

Abstract Submitted
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Moving in the Right Direction: Evolution of Protein Structural Vibrations with Functional State and Mutation KATHERINE NIESSEN, MENG YANG XU, SUNY University at Buffalo, Physics, EDWARD SNELL, Hauptman-Woodward Medical Research Institute, Buffalo, NY, ANDREA MARKELZ, SUNY University at Buffalo, Physics — Long-range intramolecular vibrations may enable efficient access to functionally important conformations. We examine how these motions change with inhibitor binding and mutation using terahertz anisotropic absorption and molecular modeling [1,2]. The measured anisotropic absorption dramatically changes with 3NAG inhibitor binding for wild type (WT) free chicken egg white lysozyme (CEWL). We examine the evolution of internal motions with binding using normal mode analysis to calculate an ensemble averaged vibrational density of states (VDOS) and isotropic and anisotropic absorptions for both WT and a two residue (R14 and H15) deletion mutant which has a 1.4 higher activity rate [3]. While the VDOS and isotropic response are largely unchanged with inhibitor binding, the anisotropic response changes dramatically with binding. However, for the mutant the calculated unbound anisotropic absorption more closely resembles its bound spectrum, and it has increased calculated mean squared fluctuations in regions overlapping those in its bound state. These results indicate that the mutant's enhanced activity may be due to a shift in the *direction* of vibrations toward those of the bound state, increasing the sampling rate of the bound conformation. [1] DOI: 10.1007/s12551-015-0168-4 [2] DOI: 10.1038/ncomms4076 [3] DOI: 10.1006/jmbi.1999.2572

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