

Mechanoenzymatics: Conformational Dynamics of Biomolecules

Proteins are biological nanomachines. Virtually every function in the cell is carried out by proteins -- ranging from protein synthesis, ATP synthesis, molecular binding and recognition, selective transport, sensor functions, mechanical stability, and many more. The combined interdisciplinary efforts of the past decade have revealed how many of these functions are effected on the molecular level, and how. Computer simulations of the atomistic dynamics play a pivotal role in this enterprise, as they offer both unparalleled temporal and spatial resolution.

Three recent examples will illustrate this progress, and also the limitations of this approach. The first example focusses at the elastic muscle protein titin. The conversion of mechanical stress into a biochemical signal in a muscle cell requires a force sensor. Titin kinase, the (only) catalytic domain of titin, has been suggested as a candidate. As our simulations have shown, its activation requires major conformational changes resulting in the exposure of its active site. The second example reveals how F-ATP synthase converts mechanical energy into the synthesis of ATP, and addresses the question how energy is stored transiently in this enzyme. The third example focusses at the mechanism of tRNA translocation by combining results from X-ray crystallography, single particle cryo-electron microscopy, and atomistic simulations.