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Patch-Surfer 2.0: Efficient and Accurate Algorithm for Comparing Ligand-Binding Sites of Proteins

A novel software tool uses a localized patch-based analysis of enzyme binding pockets to predict optimal ligand-binding molecules, offering improved results for pharmaceuticals development and ligand-protein interaction modeling.

Researchers at Purdue have developed a software tool called "Patch-Surfer 2.0" that can take an enzyme binding pocket as an input, and compares the queried binding pocket to known ligand binding pockets in its database. From there, the software predicts ligands that could bind strongly to the input binding pocket. Other binding pocket-ligand modeling software's primarily identify possible ligands for a given binding pocket by analyzing the whole protein structure, and determining what ligands could fit in the binding pocket. These other approaches have difficulty with proteins that have very different global structures but bind to the same ligand molecules.

The researchers devised an updated protein-ligand binding interaction system, which avoids this issue and improves on the previous version of the program. To get around the issue of being unable to predict different structured molecules binding to the same ligand, the researchers took a more local approach, and split up the binding pockets into a set of small, local "patches" which are subsequently evaluated for their geometric shape, surface electrostatic potential, hydrophobicity, and concavity. These patches are then compared to a database of patches with known ligand binding geometries to generate a ranked list of ligands that would bind optimally to the queried binding pocket.

Technology Validation:

The software's ability to predict possible ligands that could bind to a queried binding pocket was verified by comparing its performance to other ligand-binding modeling software systems such as APoc and eF-Seek. Fifteen ligands were chosen, and the area-under-the-curve (AUC) was calculated for each ligand, using each software. It was found that Patch-Surfer 2.0 showed

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a higher relative partial AUC than eF-Seek for all but one ligand, and Patch-Surfer 2.0 showed a higher AUC for 13 of the ligands as compared to the APoc software.

Advantages:

- Improved ligand searching ability

- Better results than similar programs

Applications:

- Pharmaceuticals development

- Modeling Ligand-Protein interactions

TRL: 6

Intellectual Property:

N/A, N/A, N/A

Keywords: Patch-Surfer 2.0, enzyme binding pocket, ligand prediction, protein-ligand binding, local patch approach, geometric shape evaluation, surface electrostatic potential, hydrophobicity, concavity, pharmaceuticals development, ligand-protein interactions, binding pocket comparison