BBB seminar (BMED380)

SCAN ME

Thursday, December 1, 14:30 at the BBB, Auditorium 4

High-fidelity biomolecular modelling

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Although molecular dynamics (MD) simulations are a widely used tool in biosciences, they often actually fail to provide a veritable description (e.g., matching NMR data within experimental accuracy) of the conformations and the dynamics of the molecules simulated—a crucial prerequisite for using MD to intuitively interpret experiments. These failures can largely be attributed to the quality of the underlying MD models (force fields), improvement of which is hindered by the lack of comprehensive comparison to experiments, and outdated approaches, such as hand-tuning parameters.

We address these issues by combining an evolutionary optimization algorithm with experimental, atomistic resolution target data (C–H bond order parameters measured with NMR) to create an automated tool for building high-fidelity MD models. Using this approach, we have created the first phospholipid models that capture the conformational ensemble sampled by a bilayer lipid. They also represent well the lipid dynamics (as demonstrated by comparison to NMR relaxation times) and the overall bilayer structure (as quantified by comparison to small-angle x-ray scattering form factors).

As an application of this 'computational microscope', we quantify the conformational ensemble sampled by POPC (1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine)—a demanding task for any other method outside simulations when considering an intrinsically disordered molecule—and compare the most prevalent conformations to the consensus structures predicted by the early pioneers of lipid NMR as well as the conformations present in crystalline state.

Chairperson: Harald Barsnes <harald.barsnes@uib.no>, Dept. of Biomedicine