Molecular Optimization Using Multi-Objective Computational Methods: A Survey

Christos A. Nicolaou, Constantinos K. Pattichis
University Of Cyprus, Medical Informatics Lab, Department of Computer Science
75 Kallipoleos Str., P.O.Box.20537, CY-1678 Nicosia, CYPRUS
Email: csp4cn1@cs.ucy.ac.cy

Improving the profile of a molecule for the purposes of the drug discovery process requires the simultaneous optimization of numerous, often competing objectives. Traditionally, standard chemoinformatics methods ignored the problem and focused on the sequential optimization of each single biological or chemical property. This approach, known as Single Objective OPtimization (SOOP), strives to discover the single optimal solution. Implicitly, SOOP-based methods assume that the optimal solution for any objective will also be the optimum for the other objectives. However, when the objectives are conflicting, as is often the case in molecular optimization problems, the individual optima corresponding to the numerous objectives may vary substantially. Multi-Objective OPtimization (MOOP) methods introduce a new notion for optimality founded on compromises and trade-offs among the various objectives. Their aim is to discover a set of satisfactory trade-offs and through them the global optimal solution by optimizing simultaneously numerous dependent properties.

MOOP methods have only recently been introduced to the field of chemoinformatics. In this paper we first present a brief introduction to issues related to multi-objective optimization[1] and then survey the application of MOO methods such as MoQSAR[2] and Pump-RP[3] to the field of chemoinformatics. We also present the current work performed in our lab in the MOOP field.

1. Yann, C.; Siarry, P. Multiobjective optimization : principles and case studies. Berlin, New York: Springer, c2004, 2003.
2. Nicolotti, O.; Gillet, V. J.; Fleming, P. J.; Green, D. V. S. Multiobjective optimization in quantitative structure-activity relationships: Deriving accurate and interpretable QSARs. *J. Med. Chem.* 2002, *45*, 5069-5080.
3. Stockfisch, T. P. Partially Unified Multiple Property Recursive Partitioning (PUMP-RP): A New Method for Predicting and Understanding Drug Selectivity. *J. Chem. Inf. Comput. Sci.*; 2003; *43*(5); 1608-1613.