Evidence of Mechanical Regulation on Thiol/disulfide Exchange from TPS and QM/MM Study

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Abstract: The ability of mechanical force to regulate chemical reactions has interested generations of researchers and theoretical efforts have been taken to understand this mechanical phenomenon. [1] As evidences that force tilted the free energy profile and thus shifted transition state (TS) accumulated, more advanced model other than Bell's model have been proposed to describe the force-dependency of rate constant. [2] Here, by the combination of TPS and QM/MM we investigated thiol/disulfide exchange under forces ranging from 200pN to 2nN. The total simulation time added up to 20ns. We demonstrated that at low force reactions went along almost the same pathway while reaction paths became diverged at high force, which rationalized the limitation of Bell's model. A new model, which is expected to be valid at any applied force , is also proposed. We suggested that TS moved towards reactant state (RS) along reaction coordinate (R_C) driven only by the component of force along R_C and broad reaction pathways became possible at high force.

[1] M. K. Beyer, H. Clausen-Schaumann, *Chem Rev*, **2005,** *105*, 2921-2948.
[2] O. K. Dudko, G. Hummer, A. Szabo, *PNAS,* **2008,** *105,* 15755-15760.