

Modeling ligand binding in protein targets

Scott Lovell, Ph.D.

Modeling ligand binding in protein targets

University of Kansas / SSGCID

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Introduction: Protein structure and X-ray Crystallography Laboratory (PSXL)

- High throughput structural biology
 - Crystallography and Cryo EM
- Structural Biology Center at KU
 - Protein Production, Computational Chemical Biology, High Throughput Screening, Mass Spectrometry, NMR Infectious Disease Assay Development and Chemical Synthesis

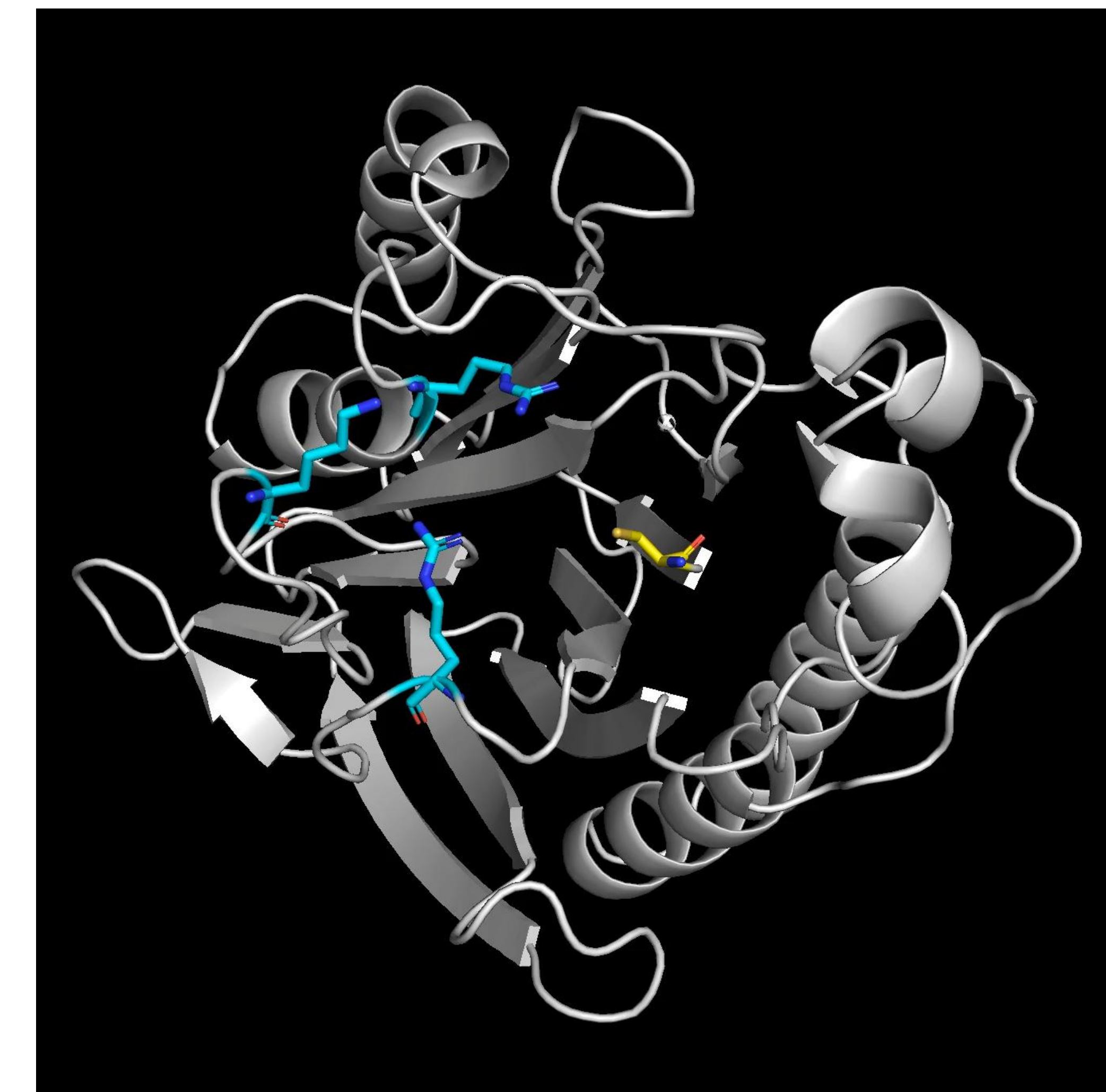
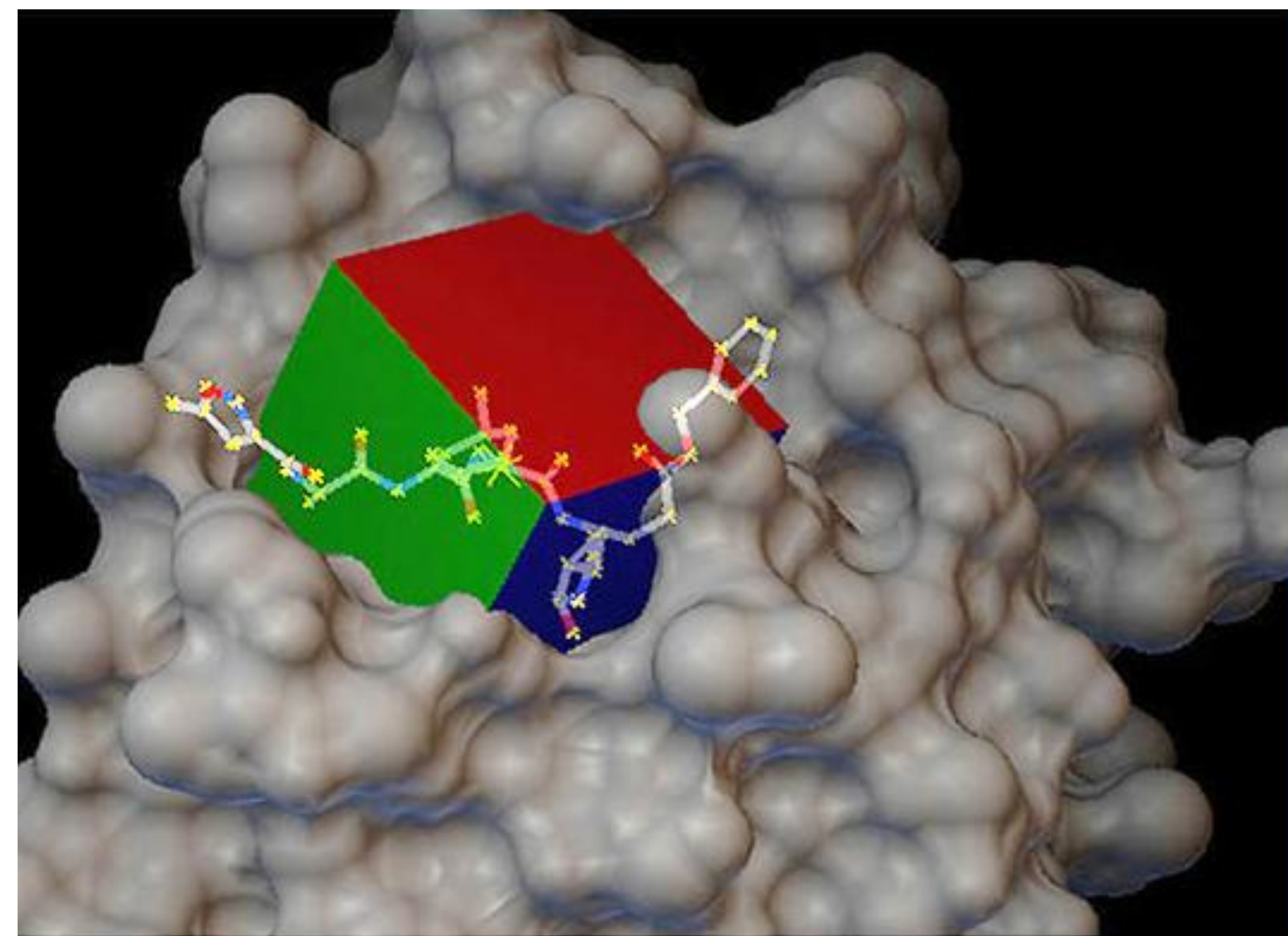


Methods for modelling protein:ligand binding

1. Docking methods: Modelling of a ligand in a protein pocket
2. Virtual screening: Identification of compounds for inhibitor development
3. Molecular dynamics simulations: Sampling conformational states of a time trajectory
4. Case Study: in silico inhibitor development
5. Preparing files for ligand modelling and software applications
6. Ligand modelling examples and analysis in the BioViz lab

General docking approach

- Computationally predict the binding mode(s) of molecules (ligands) to a protein
 - Add hydrogens to protein/ligand
- Setup a grid around the for docking search
- Sample the binding conformations (pose)
- Scoring based on binding free energy

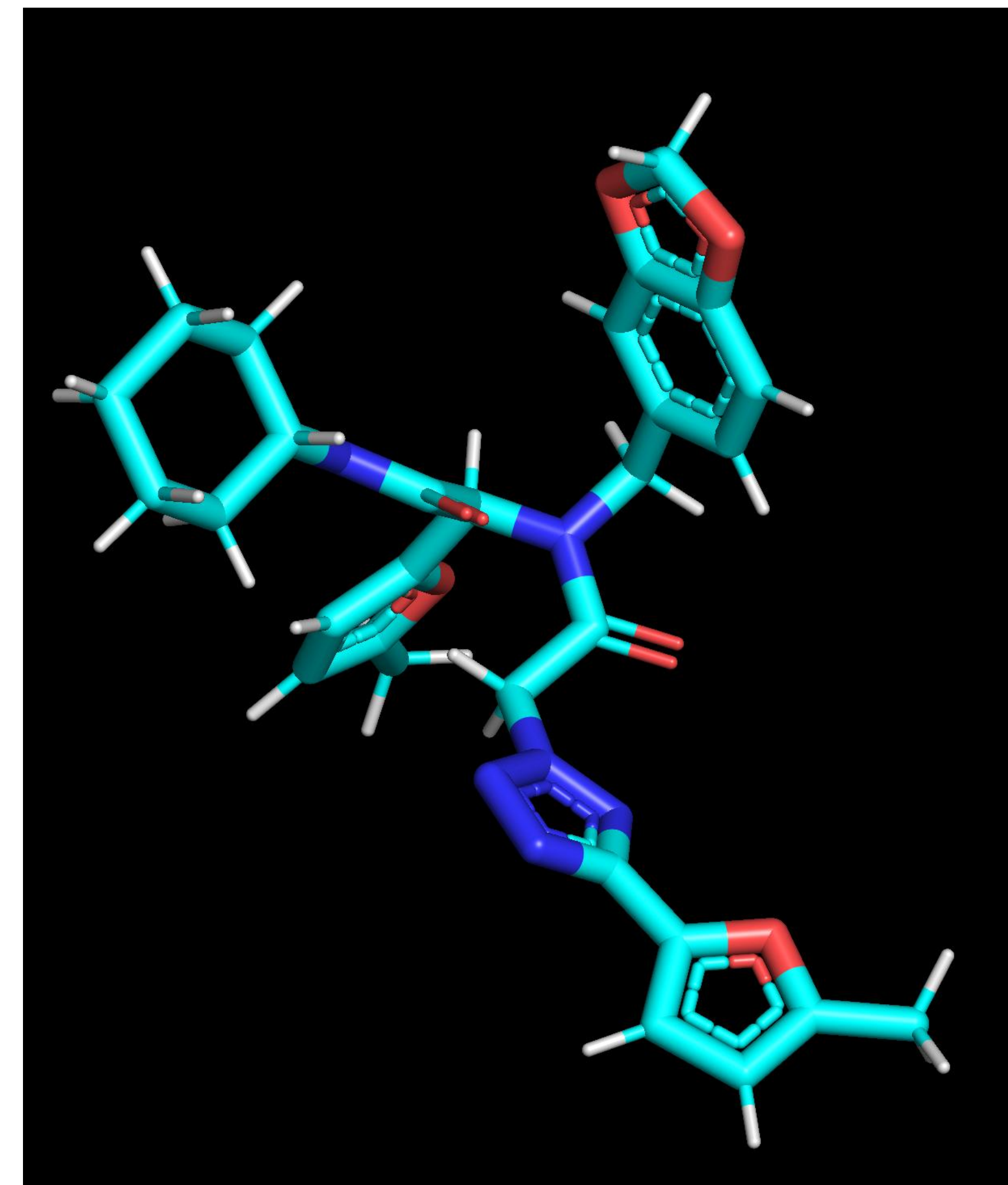


Preparation for ligand modelling

- Large cavity in protein used to test for potential ligand binding
- Protein model loaded into docking application
 - Hydrogen atoms are added in idealize positions
- Ligand molecule is loaded and hydrogen atoms added

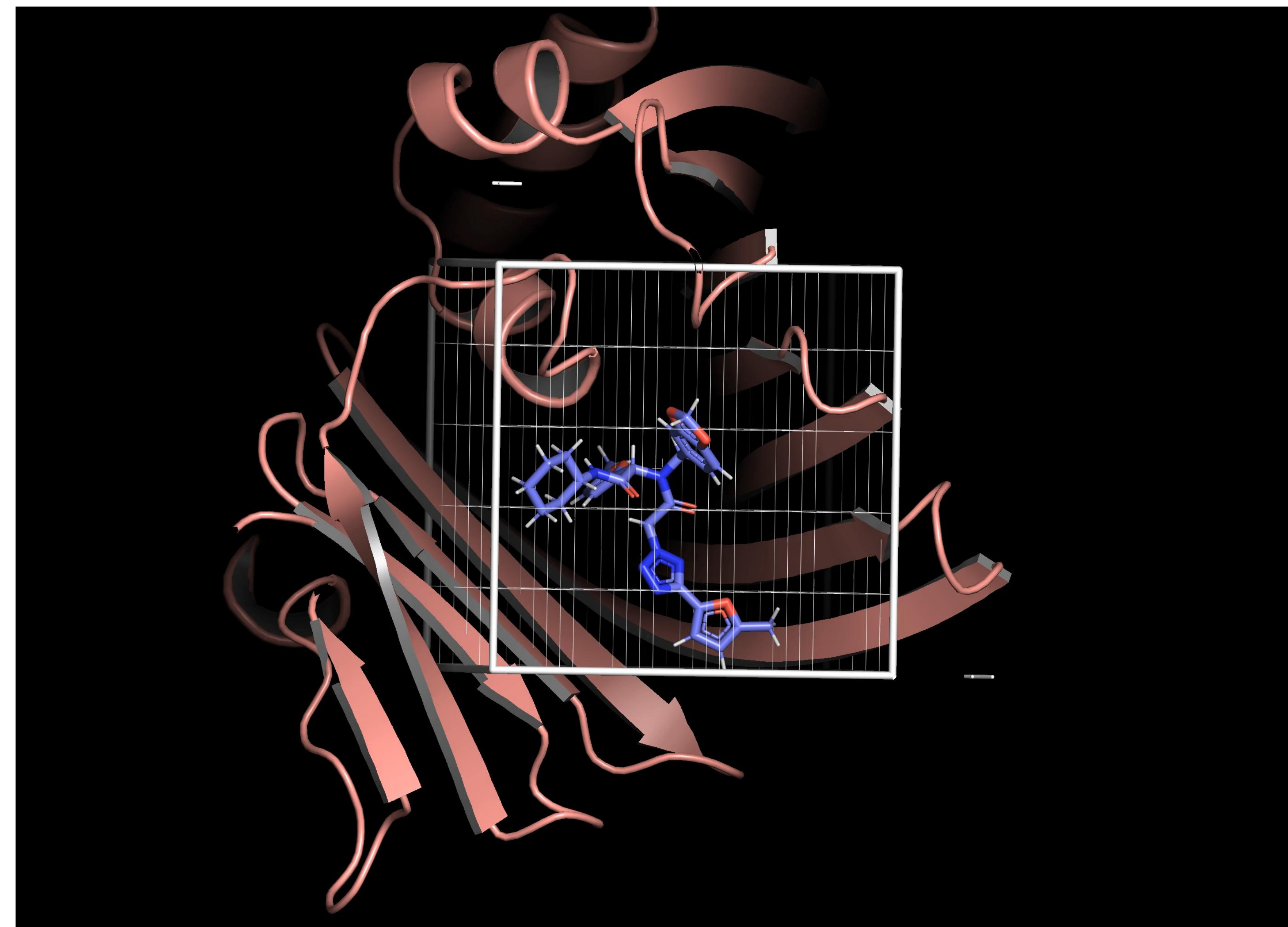


Ligand to dock

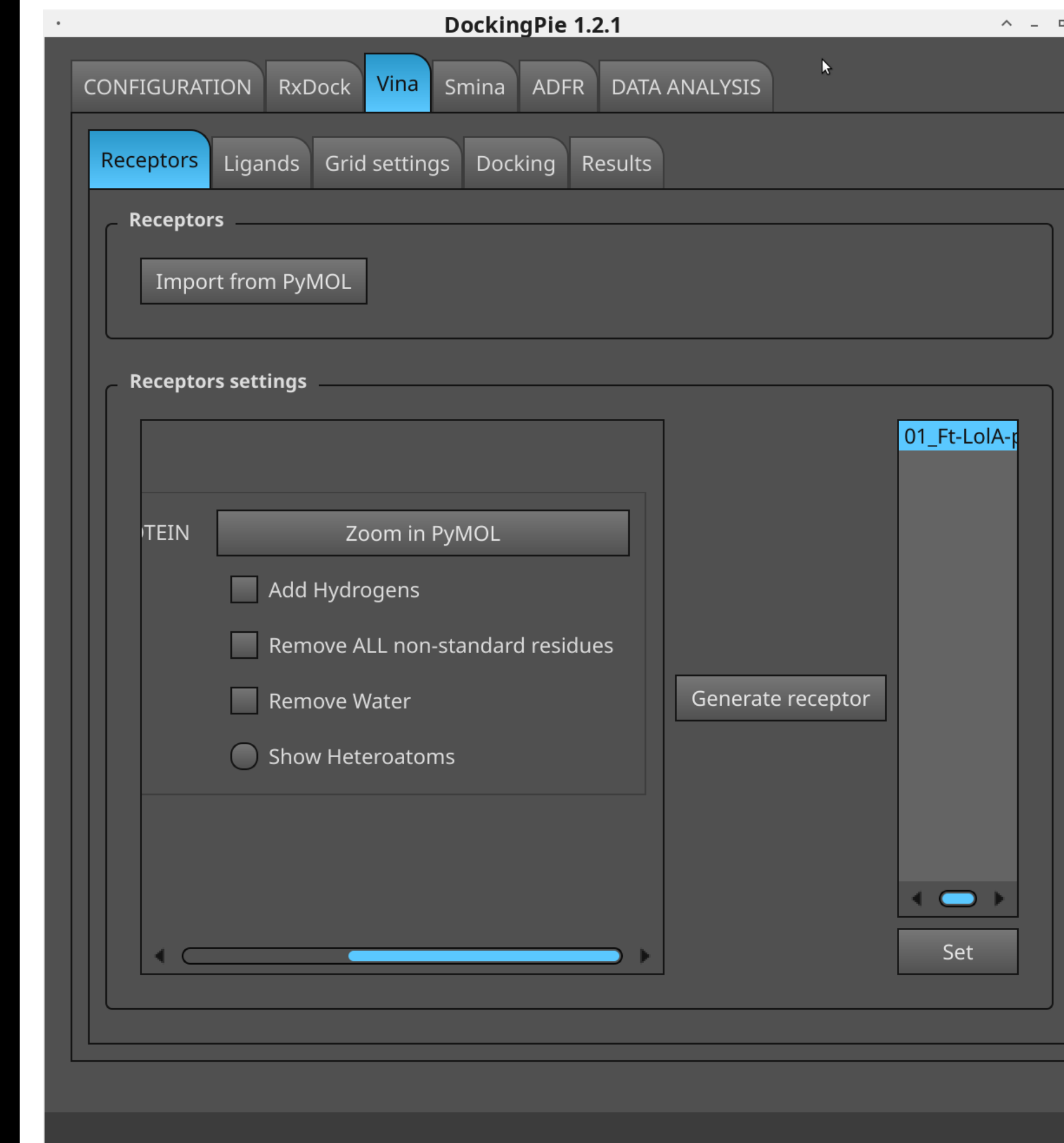


Ligand search parameters

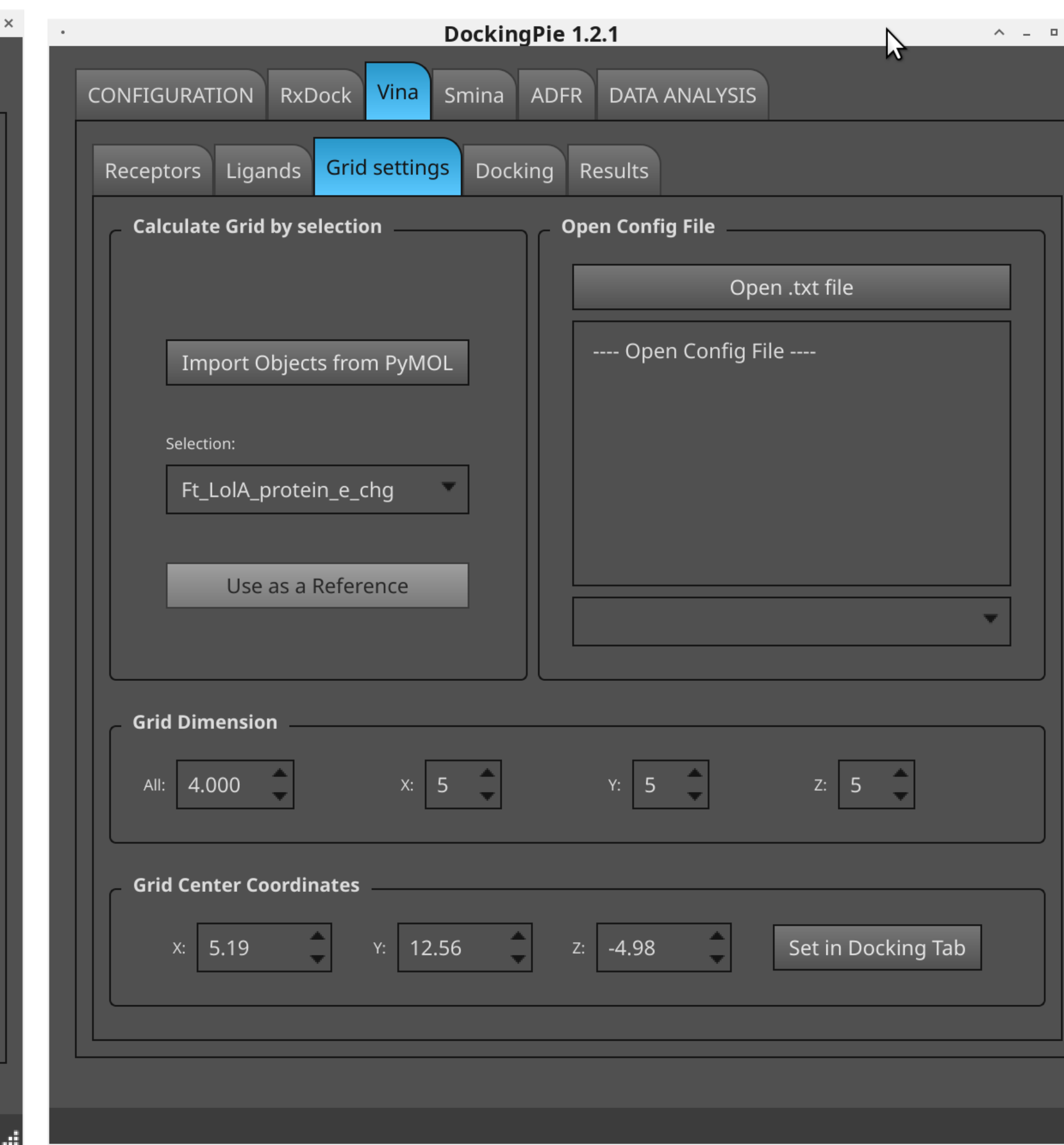
- The search grid is centered near the region of interest (cavity) and set in the x,y,z directions to encompass the desired area



Protein/Ligand Setup

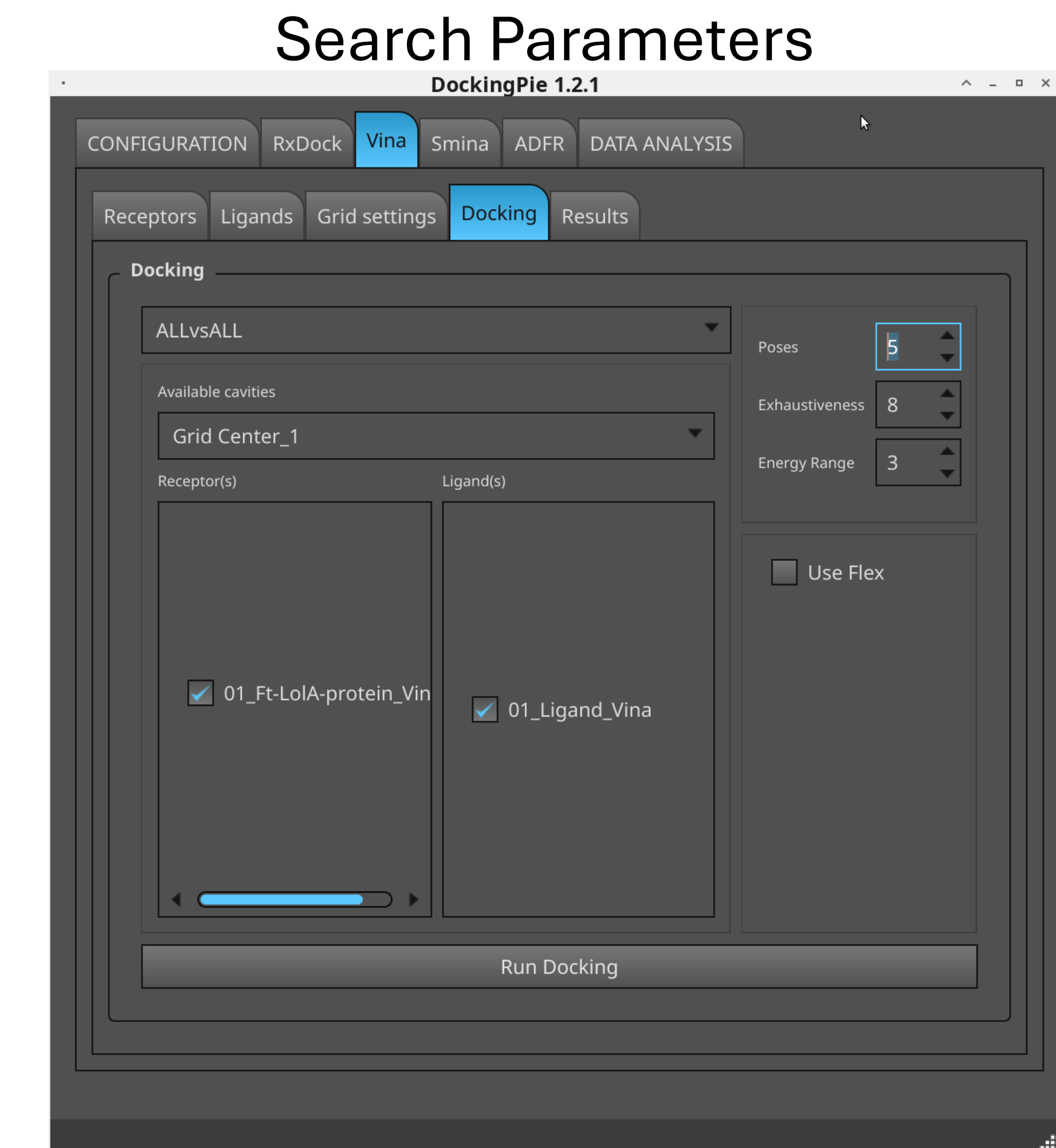
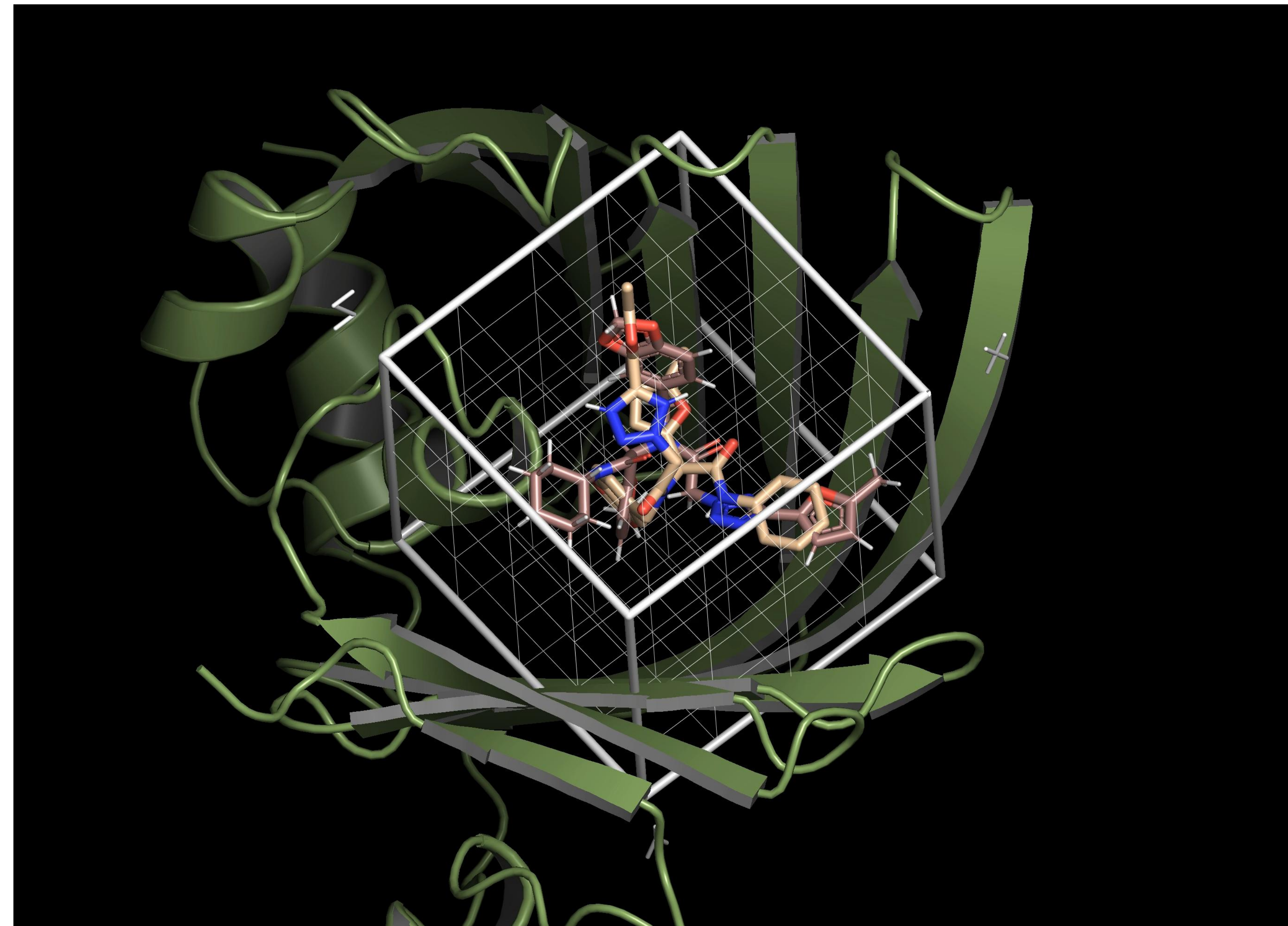


Grid Settings



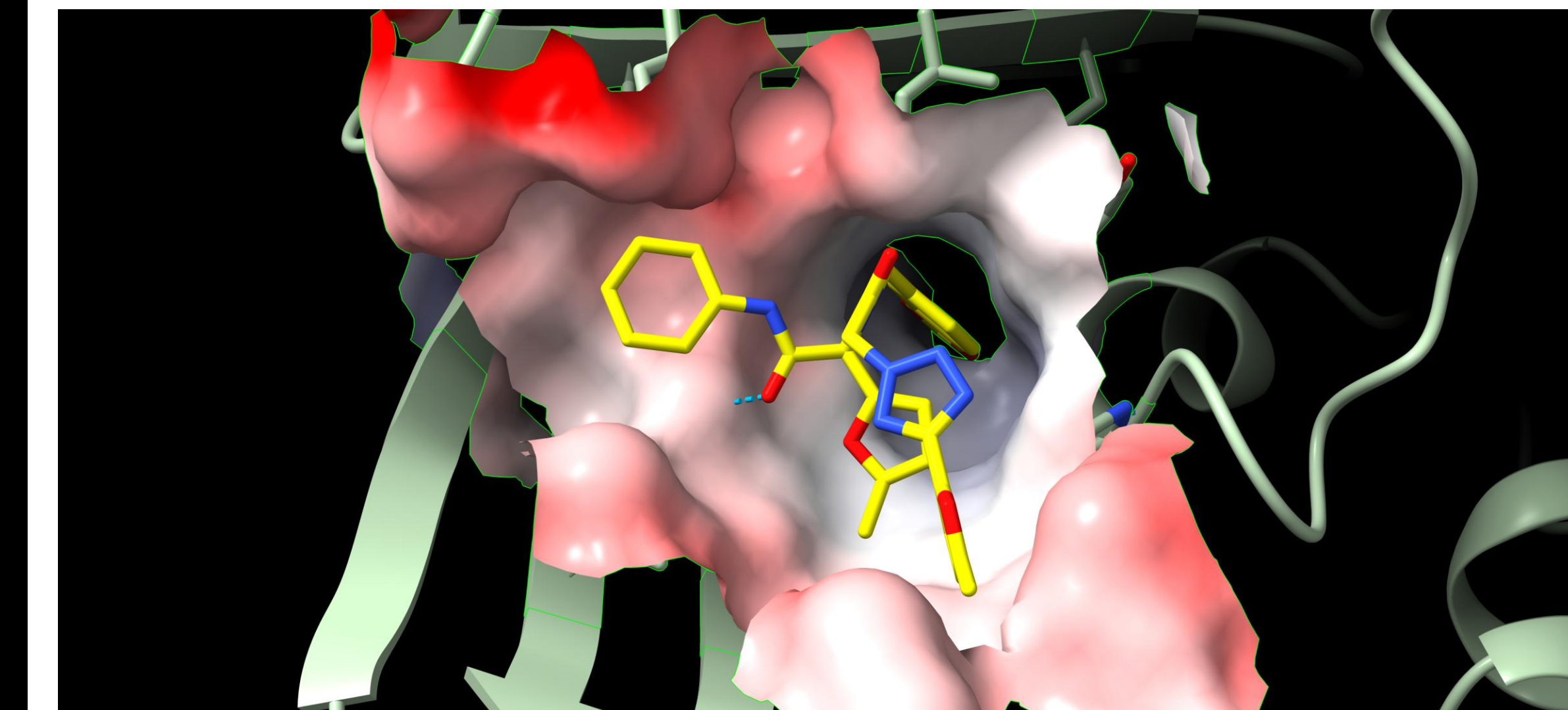
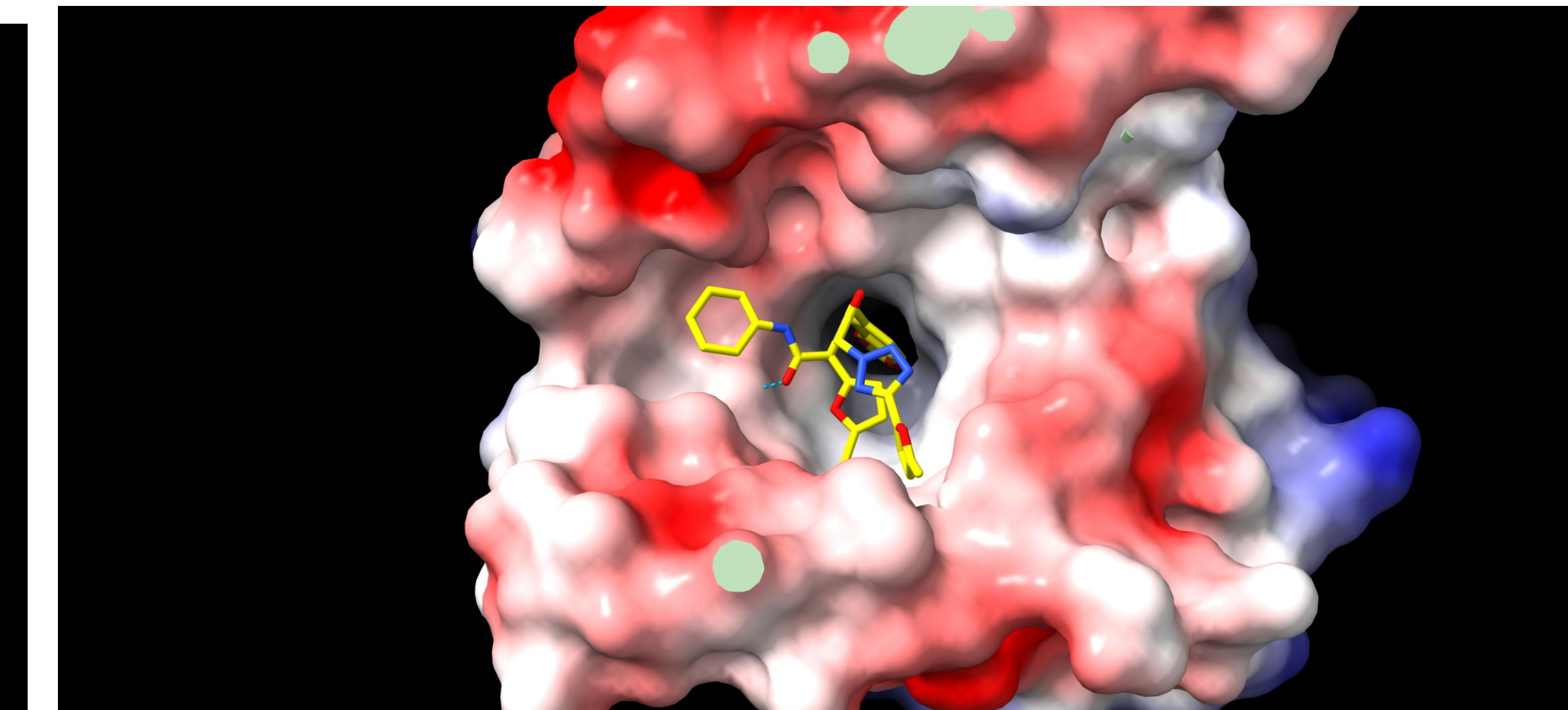
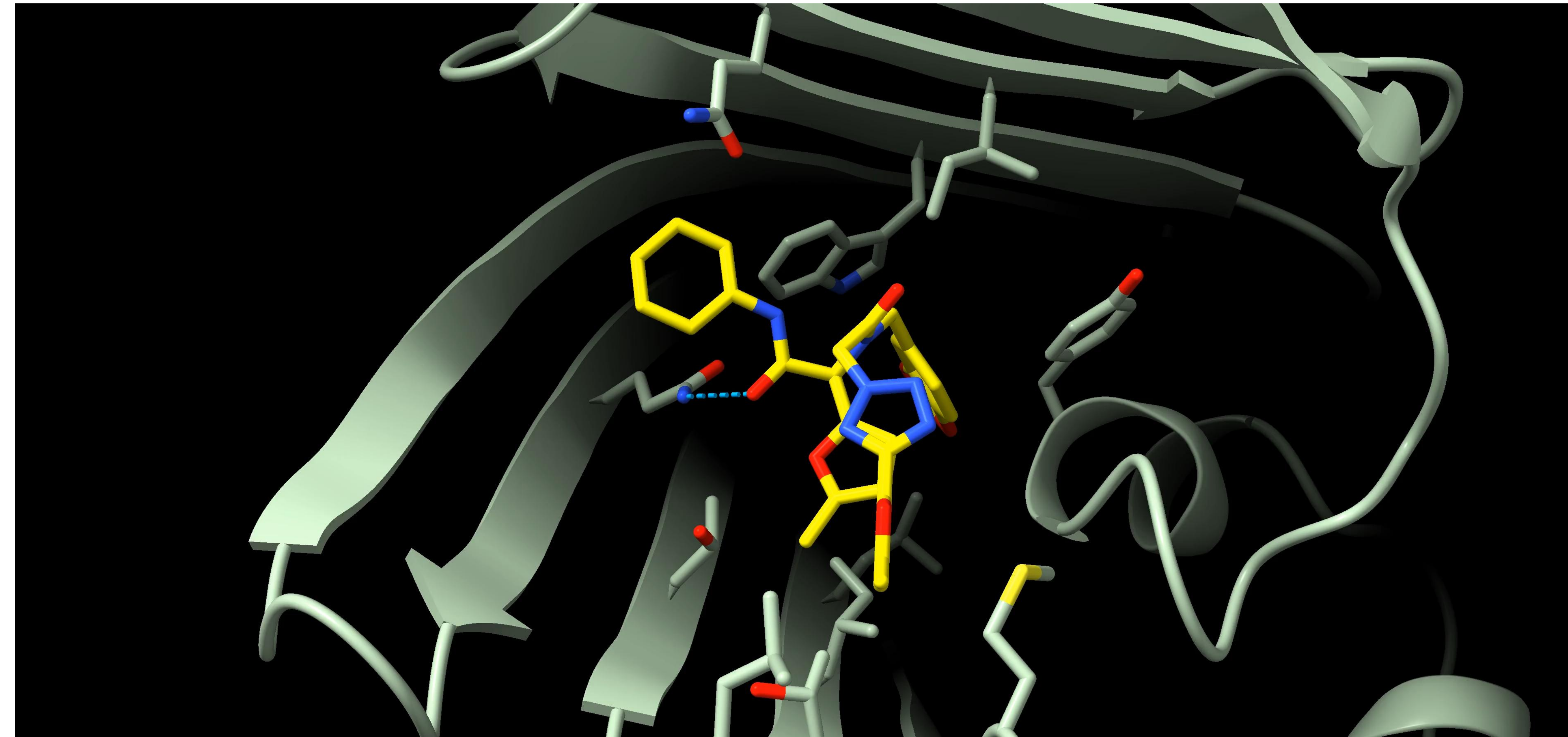
Ligand search parameters and results

- One would typically search for multiple poses within the grid space
- Results are filtered for “top” poses
 - Binding free energy



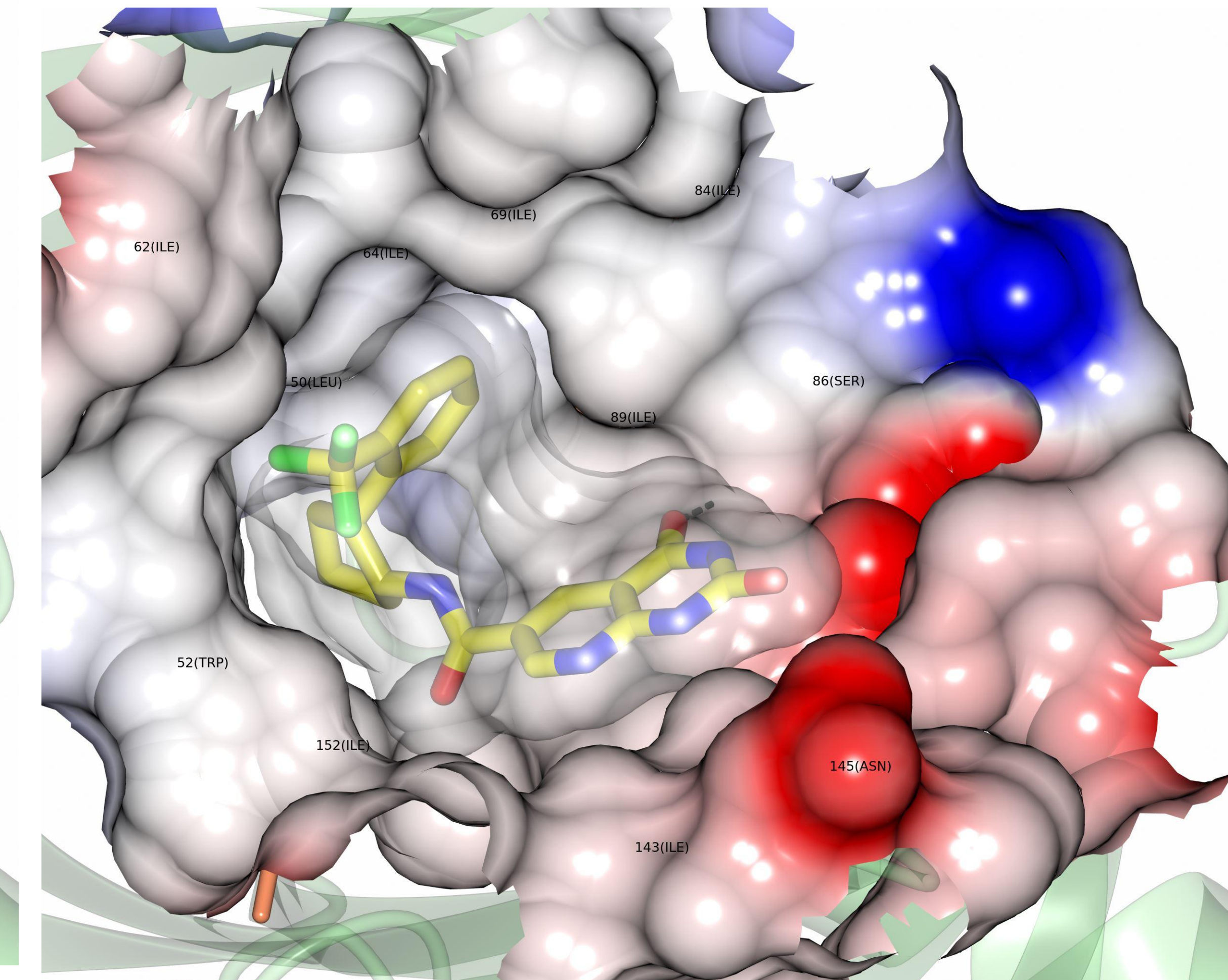
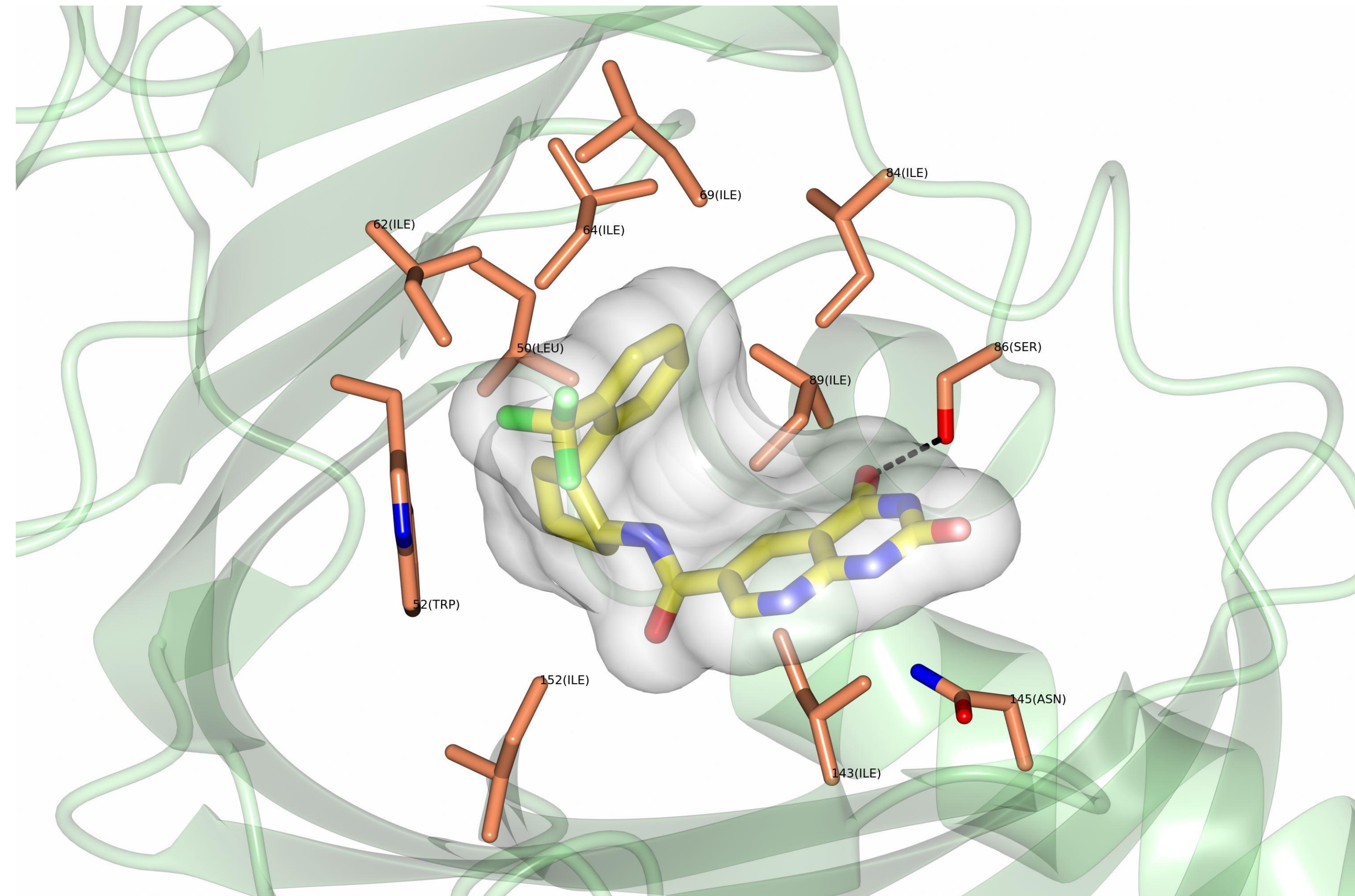
Analysis of the results

- Software: Pymol, CCP4mg, Coot, ChimeraX
- Analyze features such as hydrogen bonds, hydrophobic interactions, electrostatics, pocket environment



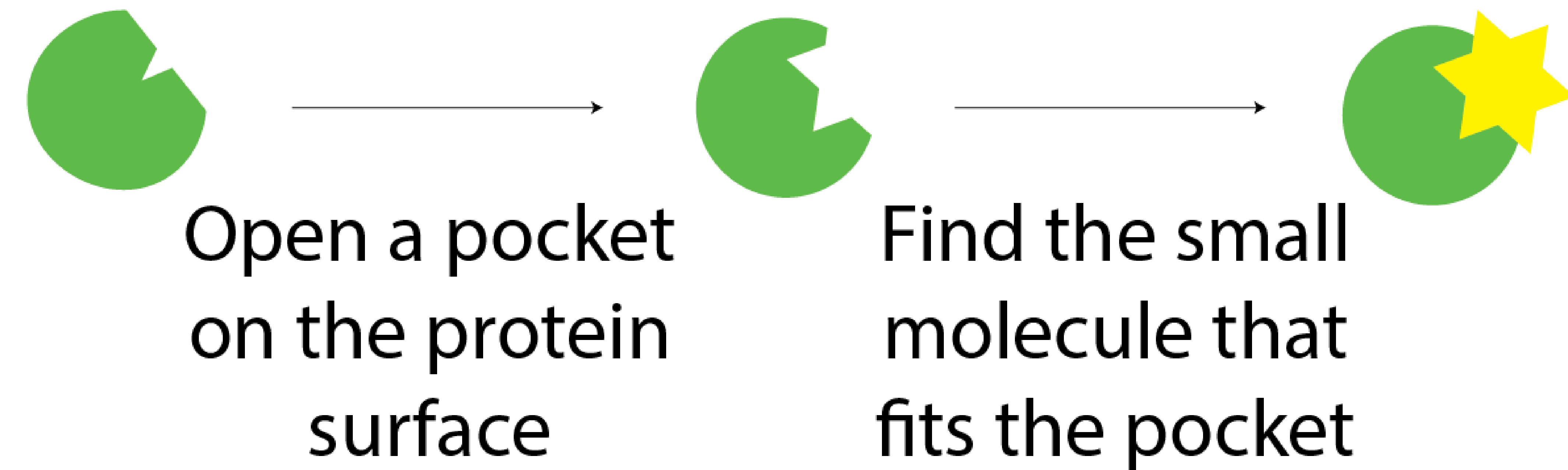
Evaluation of a docked ligand

- Hydrogen bond interactions
- Pocket characteristics
 - Hydrophobic and charged regions
- Various software packages for analysis



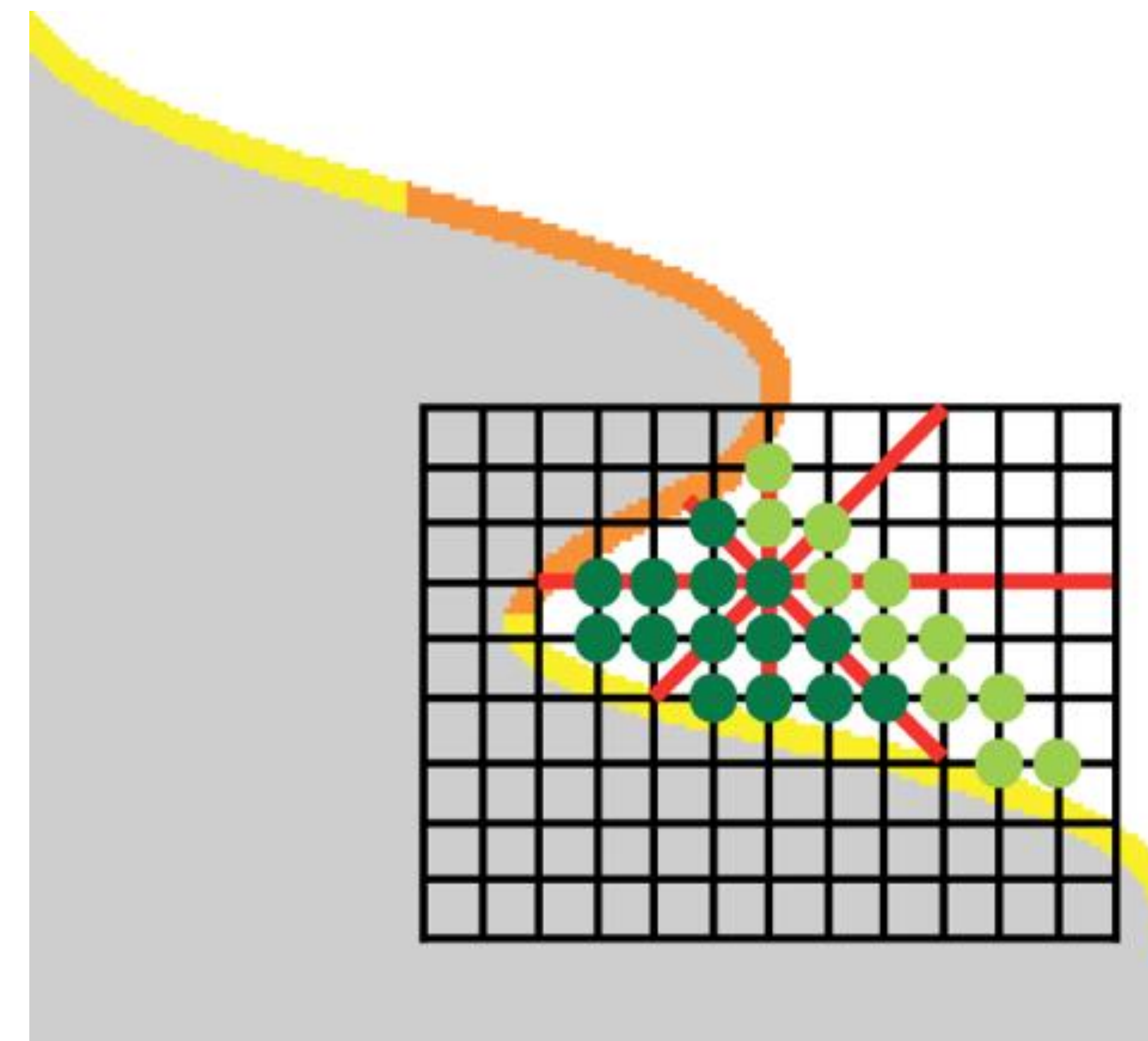
Advanced docking methods

- Docking multiple ligands to a protein target
 - In silico screening protein targets for lead compound identification
- Strategy:
 - Use a structure without a small molecule,
 - predict a conformation with a pocket
 - search for compounds that have shape and chemical complementarity.



Pocket optimization

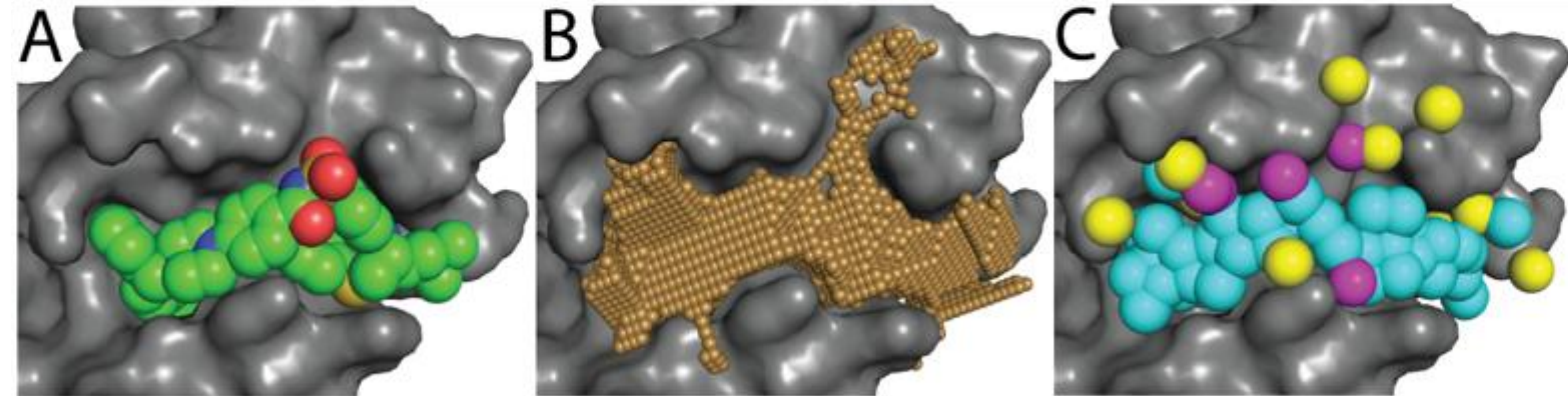
- Apply a biasing potential to drive the ensemble towards pocket containing conformations
 - Biasing potential is a proxy for binding free energy
 - Bias towards low energy conformations
- This can be a structure prediction problem
 - Given a template (unbound) structure one needs to identify conformations that satisfy energetic and pocket constraints



Johnson and Karanicolas, PLoS Comput Biol 2013

Exemplar screening

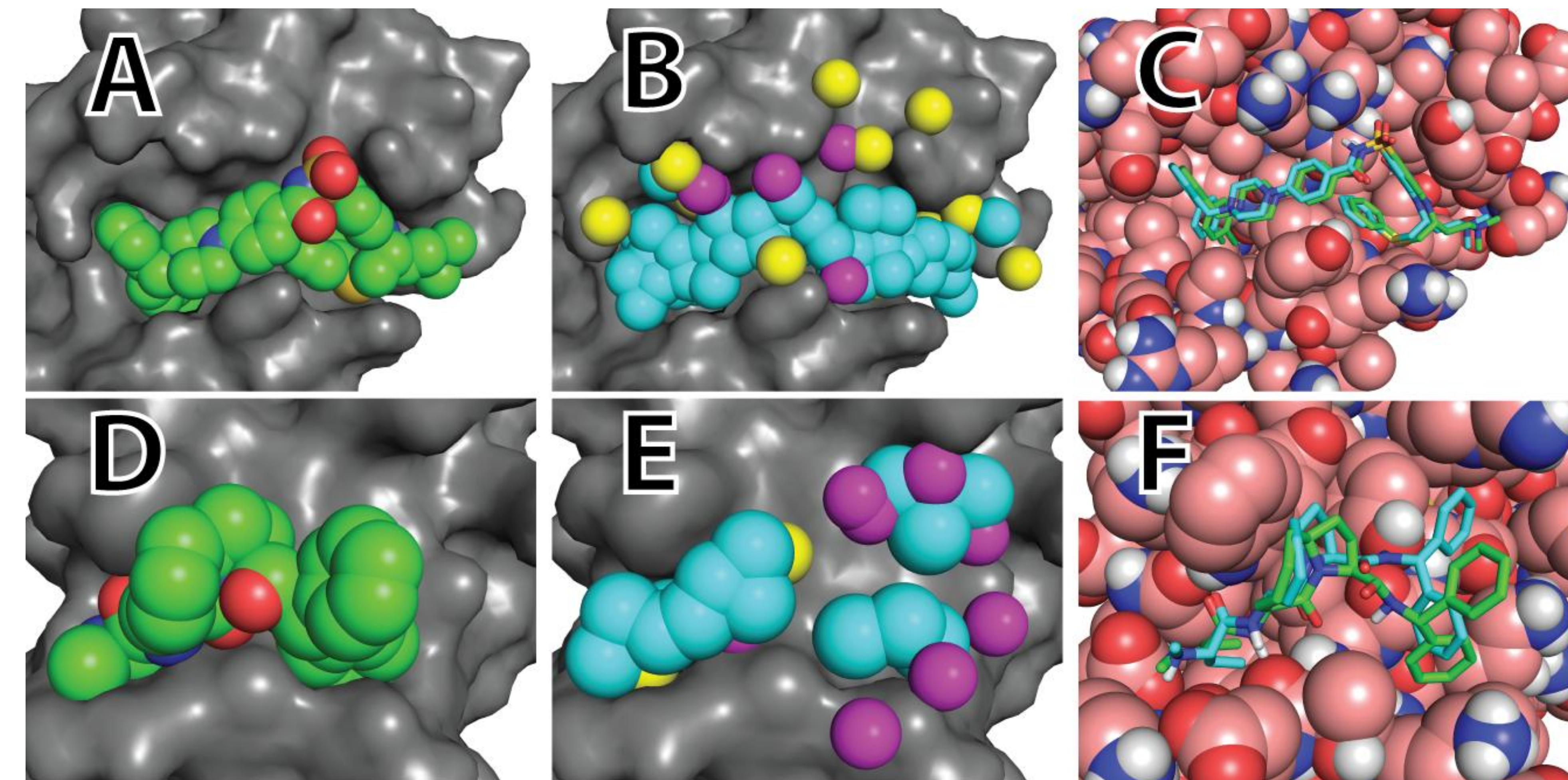
- Identify pockets
- Identify ideal location for donors and acceptors
- Fill pocket with carbon atoms
- Cluster exemplar points



(Johnson and Karanickolas, 2015)

Ligand placement via exemplar

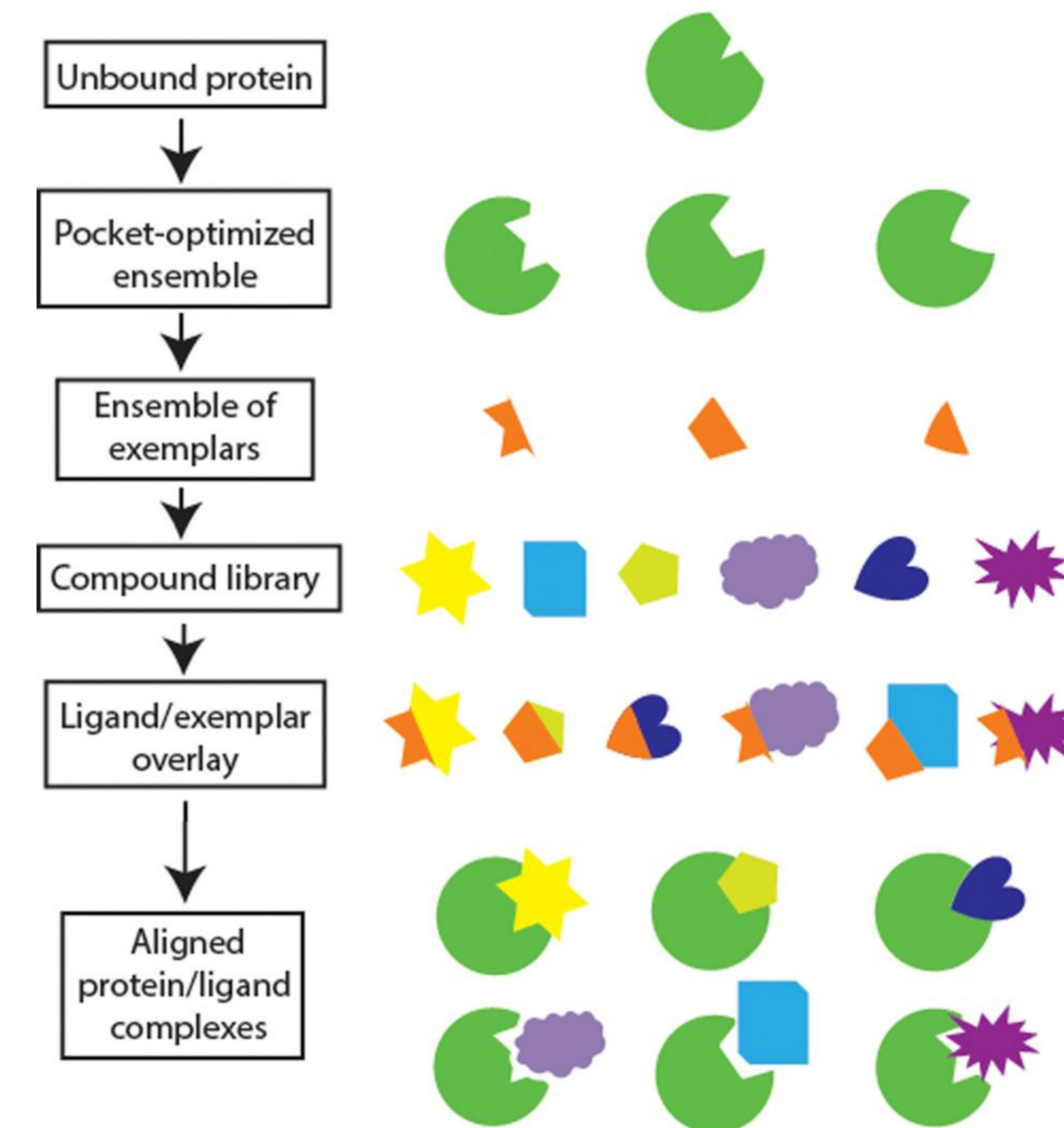
- Rapid Overlay of Chemical Structures (ROCS) developed by OpenEye software
- Fast shape comparison of ligand to exemplar by Gaussian representation of atoms
- Can screen large number of compounds using a computing cluster



Johnson and Karanicolas, JCIIM 2016

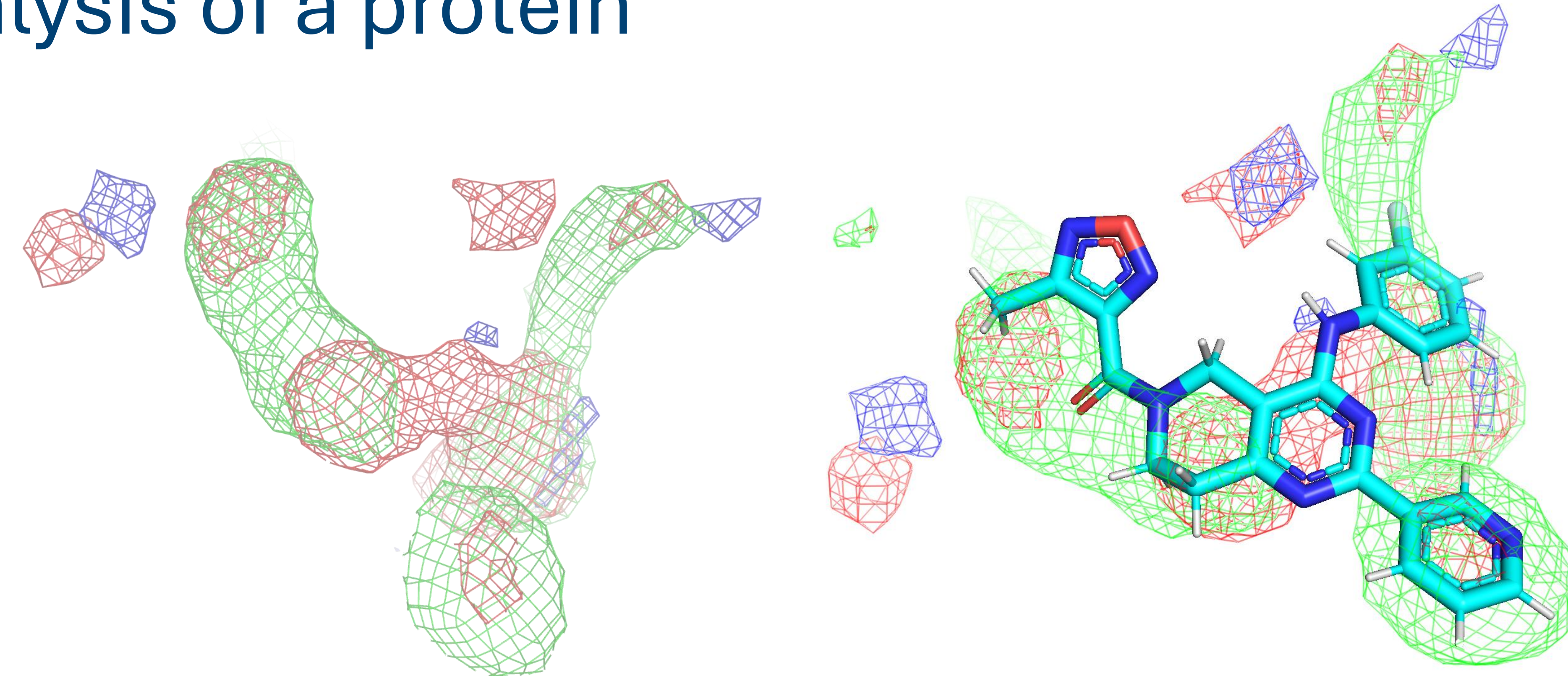
Screening structural ensembles

- Perform pocket optimization
- Assess pocket druggability (select pockets with tighter binding potential)
- ROCS exemplar screen (Rapid Overlay of Chemical Structures)
- VScreenML (active vs decoy classifier)



Site Identification by Ligand Competitive Saturation (SLICS) analysis of a protein

- Map of the interior pockets of the protein.
- Zones where the energy of a hydrophobic (green), donor (blue), or acceptor (red) are present
- Filter for ligands that fit uniquely to each protein target
- Identify compounds that might uniquely target individual targets (singles)
- Example: pyridine ring and the shape of the ligand similar shape to the pocket

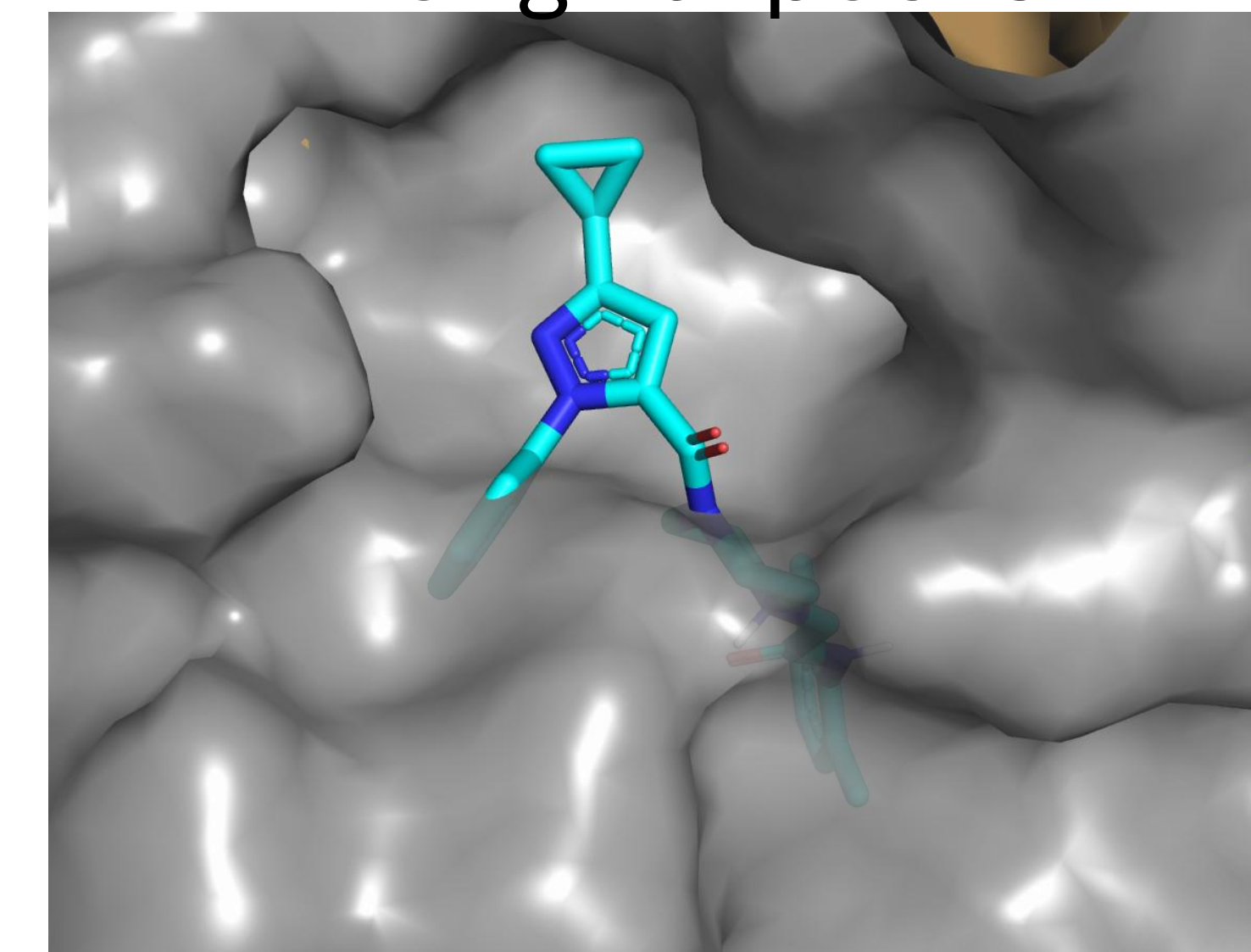


Example: In silico compound library screening

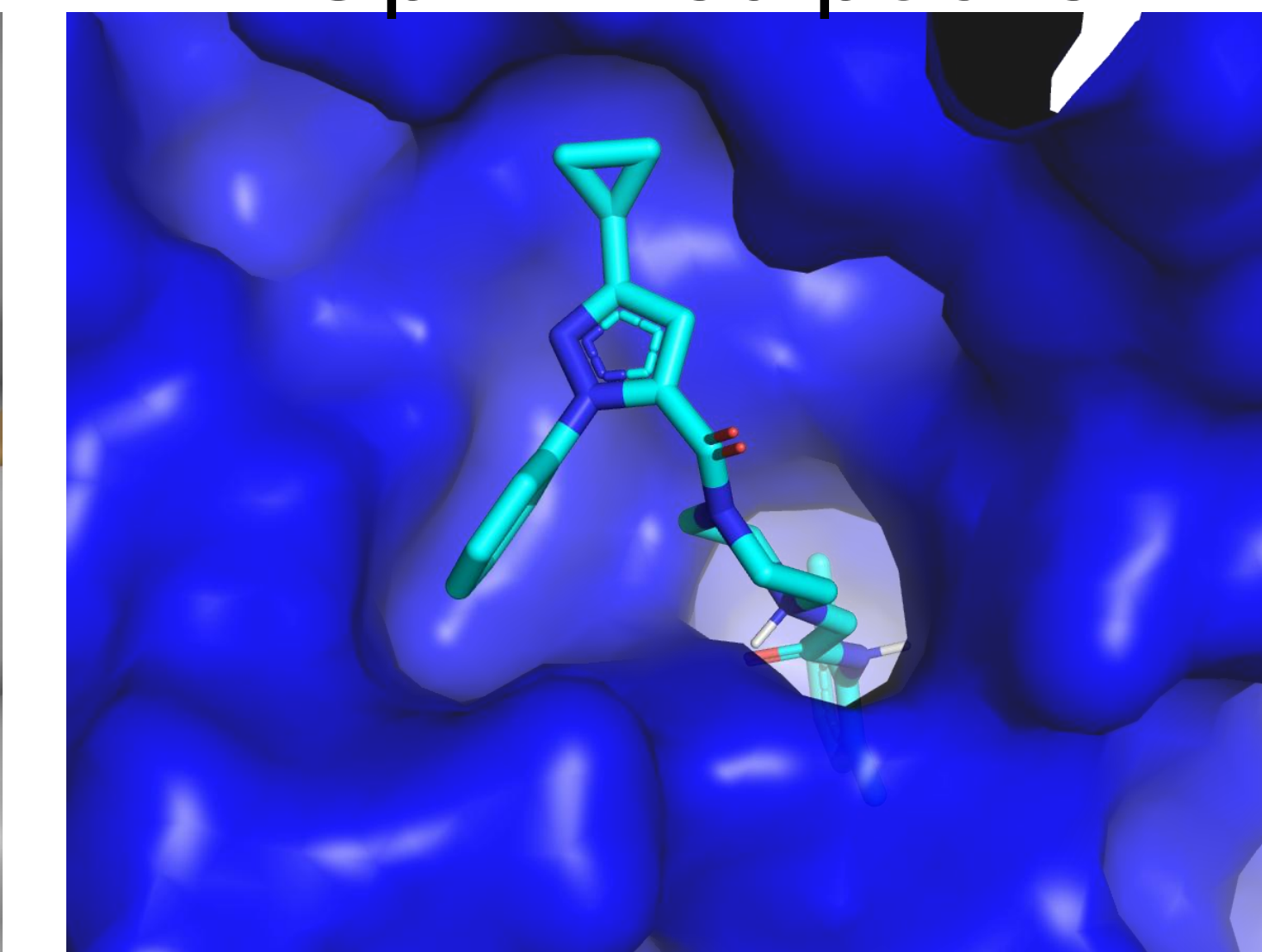
- Multiple protein target homologs
- Screened using the ZINC library
- ROCS and SILCS methods utilized
- Pocket optimization suggests deepening of the pockets during simulations supporting compatibility with binding

Homolog 1

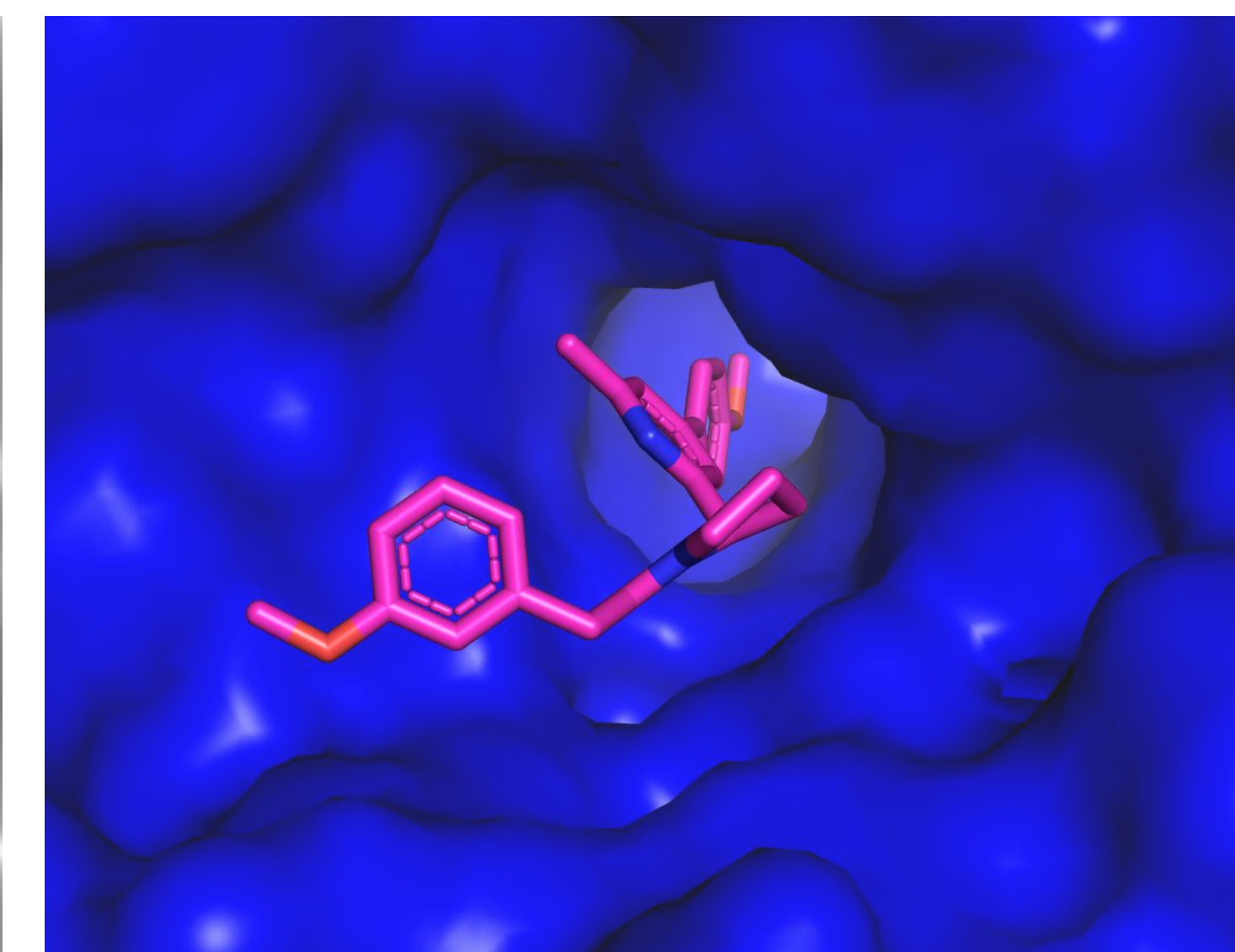
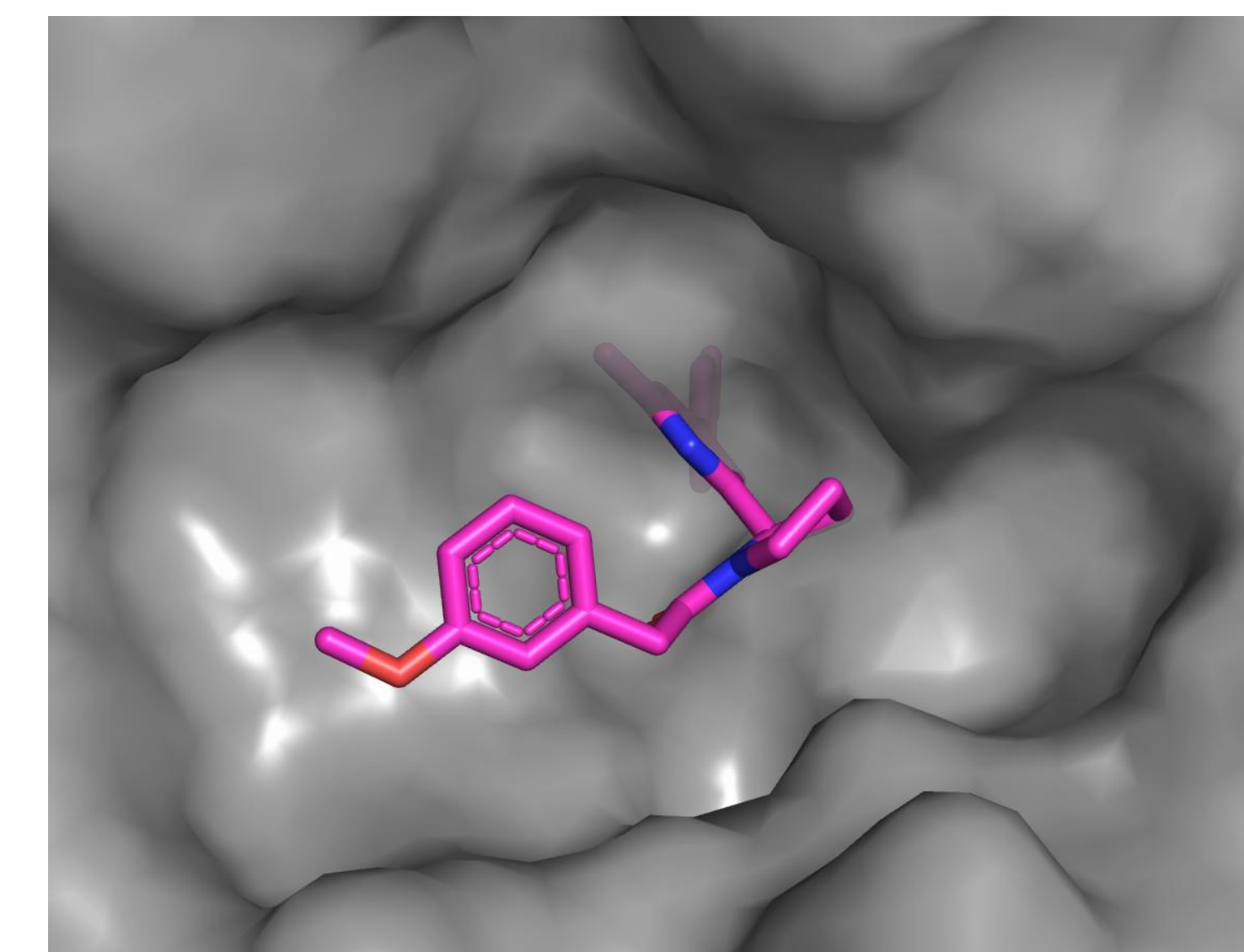
original pocket



Optimized pocket

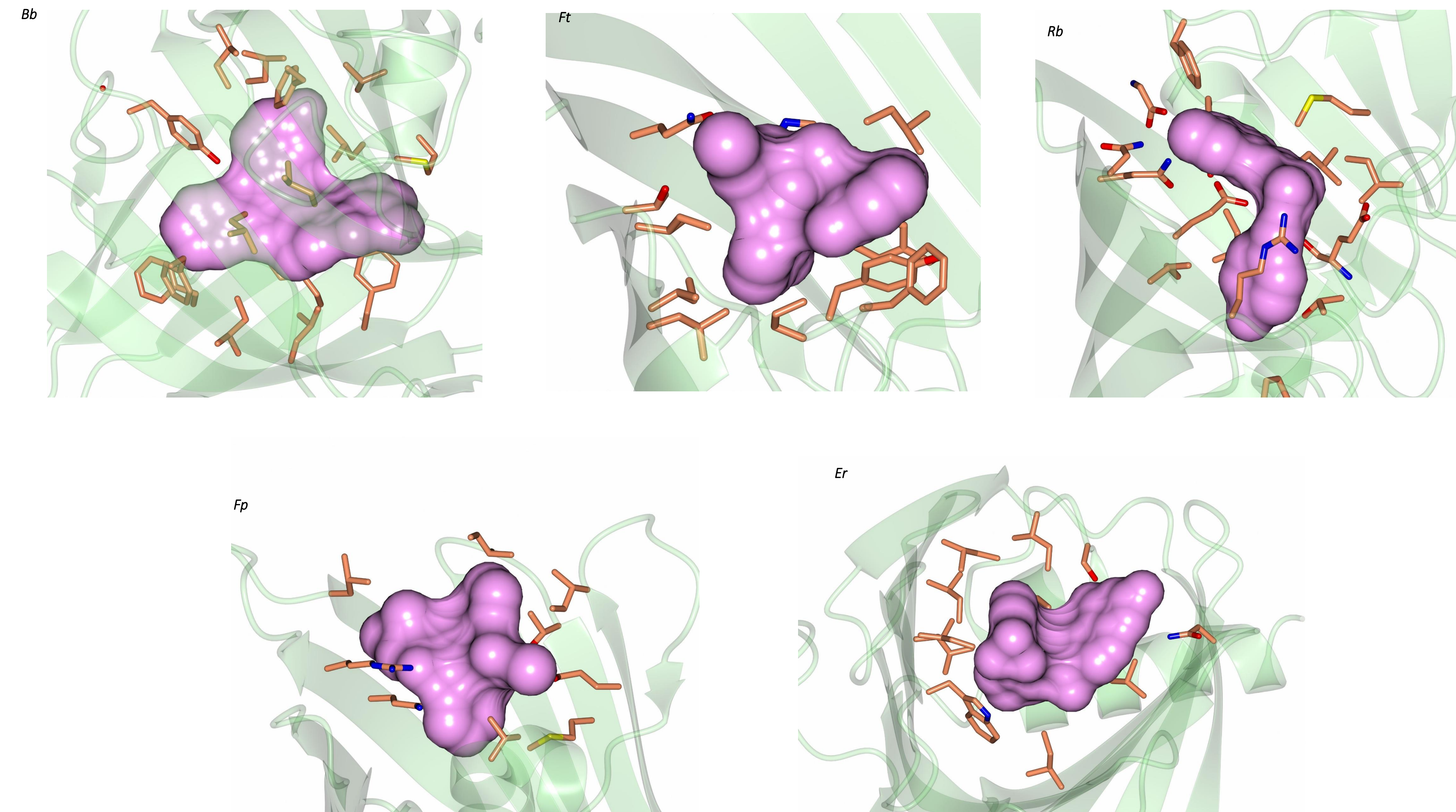


Homolog 2



Pocket comparison between protein homologs

- Map the differences/similarities amongst homologs
- Screen for compounds that might bind to various proteins
- Identify compounds that are selective



Top hits from in silico screening

- Diverse chemical functionality
- Differences in pocket depth between homologs

Homolog 1



Homolog 2



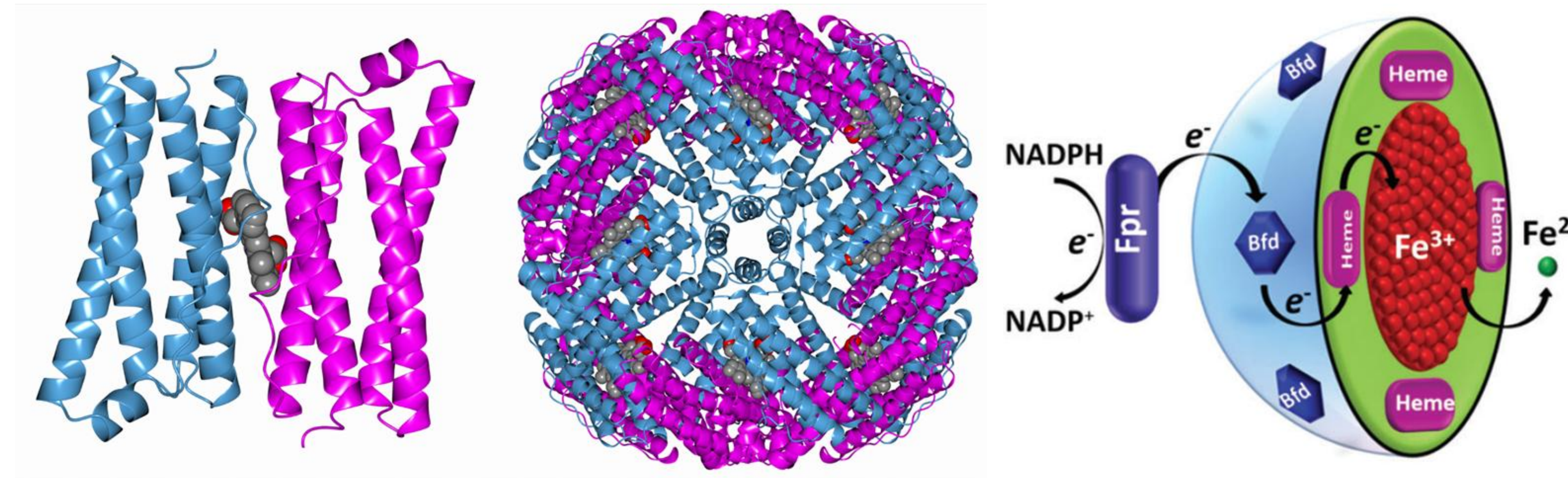
Molecular dynamics (MD) simulations

- Modelling protein physical motions over time
Generates a trajectory of minimized states.
 - Various conformational states sampled
- Can be used to identify dynamic regions near or at a ligand binding pocket

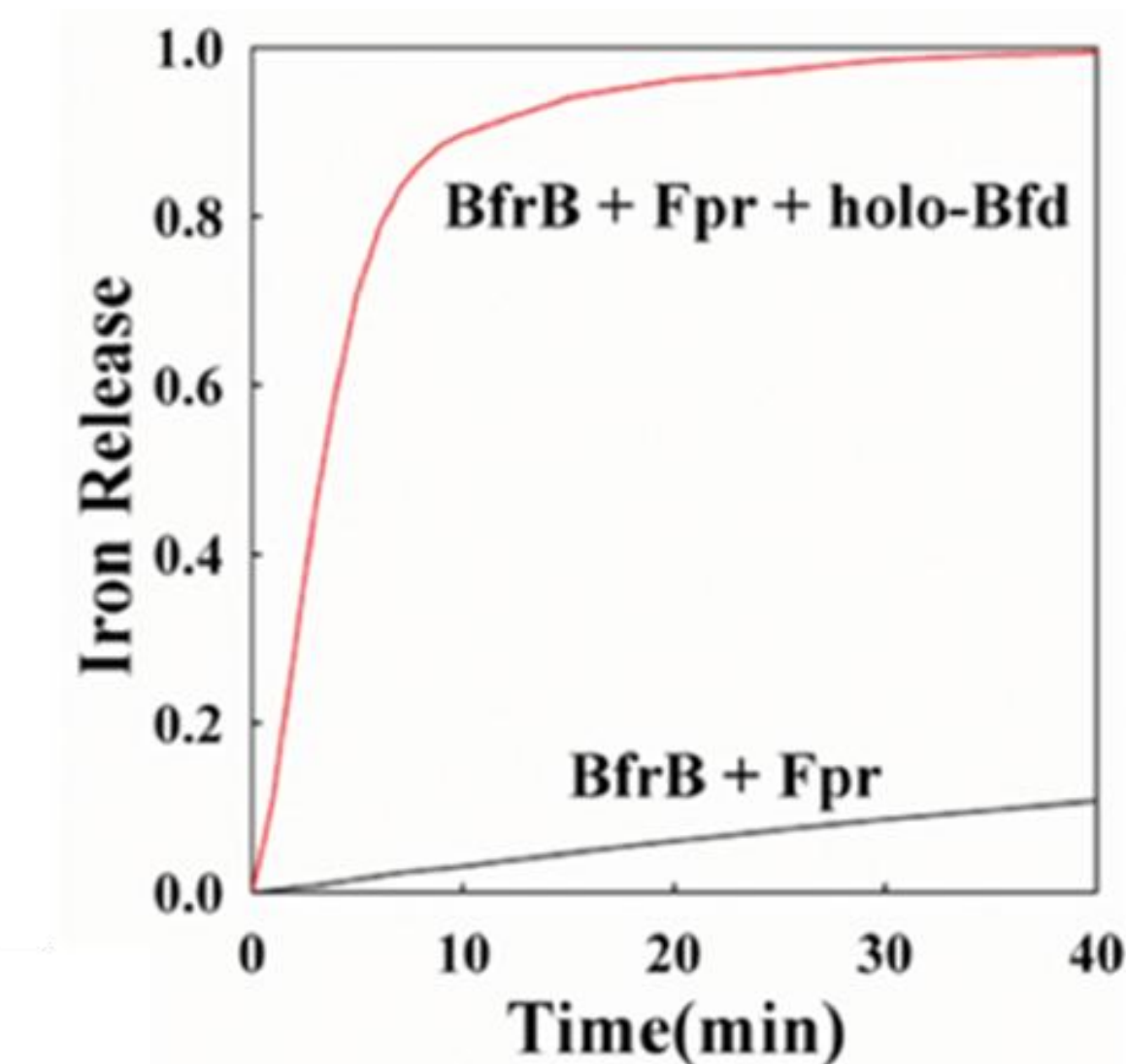


Real world example: Bacterioferritin (BfrB) from *Pseudomonas aeruginosa*

- Iron storage and mobilization
 - Bacterioferritin (Bfr): stores 3,000 Fe ions (Fe^{3+})
 - Fe^{2+} oxidation to Fe^{3+} in the ferroxidase center
 - BfrB subunit (18 kDa): 24 mer assembly
- Bacterioferritin-associated ferredoxin (bfd) binds to Bfr and reduces Fe ions in the core for mobilization

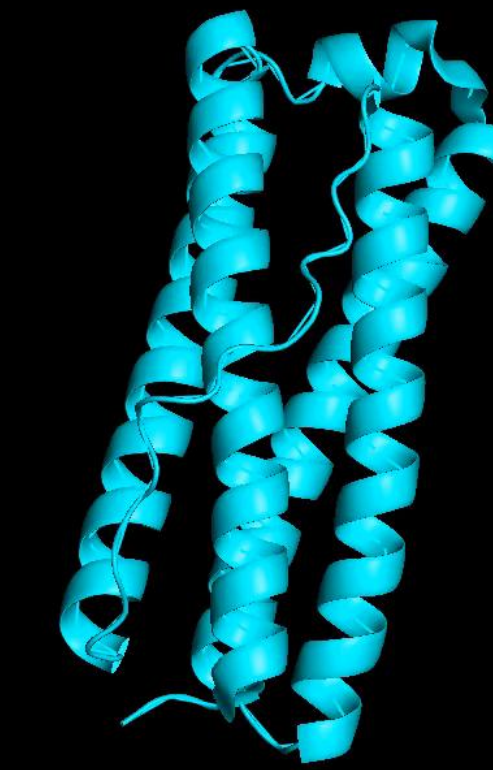


Weeraratunga, *etal.*, Biochemistry, 2010.



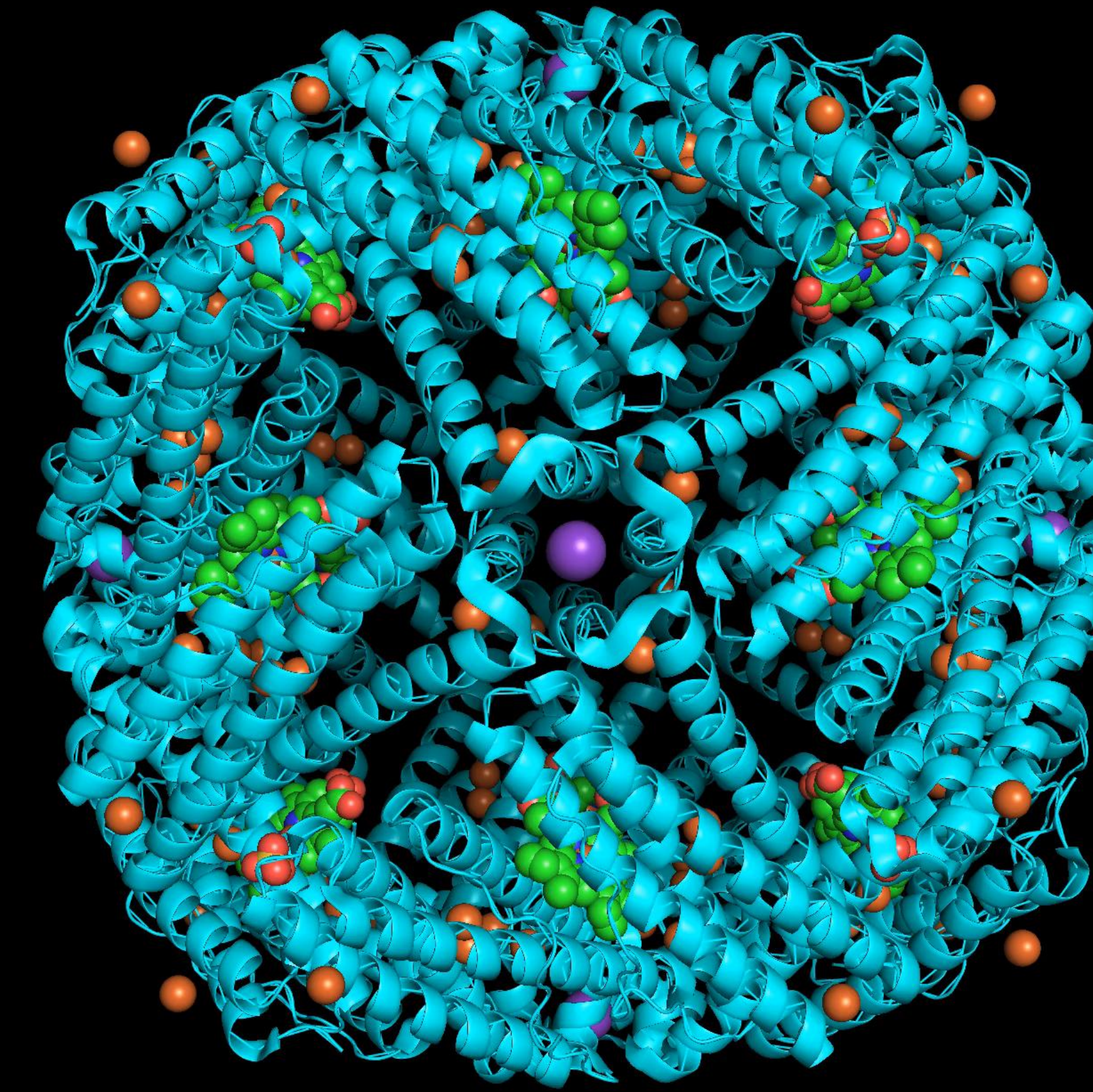
Bfr 24-mer Assembly

- Bfr dimerizes and binds a heme molecule
- The dimers assemble into a 24 meric structure
- The core has a ~90 Å diameter



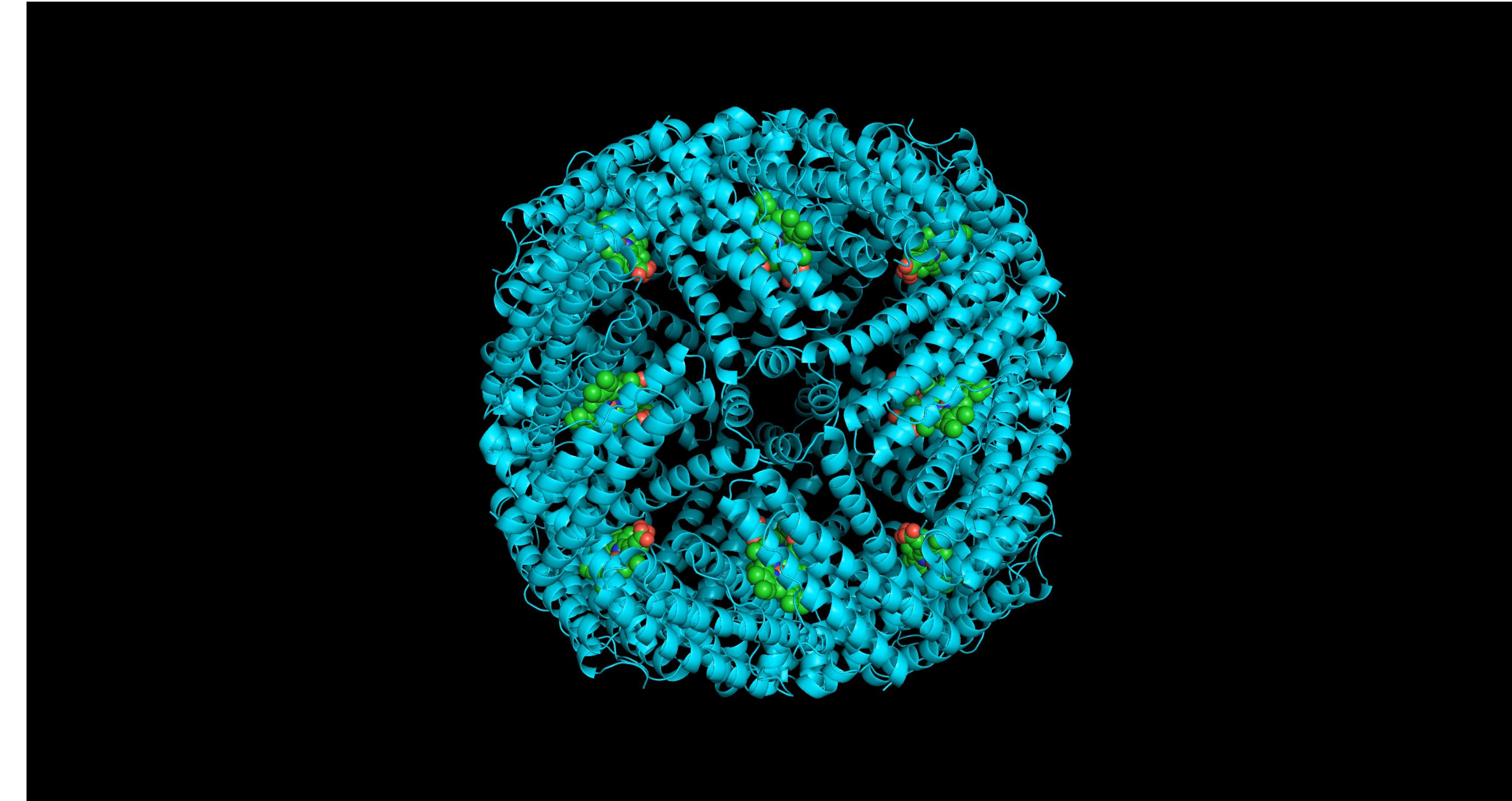
Bfr iron transport to the core

- Fe^{2+} bind to an external site coordinated by His residues
- The Fe^{2+} mobilizes to the ferroxidase center of each subunit where oxidation to Fe^{3+} occurs
- The iron ion then binds to a site at the interior before moving into the core



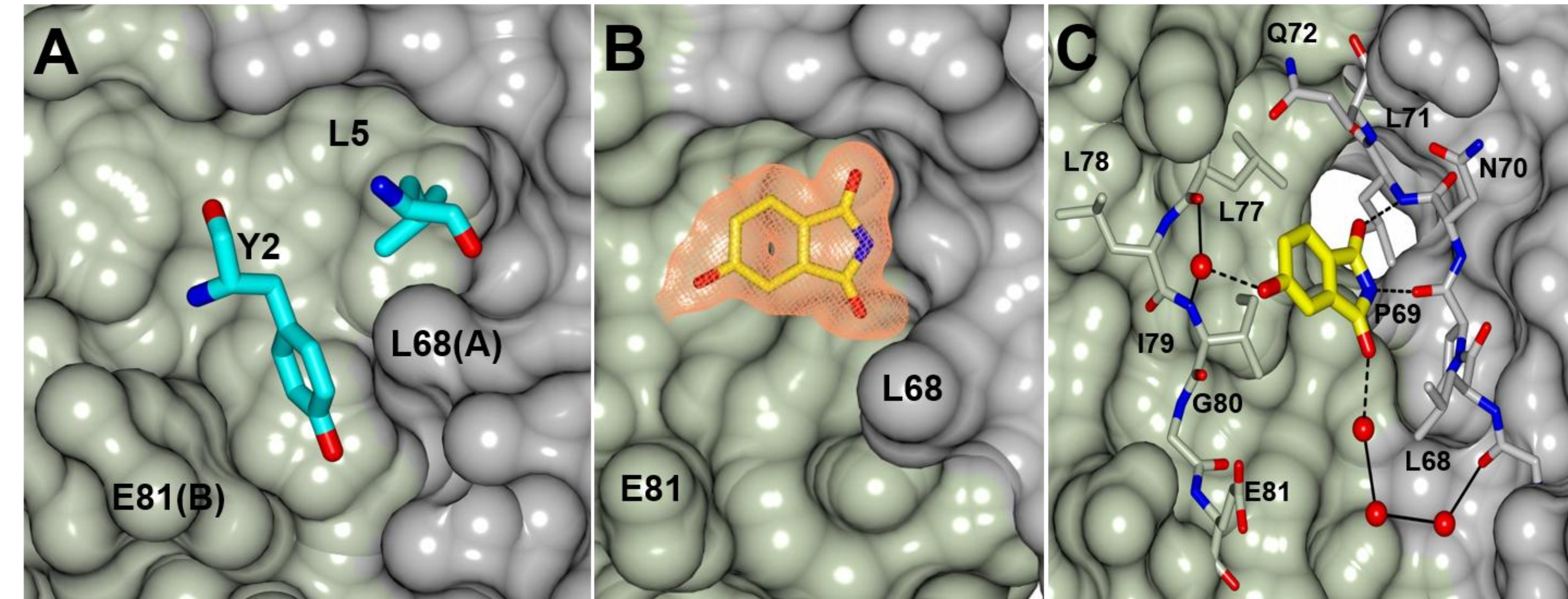
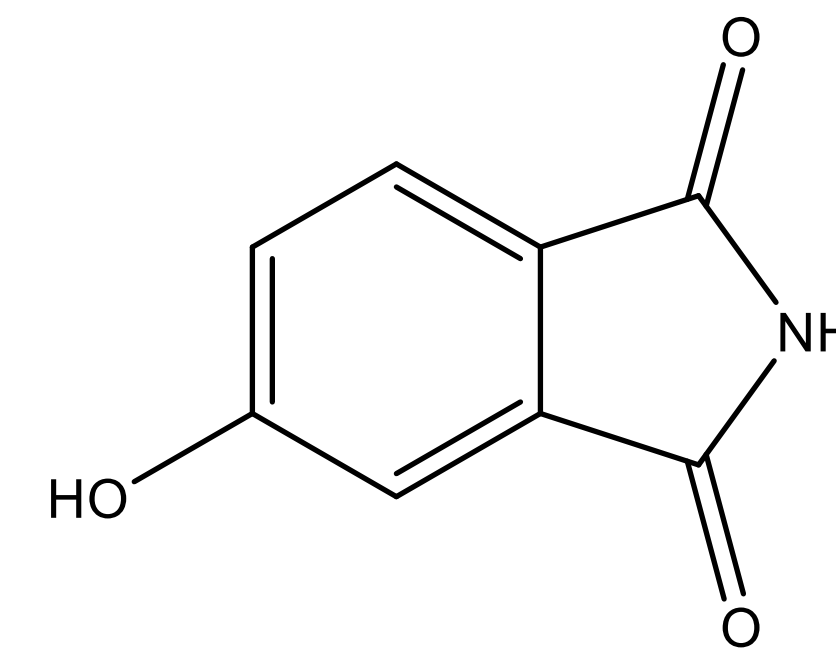
Bfr:Bfd protein complex

- Bacterioferritin associated ferredoxin (Bfd) binds to a pocket of Bfr
- Reduces Fe^{3+} to Fe^{2+} for mobilization
- Could the pocket be targeted for ligand binding



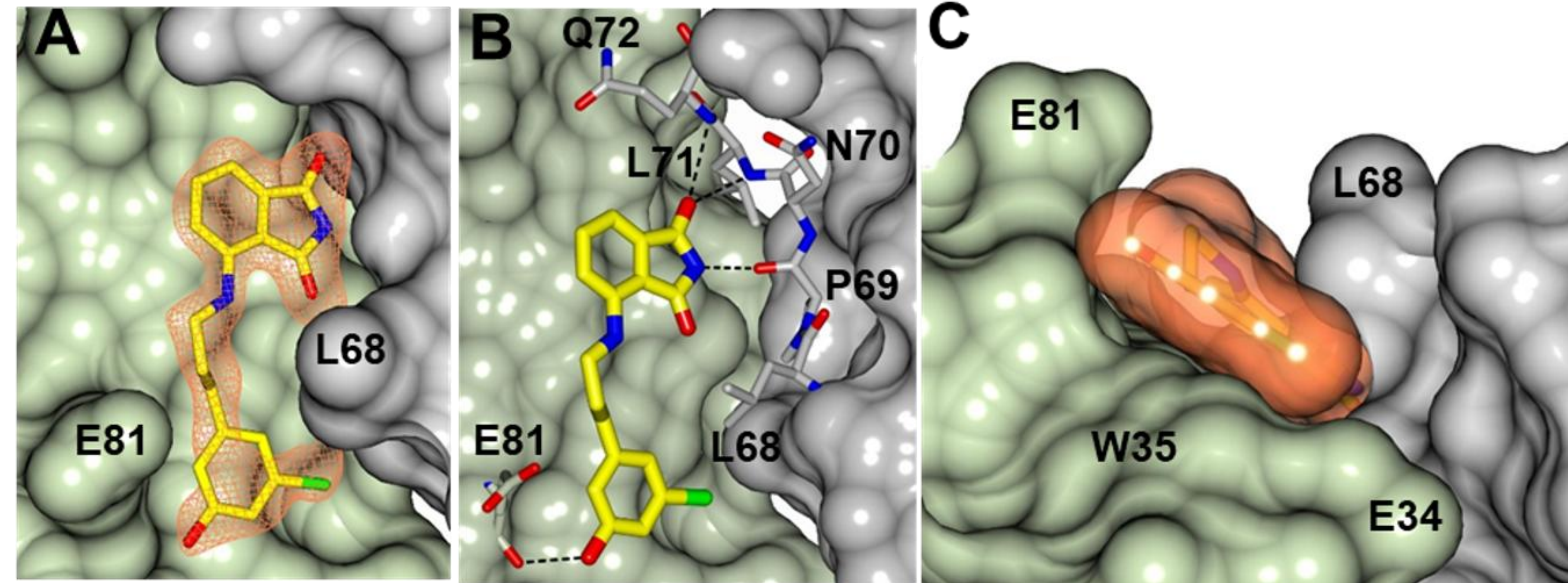
Computational design of Bfr:Bfd inhibitors

- Y2 of Bfd binds in a pocket formed by L68 and E81 of Bfr subunits in a dimer
- L5 of Bfd binds within a secondary pocket of the Bfr dimers.
- Computational screening (docking) of a virtual library identified 5-hydroxyphthalamide as a top hit



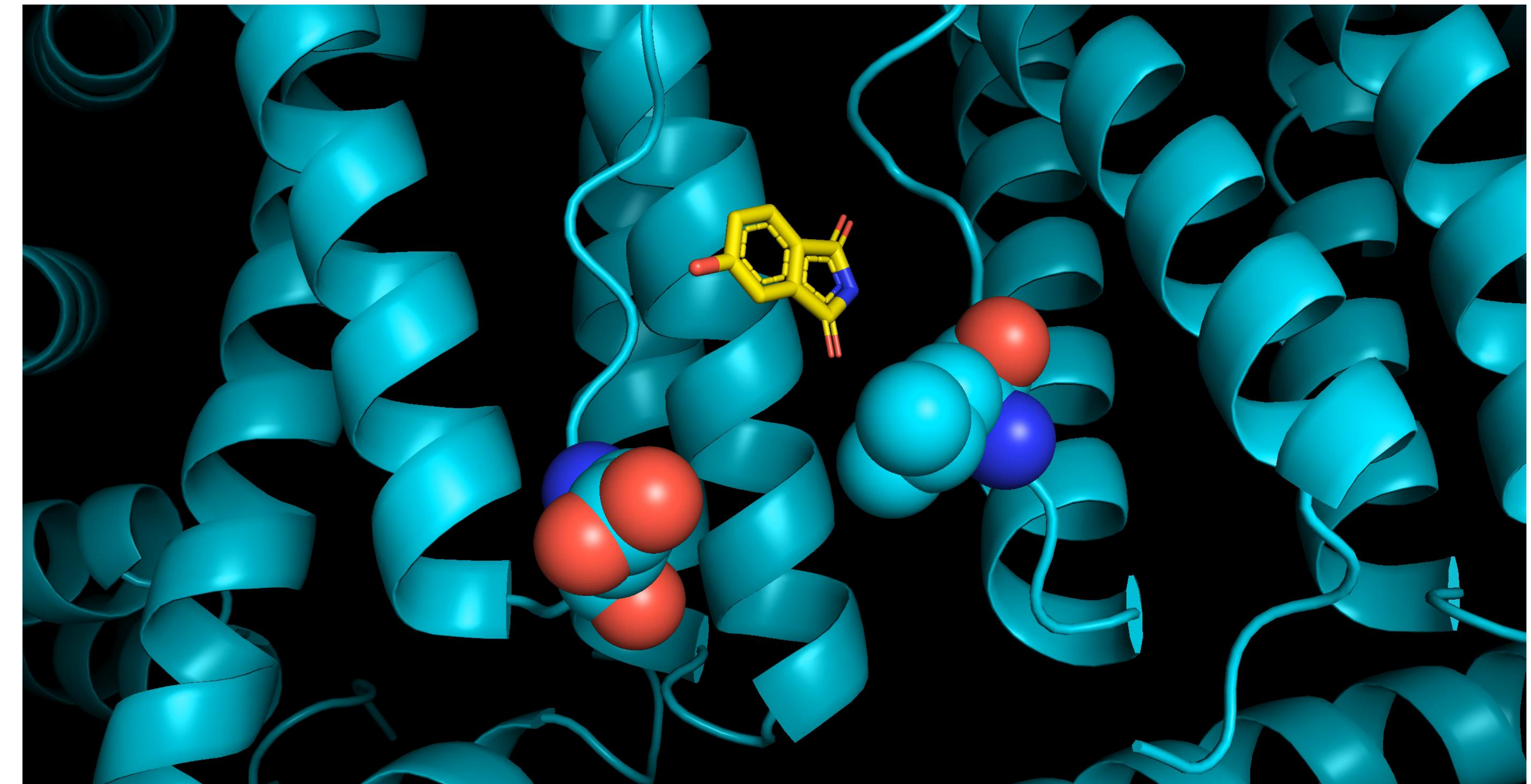
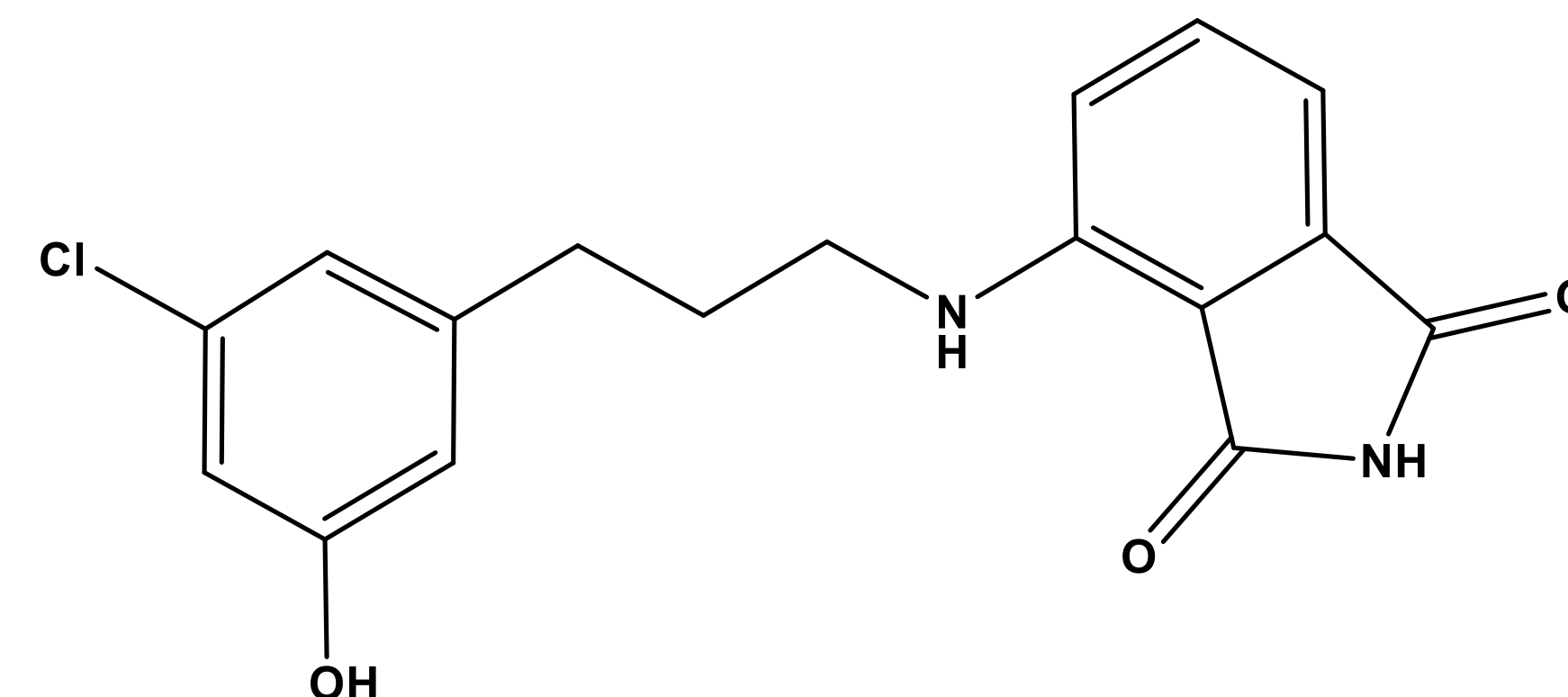
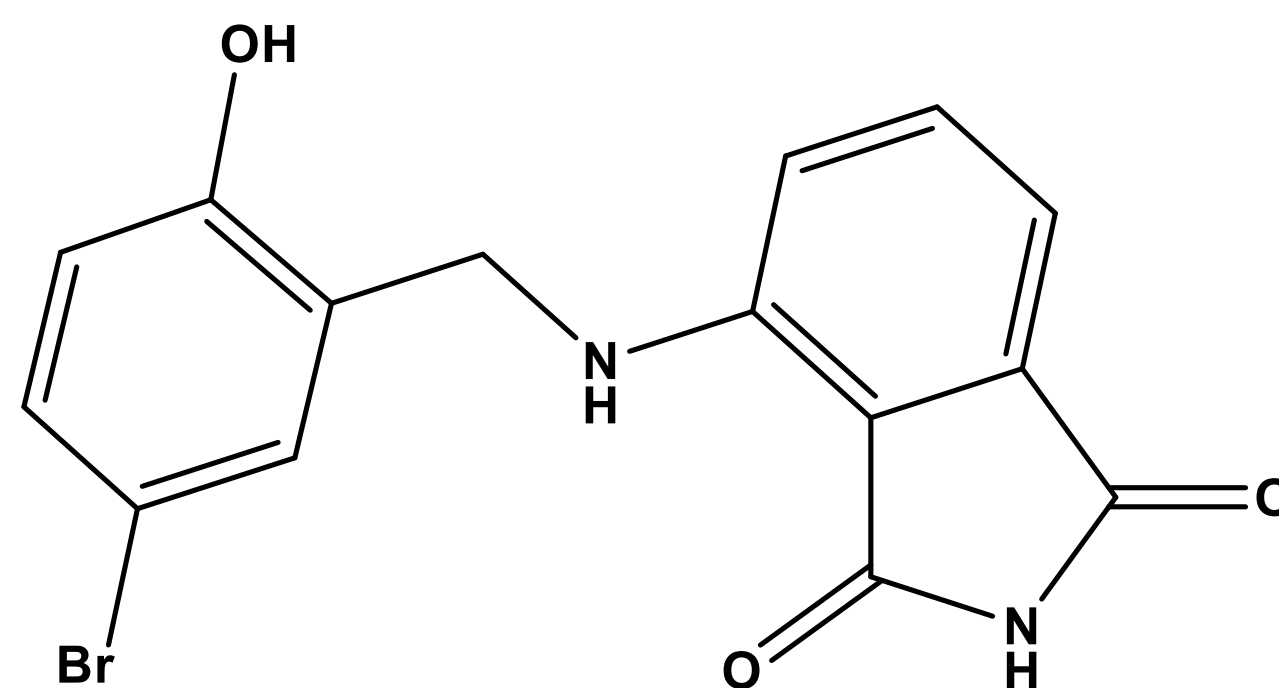
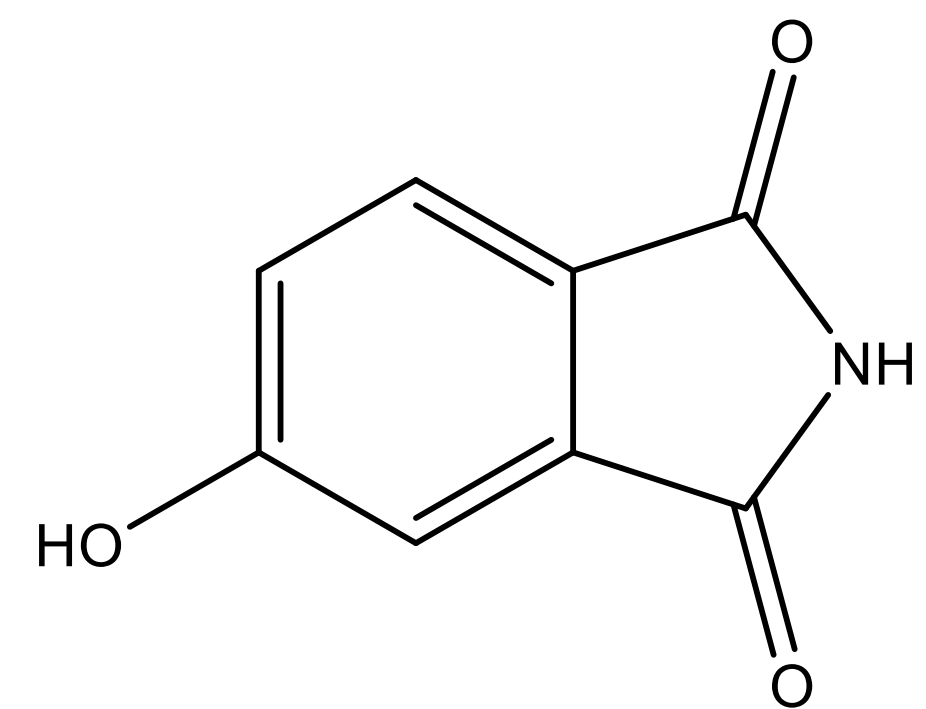
Using a computationally derived hit as the basis for inhibitor development

- Adding aryl ring substituents with 1 or 3 carbon linkers improves affinity (6 μ M)
- Aryl rings bind in the L68/E81 cleft and mimic Bfd binding



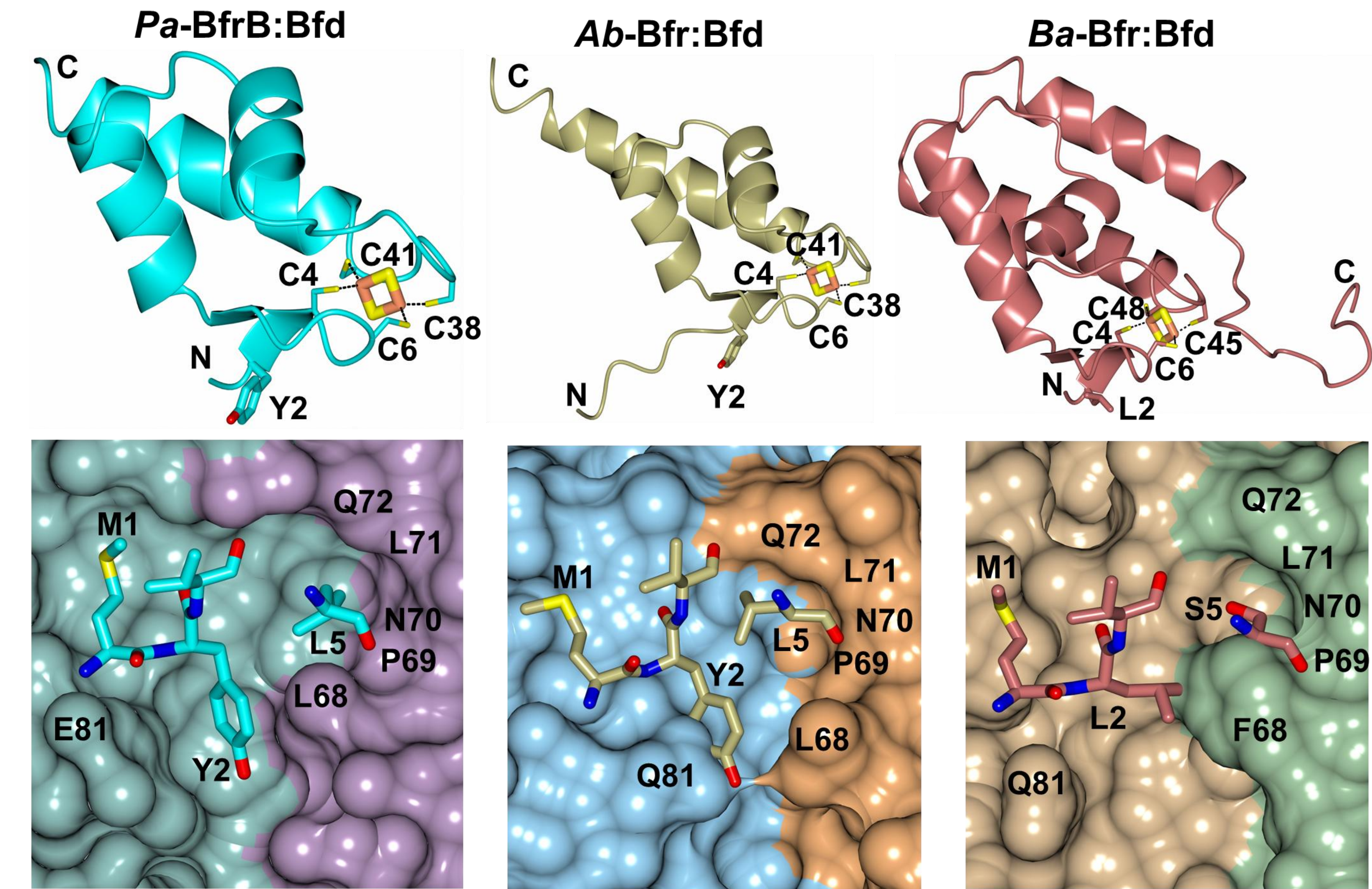
Expanding the computationally derived fragment to potent inhibitors

- The 5-hydroxyphthalimide served as the basis for inhibitor expansion into the aryl ring binding pocket.



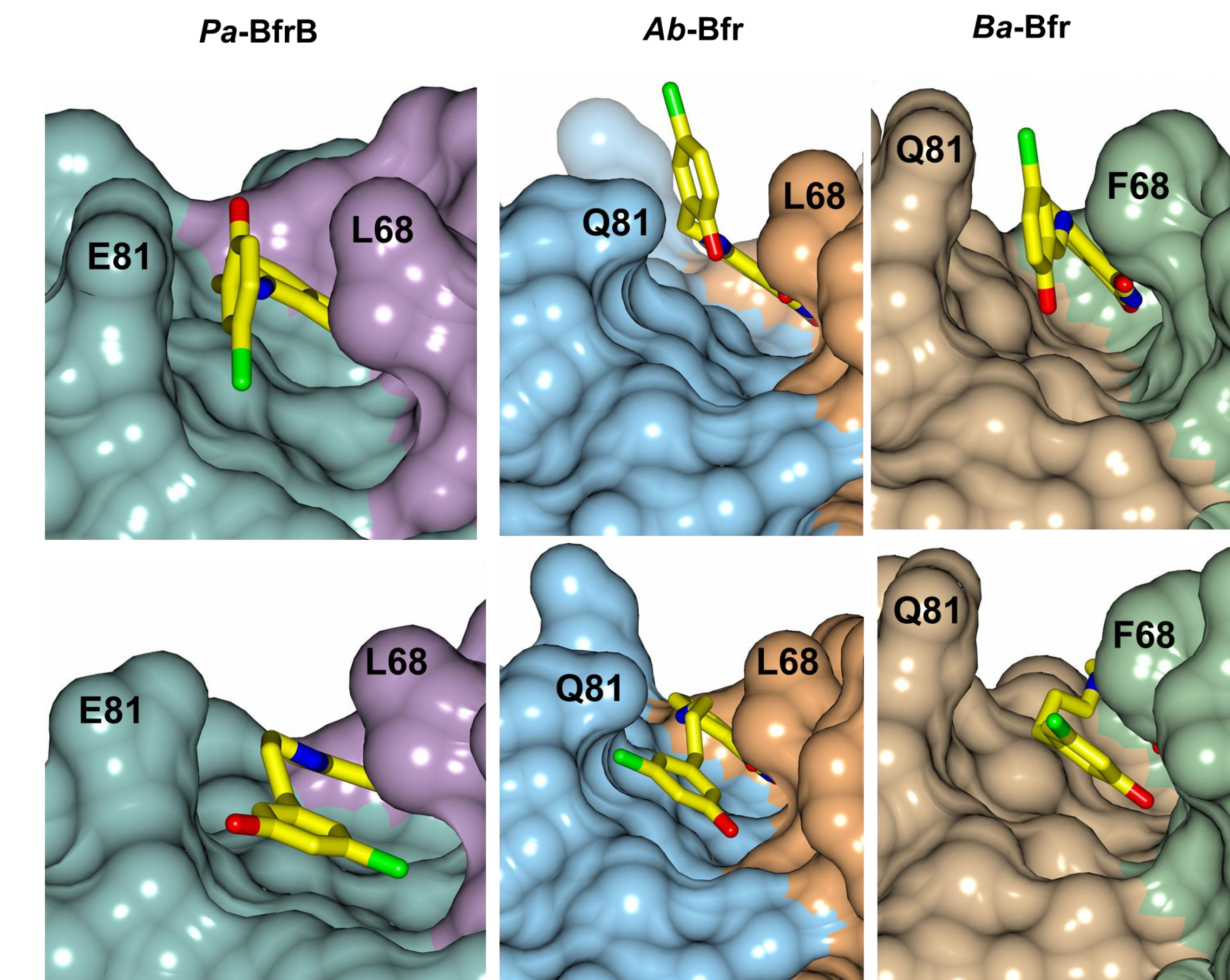
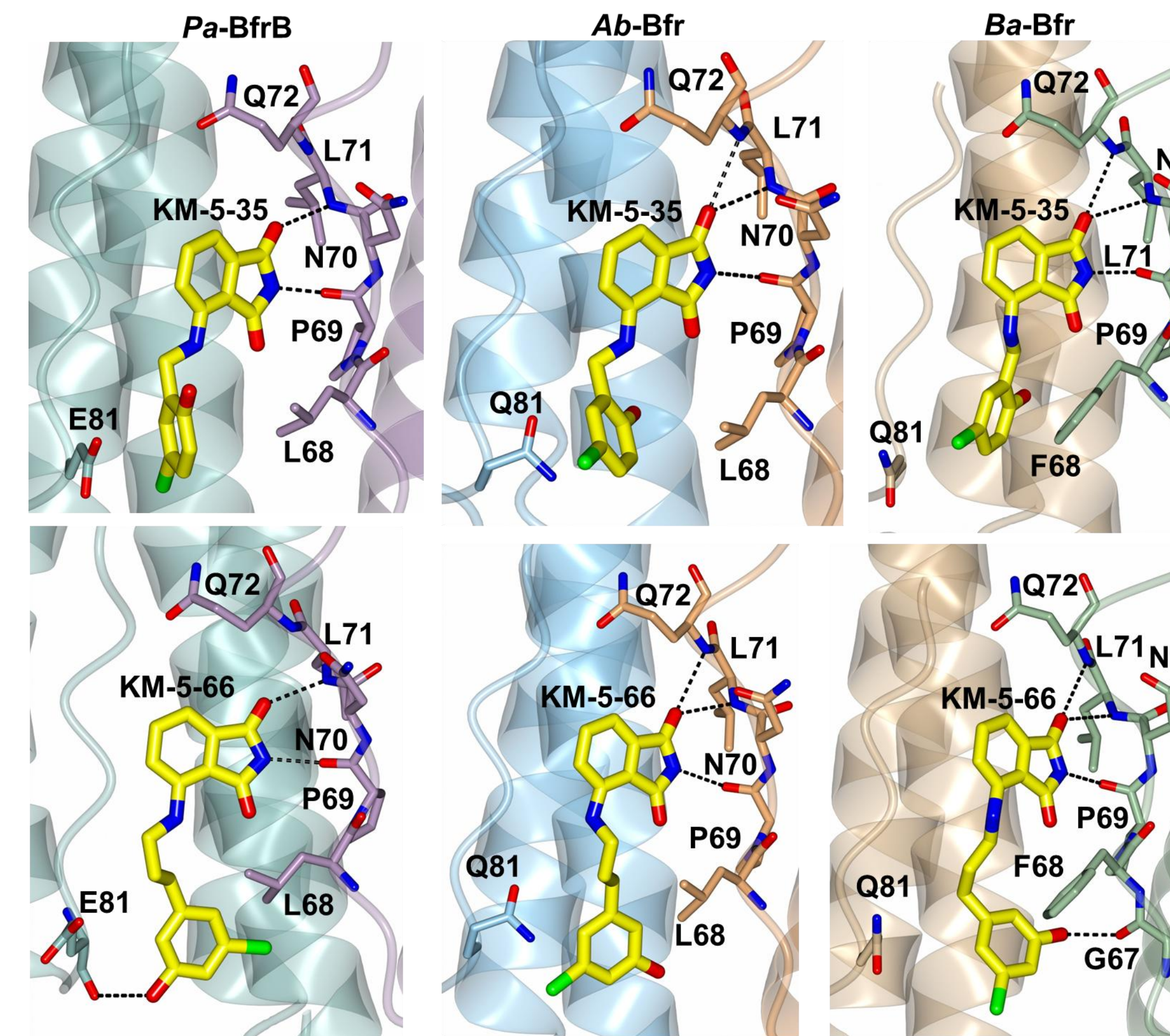
Modelling ligand binding in *Acinetobacter* and *Brucella* Bfr proteins

- The Bfd protein structures were modelled using alphafold 3 and fit to the *Acinetobacter* and *Brucella* Bfr crystal structures.
- Similar residues Y2/L5 (*Acinetobacter*) and L2/S5 (*Brucella*) bind to the pockets of each respective Bfr protein.



Docking *P. aeruginosa* inhibitors to *Acinetobacter* and *Brucella* Bfr proteins

- Inhibitors containing a 1 and 3-carbon linker between the phthalimide and aryl ring were docked in the Bfd binding pocket of each Bfr protein
- Similar binding modes are predicted

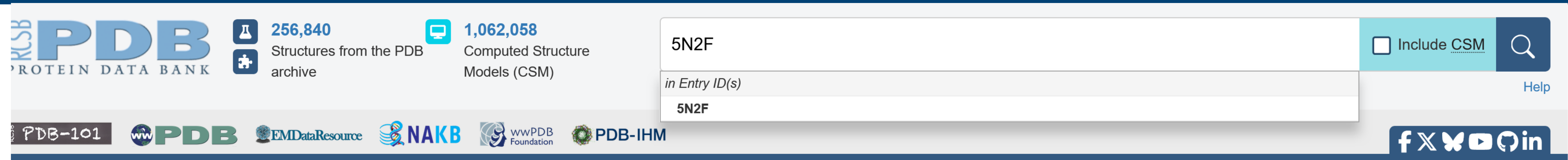


Applications for modelling protein:ligand complexes

- Alphafold 3: Allows modelling of select ligands (eg. NAD, ATP, heme, etc.). DNA, RNA and ions. Small list of ligands to select.
- Autodock vina: Stand alone software for various ligand modelling applications
- Swissdock: Online server that is user friendly. Upload protein and ligand files
- Pymol/docking pie: Separate plugin that provides various docking applications
- DiffDock: AI docking. Some web base interfaces but usually installed locally
- CB-Dock2: Web server based. Automated cavity detection and ligand docking
- Inputs: Need a protein coordinate file and some ligand description file

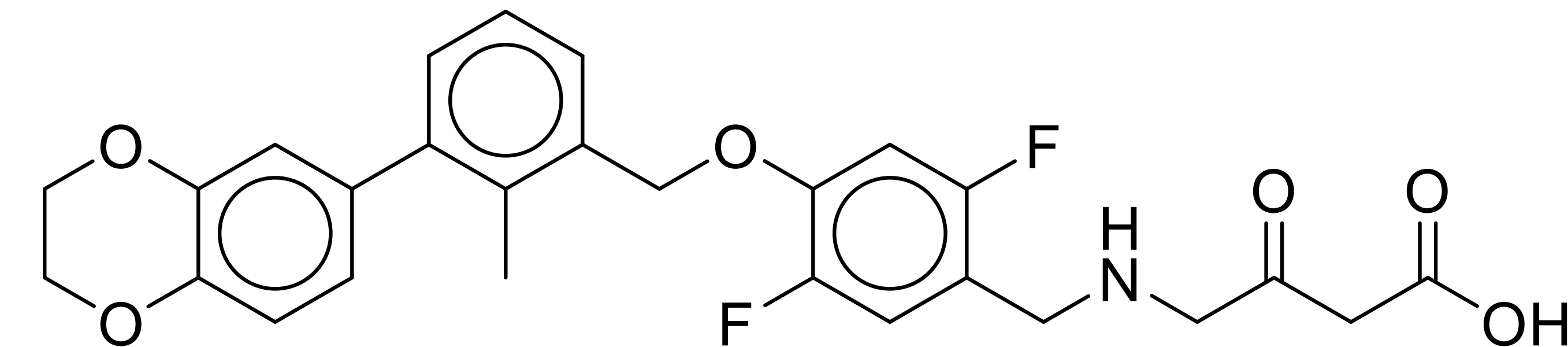
Protein structure file

- PDB file: Downloaded from <https://www.rcsb.org/> or <https://www.ebi.ac.uk/pdbe/>
 - Need the 4-letter code (e.g. 5N2F)
- Alphafold model
- Unpublished crystal structure



Ligand description file

- Structure data file (SDF): text-based coordinates
- Ligand PDB file



- Smiles string: Cc1c(COc2cc(F)c(CNCC(=O)CC(O)=O)cc2F)cccc1c3ccc4OCCOc4c3
- Can be downloaded from the PDB if the ligand is known. (3-letter code: eg. 8HW)
- ChemDraw: Ligands can be constructed and exported in these formats

Structure and ligand with Alphafold3

- The protein sequence is pasted and ligand selected for modelling.
- Output files containing the modeled ligand can be downloaded

AlphaFold Server allows you to model a structure consisting of many biological molecules [Learn more](#)

sequence

Entity type: Protein Copies: 1

SKISIIYKQSF	SFPRVSTAPV	IKNMQVEQTY	LMIKPDGIQR	QVVGEIISRF	EKRGYRIAAM
KLTIATPAIL	EEHYAEHKGK	PFLPGLIEKM	TGPVLCMVFE	GVDVIAQARK	MMGSTRPGEA
APGTIRADFC	QQAGRNLHG	SDSAESAKRE	ISLWFKPEEI	QSYKLALSDY	IFE

Entity type: Ligand Copies: 1

ATP – Adenosine triphosphate

[Save job](#)

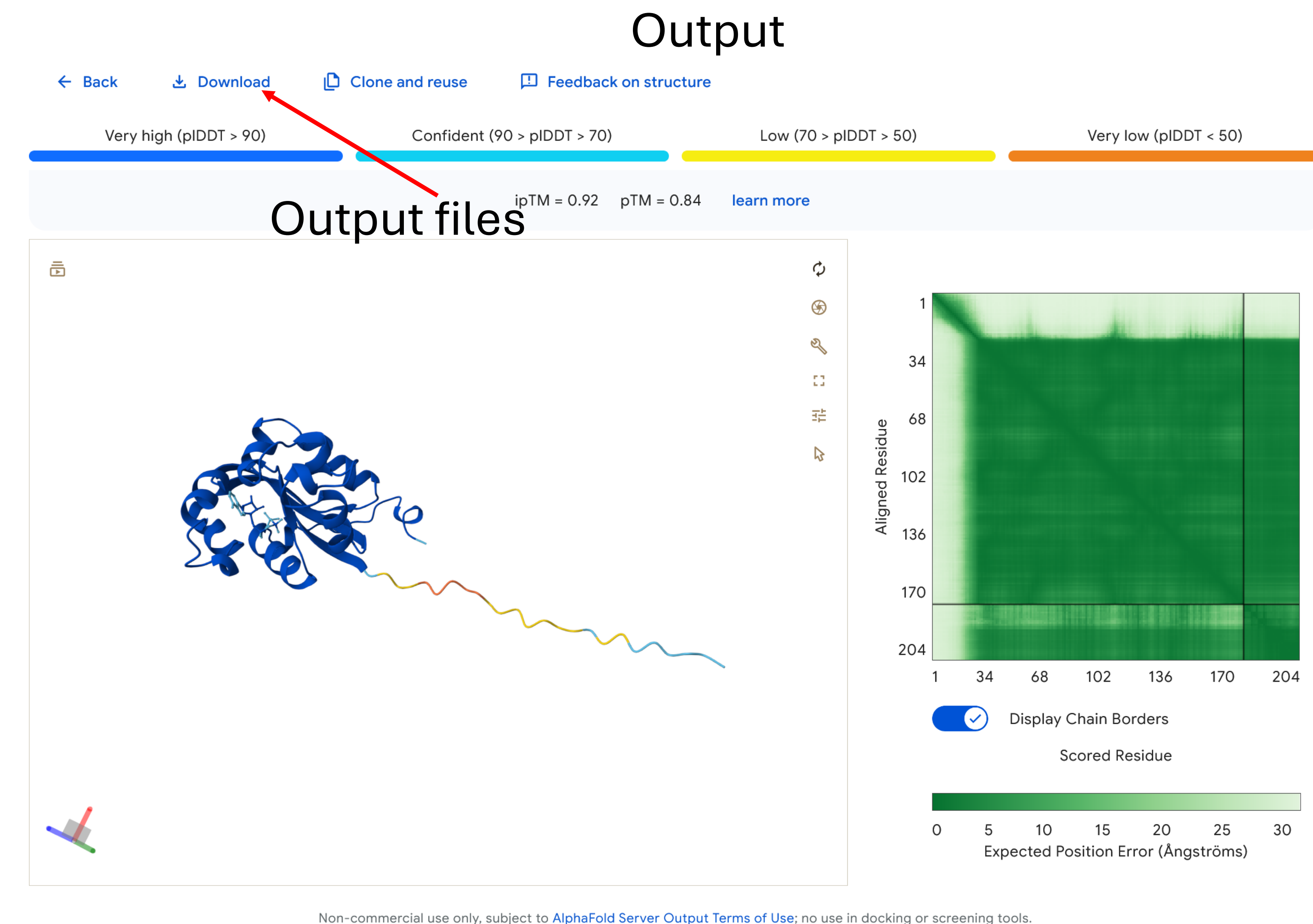
[Continue and preview job](#)

Search History

☒ Completed
 ☒ Saved draft
 ☒ In progress
 ☒ Examples
 ☒ Failed

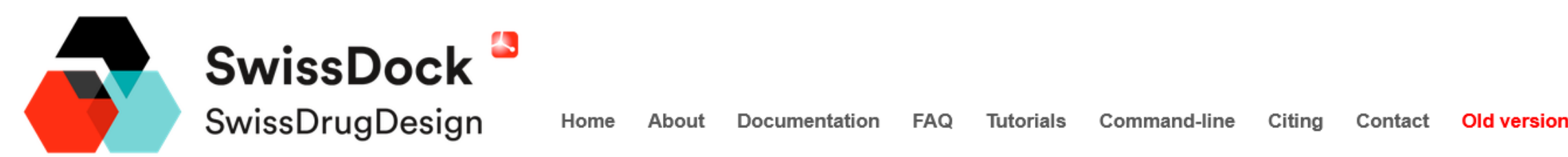
Name	Modified
☐ ☒ 2026-07-06_09:59	2026-07-06 10:02

Ligand selection



Swissdock

- Various options for ligand input
- Protein target added using PDB code or uploading your file
- The search space (grid) is chosen
- Output models can be viewed



Important information: Due to the discontinuation of ChemAxon support for academic websites, SwissDock has been modified to no longer rely on their software. We sincerely apologize for any inconvenience this transition may cause and thank our users for their understanding.



Don't know where to start? Try with an example: binding of **SNJ-1715 (CCD ID 0m6)** to **calpain-1 catalytic subunit (PDB ID 2g8e)**, of **WRR-99 (r99)** to **cruzipain (1ewl)**, or of **dabrafenib (p06)** to **B-Raf (5hie)**.

1 - Submit a ligand

Provide a SMILES

... or upload a Mol2 file or a PDBQT file

... or input, or modify, or check the molecule **using the sketcher**

... or use the **advanced search**

☒

2 - Submit a target

Provide a PDB id (e.g. 5hie)

... or upload a PDB file or a PDBQT file LemaA.18205.a.B2_AF-Q4QIU2-F1-model_v6.pdb

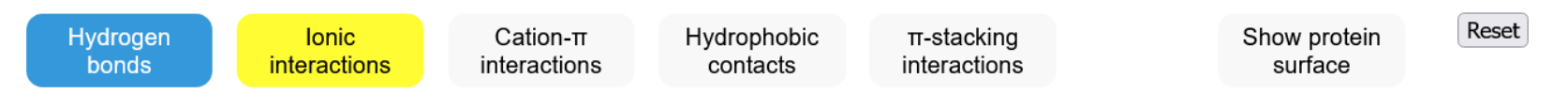
... or use the **advanced search**

☒

3 - Define search space

Search box center A

Search box size A



4 - Select parameters

Sampling exhaustivity

☒

This job is estimated to take 0:01:03 (h:mm:ss).

5 - Start docking

Enter an email (optional)

Enter a docking name (optional)

Query

Ligand N[C@@H](CCSC[C@H]1O[C@H]([C@H](O)[C@@H]1O)n2cnc3c(N)ncnc23)C(O)=O

Target LemaA.18205.a.B2_AF-Q4QIU2-F1-model_v6.pdb

Method AutoDock Vina

Date July 6, 2026, 5:21 pm UTC

Parameters:

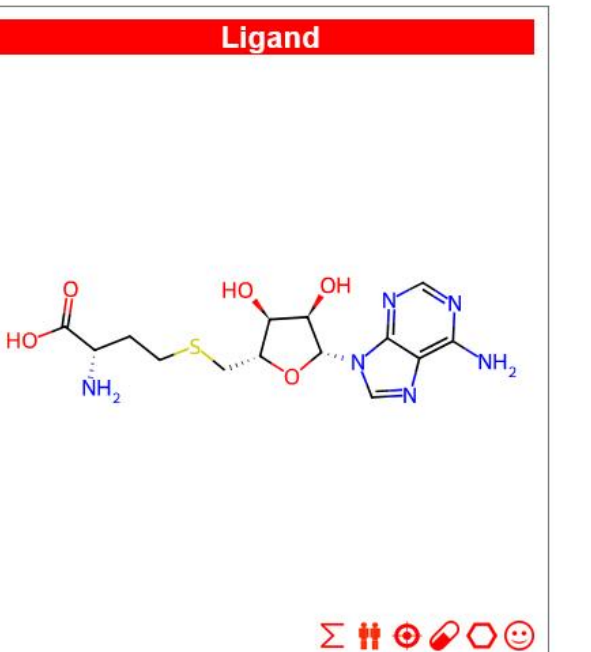
Box center: 11 - 12 - -4 Sampling exhaustivity: 4

Box size: 22 - 22 - 22

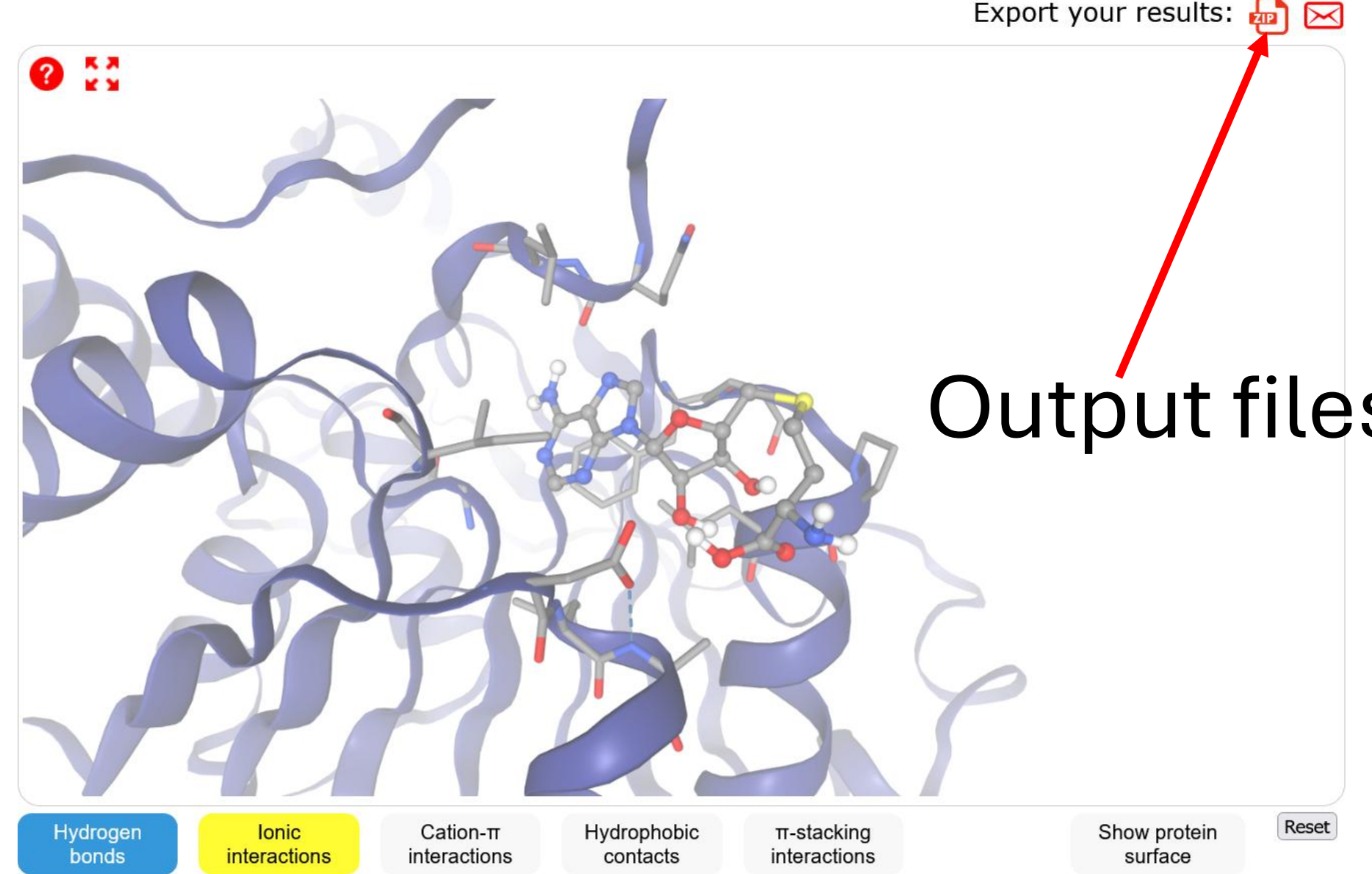
If you publish these results, please, cite the following papers:

Bugnon M, Röhrig UF, Goullieux M, Perez MAS, Daina A, Michielin O, Zoete V. SwissDock 2024: major enhancements for small-molecule docking with Attracting Cavities and AutoDock Vina. *Nucleic Acids Res.* 2024

Eberhardt J, Santos-Martins D, Tillack AF, Forli S., AutoDock Vina 1.2.0: New Docking Methods, Expanded Force Field, and Python Bindings. *J. Chem. Inf. Model.*, 2021



Results



Output files

Model	Calculated affinity (kcal/mol)
1	-5.190
2	-5.001
3	-4.873
4	-4.870
5	-4.797

CB-Dock2

- Protein and ligand files are uploaded and prepared automatically
- Cavities are detected
- Docking within the detected cavities


CB-Dock2
 Cavity-detection guided Blind Docking

[Home](#)
[Dock](#)
[Example](#)
[Manual](#)
[Contact](#)

Upload Protein
 Select a protein file (pdb format) [Example: MDM2.pdb (PDB: 4HG7)] [Submitted Protein: LemaA.18205.a.B2_AF-Q4QIU2-F1-model_v6_N-truncated.pdb]

ATOM	368	CZ	ARG	A	49	-9.247	-24.586	-7.491	1.00	69.06	C
ATOM	369	N	GLU	A	50	-9.424	-16.735	-7.830	1.00	86.38	N
ATOM	370	CA	GLU	A	50	-8.861	-15.714	-8.699	1.00	86.38	C
ATOM	371	C	GLU	A	50	-8.676	-16.322	-10.091	1.00	86.38	C
ATOM	372	CB	GLU	A	50	-7.534	-15.229	-8.104	1.00	86.38	C
ATOM	373	O	GLU	A	50	-8.219	-17.461	-10.215	1.00	86.38	O
ATOM	374	CG	GLU	A	50	-7.782	-14.518	-6.770	1.00	86.38	C
ATOM	375	CD	GLU	A	50	-6.503	-14.106	-6.048	1.00	86.38	C
ATOM	376	OE1	GLU	A	50	-6.607	-13.157	-5.247	1.00	86.38	O
ATOM	377	OE2	GLU	A	50	-5.465	-14.788	-6.118	1.00	86.38	O
ATOM	378	N	LEU	A	51	-9.103	-15.593	-11.117	1.00	88.56	N

Remove file

Upload Ligand
 Select a ligand file (mol2, mol, sdf, pdb format) [Example: Nutlin-3a.sdf] [Submitted Ligand: SAH_ideal.sdf]

Upload Local Draw Ligand

SAH
 CCTOOLS-0920241012
 46 48 0 0 1 0 0 0 0 0999 V2000
 0.6630 0.7420 6.8430 N 0 0 0 0 0
 -0.6680 0.5580 6.2510 C 0 0 0 0 0
 -0.5530 -0.3150 5.0000 C 0 0 0 0 0
 0.3650 0.3650 3.9850 C 0 0 0 0 0
 0.5810 -0.6690 2.5810 S 0 0 0 0 0
 -1.5730 -0.1120 7.2510 C 0 0 0 0 0

Remove file

More parameters
 Other customizable parameters

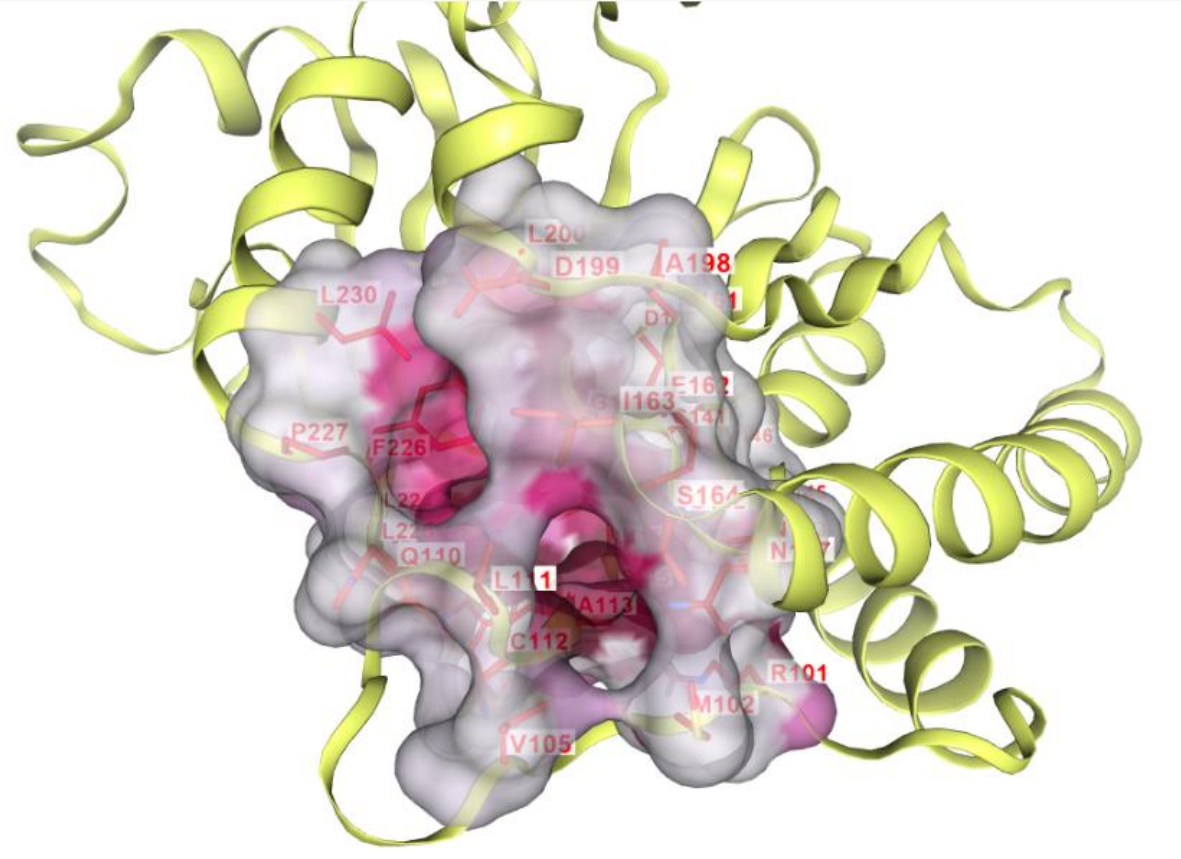
Enter your email address to receive the results (optional)

[Search Cavities](#)
[Auto Blind Docking](#)


 Structure-based cavity detection

Detected pockets from the input structure (Submitted Protein: LemaA.18205.a.B2_AF-Q4QIU2-F1-model_v6_N-truncated.pdb)
 Tips: Click the table below to view the pocket information. Select the checkbox in the table below to mark the pockets you are interested in for blind docking. Click the residue in the sequence list to view the residue you are interested in.

Query
 A VTPRE LGSGSPHDPI HPLRLTPNG SGCYHCTEE CCCVEFEKIL SNTYARVPKK RIVE SGARQ LCAKSL LTPF VTRLRLMNI TEKDFY F5 CGN6SVLFQV AFMTGAKCVG VEISEH AD
 170.....180.....190.....200.....210.....220.....230.....240.....250.....260.....270.....280.....
 V AREAWQLLRQ VLEKQYDRPM PRVEIITADL AELLSTPTVF DEEEGQTAIL HSNLLFFKPL THFLSERLRS APVGTILCF DDLYPHARSV ASYRDPGAFE LFEMKDYFWQ EMSVECSM
 290.....
 E GRFFIHTRK



CurPocket ID	Cavity volume (Å³)	Center (x, y, z)	Cavity size (x, y, z)
⊙ C1	1537	-1, 12, -3	19, 17, 15
○ C2	691	-14, 1, 4	13, 15, 9
○ C3	211	7, 3, -20	10, 12, 13
○ C4	151	-18, -17, -3	7, 6, 8
○ C5	81	16, 2, 6	8, 5, 4

[Download CurPockets](#)

Center Fullscreen Show Surface Hide Pocket Hide Label

Docking at the selected pockets
 Tips: Select the checkbox in the table above to mark the pockets you are interested in for blind docking.

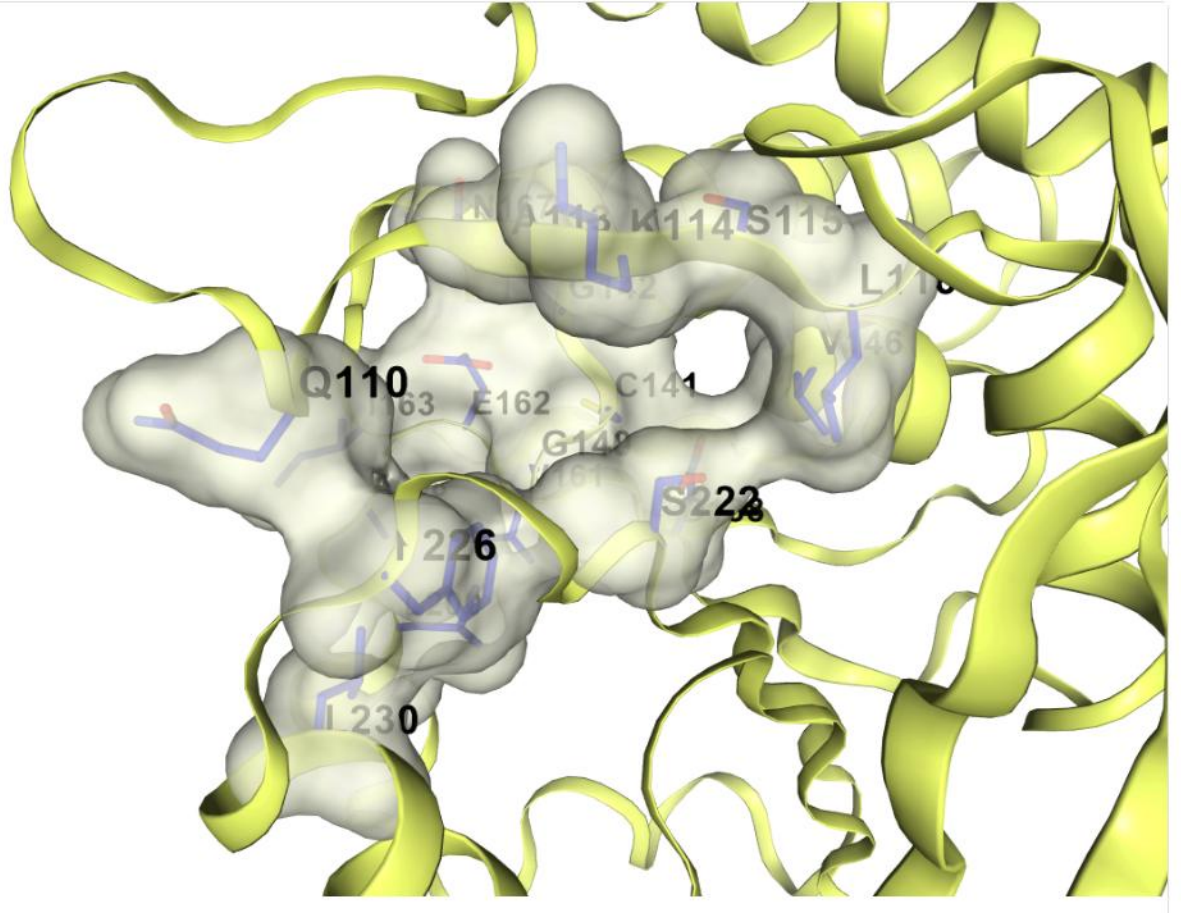
Submitted Protein LemaA.18205.a.B2_AF-Q4QIU2-F1-model_v6_N-truncated.pdb
 Submitted Ligand SAH_ideal.sdf
 Selected CurPockets ☒ C1 ☒ C2 ☒ C3 ☐ C4 ☐ C5
[BlindDock](#)


 Template-based cavity detection

Detected pockets from referring homologous proteins (Submitted Protein: LemaA.18205.a.B2_AF-Q4QIU2-F1-model_v6_N-truncated.pdb)
 Tips: Click the table below to view the pocket information. Click the residue in the sequence list to view the residue you are interested in.

8fjm
 B --KGELGAGT PHEPYNLPLR GNPNGSGCH CLADQCHCVF FERLLDATFR RLDIKR-----5 LPTFVSRMV RLMEITSEDY FYD6CGNGS ILFQVAFLTG ARCVGTEISE HNAKVAK
 ..171.....181.....191.....201.....211.....221.....231.....241.....251.....261.....271.....281.....
 KAW EVIRPELEGS SGRSMSEVNI ITSDMTKILA DERLFESERG KTVILLNLL FPKSTHYLS ERFRRVPSGT RILCFDDLVP HRSVAIAIRD PEAFRLFAMT DYRWQECVSVE WCTRDGPF
 .291....
 FI HRRR

Query
 A VTPRELGS GS PHDPIHLPLR RTPNGSGCYH CTTEECCEVE FEKILSNTYA RVPKKRMVEV SGARQLCAKSL LTPFVTRLV RLNMITEKDT FYD6CGNGS ILFQVAFMTG AKCVGTEISE HADVA
 ..175.....185.....195.....205.....215.....225.....235.....245.....255.....265.....275.....285.....
 REAW QLLRQVLEKK YDRPMRVEI ITADLAELLS TPTYFDEEG QTAILSNLL FPKPTHYLS ERLRSAPVGT RILCFDDLVP HARSVASYRD PGAFELFEMK DYFWQEMSVE WCSMEGR
 ..295....
 FFI HTRK



FitPocket ID	Template ID	Template Protein	Template Ligand	FP2	Pocket Identity	Pocket RMSD	Co
⊙ F1	t1	8fjm	SAH	1.0	0.73	0.46	C1

Center Fullscreen Show Surface Hide Pocket Show Template(Pro) Show Template(Lig)

Hide Label

Docking with homologous protein complex guidance

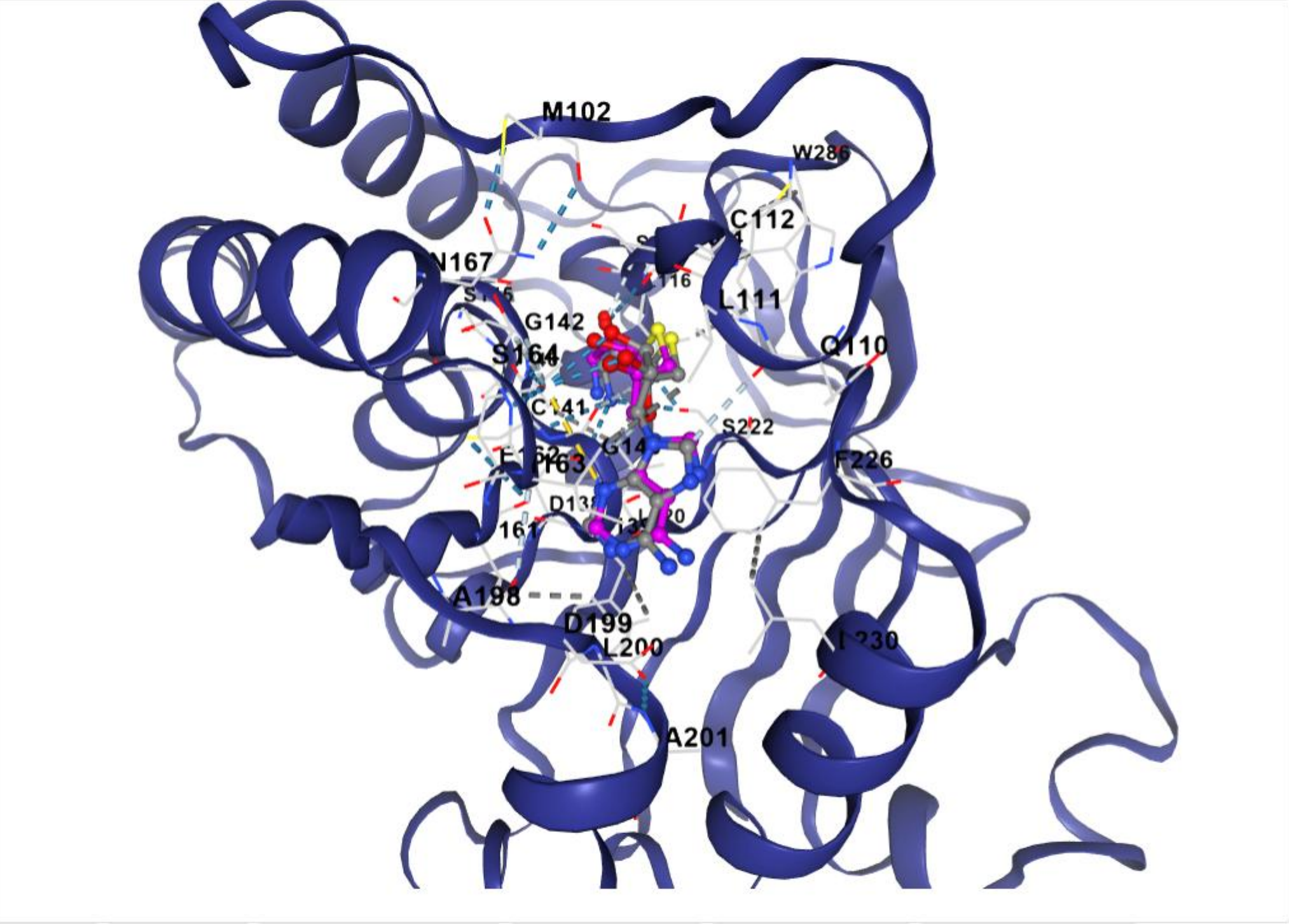
Submitted Protein LemaA.18205.a.B2_AF-Q4QIU2-F1-model_v6_N-truncated.pdb
 Submitted Ligand SAH_ideal.sdf
 Detected FitPockets 1
[Template-based Docking](#)

CB-Dock2 Results

- Interactive analysis of the ligand modelling
- A PDB file containing the protein:ligand can be downloaded

☑ Docking with homologus protein complex guidance

Submitted Protein LemaA.18205.a.B2_AF-Q4QIU2-F1-model_v6_N-truncated.pdb	Submitted Ligand SAH_ideal.sdf	Detected FitPockets 1	Hide
---	---	--------------------------	----------------------



FitPocket ID ⓘ	FitDock 1⚙ score	Template 1⚙ ID	Contact residues	Download
⦿ F1	-7.2	t1	View	Ligand [MOL2] , [PDB] Protein-Ligand [PDB]

Center Fullscreen Hide Template(Lig) Ligand Style ▾ Color Ligand ▾ Receptor Style ▾
Color Receptor ▾ ⚙ 📷 ?

Output files

DiffDock-L though Neurosnap website

- Fee for use (credits)
- Various computational applications

Use DiffDock-L

Official Neurosnap webserver for accessing DiffDock-L online.

Ligand/Drug Design & Screening

Molecular Docking & Interactions

Affinity Prediction

Protein-Ligand Docking

Virtual Screening

Overview

Features

Statistics

API Example

Similar

Video Tutorials

Overview

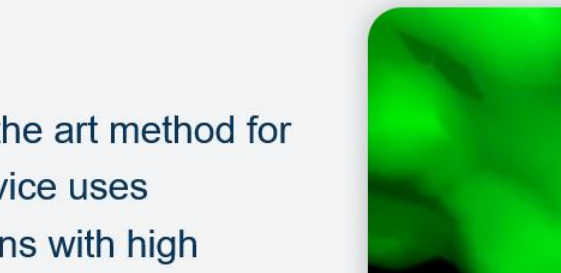
DiffDock-L is the newer and better version of DiffDock, a state of the art method for molecular docking and drug binding structure prediction. This service uses DiffDock-L and AutoDock VINA to predict protein-ligand interactions with high accuracy.

Neurosnap Overview

The DiffDock-L online webserver allows anybody with a Neurosnap account to run and access DiffDock-L, no downloads required. Information submitted through this webserver is kept confidential and never sold to third parties as detailed by our strong [Terms of Use](#) and [Privacy Policy](#).

View Paper

How To Use



✓

Add Structures (1/1)



Upload protein structures by clicking here or dragging and dropping your files

✓

Successfully added entry with file name "5n2f_protein_only.pdb".

Structure Restrictions:

- Supported file formats: .pdb
- Maximum allowed models per file: 1
- Minimum allowed chains per structure: 1
- Maximum allowed chains per structure: 50
- Minimum allowed sequence length per structure: 5
- Maximum allowed sequence length per structure: 2048
- Residue gaps are NOT allowed
- Nucleotides are automatically removed and should ideally be removed to prevent ambiguities
- Non-biopolymer small molecules such as ligands are automatically removed and should ideally be removed to prevent ambiguities
- Water molecules are automatically removed and should ideally be removed to prevent ambiguities

5n2f_protein_only

Models: 1 | Chains: A, B | Residues: 250 | Atoms: 2000 | Explicit Bonds 0

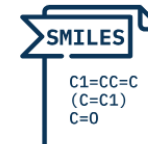






Upload Small Molecules

 Upload SDF or PDB files

 Enter SMILES or CCD codes

 Database Search (PubChem)

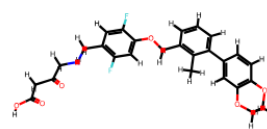
✓ Successfully added entry to list.

Upload your small molecule as a file. Note that some tools also support PDB files which then are automatically converted to an equivalent SDF formatted file. These PDB files should be monomeric unless specified otherwise.

Supported file extensions for uploads include: .sdf.

 Upload small molecule structure(s) by clicking here or dragging and dropping your files

Added molecules (1/1)



Uploaded File: 8HW_ideal.sdf







Molecular Summary: Atoms: 61 | Bonds: 64
Molecular Weight: 497.16499 Da
Canonical SMILES: [H]OC(=O)C([H])([H])C(=O)C([H])([H])N([H])C([H])([H])c1c([H])c(F)c(OC([H])([H])c2c([H])c(...

DiffDock-L output

- Results contains 100 ligand models ranked from top to bottom score
- Ligand poses can be viewed through a graphic interface
- Download all or selected models

Visuals

Explore the job's output with interactive plots, charts, and other visualization tools.

Sequence of /api/job/file/6... Chain 1: Polymer 1 (/... A

10 20 30 40 50 60 70 80 90 100 110 120 130

AFTVTVPKDLVVEYGSNMTIECRFPVEKQLDLAALIVTWEMEDRNIIQFVHGEEELRVQHSSTYRQARLLLDQLSLGNAALQITTVKLQDAGVYRCMLSYGGADYKRITVKVNAFYAAALEHHH

Show Best

Show Top 5 Best

Show Top 10 Best

Show Top 25 Best

Show All (max 250)

Structure Tools

Structure

2 structures

Nothing Focused

Quick Styles

Apply Representation

Default Cartoon Spacefill Surface

Apply Style

Default Illustrative

Components

2 structures

Preset + Add

Polymer Cartoon

All Ball & Stick

Measurements

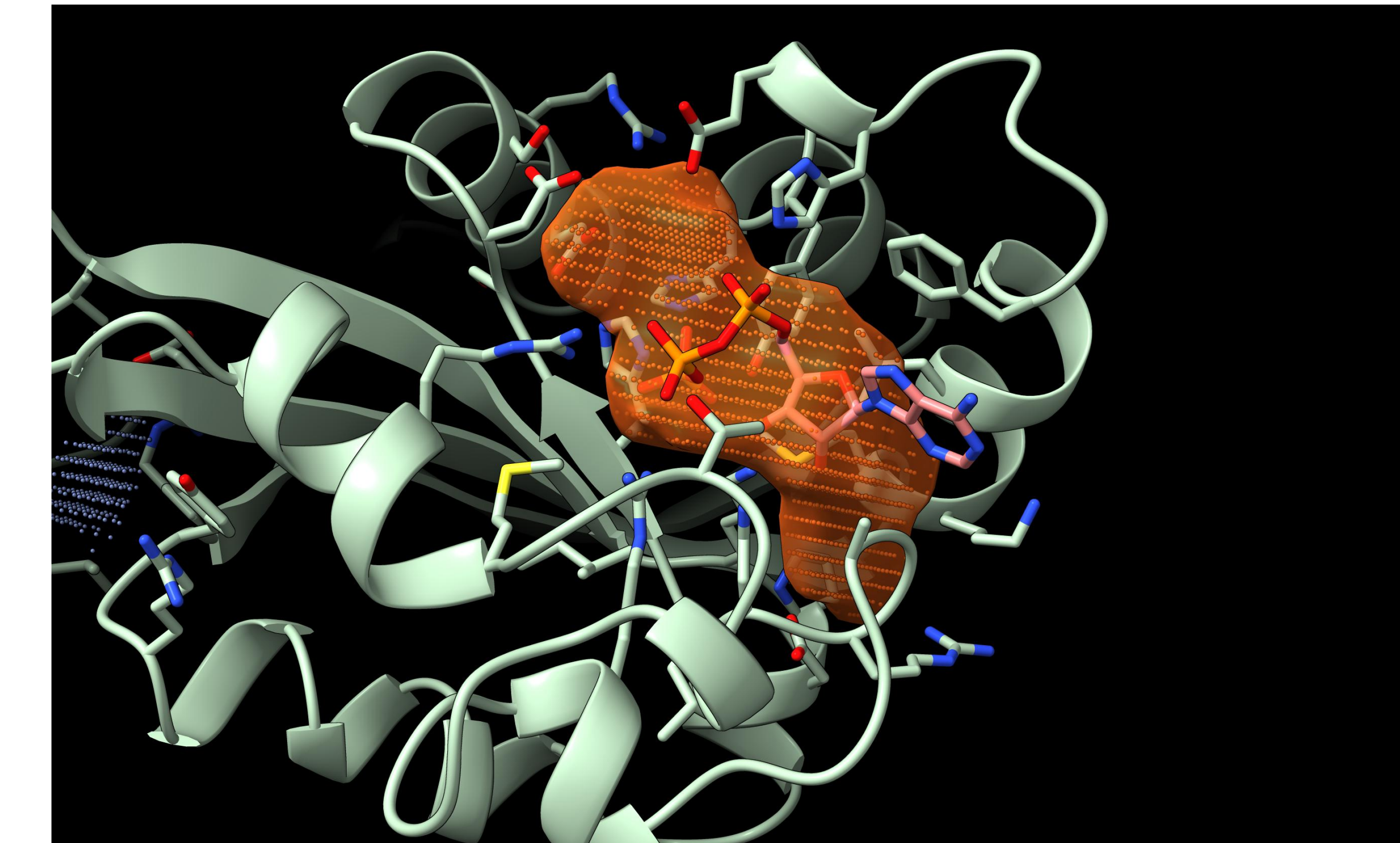
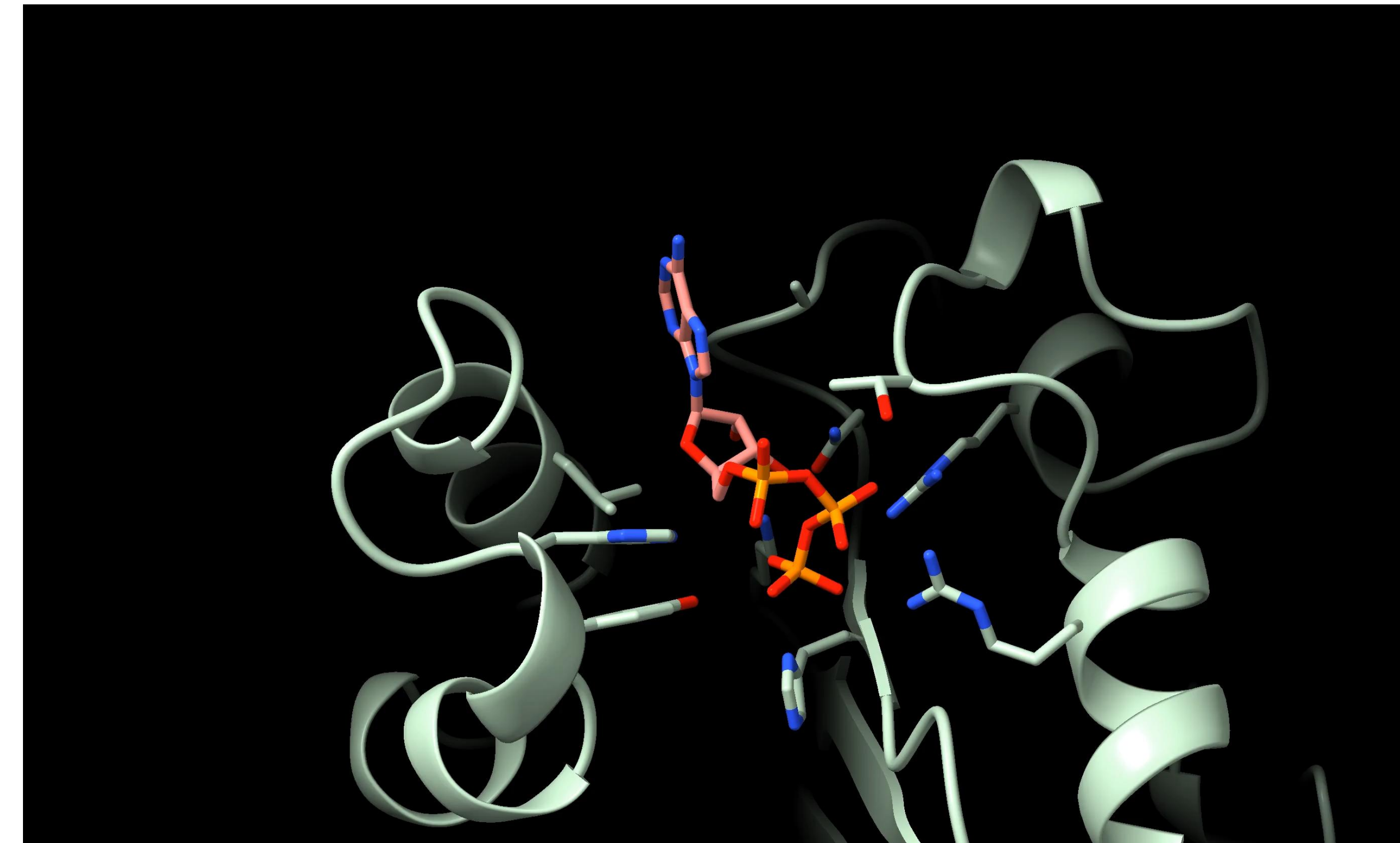
+ Add

Export Animation

Export Geometry

Protein:ligand complex modelling examples

- Example 1. Nucleoside-diphosphate kinase from *Cryptosporidium parvum*
 - Catalyzes the reversible exchange of phosphates from NTP to NDP ($\text{XDP} + \text{YTP} \leftrightarrow \text{XTP} + \text{YDP}$)
 - Uniprot Q5CR64
 - Modelling ATP and GTP bound states using Alphafold 3



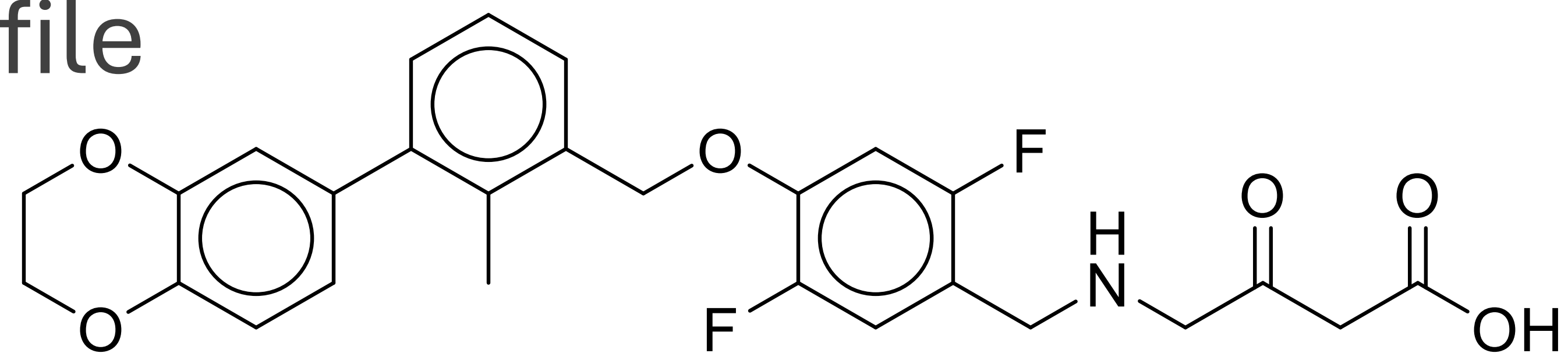
Example 2

- Glyceraldehyde-3-phosphate dehydrogenase from *Neisseria gonorrhoeae*
- Uniprot B4RPP8
- Involved in glycolysis
 - $\text{glyceraldehyde-3-phosphate} + \text{NAD}^+ + \text{Pi} \rightleftharpoons \text{1,3-bisphosphoglycerate} + \text{NADH}$
- Modelling NAD bound form using Alphafold 3



Example 3

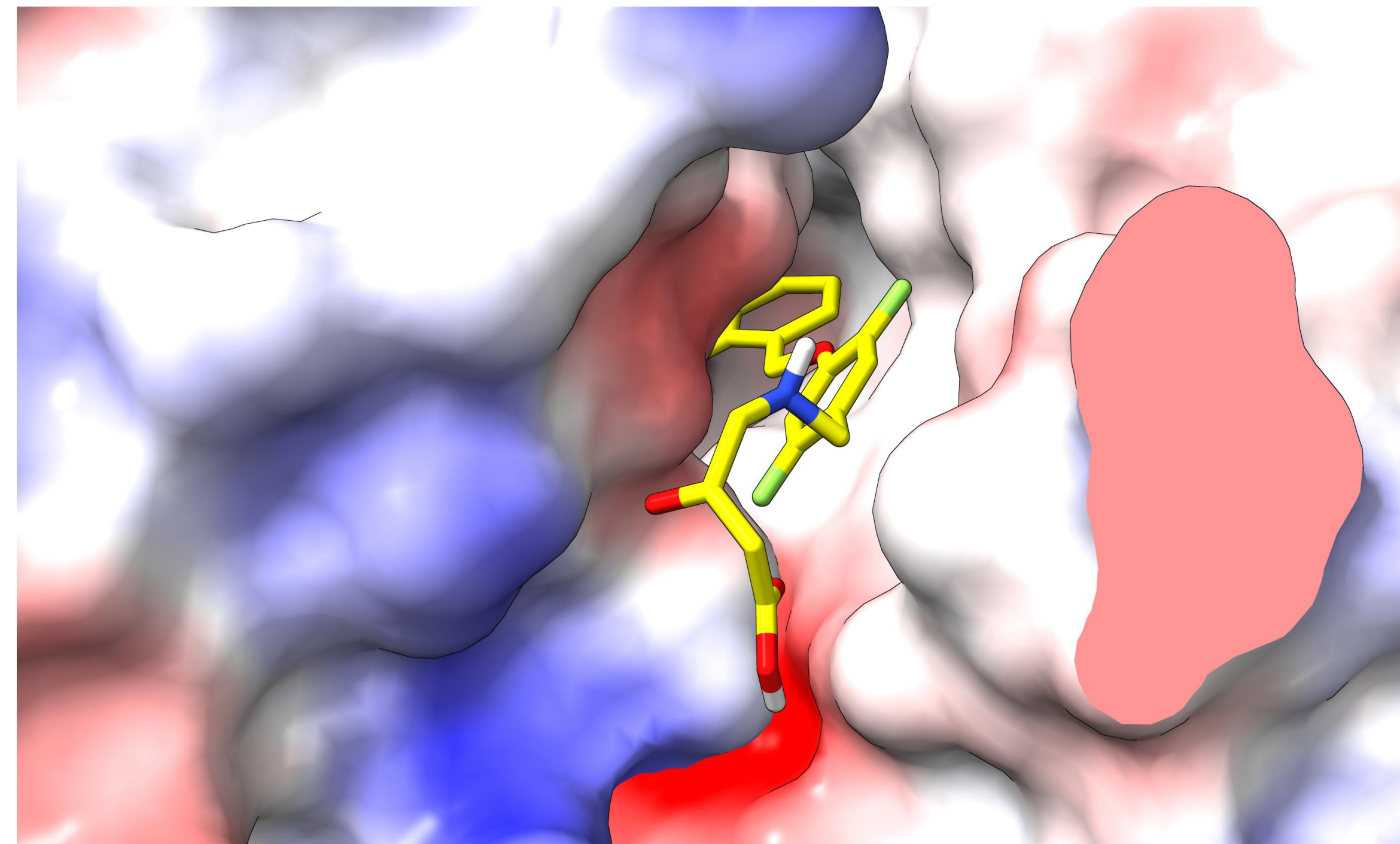
- Programmed cell death-ligand 1 (PD-L1)
- Uniprot Q9NZQ7
- Modelling a novel inhibitor with CB-Dock 2
- Protein model from the PDB input
- Ligand smiles or sdf file



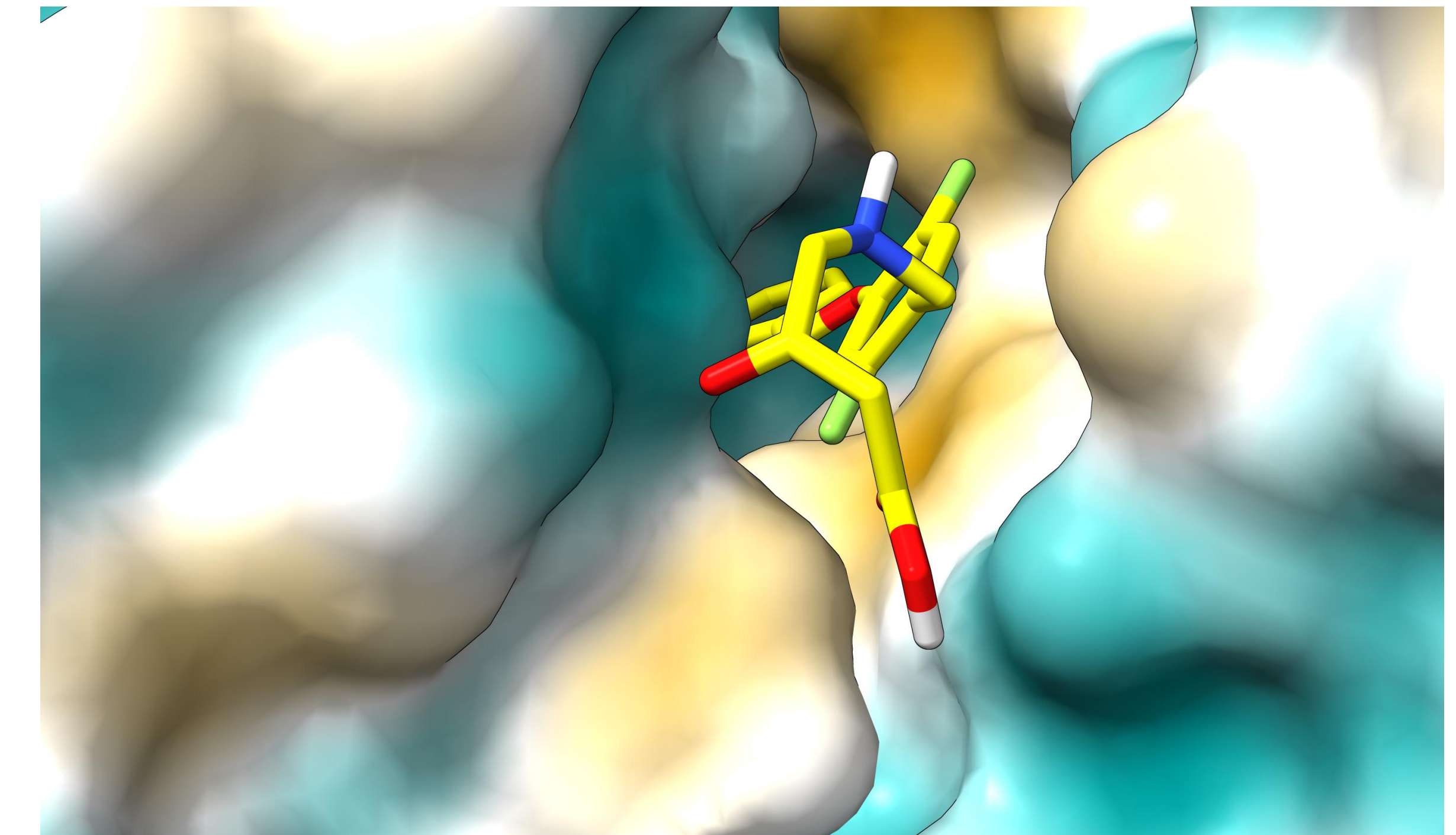
ChimeraX commands for ligand analysis

- ChimeraX commands:
- View ligand (centers on ligand molecule)
- Find cavities (Need PyKVFinder plugin installed)
- hbonds ligand (show hydrogen bond contacts to the ligand)
- coulombic protein (show electrostatic surface of the protein)

electrostatic surface



Lipophilicity surface potential



Questions