that confinement affects Grotthuss diffusion (i.e., proton-hopping mechanism)^{47–49} as well as the auto-ionization equilibrium of water.⁵⁰ Both processes are sensitive to the local hydrogen-bond network and are thus influenced by the geometry and size of the confined space.

A CNT's atomic structure, determined by its chiral indices (m, n), strongly influences its electronic properties. The chiral indices are defined by the vector $\vec{c} = m\vec{a} + n\vec{b}$, where $\vec{a}$ and $\vec{b}$ are the unit vectors of a graphene lattice. The vector $\vec{c}$ describes the direction in which a graphene sheet is rolled into a tube. Armchair CNTs correspond to $m = n$, zigzag CNTs to $n = 0$, and any other combination ($m \neq n$) yields a chiral CNT. Armchair CNTs behave as quasi one-dimensional metals along the tube axis, whereas zigzag nanotubes are semiconducting. The band gap is further influenced by the nanotube radius and curvature, with particularly pronounced effects for the smallest nanotubes.

In the present study, three zigzag CNTs with radii ranging from approximately 4 to 8 Å are investigated ($(N,0)$ CNTs with $N = 10, 15, 20$) to assess how confinement size influences the structural and dynamical behavior of confined water. To address the aforementioned modeling limitations, the CNTs are treated as fully flexible entities. The MB-pol^{51–57} potential is employed to model water. This advanced model explicitly includes many-body and polarization effects and accurately reproduces the properties of water across a wide range of temperatures and pressures.^{55,57–59} We therefore consider MB-pol suitable for simulations in confined spaces, since an accurate description of phase transitions within confinement is essential. In order to fully account for polarization effects in both water and the CNTs, the Dreiding⁶⁰ force field with polarizable carbon atoms is employed to model the CNTs.

An overview of all systems studied is given in Table 1. To quantify the effects of CNT–water polarization, each simulation was run with and without accounting for carbon polarization. Additional simulations compare water packing and diffusivity in a single CNT ($N_{\text{pol}}^{\text{single}}$ vs $N_{\text{pol}}^{\text{single}}$ for $N = 10, 15, 20$) against those with CNTs arranged in a tightly stacked configuration mimicking a VANTA ($N_{\text{pol}}^{\text{stacked}}$ vs $N_{\text{pol}}^{\text{stacked}}$). This allows us to

examine possible interactions between water in adjacent nanotubes. Furthermore, the flexible TIP4P/2005f⁶¹ water model, which has been used in previous CNT studies,^{62,63} is employed to assess how the choice of water model impacts the confined water properties. For brevity, we use the subscript “TIP4P” to indicate systems in which this model was used (e.g., $N_{\text{TIP4P}}^{\text{single}}$ vs $N_{\text{TIP4P}}^{\text{stacked}}$). Carbon atom polarizability was not considered in systems employing the TIP4P/2005f water model. Three independent replica simulations were carried out for each production run. An additional MB-pol bulk water simulation was carried out for reference. Unless stated otherwise, all reported results correspond to averages over these replica simulations.

RESULTS AND DISCUSSION

Density Distributions

To quantify the spatial arrangements of water (see exemplary systems in Figure 1a–d), density distributions were calculated. All density distributions (Figure 2a–c) qualitatively agree with previously reported results for CNTs of similar radius.^{11,64} However, there are distinct deviations when comparing the

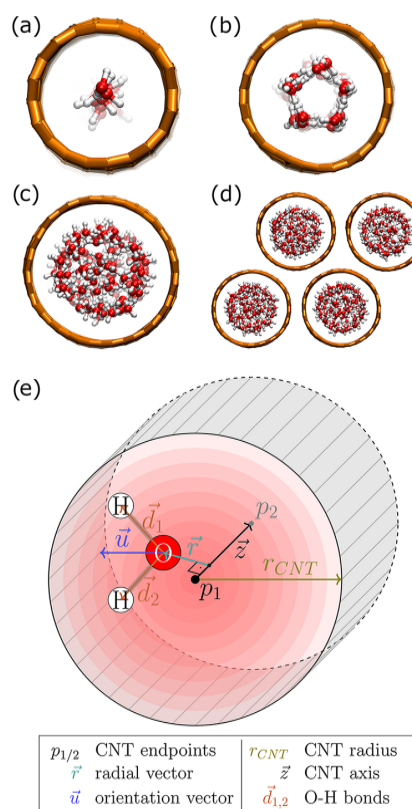


Figure 1. Snapshots of the single-CNT systems (a) $10_{\text{pol}}^{\text{single}}$, (b) $15_{\text{pol}}^{\text{single}}$, (c) $20_{\text{pol}}^{\text{single}}$ and exemplary stacked-CNT system (d) $20_{\text{pol}}^{\text{stacked}}$. The water is shown in a ball-and-stick model, the CNT in bond depiction (color code: oxygen = red; hydrogen = white; carbon = orange). (e) Scheme of a CNT with radial layers in the tube (red shades) and a water molecule. Key vectors: CNT radius r_{CNT} (olive), center axis z between end points p_1 and p_2 (black), radial vector $\vec{r}$ (teal), bond vectors $\vec{d}_1$ and $\vec{d}_2$ (orange), and their bisector $\vec{u}$ (blue).

Table 1. Overview of the Production Runs of the $(N,0)$ CNT Systems N^a

system N	n_{CNT}	n_{C}	$l_z/\text{\AA}$	$n_{\text{H}_2\text{O}}$
$10_{\text{pol}}^{\text{single}}/10_{\text{pol}}^{\text{single}}/10_{\text{TIP4P}}^{\text{single}}$	1	1000	107.3	39
$15_{\text{pol}}^{\text{single}}/15_{\text{pol}}^{\text{single}}/15_{\text{TIP4P}}^{\text{single}}$	1	1020	72.85	125
$20_{\text{pol}}^{\text{single}}/20_{\text{pol}}^{\text{single}}/20_{\text{TIP4P}}^{\text{single}}$	1	1120	59.92	215
$10_{\text{pol}}^{\text{stacked}}/10_{\text{pol}}^{\text{stacked}}/10_{\text{TIP4P}}^{\text{stacked}}$	4	4000	107.2	156
$15_{\text{pol}}^{\text{stacked}}/15_{\text{pol}}^{\text{stacked}}/15_{\text{TIP4P}}^{\text{stacked}}$	4	4080	72.80	500
$20_{\text{pol}}^{\text{stacked}}/20_{\text{pol}}^{\text{stacked}}/20_{\text{TIP4P}}^{\text{stacked}}$	4	4480	59.92	860

^aThe following is listed for each system: the number of CNTs, n_{CNT} , the carbon atom count n_{C} , the axial z-axis length l_z and the number of confined water molecules $n_{\text{H}_2\text{O}}$.

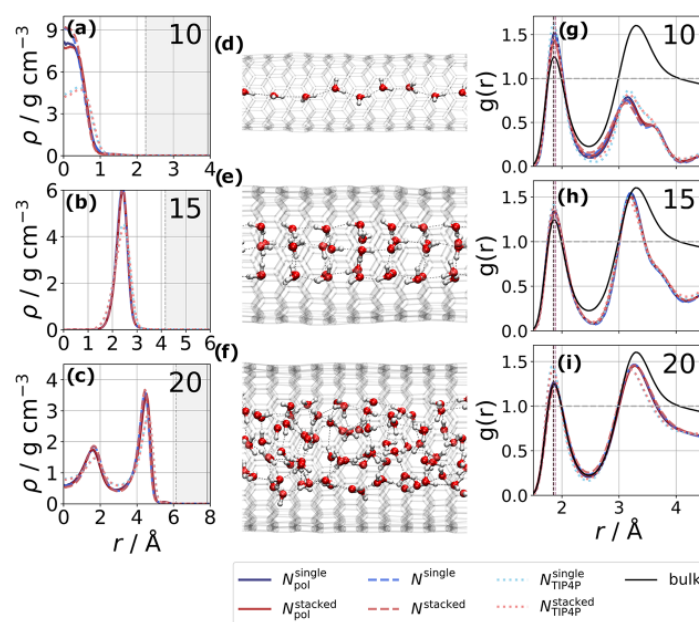


Figure 2. (a–c) Comparison of the density distributions of water within a given CNT. The area colored in light gray corresponds to the area occupied by the carbon atoms (carbon van-der-Waals radius); (d–f) side view of the CNTs filled with water. Water is shown in a ball-and-stick model, the CNT in bond depiction (color code: oxygen = red; hydrogen = white; carbon = gray/transparent); (g–i) intermolecular radial distribution functions between the hydrogen and oxygen atoms of the confined water. The positions of the maxima are shown as vertical, dashed lines. The bulk reference distribution in black; Top = systems 10; center = systems 15; bottom = systems 20.

density profiles obtained from MB-pol and TIP4P/2005f simulations (compare dotted with solid and dashed lines). In Systems 10, water molecules form a single-file chain along the CNT axis.⁶⁵ For MB-pol, water molecules preferentially occupy the center of the CNT, with a slight density shift toward the CNT wall when accounting for carbon polarization, yielding a shallow plateau for $r = 0.0 - 0.3$ Å. In comparison, water shifts toward the carbon wall in TIP4P/2005f simulations, reaching a maximum density at $r = 0.5$ Å. Intermolecular radial distribution functions (RDFs) between oxygen and hydrogen atoms reveal no significant differences in hydrogen-bond length across the models, with maxima of $g(r)$ located at $r = 1.85 - 1.88$ Å (see Figure 2g–i and Table S5 in SI). The RDFs are scaled such that the integral up to the first minimum is equal across all methods. The maxima of $g(r)$ are largest for the TIP4P/2005f model across all CNT radii, indicating a tendency toward a more rigid network.

The density distributions of systems 15 exhibit a distinct peak at $r = 2.5$ Å, describing the tubular arrangement of water molecules within the confinement (Figures 1b and 2e). The arrangement can be simplified as an ice-like structure with pentagonal rings of five water molecules in radial planes, stacked along the CNT axis.¹⁶ A similar structural motif has been reported in literature for CNTs of comparable radius.^{64,66} Differences between the models are minor, with slightly broader maxima for the 15_{TIP4P} systems, while the density profiles for systems simulated with MB-pol are almost identical.

The most complex density profiles emerge in systems 20, showing two maxima at $r = 1.6 - 1.8$ Å and $r = 4.4 - 4.6$ Å, corresponding to two distinct tubular layers (Figure 1c). Notably, the density never falls below 0.4 g cm^{−3} for $r < 4.8$ Å, suggesting exchange of water molecules between layers. This is

especially the case for 20_{TIP4P}^{single} and 20_{TIP4P}^{stacked}, where minima and maxima are least pronounced, indicating more frequent interlayer motion. A noticeable shift also occurs for TIP4P/2005f, with both maxima located at larger values of r relative to MB-pol.

For all models, comparing the density profiles of the single and stacked CNT configurations (red versus blue in Figure 2) shows good agreement, highlighting that stacking of multiple CNTs does not affect the radial density distributions of confined water (Figures S11–S13 in the SI). Differences when modeling polarizable and nonpolarizable CNTs are also minor (Figures S14–S16 in the SI). Still, subtle shifts are observed in systems 10_{pol}, where part of the density is shifted away from the tube center, reducing the maximum at $r = 0$. In the wider systems 20_{pol}, the density maximum of the outer tubular layer is slightly displaced toward the wall compared to the nonpolarizable CNT systems, while the inner maximum moves inward. A small additional peak appears at $r \approx 5.5$ Å (Figure S16 in the SI), which reflects hydrogen atoms approaching the interface to enhance the water–wall interactions.

Angular Distribution

Additional insight is gained by analyzing the orientational distributions of the confined water molecules. Three angles are considered, which are defined as follows (see Figure 1):

1. θ : the angle between the radial vector $\vec{r}$ (pointing from the CNT center axis toward the water molecule's oxygen) and the water's bisector $\vec{u}$.
2. β : the angle between the CNT's axis $\vec{z}$ and the water's bisector $\vec{u}$.
3. ϕ : the angle between the CNT's axis $\vec{z}$ and either of the O–H bond vectors $\vec{d}_1$ or $\vec{d}_2$.

For $\theta = 0^\circ$, the bisector $\vec{u}$ points directly toward the CNT wall, while at $\theta = 180^\circ$ it points toward the CNT axis; $\theta = 90^\circ$ indicates that the bisector is tangential to the wall. For $\beta = 0^\circ$, $\vec{u}$ aligns with the CNT axis, whereas $\beta = 90^\circ$ indicates that the bisector lies in a plane orthogonal to the CNT axis. The same is true for ϕ and the alignment of $\vec{d}_{1,2}$. Due to the CNT symmetry β and ϕ are mirror-symmetric at 90° . The angular distributions of θ and β are shown in Figure 3a–f as a function of the relative

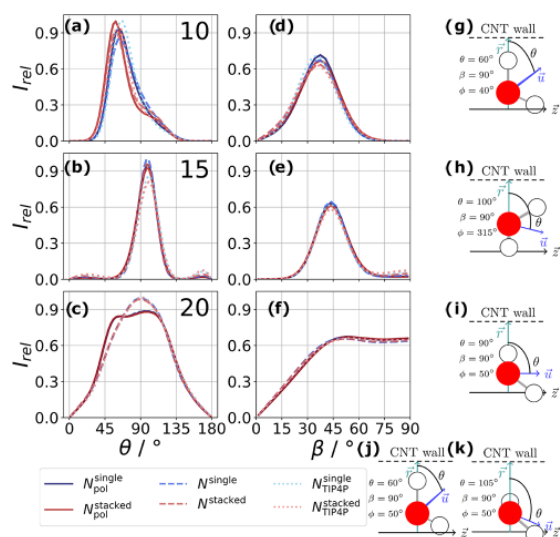


Figure 3. (a–c) Angular distributions of the angle θ between the radial vector $\vec{r}$ of the center axis and the bisector of the water O–H bonds $\vec{u}$; (d–f) angular distributions of the angle β between the center axis $\vec{z}$ of a given CNT and the bisector of the water O–H bonds $\vec{u}$. Both angles are plotted against the relative intensity I_{rel} ; (g–k) schematics showing a water molecule at exemplary orientations, at the most populated angles θ, β and ϕ for a given CNT size; top = systems 10; center = systems 15; bottom = systems 20.

intensity I_{rel} . (Distributions of ϕ are similar across all systems of a given CNT size and are provided in Figure S19 in the SI.) For each CNT size, I_{rel} is normalized to the highest observed peak among all models. Using the three defined angles, the most probable orientation of a water molecule within the confinement can be constructed, depicted in Figure 3g–k (g: 10; h: 15; i–k: 20).

In the narrowest tubes (systems 10), the angular distributions exhibit pronounced maxima at $\theta \approx 60^\circ$ and $\beta \approx 40^\circ$. This corresponds to an orientation in which one O–H bond points toward the CNT wall while the other O–H bond is directed more along $\vec{z}$ (see Figure 3a,d,g for visualization). The driving force for this orientation is the one-dimensional hydrogen-bond wire formed between nearest-neighbor water molecules along the single-file chain inside the CNT (Figure 2d). This single-file hydrogen-bond arrangement enforces a specific tilt of each water molecule, consistent with previous observations of oriented single-file water in hydrophobic nanopores.^{65,67} The choice of water model and CNT stacking configuration both have a minor effect: Using the MB-pol model and modeling stacked systems both impact the water molecule orientation, favoring smaller θ and β angles (i.e., water molecules are more aligned along the tube) compared to the other systems.

For the intermediate diameter systems 15, the distributions have maxima at $\theta \approx 100^\circ$ and $\beta \approx 42^\circ$. This orientation aligns with the visual observations of water forming stacked pentagonal rings within the CNT (Figures 1b and 2e). Within each pentagon, the water molecules form in-plane hydrogen bonds. However, each water also has one hydrogen pointing out of the pentagon plane toward the adjacent rings, which distorts the ideal pentagonal geometry slightly but maximizes the O···H interaction between neighboring rings. This arrangement—essentially a single-walled ice-like nanotube of pentagonal cross-section—has been reported in previous simulations for water confined in similarly sized CNTs.¹⁶ Variations in the water model or CNT stacking have a negligible effect on these angular distributions for 15, indicating a robust structure dominated by the water–water hydrogen-bond network within and between the rings.

In the largest confinement (systems 20), water molecules have substantially more orientational freedom, yet the confinement still imposes noticeable ordering. All angles in the range $45^\circ < \beta < 90^\circ$ occur with comparable probability, whereas configurations with $\beta < 45^\circ$ (water bisector more aligned with the tube axis) are increasingly unfavorable. This trend underscores that even in the widest CNT we considered, the water molecules' orientations are biased by the confining walls—an effect noted in previous studies as well, wherein interfacial water tends to align parallel to hydrophobic surfaces to maximize hydrogen bonding in the first adsorbed layer.^{5,16} The most striking feature in systems 20 is found in the θ distribution. With nonpolarizable CNTs combined with either MB-pol or TIP4P/2005f water, θ displays a clear peak around 90° , with I_{rel} falling off toward smaller and larger angles. However, when carbon polarizability is included in the simulations with MB-pol, the θ profile is dramatically altered: the intensity for intermediate angles between 30° and 70° is enhanced at the expense of the intensity in the 70° – 120° range. As a result, the θ distribution in 20_{pol} becomes broad and flattened, with a plateau between roughly 55° and 110° . Water molecules in the polarizable-carbon case tilt more toward the wall than in the nonpolarizable case, as illustrated by the schematics in Figure 3i–k. In contrast to the small systems (10), the distinction between single and stacked CNT configurations has no noticeable effect on the angle distributions. This showcases that, depending on the confinement size, different factors dominate the orientational preference: in the narrow tube (10), the geometric arrangement (single vs stacked CNT) plays a role in modulating orientations, whereas in the wider tube (20), the polarization of the carbon atoms governs the water orientation, overwhelming any subtle effects of the CNT stacking geometry.

To further elucidate the shift in θ observed for systems 20 upon including carbon polarizability, we computed combined angle-radial distribution functions, revealing how preferred orientation of water molecules vary with radial position in the CNT (Figure 4a). As an example, Figure S20 in the SI shows θ distributions for water at $r = 4.0 - 4.8$ Å (the first hydration layer at the interface) in $20_{stacked}^{stacked}$ vs $20_{pol}^{stacked}$. All occurrences are normalized to the global maximum and expressed as I_{rel} . Additionally, following a similar approach used in previous studies,⁶⁸ radial Sections S0–S2 are defined, based on the radial density distributions (Figure 4b and Table S6 in the SI). Sections S0 and S1 are separated by the minimum in the corresponding radial density profile, marking the boundary between the distinct tubular water layers. Section S2 comprises the water molecules located at the largest radial distances, closest

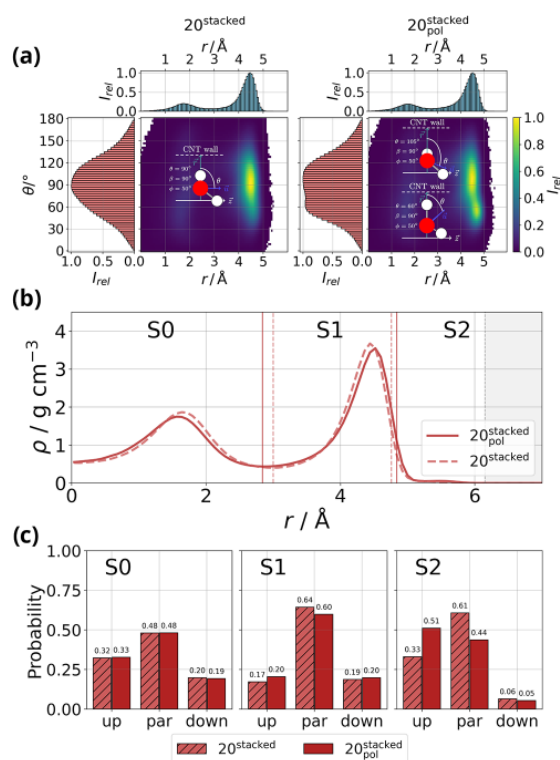


Figure 4. (a) Combined distribution function of systems 20^{stacked} and $20^{\text{stacked}_{\text{pol}}}$. The schematics (also shown in Figures 3i–k) show the favored orientation of water molecules at the respective maxima. Please note, the larger distances (5 $\text{\AA}$) indicate a close distance to the CNT wall, while small distances indicate the location at its center axis. (b) Density distributions of systems 20^{stacked} and $20^{\text{stacked}_{\text{pol}}}$. The density distributions are divided into three sections, labeled S0–S2 (see Table S6 in the SI). (c) Water orientation probability function of the angle θ for each identified Section S0–S2. The orientation is grouped into three groups: up ($0^\circ \leq \theta < 60^\circ$); par ($60^\circ \leq \theta < 120^\circ$); down ($120^\circ < \theta \leq 180^\circ$).

to the CNT wall. The section starts at the radial increment where the density is less than half of the maximum value observed in S1.

The observed water orientations are sorted into three groups (Figure 4c): Facing toward the CNT up ($0^\circ \leq \theta < 60^\circ$); In a parallel orientation with respect to the CNT wall par ($60^\circ \leq \theta < 120^\circ$); Facing toward the CNT center down ($120^\circ < \theta \leq 180^\circ$).

In the nonpolarizable case, 20^{stacked} , the most populated orientation at the interface occurs at $r = 4.4$ $\text{\AA}$ with $\theta \approx 90^\circ$, corresponding to the configuration depicted in the schematic (also shown in Figure 3i). Up to this distance, the $20^{\text{stacked}_{\text{pol}}}$ distribution follows the same trend. However, at slightly larger radii ($r = 4.6$ $\text{\AA}$ and beyond), the polarizable-carbon system develops a new preferred orientation. An additional peak emerges at $\theta \approx 60^\circ$, which becomes more pronounced at $r = 4.8$ $\text{\AA}$. Concurrently, the original peak seen in 20^{stacked} at $\theta \approx 90^\circ$ shifts to larger angles of $\theta \approx 105^\circ$ in the polarizable system ($20^{\text{stacked}_{\text{pol}}}$). This results in two new water orientations near the CNT wall when carbon polarization is included, as shown by the schematics in Figure 4 and Figure 3j,k. At $\theta \approx 105^\circ$, one O–H bond of the water molecule is rotated slightly away from the wall,

compared to the configuration at $\theta \approx 90^\circ$, while the other O–H bond remains roughly pointing toward the CNT interior. By contrast, for $\theta \approx 60^\circ$, one O–H bond of the water molecule points directly toward the carbon wall. The rise in intensity of these $\theta \approx 60^\circ$ orientations at $r > 4.6$ $\text{\AA}$ correlates with our earlier observation (from the density profiles) that hydrogen atoms at the interface move closer to the CNT wall when carbon polarization is included. These combined angle–radius distribution functions also demonstrate that the shift in the overall angle distribution of θ (Figure 3c), i.e., the tilt of the water bisector relative to $\vec{r}$, originates from the interfacial water layer. This effect is especially present comparing the probability distributions shown in Figure 4c: In Section S0, the preferred orientation is parallel to the CNT wall. This orientation is even more prevalent in Section S1, where 60–64% of all analyzed orientations are in the “par” category. For both sections, 20^{stacked} and $20^{\text{stacked}_{\text{pol}}}$ are in good agreement, especially for S0. However, significant differences are observed for Section S2, which describes the molecules closest to the CNT surface. While the “down” orientation is generally depopulated compared to S0 and S1, the preferred orientation of water shifts from a parallel alignment with respect to the CNT wall to water molecules facing the carbon wall when carbon polarization is considered. This is accompanied by an 18% increase in the probability of finding a water molecule facing toward the carbon wall (“up”), comparing 20^{stacked} and $20^{\text{stacked}_{\text{pol}}}$. Thus, carbon polarization selectively stabilizes configurations in which a water molecule’s bisector tilts toward the wall, altering the preferred orientation of the molecules nearest to the CNT surface.

In summary, for the smaller confinements (10 and 15), including carbon polarization has a minimal effect on water orientations. This suggests that the dominant factor governing both radial positions and orientations in those systems is the interaction between neighbor water molecules and the formation of the hydrogen-bond network. In the tight one-dimensional chain of 10 or the pentagonal ring network of 15, a given water molecule’s orientation is strongly constrained by its neighbors, implying that any significant reorientation would disrupt the favorable hydrogen-bond angles in the chain or ring, incurring an energy penalty. As the confinement size increases, this constraint relaxes and water has more orientational freedom, allowing subtler effects like carbon polarization to play a greater role. Indeed, in the largest tubes (20), the influence of polarizable carbon on water orientation becomes significant, indicating a crossover where the water–CNT interactions (enhanced by CNT polarizability) start to compete with or even outweigh the water–water hydrogen-bonding interactions in determining how molecules orient near the interface.

Infrared Spectra

Infrared (IR) spectra were computed for all systems using the MB-pol potential energy surface and the MB- μ dipole moment surface. Comparisons between the single and stacked CNT configurations, as well as with and without explicit treatment of carbon polarization, are provided in the SI (Figures S21–S23). In general, the spectra are in excellent agreement across all systems, with only minor deviations. Most notably, in system 20, we observe a modest increase in relative intensity $I(\omega)$ upon including carbon polarization. This effect arises from a slight increase in the water dipole moment magnitude due to stronger CNT–water interactions when carbon polarization is included. Given the high degree of consistency among systems of the same diameter, we selected the spectra of systems $N^{\text{stacked}_{\text{pol}}}$ for further

comparison. These are shown in Figure 5 alongside a reference MB-pol bulk⁶⁹ spectrum. Figure S24 in the SI provides an

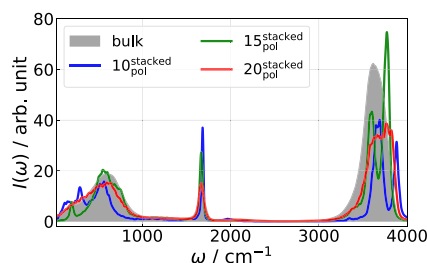


Figure 5. Infrared spectra of all systems $N_{\text{pol}}^{\text{stacked}}$ are shown together with a MB-pol bulk reference spectrum (gray area).⁶⁹

additional comparison of the water's bond stretching modes to an experimental spectrum of confined water in CNTs with diameters ranging from 0.7 to 2.1 nm.⁷⁰ Nuclear quantum effects are accounted for by applying a frequency correction of 175 cm^{-1} to the computed spectra, yielding a very good agreement with the experimentally observed O–H stretching bands.⁷¹

As evidenced by the IR spectra, the librational modes ($\omega < 1000 \text{ cm}^{-1}$) of water are generally red-shifted under confinement for all the CNTs studied. The librational dynamics of water in these CNTs are strongly influenced by confinement, with each CNT diameter producing different peak positions. An effect, which is especially present in the smallest CNT studied. For system 10 the broad librational band splits into distinct peaks at approximately 150 cm^{-1} , 300 cm^{-1} , while for system 15 peaks emerge at approximately 200 cm^{-1} and 600 cm^{-1} . These features emphasize the ice-like nature of the confined water, in which librational modes are suppressed while others are enhanced.^{72–75} Conversely, the O–H bond stretching modes ($\omega > 3200 \text{ cm}^{-1}$) are generally blue-shifted relative to bulk water. For systems 10 and 15, the O–H stretching band splits into two distinct peaks, consistent with previous theoretical and experimental studies.^{66,67,70} The higher-frequency component is assigned to dangling or weakly hydrogen-bonded O–H groups, whereas the lower-frequency peak correspond to O–H stretches within a hydrogen-bond network. These confinement-induced spectral features directly reflect the altered hydrogen-bonding environment within the subnanometer CNTs. In bulk water, each molecule participates in several hydrogen-bonding interactions, forming a fluctuating hydrogen-bond network. Under confinement, however, the imposed high structural order perturbs this network and generally reduces the number of formed hydrogen bonds per water.^{66,76}

As discussed above, the water molecules in systems 10 form a single-file chain. One hydrogen atom of each water molecule points to its neighbor along the chain, while the oxygen atom accepts a hydrogen bond from the adjacent molecule on the opposite side. The second hydrogen atom, however, remains unbound and points radially toward the CNT wall, giving rise to the high-frequency peak at $\omega > 3800 \text{ cm}^{-1}$ (see Figure 3g). By contrast, the axially oriented O–H stretch (which participates in a hydrogen bond along the chain) is comparatively red-shifted, as the stronger hydrogen bonding stabilizes this vibrational mode.

In systems 15, the water molecules adopt an ice-like, pentagonal ring arrangement. Here, in-plane hydrogen bonds (oriented roughly radially toward the CNT's center axis)

stabilize the pentagonal rings and give rise to the spectral feature at $\omega \approx 3500 \text{ cm}^{-1}$. In contrast, the out-of-plane hydrogen bonds connecting adjacent pentagonal layers are weaker and produce the blue-shifted stretching mode.⁶⁶ Thus, the observed spectral splitting is not simply a matter of an O–H bond's orientation toward the CNT wall, but it must be understood in the context of the local molecular arrangement and the resulting hydrogen-bond network, which are governed by the confinement geometry.

Finally, in systems 20, orientational and positional constraints on the water molecules are the least pronounced. As a result, no splitting is observed in the O–H bond stretching band, and the overall spectrum is closest to that of bulk water, indicating that confinement effects diminish with increasing CNT diameter.

Hydrogen Bond Lifetimes

We computed the intermittent hydrogen-bond lifetimes (τ_{HB}) for all the 20 systems and the results are listed in Table 2. The

Table 2. Intermittent Hydrogen Bond Lifetimes τ_{HB} , along with the Standard Deviations Calculated from the Three Replica Simulations^a

system	single (τ_{HB} /ps)	stacked (τ_{HB} /ps)
20 _{pol}	4.9 (± 0.1)	4.1 (± 0.1)
20	5.2 (± 0.1)	4.1 (± 0.1)
20 _{TIP4P}	6.8 (± 0.2)	5.1 (± 0.0)

^aThe calculated intermittent hydrogen bond lifetime for the MB-pol bulk simulation is $\tau_{\text{HB}} = 3.2 \text{ ps}$.

intermittent approach^{77,78} monitors hydrogen-bond breaking and reforming over time, thereby allowing the determination of τ_{HB} , which measures how long, on average, a pair of water molecules remains bonded (including periods during which the hydrogen bond is temporarily broken and then reforms). Hydrogen bonds were identified using a geometric criterion optimized for water at hydrophobic interfaces.⁷⁹ Accordingly, two water molecules were considered hydrogen-bonded if the oxygen–oxygen distance r_{OO} was less than 3.5 Å and the angle $\angle(\text{H}–\text{O} \cdots \text{O})$ was below 50°. The corresponding correlation plots are shown in Figure S25 of the SI.

Water in all confined systems exhibit longer τ_{HB} than the MB-pol bulk value (3.2 ps), a trend consistent with previous studies of confined water.¹¹ Among the models, TIP4P/2005f predicts significantly longer lifetimes, with an increase of τ_{HB} of up to 39 for single CNT systems and 24 for stacked systems compared to the MB-pol models. This is consistent with the RDF analyses presented above and suggests that TIP4P/2005f tends to make hydrogen bonds stronger in the CNT- confined environment. When water is modeled with MB-pol, introducing carbon polarizability (model 20_{pol}) slightly reduces τ_{HB} in the single-CNT systems, likely because the enhanced water–CNT interactions decrease the rigidity of the hydrogen-bond network and thereby shorten the hydrogen-bond lifetime.

Comparing single versus stacked CNTs reveals a significant effect: τ_{HB} decreases by ~ 20 in the MB-pol models and by ~ 25 for TIP4P/2005f when the CNTs are stacked. Conceptually, the presence of adjacent CNTs appears to introduce additional intertube water–water interactions that perturb the hydrogen-bond network inside each tube. This intertube coupling destabilizes individual hydrogen bonds, leading to shorter lifetimes. In the context of the intermittent hydrogen-bond picture, the reduced τ_{HB} in stacked config-

urations implies higher mobility of the confined water. Water molecules do not remain hydrogen-bonded to the same neighbors as long as they do in an isolated CNT.

Residence Times

To assess how these findings impact the lateral diffusive properties of the confined water, residence times (τ) were calculated for all 20 systems. Averages were computed, where applicable, over all CNTs within the same system. Two distinct radial layers were defined based on the minima positions $r_{\min}$ in the density distributions (Table 3): Layer 1 ($0 \text{ \AA} < r < r_{\min}$) and

Table 3. Positions of the Density Minima $r_{\min}$ from the Density Profiles Shown in Figure 2 for All Systems Modeling 20,0) CNTs Systems 20)

system	single ($r_{\min}/\text{\AA}$)	stacked ($r_{\min}/\text{\AA}$)
20 _{pol}	2.84	2.84
20	3.00	3.00
20 _{TIP4P}	2.92	3.00

Layer 2 ($r_{\min} < r < 6.5 \text{ \AA}$), with r being the center-of-mass (COM) radial position of a water molecule at any given time step. This definition was applied to all systems.

For each system, τ was obtained via exponential fit of the corresponding residence-time correlation function shown in Figure S26 of the SI. The τ values, together with the average water population $\langle n_{\text{H}_2\text{O}} \rangle$, are listed in Table 4. The populations

Table 4. Residence Time τ and Average Population $\langle n_{\text{H}_2\text{O}} \rangle$ Per Layer are Listed for All Systems Modeling 20,0) CNTs Systems 20)

layer	system	single		stacked	
		(τ/ps)	($\langle n_{\text{H}_2\text{O}} \rangle$)	(τ/ps)	($\langle n_{\text{H}_2\text{O}} \rangle$)
1	20 _{pol}	22.5 (± 0.4)	50	19.6 (± 0.3)	50
1	20	26.3 (± 0.3)	55	21.9 (± 0.4)	55
1	20 _{TIP4P}	21.5 (± 0.7)	54	17.4 (± 0.2)	55
2	20 _{pol}	83.7 (± 1.3)	165	75.2 (± 0.9)	165
2	20	82.5 (± 1.3)	160	71.8 (± 1.4)	160
2	20 _{TIP4P}	72.5 (± 1.9)	161	58.9 (± 0.7)	160

of water molecules in each layer fluctuate only slightly over the course of the simulations (Figure S27 in the SI). Layer 1 consistently contains about 50–55 molecules, while Layer 2 accommodates around 160–165, i.e., approximately 75% of the confined water. Accounting for carbon polarizability (20_{pol}^{single}/20_{pol}^{stacked}) increases the average number of molecules in Layer 2 by about five (see Table 4), which corresponds to a noticeable $\sim 9\%$ reduction in density in Layer 1. The generally longer residence times in Layer 2 reflect that most molecules occupy the outer tubular region.

The sizable differences in $\langle n_{\text{H}_2\text{O}} \rangle$ for 20_{pol} relative to 20 and 20_{TIP4P} directly impact the residence times and preclude a conclusive model-to-model comparison. In addition, as discussed above, the positions and amplitudes of the minima and maxima in the density distributions change with the choice of water model (Figure 2c). While defining layers by $r_{\min}$ partly accounts for this, the altered average structuring inherent to each model also affects the layer residence times. Nevertheless, when comparing 20 and 20_{TIP4P}, the smallest τ values are observed with TIP4P/2005f, indicating enhanced crossing between layers. Based on the hydrogen-bond lifetimes, this effect is not

directly governed by the dynamics within the hydrogen-bond network. Rather, it reflects structural differences in the confined water when using TIP4P/2005f, with a more populated interlayer region and a less distinct separation between layers, which is consistent with less distinct minima and maxima in the corresponding density profiles (Figure 2c).

A consistent trend emerges when comparing single to stacked CNTs: τ decreases in the stacked configurations by approximately 10–20% across all models, highlighting the importance of intertube interactions. Because the $\langle n_{\text{H}_2\text{O}} \rangle$ averages are very similar between single and stacked systems, this comparison is robust. In the context of the discussions in previous sections, this result can be rationalized as follows: while the local hydrogen-bond network primarily governs structure and orientation, additional interactions in stacked CNTs (between water and carbon atoms in adjacent tubes, and between water molecules across tubes) perturb the energy landscape, reduce hydrogen-bond lifetimes, and seemingly facilitate layer crossing, thereby shortening the residence times.

Mean Square Displacement

Mean square displacements (MSDs) were calculated for each system, with the results shown in Figures S28–S30 of the SI. In the 10 systems, the water molecules form a single-file chain that enforces a collective translational motion, such that all molecules within the same CNT share the same long-range displacement (i.e., they effectively diffuse as one).⁸⁰ A similar effect occurs in the 15 systems, where the stacked pentagonal ring structure configuration (an ice-like configuration) leads to correlated dynamics within each CNT.¹⁶ In both cases, the effective number of statistically independent water trajectories is determined by the number of CNTs rather than the total number of water molecules. This effect is less pronounced in the 20 systems, but still present. Therefore, to ensure robust statistics, we only considered stacked systems for the MSD analysis. Still, the MSDs from individual replica simulations exhibit large variations across all systems. The corresponding self-diffusion coefficients obtained for each system N^{stacked} are summarized in Table 5, along with the standard deviations

Table 5. Self-Diffusion Coefficients of Water D^{pol} , and D^{TIP4P} for the Systems N^{stacked} together with the Standard Deviation from the Replica Simulations, Given in Units of $\text{\AA}^2\text{ps}^{-1}$

N	D^{pol}	D	D^{TIP4P}
10 ^{stacked}	30.1 (± 4.5)	26.9 (± 4.7)	15.4 (± 4.5)
15 ^{stacked}	12.1 (± 5.4)	17.0 (± 3.1)	11.8 (± 7.3)
20 ^{stacked}	0.9 (± 0.2)	1.6 (± 0.4)	1.3 (± 0.4)

^a(D : MB-pol model; D^{pol} : MB-pol model with explicit carbon polarization; D^{TIP4P} : TIP4P/2005f model; bulk MB-pol reference:⁵⁵ $D_{\text{bulk}} = 0.28 (\pm 0.04) \text{ \AA}^2\text{ps}^{-1}$).

across replicas. Despite some variability across the replica simulations, a consistent trend is observed: the self-diffusion coefficients are significantly higher than in bulk water,⁵⁵ especially for water confined in the (10,0) CNT (consistent with previous simulations of single-file water in nanotubes).⁸¹ As the CNT diameter increases, this enhancement of diffusion decreases rapidly. Apart from this overall trend, the only significant model-dependent difference is observed in the 10 systems, where TIP4P/2005f yields diffusion coefficients

roughly half of those obtained with the MB-pol model, which is well beyond the estimated statistical uncertainties.

CONCLUSION

From the present analysis of water confined in CNTs, three main findings emerge. First, the MB-pol model provides an accurate description of the water structure and dynamics under confinement. It reproduces the preferred arrangements observed across CNTs of varying size, namely single-file chains, pentagonal rings, and two-layer structures, supporting its general applicability. Additionally including carbon polarizability in the CNT model provides the most detailed description of the studied systems, enabling a quantitative description of the interfacial orientation of water at CNT walls. In addition, IR spectra computed from the simulated dipole moments provide further insights into the librational and O–H stretching modes of nanoconfined water.

Second, explicitly modeling carbon polarizability has a measurable effect on water structure and orientation, particularly in wider CNTs, where interfacial molecules respond more strongly to CNT–water interactions. Water molecules tilt toward the wall, and hydrogen-bond lifetimes are slightly reduced (at least in single-CNT systems). This indicates that accounting for carbon polarizability is especially important when probing the behavior of interfacial water. The magnitude of these effects appears to depend on tube size, suggesting that carbon polarizability is critical when studying wider CNTs but negligible for the smallest CNTs.

Third, stacking multiple CNTs has a pronounced impact on water dynamics. In stacked configurations, interactions between water molecules in adjacent tubes perturb the local energy landscape within a CNT and reduce hydrogen-bond lifetimes. Layer crossing is facilitated in CNTs with multiple radial water layers, leading to increased lateral mobility. This phenomenon is robust across all models considered and, to the best of our knowledge, has so far received comparatively little attention. Our results highlight that intertube interactions are crucial determinants of water dynamics in CNTs and warrant further investigation.

Overall, the results underscore that water structure and dynamics are strongly governed by the degree of confinement, and that explicitly accounting for carbon polarizability and intertube (stacking) interactions is critical for accurate modeling of confined water.

METHODS

Simulations

Molecular dynamics simulations were performed using LAMMPS,⁸² with the workflow outlined in Figure S1 in the SI. All simulation boxes were generated using PACKMOL.⁸³ Preliminary simulations were carried out to fill (N,0) CNTs ($N = 10, 15, 20$) with water, using a CNT of approximately 40 Å in length and 2000 water molecules. An exemplary simulation box is shown in Figure S2 in the SI. CNTs were modeled using the fully flexible Dreiding force field,⁶⁰ with the functional form and parameters listed in the SI. Throughout the simulation protocol, we used the Nosé–Hoover approach for thermostatting. Angular and translational momenta of the CNTs were rescaled every 100th time step throughout the equilibration to avoid drifts and tilts of the tube. The TIP4P water model⁸⁴ was used to pre-equilibrate the system for 0.5 ns at a time step of 0.5 fs in an NpT ensemble at 298 K and 1 atm with periodic boundary conditions applied. The time step, temperature, and, when applicable, pressure were not changed throughout the work flow. The water model was then switched to MB-pol^{51–55} using the MBX⁸⁵ software. After a further 0.5 ns

equilibration in an NpT ensemble, the ensemble was switched to NVT for another 0.5 ns.

The total confined mass within a given CNT was calculated for every 1000th frame, using a new tool in CONAN,⁸⁶ with more information provided in the next sections. The average loading mass during the NVT runs are shown in Table 6.

Table 6. Listed are the Average Confined Mass Per Å, m_{avg} , the Average Length of a Given CNT, l_{avg} , the Average CNT Unit Cell Length, $l_{\text{unit}}^{\text{avg}}$, during the Equilibration in NVT Ensemble^a

CNT	(10,0)	(15,0)	(20,0)
$m_{\text{avg}}/\text{a.u.}$	6.56	31.0	64.7
$l_{\text{avg}}/\text{Å}$	41.4	41.4	41.4
$l_{\text{unit}}^{\text{avg}}/\text{Å}$	4.28	4.28	4.28
$n_{\text{unit}}^{\text{atoms}}$	40	60	80
$r_{\text{CNT}}^{\text{avg}}/\text{Å}$	3.97	5.92	7.87

^a $n_{\text{unit}}^{\text{atoms}}$ is the number of atoms that comprise a unit cell of a given CNT.

To minimize the influence of packing effects at the open ends, the first 2 Å within the CNT at both ends were not considered when calculating the average confined mass per angstrom (m_{avg}). The development of the total confined mass within the CNTs per frame during the NpT and NVT ensemble are shown in Figures S3 and S4 in the SI, respectively, and discussed. During the NVT runs, the average CNT radii $r_{\text{CNT}}^{\text{avg}}$ were collected and used to calculate the atomic polarizabilities of carbon α_{C} , detailed in the next section.

Periodic CNTs were constructed and filled with water, with details provided in Table 1. The length l_{c} of a CNT and the respective number of water molecules was chosen to match m_{avg} . The filled periodic CNTs were modeled as a single entity in simulation boxes measuring $25 \times 25 \times l_{\text{c}}$ Å³ and in a stacked configuration. Initial 50 ps runs were done using the TIP4P model of water in an Np₂T ensemble before switching back to MB-pol. For the final equilibration over 0.5 ns in an Np₂T (single CNT) or Np_{aniso}T (stacked CNTs) ensemble, the atomic polarizability for all carbon atoms of a CNT is explicitly accounted for using the MBX framework. Production runs were carried out in the NVT ensemble using the MB-pol model (with and without accounting for carbon polarization) as well as the TIP4P/2005f model for water. Three replica simulations were run for 0.5 ns using different velocity seeds to let the simulations diverge, before starting separate production runs over 5 ns, where every 250th frame was stored for analysis. In systems using the MB-pol water model, additional replica simulations were carried out in the NVE ensemble over 0.1 ns with every eighth frame stored to calculate IR spectra. Reference bulk simulations were carried out over 0.1 ns in the NVT ensemble, starting from an equilibrated system using 256 water molecules.

Trajectories were analyzed using CONAN⁸⁶ with newly developed functions. Diffusion coefficients were calculated using msdiff.⁸⁷ Hydrogen bond lifetimes and radial distribution functions were computed using Travis.^{88,89} VMD^{90,91} was employed for visualization purposes and figure rendering.

Polarizability of CNTs

The atomic polarizability of carbon atoms is of anisotropic nature in CNTs. By convention, the axial polarizability $\alpha_{\parallel}$ is defined as the polarizability along the CNT's axis, while the radial polarizability $\alpha_{\perp}$ is oriented perpendicular to the tube wall, pointing toward the center of the CNT. Notably, the axial polarizability $\alpha_{\parallel}$ is known to correlate inversely with the electronic band gap of the CNT. Structures with a large band gap exhibit a low $\alpha_{\parallel}$, whereas quasi-metallic CNTs with small band gaps display significantly larger values. For example, the (15,0) CNT, which is nearly metallic and exhibits a very small band gap, has a particularly large $\alpha_{\parallel}$.⁹² Both components of the polarizability play distinct roles. The axial polarizability $\alpha_{\parallel}$ is more relevant for describing dynamical properties such as the diffusion of molecules along the tube axis,^{93,94} whereas the radial polarizability $\alpha_{\perp}$ plays a more dominant

role in static interactions, particularly affecting packing effects within the confinement. The radial polarizability $\alpha_{\perp}$ correlates with the CNT radius $r_{\text{CNT}}^{\text{CNT}}$, following the equation³²

$$\alpha_{\perp} = 0.4 \left(\frac{r_{\text{CNT}}^{\text{CNT}}}{1.3} \right)^2 \quad (1)$$

For our study, we assume the polarizability to be isotropic.

The atomic polarizability $\alpha_{\perp}$ of a given CNT carbon atom is derived by multiplying $\alpha_{\perp}$ with the length of the unit cell and dividing it by the number of atoms per unit. The calculated values are given in Table 7, alongside values found in literature, $\alpha_{\perp}^{\text{lit}}$.

Table 7. Listed are the Radial Polarizabilities of the CNTs, Found in Literature, $\alpha_{\perp}^{\text{lit}}$, and Derived by eq 1, $\alpha_{\perp}^{\text{eq}}$

$N_{\text{pol}}^{\text{single/stacked}}$	$\alpha_{\perp}^{\text{lit}}/\text{\AA}^{295}$	$\alpha_{\perp}^{\text{eq}}/\text{\AA}^2$	$\alpha_{\perp}^{\text{atom}}/\text{\AA}^3$
10	10.2	11.10	1.189
15	19.3	20.82	1.485
20	32.2	33.66	1.800

^aFrom $\alpha_{\perp}^{\text{eq}}$, the atomic carbon polarizabilities $\alpha_{\perp}^{\text{atom}}$ are calculated and later used in systems the $N_{\text{pol}}^{\text{single/stacked}}$.

Average CNT Filling

The first step in calculating the average confined mass within a given CNT is to identify the part of the simulation box that corresponds to the confined space within the tube. As the CNT is modeled as fully flexible, this is done repeatedly for each frame analyzed. For CNTs of finite length, the center axis is defined by two center points at the open ends of the tube, p_1 and p_2 . Both are determined based on molecular bond information obtained during the initial CONAN molecular identification. Applying a maximal carbon–carbon bond length criterion of 2 Å, the terminal carbon atoms are identified.

The bonding information further reveals which atoms belong to each open end of the CNT. Based on this, two separate rings are constructed, with periodic boundary conditions (PBC) taken into account. The geometric centers of these rings define the end points p_1 and p_2 of the CNT axis (see Figure 1).

For periodic CNTs, a carbon atom is randomly selected as a reference. Using a small positional tolerance, all other atoms that share the same coordinate along the periodic axis are identified. These atoms form a representative ring due to the translational symmetry of the nanotube. The geometric center of this ring defines p_1 . The corresponding point p_2 is constructed by translating p_1 along the periodic direction

$$p_2 = p_1 + l_{\text{dim}} \quad (2)$$

where l_{dim} is the box length in the periodic dimension. The CNT radius, r_{CNT} , is calculated as the mean distance of the ring atoms to the ring center in the first analyzed frame and subsequently used as a fixed parameter. For an atom in the simulation box with the position vector $\vec{x}$ to be within the structure, it must fulfill the conditions

$$(\vec{x} - \vec{r}_1) \cdot (\vec{r}_2 - \vec{r}_1) \geq 0 \quad (3)$$

$$(\vec{x} - \vec{r}_2) \cdot (\vec{r}_2 - \vec{r}_1) \leq 0 \quad (4)$$

$$\frac{(\vec{x} - \vec{r}_1) \times (\vec{r}_2 - \vec{r}_1)}{|\vec{r}_2 - \vec{r}_1|} \leq r_{\text{CNT}} \quad (5)$$

The sum of the masses of all the atoms found within the CNT at a given time step yields the confined mass. Averaging over each analyzed frame gives the average mass m_{avg} . Parts of the confined volume at the open ends of the CNTs can be neglected when calculating m_{avg} with the cutoff set by the user. The average CNT radius, $r_{\text{CNT}}^{\text{avg}}$, is also computed on the fly.

Density Distribution

Within CNT confinement, water forms radial layers at the solid–liquid interface, a phenomenon extensively described in the literature.^{11,34,64}

The number of radial layers depends on r_{CNT} . Density distributions are constructed by dividing the radial space into user-defined increments (see red circles in Figure 1e). During the trajectory analysis, each atom inside a CNT is sorted into radial bins according to its radial distance from the center axis r_{rad} and weighted by its atomic mass. In postprocessing, the density for each increment is calculated by dividing the total mass by the number of analyzed frames and the volume of each increment. While each radial bin spans the same radial length, their volumes increase with distance from the center, which is taken into account when computing the density. In this work, the radial distance from the center of a given CNT to its wall was divided into 100 increments. The three replica simulations for each system are in good agreement, with noticeable deviations occurring only for the 10^{single} and 10^{TIP4P} cases, where the maximum density slightly differs among replicas (Figures S5–S10 in SI).

Angular Distribution

Angular distributions were calculated by expanding the scheme used to calculate density distributions. Two vectors are defined for which the angle is calculated (Figure 1e). The vector $\vec{z}$ represents the CNT center axis, and $\vec{r}$ is the radial vector between the center axis and the COM or a representative atom of the studied molecule. The vector $\vec{r}$ is constructed as such that the angle between $\vec{z}$ and $\vec{r}$ is always 90°. The bond vectors are defined as $\vec{d}_1$ and $\vec{d}_2$, and their bisector $\vec{u}$ is obtained by first normalizing the bond vectors to eliminate bond stretching effects and then taking the mean. In Figure 1e, $\vec{r}$ connects the center axis to the oxygen atom, while $\vec{d}_1$ and $\vec{d}_2$ are the O–H bond vectors, with $\vec{u}$ as their bisector.

Alternatively, vectors (e.g., the dipole moment) can be read directly from the trajectory file. During the analysis, angles are calculated and sorted into radial bins based on the molecule's COM position. Plots are generated to visualize the distribution of angles for each radial increment.

Residence Times

The radial residence time $\tau_{l,c}$ of molecules in a given layer l within a CNT c is determined through a survival correlation function. The number and extent of radial layers within a given CNT are manually defined, and in each analyzed frame of the trajectory, every molecule is assigned to a layer based on its COM position. The analysis allows to manually define a transient tolerance time t^* , which defines the time a molecule may leave a given layer before returning. Below the defined time threshold, the residence within a layer is considered to be continuous. For the analyses, we set $t^* = 2$ ps. Over the course of the simulation, each molecule generates residence intervals from $[t_{\text{start}}, t_{\text{end}}]$, during which the position within a layer is considered uninterrupted. From these segments, the survival correlation function $C_{l,c}(t, t^*)$ is obtained as

$$C_{l,c}(t, t^*) = \frac{N_{l,c}(t, t^*)}{D_{l,c}(t, t^*)} \quad (6)$$

$D_{l,c}(t, t^*)$ is the number of start times and $N_{l,c}(t, t^*)$ the number that survive until time t . By definition $C_{l,c}(0, t^*) = 1$. Assuming an exponential decay, the residence time $\tau_{l,c}$ is obtained through a fit

$$C_{l,c}(t, t^*) = e^{-t/\tau_{l,c}} \quad (7)$$

$$\tau_{l,c} = \frac{t}{\ln(C_{l,c}(t, t^*))} \quad (8)$$

Mean Square Displacement

The mean square displacement (MSD) of the confined water molecules is obtained from their COM movement. In each frame, the COM of each molecule is calculated from the atomic masses and coordinates. Periodic boundary conditions are accounted for by unwrapping the atomic positions x . Between successive analyzed frames, the COM displacements are calculated and stored. Using all possible time origins and averaging over all molecules yields the MSD as a function of observation time τ . The maximum correlation depth is defined by $\tau_{\text{max}} = n \cdot \Delta t$, with Δt as the time step and n as the number of subsequent frames

contributing. $\tau_{\max}$ is user defined through n . The MSD is then calculated using the standard equation

$$\text{MSD}(\tau) = \langle |x(\tau) - x| ^2 \rangle \quad (9)$$

■ ASSOCIATED CONTENT

■ Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsnano.5c17458>.

Workflow scheme; Functional form of the force field and according parameters; Description of the filling procedure of the CNT; Density distributions of water in CNTs; Intermolecular radial distribution functions: Angle distributions; Combined density-angle distribution; Infra-red spectra; Hydrogen bond lifetime correlation plots; Layer population distribution; Residence time correlation plots; Mean square displacements (PDF)

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Notes

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Appendix: The adsorption of drugs on nanoplastics has severe biological impact

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Note: This publication is based on the master thesis “Adsorption of Tetracycline on Nanoplastics”.¹⁸⁷ However, all calculations were redone with slightly differing setup, new MD simulations were included, all analyses were redone, and numerous new analyses were performed for this publication, making it entirely novel. For this reason, the publication is included in this cumulative work.

Own contributions

- Running all MD simulations and geometry optimizations.
- Participating in the analysis of the trajectories and optimized NP geometries.
- Partially curating and visualizing the results
- Contributions to the writing of the manuscript.

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OPEN The adsorption of drugs on nanoplastics has severe biological impact

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Micro- and nanoplastics can interact with various biologically active compounds forming aggregates of which the effects have yet to be understood. To this end, it is vital to characterize these aggregates of key compounds and micro- and nanoplastics. In this study, we examined the adsorption of the antibiotic tetracycline on four different nanoplastics, made of polyethylene (PE), polypropylene (PP), polystyrene (PS), and nylon 6,6 (N66) through chemical computation. Two separate approaches were employed to generate relevant conformations of the tetracycline-plastic complexes. In the first approach, we folded the plastic particle from individual polymer chains in the presence of the drug through multiple separate simulated annealing setups. In the second, more biased, approach, the neat plastic was pre-folded through simulated annealing, and the drug was placed at its surface in multiple orientations. The former approach was clearly superior to the other, obtaining lower energy conformations even with the antibiotic buried inside the plastic particle. Quantum chemical calculations on the structures revealed that the adsorption energies show a trend of decreasing affinity to the drug in the order of N66 > PS > PP > PE. In vitro experiments on tetracycline-sensitive cell lines demonstrated that, in qualitative agreement with the calculations, the biological activity of tetracycline drops significantly in the presence of PS particles. Preliminary molecular dynamics simulations on two selected aggregates with each plastic served as first stability test of the aggregates under influence of temperature and in water. We found that all the selected cases persisted in water indicating that the aggregates may be stable also in more realistic environments. In summary, our data show that the interaction of micro- and nanoplastics with drugs can alter drug absorption, facilitate drug transport to new locations, and increase local antibiotic concentrations, potentially attenuating antibiotic effect and at the same time promoting antibiotic resistance.

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Through the degradation of plastics, particles with a wide variety of sizes, shapes, and compositions are formed^{1–5}. Over the past few decades, it has become evident that micro- and nanometer-sized fragments of these pollutants (micro- and nanoplastic particles, MNPs) are present in our environment^{1,2,6,7}. Beyond the fact that these artificial materials enter the human body⁸, organs^{9–14}, or even individual cells¹⁵ of living organisms, their physiological and environmental effects are not yet fully understood^{16–18}. Numerous studies have focused on understanding the consequences of absorbing MNPs, and reached alarming conclusions^{5,15,19–25}. While it is clear that decreasing the MNP intake is necessary to mitigate the risks, more research is needed to identify the particular kinds of MNPs that pose a health and environmental danger.

When assessing the possible effects of MNPs, it is crucial to consider their interactions with other compounds in natural and artificial environments. These materials can adsorb a wide variety of substances and, through a “Trojan horse” effect, deliver them into living organisms. Compounds called endocrine disruptors (EDCs)²⁶ that enter life forms through this mechanism can trigger severe toxic effects on the hormonal level, which is suspected to be linked to the increased incidence of cancer cases worldwide⁵, but also male infertility²⁷.

The interaction of MNPs with medicinal drugs can also have severe consequences. First, through the aforementioned “Trojan horse” effect, residual drugs in waste water²⁸ can be shuttled into the body of humans and animals, resulting in unintended physiological changes^{29–33}. Second, it is conceivable that when MNPs are present in the digestive tract of the patient while undergoing medical treatment through oral delivery, interactions between the drug and the MNP particles may slow down, or even hinder the absorption of the drug into the blood stream, thereby altering the pharmacokinetics of the medication. This hypothesis must be rigorously tested with the ever-increasing particle load in humans due to the rising concentration of MNPs in the environment.

However, when considering MNP-drug interactions, antimicrobial agents deserve special attention, as the possible negative effects can be significantly exacerbated by these compounds. The presence of antibiotic drugs in the environment is of great concern even without their interplay with MNPs³⁴. Depending on the exposure level, bacteria exposed to these compounds may exhibit intrinsic, adaptive and acquired resistance (i.e. positive selection above minimal selective concentration, MSC). Still, even much below MSC, the persistence of resistance genes may increase³⁵. Due to this evolutionary pressure, and the continuous release of antimicrobial compounds by their anthropogenic use and misuse, the abundance of resistance genes has been observed to increase in the environment³⁶. The emergence and spread of resistant strains is highly alarming, since common infectious diseases have become a global threat. The findings above prompted the definition of new strategies and policies for assessing drugs’ environmental and human health risks³⁷, including the potential contribution to antimicrobial resistance when selecting the compound’s Predicted No Effect Concentration. As the most common form of bacterial life³⁸, biofilms are bacterial populations embedded in self-produced heterogeneous matrices where diffusion, sorption³⁹ and biotransformation⁴⁰ of antimicrobial chemicals may occur. MNPs provide a surface for microorganisms to colonize, serving as a vector for transportation and spread⁴¹. The local increase in drug concentration induced by the MNP leads to the exposure of bacteria to higher quantities of the drug than in the absence of the plastic, increasing the chances for resistance to develop. Furthermore, both microplastics and biofilms seem to facilitate the transfer of resistance genes between the microbes^{42,43}. However, a deeper and more structured understanding of analyte-MNP, analyte-biofilm, and biofilm-MNP interactions may be required to bridge knowledge gaps regarding the development and spread of antimicrobial resistance in complex environmental matrices.

Thus, beyond being potentially toxic themselves, MNPs can also offer a platform, at which resistant strains of bacteria can be produced. If a post-antibiotic era is to be avoided, all possible actions need to be taken to explore and eliminate the sources of resistance, and the connections with plastic waste need to be unveiled. Understanding the key features of drug adsorption on MNPs is essential in this endeavour. Several studies have been published throughout the last decade that focused on the interaction of MNPs and antibiotics^{44–49}, including a broad-spectrum antibiotic, tetracycline (TC, see Fig. 1). The importance of this particular drug is underscored by the fact that it is on the WHO’s list of essential medicines, despite its significantly eroded versatility. Further loss of its efficacy will have a devastating effect on the treatment of some severe infections, including malaria and syphilis.

TC binds spontaneously to polyethylene (PE), polypropylene (PP), polystyrene (PS), and polyvinyl chloride (PVC)^{44,49}, following a multilayer adsorption mechanism⁴⁹, changing the morphology of the MNP particle⁴⁸. The interactions that drive this adsorption include polar and $\pi - \pi$ interactions, making PVC⁴⁸ and PS the strongest adsorbents among the investigated MNPs, followed by PP and finally PE⁴⁵. Weathering introduces polar functional groups to the plastics, such as carbonyl groups, which enhance adsorption^{47,50}. Organic and inorganic substances can also significantly affect sorption^{44–46,50}, therefore the particular matrix, in which the binding occurs, has to be considered in the experimental setups and their interpretation.

In the present article, we use a theoretical chemical and molecular biological approach to characterize how TC interacts with a variety of nanoplastics, and to observe how the biological activity of the drug is altered by the presence of these plastic pollutants. Since this antibiotic interacts weaker with MNPs than many other antibiotics (ciprofloxacin, amoxicillin, sulfadiazine, trimethoprim)⁴⁴, investigating TC should be more challenging for modeling than the others. For the same reason, any effects found for TC in the experiments should be stronger with the other drugs, providing a careful underestimation for the general biological impact of MNP-drug interactions. We chose four kinds of pristine plastics for our study, including the plastics produced in the most significant quantities such as polyethylene (PE), polypropylene (PP), and polystyrene (PS), which are also the most prevalent in the environment, and nylon 6,6 (N66), which has been shown to have severe effects on biomolecules (see Fig. 2)^{51,52}. Note, in the following, we use only NP as an abbreviation for the micro- and nanoplastic (MNP) because the size of our investigated subjects does not exceed the nanoscale.

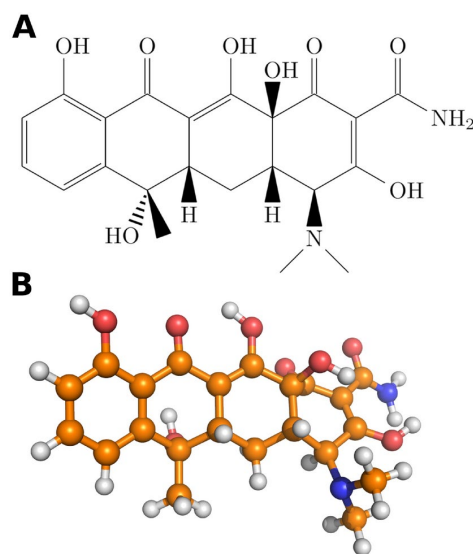


Fig. 1. Lewis structure (**A**) and ball-and-stick representation (**B**) of the antibiotic tetracycline (carbon: orange; hydrogen: white; oxygen: red; nitrogen: blue).

Methods

Theoretical chemical calculations

Exploring the conformational space of macromolecular systems is a difficult task, and beyond a certain size only stochastic methods are available. One of these methods is simulated annealing (SA)^{53–58}, which relies on a temperature program, heating up the system to an often unphysically high temperature, and then gradually cooling it down. The high kinetic energy of the atoms allows the facile exploration of the conformations of the system, while the gradual cooling depopulates the higher energy structures. This approach can find the global minimum of the potential energy surface of any system, if the rate of cooling is infinitely low; in any other (i.e. realistic) cases it may produce energetically higher lying minima. Thus, a careful design of the simulated annealing setup is necessary, and it is highly advantageous to perform several parallel SA runs that produce multiple conformations⁵⁸.

In order to obtain several conformations of the drug molecule TC with the nanoplastic, we adapted a workflow from our earlier established⁵¹ simulated annealing protocol. First, the polymer chains that the plastic particle is to be composed of were placed in a periodic box. The box size was chosen to be large enough to avoid close self-interactions between the opposite ends of the same polymer chain, but small enough to prevent the individual chains from floating apart, e.g. 150 Å. On this system, a molecular dynamics run of 20 ns was performed in the canonical ensemble with the temperature gradually decreasing from 1200 to 200 K. The radius of gyration of the particle and the mobility of the chains within were monitored through the simulation, showing the phase transition temperatures at which first, the polymer chains condense into a single cluster (defining T_{start}), and second, their mobility becomes so limited that they do not explore their conformational space anymore (defining T_{end}). These two temperatures were taken as the two extreme points for the subsequent simulated annealing runs. Then, 50 separate starting conformations were generated, and on each of these a simulated annealing run was performed in the canonical ensemble for 20 ns, cooling gradually from the obtained T_{start} to the T_{end} temperature.

Next, we built the TC@NP system in two separate ways. In one approach, we carried out a complete refolding of NP in the presence of the TC through the same temperature program designed for the neat plastic, i.e., SA was applied to the TC@NP systems as well. We again performed these simulations on 50 different starting structures, so that we received an array of conformations at the end. In the other approach, we placed the TC on the pre-folded NP surface that was found as the lowest energy structure of the simulated annealing runs of the pure plastic. We term this FP (for free particle) approach. The TC was attached to the surface of the plastic in various systematically chosen orientations. A 1 ns molecular dynamics simulations run at 200 K followed to adjust the position and orientation of the drug. These two processes led to a total of 104 aggregates for each NP.

To characterize the binding modes of the chosen drug TC to the various plastics, each of the obtained multiple conformations underwent a geometry optimization based on the OPLS-AA^{59,60} force field. Subsequently, we carried out semi-empirical quantum chemical calculations with implicit aqueous solvation, using the xtb program⁶¹, and the GFN2-xTB method⁶². The structures were all fully geometry optimized. The binding modes and sorption energies discussed in the paper were obtained from these quantum chemical calculations. The methodology is described in the Supporting Information (see Supplementary Fig. S2).

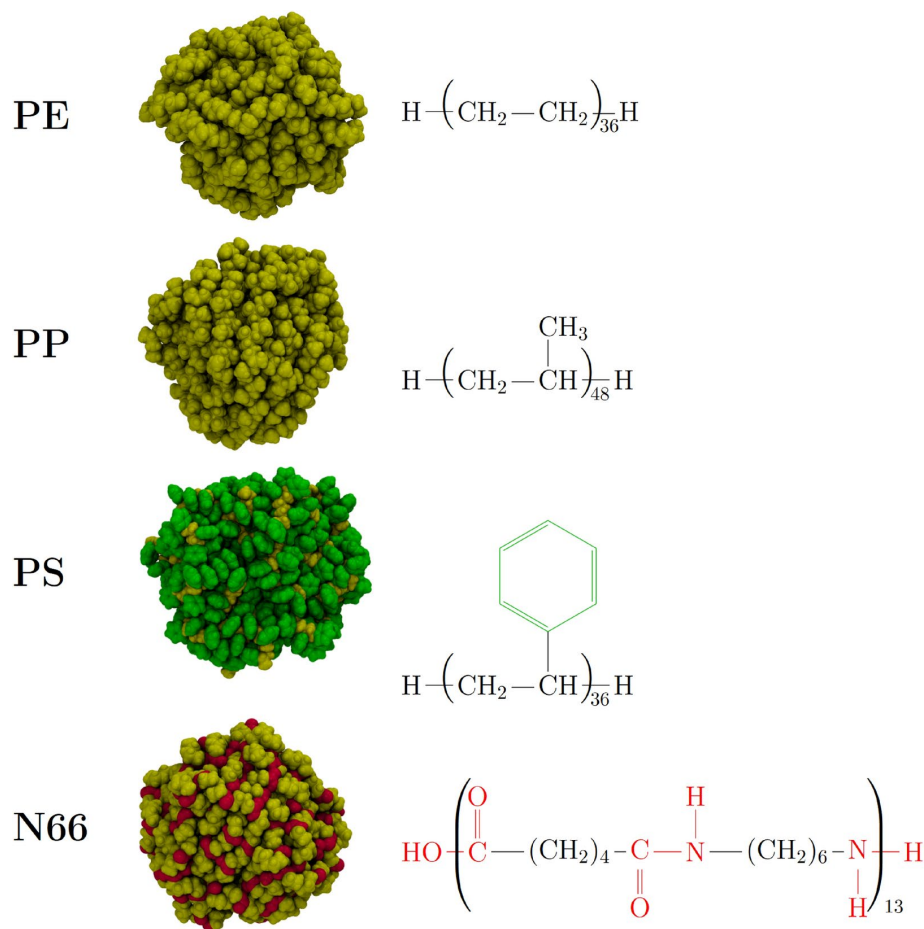


Fig. 2. Ball-and-stick structures and Lewis formulae of the four investigated NP particles; characteristic functional groups of polystyrene (PS, phenyl groups) and nylon (N66, amide units) are highlighted in green and red, respectively. The composition and number of polymer chains use of each NP are given in Supplementary Table S1.

	Size (supplier)/ μm	ζ potential	Size (measured)/nm	PDI (measured)
PET	—	−34.30	1090	0.26
PE	0.2–9.9	−34.72	n.d.	n.d.
PS 1 μm	1.11	−71.75	1158	0.05
PS 0.25 μm	0.252	−64.51	258.3	0.01

Table 1. Particle characterization of the studied plastic particles. The sizes are given as listed by the commercial supplier. Micro- and nanoplastic particles were additionally analyzed for ζ potential, size distribution and polydispersity index (PDI) (1 mg particles in 1 mM KCl).

To study the temperature influence and solvation behavior of the TC@NP aggregates, we performed two molecular dynamics simulations for each type of plastic, with 32000 water molecules explicitly modeled using the LAMMPS⁶³ program package with the OPLS-AA force field for the NP and TC, and the SPC/E⁶⁴ water model. The bond and angle terms of water were constrained throughout the simulations using the SHAKE⁶⁵ algorithm to allow for a time step of 1 fs. Pairwise interactions were computed up to a cut off distance of 10 Å. Coulombic interactions for larger distances were computed using the particle-particle particle-mesh method. The equilibration process was initiated with a minimization with the convergence criteria set to 10^{-4} kcal mol^{−1} for the energy and 10^{-4} kcal mol^{−1} Å^{−1} for the force term. After convergence, a simulation in a microcanonical

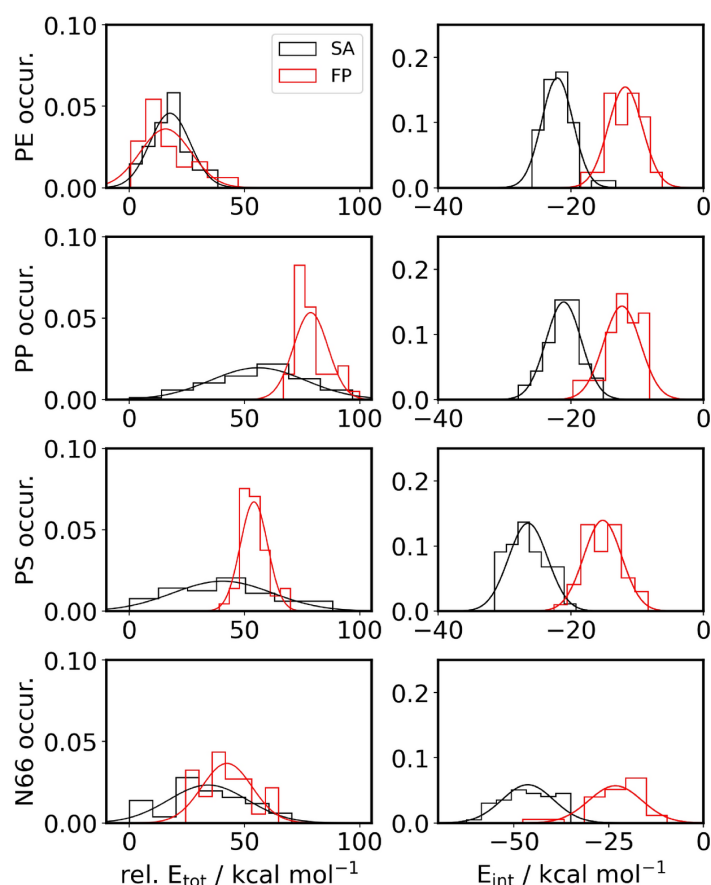


Fig. 3. The distribution of relative total energies referenced to minimum value (left) and the interaction energy for the different NP with TC (right) are presented as histograms with bins of 7 chosen according to Sturge's rule. The normal distribution plots are only to guide the eye.

ensemble was performed to further remove hotspots in the initial configuration over 50 ps, while explicitly rescaling the temperature of the system at 500 K. The temperature was then adjusted in a short NVT ensemble to 293.15 K via a temperature ramp over 100 ps. After the thermal adjustment, the setup was changed to an NpT ensemble to adjust the density over 5 ns. The box volume was averaged over the last 3 ns before adjusting the cell vector to the calculated value. The final cell vectors are listed in the Supporting Information (see Supplementary Table S2). For the final equilibration phase of 0.7 ns and the subsequent production run, the NVT ensemble was used. In the production run of 50 ns, every 10,000-th time step was saved to the trajectory file and later used for analysis. The processing of the trajectories and all of the analyses presented in this paper were carried out using the TRAVIS program suite^{66,67}.

Molecular biology experiments

Microplastic particles were either purchased commercially—polystyrene (PS, microParticles GmbH, Germany; 250 nm or 1.1 μm mean particle size, 5% or 10% w/vol in aqueous solution), polyethylene (PE, Cospheric LLC, United States; size range 0.2–9.9 μm , dissolved at 100 mg/ml in 1% Tween20)—or produced in the lab—polyethylene terephthalate (PET, mean size range of $1.9 \pm 0.3 \mu\text{m}$, dissolved at 630 $\mu\text{g}/\text{ml}$ in 0.5% Tween 20) using a variation of the protocol of Rodríguez-Hernández et al.⁶⁸ PS particle characterization was performed measuring ζ potential, size and polydispersity index (PDI) on a Zetasizer Pro device (Malvern Pananalytical, Malvern, United Kingdom). Data analysis was performed using ZS Xplorer software. ζ potential, size and PDI of 1 mg particles were measured in 1 mM KCl solution (see Table 1). DLS measurements for PE particle were not possible due to the high particles size range. For scanning electron microscopy (SEM) PET particles were dried and mounted on aluminum stubs with conductive tape and Au sputter-coated for 120 s at 50 mA using a sputter-coating device Q150R ES from Quorum Technologies Ltd. (East Grinstead, UK). The SEM images (see Supplementary Fig. S19) were measured using a JEOL JSM-6510 scanning electron microscope from JEOL GmbH (Eching/Munich, Germany). SEM images of commercially supplied particles are provided by the company on request via <https://www.microparticles-shop.de/>, or <https://www.cospheric.com/>. A platinum ATR

	PE				PP			
	SA	SA ^B	FP	FP ^B	SA	SA ^B	FP	FP ^B
Mean	18	18	16	16	56	56	79	79
σ	9	1	11	2	20	3	7	1
95 % conf.	3	–	3	–	6	–	2	–
skew	0.32	0.03	1.00	0.16	–0.47	–0.06	1.09	0.16
kurt	–0.16	–0.02	0.26	0.08	–0.23	–0.02	0.46	0.07
xMed	17	18	12	16	60	56	77	79
xlow	0	13	0	10	0	45	67	75
xhi	38	22	47	24	97	66	100	85
	PS				N66			
	SA	SA ^B	FP	FP ^B	SA	SA ^B	FP	FP ^B
Mean	40	40	54	54	34	34	42	42
σ	22	3	6	1	17	2	11	2
95 % conf.	6	–	2	–	5	–	4	–
skew	0.20	0.04	0.46	0.00	–0.07	–0.02	0.29	0.01
kurt	–0.65	–0.04	0.88	–0.04	–0.52	–0.03	–0.56	–0.04
xMed	41	40	54	54	31	34	42	42
xlow	0	30	39	51	0	25	24	35
xhi	88	51	70	58	70	42	65	49

Table 2. Relative total energy in kcal/mol: Collection of mean, standard deviation (σ), skewness (skew), kurtosis (kurt), x-median (xMed), lowest x-value (xlow) and highest x-value (xhi) for histogram and bootstrapped histogram. SA: simulated annealing approach; SA^B: SA bootstrapped; FP: fixed particle approach; FP^B: fixed particle bootstrapped.

alpha from Bruker (Billerica, USA) with its software OPUS 7.5, was used for FTIR-measurements of all particles (see Supplementary Fig. S20). Light microscopy was performed on an Invitrogen EVOS FL imaging system (see Supplementary Fig. S19). Both mouse (Cebpa^{p30/p30} shCebpa) and human (MV4:11 shRen.713) cell lines were cultured as described previously (Schmidt et al.⁶⁹ and Skucha et al.⁷⁰, respectively). In these cells, expression of the shRNA and the fluorescent reporter protein is under the regulation of a tetracycline-controlled promoter (Tet-On)⁷¹. Microplastic samples were pre-incubated in fetal bovine serum (FBS) for 20 minutes at room temperature, before incubation at given concentrations with tetracycline (CycloPel 300mg capsules, Pelpharma, Cat# 136100, diluted to 16 $\mu\text{g/mL}$ in cell culture medium) at 37 °C for 1 h. Tetracycline $\pm$ microplastic was added to the cells for 45 h before measuring the induction of the reporter on the IQue3 (Sartorius). Data were analyzed using Forecyte 10.0 and FlowJo 10.4.2 and statistical analysis was done with Excel (2308) and GraphPad Prism (6.01). To evaluate the statistical significance of the differences in adsorption rates among various experimental conditions, we conducted a One-Way Analysis of Variance (ANOVA). This method was selected as it allows for comparison of means across multiple groups, providing insights into whether any significant differences exist.

Results

Conformational analysis

The obtained structures of the neat NPs resemble the known features of bulk plastics of the same material, indicating that simulated annealing works reasonably well for these systems. For instance, the most stable N66 particle exhibits a clear structure, in which the amide groups line up to form long chains through hydrogen bonding (red in Fig. 2) that repeat across the roughly spherical plastic, analogously to the crystal structure of this highly crystalline polymer. The folding of multiple chains of these hydrogen bonds into a sphere produces a complex network of mesoscopic structures, as shown in Fig. 2. The three remaining plastics—in which the chains are held together only by weak intermolecular interactions—are often amorphous, also represented in the hereby obtained geometries, lacking any clearly recognizable features. The detailed structure of these particles has been described elsewhere^{51,52}.

The surface structure of the particle determines its solvation and the interactions with any molecule that is adsorbed on its surface. Both PE and PP consist solely of non-polar functional groups, therefore their surface lacks hydrogen bonding sites. However, the surface of PP should be rougher due to the presence of the methyl groups that hinder the close alignment of the polymer chains. The PS particle exhibits a significant portion of its phenyl functionalities at the surface, pointing away from the rest of the plastic (Fig. 2). The resulting surface contains many cavities and voids, which may affect adsorption processes. N66, on the other hand, has several polar amide groups on its surface, which can form multiple hydrogen bonds with either the aqueous solvent, or the molecule to be adsorbed. Due to these differences in the structure of the various MNPs investigated here, the tetracycline molecule is expected to behave differently when interacting with each particular NP.

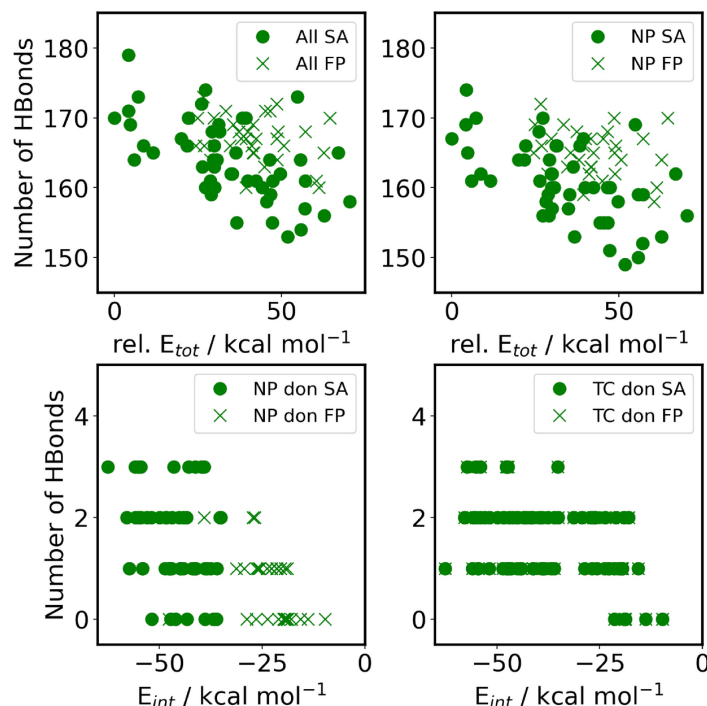


Fig. 4. Number of hydrogen bonds in TC@N66 against energies. Each symbol represents an aggregate conformer. Upper left: All hydrogen bonds in the system versus relative total energies. Upper right: All hydrogen donated and accepted by the NP versus relative total energies. Lower left: All hydrogen bonds accepted by the TC molecules versus interaction energies. Lower right: All hydrogen bonds donated by the TC molecule versus interaction energies. (Hydrogen bonds against the index see Supplementary Fig. S8.

Employing the two separate strategies described in the Methods section and the Supporting Information, we produced 104 conformations for each plastic. Simulated annealing is a conformational search approach, and its aim is not to generate a thermodynamic ensemble; hence, strictly speaking, only the lowest energy structures are thermodynamically meaningful. Yet, since it is a stochastic algorithm, the geometries produced can be considered to be a random sample from the conformational space. Similarly, we distributed the TC in the FP approach over the whole NP, producing random orientations (see Supplementary Fig. S1). Therefore, the geometries obtained can be seen as an extension of that sample. Thus, comparing the resulting structures in terms of geometry and energy can lead to a more detailed understanding of TC-NP interactions and allow for a more sophisticated approach to produce the present macromolecular clusters.

It must be stressed here that the inherent features of the SA and FP methods determine some differences in the meaning of the data. First, the plastic is refolded in the SA approach, the relative energies of the structures produced may result from the imperfect alignment of the polymer chains. On the other hand, in the FP method, an already reasonable plastic structure is selected. Therefore, the energy differences are all related solely to the plastic-TC interaction. However, shown below, it is essential to select the proper neat plastic structure for FP if the energies are to be compared directly to those obtained from SA. Second, the refolding allows the plastic to better adjust to the molecule it should interact with, and therefore the ideal modes of plastic-TC interplay can be tracked. In contrast, in FP, only a limited adjustment of the surface to the drug can be expected. Third, somewhat related to the previous point, if the drug should penetrate the plastic particle, i.e., diffuse in between the chains, FP will not be able to recognize the full extent of the complex adsorption behavior that is the focus of our study.

The relative total energies of the structures vary considerably (Table 2 and left side of Fig. 3), in the range of up to 100 kcal mol⁻¹, which underscores the need for multiple folding attempts to ensure that higher energy conformations and the related erroneous conclusions regarding structures and energies can be avoided. As expected, the FP data (shown in red in Fig. 3) scatters less, as these conformer aggregates differ exclusively in their surface structure. This finding, together with the higher energy values of xlow in Table 2 shows it is inferior to the SA approach. For PE the scatter is the lowest and SA as well FP exhibit similar distributions.

The scatter in SA is greatest in case of PP and PS, as shown by the standard deviation (σ), the x-median (xMed) and highest x-value (xhi) numbers in Table 2. Note the bootstrapping (SA^B values) of this data reduces the standard deviation to about 3 kcal/mol. Further note, the bootstrapping does not find lower energy values but works within the range of the original data, which is why xlow never reaches 0. The two plastics (PP and PS) are, presumably, due to the functional groups branching off the backbone, apparently more complicated to fold.

In other words, the roughness of the chains should produce higher barriers between the minima, which hinders the rearrangement from a high-energy structure into a more stable one. This feature makes simulated annealing more likely to get trapped in a higher energy structure, making SA much more sensitive to the particular setup of the procedure. Thus, the refolding of the TC@NP complexes by the SA approach yields a higher portion of thermodynamically unstable or metastable structures than in the case of the other two plastics (cf. σ , xMed and xhi values in Table 2).

Similarly, the different conformations of a N66 polymer chain should exhibit significant barriers since the rearrangement between them may necessitate breaking hydrogen bonds between the amide groups. This not only makes the SA approach more likely to result in a higher energy structure but also makes the differences in the relative energies between the various conformations larger, as a single hydrogen bond can be more than 10 kcal mol⁻¹ in strength. Hydrogen bonds can be observed and counted within the structures by defining a distance criterion (3.5 Å) and an angle N-H...O cutoff (30°), exhibiting total numbers between 150 and 180. These values show a common trend with the total energy of the structure. However, there are apparently other effects at play (Fig. 4), which prompted us to refrain from a linear regression analysis. Furthermore, although the repeating sequences of the hydrocarbon and amide moieties create a well-defined surface, they also make different sites that can interact with the tetracycline with varying strengths. Thus, the number of hydrogen bonds between the drug and the nanoplastic varies greatly, strongly affecting the interaction energy between the two compounds (see right side of Fig. 3 and Table 3).

A lower scatter in the relative total energies was found since the same structure was taken for each plastic for FP (Fig. 3). However, as the plastic particle cannot adjust to the drug, and hence the drug cannot enter the particle, using a pre-folded particle to study drug-plastic interplay can lead to an underestimation of the stability of the corresponding complexes and the strength of the interaction. In contrast, when refolding the plastic structure in the presence of the TC, the polymer chains can adjust to the TC molecule, and choose the best possible conformation to maximize the sum of NP-NP and NP-TC interplay. This difference can be clearly demonstrated via the example of the interaction of the N66 particle with TC. The FP approach has a significantly higher propensity of creating structures with fewer hydrogen bonds between drug and plastic, yielding substantially less stable structures than the SA method (Fig. 4). According to the data in Table 2, it is evident that refolding the plastic to let it adjust to the drug produces significantly more stable structures, with differences between the most stable structures from the SA and FP approaches of up to 66.7 kcal mol⁻¹. It should be, however, also mentioned here that the sizable difference in total energies between the structures obtained through these two approaches partly stems from the reference structure in the FP method. We selected the folded plastic structure that exhibited the lowest energy according to the molecular mechanical force field calculations at the end of the energy minimization after the simulated annealing of the plastic. However, the semi-empirical quantum chemical energies, after geometry optimization, showed a slightly different trend, shifting the reference energies significantly. However, the interaction energies—used as reference the neat plastic particle with an identical geometry to that within the complex—also indicate a superior performance of the SA approach.

	PE				PP			
	SA	SA ^B	FP	FP ^B	SA	SA ^B	FP	FP ^B
Mean	-22.0	-22.0	-11.8	-11.8	-21.1	-21.1	-12.3	-12.3
σ	2.4	0.3	2.6	0.4	2.7	0.4	2.8	0.4
95 % conf.	0.7	–	0.8	–	0.8	–	0.9	–
skew	1.07	0.16	-0.29	-0.02	-0.06	-0.02	-0.75	-0.12
kurt	2.12	0.00	-0.24	0.03	0.37	0.02	0.20	-0.02
xMed	-22.2	-22.0	-11.5	-11.8	-21.0	-21.1	-12.0	-12.3
xlow	-25.9	-23.1	-18.5	-13.2	-27.9	-22.5	-19.7	-14.1
xhi	-13.3	-20.5	-6.2	-10.2	-15.1	-19.5	-8.2	-10.8
	PS				N66			
	SA	SA ^B	FP	FP ^B	SA	SA ^B	FP	FP ^B
Mean	-26.4	-26.4	-15.2	-15.2	-46	-46	-23	-23
σ	2.9	0.4	2.9	0.4	7	1	7	1
95 % conf.	0.8	–	0.8	–	2	–	3	–
skew	0.36	0.08	-0.03	0.00	-0.23	-0.03	-1.41	-0.24
kurt	-0.70	0.03	-0.03	-0.01	-0.79	-0.03	3.27	0.08
xMed	-27.1	-26.4	-14.9	-15.2	-46	-46	-21	-23
xlow	-31.5	-28.1	-22.6	-16.7	-63	-50	-48	-29
xhi	-19.3	-24.8	-8.3	-13.8	-35	-43	-10	-19

Table 3. Interaction energy: collection of mean, standard deviation (σ), skewness (skew), kurtosis (kurt), x-median (xMed), lowest x-value (xlow) and highest x-value (xhi) for histogram and bootstrapped histogram. SA: simulated annealing approach; SA^B: SA bootstrapped; FP: fixed particle approach; FP^B: fixed particle bootstrapped.

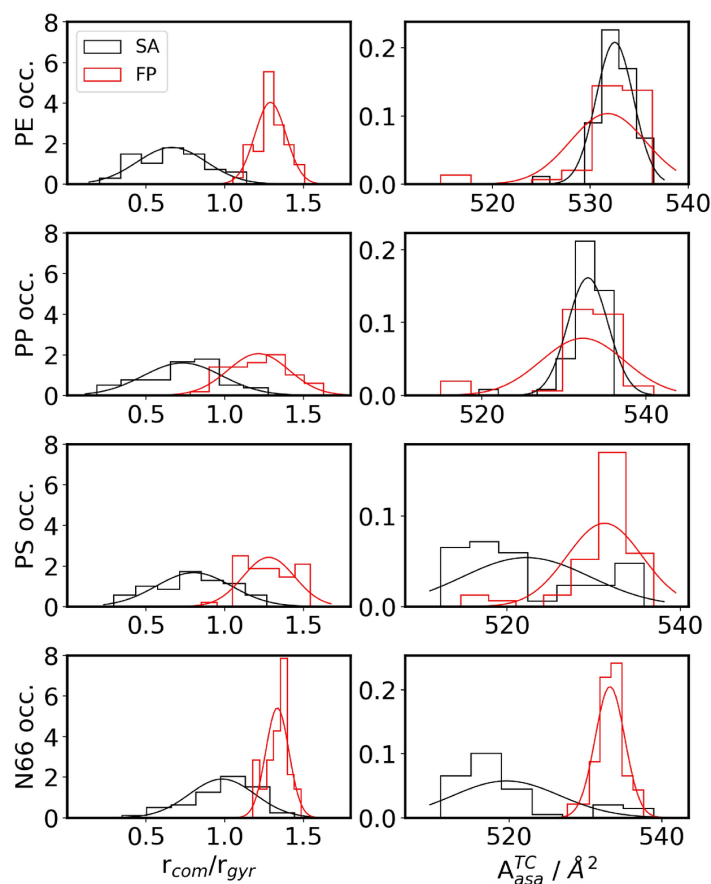


Fig. 5. Left: Occurrence of ratio of center of mass distance (TC to NP) divided by the radius of gyration of the NP. Right: Occurrence of accessible surface area A_{asa}^{TC} for TC. The histograms are done with bins of 7 according to Sturge's rule. The normal distribution plots are only given to guide the eye.

Analyzing the structures and correlating plastic-drug interaction energies and the total relative energies with the way TC is situated on the NP provide essential information on how this antibiotic prefers being adsorbed on the plastic surfaces considered here. Tetracycline has multiple polar functional groups, concentrated predominantly on one side of the molecule, see Fig. 1. This almost amphiphilic structure determines the modes of interaction between TC and the NP. On polyethylene, the less polar side of the molecule is attached to the plastic, while the carbonyl, hydroxyl and amide groups point toward the aqueous solvent. On N66, the alignment of TC is opposite, and the polar-polar interaction between the particle and the antibiotic is apparently stronger than the solvation of these very groups.

It is interesting to point out that the drug molecule in the SA approach, which produces the more stable TC@NP structures, the drug molecule is often situated “inside” the particle, buried beneath the polymer chains. A similar observation was made by molecular dynamics simulations of a peptide adsorbed on the surface of a NP³². The driving force for the SA to produce such conformations should be that if the polymer surrounds the tetracycline, they interact through a larger interface, stabilizing the structure, provided that the drug-plastic interactions can compensate for the disrupted plastic-plastic interplay. This finding is in line with the swelling of plastic surfaces in hydrophobic media, which involves the solvent molecules penetrating the interfacial region of the polymer, loosening the entangled structure of the plastic.

If a molecule, adsorbed onto the surface of a nanoplastic particle, can diffuse in between the polymer chains, this would have significant consequences. In case of the most frequently investigated nanoparticles—built from e.g. metals, metal oxides, silicates—it has been discussed that their composition does not necessarily play a pivotal role in their toxicity, as its environment, for instance a cell may sense and respond to only the molecules that cover the surface, i.e., the corona^{72,73}. Plastic nanoparticles possess, however, a property that makes them significantly different from materials mentioned above, namely that they are composed of polymer chains that may be associated only through weak secondary intermolecular forces. Thus, instead of having a distinct border between the particle and its corona, these two materials may mix, forming a heterogeneous droplet composed

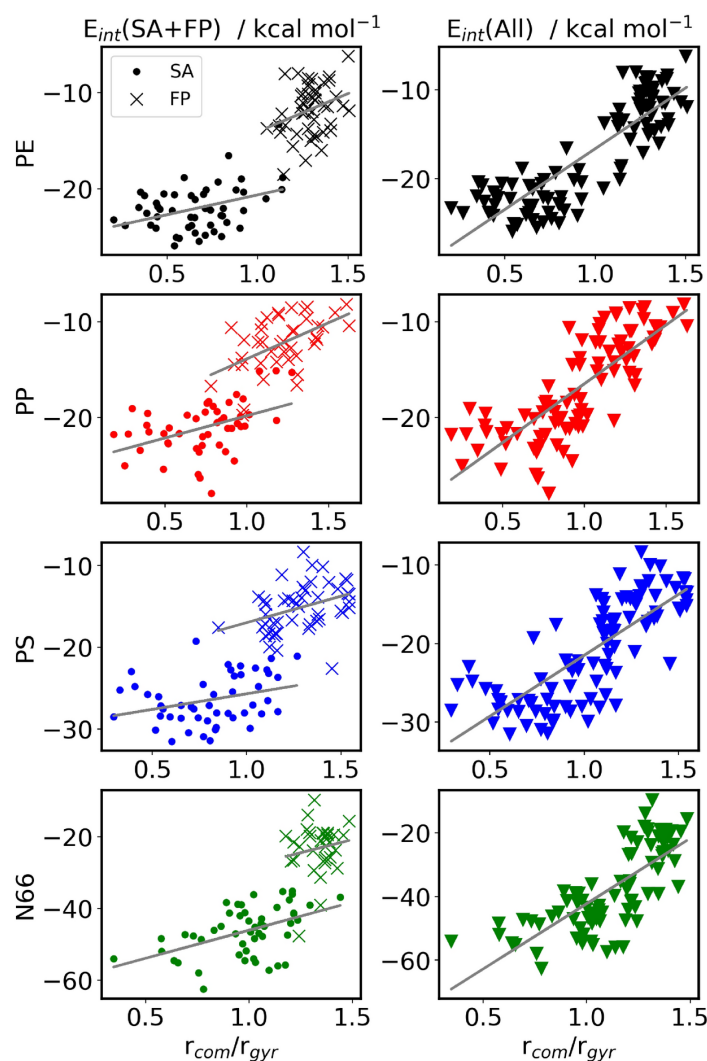


Fig. 6. The ratio of center of mass TC versus NP and the radius of gyration plotted against the interaction energy.

of a mixture of multiple compounds. Furthermore, the capacity of a nanoparticle to carry environmental molecules—e.g. drugs, endocrine disruptors, heavy metals, pesticides—should be higher, if the whole volume of the species is accessible for these compounds rather than just its surface.

To quantify this effect, we defined the ratio of the drug-plastic centers of mass distance (r_{com}) and the radius of gyration (r_{gyr}), see Fig. 5 left. Assuming a perfect, homogeneous sphere, this ratio converges to a value of $r_{com}/r_{gyr} = 1/\sqrt{3/5} \approx 1.29$ for a particle sitting directly on the surface. However, due to the NPs rough surface structure and empty spaces within the particle, r_{gyr} is generally larger for all investigated structures. Additionally, the r_{com} does not contain information regarding the orientation of the TC with respect to the NP. Therefore, the ratio has certain limitations in its accuracy to predict the TC position, but from visual observation of the analyzed structures, we found that the values of r_{com}/r_{gyr} , for structures with the TC positioned on a NPs surface, mostly lie in a range of 1–1.4. As a crude approximation and for simplicity we decided to characterize structures with ratio below 1 as the TC being inside the NP. For all plastic particles we observe that the scatter for the SA method is wider than that for the FP approach, which is particularly the case for PE and N66. Supplementary Table S3 shows the corresponding statistics. Additionally, the FP approach, apparent for obvious reasons, shows higher values of the ratio, i.e., the conformers do not show the TC molecule inside of the NP as opposed to the SA conformers. Interestingly, and in contradiction to the very hydrophilic nature, the TC can enter the PE and the PP in more cases than the N66 where the TC molecule is found closer to the surface than deep inside of the NP, i.e., the mean of the ratio is 1 for N66 and 0.7 for PE as well as for the PP.

Plastic	ΔE_{int}	ΔE_{reorg}^{NP}	ΔE_{reorg}^{TC}	ΔE_{ads}	A_{asa}^{TC}
PE	-23.2	8.7	10.3	-4.3	530
PP	-22.0	1.0	10.3	-10.6	536
PS	-25.2	1.6	12.0	-11.6	518
N66	-36.0	1.9	15.0	-19.1	518

Table 4. Interaction energies (ΔE_{int}), reorganization energies for the plastic particle (ΔE_{reorg}^{NP}) and tetracycline (ΔE_{reorg}^{TC}), sorption energies (ΔE_{ads}) and accessible surface area of tetracycline (A_{asa}^{TC}) for the most stable obtained tetracycline-nanoplastic aggregates. All energies are given in kcal mol⁻¹.

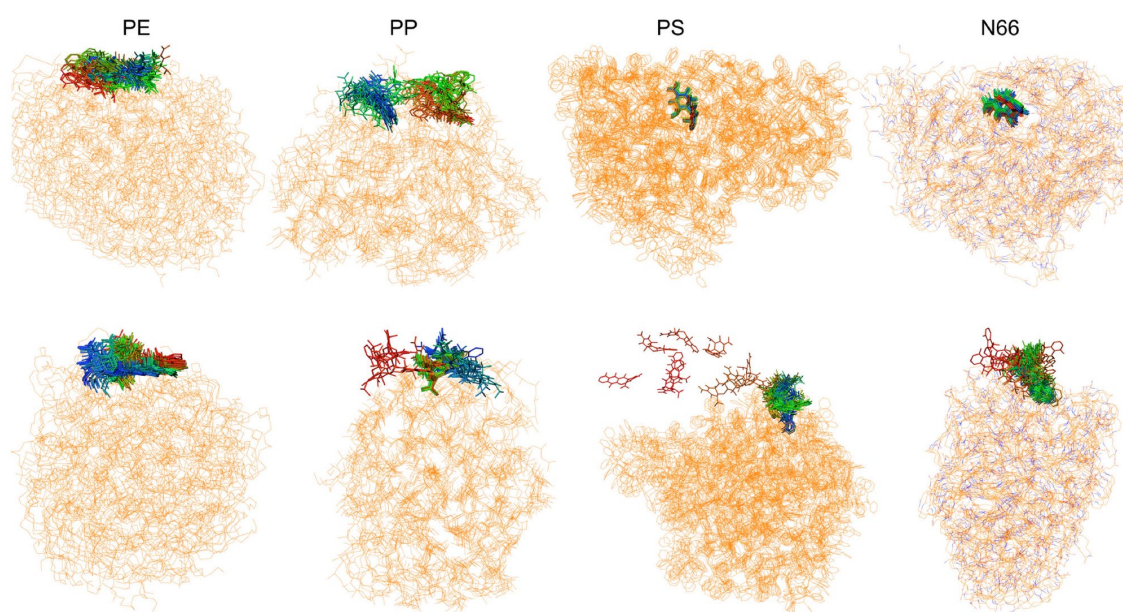


Fig. 7. Snapshots of the MD simulations of the tetracycline-plastic systems. 100 snapshots are overlapped with the tetracycline shown in color-changing-with-time. Water molecules are omitted for clarity. Start: Red, Middle: Green; and End: Blue; Above: trajectory starting from a small r_{com}/r_{gyr} ratio; Below: trajectory starting from a large r_{com}/r_{gyr} ratio.

When plotting the interaction energies (ΔE_{int}) against r_{com}/r_{gyr} for all the structures obtained, it becomes apparent that there is a notable, albeit somewhat weak correlation between these two quantities, with a stronger interplay when the drug molecule is inside the plastic particle (Fig. 6). As approaching from the larger r_{com}/r_{gyr} values—i.e., from the structures with the TC excluded from the plastic particle—the slope of this correlation is quite large. Thus, if the TC is closer to the surface, the energy decreases significantly, as the drug/plastic interface grows. However, when the $r_{com}/r_{gyr} = 1$ value is reached, the slope becomes smaller, since from this point on the plastic has already covered most of the antibiotic, and therefore burying this molecule deeper into the particle does not produce significant further stabilization. Thus, in the structures with the TC inside the plastic, the energy of the system will probably exclusively depend on the efficiency of the polymer chains' packing. In agreement, the total energies of these structures exhibit a different trend, and in contrast to the ΔE_{int} , the structures with the minimal ΔE_{tot} do not necessarily correspond to structures with low r_{com}/r_{gyr} ratios (see Supplementary Fig. S12).

After observing this common trend between interaction energy and r_{com}/r_{gyr} ratio, and the finding that the more the TC is inside the NP the stronger it interacts with the plastic, the accessible surface area (A_{asa}^{TC}) of the TC puts these results into a different perspective. Figure 5 (right) plots this measure for all plastic particles. For the FP approach, all particles behave similarly, with a mean value of 533 Å² (see Supplementary Table S4 and Supplementary Fig. S13). This value also coincides with that obtained from the SA approach in case of PE and PP. These are the NPs, in which the TC is buried most. For PS and N66, however, lower average A_{asa}^{TC} values were found with 522 and 520 Å², indicating that the antibiotic adopts a more compact conformation, associated with a higher reorganization energy ΔE_{reorg}^{TC} (see Table 4 for the values of the most stable TC-NP aggregates), to maximize its interaction with the given NP.

Plastic	AD		A		D	
PE	5.334	5.452	3.828	3.976	1.506	1.476
PP	5.428	6.034	3.876	4.394	1.552	1.640
PS	0.268	4.872	0.030	3.444	0.238	1.428
N66	0.896	4.814	0.884	3.960	0.012	0.854

Table 5. The average hydrogen bond number with AD/A/D indicates acceptor and donor hydrogen bonds from the TC molecule to water. First value: trajectory starting from the small $r_{\text{com}}/r_{\text{gyr}}$ ratio; Second value: trajectory starting from the large $r_{\text{com}}/r_{\text{gyr}}$ ratio.

While TC clearly penetrates less into N66 and remains closer to the surface, the average accessible surface area of TC is the smallest in these complexes (cf. Fig. 5 left and right), highlighting that the driving force behind the more compact conformation is to maximize the favorable interactions with the NPs and is not caused by the embedded position within the NPs. This implies that in case of PE and PP, the TC is in a relatively large void, arising from packing effects within the NP.

The interaction energies (ΔE_{int} , see Fig. 6 and Table 4) were found similar for the three polyolefins PE, PP, and PS, as they are all similar in interacting with tetracycline solely through weak van der Waals forces. The strongest interaction can be observed for N66, which—as discussed above—offers a multitude of hydrogen bond donor and acceptor sites to the antibiotic (Fig. 4). However, rearranging the polymer chains in this plastic to make the cavity for the drug requires more energy due to the strong interactions between the amide moieties of N66, making the structure with TC attached to the surface, rather than embedded, energetically more favorable. In the case of PP and PS, the substituents that are attached to the backbone of the polymer chain hinder these chains from being packed very close to each other, leaving significant voids in the structure of the plastic itself. In the presence of these cavities, the reorganization of the plastic in the adsorption process is less demanding energetically compared to PE.

The combination of the effects above results in the adsorption energies (ΔE_{ads}) presented in Table 4. Interestingly, although the ΔE_{int} data were similar for all polyolefins, the ΔE_{ads} values were more negative for PP and PS, due to the lower reorganization energy of the plastic upon adsorption. The high ΔE_{int} found in the case of N66 yields the most negative adsorption of the four hereby investigated plastic materials.

Tetracycline on and in nanoplastics solvated in water

Based on the SA and FP calculations, we found that the present drug-polymer systems form low-energy aggregates with the tetracycline, with thermodynamically favorable adsorption. Moreover, the drug often prefers being inside the plastic particle, fully covered by the polymer chains. For the formation of these conformations, the polymer chains must be mobile enough for the antibiotic to penetrate the particle. Therefore, we investigated two TC@NP structures of each type of plastic in water using molecular dynamics simulations to gain preliminary knowledge about their stability concerning temperature and solvation. The investigated structures were selected from the SA approach, with the two structures of each plastic being those with the highest and lowest $r_{\text{com}}/r_{\text{gyr}}$ ratio, of all structures lying within 20 kcal mol^{−1} of the energetically best TC@NP structure. We paid special attention to the solvation of these aggregates, and the mobility of the molecules they are comprise.

The mobility of the chains can be expressed through the root mean square deviations (RMSDs, Supplementary Fig. S16), which describe how much the atoms of the TC@NP system rearrange over time. It is visible that the plastics exhibit significant differences in their mobilities. The least mobile structures are PS chains, which have the largest functionalities attached to the polyolefin backbone that can provide significant friction or steric hindrance in their rearrangement. Similarly, the movement of the N66 macromolecules is hindered by the strong hydrogen bonds between the amide groups, although the hydrocarbon units in between may have some mobility. The rearrangement of PE is somewhat more significant, but that of PP is remarkable, showing almost two times larger deviations with respect to the starting structures.

These results show that while the simulation time is limited compared to the time scale of macromolecular motion, at least PP is capable of rearranging enough to accommodate drug molecules within, e.g. tetracycline. In case of this particular drug, however, radial diffusion can occur in both directions. In case of the low $r_{\text{com}}/r_{\text{gyr}}$ ratio simulations with PE and PP, the moieties that covered TC, and separated it from the aqueous solvent, rearranged in a way that TC was uncovered already during the equilibration phase. This change allowed the polar, hydrophilic substituents of TC to interact with the water molecules, resulting in the stabilization of the system.

In agreement, plotting the radial position of the TC in or on the NP (r_{COM}) as a function of time shows that the drug diffuses significantly on top of the PP and N66 particles (see Supplementary Fig. S17). It is also notable that in case of PS, the drug detached from the surface during the equilibration. However, it found its way back to the plastic over the course of the subsequent production run, apparently finding a stronger binding site. The fact that the drug was spontaneously adsorbed on the PS represents the affinity of these compounds toward each other, indicating that the complexes obtained here are not metastable states.

Interestingly, except for PS, the r_{gyr} values also change significantly for the particles, especially with small $r_{\text{com}}/r_{\text{gyr}}$ ratio (see Supplementary Fig. S17). Over the course of the simulation, these systems seem to shrink, obtaining a more compact packing of the polymer chains. This process appears to be slower than the range of the present simulations, and would presumably continue after the 50 ns of physical time that was simulated here.

Considering the $r_{\text{com}}/r_{\text{gyr}}$ ratios, it is visible that the shrinking of the particles and the radial movement of the TC results in an overall rearrangement of the TC@NP complex. For most plastics, this mobility is more intensive in the first quarter of the simulation. The movement of the TC can be shown by overlaying its position through the 50 ns run (Fig. 7). It is clearly visible that the TC molecule rearranges and drifts notably. In case of PP, this movement is especially striking, in accordance with the aforementioned dynamics of the TC@NP complex.

The dynamics of the system can also be observed by the development of the number of hydrogen bonding interactions between the TC and the neighboring water molecules over time (see Table 5 and Supplementary Fig. S18). In case of the simulations with the TC at the surface—i.e., with large $r_{\text{com}}/r_{\text{gyr}}$ ratio—the number of hydrogen bonds is high, many of the hydrogen bond donor and acceptor sites are occupied with a water molecule. In case of the PS particle, the re-adsorption of TC can be followed through the number of hydrogen bonds, gradually as the plastic prevents access of the water molecules to the drug. This suggests that via the alignment of the TC at the surface of the plastic, the polymer chains rearrange so that the drug is covered more and more as the simulation progresses further.

For the simulations, starting from the antibiotic within the plastic particle—i.e., having a low $r_{\text{com}}/r_{\text{gyr}}$ ratio—significant differences can be observed. N66 and PS keep the TC inside the particle, and therefore, water molecules cannot approach the hydrogen bonding sites of the drug (see Supplementary Fig. S18). Furthermore, the hydrogen bonding sites of N66 can form interactions with TC, as discussed above; hence, they effectively compete with water for the antibiotics. In the case of PE and PP, as the polymer chains make way for the water molecules already during the equilibration phase, the number of hydrogen bonding interactions between the solvent and the drug is similarly high to that in the simulations starting from structures with the TC on the surface of the plastic (see Supplementary Fig. S18).

Experimental proof for the relevance of tetracycline-plastic interactions in biological media

Earlier experiments showed that dissolved organic matter decreases the ability of MNPs to adsorb TC^{45,49}. However, in a more complex matrix that is present in biological systems, the intricate network of intermolecular interactions can cancel such effects, and despite the presence of organic substances, a significant amount of TC is adsorbed by the MNP. Thus, to test changes induced by microplastics in the cellular effect of tetracycline, we used two cell line models in which tetracycline-induced gene expression can be measured via the induction of a fluorescent reporter. We found that incubation of cells with all three types of microplastics tested (PS, PE and PET) caused a significant reduction of the tetracycline-induced expression (40–50%) of the reporter protein in both human and mouse cell lines after 45 h (Fig. 8).

Summary and conclusion

In this work, the interaction of nanoplastics with biologically active compounds was investigated, on the example of the antibiotic drug tetracycline, through theoretical chemical methods and in vitro experiments. We chose two alternative strategies to generate thermodynamically relevant conformations, both relying on simulated annealing molecular dynamics. In the first approach (SA), the plastic was folded through simulated annealing in the presence of the tetracycline. Since the folding, due to the limited simulation time of the annealing, may result in high energy structures, we performed this process 50 times for each plastic-tetracycline system from different

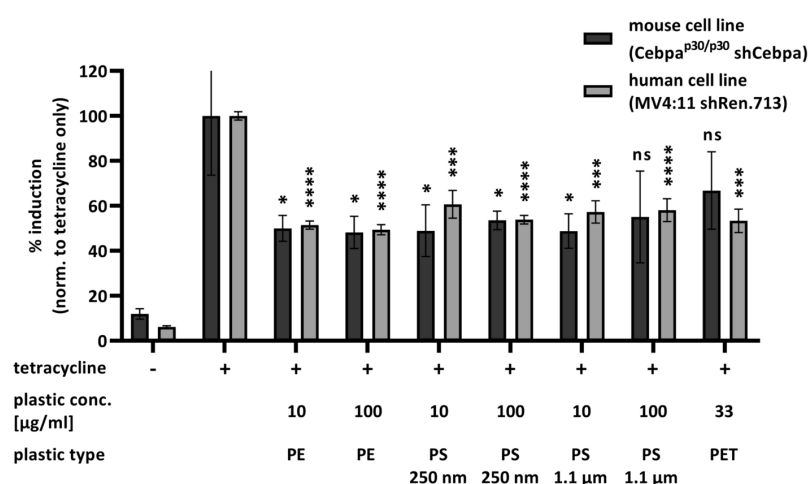


Fig. 8. Effects of polystyrene (PS, 250 nm or 1.1 µm mean particle size), polyethylene (PE, size range 0.2–9.9 µm) or polyethylene terephthalate (PET, 1.9 µm mean particle size) microplastic particles at given concentrations on tetracycline-induced expression of a dsRed or IRFP670 fluorescent reporter in mouse or human cells, respectively. The percentage of dsRed or IRFP670 induction was normalized to the effects of tetracycline only [16 µg/ml] (n = 3). Statistical significance *p < 0.05, ***p < 0.001, ****p < 0.0001 was assessed by a two-tailed t-test. ns not significant.

starting geometries. In the other strategy (FP), we first folded the neat plastic, and then placed the tetracycline in several orientations onto the surface of the best structure found, followed by a short molecular dynamics run. The 104 obtained structures from the two methods underwent a semiempirical quantum chemical geometry optimization with an implicit solvent model, which gave the accessible most accurate relative energies for the different geometries.

The difference between the two approaches becomes apparent when analyzing the structure and energy of the aggregates obtained. While folding the plastic in the presence of the tetracycline can result in high energy structures, it allows the reorientation and adjustment of the polymer chains to the drug. It is, therefore, not bound by the starting geometry of the plastic particle. For all plastics, the SA method produced the most stable plastic-tetracycline complexes. Even more interestingly, in many low energy structures the drug was situated inside the plastic particle, suggesting that such compounds can be bound not only onto the surface of nanoplastics but can diffuse in between the chains. Such a process should be similar to the swelling of plastic surfaces and polymer network in solvents. The experimentally observed morphological changes of MNPs upon adsorption of TC, reported recently, appear to support this finding⁴⁸. These results clearly suggest the superiority of the SA approach over the FP. Therefore, in computational studies, we recommend using this method to create the most stable starting structures.

The resulting adsorption energies show a clear trend, indicating an affinity to the drug decreasing in the order of N66 > PS > PP > PE, in very good qualitative agreement with earlier experimental observations⁴⁵. The values themselves are between $\Delta E_{ads} = -4.3$ and -19.1 kJ mol⁻¹. These values suggest that the adsorption can be in the range that is exothermic enough to make a physical difference in a suspension having both micro- and nanoplastics and this particular drug, but not too exothermic, hence the drug can be delivered from an external source and released in the human body. Verifying the computational results above, experiments with cell line models were conducted, based on tetracycline-induced gene expression. The experiments showed that the effect of tetracycline on the cells decreased significantly in the presence of the plastics.

We performed equilibrium molecular dynamics on selected low-energy structures to observe if the complexes produced in the methods above are stable in terms of temperature and water solvation. These simulations confirmed the affinity of the plastics to the antibiotic, and showed that the chains rearrange already within 50 ns. Furthermore, the tetracycline molecule also appears to drift on the nanoplastic particle's surface. These findings suggest that the mobility of both the plastic and the drug is high enough to allow the radial diffusion of the adsorbed molecule into the inner domain of the particle.

The results above from the simulated annealing, quantum chemistry, and experimental data clearly indicate that the interaction of micro- and nanoplastics with drugs can significantly impact on the environment and human health through multiple mechanisms. First, as shown by the experiments, the absorption of the drug into the human body can be altered if they are ingested together with plastics. Second, the adsorption energies indicate that the adsorption to the plastic is reversible, and the drug may be carried and delivered at a different location later, perhaps even in a different organism. Third, due to the adsorption's thermodynamically favourable nature, the local concentration of antibiotics can be increased at the surface of the particles, which may induce the development of antibiotic-resistant bacterial strains. This is especially the case for those plastics that exhibit more affinity to the given drug, collecting it more efficiently from the given matrix, even at lower concentrations. All these effects are enhanced by the hereby observed effect that the adsorbed molecule—through swelling its polymeric network—can penetrate the plastic particle, making thereby much of its volume available to accommodate the adsorbed molecule than just the immediate surface area. In summary, the results above show that MNPs can pose a variety of direct health risks, as they can carry unwanted drugs into the body, may interfere with medical therapy, and can contribute to the development of antibiotic resistant strains of bacteria.

Data availability

All generated geometry-optimized NP and TC@NP structures are publicly available. The molecular dynamics trajectories analyzed for this study are available on request from O.H. or B.K. due to their size. All data sets resulting from the analyses of the geometrically optimized structures and the MD trajectories are also publicly available and stored on zenodo (<https://doi.org/10.5281/zenodo.12167648>).

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Author contributions

O.H. and B.K. conceptualized and drove the project. L.D. ran the molecular dynamics simulations and performed all geometry optimizations. L.D., P.R.B., and P.Z. analyzed the trajectories which were carried out under guidance of B.K.. P.Z. developed analysis tools for further investigation. B.K., P.Z., and L.D. carried out bootstrapping. B.K., P.Z., L.D., P.R.B., and O.H. curated the data and visualized the results in the respective tables and figures. L.Ke. and F.G. designed the experiment. G.M., V.K., V.P., L.Ko. and L.Ke. performed the experiment and visualized the experimental results. V.B., B.P., and O.H. had the original idea of the subject to study. L.Ke. supervised the experimental part, while O.H. and B.K. supervised and financed the computational part. O.H. took the lead in writing the manuscript with the help of B.K., L.D., P.Z. and P.B.. O.H. came up with the overall direction of the project. All authors discussed the results, as well as reviewed and edited the manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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Appendix: Building Nanoplastic Models for Molecular Calculations

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Own contributions

- Participating in analyzing the trajectories and NP geometries.
- Partially curating raw data, setup of the NP database.
- Participating in the visualization of results and creation of schematics.

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Building Nanoplastic Models for Molecular Calculations

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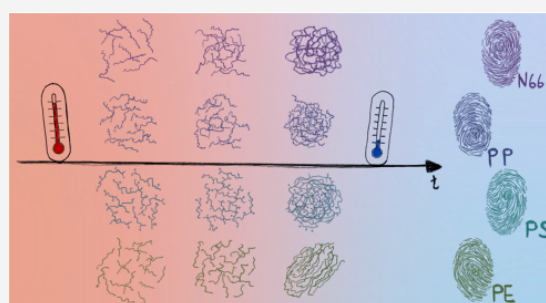


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Supporting Information

ABSTRACT: In exploring the toxicity of micro- and nanoplastics, molecular simulations of plastic nanoparticles have been gaining traction recently. Modeling of nanoplastics involves the folding of multiple polymeric chains into an entangled particle, which is a challenging process, necessitating thorough optimization of the folding procedure. In this contribution, we use the simulated annealing procedure in a systematic workflow for preparing stable nanoplastic structures for the first time, based on the CHARMM36 force field. On the structures prepared with the fine-tuned protocol, we carry out quantum chemical geometry optimizations with the GFN2-xTB method, followed by benchmarking single-point calculations with GGA and hybrid DFT functionals. We further demonstrate the applicability of this approach through four plastic systems, including polyethylene, polypropylene, polystyrene, and nylon-66. Remarkably, the geometry of the resulting most stable assemblies show similarities to features observed earlier theoretically and experimentally for such systems. For polyethylene, a highly ordered, crystalline structure is obtained, in which the polymer chains possess long sections with all C–C–C–C units in *trans* configuration. For polypropylene and polystyrene, helical structures are observed, formed by alternating *gauche* and *trans* configurations along the backbone. For nylon-66, the structure-directing effect of the hydrogen bonds between amide moieties complicates the folding, resulting in parallelly arranged hydrogen bonding chains throughout the particle. Especially, we make the whole set of optimized structures available for the community in an online repository, with hopes of advancing simulation studies in the field, even making ensemble simulations accessible.



INTRODUCTION

The mechanical, chemical, and biological fragmentation of plastic waste produces micro- and nanoplastics (MNPs) of various compositions, sizes, and shapes. These particles are ubiquitous in many kinds of natural and artificial environments,^{1–9} and even more alarmingly, in animal and human tissues.^{10–14} The presence of MNPs in the body has been suggested to be connected to the increasing incidences of e.g., autoimmune and neurodegenerative diseases, as well as various forms of cancer.¹⁵

In efforts to unveil the adverse effects of MNPs, molecular simulations have been playing an increasingly important role due to several reasons.^{16–33} The diversity of MNPs and the complexity of their interactions hamper the characterization of their interplay with biomolecular systems. Experiments themselves are complicated by difficulties in detecting organic particles in biological media, which are inherently complex colloidal systems. These problems are even more restraining when approaching the lower size range of MNPs, i.e., nanoplastics (NPs, $d < 100$ nm). On the other hand, these

minute particles are probably the most relevant in terms of toxicity, as their sheer size being at least 2 orders of magnitude smaller than a eukaryote cell suggests that they are capable of modifying the delicate biochemical balance of living organisms at the molecular level. Fortunately, theoretical chemistry methods suffer from the very opposite problem – as larger systems usually require increasingly larger computational resources to handle, nanoplastics become an ideal target for these methods. Therefore, the structural insights provided by any means of theoretical chemistry, including simulations, offer significant help in this endeavor, defining systematic directions

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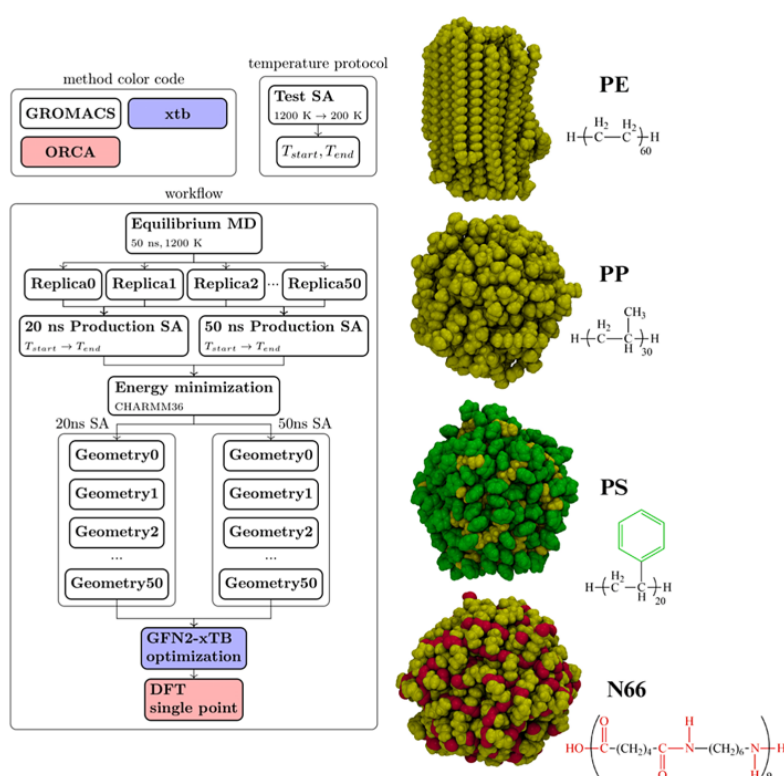


Figure 1 Left: Flowchart of the workflow applied in this work. Right: Ball-and-stick representation of the most stable GFN2-xTB structures, and Lewis structural formulas of the hereby investigated polymer chains. Color code: yellow: carbon and hydrogen atoms, green: phenyl groups; red: polar moieties in N66. The very crystalline structure of PE versus the more unordered structures of the other kinds of plastics stands out.

for the corresponding experimental research and a clearer way of interpreting the results.

Research in this field through theoretical calculations is highly dependent on the nanoplastic model that is used. A faulty structure, with energy hotspots from an unphysical orientation of the polymer chains with respect to each other, can lead to severe artifacts, and thus to erroneous conclusions. Unfortunately, no reasonable structures from experiments are available in such a resolution that it could provide a basis for validation, owing to the high variety of the particles, experimental difficulties, and to some extent also the dynamic behavior (i.e., the high mobility) of the polymer chains constituting the given particle. In modeling practice, these structures are created from one or more polymer chains, by folding them into a globular assembly prior to the simulations of interest, which for the aforementioned reasons should be a low-energy conformation of these particles in the gas or aqueous phase.

Although NPs are small from the experimental perspective, they are still too large (containing atoms between $10^3 < N < 10^7$) to employ systematic conformation search algorithms to find the best possible structures in the folding procedure. Promising possibilities are offered by, for instance, the BUPO method³⁴ or the GOAT approach³⁵ i.e., a new global optimization algorithm that is able to optimize such large structures. Furthermore, modern enhanced sampling techniques like replica exchange molecular dynamics (REMD) or even Boltzmann-weighted reservoir or non-Boltzmann-

weighted reservoir REMD, as well as metadynamics, accelerated MD, and homology modeling, cannot be easily applied to the current systems. Instead, simulated annealing (SA)^{36–38} methods remain the preferred choice, as these are easier to apply simply for computational reasons.

In SA, the system is simulated in a Monte Carlo or molecular dynamics (MD) environment at a high (often even unphysical) temperature, which allows the simulation to explore a large portion of conformational space. Then a gradual cooling is performed, which depopulates high-energy conformations and ideally converges to the global minimum of the potential energy surface. In the case of an infinitely slow cooling protocol, the global minimum will be obtained, but in realistic setups the resulting geometry is often a higher energy structure. Thus, it has been shown that performing several SA simulations increases the chance of finding the low-lying minima.³⁹ However, to minimize the number of irrelevant conformations, it is necessary to fine-tune the approach and adjust it to the problem at hand.²¹ This optimization and the subsequent application in a multitude of SA runs to generate the best structures consume significant computer time. Thus, the identified optimal settings for the SA procedure should be made available for the community, as well as any high-quality structures found, in order to increase accuracy and reproducibility, while facilitating the use of reliable structures for further MNP research.^{40,41}

In the present contribution, we build models for four kinds of plastics: polyethylene (PE), polypropylene (PP), polystyr-

ene (PS), and nylon-66 (N66) using SA. We optimize and evaluate the folding procedure, and discuss the energetics and structural characteristics of the resulting particles. Through tracking and characterizing the folding process, we identify the features that make the lowest energy conformations so stable. Furthermore, for the aforementioned reasons, we have set up an online library containing optimized, low-energy models of these structures, which will be updated with newer structures produced even after the publication of the present results. These inputs will be freely available and can be used in single or ensemble simulations.

METHODS

Molecular Dynamics Simulations

For the simulated annealing and standard molecular dynamics simulations, the Gromacs 2020.3 program was used,^{42,43} along with the CHARMM36 force field⁴⁴ which we will refer to as CHARMM in the following if brevity is needed to estimate the interactions between the atoms within the system. For the polymers, force field parameters were obtained from the CGenFF web interface.^{45–47} The leapfrog algorithm with a 1 fs time step was used for integrating the equations of motion. The temperature was controlled through a modified Berendsen thermostat, with a time constant of 100 fs. The bonds involving hydrogen atoms were constrained through the simulations. The particular workflow and further settings of the simulations were subject to the present development (Figure 1), and therefore, will be discussed in the main part of the paper.

Quantum Chemical Calculations

The last geometries of all production simulated annealing runs underwent an energy minimization with the CHARMM36 force field. The resulting geometries were then subjected to a full geometry optimization with the semiempirical quantum chemical method GFN2-xTB, using the xtb program.^{48,49} Such optimizations require significantly higher CPUh and memory demands with standard electronic structure methods (for timings, see Table S3), which would not be feasible to perform for the current large number of structures. Quantum chemical single-point calculations of the structures optimized with GFN2-xTB were conducted with the BP86^{50,51} functional. For selected CHARMM36 and GFN2-xTB structures, single-point calculations were also performed using the B3LYP,⁵² BP86,^{50,51} PBE,⁵³ PBE0,⁵⁴ and ω B97X-D3⁵⁵ functionals (Figure 1). The def2-SV(P)⁵⁶ basis in combination with the def2-MTZVP/J auxiliary basis for the Coulomb-fitting and the D3 dispersion correction with Becke–Johnson damping⁵⁷ were employed for all these DFT calculations. All other parameters were set to default values. In addition, calculations with the long-range corrected hybrid functional ω B97X-D3⁵⁸ and low-cost DFT methods, such as R2-SCAN-3c^{59,60} and PBEh-3c⁶¹ were performed. All single-point calculations were carried out with the Orca program⁶² version 6.0.1.

Structural Analysis of Nanoplastics

To analyze the structural features of the plastics resulting from the SA procedure, we used our recently developed code, MakroLyzer.⁶³ Designed for the characterization of macromolecular systems, MakroLyzer leverages graph theory to identify monomeric units and to define the backbone of the plastic chain. Available functions include calculating the radius of gyration (R_g), end-to-end distance of linear polymer chains

($\vec{r}_n$), anisotropy factor ($\langle \chi^2 \rangle$), asphericity parameter (b), and evaluating local conformations of C–C–C–C quadruplets along the backbone. Furthermore, a parameter to quantify orientational order is available in the program, based on the second Legendre polynomial (P_2). Number of hydrogen bonds for N66 were also calculated with MakroLyzer, with an O–N distance cutoff of 3.5 Å, an O–H distance cutoff of 2.5 Å, and a H–N...O angle cutoff of 30°. Further details can be found in ref 63.

RESULTS AND DISCUSSION

Generating Nanoplastic Models

As discussed above, one of the main difficulties regarding the discussion of the toxicity of micro- and nanoplastic particles is the extremely high variation of these materials, in terms of composition, molecular structure, size, and shape. Clearly, it is impossible to simulate infinite kinds of particles that might be present in the environment as pollutants. Thus, the aim of any study in this complex field can only be to investigate a large enough ensemble, i.e., a few selected particle types, and then carefully generalize the conclusions based on the assumption that other particles would behave similarly in the same local environment. Accordingly, our goal in this paper is not to generate all conceivable kinds of nanoplastic models, but to establish a standard workflow to create these structures and identify all potential issues that can complicate their production. Furthermore, we also aim to generate several reasonable structures, which will be openly available and readily usable as starting points in molecular simulations or other theoretical calculations. The multiple structures (i.e., a conformational ensemble) that will be made accessible will also enable ensemble simulations^{64,65} to be carried out, so that a better sampling of phase space and a deeper understanding of the physicochemical behavior of the corresponding particles can be achieved.

In this article, we chose very simplistic model polymers, without any branching or cross-links, but the protocols developed here can be extended to these more complex macromolecules in a follow-up work. For choosing the length of the polymer chain, the limiting factor was the force field fitting by the CGenFF interface,^{45–47} allowing a maximum of 384 atoms for a single molecule. Although it would be possible to generate a force field by other means for a longer polymer chain (e.g., fitting them anew), that was not the goal of the present study. Furthermore, within these limits, we could define macromolecules that should as much as atomistic simulations allow in terms of size and simulation time⁶⁶ exhibit polymer-like features, and should generate a core and surface structure that are realistic for nanoplastics. In the case of vinyl-type polymers (PP, PS), the tacticity of the structure i.e., the relative stereochemical arrangement of adjacent monomer units was considered carefully. Since commercially available PP has a high isotactic index, we also built an isotactic structure for this plastic. PS, on the other hand, is mostly atactic, and therefore, we chose to generate this kind of structures in our simulations. The total size of the systems was chosen to add up to nanoparticles of ca. 3–5 nm in diameter. The composition of the polymer molecules and the number of chains are presented in Table 1.

To prevent the formation of solvent inclusions inside the plastic, we performed all SA runs in the gas phase. At higher temperatures, the diffusion of vaporized polymer chains

Table 1 Characteristics of the Nanoplastic NP Models and Corresponding Settings for the Simulated Annealing

NP	chain	N_{chain}	N_{mon}	N_{atoms}	$N_{\text{ha}}/N_{\text{chain}}$
PE	$\text{C}_{120}\text{H}_{242}$	9	60	3258	120
PP	$\text{C}_{90}\text{H}_{182}$	13	30	3536	90
PS	$\text{C}_{160}\text{H}_{162}$	12	20	3864	160
N66	$\text{C}_{108}\text{H}_{200}\text{N}_{18}\text{O}_{19}$	11	9	3795	145
NP	$M_{\text{chain}}/\text{g mol}^{-1}$	N_{bf}	$T_{\text{start}}/\text{K}$	T_{end}/K	ABC/ $\text{\AA}$
PE	1685.20	19476	620	210	220
PP	1264.40	21112	540	210	110
PS	2084.99	30768	700	270	100
N66	2054.84	26730	700	310	230

^aChain: chemical composition of each individual chain; N_{chain} : number of polymer chains in each NP; N_{mon} : number of monomer units in each chain; N_{atoms} : total number of atoms in the nanoplastic particle; $N_{\text{ha}}/N_{\text{chain}}$: number of heavy atoms per chain; M_{chain} : molecular weight of an individual chain; N_{bf} : number of basis functions for whole nanoplastic particle with the def-SV(P) basis set; T_{start} : starting temperature of the cooling by simulated annealing; T_{end} : end temperature of the cooling by simulated annealing; ABC: cell vector of the cubic periodic box used for the simulations.

through infinite space could obstruct aggregation; therefore, periodic boundary conditions were employed, with a larger box size than the length of a single chain in the given system (Table 1). The polymer chains were placed randomly in the simulation box using the packmol software.⁶⁷ In order to increase the efficiency of individual SA runs, we aimed to keep the cooling rate as slow as possible. To do so, one can increase the simulation time, which can become costly when performing multiple SA run replicas. The other possibility is to avoid simulating at temperatures that are ineffective for separating stable and unstable conformations and focus the computational efforts on cooling through that temperature range that produce the best possible outcome. Thus, the SA should be restricted to an interval that is low enough to keep the individual chains associated yet high enough to allow enough mobility for producing relevant conformational changes. In other words, we direct SA in a manner that the gas and solid phases are avoided, and runs roughly from the boiling to the freezing point of a liquid droplet.

Due to the varying molecular weight, rigidity, and the nature of intra- and interchain interactions, the plastic models taken here have different boiling and freezing points, and therefore, should have different SA setups. Thus, for each plastic, an initial test SA run was performed, cooling from 1200 to 200 K over 20 ns, in which the ideal temperature range was estimated (Figure 1). Similarly to our previous preliminary study,²¹ the condensation of molecules into a particle and changes in mobility were monitored by tracking the radius of gyration R_g and root-mean-square displacement (RMSD) of the system with the temperature. During cooling, a distinct drop in the radius of gyration marked the starting (T_{start}) temperature, whereas the temperature below which the RMSD values showed no more changes was taken as the end point (T_{end}) for the cooling program in the production SA runs. The resulting optimal settings are listed in Table 1, while the temporal development of R_g and RMSD in this test SA run is shown in the Supporting Information.

The obtained ideal T_{start} and T_{end} data show some notable trends. Some effect of the molecular weight of the chains is observable. The herein investigated PE chain condenses into a

single particle at approximately 620 K, whereas the smaller PP chains need a lower T_{start} , and the largest PS strains a higher one. These three kinds of macromolecules are held together by weak van der Waals forces. However, N66 has polar groups which provide additional dipole–dipole cohesion between the strands and greater rigidity. Accordingly, N66 has high optimal T_{start} and T_{end} values.

In achieving a sufficient sampling of phase space, it has been demonstrated repeatedly^{64,65} that conducting multiple replica simulations has a remarkable advantage over a single one. This is even more so for SA, in which case the output is essentially a single structure from each run, even if produced by a multitude of shifts of delicate conformational equilibria upon the slow cooling of the system. Since during the cooling the system can be trapped in slightly or even severely disadvantageous conformations, performing multiple SA simulations becomes essential.³⁹ Thus, after determining the temperature intervals, we created a series of starting geometries through a 50 ns equilibrium MD run at a constant 1200 K temperature (Figure 1), harvesting coordinates every 1 ns, yielding 51 input geometries, which were used in the subsequent production SA runs.

In each of the 51 input structures, new velocities have been assigned, and each structure underwent an SA run, reaching T_{end} from T_{start} over 50 ns. To test the effect of the cooling rate, the procedure was repeated on the same set of starting geometries with an identical temperature interval setting, but cooling over 20 ns. Thereafter, each of the 102 structures underwent an energy minimization procedure with the force field, to remove any remaining energy hotspots from the system (Figure 1).

In order to obtain more reliable relative energies for the validation of the force field results, as well as reference input structures for later quantum chemical (QC) calculations, we performed full geometry optimizations with semiempirical GFN2-xTB and subsequent BP86/def-SV(P) single point calculations on the structures after energy minimization. Furthermore, from each set of geometries four kinds of plastics each energy minimized with the CHARMM36 force field or geometry optimized with GFN2-xTB we selected the lowest energy structure (henceforth called rank 0) and the 20th lowest energy geometry (henceforth referred to as rank 19), and calculated single point energies on them with various DFT methods (Figure 1, Table 2). The size of these systems renders such an endeavor far from trivial due to the large memory and computer time demand (Table S3). These geometry optimizations and single point energy calculations on the 102 structures of each plastic gave a wide variety of geometries and total energies. This array of data allows testing how well the chosen force field describes the interactions within the nanoplastics, i.e., if these interactions add up to the near correct driving forces toward the right conformations, and thus how well it can be employed for the SA procedure.

Correlating the CHARMM36 and the corresponding GFN2-xTB relative energies (Figure 2) shows a good common trend for PE, PP, and PS, indicating that the conformational features preferred by the force field are consistent with those by the quantum chemical calculations. Thus, it can be assumed that a good SA approach based on the CHARMM36 force field is driven toward reasonable, low-lying minima on the potential energy surface in the case of these plastics. To make correlations comparable for the different plastics, the effect of system size had to be eliminated; hence, we present the

Table 2 Comparison of Different Methods for Two Selected Conformers for Each Plastic

method	PE (kJ/mol)	PP (kJ/mol)	N66 (kJ/mol)	PS (kJ/mol)
GFN2-xTB geometries				
CHARMM36	545.3	26.9	298.1	113.1
GFN2-xTB	360.3	42.4	133.8	90.3
BP86-D3BJ	509.8	56.7	347.4	169.4
PBE-D3BJ	452.8	69.8	338.4	131.5
PBE0-D3BJ	474.7	63.2	334.6	131.8
B3LYP-D3BJ	509.6	60.4	347.4	156.4
ω B97X-D3	536.1	49.2	361.4	145.3
R2-SCAN-3c	514.9	34.1	335.7	89.0
PBEh-3c	427.0	51.2	287.1	64.8
CHARMM36 geometries				
CHARMM36	600.3	104.6	141.5	125.6
GFN2-xTB	267.8	79.3	92.9	82.8
BP86-D3BJ	537.0	142.7	155.8	239.6
PBE-D3BJ	375.6	123.1	145.1	187.4
PBE0-D3BJ	413.2	137.3	170.5	180.9
B3LYP-D3BJ	501.4	139.6	152.1	204.0
ω B97X-D3	515.4	155.3	191.3	210.0
R2-SCAN-3c	426.3	149.3	183.4	132.7
PBEh-3c	355.6	129.3	198.9	126.5

^aGiven is the energy difference in kJ/mol between the most stable conformer (rank 0) and the conformer that is ranked as 19 considering the corresponding energies of the CHARMM36 and the GFN2-xTB optimized structures. The basis set for the BP86, PBE, PBE0, B3LYP, and ω B97X-D3 calculations is in all cases def-SV(P).

energies scaled to the number of heavy (non-hydrogen) atoms. In this measure, the relative energies of the obtained structures are only up to about a kJ mol⁻¹ for PE and a few tenths of a kJ mol⁻¹ for PP, PS, and N66, whereas the difference in relative energies calculated with the force field and GFN2-xTB also only amounts up to about 0.1–0.2 kJ mol⁻¹. These circumstances lead to relatively low correlation coefficients, except for PE, where the relative energies per number of heavy atoms are the most diverse. Reassuringly, in the case of the hydrocarbon molecules, the two methods agreed on which

structure has the most stable geometry, while for N66, a slight discrepancy was observed in this matter, see Figure 2 lower right panel yellow entries above the line. However, when comparing the CHARMM36, DFT, and semiempirical relative energies $\Delta E_{\text{rel}}^{0-19}$ of the 20th lowest energy conformer with respect to the lowest located minimum (Table 2), the force field data do not deviate significantly from the higher-level QC results. Thus, the low degree of correlation in Figure 2 cannot be considered a basis for criticizing the quality of the force field. GGA and hybrid functionals exhibit low variation in $\Delta E_{\text{rel}}^{0-19}$, particularly when performed on the geometries obtained from the optimization from the GFN2-xTB data. Among the DFT results, R2-SCAN-3c and PBEh-3c calculations produced the smallest $\Delta E_{\text{rel}}^{0-19}$ values, most apparently in the case of PS. This may be due to the BSSE correction included in these calculations, since BSSE should be somewhat larger in the more closely packed rank 0 structures.

Due to the sheer size of the systems, these small differences add up to large relative total energies, even 1200 kJ mol⁻¹ in case of PE (Figure 3). This wide distribution of energies indicates the diversity of structures that resulted from our procedure (Figure S4). In fact, in some of the least stable conformations, the chains aggregated not into one, but two particles. The formation of such undesired structures could be avoided by choosing a smaller periodic box that would force the chains close enough to each other. However, this could give rise to other issues due to the length of each chain, for instance, the formation of a loose, infinite network of macromolecules that reaches across the periodic box. Furthermore, these split structures do not create a strikingly separate cluster of data in the energy distributions (Figures S3 and S4), nor in the correlation between the force field and quantum chemical energies; instead, the changes in the conformations are rather continuous between the most and least stable geometries. Thus, we decided not to vary the box size, and leave the data as is.

The wide distribution of relative energies is, on one hand, reassuring, as it shows that the chosen procedure samples the conformational space thoroughly, while producing different input structures is also desirable for ensemble simulations.^{64,65}

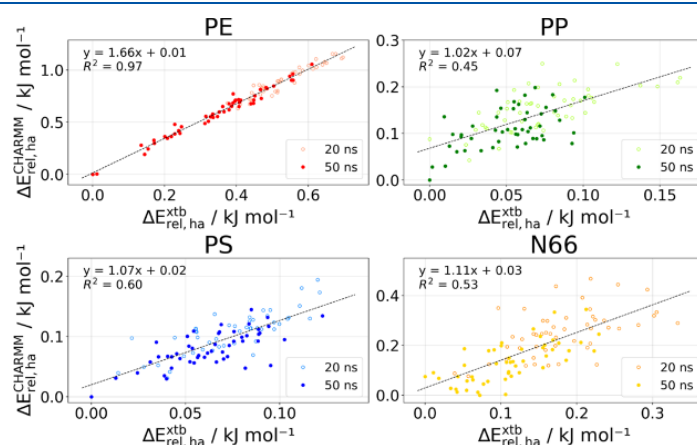


Figure 2 Correlation between relative GFN2-xTB (x-axis) and CHARMM36 (y-axis) energies, given in kJ mol⁻¹ for all NPs. Please note the different scales of the axes. The linear regression includes all obtained structures of 20 ns (open symbols) and 50 ns (filled symbols) of a given plastic. The relative energies are scaled to the number of heavy atoms (ha), see Table 1.

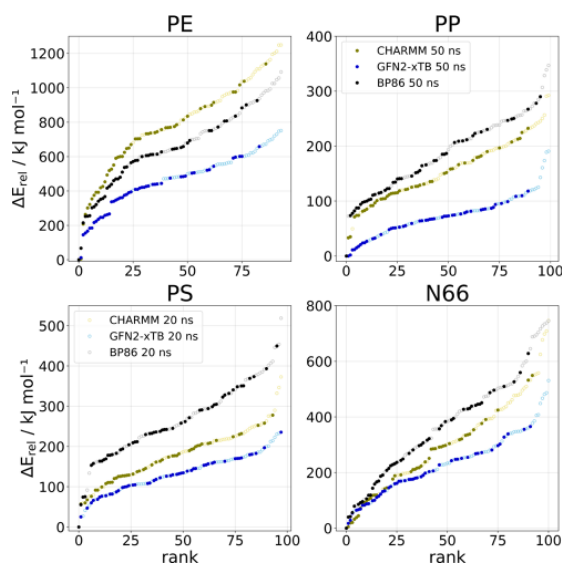


Figure 3 Relative energies of different methods (CHARMM36, in olive, GFN2-xTB, dark blue, and BP86, black) plotted against their rank in relative energies ΔE_{rel} , i.e., the lowest relative energy is zero and has the rank zero, the next lowest relative energy has rank 1 and so on. Full symbols refer to 50 ns, and lighter open symbols refer to 20 ns structures. Please note that each method curve is sorted individually and therefore the same rank may relate to different conformers (indices).

However, on the other hand, it is also apparent how likely it is for the individual SA runs to converge into a high-energy, even unstable structure. In other words, the chance of successfully finding the most stable conformation thus, the global minimum of the potential energy surface is quite low. This is especially apparent when ranking the geometries based on their energies and plotting the relative energy of the structures against their rank (Figure 3). Even among the lowest energy structures (with low rank, on the left side), the most stable conformer (rank 0) seems to have a distinguished position, as all the conformations that follow exhibit an already high relative energy, resulting in a steep ascent of the curve.

Since we chose the starting points randomly with random velocities, it is reasonable to consider the obtained array of relative energies to be statistically distributed. If the SA approach were robust, most of the structures that it produces would have the same, lowest energy, as most replicas runs would converge to the global minimum. If uncertainties rise, some of the simulations should result in higher energy structures, and eventually would produce a maximum probability i.e., an expected value at a relative energy different from 0. This latter behavior can be seen in Figure 4 for all four plastic models, depicting that the majority of the structures obtained are high in energy, and only a few similarly good conformations are obtained out of the 102. In fact, the lowest energy structures are in all cases far outside the shown 95 confidence interval (Figures 4 and S4–S6). Thus, together with the discussion above, this data set clearly demonstrates that finding low-energy structures is a rare event; hence, multiple replica SA runs are necessary if such structures are to be obtained.

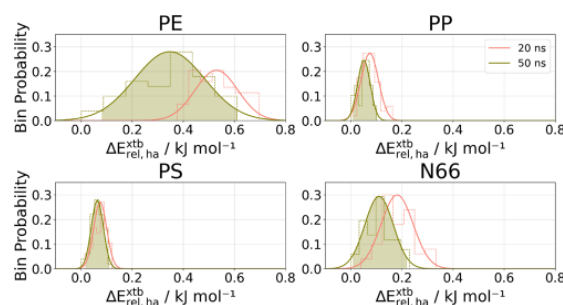


Figure 4 Bin probabilities for the relative GFN2-xTB energies for all plastics scaled to the number of heavy atoms of the respective NP. All relative energy data points are grouped into seven bins. The bin probabilities are defined such that the sum of all y-values of the bins is 1. The Gaussian functions are fitted over all relative energy values and scaled such that the maximum y-value corresponds to the maximum y-value of the largest bin probability. The shaded area indicates the 95 confidence level of the Gaussian.

The probability distributions provide further information regarding the ideal setup for the SA runs. Splitting these functions based on whether the corresponding structures originate from a 20 ns or a 50 ns run demonstrates the difference in quality between the two cooling rates in terms of outcome (Figures 3 and S4–S6). In all cases, the 50 ns runs produced significantly lower energy structures, underscoring the importance of slow cooling, that is, a long simulation time.

The intermolecular interactions between the chains within the PE, PP, and PS particles are dominated by weak dispersion forces. However, the two domains of N66, namely the amide groups and the hydrocarbon moieties that connect them, have very different sets of intermolecular behavior in terms of directionality and strength. While the polar amide units form strong and directional hydrogen bonds with each other, the hydrocarbon units are governed by the aforementioned weak dispersion forces. This dual behavior may pose significant problems when folding the N66 chains through SA. The sheer strength of these hydrogen bonds makes N66 slowly associate, even through the 1200 K simulation that produces the 51 input structures. Thus, about half of the SA runs started from a preaggregated state (Figures S7 and S8). One could argue that the formation of a droplet reduces the mobility of the chains and, consequently, the starting structures do not differ from each other enough; therefore, they should converge into the same or at least very similar conformations. However, the data shows otherwise: the expected total relative energy of the 50 ns long SA runs that started from the preaggregated structures was slightly lower (Figure S7 bottom). In agreement, although the most stable conformation found came from an SA run with a dissociated starting structure, the second-best was derived from a preaggregated structure (Figure S7 bottom). For the 20 ns SA runs, the difference is even clearer, as the associated starting structures gave markedly better results, including the expected value and the most stable structures (Figure S7 top). This interesting trend can be rationalized by the dissociated states using some of the simulation time in the production SA run for the aggregation, leaving only a part of the 20 ns to observe the rearrangements within the droplet. Moreover, when the association finally occurs, the temperature is already significantly cooler than the set T_{start} potentially hindering some of the larger conformational changes. On the other hand,

the 50 ns simulations are apparently long enough to overcome the time and temperature interval lost to the aggregation process. This finding indicates that the latter cooling rate is sufficiently slow even for this most difficult plastic model.

Geometric Features of Nanoplastic Particles

Geometric Measures along the Folding The ideal geometries of polymer particles should be governed by a delicate balance between multiple effects. In bulk plastics, the intra- and intermolecular interactions often lead to well-defined crystal structures, as described in many textbooks.⁶⁸ However, the present systems are nanoparticles, which can even be considered a cluster of a few polymer chains. This limited size results in a significant relative surface area, in which the molecules and functional groups at the surface have an imperfect embedding in the crystal structure, missing stabilizing interactions. Thus, the very interplay between the chains that generates a certain structure in the bulk of amorphous or crystalline plastics may induce a distortion in this characteristic order in the particles, in order to achieve a spherical shape and thereby minimize the proportion of interfacial polymer segments. Thus, depending on the polymer in question and the size of the particle, the obtained geometries here may show significant differences compared to those observed in the bulk solid phase.

The 3D geometry of the lowest energy structures exhibits some order (Figure 1 right), most strikingly in the case of PE. Here, the polymer chains are ordered in a manner that they run parallel to each other, stretched out in an almost all-*trans* conformation along their length. This parallel orientation of the chains can be considered an additional driving force that allows their close packing without any voids in between, and thereby stronger inter- and intramolecular interactions. This alignment, in fact, closely resembles that in the crystal structure of high-density PE.⁶⁹ The tendency to exhibit this behavior is especially recognizable in the development of the local conformations and order during the folding of this lowest energy structure (Figures 5 and 6). The proportion of C–C–

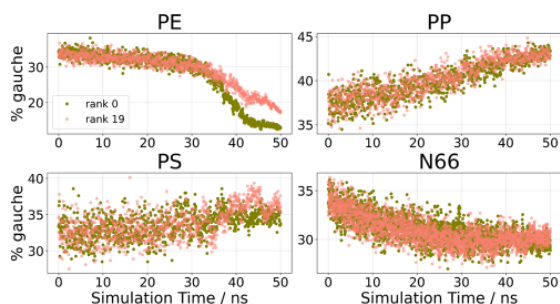


Figure 5 Percentage of gauche dihedral orientation or local conformation within the plastic versus the time along the folding trajectory of the global minimum structure and the one having rank 19, see Table S2.

C–C quadruplets in the backbone that are in *gauche* conformation suddenly decreases, whereas the order suddenly increases from about 35 ns in the corresponding trajectories.

The structural changes in the plastic particle at this point in the folding procedure are further underscored by the radius of gyration data (R_g , Figure 7), which also experiences a slight increase (see inset). Thus, the depopulation of high-energy

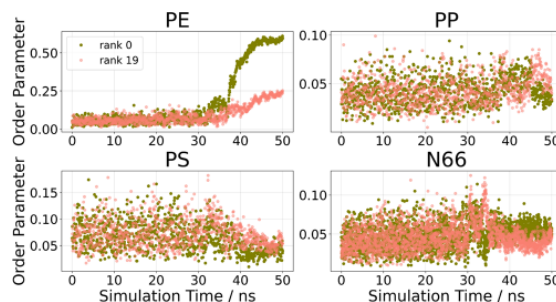


Figure 6 Order parameter P_2 for each of the plastics along the folding trajectory time of the global minimum structure (rank 0) and the one having rank 19, see Table S2.

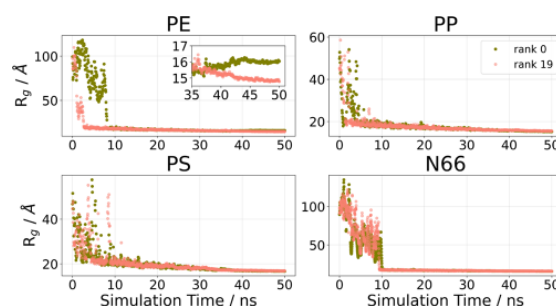


Figure 7 Radius of gyration for each of the plastics along the folding trajectory time of the global minimum structure (rank 0) and the one having rank 19, see Table S2.

structures leads to the formation of bundle-like structures with long, all-*trans* chains, and hence, this feature should be characteristic of stable PE geometries. To test this hypothesis, it is worth considering how the order parameter and the percentage of *gauche* conformations develop in the SA run that produces a less stable particle (see entries in salmon in Figures 6 and 7 for the structure with rank 19 in energy). The discussion above and the data suggest that the higher energy of this geometry may arise from the lack of order. The structure-determining effect for PE is, therefore, order, while the tendency toward producing a smaller surface area is sacrificed.

The distribution of the local conformations along each chain, and its temporal development, shows interesting trends (top two panels, Figure 8). From 35 ns on in the SA, at which point order arises in the particle, short all-*trans* sections start to appear in small yellow patches (check any vertical line in the top two panels at 35 ns) in the system at a few points, and they expand over time to cover a larger portion of the chain starting from these nucleation points. Interestingly, in some cases, these nucleation sites migrate, transferring *trans* or *gauche* conformations along chains. This is in alignment with Milano and co-workers,⁷⁰ where the idea of nucleation inducing structure in a plastic nanoparticle has been exploited in aiding the folding of pristine and aged nanoplastics via the introduction of an ordered chain as a crystal seed into the system.⁷⁰ In future studies, a combination of our approach together with the seed idea⁷⁰ may be explored.

In the final structures, the C–C–C quadruplets are predominantly in *trans* conformation, having long all-*trans* sections in the strands (large yellow areas in Figure 8 top two panels, and bottom), but the remaining few moieties in *gauche*

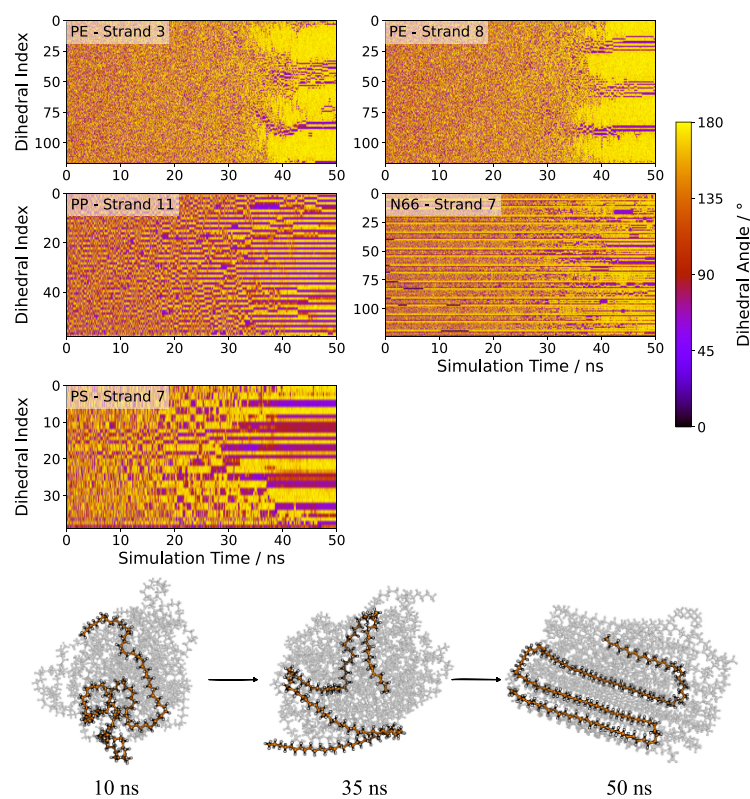


Figure 8 Distribution of dihedral angles along chains 3 and 7 in the course of the simulated annealing run for PE, alongside chain 11 for PP and chains seven for PS and N66, respectively. The data shown here is for the simulation yielding the most stable structure (rank 0). Each panel corresponds to a single strand of the corresponding particle, and any vertical line therein describes the conformation of that strand at a given time. The time development of one dihedral can be followed from left to right along a horizontal line. Below we show ball-and-stick representation of the rank 0 PE particle with strand 8 highlighted in orange (carbon atom) and white (hydrogen atom) while the rest of the plastic is given in gray shades.

conformations play a significant role in the overall structure, as they allow hairpin turns to form. These turns are necessary for packing the particle into a compact object, and they are apparently achieved by a short sequence of alternating *trans* and *gauche* units. In good agreement, it has been shown through both experiments and theoretical calculations that long alkane chains tend to prefer *trans* conformations in their C–C–C–C units, and they form hairpin structures only beyond a threshold in length.^{71–73} This value changes depending on the force field or electronic structure method and the medium, but the most accurate coupled cluster calculations⁷² and experiments⁷³ suggest it to be about the length of 16–18 carbon atoms for isolated molecules in the gas phase. In the present case, despite the simultaneous presence of multiple molecules during the packing, the length of the all-*trans* sections is surprisingly similar to these numbers, albeit slightly larger, stretching through roughly 20–30 carbon atoms.

In the case of PP and PS, order is less apparent, owing to the methyl and phenyl groups attached to the backbone, which hinder the perfect alignment seen for PE. These plastics, depending on their tacticity, can form a high diversity of microscopic structures, often including left- and right-handed helices.⁷⁴ To form these helices, PP and PS, unlike high-density PE, feature a high proportion of *gauche* C–C–C–C

sections within the backbone, forming alternating *gauche-trans* sequences.⁷⁴ This should lead to a theoretical ratio of $\approx 50\%$ of the two local conformations for these plastics.

Interestingly, in excellent agreement with this previously observed structure,⁷⁴ but in contrast to PE, for PP, the percentage of *gauche* conformations does not decrease, but rather increases throughout the SA run (Figure 5). The percentage of C–C–C–C units in *gauche* conformation reaches about 45% in the best structure, very close to the theoretical 50% ratio, with the alternating *gauche-trans* sequences clearly visible in the structure of the chain (see Figure 8 middle left panel and Figures S11 and S12). One could argue that these helical structures would occur only in the gas phase, and their presence in the particle is only an artifact of a too sudden cooling protocol, trapping the macromolecules in these conformations. However, the onset of this peculiar structure is at 30 ns into the simulation (Figures S11 and S12), long after the aggregation of the macromolecules was completed (<10 ns, Figure 7 upper right). These findings consistently indicate that forming these helical structures along the PP chain is beneficial energetically in the nanoparticle, while also demonstrating a certain quality for the folding process of the lowest energy structure.

The best obtained geometry for PP is visually (Figure 1) significantly more spherical than that for PE. The higher

preference for compact structures is suggested by the development of the R_g values, decreasing monotonously in the SA run from ≈ 10 ns physical time on (Figure 7). Furthermore, whereas the structures with the lowest (Figure 5, olive entries) and 20th lowest energies (Figure 5, salmon entries) produce similar percentages of *gauche* conformations in their backbones, the R_g is somewhat lower for the former (Figure 7). The data above, therefore, indicates that the PP particle has a high proportion of helices, and these helices do not require a rod- or bundle-like structure to form, as observed for the all *trans* chains of PE, but they can just as efficiently fold into a compact, highly spherical object.

Visual inspection of the most stable PS particle suggests that the backbone of the chains is situated closer to the center of mass of the whole object, with the bulky phenyl groups pointing outward, making the surface rugged. The percentage of C–C–C–C units in *gauche* conformation shows an increasing trend through the whole SA run that produces this structure, although the change is less pronounced than in the case of PP. In the resulting geometry, the final value is lower than for the lowest energy PP particle (35, Figure 5). In agreement, longer sections in all-*trans* configuration can be observed (lower left panel of Figure 8 and Figures S11 and S12). It is possible to interpret these results through the aforementioned arrangement of the interfacial section of the chains, with the preference of the phenyl rings to point outward, which overrides the need to form alternating *gauche-trans* sequences of helical geometries. Interestingly, the order parameter P_2 continuously decreases in the SA run. These trends and structural features are also characteristic of the 20th lowest energy geometry. The only parameter, in which a notable advantage can be found for the lowest energy structure is the R_g , suggesting that the energetically decisive feature of this particular geometry is its compactness.

N66 differs from the examples above, since it has a dual character from the mutual presence of nonpolar hydrocarbon units and polar, hydrogen-bonding amide groups. It is apparent from the structure that the amide groups are spatially close to each other, forming chains of hydrogen bonds (cf. Figure S32), which stretch throughout the entire particle. While this is in full agreement with the crystal structure of the bulk N66,⁷⁵ the present structure is clearly less ordered than the crystal. In that experimentally known structure, polymer chains are running parallel next to each other in an all-*trans* configuration, aligned in a way that their amide groups can form hydrogen bonds with each other. The percentage of C–C–C–C units in a *gauche* configuration is low in the most stable geometry we found (30), but it is higher than that in the case of the PE particle above. The importance of this geometric property is established by its decreasing trend throughout the SA run that leads to this structure. However, interestingly, the decrease in the prevalence of *gauche* units reaches a plateau after the first half of the SA run i.e., at high temperatures which is strikingly different from the behavior of the PE particle, in which case the dihedral angles found their ideal position only in the last third of the simulation, i.e., at lower temperatures (Figures 5 and 8 middle right panel).

P_2 monotonously decreases during the SA run, as well as the R_g . Hydrogen bonding is clearly a considerable driving force when forming the particle, as in the SA run yielding the most stable geometry, the number of hydrogen bonds monotonously increased over time. The fact that the number of hydrogen bonds monotonously increases, whereas the rearrangement of

the C–C–C–C units into *trans* conformation stops early in the simulation, could be interpreted as an artifact of the folding arising from the structure of N66 itself. The differences in the interactions in the polar and nonpolar domains within the N66 particle may hinder an efficient packing of the particle during the production SA runs. The prominent strength and directionality of hydrogen bonds between amide groups provide, even at a high temperature, a driving force for the formation of the structures, in which the number of hydrogen bonds is maximized. However, the aliphatic links in between move freely at this temperature, due to the significantly weaker intra- and intermolecular interactions that govern their conformations. Thus, while an N66 structure is being created in an SA setup, the hydrogen bonds form very early in the process, at a temperature at which the *trans* and *gauche* conformations within the hydrocarbon links are not yet separated in their occurrences. However, at lower temperatures, which would shift the conformational equilibria related to the nonpolar regions toward the desired structures, the hydrogen bonds have already formed a rigid network, hindering the movements required to produce low-lying minima. In our attempt to address this issue, we aimed at scaling down Coulombic forces within the system, which are used in force field calculations to describe hydrogen bonding. Thus, in another set of computer experiments, we performed 50 ns long production SA runs on the original 51 replica geometries, in which we used $\epsilon = 4$ and $\epsilon = 40$ settings for relative permittivity. The resulting structures underwent an energy minimization as described above, with the default $\epsilon = 1$ setting, and then a geometry optimization with the GFN2-xTB QC method. The obtained energies were significantly higher than those from the original folding procedure without the dielectric medium, which we attributed to a nonideal alignment of the hydrogen bonding units due to the scaled-down Coulombic interactions. To mitigate this issue, we performed an additional 20 ns SA run on each structure, in a temperature range of 350–300 K, which was the lower end of the original temperature interval and therefore should only offer a minimal further advantage at most over the simulations above. After the energy minimization, one structure from the $\epsilon = 4$ set was found 35 kJ mol^{−1} lower in energy than the best structure from the unscaled simulations. However, considering the average energies and their distribution, this approach did not show a clear advantage over the protocol with the default settings in Figure 1, and the single hit can be considered only accidental, originating from the overall larger number of replica simulations. Thus, one can conclude that the effect of this hypothetical artifact is negligible.

Based on the information above, an intriguing structural picture emerges. The most important feature in the N66 system is the number of hydrogen bonds. In case of such a small particle, however, the relative surface area is considerable, which if the order within the particle would mimic that of the crystal could leave many of the hydrogen bonding sites free. Instead, the hydrocarbon chains are partly curled, distorting the preferred orientation of the chains, which results in a smaller surface area and a lower number of noninteracting, free amide groups, which brings enough stabilization to compensate for the faulty local conformations of the hydrocarbon units.

Conformational Ensemble The methodology above produced several (about 100 each) nanoplastic geometries of each polymer type, which differ not only in stability but also in

their shape, local conformations, and alignment of their chains. Whereas one may refrain from using the least stable of these structures for calculations, as they might contain unrealistic structural features, considering multiple low-energy geometries could provide more information and a deeper understanding than only the most stable one. Using multiple conformations may allow exploration of the effects of the surface structure, which is different in each case. Furthermore, running parallel ensemble simulations^{64,65} is highly advantageous for obtaining a better sampling of phase space and thereby arriving at physically more correct and reliable conclusions.

To support any such attempt, we chose the five lowest energy structures for each plastic type and characterized them in detail based on their geometry (Table 3). The relative

Table 3 Quantities of Interest for the Different Plastic Particles with Certain Rank According to Their Relative Energies

rank	ΔE_{rel}	$\rightarrow_n$	R_g	2	b	P_2	HB
PE							
0	0.0	29.43	16.07	0.18	107.91	0.56	
1	12.4	23.80	16.57	0.27	142.38	0.51	
2	145.5	22.95	15.79	0.17	103.40	0.52	
3	155.7	19.62	15.16	0.08	60.65	0.42	
4	166.6	27.72	15.72	0.15	93.88	0.55	
PP							
0	0.0	22.93	15.24	0.01	13.02	0.19	
1	0.0	20.71	15.23	0.01	17.21	0.24	
2	1.9	22.15	15.31	0.03	37.23	0.13	
3	11.1	21.99	15.25	0.00	14.42	0.21	
4	11.8	22.95	15.36	0.01	17.57	0.18	
PS							
0	0.0	20.10	16.37	0.01	20.59	0.32	
1	24.9	20.16	16.52	0.03	46.35	0.28	
2	27.2	19.75	16.40	0.00	11.72	0.33	
3	41.3	20.88	16.57	0.02	31.14	0.30	
4	47.0	22.80	16.53	0.02	34.68	0.33	
N66							
0	0.0	30.10	15.85	0.01	25.70	0.20	173
1	17.6	21.26	15.87	0.03	33.59	0.17	173
2	29.0	24.05	15.85	0.03	39.46	0.16	164
3	53.8	26.45	15.82	0.00	16.12	0.20	168
4	62.1	22.10	15.68	0.01	19.02	0.17	164

^aGFN2-xTB relative energies: ΔE_{rel} (in kJ mol^{-1}); average end-to-end distance: $\rightarrow_n$ (in Å); radius of gyration: R_g (in Å); anisotropy factor: 2 ; asphericity parameter: b ; order parameter: P_2 ; total number of hydrogen bonds: HB (only for N66). All quantities are calculated as described in Ref 63.

energies are diverse, in agreement with the observation above that finding low-energy minima on the potential energy surface is a rare event in the SA procedure performed here. The highest energy differences among the five best structures can be found for PE (167 kJ mol^{-1}), in which a very well-defined order is required for stability. This plastic is followed by N66, in which case variations in hydrogen bonding produce a large energy penalty due to the strength of this interaction. For PP and PS, all five structures are within 12 and 47 kJ mol^{-1} , respectively.

The R_g values show relatively low variations, indicating that all compounds here are relatively compact. In PE, 2 and b values are generally high due to the rod-like shape of the low-

energy structures, and they exhibit large differences among the selected five geometries. For the other three compounds, 2 is low for all geometries, showing that in terms of overall shape, the particles here were folded into a form within which mass is distributed equally along all three dimensions of space. However, in b , notable variations can be observed, with both very high and very low values (c.f. rank 0 and 2 of PP, or rank 1 and 2 for PS in Table 3). Orientational order P_2 displays significant variations in PE, while for PS and N66, the differences are low. Finally, the number of hydrogen bonds in the N66 particles varies significantly, suggesting that the number of amide groups available for donating or accepting hydrogen bonds to or from any molecule interacting with the particle may also change at the surface, which may be influential when investigating a molecule at the surface of these particles. Thus, based on these data, although the low-energy geometries produced here have certain similarities in some characteristic structural features, they also show several differences, which make them promising candidates as inputs for future ensemble simulations.

CONCLUSIONS

In recent years, many simulation studies have appeared that address the physics, chemistry, and toxicology of nanoplastics. However, to make the most out of the predictive power of theoretical chemistry, it is necessary to use representative model structures of these materials, which have low energy and a realistic build. Thus, the methods to create nanoplastic models must be evaluated and standardized, and the structures that are proven to be of high quality should be shared with the community for further use.

We used simulated annealing (SA) to generate ca. 100 geometries for each of four chosen polymer systems, namely polyethylene (PE), polypropylene (PP), polystyrene (PS), and nylon-66 (N66). The size of these models was chosen to contain up to 4000 atoms, which is large enough to be on the nanometer scale (ca. 4–5 nm) but small enough to be handled even with quantum chemical methods. The cooling rate of the SA was optimized systematically, with test simulations determining the best possible temperature range in which the polymer chains, despite aggregating into a single particle, remain mobile enough to undergo conformational changes. It is shown that 50 ns long SA runs are necessary and sufficient for these systems.

In our motivation to achieve the highest possible accuracy, the obtained structures were all investigated through quantum chemistry. By using the semiempirical GFN2-xTB method, full geometry optimization for these very large systems became available. Single-point energy calculations with DFT methods, on the other hand, provided an excellent benchmark for the employed CHARMM36 force field and GFN2-xTB. The data showed that the force field used here is applicable to create low-energy structures, as it estimates the driving force to these geometries with an uncertainty comparable to that of quantum chemical methods. The resulting structures vary greatly in energies, including the most stable ones, showing that many SA runs are necessary if high-quality geometries are to be found.

Dissecting geometric features of the systems reveals that the PE particle prefers an all-*trans* conformation along the chains, with a length of 15–20 carbon atoms. These sections are interrupted by *gauche-trans* sequences that produce hairpin turns, in good agreement with previous high-level quantum

chemical and experimental data.^{72,73} These turns fold the chains into a compact rod-like shape. In case of PP and PS, helical structures were observed, characterized by alternating *gauche* and *trans* sections along the backbone. This is in good agreement with earlier literature.⁷⁴ For N66, hydrogen bonding between the amide moieties was found to be the most important structure-directing effect, whereas the hydrocarbon groups between them provide the necessary flexibility to maximize these interactions, allowing the chains to coil into a highly spherical motif.

Considering five of the lowest energy structures allows simulating conformational ensembles, which can give access to more accurate and reliable data, and thereby a better understanding of the behavior of these materials can be achieved. The energy and structure of these minima are diverse, which serves this purpose well. Through publishing the nanoplastic structures obtained here in an online repository, we aim at standardizing the corresponding simulations and rationalizing computational efforts in future studies that will not necessitate performing the lengthy and expensive folding procedure. In the future, we plan to update this database and expand it with more particles, built from either from other polymers, or having different sizes, and additional functionalization.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are openly available in a repository on GitHub at: <https://github.com/kirchners-manta/Nanoplastics>.

■ Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.jpcb.5c06528>.

Figures with more information on the energetics and structure of the nanoplastic particles (PDF)

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Notes

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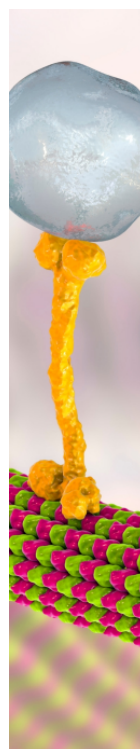
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Appendix: Nanoplastics can build themselves

Katrin Jonas,^a Barbara Kirchner,^a Oldamur Hollóczki,^b Leonard Dick^a

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Own contributions

- Conceptualizing and leading the project
- Partly running the MD simulations and participating in their analysis.
- Writing the introductory part, parts of the discussion, and the conclusion.

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Nanoplastics Can Build Themselves

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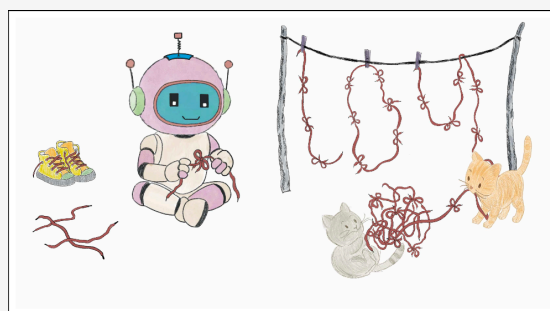
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ABSTRACT: To understand nanoplastics through modeling, e.g., to assess their toxicity and environmental impact, reliable starting structures are required. In this study, we present a new approach to generate nanoplastic particles from classical molecular dynamics simulations. Starting with the initial aggregation of monomer units and allowing for their subsequent growth into polymer strands yields stable aggregates with polymers of diverse length, avoiding the need to define the number of polymer units with a set length *a priori*. The generated particles are compared to existing model nanoplastics and show agreement in terms of structural characteristics and energetics. The novel approach is computationally efficient and allows for a greater diversity of structures than approaches with predefined chain lengths.



Nanoplastics (NPs) are widespread across the environment, and can be found in soil, water, and the atmosphere, both in urban and remote areas,^{1–6} originating from, e.g., the abrasion of car tires, mechanical wear of clothing or originating from biological, chemical, or physical degradation of plastic waste.^{7–9} An increasing number of studies show that NPs are found across the food chain^{10,11} as they have been detected in plants, animals, and also humans.^{5,8,12} These nanoparticles can cross biological barriers,^{13,14} allowing them to enter many tissues, making research on their toxicity essential.^{1,5,15–17} Previous theoretical and experimental studies have shown that nanoplastics exhibit bioactivity toward proteins,^{18–21} interact with antibiotics other drugs,^{22,23} and potentially alter the structure of DNA.^{24,25} Besides the bioactivity, NPs also interact with other materials, forming an eco-corona through heteroaggregation.^{26,27}

In revealing the effects above, theoretical calculations and molecular modeling played an important role, in many cases leading the way to experiments, or provided a molecular insight into reveal the origin of toxicity of NPs. Thus, theory and simulations became an indispensable tools in uncovering and mitigating the environmental and health effects of these pollutants. However, the diversity and complexity of the physical, chemical, and biological processes that yield NPs leads to an immense variety among NPs, hence if their effects are to be understood, this diversity needs to be taken into account.²⁸ Thus, similarly to experiments, theoretical calculations aiming at modeling the underlying physicochemical effects must also consider various NP structures.²⁹

In generating plastic nanoparticle models — often relying on atomistic or coarse-grained force fields^{30–33} — one possibility is using simulated annealing.^{30,34,35} In this setup, polymer

strands with predefined length are heated up to a high temperature, ensuring sufficient movement and rearrangement of the polymer strands to explore their conformational space. Subsequently, a cooling protocol is started to decrease the population of high-energy conformations. In principle, the global minimum on the potential energy surface (PES), i.e., the most stable NP conformer, can be found with an infinitely slow cooling. To compensate for the limits in simulation time, multiple runs should be performed to ensure finding low-energy NP structures.^{22,35} Programs such as *Polymer Builder*,³⁶ or *pyPolyBuilder*,³⁷ which enable users to create complex polymer systems, are also possible choices for producing NPs. Other studies define semicrystalline fragments using a “crystal seed”, around which further polymer chains can aggregate.³⁸

A shared conceptual limitation of all previous studies, however, is that the degree of polymerization (i.e., the number of monomer units per macromolecule) and the total number of polymer molecules that comprise a NP are defined beforehand, which — albeit can produce useful molecular level information — fails to represent the aforementioned diversity of NPs. This constraint limits the accessible set of possible NP configurations in three ways. First, the degree of polymerization directly determines the number of its rotatable bonds. Compared to short polymer strands, longer polymers have a much larger conformational space and tend to form more

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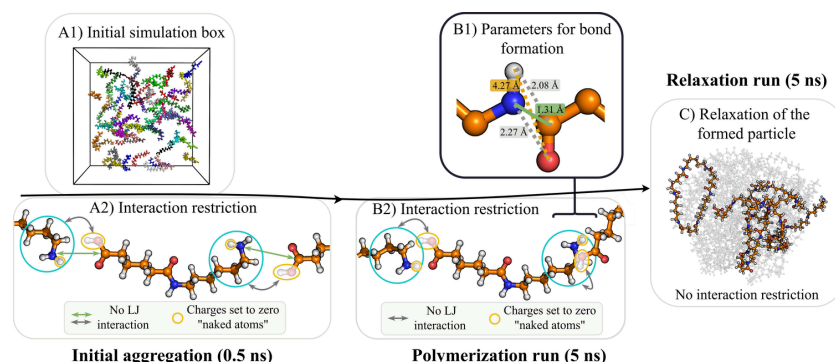


Figure 1. Workflow to generate NPs. A1) Initial simulation box containing monomer units. A2) Interaction restrictions during the initial aggregation. B1) Equilibrium distances during the polymerization run enforced through Lennard-Jones parameters. B2) Interaction restrictions during the polymerization simulation run. Note that the only difference to A2) is the activated LJ interaction between the atoms connected via the green arrow. C) Relaxation run and final N66 NP, with two highlighted polymer strands. (color code: carbon = orange; oxygen = red; nitrogen = blue; hydrogen = white).

entangled arrangements with neighboring strands. This results in a more complex PES, substantially increasing the sampling effort required to obtain a set of energetically stable NPs. Second, with a given length, the ratio of end-groups to monomer units is defined. For polymers such as nylon-66 (N66), these end-groups are functional groups and engage in hydrogen bonding and proton transfer reactions, which may directly influence the local polymer packing and arrangement, as well as the surface charge. When only short chains are considered for aggregation, the density of terminal groups in an NP is particularly high, impacting the particle's internal crystallinity. Third, in most approaches, in which the user has to define the macromolecule that is used to generate the particle, ring structures are often ignored, which could otherwise have an impact on the structure through packing effects or the lack of end groups.

A possible way to mitigate the shortcomings above is to start creating the NP from monomers and polymerize them in the process, which would allow the development of varying chain lengths. Approaches for simulating reactions in comparatively large systems already exist, such as reactive force fields like ReaxFF³⁹ and template-based methodologies, like REACTER,⁴⁰ implemented in LAMMPS. Since reactive force fields encode the reactivity directly into the potential, enabling bonds to “naturally” break and form, they are computationally demanding and require specialized parametrizations. REACTER,⁴⁰ by contrast, operates on conventional, nonreactive force fields and can in principle be used to simulate polymerization processes and generate polymers without prescribing chain lengths. However, this method requires the construction of explicit reaction templates for each reaction pathway.

Here, we introduce a novel approach for generating NP models, where number and lengths of the polymer strands that form the particle are not predefined. Demonstrated for N66, the created NPs are solely determined by the total number of monomers (N_{mono}), with the number of macromolecules as well as the degree of polymerization being allowed to vary, as determined by the simulation. N66 is composed of two components, hexamethylenediamine ($\text{H}_2\text{N}(\text{CH}_2)_6\text{NH}_2$) and adipic acid ($\text{HOOC}(\text{CH}_2)_4\text{COOH}$). For simplicity, in this work we will refer to monomers, defined as the repeating unit

resulting from the condensation of one hexamethylenediamine unit and one adipic acid unit, i.e., $\text{HOOC}(\text{CH}_2)_4\text{CONH}(\text{CH}_2)_6\text{NH}_2$ (Figure 1). The generated NP structures are in the size range of $N_{\text{mono}} = 70\text{--}130$.

Generating the NPs follows a three-step procedure. Initially, individual monomer units are randomly placed within a simulation box, see Figure 1A1. A preliminary aggregation of the individual units into a single particle is driven by van der Waals interactions and the formation of a hydrogen bond network through a 0.5 ns simulation run at 400 K. The elevated temperature allows for sufficient movement and orientational freedom of the monomers. To achieve an arrangement of the monomers resembling that in a polymer, terminal groups (carboxyl – OH group and one of the amino hydrogen atoms) are treated as “naked atoms” (Figure 1A2, yellow), i.e., selectively switching off the LJ interactions between the –OH and the terminal $-(\text{CH}_2)_3\text{NH}_2$ group (Figure 1A2, blue). This allows the terminal carbon and nitrogen atoms to come into close proximity, while the emerging structure within the particle is governed solely by partial intermolecular monomer–monomer interactions, excluding terminal groups.

After the initial run, a polymerization procedure is performed, in which the monomers are allowed to connect to form macromolecules: through a simulation at 400 K over 5 ns, LJ interactions between spatially close carboxyl carbon and nitrogen atoms are reset in a manner that they can mimic covalent N–C bonds (Figure 1B1/2) with an equilibrium bond length of 1.31 Å (Figure 1B1). The newly formed amide bond should assume a *trans* conformation, as seen in experiments. To achieve this goal without needing to redo the topology of the molecule, we also adjusted the N...O, C...H and H...O Lennard-Jones parameters within the amide unit to mimic reasonable conformation distances ($\text{N}\cdots\text{O} = 2.27$ Å, $\text{C}\cdots\text{H} = 2.08$ Å, and $\text{H}\cdots\text{O} = 4.27$ Å), as shown in Figure 1-B1. Subsequently, using MakroLyzer,⁴¹ “naked atoms” are discarded wherever a new bond is formed (N–C distance below or equal to a cutoff value of 1.69 Å), resulting in an NP consisting of polymer strands of varying length. The cutoff value was obtained by multiplying the sum of the covalent radii of N and C by a factor of 1.15, making sure bond vibrations are considered. For the final simulation run, the bonding and

nonbonding interactions within the force field were newly defined, describing the new amide unit through bonding terms. Consequently, all N–C pairs, with distances lower than or equal to the cutoff value, are treated as bonded in the relaxation run. At a temperature of 300 K, the particles were relaxed over 5 ns, with a subsequent energy minimization. Further technical details of the protocol, which were not the subject of the present development.

To test the described ansatz, six kinds of systems were constructed (Table 1), with 50 replica systems for each. Each

Table 1. System Name, Number of Used Monomer Units N_{mono} , Number of Initial Minimal Units N_{unit} and the Box Length l of the Systems Studied^a

System	N_{mono}	N_{units}	$l/\text{\AA}$	replicas
M70	70	70	80	50
M99	99	99	90	50
M130	130	130	100	50
D70	70	35	80	50
D99	99	49.5	90	50
D130	130	65	100	50

^aThe simulations of D70, D99 and D130 were started from dimer units. In the case of the D99 systems 49 dimer units and one monomer unit were used.

replica system was constructed by placing initial minimal units randomly into a simulation box. For the first three groups of starting structures, configurations containing 70, 99, and 130 monomer units (labeled as M70, M99, and M130, respectively), were chosen. As intended, through the simulation, polymerization of the monomers spontaneously occurred, and a compact particle composed of macromolecules with very diverse degree of polymerization was formed. Some of the polymers emerging from our approach are so large that they span across the particle. Furthermore, ring structures were also observed in the final particles, with sizes as low as two monomer units and up to 47 for a M130 system. An example for the obtained NPs can be seen in Figure 1C of the M70 set of configurations, with two macromolecules, a ring and a linear chain highlighted.

To test what impact the length of the initial building blocks has on the resulting structure, we performed the procedure described above using dimers instead of monomers as starting molecules, labeled as D70, D99 and D130. To maintain comparability, the number of monomer units in these systems was identical to systems M70, M99, and M130, respectively, which meant an additional monomer unit for system D99. The final NP particles are compared in terms of geometry and energy to those from our previous study, where N66 particles were generated using 11 polymer strands, consisting of nine monomer units each.³⁵ As discussed in detail in the Supporting Information, the hereby obtained structures are found to be similar in terms of relative energy compared to the earlier structures, while being spread through a larger range.

No quantitative trend in energy can be identified comparing the M-systems to the D-systems. However, structural differences between the sets of configurations are observed. Figure 2 depicts the frequency of the monomers per macromolecule as well as the number of macromolecules found in each NP, for the M70 and the D70-systems. The results obtained for the other M- and D-systems are shown in the Supporting Information, where similar trends were observed. The majority

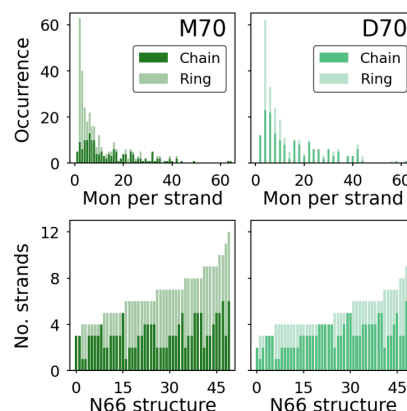


Figure 2. Comparing the final NP structures from M70- and D70-sets. Top: Occurrences of the number of monomers per strand. Bottom: NP structures sorted by the number of polymer strands forming the NPs. The polymer strand counts are divided into their polymer chain and polymer ring contributions.

of rings that were formed during the simulations consist of fewer than ten monomers, and fewer rings were formed when starting from dimers. The largest proportion of rings contain two and four monomers per ring in M- and D-systems, respectively. Chains show a wider distribution, with the most common lengths being between five and ten, being longer in the case of the D-systems.

We use the Herfindahl–Hirschman Index (HHI)⁴² to characterize the composition of our plastic particles. The HHI is frequently used in macroeconomics to calculate how equal the portion of the market that each company controls is, quantifying the difference between monopoly and competitive markets. Adapting it to the nanoparticles in our systems through

$$\text{HHI} = \sum_{i=1}^N \left(\frac{x_i}{\sum_{j=1}^N x_j} \right)^2 \quad (1)$$

where N describes the total number of macromolecules formed in a specific NP, whereas x_i and x_j are the number of monomers in the i^{th} and j^{th} macromolecule, respectively, allows quantifying the structures along a scale between two extremes: an NP composed of a single, long molecule ($\text{HHI} = 1$), or an NP formed as a mere cluster of monomers ($\text{HHI} = \frac{1}{\sum_{j=1}^N x_j} = \frac{1}{N_{\text{mono}}}$). Table 2 shows the statistical distribution of HHI for each kind of system, including the reference structures.³⁵

The reference NPs consist of 11 strands, each of which is made up of nine monomers, resulting in an HHI of 0.09. The minimum HHI values for all of our systems are larger than those of the reference, indicating the formation of comparatively large strands, which supports the observed distribution in the top row of Figure 2. When comparing the different systems, we observe that the mean and median HHI values decrease as the number of monomers increases. This suggests that a single dominating polymer molecule is more unlikely to form when moving toward larger systems. All mean and median HHI values are smaller than 0.40. Thus, we do not find large monopolization in our systems, which means that our

Table 2. Mean HHI, Its Standard Deviation as Well as the Median, Minimum and Maximum HHI Values for Each Particle, Including the Reference (“ref”)³⁵

system	mean $\pm$ std	median	min	max
ref.	0.09 $\pm$ 0.00	0.09	0.09	0.09
M70	0.32 $\pm$ 0.14	0.29	0.13	0.84
M99	0.30 $\pm$ 0.14	0.27	0.10	0.85
M130	0.18 $\pm$ 0.05	0.18	0.10	0.34
D70	0.36 $\pm$ 0.12	0.35	0.17	0.80
D99	0.24 $\pm$ 0.09	0.22	0.13	0.62
D130	0.20 $\pm$ 0.07	0.19	0.11	0.44

particles are, on average, built of multiple small-to-medium sized macromolecules. For all systems, the median HHI is slightly smaller than or equal to the mean values, indicating that the indices for the particles in the respective systems are mostly concentrated around the mean and median values with a few outliers to larger values.

The structure of the resulting particles is of key importance, since the arrangement of molecules, especially on their surface, determines their interaction with their environment in the modeling studies they are intended for. We calculated six properties for the obtained NPs with our analysis program MakroLyzer,⁴¹ as shown in Figure 3. Among the properties, the number of hydrogen bonds, N_{HB} , is an important feature for the hereby investigated polymer, as this interaction dominates also the crystal structure of bulk N66. Next to the amide moieties, the terminal $-\text{COOH}$ and $-\text{NH}_2$ groups may be involved in this interplay. To ensure comparability between the results for the different NPs, the terminal groups were not included into the hydrogen bond analysis. The presence of a hydrogen bond was calculated by using geometric criteria, defining <3.5 Å for the $\text{N}\cdots\text{O}$ distance, <2.5 Å for the $\text{H}\cdots\text{O}$ and distance, and a cutoff angle of $<30^\circ$ for the angle enclosed by the $\text{N}-\text{H}$ vector and the $\text{H}\cdots\text{O}$ vector.

The radius of gyration quantifies the extent of the particle in space; i.e., it can give an estimate of the overall compactness.

N_{HB} was normalized by the total mass of the respective particle m_{tot} to ensure compatibility between the particles of differing size. The anisotropy factor as well as the asphericity parameter are defined by the eigenvalues of the gyration tensor.⁴³ These two parameters measure the uniformity of the particle and its similarity to a perfect sphere, respectively, thereby describing its overall shape. The order parameter is obtained as the largest eigenvalue of the Q-tensor, an orientational order parameter often used to determine order in liquid crystals.⁴⁴ This quantity leverages the distance between two atoms to form a “molecular” vector. The *gauche* ratio refers to the share of neighboring C–C–C–C quadruplets that are in a *gauche* conformation (as opposed to *trans*), based on the dihedral angles along the backbone of each polymer strand. More information regarding the analyses is given in the [Supporting Information](#).

Both R_G and N_{HB} increase for larger plastics, while the $N_{\text{HB}}/m_{\text{tot}}$ ratio shows very similar trends for all NPs studied. For R_G , there is a slight increase for the **D** system compared to the **M** systems, while no significant variations are observed when comparing the number of hydrogen bonds obtained from systems of equal size.

Due to the lack of an interacting medium, the atoms can only partake in stabilizing interactions within the particle, leaving the surface a high energy domain. Thus, minimizing the surface-to-volume ratio is a driving force for the formation of compact particles. Since a sphere has the lowest possible surface-to-volume ratio, the most energetically stable structures should exhibit rather low values for the anisotropy factor and the asphericity parameter. On the other hand, a close and efficient packing of the atoms within the NP can strengthen the individual interactions, even if it requires sacrificing sphericity.

Interestingly, the shape of the particles is apparently influenced by variations in the size of the starting units. For the NPs containing 99 or 130 monomers, the anisotropy factor and the asphericity parameter are significantly larger for the **D**-systems than for the **M**-systems. Although to a smaller extent,

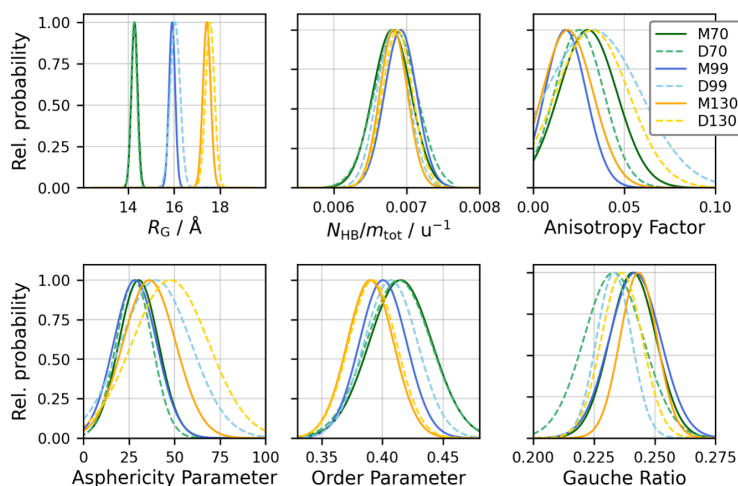


Figure 3. Relative probability of different structural properties for the six investigated systems. For the calculation of the hydrogen bonds, a donor–acceptor cutoff of 3.5 Å, a hydrogen-atom-acceptor cutoff of 2.5 Å, and an angle cutoff of 30° was used. End-group oxygen and nitrogen atoms were not considered as acceptor or donor atoms. For the order parameter determination, boxes of $10 \times 10 \times 10$ Å³ were constructed and molecular vectors of size 3 were used. Detailed information about the structure parameters is provided in the [Supporting Information](#).

the opposite trend is shown by the smallest considered systems (D70 > M70).

Generally, for all systems of the same size, the *gauche* ratio is larger for the M-systems compared to the D-systems. The order parameter decreases with increasing system size, being slightly larger for the D99 and D130 systems. The small *gauche* ratios and large order parameters found for the D-systems indicate more crystalline particle structures compared to their M counterparts.

Figure 4 shows the spread of the same six structure parameters over all systems investigated in this study compared

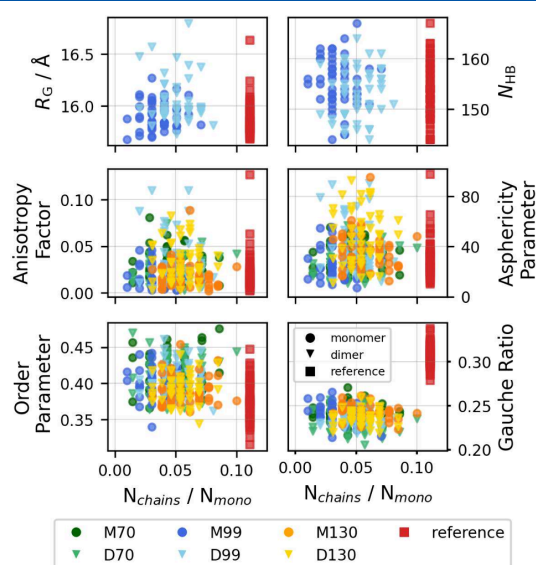


Figure 4. Structural properties against $\frac{N_{\text{chains}}}{N_{\text{mono}}}$ for the six investigated systems as well as the reference data.

to the reference structures. N_{chains} corresponds to the number of chain-like macromolecules in a NP, thus ring polymers are not included into this count. All properties are shown in dependence of the N_{chains} to N_{mono} ratio, since the number of chains is proportional to the number of end-groups in the corresponding system and thus, as discussed above, may influence the characteristics of a NP. For R_G and N_{HB} only the results for the systems M99, D99, and the reference are shown to maximize comparability.

R_G , N_{HB} , the anisotropy factor and the asphericity parameter, calculated for the newly generated structures, cover a similar range compared to the reference structures, while the order parameter and *gauche* ratio deviate. Note that the end-group oxygen and nitrogen atoms were excluded as hydrogen bond acceptors/donors, to ensure comparability between particles containing the same number of monomers but different numbers of end-groups. Since R_G , the asphericity parameter, and the anisotropy factor are all measures of the spatial extension or uniformity, the particles in the reference system and our systems appear to be similar in shape. Interestingly, the *gauche* ratio is much smaller for our systems than for the reference systems, while the order parameter is slightly higher on average. As previously mentioned, the N–C bonds formed in the process here are oriented into *trans* configurations

during the initial polymerization simulations. During the relaxation phase of the simulation, the bonds may rearrange again, but a bias toward more *trans* conformations cannot be ruled out.

However, this conformation at the amide groups closely resembles the crystal structure of N66, and their prevalence can be, therefore, considered realistic, indicating a well-aligned cluster of polymer strands. Density estimates for the particles can be found in the Supporting Information. These values are in good agreement with the experimental densities, indicating that the particles generated by our approach are physically reasonable. While our method slightly underestimates the particle density, this discrepancy is probably due to the density estimation procedure employed in the model. All discussed structural properties were additionally recorded during the relaxation run for each simulation (see the Supporting Information), and they show only a slight variation during the relaxation simulation. This finding indicates that all main structural arrangements occur during the aggregation and polymerization runs.

In summary, we successfully generated NPs using a novel approach, which allows for the stepwise aggregation and subsequent polymerization of monomer units. The number and lengths of polymer chains are treated as variables, which allows for great diversity in the structures. This diversity is a cornerstone of NP research, and the ability to generate an array of geometries within a single setup can be an asset in discovering what the effects of this structural heterogeneity on the environment and human health can be. The generated NPs were compared using their individual N_{chain} to N_{mono} ratio to allow for size-independent comparison of the particles. Energetically and structurally, the formed particles cover a wide range. In the context of comparing the novel particles to reference structures, the NPs obtained using the new approach are similar in terms of energy and structure. However, an overall higher order parameter is observed together with a reduction in the *gauche* ratio in the backbone of the polymer, indicating a higher crystallinity within the NPs. Interestingly, using dimers as starting units also impacts the NP structure, leading to more ordered particles, overall longer polymer strands and a reduced polymer ring formation. The approach is computationally efficient and can be used as a foundation for further structural refinements based on other methods, as well as for the future modeling of functionalized NPs.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.jpclett.6c01194>.

Computational details, size-independent energy comparison, and structural quantities with supporting tables and figures (PDF)

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Notes

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List of Figures

1.1	Schemes describing the intra- and intermolecular interactions between atoms.	10
1.2	LJ potential $U_{\text{LJ}}(r_{ij})$ in relation to the distance r_{ij} between two atoms i and j	11
1.3	Schemes depicting a simulation box of atoms surrounded by periodic images. The radial cutoff distances of exemplary atoms are shown.	13
2.1	Compositions of ILs from anions, cations, as well as their functionalization.	17
2.2	Carbon allotropes and their connection.	20
2.3	Description of the ZIF-8 and the N66 NP structure from individual building blocks to the final structure.	23
2.4	Schematic depicting a flowchart of CONAN.	25
2.5	Flowchart of the molecular recognition in CONAN.	26
2.6	Flowchart of the structure recognition in CONAN.	28
2.7	An overview of exemplary systems studied, utilized analysis methods and the visualization of the results.	29

List of Acronyms

B

B3LYP Becke-3-LYP

B88 Becke 88

BSSE basis set superposition error

C

CNT carbon nanotube

COM center of mass

CVD chemical vapor deposition

D

DFT density functional theory

E

EDLC electric double-layer capacitor

ESW electrochemical stability window

F

FF force field

G

GGA generalized gradient approximation

GTO Gaussian-type orbital

H

HB hydrogen bond

HF Hartree-Fock

HHI Herfindahl Index

I

IL ionic liquid

IR infrared

L

LCAO linear combination of atomic orbitals

LDA local density approximation

LJ Lennard-Jones

LSDA local spin density approximation

M

MD molecular dynamics

mGGA meta-GGA

MNP micro- and nanoplastic

MOF metal-organic framework

MSD mean square displacement

N

N66 nylon 6,6

NP nanoplastic

P

PBC periodic boundary condition

PBE Perdew-Burke-Ernzerhof

PE polyethylene

PES potential energy surface

PIP permutationally invariant polynomial

PP polypropylene

PS polystyrene

Q

QM quantum mechanics

R

List of Acronyms

RDF radial distribution function

RTIL room temperature ionic liquid

S

SA simulated annealing

SBU secondary building unit

SiIL salt-in-ionic liquid

STO Slater-type orbital

T

TC tetracycline

U

UCSD University of California San Diego

V

VANTA vertically aligned carbon nanotube array

vdW van der Waals

Z

ZIF zeolitic imidazolate framework

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