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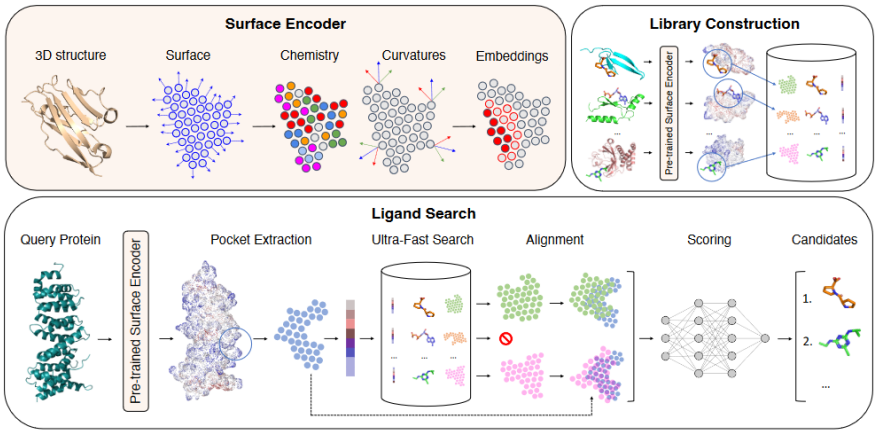
Licensing Opportunity

TTO – Technology Transfer Office

Decoding surface fingerprints for protein-ligand interactions



Surface encoding workflow of dMaSIF (top left), library construction (top right), and ligand / search pipeline (bottom)

Ref. Nr

6.2392

Keywords

deep learning
binding affinity predictor
ligand discovery
ligand design
druggable small molecule

Intellectual Property

US 18/621,39
priority 30.03.2023

Publications

https://doi.org/10.1101/2022.04.26.489341

Date 09/10/2024

Description

Computational workflow for high-throughput fragment-based screening and binding affinity prediction, using state of the art protein surface embedding framework (dMaSIF). Ligand and fragment searching methodology based on geometric deep learning applied to surface representations of binding pockets and binding affinity prediction model. Performs on par with the state of the art and outperforms a recent deep learning-based method.

Identified fragments can be further combined into novel ligands. Using the structural data, our ligand discovery pipeline learns the signatures of interactions between surface patches and small pharmacophores.

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Advantages

- docking and screening of compounds and targets for which co-crystallised structures are not available
- method enabling the screening without the costly step of first docking candidate molecules
- Facilitated design of ligands based on the target's surface information
- The binding affinity predictor is capable of predicting the affinity of a given protein-ligand pair, requiring only limited information about the ligand pose
- The framework may significantly reduce the experimental screening load and ultimately reveal novel chemical compounds for targeting challenging proteins chemical and geometric features of the target pocket

Applications

- design of ligands based on the target's surface information
- designing / identifying novel chemical compounds for targeting challenging proteins
- finding small molecules that engage "hard-to-drug" protein targets