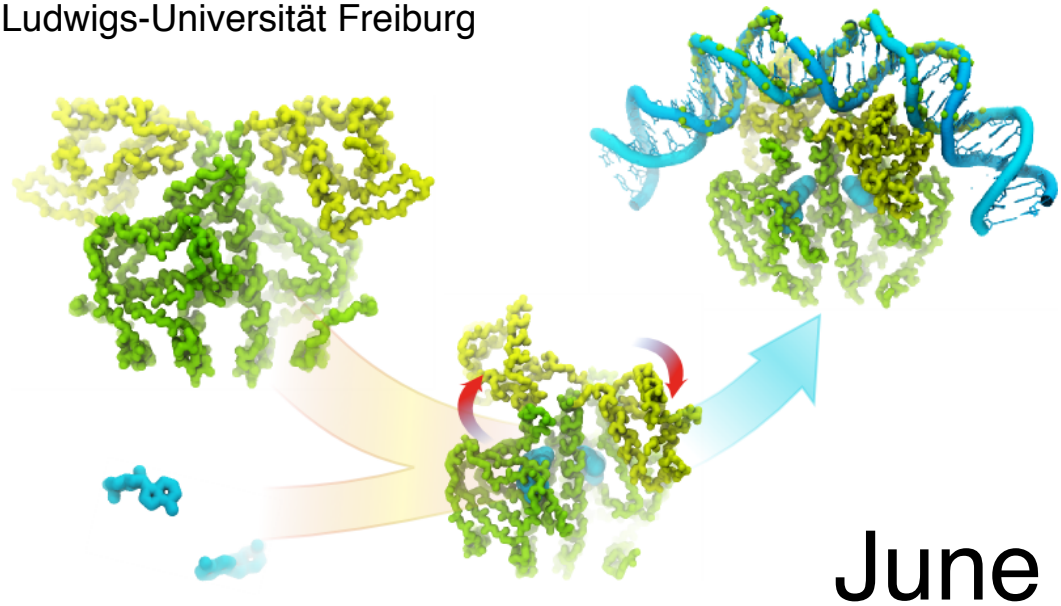
Physikalisches Institut

Albert-Ludwigs-Universität Freiburg



June 27

Free Energy Guided Sampling

Amedeo Caflisch

University of Zurich

We have developed a method called FEGS (Free Energy Guided Sampling) which uses the cut-based free energy profile and Markov state models to efficiently explore the conformational space of peptides and proteins by conventional MD at constant temperature. The efficiency and accuracy of FEGS was demonstrated by applications to the alanine dipeptide and the reversible folding of a 20-residue beta-sheet peptide (Beta3s). The former illustrates in a human-comprehensible manner its speedup efficacy, as the two-dimensional free energy surface converges faster by more than one order of magnitude for FEGS than CS. The latter peptide is a challenging system because of the complex denatured state consisting of enthalpic traps and an entropically stabilized non-native helical basin. FEGS generates a converged cut-based free energy profile of Beta3s by sampling mesostates about one order of magnitude faster than conventional sampling. The FEGS method is a reaction-coordinate-free approach, and samples heuristically. No additional information is needed except for a starting conformation. Moreover, it does not need to bias the energy function. Therefore the simulation code, force field parameters, and/or coarse-grained models do not need to be modified. It samples at the temperature of interest, and does not visit regions of conformational space visited only at elevated temperature. The FEGS sampling makes possible also investigating local movements, such as ligand binding/unbinding and conformational transitions involving localized structural elements.

Molecular Dynamics Seminars 2012

Seminar Room of Gustav Mie Haus, Ground Floor, 16:15

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