A molecular-modeling toolbox aimed at bridging the gap between medicinal chemistry and computational sciences

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 1555243
Author(s) Eid, Sameh; Zalewski, Adam; Smiesko, Martin; Ernst, Beat; Vedani, Angelo
Author(s) at UniBasel Vedani, Angelo ; Smiesko, Martin ; Ernst, Beat ;
Year 2013
Title A molecular-modeling toolbox aimed at bridging the gap between medicinal chemistry and computational sciences
Journal International Journal of Molecular Sciences
Volume 14
Number 1
Pages / **Article-Number** 684-700
Keywords computer-aided drug discovery, structure-based design, multi-dimensional QSAR, molecular dynamics, single-click molecular modeling
In the current era of high-throughput drug discovery and development, molecular modeling has become an indispensable tool for identifying, optimizing and prioritizing small-molecule drug candidates. The required background in computational chemistry and the knowledge of how to handle the complex underlying protocols, however, might keep medicinal chemists from routinely using in silico technologies. Our objective is to encourage those researchers to exploit existing modeling technologies more frequently through easy-to-use graphical user interfaces. In this account, we present two innovative tools (which we are prepared to share with academic institutions) facilitating computational tasks commonly utilized in drug discovery and development: (1) the VirtualDesignLab estimates the binding affinity of small molecules by simulating and quantifying their binding to the three-dimensional structure of a target protein; and (2) the MD Client launches molecular dynamics simulations aimed at exploring the time-dependent stability of ligand-protein complexes and provides residue-based interaction energies. This allows medicinal chemists to identify sites of potential improvement in their candidate molecule. As a case study, we present the application of our tools towards the design of novel antagonists for the FimH adhesin.
Publisher Molecular Diversity Preservation International
ISSN/ISBN 1661-6596 ; 1422-0067
edoc-URL http://edoc.unibas.ch/dok/A6083580
Full Text on edoc Available;
Digital Object Identifier DOI 10.3390/ijms14010684
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/23344039
ISI-Number WOS:000314048800043
Document type (ISI) Article