MAR09-2008-007132

Abstract for an Invited Paper
for the MAR09 Meeting of
the American Physical Society

Kinetic parameters of association and dissociation between single molecules measured by single-molecule force spectroscopy

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This presentation is focused on development of experimental scanning probe microscopy (SPM) approaches to quantify kinetic parameters of association and dissociation between receptor–ligand pairs. The potential of mean force (pmf) between interacting molecules is quantified by single molecule force spectroscopy (SMFS) approach. In SMFS molecules are allowed to interact and form molecular bond. Consequent measurements of rupture forces are used to characterize the attractive part of the pmf by extracting the distance from the equilibrium to the transition state, the rate of dissociation at no force and the activation energy. Factors affecting accuracy of the measured kinetic parameters are discussed including effects of the polymeric tether stiffening and possible contribution of non-single molecule events to the statistics of rupture forces. The developed SMFS method accounts for pertinent systematic errors and is tested using specific biotin-streptavidin interactions. The measured kinetic parameters show quantitative agreement with theoretical predictions. In addition, a new single-molecule approach to measure the activation energy of association is proposed. This approach uses the dependence of the probability to form molecular bonds on probe velocity when one of the interacting molecules is tethered by a flexible polymeric linker to the AFM probe. The application of the developed method to study interactions between biomolecules is demonstrated with measurements of the activation energy of biotin-streptavidin association.