Welcome to CSDU

Protein-ligand docking 101 - running a simulation in GOLD

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advancing structural science

Learning outcomes for today

- Familiarity of proteins, ligands, and functional waters.
- Familiarity of what protein ligand docking is and why you might want to perform it.
- Familiarity with the GOLD interface and a step by step guide of the basic functionality.
- Where to get started with your docking simulation.
- How to run a standard protein-ligand dock with GOLD.

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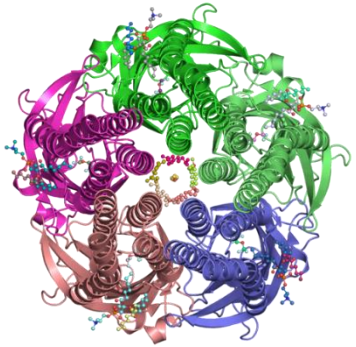
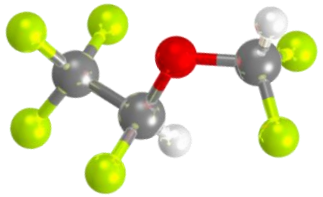
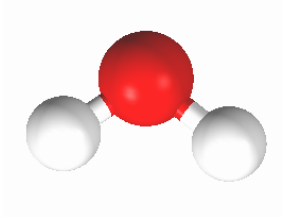
Proteins and ligands



Proteins are large biomolecules and macromolecules that comprise of one or more long chains of amino acids.



Ligands are small molecules that bind to the protein and can change the protein function.



Functional waters are found in the binding site of a protein and mediate the interactions between the ligand and the protein.

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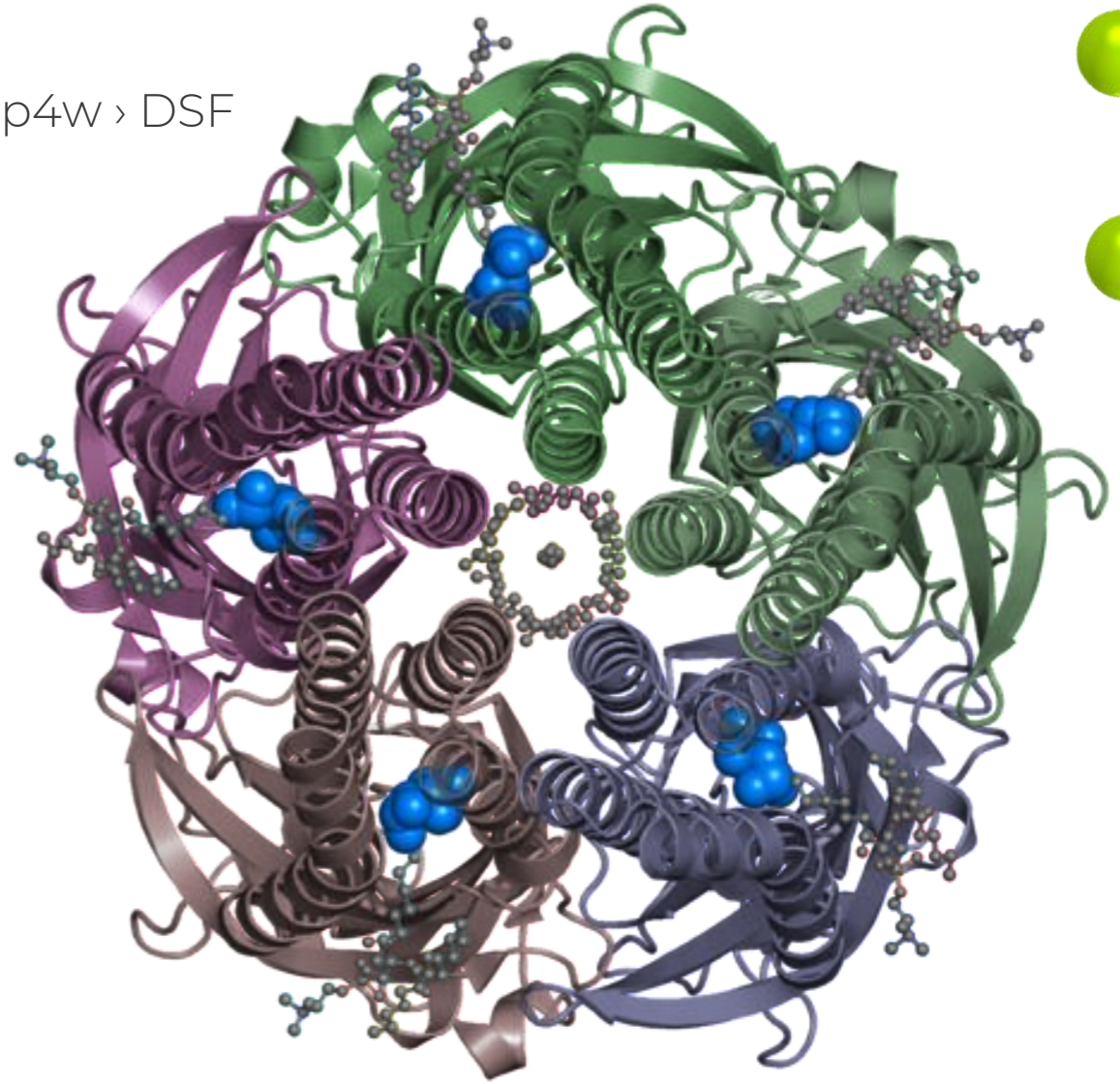
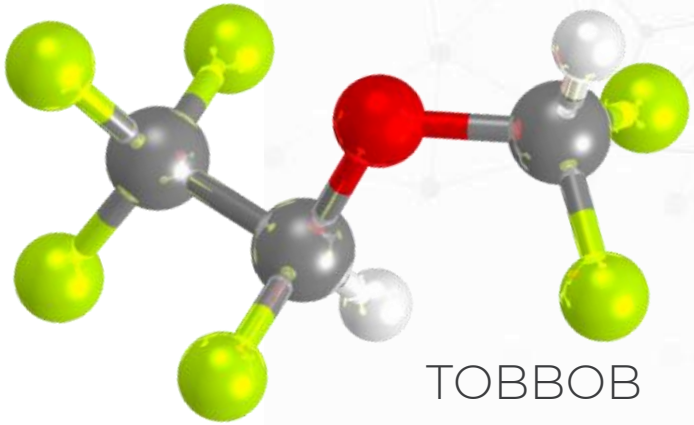
Connecting chemistry and biology

3p4w › DSF





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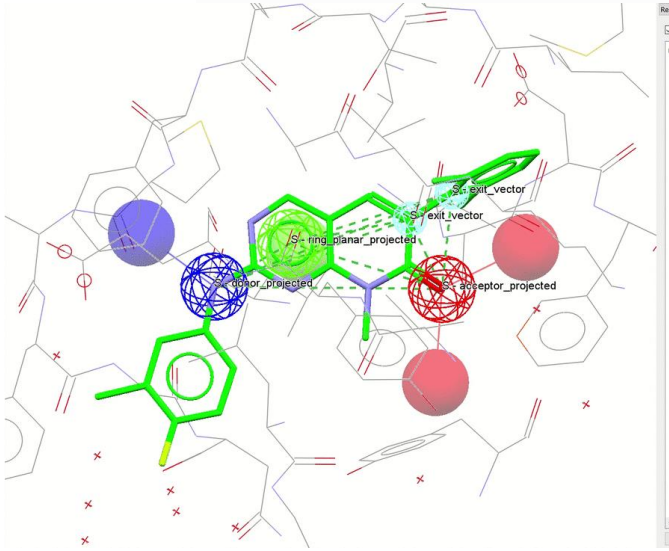

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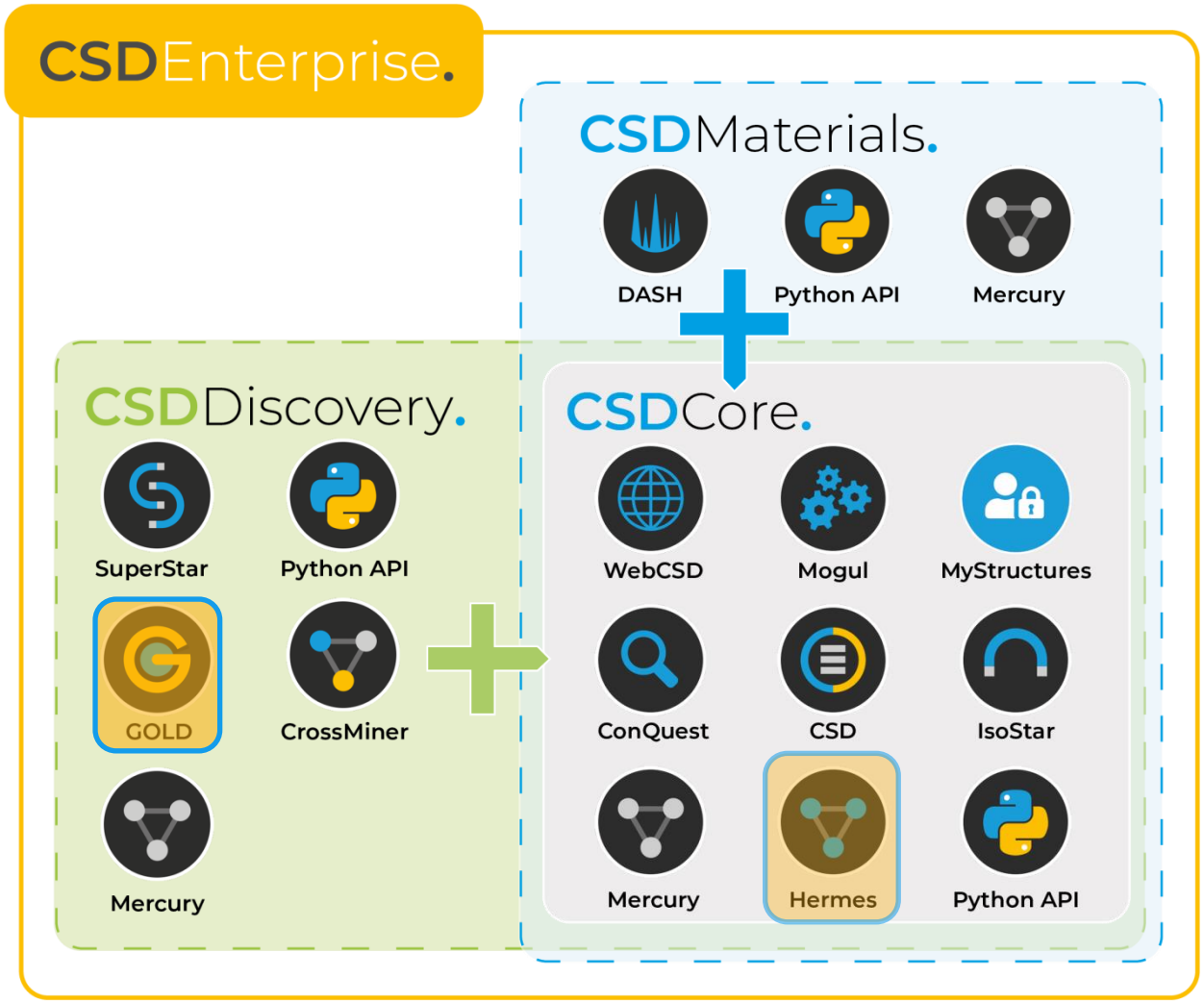
The CSD software



Professional Services

Research & Knowledge partnerships

CSDCommunity.

Mercury
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Educational
Access
MyStructures

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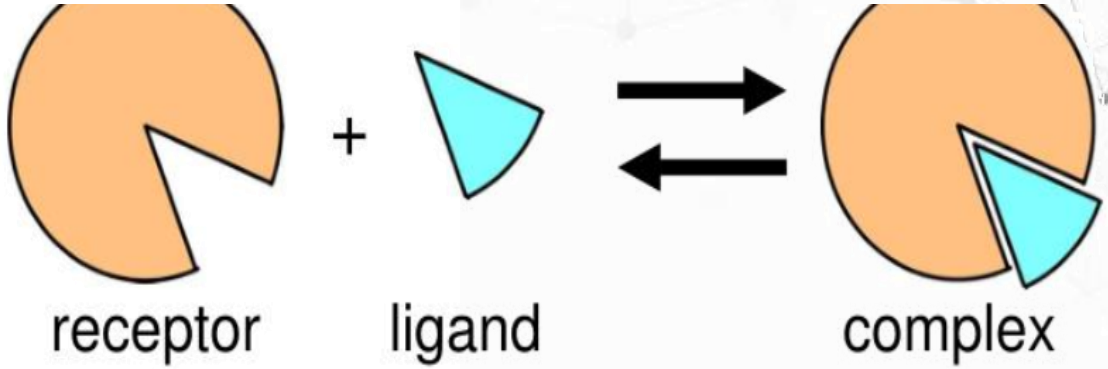
Docking



Docking studies are computational techniques for the exploitation of the possible binding modes of a substrate to a given receptor, enzyme or other binding site.

Glossary of Terms Used In Computational Drug Design, *Pure&Appl. Chem.*,Vol. 69, No. 5, pp. 1137-1152, 1997

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GOLD: Protein-Ligand Docking Software

- GOLD has proven success in virtual screening, lead optimisation, and identifying the correct binding mode of active molecules.

- Relied on by researchers in academia and industry worldwide.

- Reliable
- Flexible
- Configurable

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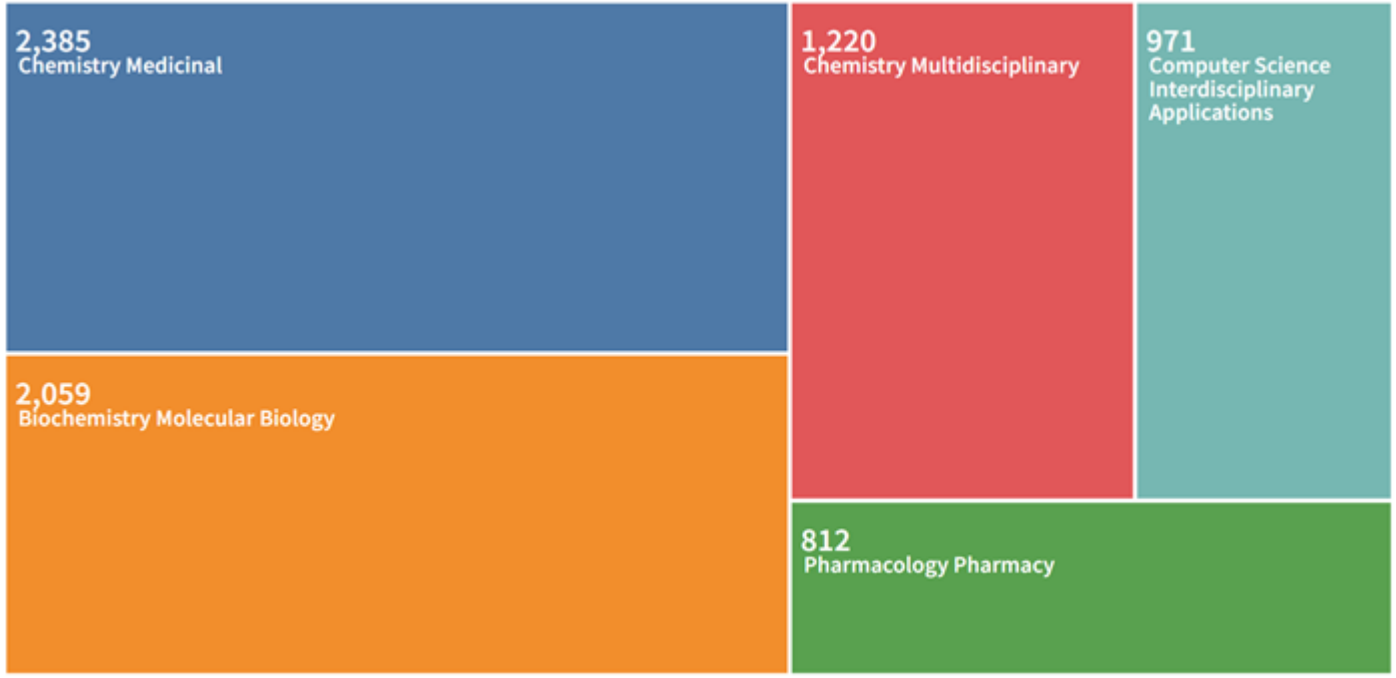
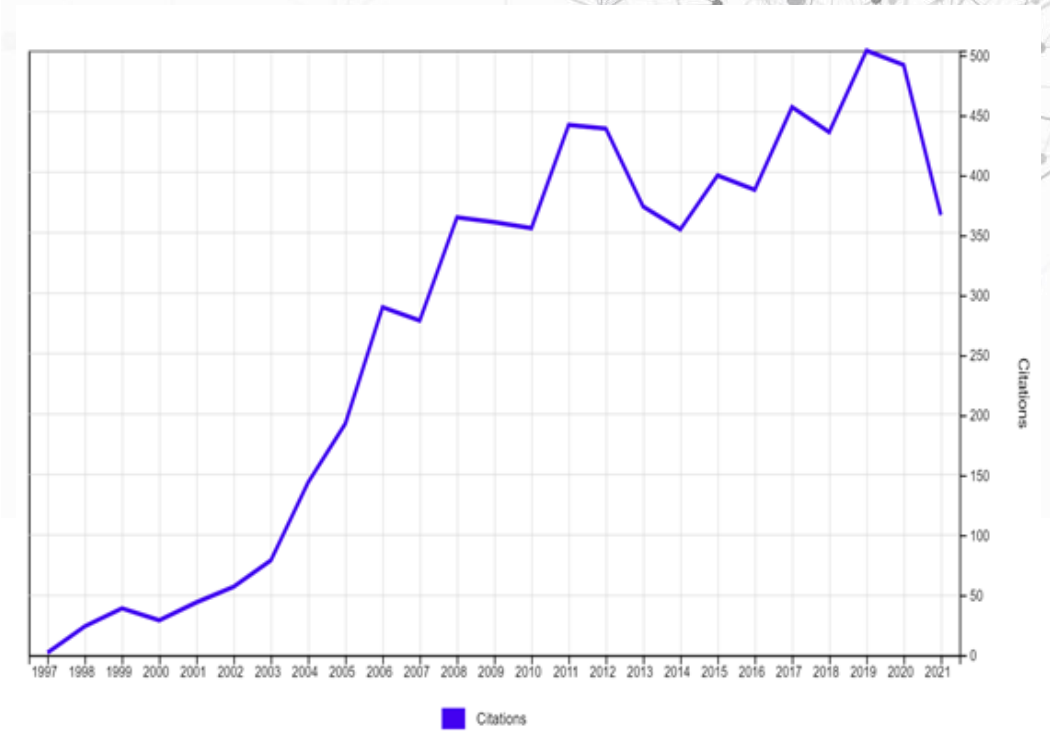
GOLD docking in research





Development and validation of a genetic algorithm for flexible docking, *J. Mol. Biol.*, Vol. 267, pp. 727-748., 1997. DOI: https://doi.org/10.1006/jmbi.1996.0897

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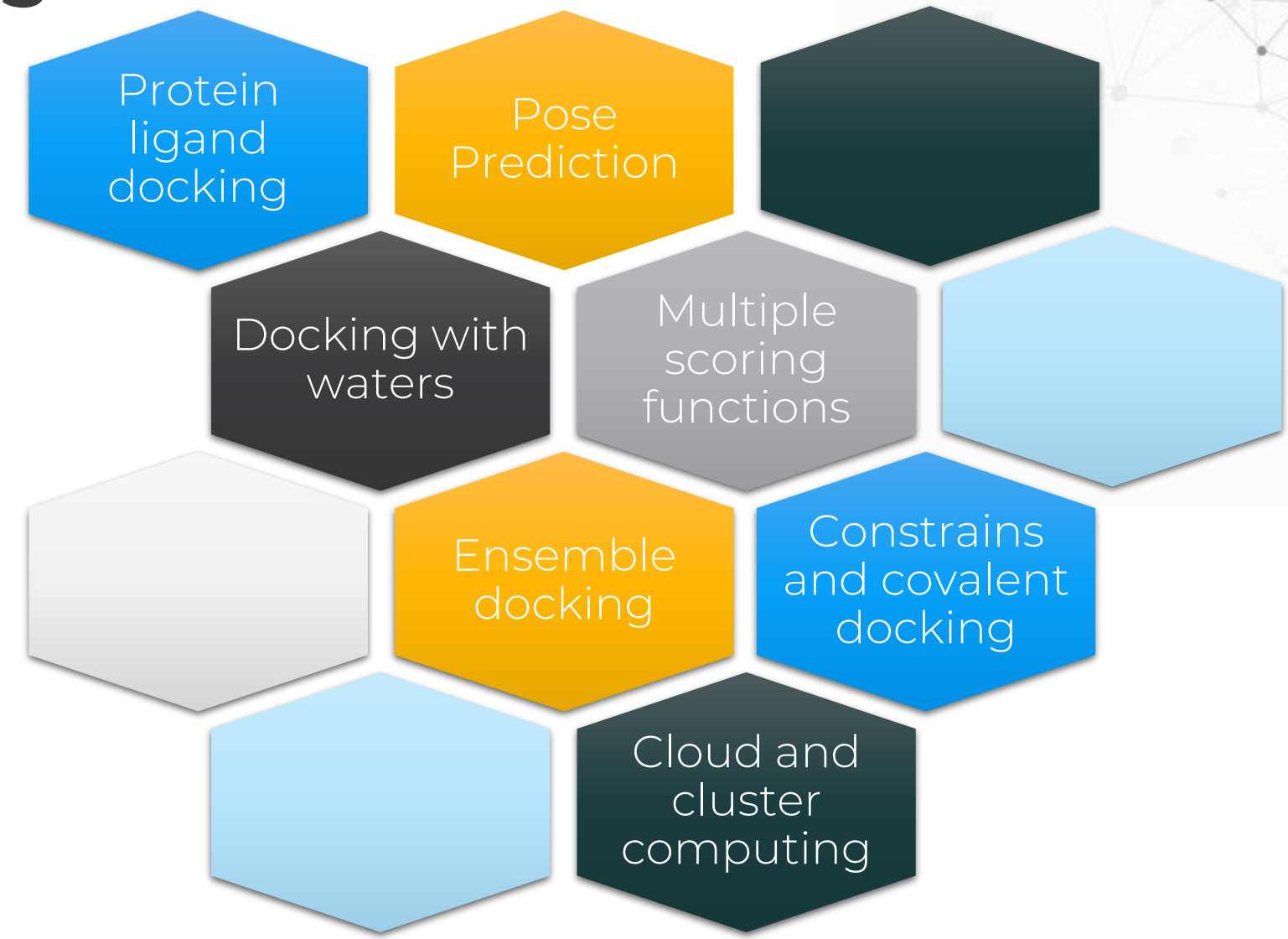
GOLD: The all in one molecular docking package



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What are we going to learn today?

- Protein-ligand docking of a Kinase inhibitor
  - We would learn how to…
    - Import a protein co-crystal from the Protein Data Bank (PDB).
    - Prepare the protein crystal structure for docking.
    - Perform molecular docking experiment in GOLD.
    - Analyse the results obtained from docking experiment.

Molecular Recognition of Receptor Sites Using a Genetic Algorithm with a Description of Desolvation, *J. Mol. Biol.*, Vol. 245, pp. 43-53, 1995.

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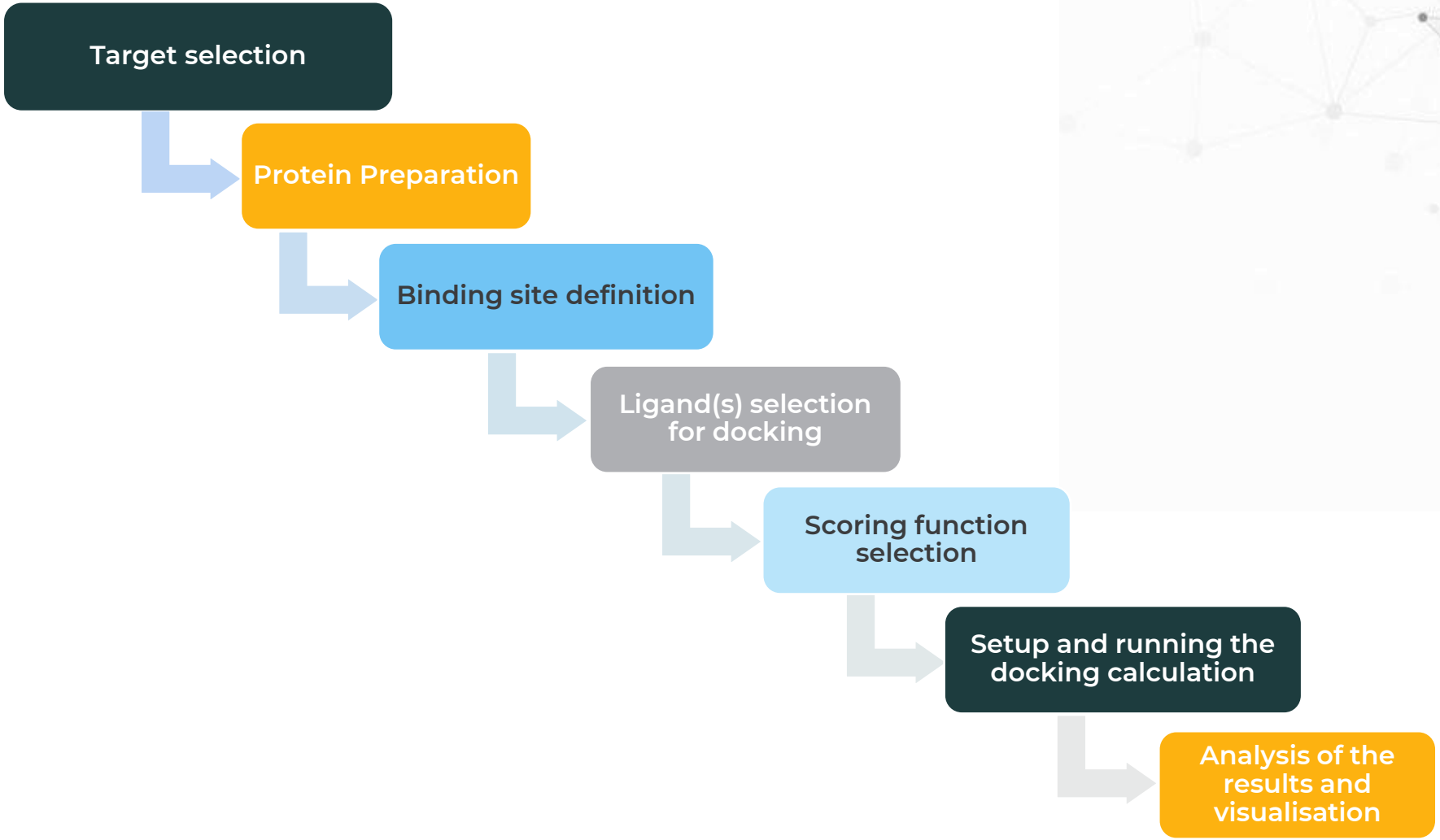
Steps in molecular docking



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Steps in molecular docking

Target selection

- Co-crystal structure of protein-ligand complex
- from PDB

Protein Preparation

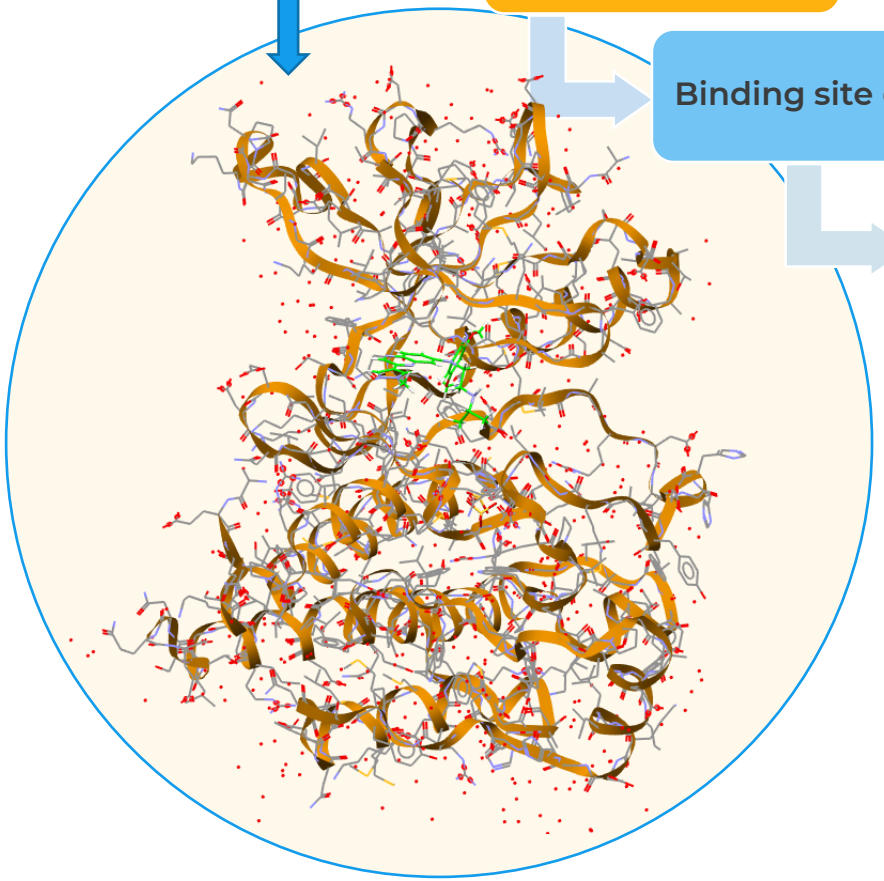
Binding site definition

Ligand(s) selection for docking

Scoring function selection

Setup and running the docking calculation

Analysis of the results and visualisation



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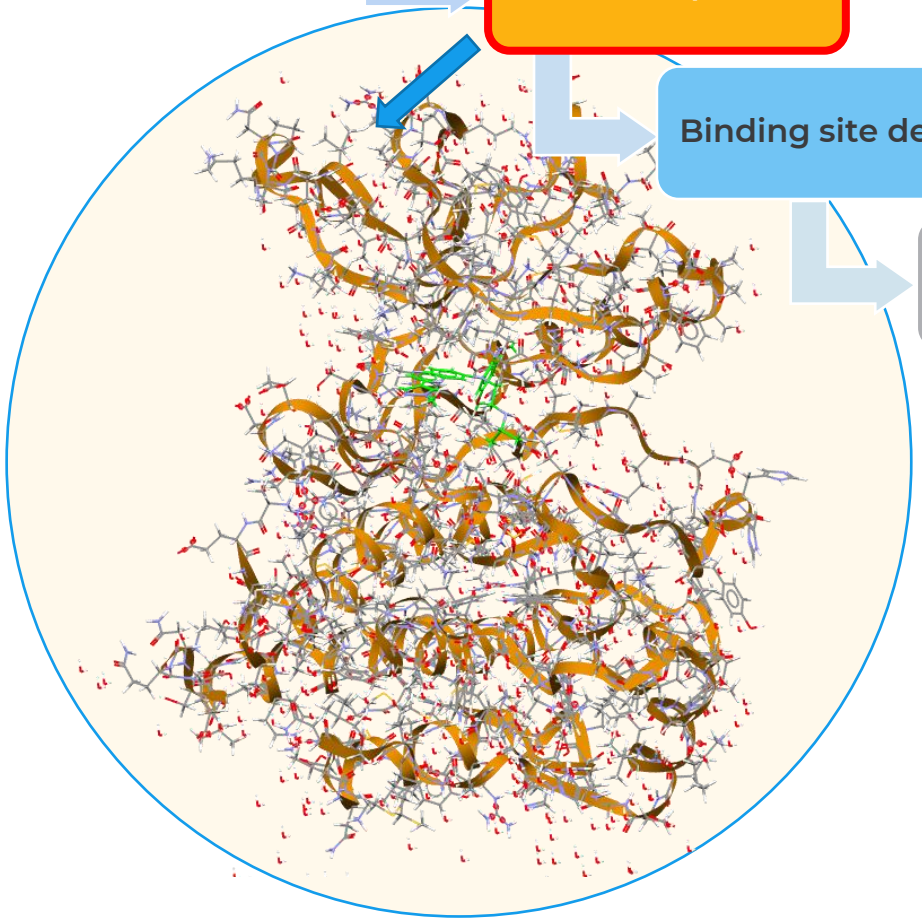
Steps in molecular docking

Target selection

Protein Preparation

- Add hydrogens



Binding site definition

Ligand(s) selection for docking

Scoring function selection

Setup and running the docking calculation

Analysis of the results and visualisation

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Steps in molecular docking

Target selection

Protein Preparation

- Add hydrogens
- Check protonation of His, Gln, Asn

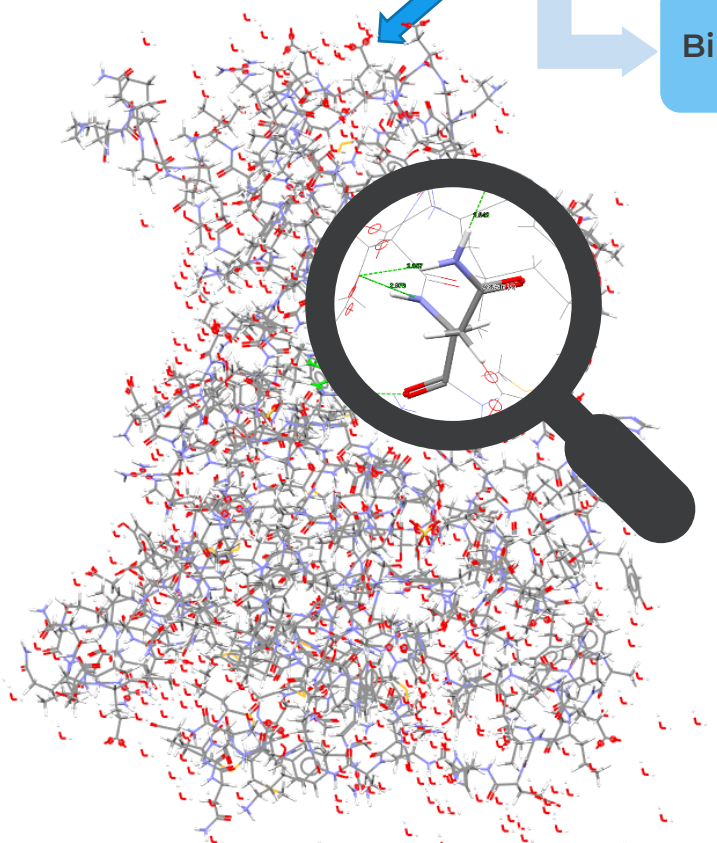
Binding site definition

Ligand(s) selection for docking

Scoring function selection

Setup and running the docking calculation

Analysis of the results and visualisation



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Steps in molecular docking

Target selection

Protein Preparation

- Add hydrogens
- Check protonation of His, Gln, Asn.
- Remove waters or retain required ones

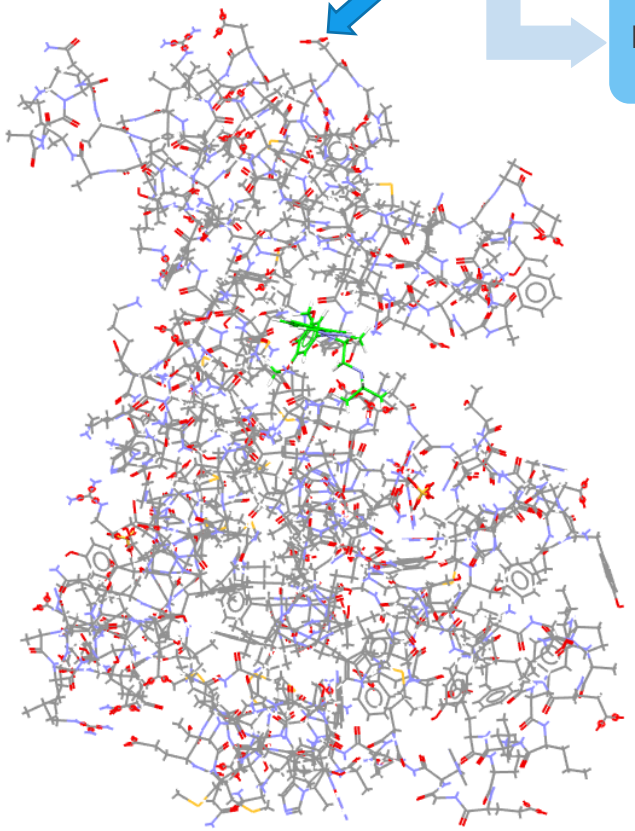
Binding site definition

Ligand(s) selection for docking

Scoring function selection

Setup and running the docking calculation

Analysis of the results and visualisation



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Steps in molecular docking

Target selection

Protein Preparation

- Add hydrogens
- Check protonation of His, Gln, Asn.
- Remove waters or retain required ones
- Extract ligand and save

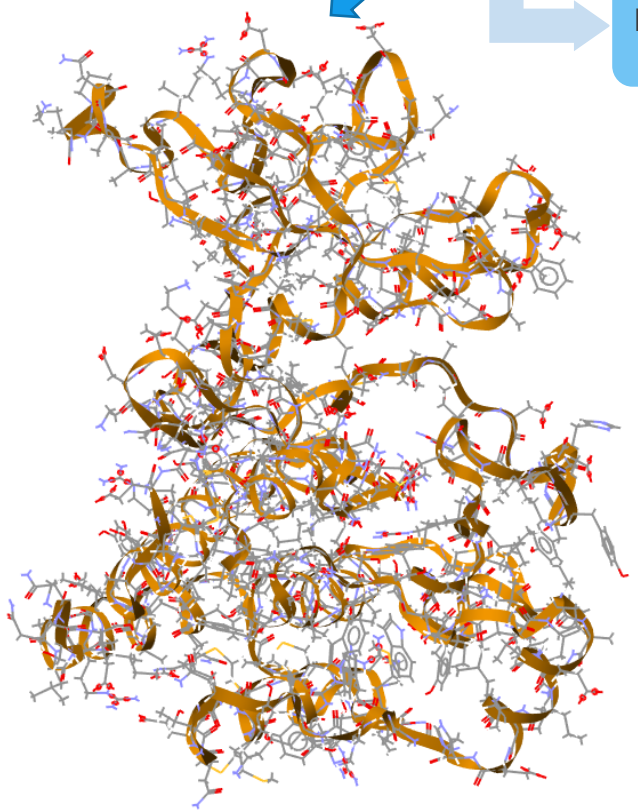
Binding site definition

Ligand(s) selection for docking

Scoring function selection

Setup and running the docking calculation

Analysis of the results and visualisation



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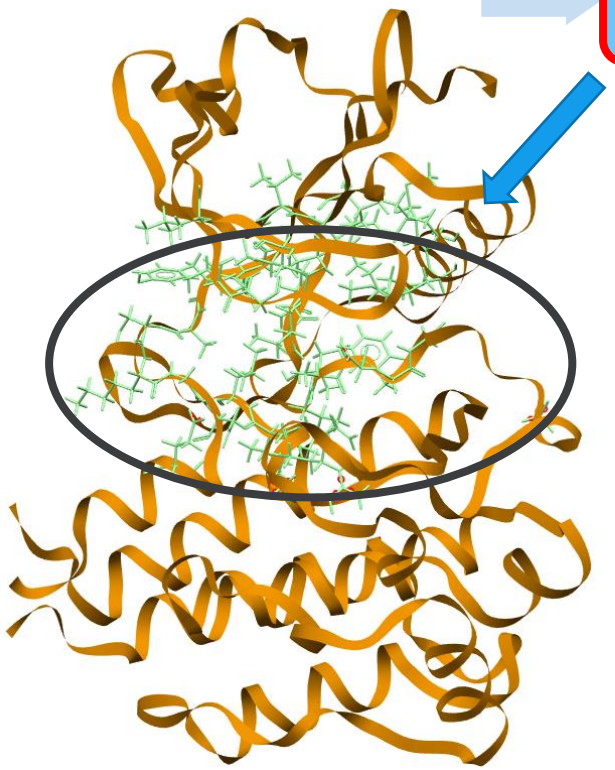
Steps in molecular docking

- Target selection
- Protein Preparation
- **Binding site definition**
  - Select the binding site for docking
- Ligand(s) selection for docking
- Scoring function selection
- Setup and running the docking calculation
- Analysis of the results and visualisation



Binding site: A specific region (or atom) in a molecular entity that is capable of entering into a stabilizing interaction with another molecular entity.

Read more in the Glossary in the handout .

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Steps in molecular docking

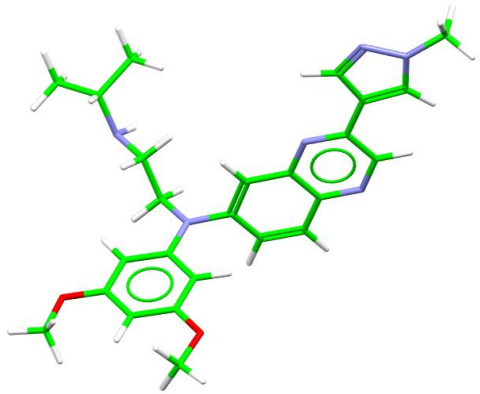
Target selection

Protein Preparation

Binding site definition

Ligand(s) selection for docking

- SDF, MOL2



Scoring function selection

Setup and running the docking calculation

Analysis of the results and visualisation

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Steps in molecular docking

Target selection

Protein Preparation

Binding site definition

Ligand(s) selection for docking

Scoring function selection

- Optionally rescoring

Setup and running the docking calculation

Analysis of the results and visualisation

Scoring functions in GOLD

- GoldScore
- ChemScore
- ASP (the Astex Statistical Potential)
- ChemPLP

Learn more in the FAQ

Scoring functions: mathematical functions used to approximately predict the binding affinity between two molecules after they have been docked.

Read more in the Glossary in the handout .

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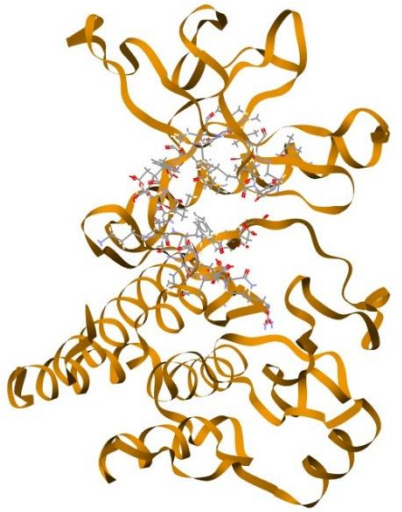
Steps in molecular docking



- Target selection
- Protein Preparation
- Binding site definition
- Ligand(s) selection for docking
- Scoring function selection
- Setup and running the docking calculation
- Analysis of the results and visualisation

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Steps in molecular docking

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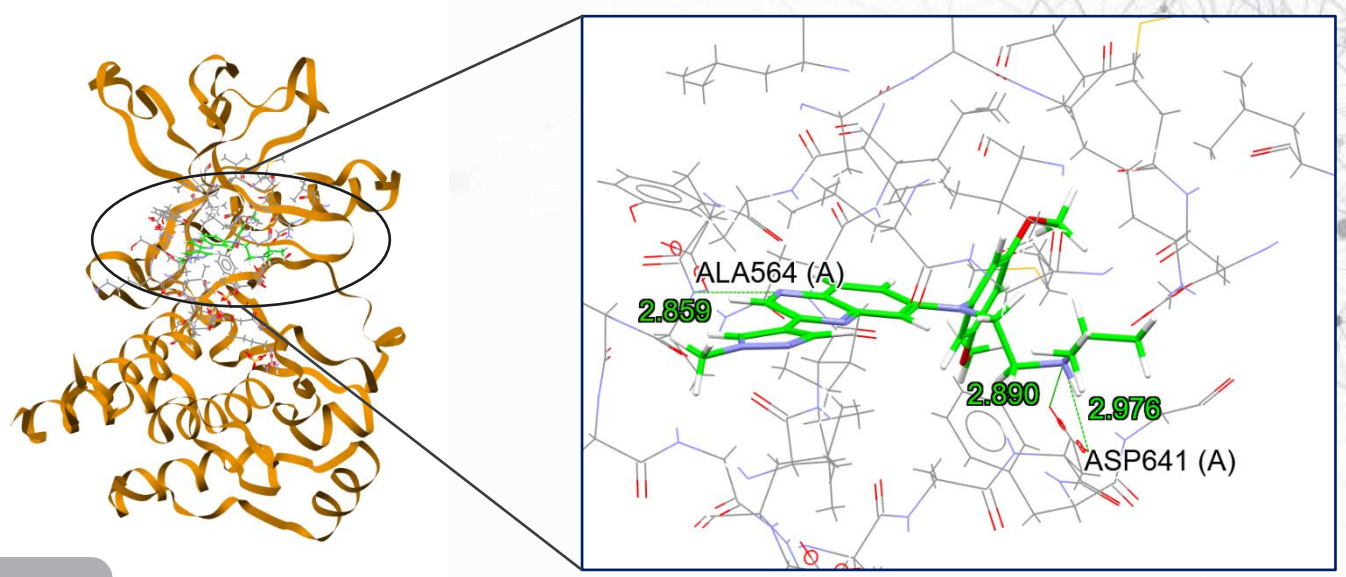

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Steps in molecular docking

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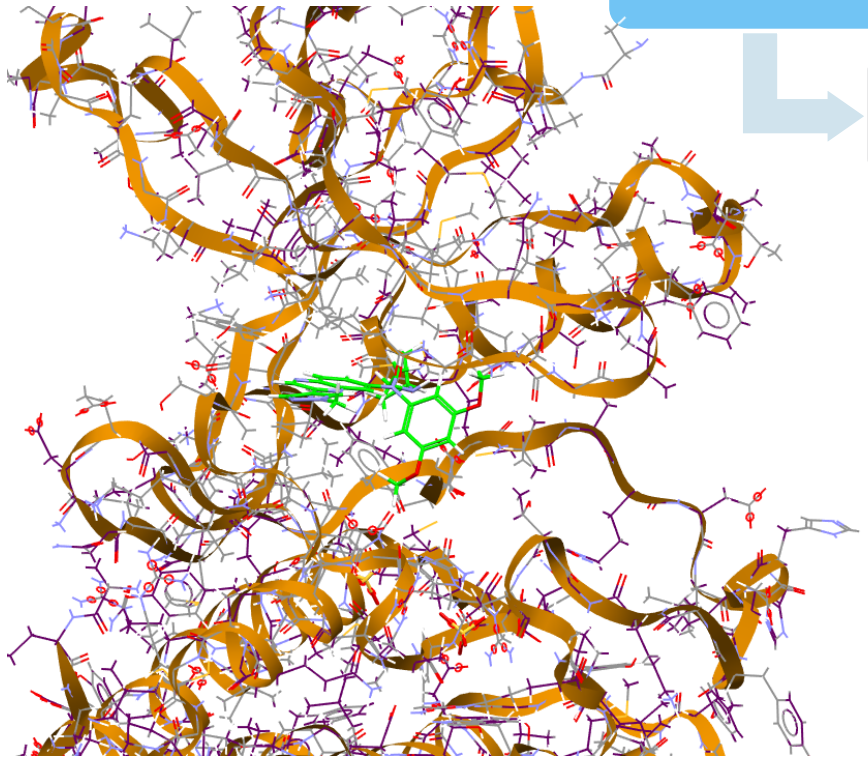

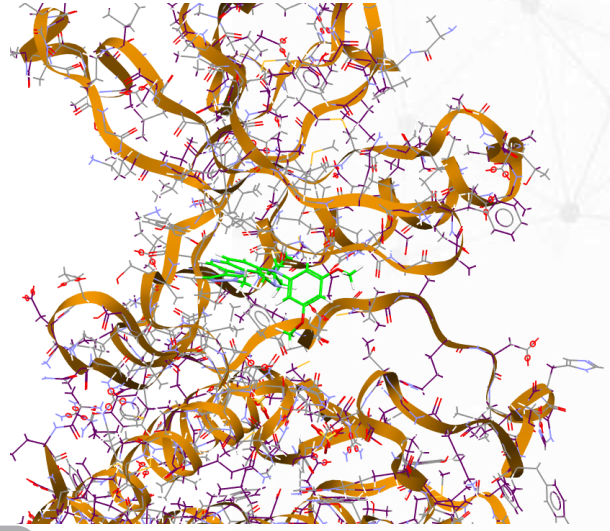

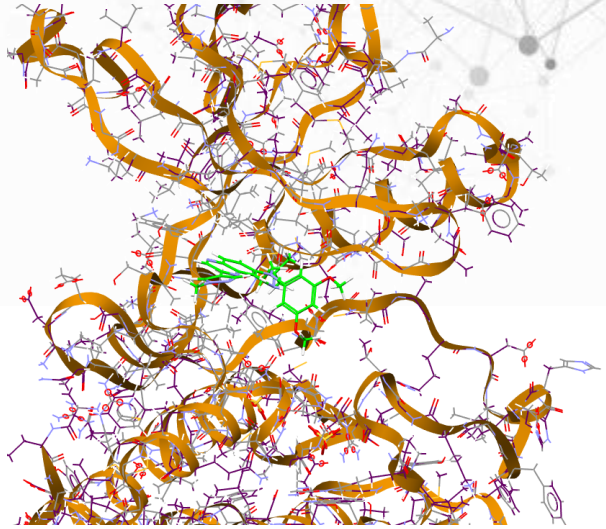

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