ChemModeling

Areas of Expertise and Capabilities

Compound Collection Analysis and Augmentation

We have found compound collections often contain structures that have been misentered, are present in several forms or are highly redundant with other compounds in the collection. ChemModeling has significant experience cleaning up structure representations and selecting diverse, representative subsets- which can considerably reduce the cost of compound screening. We can also augment an existing collection with compounds from selected vendors which are unique with respect to the existing collection and optionally are selected for their similarity to specific drug targets. Our capabilities in this area include:

- Structure normalization
- Property calculation and analysis
- Subset selection
  - Novel distance based clustering methods
  - Diverse/Representative
  - Targeted class
- Scaffold based
- 2D and 3D similarity
- Augmentation with additional chemical entities
  - Normalization of vendor databases
  - Unique to existing collection
  - Prioritize by other factors such as preferred vendor

Library Design

ChemModeling researchers have decades of experience designing general screening and targeted libraries. A significant differentiator in our approach is that we have a strong commitment to involve medicinal chemistry expertise at every step of the design process. For targeted libraries we can work with chemists to propose novel scaffolds or access an internal ideas database. Designed libraries thus will only contain relevant and synthetically accessible compounds. In conjunction with our collaborators, the designed compounds can be synthesized. ChemModeling can thus provide additional design input in the case of synthetic problems, ensuring the delivered compounds remain desirable. Our capabilities in this area include:

- Virtual Libraries are designed in conjunction with medicinal chemists
  - Reasonable synthetic routes
  - Appropriate reagents for chemistry involved
- Optimized for lead-like or drug-like properties
- Optimized for diversity or specific target
  - Unique with respect to existing collections
- Multi-objective library design
  - Physiochemical properties, matrix size and density
  - Incorporate docking scores into design
  - Incorporate 2D or 3D similarity into design
  - Include other factors such as cost and synthetic feasibility

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Lead Generation

ChemModeling researchers have a wide range of tools for generating leads and developing novel chemical entities from existing leads. Virtual screening can be employed using virtual docking methods, when a crystal structure is available, or using a wide range of similarity-based methods. Pharmacophore models can be built from crystal structures or a set of active compounds. Methods employed are typically quite fast and can be used on large collections. For greater speed, virtual libraries can be screened without the need to enumerate individual products. The advantage of having access to a wide range of tools is that ChemModeling will validate the methods for the particular application, ensuring that the results are meaningful. Often different methods turn out to be most amenable to specific problems. Our capabilities in this area include:

- Idea generation tools
- Structure based virtual screening
  - Novel methods incorporating intelligent scaffold placement
- Ligand based virtual screening
  - 2D fingerprint and substructure methods
  - 3D shape and pharmacophore methods
  - Incorporate CoMFA models into virtual screening
  - Flexible scoring function that captures custom filtering requirements
- Pharmacophore generation and searching
  - Intelligent pharmacophore generation from crystal structure
  - Pharmacophore based on ligand alignment
  - 3D flexible searching
- Screening of virtual libraries or existing compound collections

Lead Optimization

In addition to the tools used for lead generation, ChemModeling has experience with a number of additional tools for optimizing an existing lead. Techniques include hit to lead analysis for determining which hits from an HTS screen are true positives to follow-up, model building to identify features in the lead molecule which should be modified to improve potency or ADMET properties, and profiling a set of active molecules to identify key substructures or optimal physical properties. Our capabilities in this area include:

- QSAR modeling and activity prediction
- R-group analysis
- Hierarchical fragment analysis to detect privileged substructures
- Docking and scoring
- Ligand overlay and scoring
- Physical property profiling

ChemModeling is a computational chemistry services company providing in-depth technical knowledge and expert tools in support of the pharmaceutical, biotechnology and related industries.

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