An automated active site identification, docking and scoring protocol for protein targets Based on physico-chemical descriptors (AADS)

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Abstract

We report here a robust automated drug active site detection, docking and scoring protocol for proteins with known structures. The active site finder identifies all cavities in a protein and scores them based on the physicochemical properties of functional groups lining the cavities in the protein. The accuracy realized on 620 proteins with sizes ranging from 100 to 600 amino acids with known drug active sites is 100% when the top ten cavity points are considered. These top ten cavity points identified are then submitted for an automated docking of an input ligand/candidate molecule. The docking protocol uses an all atom energy based Monte Carlo method. Eight low energy docked structures corresponding to different locations and orientations of the candidate molecule are stored at each cavity point giving 80 docked structures overall which are then ranked using an effective free energy function and top five structures are selected. The predicted structure and energetics of the complexes agree quite well with experiment when tested on a dataset of 170 protein-ligand complexes with known structures and binding affinities. The AADS methodology is implemented on an 80 processor cluster and presented as a freely accessible, easy to use tool at http://www.scfbio-iitd.res.in/dock/ActiveSite_new.jsp.