

# Computer simulations of enzyme reactions

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Identification of the minimum energy path (MEP) for chemical reactions in enzymes is one of the most important problems in computational chemistry and biophysics. The structure with maximum energy along MEP approximates the transition state for the reaction process and the energy profile itself permits estimation of the transition rates. For the identification of MEP in complicated biosystems we proposed a computationally efficient algorithm, which is a hybrid of the nudged elastic band and string methods.<sup>1</sup> To illustrate the efficiency of the method I will demonstrate its several applications to study reaction mechanisms in enzymes. In particular, I will talk about the mechanism of citryl-coenzyme A formation catalyzed by citrate synthase;<sup>2</sup> the GTP hydrolysis in the EF-Tu:aa-tRNA:ribosome complex;<sup>3</sup> and mechanism of the aminoacylation reaction catalyzed by leucyl-tRNA synthetase.<sup>4</sup>

As a completely different topic, but nonetheless very important for biomolecular simulations, I will present our recent work on the development of the continuum medium implicit solvation model for the Drude polarizable force field. In this model, the electronic polarization response of the solute is computed in accord with the solvent reaction field produced by solute charges and solute polarization. The usefulness and limitation of the current model will be demonstrated in the context of its application to protein-protein relative binding free energy calculations.<sup>5</sup>

## References:

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- 2) Aleksandrov A, Zvereva E, Field M. The mechanism of citryl-coenzyme A formation catalyzed by citrate synthase. *J Phys Chem B*. 2014, 118, 17, 4505-13;
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- 4) Aleksandrov A, Palencia A, Cusack S, Field M. Aminoacylation Reaction Catalyzed by Leucyl-tRNA Synthetase Operates via a Self-Assisted Mechanism Using a Conserved Residue and the Aminoacyl Substrate. *J Phys Chem B*. 2016, 120:4388-98;
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