MD on interactions of plastic nanoparticles and bio molecules

Modelling the influence of environmental micro- and nano-plastic on proteins and biological membranes

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In Short

- Developing a representative polystyrene model (adjustable pH, functionalisations)
- Physical charactarisation via zeta potential and water contact angle simulations
- Nano particles with protein corona and lipid membrane interaction

Introduction Plastic waste is a major cause of pollution in marine systems. This can pose a high risk factor for health threats in the near future for many organisms. While plastic waste consists of a variety of differently shaped and sized structures, especially microplastic particles smaller than 5 mm are constantly degraded into nanoplastics smaller than 1 µm[1]. This happens due to biological, chemical and mechanical processes. Also, such nanoplastic particles are already found in various daily goods, such as cloths, cosmetics or water bottles and may easily enter the human body, even through the skin. Only little is known, if these particles interact with biomolecules such as proteins and lipids in our bodies and how they might perturb biological processes. Plastic nanoparticles are likely to cause aggregation or structural changes of proteins and may therefore trigger inflammatory immune responses when interacting e.g. with cell membranes. They build protein coronas and may also accumulate in our organs or brains and research is required to understand, what healthwise consequences we may expect sooner or later due to this bioconjugates.

Objective This project shall implement a basis for modelling nanoplastic properties and their influence in biological systems utilising molecular dynamics simulations (MDS). Force field parameters for one of the most produced plastics (polystyrene) with various surface functionalisations are developed. Surface and nanoparticle models will be build and the physical properties characterized (e.g. zeta potential, water contact angle, diffusion coefficient) to bring them close to experimental evidence. The interaction with human blood proteins, membranes and liposomes is investigated to understand the influence of nanoplastic particles in our protein machinery under various stress conditions e.g. pH or temperature, on a molecular level[2,3].

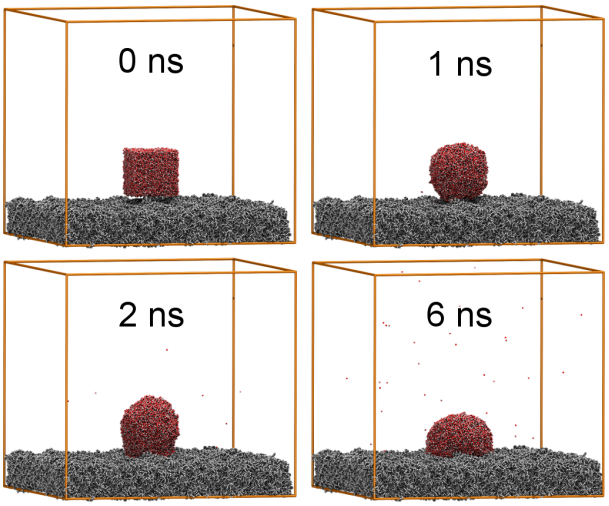

Figure 1: *Time evolution of a water (red:O, white:H) contact angle simulation on pure polystyrene (grey:C). At the end of the simulation the contact angle approaches 90 °which is in line with the literature.*

Model building For a representative plastic particle model, it is important to verify the surface properties by common physical measurement parameters and to compare them against experimental values. Artificial surface and nanoparticle models will be refined to fit experimental zeta potentials, elemental composition, diffusion and wetting properties. The simulation parameters for the polystyrene polymers need to be developed and refined. This includes the main chain repeat as well as patches used to add functionalisations for -OH and -SO_3H at the polymer backbone and -NH_2 and -COOH at the benzene ring, with selectable protonation states. From these polymers, periodic building blocks are created by high temperature simulations that allow sufficient mixing. After relaxation at physiological temperature this periodic building blocks can seemingly be repeated in any spatial dimensions to construct plastic surfaces and bodies as desired. From such bodies, also particles of any shape and size can be cut (Figure 2). By tweaking e.g. the protonation states of monomers and the amount of functionalisation, we aim to adjust the properties of our polystyrene bodies by means of surface charge, hydrophobicity and elemental composition at the surface. Characterising the wetting properties is especially important to

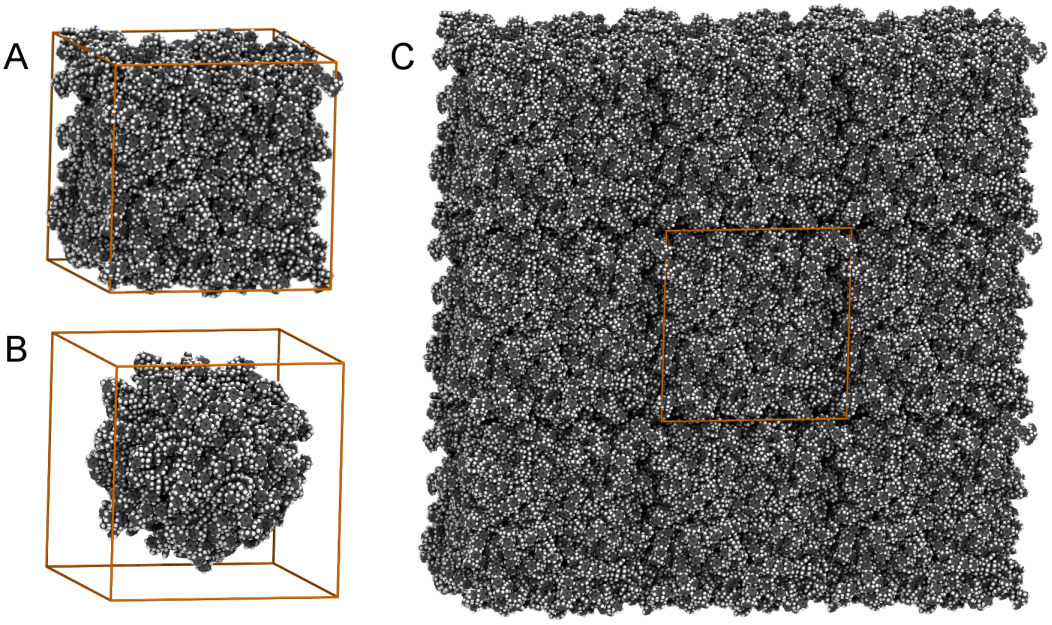

Figure 2: *Atomic representation of polystyrene bulk includes carbon (grey) and hydrogen (white). The orange box denotes the original periodic unit boundary.* ***A*** *Example of a seemless plastic building block.* ***B*** *Spherical particle clipping.* ***C*** *Assembled surface model for e.g. water contact angle simulations.*

understand later the interaction with different blood proteins and membrane systems.

Bioconjugation and membrane interactions Bioconjugation will be investigated to understand how the shape and surface modification of plastic compounds may alter protein structure and how prone nanoplastics are to cause aggregates. Bare nanoparticles and bioconjugates are subjected to lipidic systems such as membranes and liposomes to investigate how cell permeability may be influenced by protein corona formation. We aim to quantifying the binding of different types of blood proteins (human serum albumin, lysozyme, transferrin and insulin) to variously functionalised polymer surfaces. By MDS of only proteins in aqueous solution we aim to find, whether proteins change their structure or shift their conformational equilibrium while binding to the polymer surfaces. This is quantified by dihedral PCA structural landscapes[4]. Protein corona particles (bioconjugates) are constructed for different polymer modification with strong binding blood proteins to be used with membrane interaction studies. It will be studied how particles may penetrate or perturb the lipid bilayer structure and how this is controlled by the surface modification of particles. It is assumed that with a protein corona already attached to the polymer nanoparticle, the actual composition, away from binding the protein, does not influence the interaction with the lipid bilayer. However, for the bare polymer nanoparticles, a dependence on functionalisation and pH is expected.

Simulated water contact angles The simulation of water contact angles are performed according to reference [5]. A sufficiently large surface slab is placed periodically in XY direction. A cube of water is placed in the center above the surface in Z direction. During molecular dynamics simulation the water cube quickly relaxes into a sphere that builds contact with polymer slab. Ongoing, the drop will increase its contact surface area with the polymer until equilibrium is reached (Figure 1). The measurement of the contact angle is implemented in an automatic fashion by sensing the slab and droplet surfaces and fitting an 3D ellipsoid function. This allows to obtain the contact angle over time and with the relaxation process of the water droplet, the equilibrium angle can be obtained by fitting an exponential decay function.

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https://biochemie.uni-greifswald.de/biophysikalische-chemie/

More Information

[1] doi:10.1016/j.envpol.2020.114297

[2] doi:10.1038/s41598-020-64010-7

[3] doi:10.1039/D0NR04181E

[4] doi:10.1021/acs.jpcb.9b03134

[5] doi:10.1116/1.4883555