Atomistic Simulation of Biomolecular Function: Ribosomal Translation, Ligand Binding Heterogeneity, and a Dynasome Perspective

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Abstract

Ribosomes are highly complex biological nanomachines which operate at many length and time scales. We combined single molecule, x-ray crystallographic, and cryo-EM data with atomistic simulations to elucidate how tRNA translocation, the action of antibiotics, and frameshifting work at the molecular level. We show that tRNA translocation between A, P, and E sites is rate limiting, and identified dominant interactions. We further describe a new combined allosteric mechanism for erythromycin-induced translational stalling of the antibiotics sensor peptide ErmB, as well as a free energy model that can explain and predict frameshifting efficiencies. Using streptavidin/biotin as a model system with super-strong affinity, we show that the underlying free energy landscape which governs ligand binding and unbinding can be extracted from combined atomic force microscopy (AFM) and force probe simulation data, which covers loading rates of 11 orders of magnitude. We will, finally, take a more global view on the 'universe' of protein dynamics motion patterns and demonstrate that a systematic
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