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Conformational dependence of a protein kinase phosphate transfer reaction MONTIAGO LABUTE, Theoretical Division, Los Alamos National Laboratory, GRAEME HENKELMAN, Department of Chemistry and Biochemistry, University of Texas, Austin, CHANG-SHUNG TUNG, PAUL FENIMORE, BEN MCMAHON, Theoretical Division, Los Alamos National Laboratory
— Atomic motions and energetics for a phosphate transfer reaction catalyzed by the cAMP-dependent protein kinase have been calculated using plane-wave density functional theory, starting from structures of proteins crystallized in both the reactant conformation (RC) and the transition-state conformation (TC). In TC, we calculate that the reactants and products are nearly isoenergetic with a 20-kJ/mol barrier, whereas phosphate transfer is unfavorable by 120 kJ/mol in the RC, with an even higher barrier. Our results demonstrate that the phosphate transfer reaction occurs rapidly and reversibly in a particular conformation of the protein, and that the reaction can be gated by changes of a few tenths of an angstrom in the catalytic site [1]. [1] G.H. Henkelman, M.X. LaBute, C.-S. Tung, P.W. Fenimore, B.H. McMahon, Proc. Natl. Acad. Sci. USA vol. 102, no. 43:15347-15351 (2005).

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