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Accurate binding site models can be derived from low quality PDB files using an empirical geometry based force field

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Abstract

A new geometry force field based on atomic resolution regions PDB structures was recently published [1]. The new force field has now been tested in many examples not included in the original study. It is very successful in preserving geometries and computed energies in packed small molecule crystals and in atomic resolution regions of PDB structures. When applied to low quality PDB structures the force field causes small movements of those atoms with high energy features and anomalous geometries. This results in structures with energies and geometries similar to those found at high resolution. In the present work the force field was applied to binding site models selected from the entire resolution range of the PDB. A binding site model consists of a ligand and residues in close contact. Binding site models are selected if all atoms a reported, have unique coordinates, have Boltzmann factors less than 80 A^2 and do not have non-bonded clashes. These criteria are clear and easily applied and thousands of models satisfying these criteria have been found. Application of the force field to these models produces optimized models with similar energy and geometry profiles to those found in high resolution X-ray models. This process has provided a large set of consistent binding site models. The set contains many series of models where a unique binding site (100% sequence homology) is complexed with a variety ligands. This data is ideal for a broad empirical study of the effects of ligands on binding site flexibility. Tools for using this data base for exploring binding site flexibility are given in a poster at meeting[2].

Biography

Colin McMartin owns a computational soft-ware company, FLO/QXP, which specializes in force field development/application. A recent publication based on atomic resolution protein crystal geometries describes a new geometry force field as well as methods for developing complete models with explicit water and hydrogen bond networks suitable for structure based design.