Binding and catalysis to protein ensembles

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Because protein function is determined by its conformational state, understanding protein binding and catalysis depends on knowledge of the conformational ensemble. Experimental determination of the structures composing an ensemble and their interconversion dynamics remains a challenging task and motivated development of theoretical methods. On this talk I will present computer simulations of small-molecule binding and catalysis to an ensemble of protein tyrosine phosphatases generated with a coarse-grained model of the protein backbone. The results reveal formerly unknown binding modes that uncover the mechanism of inhibition. Structural characteristics previously treated as artifacts in analysis of x-ray crystallography data are shown to be features of the ensemble and can help explaining activity and regulation of this enzyme family.