# ACCELERATED MOLECULAR DYNAMICS: A VERSATILE TOOL TO STUDY PROTEIN DYNAMICS, PROTEIN FOLDING AND BIOMOLECULAR RECOGNITION

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Some important processes such as biomolecular recognition, allosteric regulation, protein folding or signal transduction, usually take place on the micro- to millisecond or even longer time scales. Low-energy states relevant for these processes may be separated by high-energy barriers, which are rarely crossed over the course of conventional molecular dynamics simulations. Accelerated molecular dynamics (aMD) enhances sampling through modification of the system's Hamiltonian in a relatively simple way (only two to four parameters are required).[1,2] In addition, it does not rely on the definition of a reaction coordinate or a set of collective variables (a priori knowledge of the underlying free energy landscape is not needed), and it conserves the essential details of the free-energy landscape. Here we focus on the potential of aMD as a tool to efficiently explore the rough free energy landscape of proteins and we discuss its applications to: 1) the study of protein folding;[3] 2) the study of biomolecular recognition and its implications for drug discovery.[4] First, the ability of aMD to accurately predict the proper native state of some fast-folding proteins will be discussed. Second, aMD will be used to simulate ligand binding events between a set of potential inhibitors and three highly flexible enzymes involved in the biosynthesis of the bacterial cell wall in *Mycobacterium tuberculosis*. The computationally predicted inhibitors exhibited good activity in a series of biological assays and represent a new class of antibacterial drug leads.[5]

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