

Rational approach in modifying enzyme specificity

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Enzymes are important reaction catalysts of the biological systems. They often have strong substrate specificity and selectivity, and are important for normal functioning of a cell. Lack of enzymes in biological systems and/or their miss functioning results with all kind of disorders in living organisms. In order to study their affinity and specificity we are, besides using the established force field and quantum mechanical methods developing simple, physically based approaches to quantify the relationships between the structural variables and enzyme activity [1]-[5].

Starting from the experimental, mostly crystal, structures we model protein mutants and their complexes with substrates and inhibitors. Molecular modelling enables us to track possible binding modes and the conformational changes that occur during binding and to study reactions in an enzyme active site. Furthermore, we correlate the molecular modelling results with the experimental, kinetic and thermodynamic data and build a QSAR (Quantitative Structure Activity Relationship) model. The QSAR model enables us to predict enzyme selectivity and/or affinity for new compounds, but also to suggest enzyme mutations that might improve its activity [3]-[5]. Therefore, the approach is the most significant in interdisciplinary researches. An example is study that we have performed on *Pseudomonas cepacia* lipase (PCL) [4]-[7], a useful biocatalyst for obtaining enantiomerically pure compounds, in particular primary and secondary alcohols and their esters.

References

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