GROMEX – Unified Long-range Electrostatics and Flexible Ionization

The German priority program 1648 "software for exascale computing" (SPPEXA) was launched successfully in January 2013 with an initial three year funding phase. The aim of the strategic initiative of the DFG is to fund HPC software in Germany. The main topics of SPPEXA involve computational algorithms, application software, system software, programming, software tools and data management. GROMEX, one of 13 interdisciplinary research consortia within the priority program engages in the first two topics. The project brings together scientists from different fields of research like computer science, mathematics and theoretical biophysics and aims to develop a flexible and unified toolbox in the field of particle-based simulations on the exascale.

Background of the Project

Simulations of biomolecular function in atomistic detail provide insights into the inner workings of living systems that are difficult or impossible to obtain experimentally. Molecular dynamics (MD) simulation methods have been a long-standing, successful tool to tackle this problem. A particularly challenging aspect of MD simulations is the realistic modeling of electrostatic interactions. The strength and long-ranged nature of electrostatic interactions makes them important determinants of biomolecular function and properties (Fig. 1). Challenges in the computational treatment of these interactions fall into two main areas.

Usability & Scalability

The calculation of long-range electrostatic interactions is the computationally most expensive part of an MD simulation. Thus, the efficiency of this calculation is decisive for the efficiency of the whole simulation. Currently applied techniques for the treatment of long-range electrostatics like the Particle Mesh Ewald (PME) method do not scale well on large numbers of processors and will thus not be capable of harnessing the full potential of future exascale computers. With the help of the Fast Multipole Method (FMM), the scalability of the electrostatics can be significantly improved (Fig. 2). The optimal time complexity O(N), with N being the number of particles in the system, allows to efficiently utilize the available and future HPC hardware. The FMM does not suffer from the same inherent communication requirements that limit the scalability of PME-based solvers and can thus scale up to millions of cores. The implementation developed at Jülich Supercomputing Centre also provides flexibility for the user. Provided with the required accuracy for the computed electrostatic energies as only input parameter, this implementation tunes the calculation such that the optimal runtime is achieved. This user-friendly error control supports the development of a truly flexible toolbox which also can be used in other areas of research dealing with long-range interactions, namely plasma physics or astrophysics.

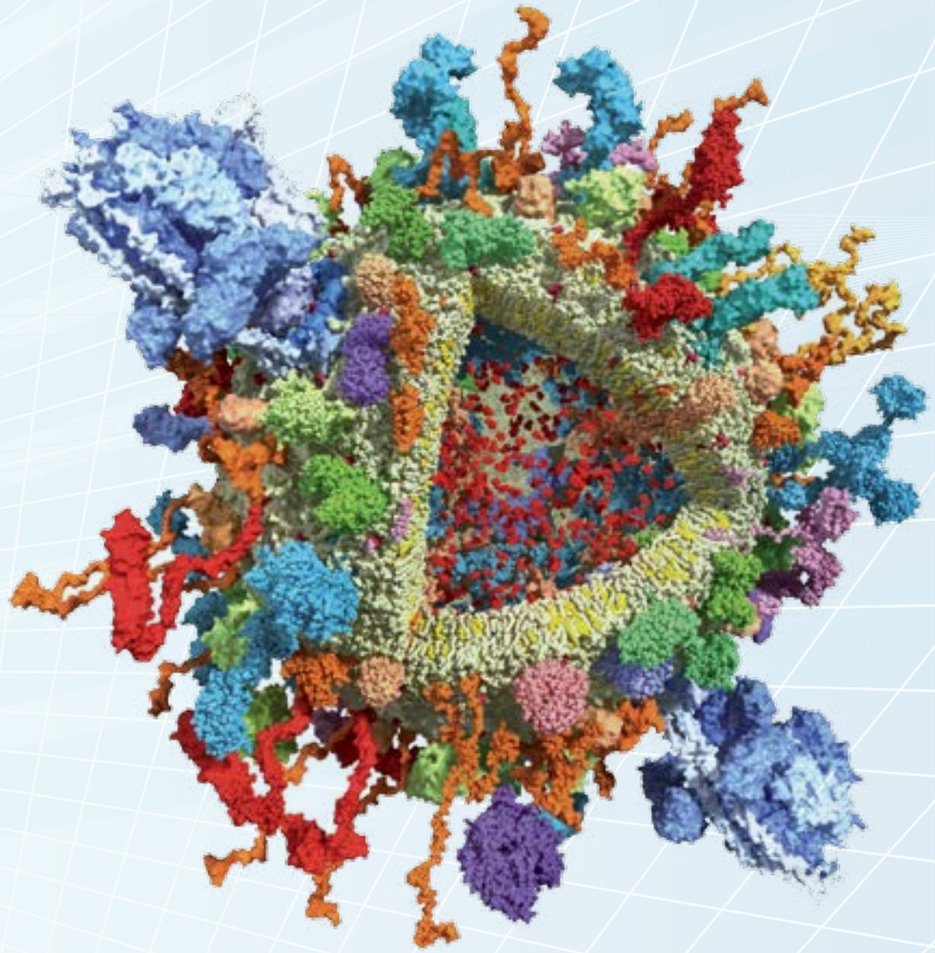

Figure 1: Functional units of biomolecular systems are often large assemblies of many different components. The simulation of these huge systems requires modern HPC computers and efficient simulation methods that take full advantage of their computational power. The figure shows an example under study at the Grubmüller department at the MPI for Biophysical Chemistry. Information between nerve cells is transmitted via messenger molecules called neurotransmitters that are transported in synaptic vesicles. The picture shows a molecular model of such a synaptic vesicle enclosed by a lipid membrane (yellow). The vesicle is filled with neurotransmitters (red spheres within the vesicle). These messenger molecules are released at the chemical synapses between nerve cells and thus transmit nerve impulses. The release of the neurotransmitters and the reloading of the vesicle involve many functional proteins, as e.g., SNARE proteins (red/orange) and V-ATPase (blue). (Figure courtesy of MPI Biophys. Chem. Jahn/Grubmüller)

Towards realistic Simulations

The treatment of biomolecular electrostatics is complicated by the fact that the charge distribution varies due to uptake and release of protons, electrons and other ions or small-molecule ligands. Here we address both tightly interlinked challenges by the development, implementation, and optimization of a unified electrostatics algorithm that will

account for realistic, dynamic ionization states (λ-dynamics) and at the same time overcome current scaling limitations. The essential idea of λ-dynamics is to enable a smooth interconversion between different protonation or other binding forms, which is crucial for MD simulations with explicit solvent molecules (Fig. 3). Improvements over previous λ-dynamics methods include that not only protonation, but also other binding reactions can be considered and that these reactions can be modeled in greater detail. The FMM allows, through its multilevel approach and spatial decomposition, to model a large variety and number of binding sites.

Additional ionization states only generate a constant computational overhead and do not require an expensive recomputation of the full interaction set. The multipole-based representation of different ionization states and sites also reduces the memory overhead and can be processed easily at very low cost.

Project Partners

- Max Planck Institute for Biophysical Chemistry, Göttingen
- Jülich Supercomputing Centre, Research Centre Jülich, Jülich
- Royal Institute of Technology, Stockholm

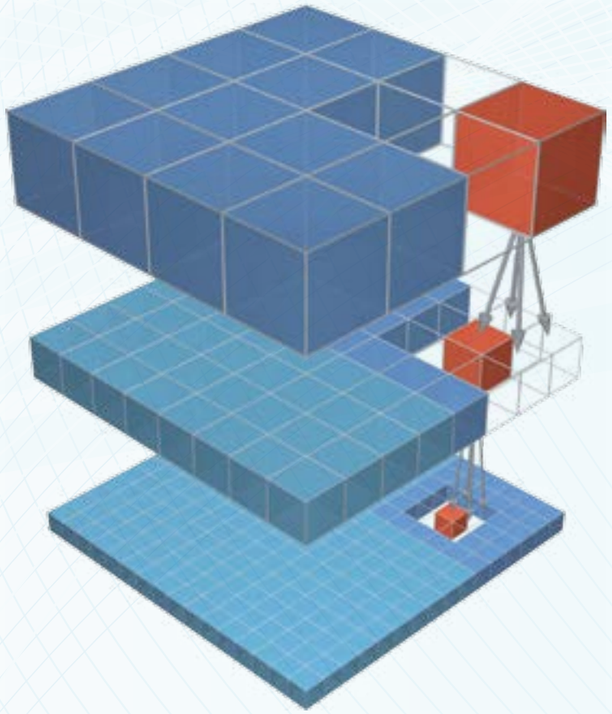

Figure 2: The figure shows the schematics of the FMM interaction set. The interaction of particles inside the depicted boxes due to their long-range forces is performed in a tree-like structure on multiple levels via box multipoles. For a given box (red) on a certain level, only a constant number of interactions (dark blue boxes) take place. The remaining interactions (light blue) are performed on a different level.

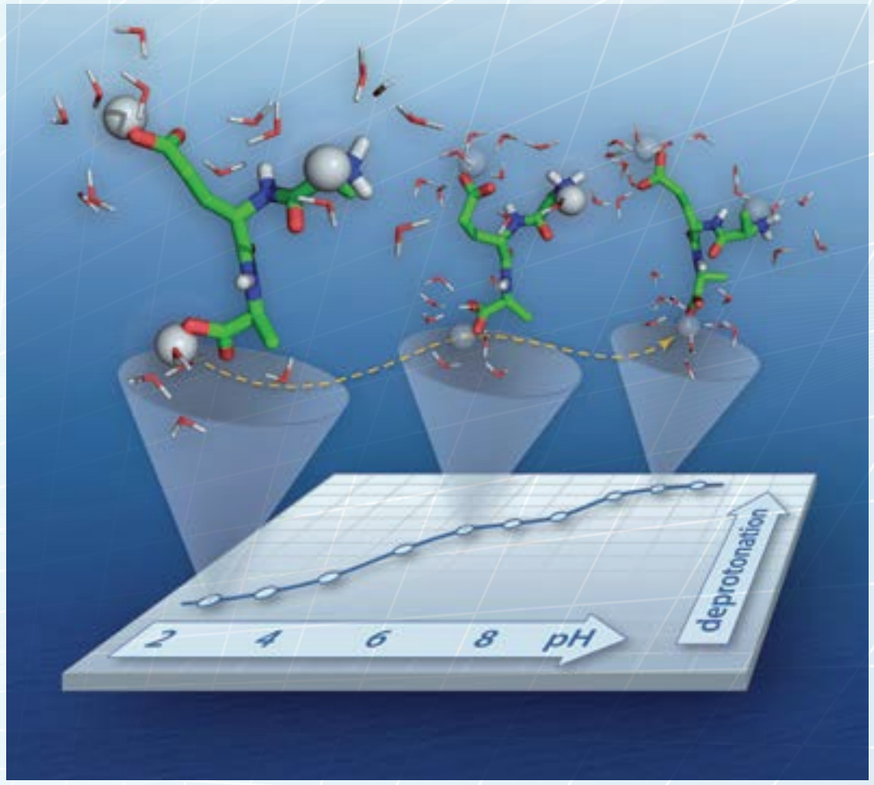

Figure 3: Binding, transfer and release of ligands, such as protons, is of central importance for the function of many biomolecules. Including these reactions in biomolecular simulations can lead to valuable insights into their influence on biomolecular function and properties. As an example, the figure shows the pH-dependent proton titration curve of a small peptide as obtained from constant-pH λ-dynamics simulations. The protonation states of the peptide's titratable groups are allowed to change dynamically during these simulations. The changes in protonation are governed by electrostatic interactions with the environment, as well as by the pH value of the surrounding solution. On top of the titration curve, the figure shows the the structures of the most probable protonation states of the peptide at selected pH values (pH 2, 6 and 10), where bound and unbound protons are depicted as opaque and faint white spheres, respectively.

References

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