MD Simulations – day 2
Analysis

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GitHub
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for Prof. Fuxreiter's course @ University of Padova
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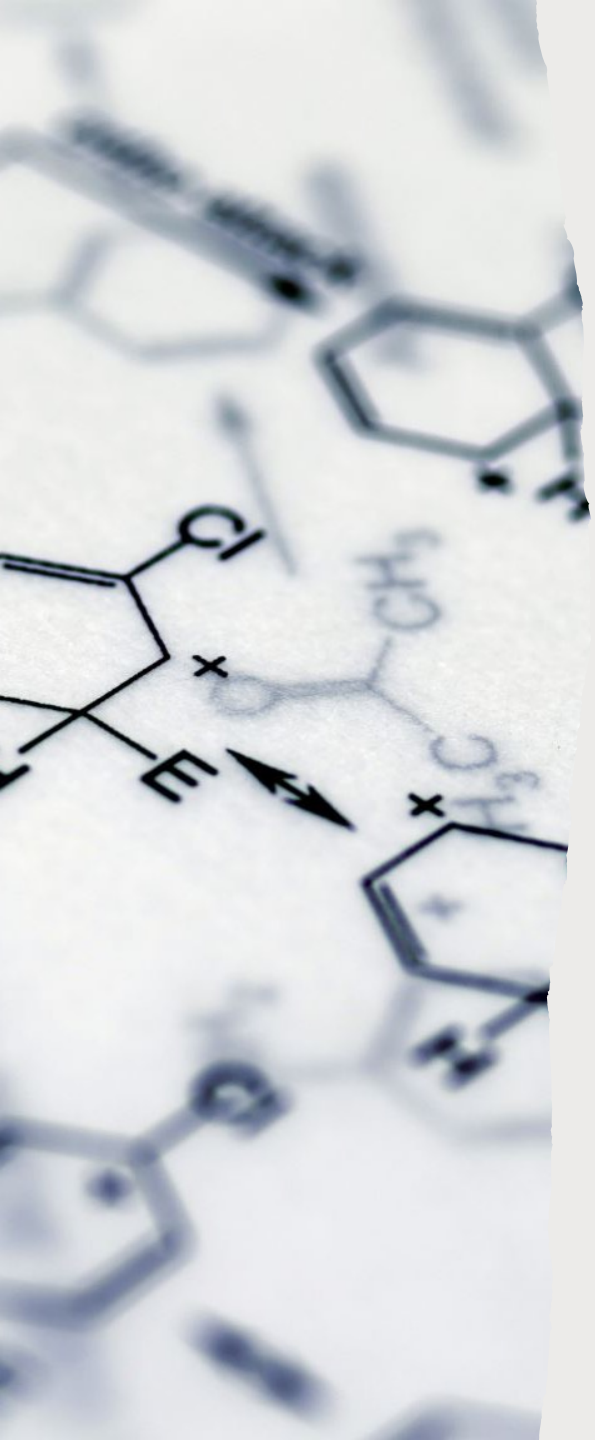
https://github.com/giorginolab/MD-Tutorial-Data



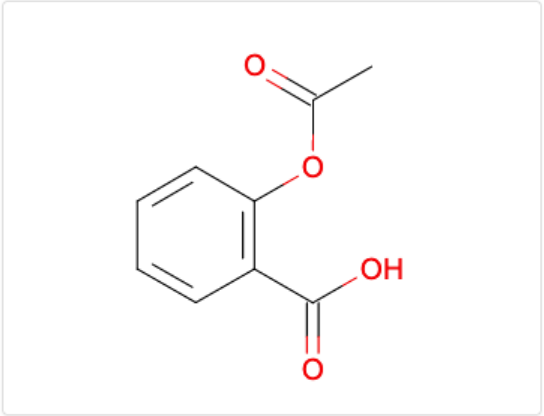
PTGS1* and **PTGS2** are the targets of nonsteroidal anti-inflammatory drugs (NSAIDs) including aspirin and ibuprofen.

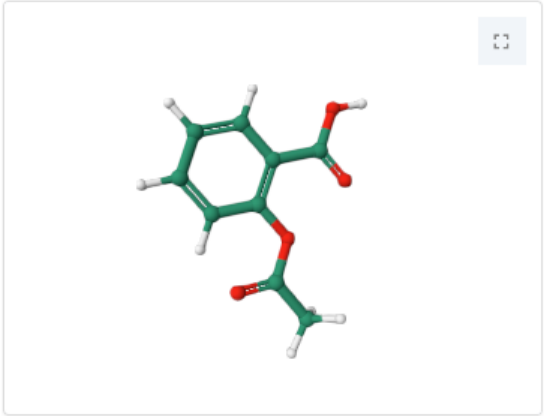
Aspirin is able to produce an irreversible inactivation of the enzyme through a serine acetylation.

Inhibition of the PGHSs with NSAIDs acutely reduces inflammation, pain, and fever, and long-term use of these drugs reduces fatal thrombotic events, as well as the development of colon cancer and Alzheimer's disease.

PTGS2 is the principal isozyme responsible for production of inflammatory prostaglandins. New generation PTGSs inhibitors strive to be selective for PTGS2, to avoid side effects such as gastrointestinal complications and ulceration.

* COX1 = Prostaglandin G/H synthase 1 = PGH1_HUMAN = P23219





Toggle Hydrogen | Toggle Labels

Display Files | Download Files | Data API

AIN

2-(ACETYLOXY)BENZOIC ACID

Find entries where: AIN

is present as a standalone ligand in 8 entries

search

Find related ligands:

Similar Ligands (Stereospecific)

Similar Ligands (including Stereoisomers)

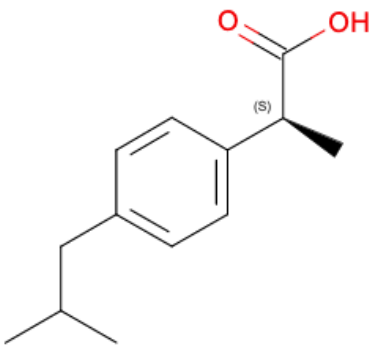
Similar Ligands (Quick Screen)

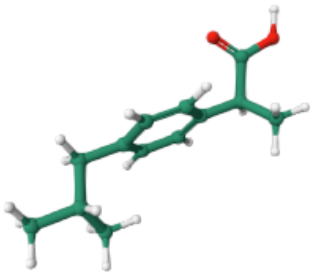
Similar Ligands (Substructure Stereospecific)

Similar Ligands (Substructure including Stereoisomers)

Chemical Component Summary	
Name	2-(ACETYLOXY)BENZOIC ACID
Synonyms	ACETYLSALICYLIC ACID; ASPIRIN
Identifiers	2-acetyloxybenzoic acid
Formula	C_9 H_8 O_4
Molecular Weight	180.157
Type	NON-POLYMER
Isomeric SMILES	CC(=O)Oc1ccccc1C(=O)O
InChI	InChI=1S/C9H8O4/c1-6(10)13-8-5-3-2-4-7(8)9(11)12/h2-5H,1H3,(H,11,12)
InChIKey	BSYNRYMUTXBXSQ-UHFFFAOYSA-N

Chemical Details	
Formal Charge	0
Atom Count	21
Chiral Atom Count	0
Bond Count	21
Aromatic Bond Count	6





Toggle Hydrogen | Toggle Labels

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IBP

IBUPROFEN

Find entries where: IBP

is present as a standalone ligand in 14 entries

search

Find related ligands:

Similar Ligands (Stereospecific)

Similar Ligands (including Stereoisomers)

Similar Ligands (Quick Screen)

Similar Ligands (Substructure Stereospecific)

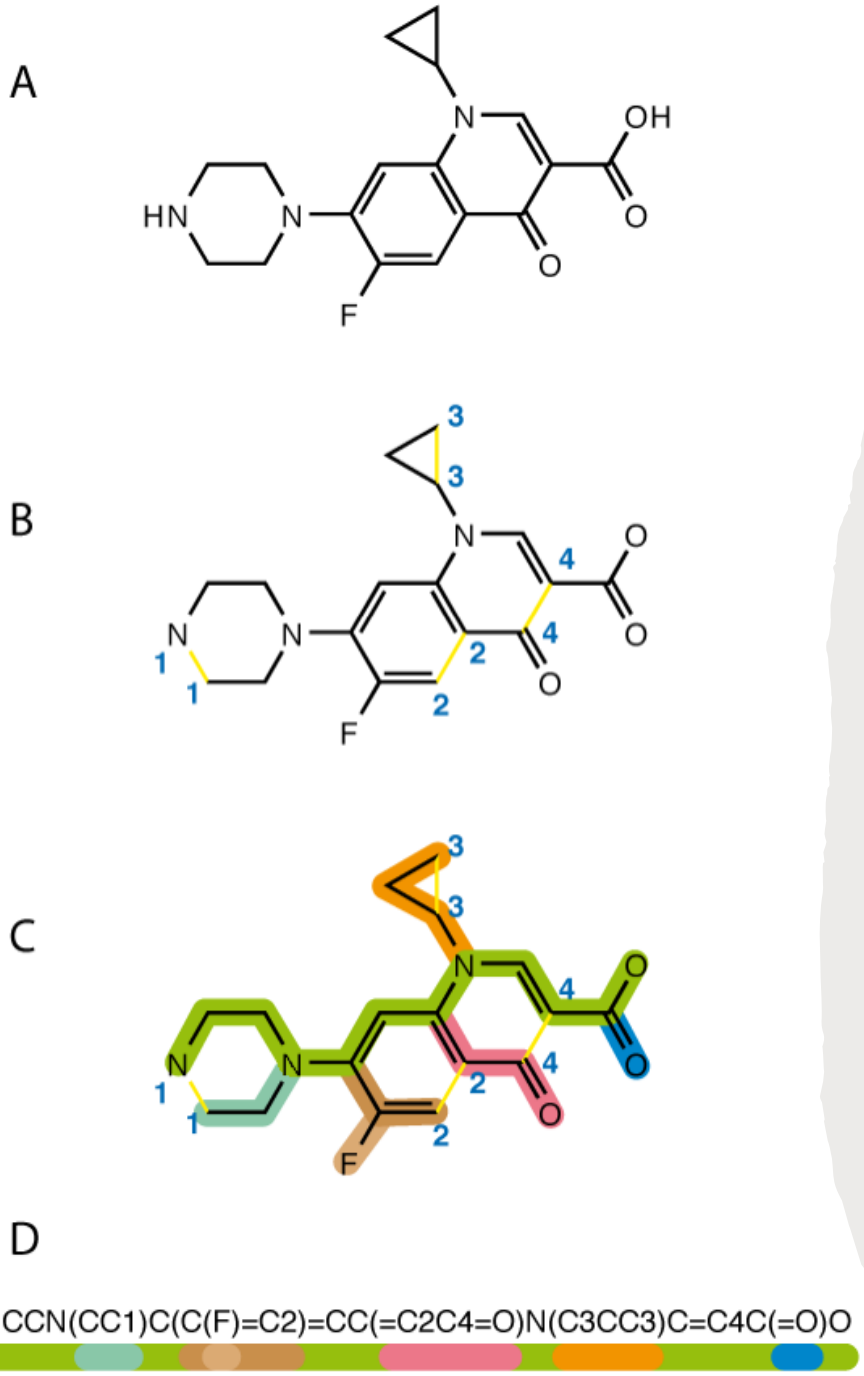
Similar Ligands (Substructure including Stereoisomers)

Chemical Component Summary

Name	IBUPROFEN
Synonyms	2-(4-ISOBUTYLPHENYL)PROPIONIC ACID
Identifiers	(2S)-2-[4-(2-methylpropyl)phenyl]propanoic acid
Formula	C_{13} H_{18} O_2
Molecular Weight	206.281
Type	NON-POLYMER
Isomeric SMILES	CC(C)Cc1ccc(cc1)[C@H](C)C(=O)O
InChI	InChI=1S/C13H18O2/c1-9(2)8-11-4-6-12(7-5-11)10(3)13(14)15/h4-7,9-10H,8H2,1-3H3,(H,14,15)/t10-/m0/s1

Chemical Details

Formal Charge	0
Atom Count	33
Chiral Atom Count	1
Bond Count	33
Aromatic Bond Count	6



- SMILES is a "1D" representation of the molecular graph.
- However, it **can** encode stereochemistry and cis/trans isomerism.
- It does **not** encode precise 2D or 3D coordinates, which must be generated.
- It is very compact and often molecular databases are distributed as such.

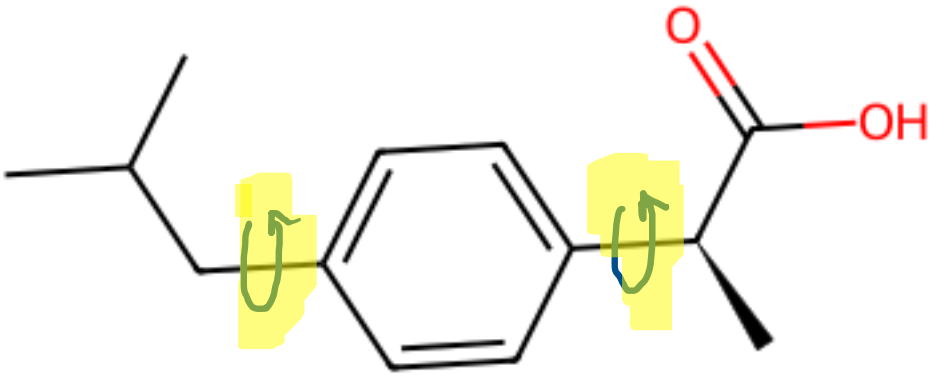
General principle

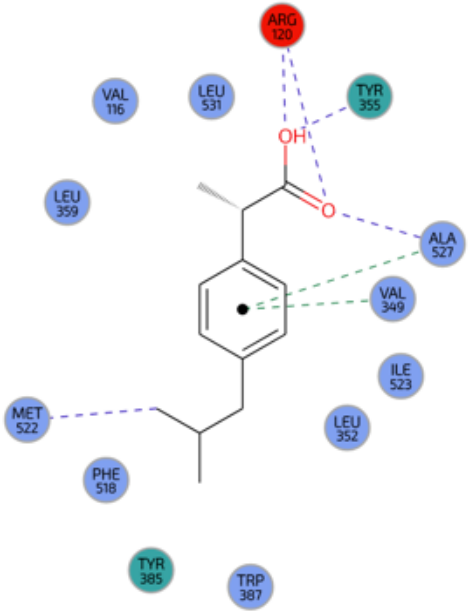
- Search a $\mathbb{R}^3 \times \mathbb{R}^3 \times \mathbb{R}^m$ space to max. score

translations

rigid rotations

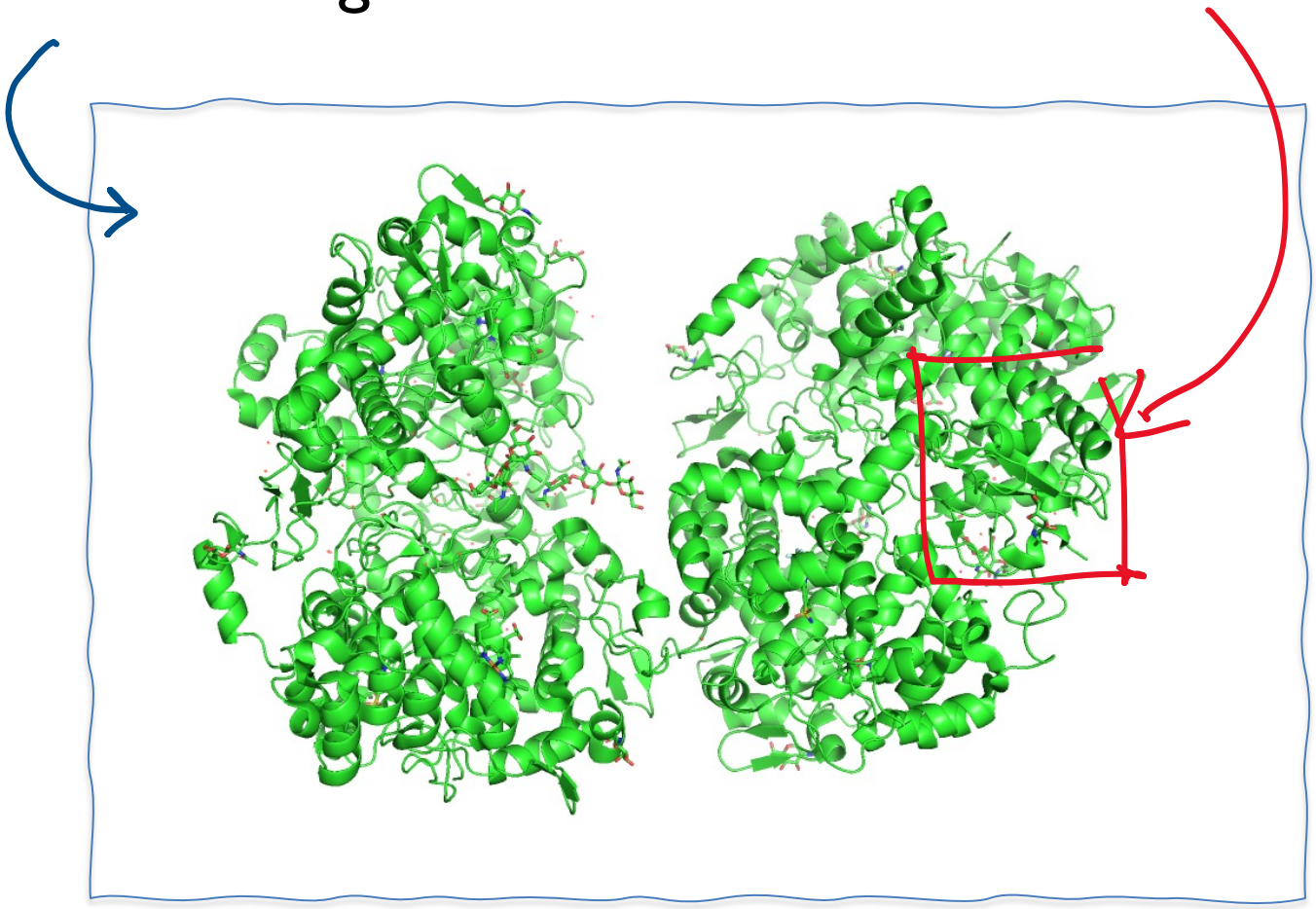
torsions





Docking types

- Blind docking
- Known-site

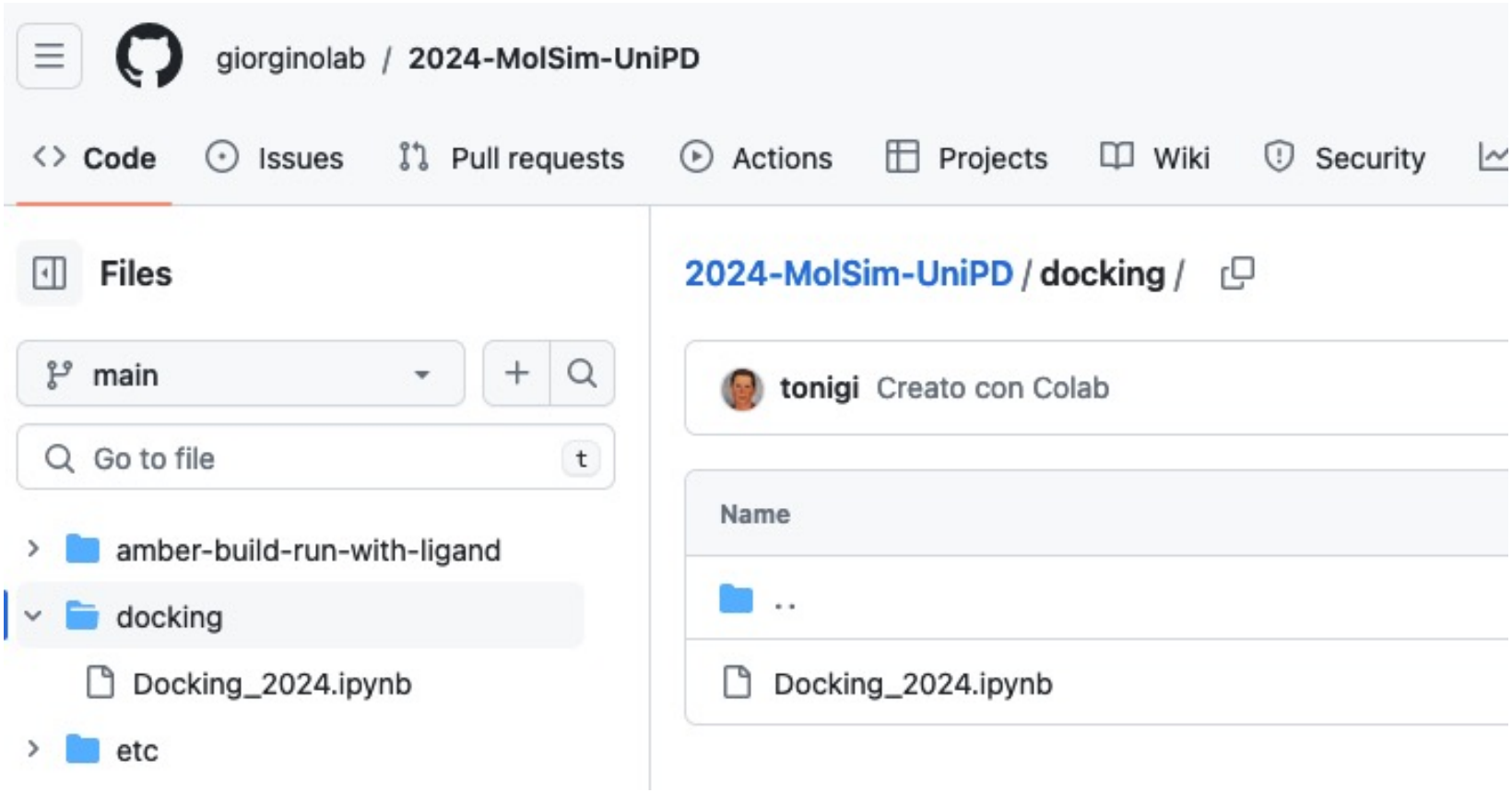


Pitfalls

- Protonation states
- Stereoisomerism
- Redocking optimism
- Receptor flexibility
- Receptor protonation states
- Thoroughness of the search
- Non-determinism

Advanced topics

- ML-based docking: diffusion models
  - DiffDock [1]
- Combine MD with docking
  - Ensemble docking [2]
- Enumeration of states
  - gypsum_dl [3]


giorginolab / 2024-MolSim-UniPD
Code
Issues
Pull requests
Actions
Projects
Wiki
Security
Files
main
Go to file
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amber-build-run-with-ligand
docking
Docking_2024.ipynb
etc
2024-MolSim-UniPD / docking /
tonigi Creato con Colab
Name
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Docking_2024.ipynb

References

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- Bender BJ, Gahbauer S, Luttens A, Lyu J, Webb CM, Stein RM, et al. A practical guide to large-scale docking. Nat Protoc. 2021 Sep 24;1–34.
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- McNutt AT, Francoeur P, Aggarwal R, Masuda T, Meli R, Ragoza M, et al. GNINA 1.0: molecular docking with deep learning. Journal of Cheminformatics. 2021 Jun 9;13(1):43.

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