Molecular modeling applications in protein biochemistry: From functional assignment to ligand recognition

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Before becoming an established research field, molecular modeling (or computational chemistry) was forged by last century developments in chemistry and physics, including the introduction of quantum mechanics. In its heart lie theoretical and empirical concepts, which implemented in computer programs, are employed to analyze or simulate the behavior of molecules in all aggregation states of matter. At one time, however, molecular modeling techniques could only be applied to small chemical systems in vacuum. Today, advances in computational power have enabled the study of increasingly complex systems, such as biological molecules. Along with new computers came new software that no more requires experts extremely experienced in using tools that were for the most part difficult to understand and apply. Molecular modeling has now been successfully applied in many areas of protein biochemistry, from function assignment to the study of ligand recognition. For instance, inspection of protein 3D structures can be of much help in assigning the function of a newly discovered gene, in designing site-directed mutagenesis experiments and in the guidance of synthetic efforts to obtain novel ligands. This talk is divided in three parts. First, developments in the molecular modeling field that enabled its application to biological systems are rapidly summarized. Next, the scope of molecular modeling applications of interest to the biochemist is presented. Finally, our experience (Biochemistry of Proteins and Peptides Laboratory, DBBM, IOC-FIOCRUZ) is reported: (i) function assignment to a new poly-A binding protein from *Leishmania amazonensis*; (ii) substrate specificity of an aspartil hemoglobinase from *Schistosoma mansoni*; (iii) small-inhibitor recognition and (iv) chromatographic behavior of snake venom thrombin-like enzymes; and (v) the Na^+ binding channel of human coagulation serine proteases.