Prediction of Biomolecular Induced-fit Flexibility Through Static Modes

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We present a new competitive approach for the treatment of biomolecular flexibility to provide an alternative to the limitations of current methodologies such as molecular dynamics and normal mode analysis. This method, called Static Mode method, is based on the "induced-fit" concept and is aimed at mapping the intrinsic deformations of a biomolecule subject to any external excitations: direct mono or multi-site contact, electrical etc... The algorithm allows obtaining a set of deformations, each one corresponding to a specific interaction on a specific molecular site, in terms of force constants contained in the energy model. Such a process can be used to explore the properties of single molecular intrinsic flexibility, as well as to predict molecular docking or molecule/surface interactions. From a modeling point of view, the interaction problem can be expressed in terms of interaction sites between the interacting entities, the molecular deformations being extracted from the pre-calculated Static Modes of each separated ones. The first applications of our method have focused on the intrinsic flexibility of biomolecules like nucleic acids and proteins (HIV-1 protease, dihydrofolate reductase). We indicate how this new methodology can be pertinent to address some issues of bio/non bio interactions.