Allosteric Modulation of Fluorescence Revealed by Hydrogen Bond Dynamics in a Genetically Encoded Maltose Biosensor

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Abstract

Genetically encoded fluorescent biosensors (GEFBs) proved to be reliable tracers for many metabolites and cellular processes. In the simplest case, a fluorescent protein (FP) is genetically fused to a sensing protein which undergoes a conformational change upon ligand binding. This drives a rearrangement in the chromophore environment and changes the spectral properties of the FP. Structural determinants of successful biosensors are revealed only in hindsight when the crystal structures of both ligand-bound and ligand-free forms are available. This makes the development of new biosensors for desired analytes a long trial-and-error process. In the current study, we conducted μs-long all atom molecular dynamics (MD) simulations of a maltose biosensor in both the *apo* (dark) and *holo* (bright) forms. We performed detailed hydrogen bond occupancy analyses to shed light on the mechanism of ligand induced conformational change in the sensor protein and its allosteric effect on the chromophore environment. We find that two strong indicators for distinguishing bright and dark states of biosensors are due to substantial changes in hydrogen bond dynamics in the system and solvent accessibility of the chromophore.

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