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CHARMM force field and molecular dynamics simulations of polyethylenimine chains

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Over more than a decade, cationic polymers have been validated as excellent gene delivery vectors, not in the least, due to their accessible chemistry, cost effectiveness, and controllable toxicity. Polyethylenimine (PEI), in particular, is one of the most commonly employed synthetic poly-cations. The predominant electrostatic interactions between the positive amino groups of these polymers and the negative phosphate groups of DNA lead to condensed polyplexes, which protect DNA from degradation and are able to enter cells via endocytosis. The specific charge pattern of protonated PEI is widely considered to be responsible for the release of the polyplexes from the endosome (via proton sponge effect), and, finally, for the release of DNA from polyplexes (prior to being processed by the nucleus). Our investigations aim to provide a new, realistic molecular mechanics force field for PEI, to be used in detailed atomistic simulations of DNA-PEI condensation. Accordingly, we tackle two major issues: (1) we develop a new atomistic CHARMM force field for PEI of arbitrary length and protonation patterns rigorously derived from high-quality *ab initio* calculations on model polymers, and (2) we perform molecular dynamics simulations, investigating the dynamic structuring of solvated PEI chains in dependence of their size and protonation state. We characterize the dynamic structure in terms of gyration radius, end-to-end distance, persistence length, radial distribution functions, coordination numbers, and diffusion coefficients. Altogether, the developed force field leads to more rigid PEI chains than other computational studies. Notably, the calculated diffusion coefficients are in excellent agreement with experimental data and validate the force field for the realistic modeling of the size and protonation behavior of linear PEI chains, whether individually or as part of polyplexes.

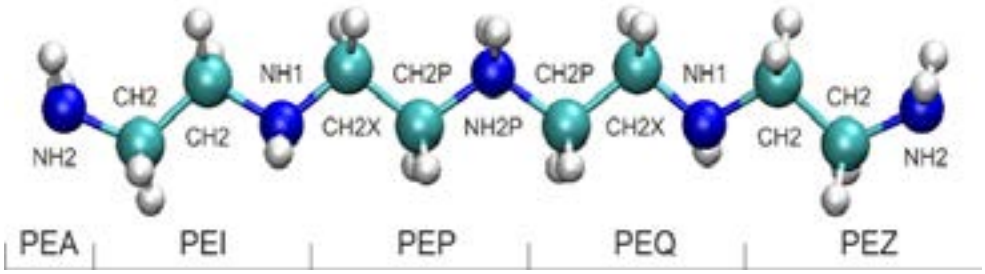

Figure 1: Protonated PEI tetramer used as model for the force field parametrization.

Biography

Titus Adrian Beu is Professor of Theoretical and Computational Physics at Babeş-Bolyai University, Romania. He has been actively involved in computational physics, material science, and chemical physics for more than 30 years. His research topics have evolved from tokamak plasma and nuclear reactor calculations in the 1980s, collision theory and molecular cluster spectroscopy in the 1990s, to simulations of fullerenes, nano-fluidic systems and biopolymers in recent years. He taught courses in general programming techniques and advanced numerical methods, general simulation methods and advanced molecular dynamics.

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