DESCRIPTION FOR THE GENERAL PUBLIC

Catalytic fields as the tool for theoretical analysis and design of biocatalysts

Since the discovery of the potential of chemical reactions, chemistry is an essential part of every industry. For this reason researchers are continuously searching for better ways to obtain products in less time and with less money. The perfect tools for obtaining these goals are catalysts - substances which significantly speed up chemical reactions by lowering the activation barrier, allowing reagents to react in milder conditions (for example at lower temperature and pressure), with higher efficiency and less harmful impact on environment. The best catalysts known in nature are enzymes, proteins evolved by evolution to speed reactions proceeding in living species. Despite of significant research effort the attempts to design theoretically enzymes to catalyze other reactions with potential use in industry or environment protection remain still unsuccessful. Such enzymes could be obtained experimentally at great cost by laboratory directed evolution, which leads to some mutations which are generally not understood. In this project we will use several computational methods developed in our laboratory to interpret the role of such mutations. Our preliminary results indicate that the major role play rotations of charged amino acid sidechains, which would require extremely long simulation time using conventional computational methods of molecular dynamics. The advantage of the method proposed in this project will be possibility of scanning millions of possible rotamers in short time, aiding theoretical design of mutants leading to better catalytic activity. The most important element of our methodology is catalytic field, i.e. charge distribution of ideal catalyst, derived by quantum chemical calculation of molecular electrostatic potentials of the transition state and substrates. It allows to analyze and build catalytic environment in bottom-up fashion avoiding numerous arbitrary assumptions which have to be made in other conventional top-down methods requiring consideration of the entire complex enzyme composed with thousands atoms. We also plan to explore other applications of catalytic fields in analysis of some enzyme features which are still fully understood.