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Structural and functional analysis of glycoprotein butyrylcholinesterase using atomistic molecular dynamics[1] AUSTEN BERNARDI, ROLAND FALLER, Univ of California - Davis — Atomistic molecular dynamics (MD) has proven to be a powerful tool for studying the structure and dynamics of biological systems on nanosecond to microsecond time scales and nanometer length scales. In this work we study the effects of modifying the glycan distribution on the structure and function of full length monomeric butyrylcholinesterase (BChE). BChE exists as a monomer, dimer, or tetramer, and is a therapeutic glycoprotein with nine asparagine glycosylation sites per monomer. Each monomer acts as a stoichiometric scavenger for organophosphorus (OP) nerve agents (e.g. sarin, soman). Glycan distributions are highly heterogeneous and have been shown experimentally to affect certain glycoproteins' stability and reactivity. We performed structural analysis of various biologically relevant glycoforms of BChE using classical atomistic MD. Functional analysis was performed through binding energy simulations using umbrella sampling with BChE and OP cofactors. Additionally, we assess the quality of the glycans' conformational sampling. We found that the glycan distribution has a significant effect on the structure and function of BChE on timescales available to atomistic MD.

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