Abstract

DNA has been an attractive target for anticancer, antitumor agents and antibiotics. While the growing number of DNA-drug complexes in structural repositories are yielding molecular insights on DNA-drug recognition principles, identification of distinct sequence-specific electrostatic potentials in the minor and major grooves of DNA has aroused keen interest in designing/identifying molecules which can bind to DNA in a sequence-specific manner. Computational protocols for examining such interactions by means of docking small molecules in the grooves of DNA are accessible. However, with the present compute-intensive docking and scoring protocols, it is nearly impossible to scan millions of molecules for DNA targeted drug discovery. This makes it necessary to develop a rapid screening protocol for scanning millions of molecules to identify potential binders to any DNA sequence of choice. RASDD (**RA**pid **S**creening of **D**NA-**D**rug) is one such utility which utilizes physicochemical properties associated with DNA as well as groove binders to rapidly scan a large library of molecules. The methodology is developed using 30 DNA-drug complexes (R = 0.85) and, when tested on 18 DNA-drug complexes, yielded a correlation (R) of 0.83 between experimental and predicted binding free energies. With RASDD protocol, it is possible to scan a million compounds against a DNA sequence of interest (AT-rich) in ~18 sec.! RASDD is freely accessible at http://www.scfbio-iitd.res.in/software/drugdesign/rasdd.jsp.