Multi-Objective De Novo Drug Design Using A Novel Evolutionary Algorithm

Christos A Nicolaou and Constantinos S Pattichis

Computer Science Department, University of Cyprus
75 Kallipoleos Str., P.O.Box.20537, CY-1678 Nicosia, CYPRUS
cnicolaou@cs.ucy.ac.cy

Drug discovery and development is a complex, lengthy process and failure of a candidate molecule can occur as a result of a combination of reasons, such as poor pharmacokinetics, lack of efficacy, or toxicity. Drugs compromise the numerous, sometimes competing objectives so that the benefits to patients outweigh potential drawbacks and risks [1]. Computer-aided drug design, widely known as de novo design, involves searching an immense space of feasible, drug-like molecules to select those with the highest chances of becoming drugs [2]. Traditionally, de novo design has focused on a single objective and ignored the presence of the multiple objectives required for drug-like behavior. Recently, methods have appeared in the literature that attempt to design molecules that satisfy multiple predefined objectives [3]. In this presentation we briefly review these methods and then describe a new multi-objective optimization algorithm that combines evolutionary techniques with graph-theory to directly manipulate molecular graphs and design molecules satisfying one or more objectives. We conclude with the presentation of the results produced by the application of our method to the *in silico* design of molecules satisfying one and two objectives.

References:

1. Nicolaou CA, Brown N, Pattichis CS: **Molecular optimization using computational multi-objective methods.** Curr Opin Drug Discov Devel. (2007) **10**(3):316-324.
2. Schneider G, Fechner U: **Computer-based d*e novo d*esign of druglike molecules.** *Nat Rev Drug Discov* (2005) **4**(8):649-663.
3. Brown N, McKay B, Gilardoni F, Gasteiger J: **A graph-based genetic algorithm and its application to the multiobjective evolution of median molecules.** *J Chem Inf Comput Sci* (2004) **44**(3):1079-1087.