TECHNOLOGY

SILCS: Site Identification by Ligand Competitive Saturation. Method for binding site identification by molecular dynamics simulation

OVERVIEW

The present invention is directed to a method of computational chemistry for identifying binding sites by molecular dynamics simulations using ligand competitive saturation. Fragment-based drug discovery relies on a simple premise: identify small molecule fragments that bind to a target region of a large molecule and then evolve or link the small molecule fragments to create a larger high-affinity molecule. In particular, the method overcomes the problem of small nonpolar molecule aggregation to allow competitive saturation in an aqueous solution at physiological conditions. More particularly, the method, when used in a two-tier approach, may determine which one of several multiple fragment molecules has a highest probability of improving binding to a surface region of a large molecule that is proximate to a bound ligand, in order to produce an optimized lead compound for drug discovery.

- Global Industry Analysts, Inc predicts that the Drug discovery Technologies market will exceed $57 Billion by 2012. This estimate includes areas other than CADD such as bioanalytical instruments, contract research organization services and pharmacogenomics.
- SGX Pharmaceuticals, a drug discovery company, was acquired by Lilly for $65M.
- Discovery Studio (Accelrys $80M/yr total revenue Discovery Studio is major source).
- Sybyl-S1.0 (Tripos-private company sales unknown).
- Gaussian 09 (Gaussian Academic site license $6000, Commercial site license $35,000).

https://www.youtube.com/watch?v=x27lnGC-U5E#t=254

APPLICATIONS

Small Molecule Drug Discovery and Design

ADVANTAGES

-Using this data, medicinal chemists can design better therapeutics in shorter amounts of time. Pharmaceutical companies calculate the value of shorter development time by determining the net present value of income from drug sales at the end of the market exclusivity period for the same amount of time the development period was shortened, typically in the hundreds of millions of dollars.
-Current methods do not take certain properties such as protein flexibility or an aqueous environment into consideration when designing drugs for binding to targets. This method is not only uses these properties in its model, but provides data for the entire surface of the target molecule not just a particular binding pocket.
-When used in a two-tier approach, may determine which one of several multiple fragment molecules has a highest probability of improving binding to a surface region of a large molecule that is proximate to a bound ligand, in order to produce an optimized lead compound for drug discovery.

STAGE OF DEVELOPMENT

-Currently used in Computer Aided Drug Design at the University of Maryland, School of Pharmacy.
-Compounds designed using SILCS will be synthesized and compared with compounds identified using other methods in ligand affinity assays.

R&D REQUIRED

Further proof of concept.

LICENSING POTENTIAL

In addition to exploring traditional licensing strategies, the University of Maryland, Baltimore is actively looking for entrepreneurs for venture creation.

CONTACT INFO

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Additional Information

INSTITUTION

University of Maryland, Baltimore

PATENT STATUS

Patent application pending in the U.S., Canada, and Europe.

CATEGORIES

- Research Tools, Antibodies, & Reagents
- Software + Algorithm

INVESTIGATOR(S)

Alex MacKerell Jr.
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EXTERNAL RESOURCES

- Computational fragment-based binding site identification by ligand competitive saturation.
- SILCS Drug Design Method

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