Mapping Enzyme Engineering by computational tools

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In this talk we will review recent studies in our lab modeling enzymatic processes on heme proteins. In particular, we will describe our efforts in coupling biophysical events, such as protein dynamics and substrate-protein interaction, with the biochemical activity.

On one hand, our in house Monte Carlo techniques coupled with protein structure prediction algorithms are used to describe these biophysical processes. A complete unbiased substrate migration and binding, for example, is possible in a 1-2 order faster manner than conventional molecular dynamics techniques[1] (see the PELE webserver at http://pele.bsc.es[2]). On the other hand, enzyme biochemistry is studied by means of QM/MM techniques. These methods allow for an electronic description of the catalytic active site.

We will show different examples addressing oxidation catalysis and long-range electron transfer processes. In particular, we will show our latest efforts in engineering different peroxidases and flavin oxidases. Additionally, we will also show how computational methodologies are (today) mature enough to provide accurate atomistic details into the mechanism of long range heme to heme electron transfer.[4,5] Our findings indicate the fine evolution of the enzyme to approach an elevated turnover rate of 5.47×106 s-1 for the ET between Cytc and CcP through establishment of a localized bridge state in Trp191.

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