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CSM-lig: small-molecule affinity

CSM-lig: a web server for assessing and comparing protein-small molecule affinities

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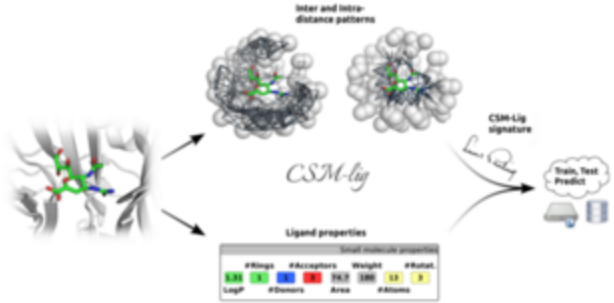
Abstract

Interactions between small molecules and proteins mediate many essential biological processes, and are central in the development of new drugs. Accurately predicting binding affinities is a challenging and difficult task, and despite being regarded as poorly predictive, scoring functions play an important role in understanding molecular recognition and in the analysis of molecular docking results.

Here we present CSM-Lig, a web server tailored to predict the binding affinity of a protein--small molecule complex based on structural signatures. CSM-Lig was first built and evaluated on the widely used 2007 and 2013 releases of PDBbind. For the two releases, CSM-lig achieved a Pearson's correlation coefficient of 0.82 and 0.86 on 10-fold cross validation. Over the PDBbind core set, a blind test of 195 diverse complexes with binding affinities ranging from millimolar to picomolar that has been used to benchmark different approaches, the models showed strong correlations of 0.75 and 0.80, outperforming well established scoring functions and predictors.

We believe CSM-Lig would be an invaluable tool for helping assess docking poses, the effects of multiple mutations, including insertions, deletions and alternative splicing events, in protein-small molecule affinity, unraveling important aspects that drive protein-compound recognition.



Available Resources

CSM-lig	Small-molecule binding affinity prediction
Related	Other resources

UNIVERSITY OF CAMBRIDGE

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Best viewed using Chrome on 1280x1024 resolution and above

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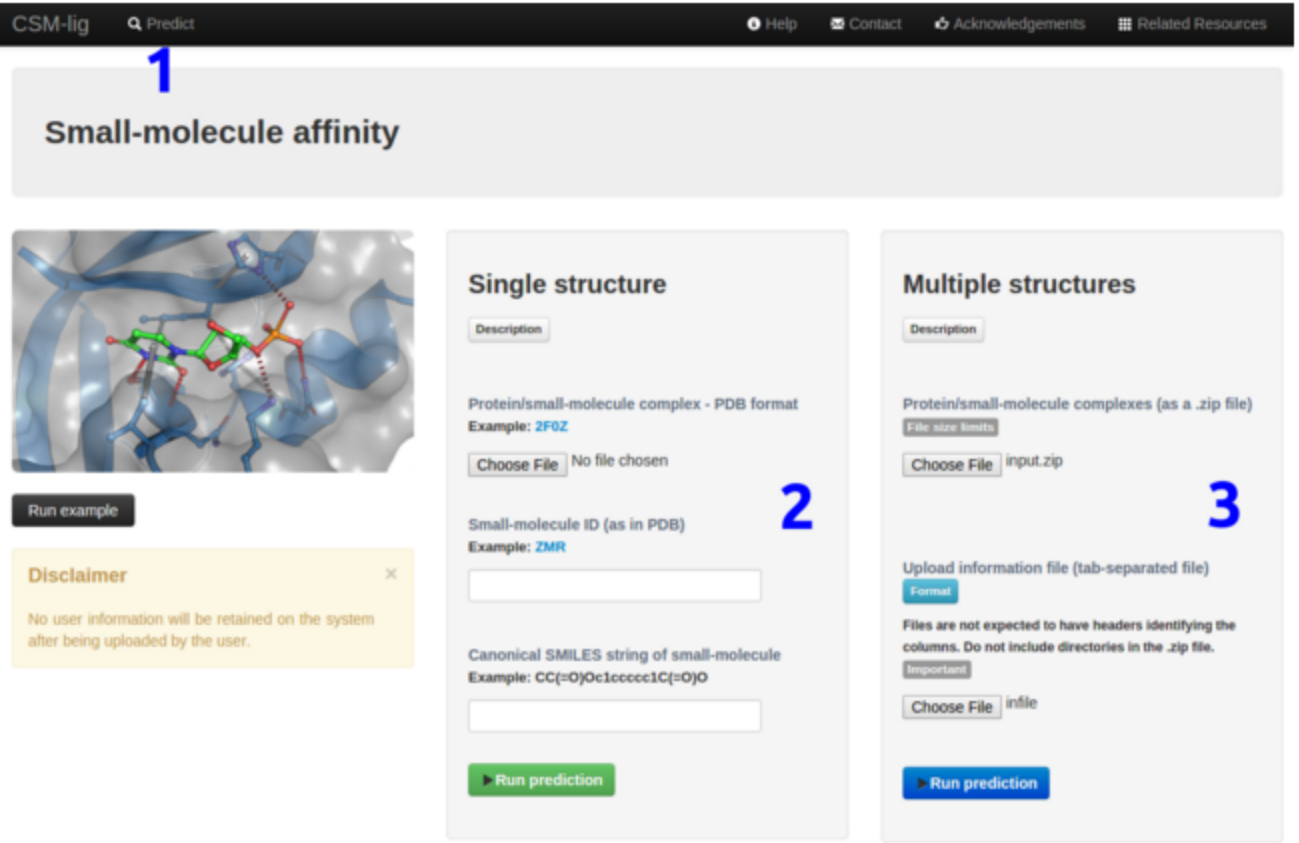
About CSM-lig

CSM-lig is a machine-learning method to predict affinities of small-molecules to proteins, which relies on distance/pharmacophore patterns encoded as graph-based signatures.

A user-friendly and freely accessible web interface was developed and allows users to submit either a single PDB structure of the protein-small molecule complex, or a compressed file with multiple structures, which could include different poses of the same complex, different ligands or multiple different proteins.

Submission page



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How to run a prediction

To run a prediction:

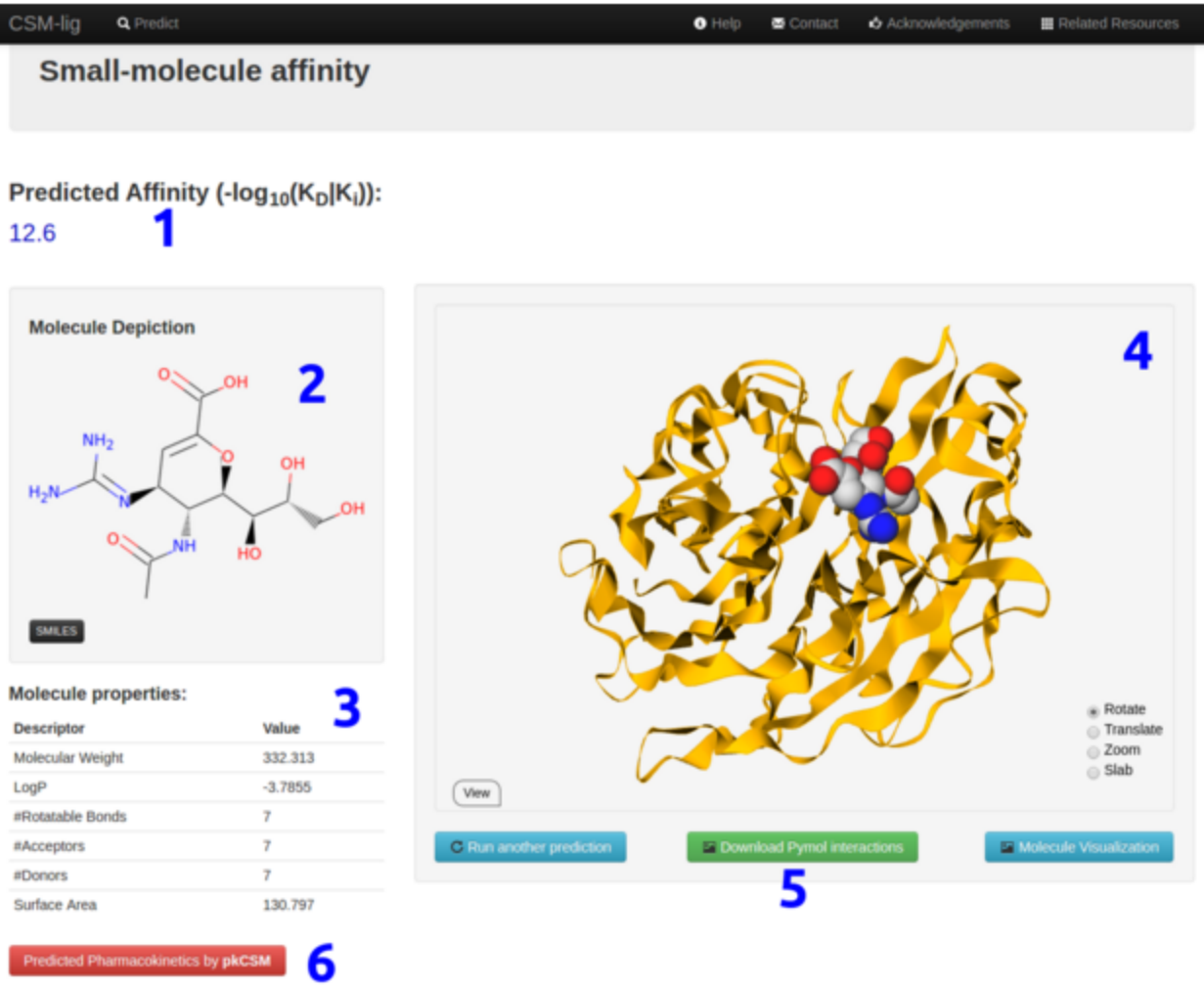
- Click on "Predict" **(1)** to open the submission page.
- Provide either:
  - A single PDB file and the small-molecule information (HET ID and SMILES string) **(2)** or
  - As input files, a compressed file with PDBs (.zip) and a tab-separated file with the molecule information (HET ID and SMILES string for each uploaded PDB)**(3)**.

Users are advised to use Canonical SMILES. Syntax non-compliant molecules or PDB files will be ignored.

Parsing Considerations

*** Water molecules** present in the uploaded PDB files are removed prior to calculation.
*** Cofactors, metals and ions** are also removed from the structure and are not considered in the structural signature calculations.

Results page



Results

For a **single molecule** prediction, your results can be displayed as follows:

- The affinity **prediction** will be shown in (1).
- A **depiction** of the small-molecule will be shown in (2). Make sure the depiction is what you are expecting for your molecule.
- A list of **molecule properties** will be calculated and shown in (3).
- An **interactive** molecular visualization of the uploaded complex will be shown in (4).
- Users have the option to download a **Pymol session file** for visualizing the ligand interactions in (5).
- There is also an option of calculating the **phamacokinetic and toxicity properties** of the ligand using the pkCSM server (6).

Results for **multiple molecules** will be shown in a tabular format, whithout molecule depiction, which can be downloaded as a tab-separated file.

Contact page

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Contact

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Get in touch

Have you come across a problem on the website or have any requests or suggestions? Please report it here!

Name

Email address

(optional)

Submit

Getting in touch

In case you experience any trouble using CSM-lig or have any suggestions or comments, please do not hesitate in contacting us either via e-mail or through the online form.