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Abstract

Information Routing in Proteins: The Case of a Therapeutic Antibody †

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Internal dynamics is the link between structure and biological function in proteins [1]. It has been shown that low-frequency dynamics is not only essential for a protein to function [2], but also that a correlation exists between a protein's activity and its specific dynamical properties [3]. Propagation of information between two or more distant sites on the protein network allows concerted, large-scale conformational changes to take place, triggering as a consequence biological responses. In this work, we aim at identifying patterns of information routing within the therapeutic antibody pembrolizumab [4], as communication channels that emerge from the underlying topology and drive the observed correlated motions. Specifically, we focus on the mutual information (MI) of the displacements of atomic positions, as computed from atomistic molecular dynamics simulations, both in presence and in absence of the bound antigen. MI is used to build network models of the antibody for each of the conformational clusters emerging from the simulations; these networks are then interpreted in the light of a graph-theoretical approach, to couple chemical detail and large-scale dynamics. Unveiling inter-residue communication pathways in may find application not only in biotechnological manipulation for improved therapeutic agents, but also in design of simplified, multi-resolution antibody models that, describing channels of information transfer at an appropriate high-resolution level, facilitate the dynamical investigation at a lower computational cost [5].

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