Structure Prediction In Computational Chemistry, Biology, and Immunology: Protein Folding and Peptide Docking

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A significant effort has been expended in the last five decades toward theoretical and algorithmic studies in *Computational Chemistry, Biology and Immunology*. In the last decade, the area of *Global Optimization* has received a lot of attention from a variety of disciplines including Chemical Engineering, and this surge of interest is attributed to three main reasons. First, a large number of process engineering, computational chemistry, biology and medicine problems are indeed global optimization problems. Second, the existing local nonlinear optimization approaches may either fail to obtain even a feasible solution or are trapped to a local optimum solution. Third, the global optimum solution may have a very different physical interpretation.

This presentation contains three parts. In Part I, we will discuss briefly our recent advances in *Deterministic Global Optimization*. The key theoretical concepts of the difference of convex functions method, denoted as α**BB**, will be presented. The αBB can address general continuous twice-differentiable problems that arise in computational chemistry, biology, and a variety of engineering and applied science problems. The αBB (i) offers theoretical guarantee of attaining an ϵ-global optimum solution in a finite number of iterations, (ii) provides valid lower and upper bounds on the global solution, and (iii) identifies local optima close to the global minimum (e.g., low energy conformations of proteins).

In Part II, we will discuss our advances in the *Protein Folding* problem.

A molecular modeling at the atomistic level via ECEPP/3 is employed for the calculation of the total potential energy. This involves the summation of the electrostatic, nonbonded, hydrogen bonding, torsional and cystine-loop contributions which are expressed in terms of the dihedral angles. The interactions with the solvent are also calculated and incorporated in the overall objective function. Two models are considered for the evaluation of the solvation effects: (a) the MSEED solvation model which is based on the solvent-accessible surface areas, and (b) the RRIGS model which is based on solvent accessible volume evaluation. The resulting objective is a highly nonconvex function that exhibits a large number of local minima. The application of the global optimization method αBB to several oligopeptides including met-enkephalin, leu-enkephalin, Ac-Ala$_4$-Pro-NHMe and decaglycine will be discussed.

In Part III, we will discuss our advances in the *Peptide Docking* problem. The determination of protein's native structure is of great importance in the peptide docking problem in order to identify the structure of the binding peptide that characterize the binding affinity of the protein molecule. Human leucocyte antigens (HLA) are cell surface molecules that form complexes with self and non-self peptides. The HLA-peptide complex is recognized by the T-cell receptor and initiates antigen specific immune responses. To quantitatively determine the binding specificity of a class II HLA molecule interacting with peptides, a novel decomposition approach is proposed that takes advantage of the topography of HLA binding grove, and examines the interactions of the bound peptide with the five different pockets. In this problem the intra as well as the inter energetic interactions are considered in order to formulate the correct objective function that reveals the binding specificity of the pocket. The obtained theoretical results are also compared with experimental binding assays.