Directed Protein Docking Algorithm

Computational means to drive one protein to bind to another in a structurally pre-defined manner

Even though the importance of developing new therapeutics has continued to increase, the methods of drug discovery have not fundamentally changed for 20 years. Most companies look for random matches with drug targets by screening vast numbers of compounds. If a match is found, medicinal chemists are engaged to find a lead molecule with suitable properties. This process is often costly and time-consuming.

Dr. John J. Love of San Diego State University has developed a technology using computational means to design, engineer and mutate proteins so they bind, or dock, to other proteins in a structurally specific and precise manner.

This technology will enable scientists to target proteins (e.g., engineered antibodies) that bind exact regions of other proteins.

The algorithm used treats the proteins as rigid bodies and rotates and translates their atomic coordinates within the bounds of the pre-defined orientation. Concurrently, protein/protein surface complementarity (i.e., goodness of fit) is rigorously assessed as a function of translational and rotational position. This is a computationally intensive process that has been rendered tractable with the incorporation of the Fourier correlation theorem. The atomic coordinates that result in the highest score (i.e., exhibit the best intermolecular surface complementarity) are then modified to further improve the fit.

Follow-on technology allows the atomic coordinates of the docked proteins to be combined and treated as one protein. Protein design algorithms are used to computationally mutate and repack the interfacial side chains in a manner analogous to the core of a well-folded protein.

Advantages Over Existing Technology

- May reduce research costs
- Identifies the structure of antibodies
- Improves lead molecule generation
- Highly selective for complementarity

Applications

- New drug discovery
- Improves specificity of current drugs

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