

BRIDGING MICROSECOND COMPUTER SIMULATIONS AND MILLISECOND BIOLOGICAL EVENTS

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ABSTRACT. Despite considerable effort to gain structural and mechanistic insight into the network of proteins utilized by higher life forms to regulate the energy conversion pathways in mitochondrial respiration, atomic-level detail of the modus operandi whereby the entire respiratory chain fulfills its homeostatic functions is still largely missing. Moreover, the dynamical complexity of the biological objects at play and their relationship constitutes an insuperable barrier for petascale supercomputing. Inspired by the ubiquity of bioenergetic protein complexes in sustaining life on the biosphere, we will turn to the cell machinery of lower organisms, focusing on prokaryotic complex I and Vtype ATPase, as models to underscore the structure and dynamics of these protein assemblies in atomistic simulations. Bridging timescales, we will decrypt the chemo-mechanical coupling in a vacuolar ATPase and the conformational transition in complex I to showcase with unprecedented detail the remarkable design of the bioenergetic network and how it avoids dissipative energy loss to transform energy from nutrients into ATP.