AN APPROACH TO EXPLORE THE LINK BETWEEN ENZYMATIC MECHANISM AND ITS CATALYTICAL FUNCTION

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The main objective of this research is to study the mechanism of an enzyme as it reaches a catalytically competent shape to carry out its reaction. Creatine kinase, an enzyme found in all vertebrates, has been chosen because it is known to undergo conformation changes in order to accomplish its catalytic role. Creatine kinase acts as a catalyst in the reversible reaction of creatine and ATP, forming phosphocreatine and ADP. Since phosphocreatine functions to store energy, creatine kinase, as a result, plays an important role in energy metabolism of cells and tissues with high energy demands. Creatine kinase appears in four major isoforms: two cytosolic and two mitochondrial. This important enzyme is implicated in a number of disease states and is used as an indicator of myocardial and skeletal muscle disorders. A combination of computational and biophysical methods is applied in order to understand the mechanism creatine kinase uses to change its shape in response to the binding of a substrate. The study focuses on multiple sequence alignment of the amino acid residues from a large and diverse dataset of creatine kinases from a variety of organisms.
The analysis of the variation of these amino acids at each position in the enzyme is then used to identify critical residues for function. Additionally, this result further suggests the residues which are highly conserved as well as highly mutatable.