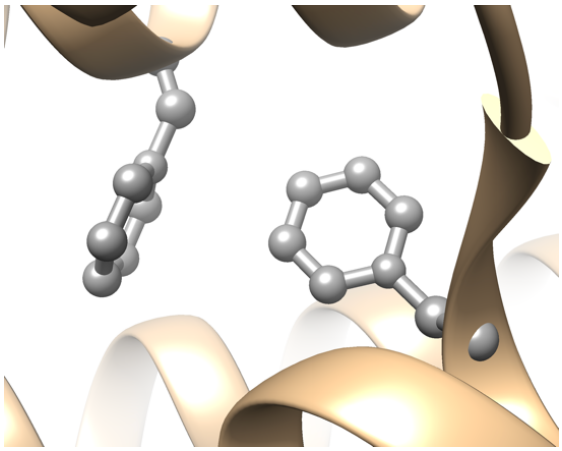
Computer-Aided Drug Design

Daina Antoine & Zoete Vincent

November 29, 2023

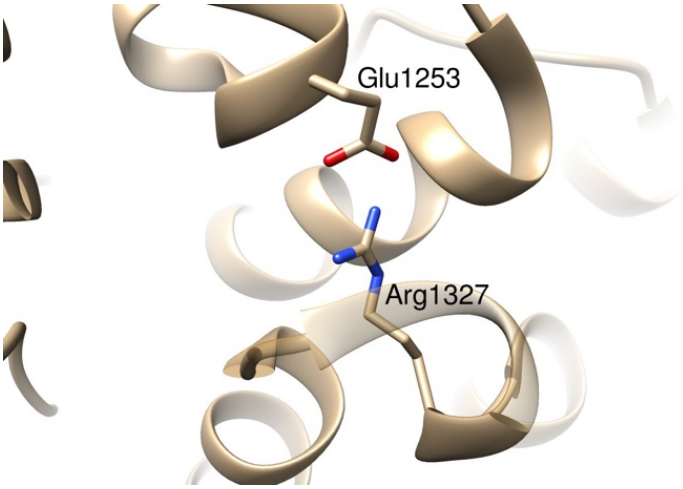
Your name:

Choose <u>one</u> answer/statement that matches best each of the 12 questions/points.
There is no penalty for bad answers.



1. In the above structure, the side chains of both amino acids displayed in ball-and-stick representation are making:

a. a hydrogen bond
b. a T-shaped π-stacking aromatic interaction
c. an ionic interaction
d. disulfide bridge



2. In the structure displayed above, the arginine (Arg1237) and glutamate (a.k.a. glutamic acid; Glu1253) residues are making:

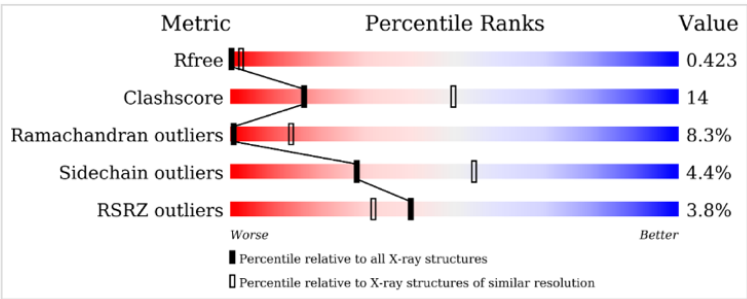
a. an aromatic interaction
b. an ionic interaction (a.k.a. salt bridge in this case)
c. a disulfide bridge
d. a cation-π interaction

3. The quality report on the X-ray structure above indicates that :
   a. the overall quality of the experimental structure will enable a fine analysis of the position of a large proportion of the atoms
   b. the overall quality of the experimental structure is limited and will, for example, only enable a qualitative analysis of the relative position of residues

Experimental Data Snapshot

Method: X-RAY DIFFRACTION
Resolution: 4.20 Å
R-Value Free: 0.444
R-Value Work: 0.381
R-Value Observed: 0.388

wwPDB Validation 3D Report | Full Report



4. Using a consensus approach to dock a small molecule on a protein could consist in
   a. performing the docking using several different software, retaining the binding mode predicted by most of these programs as the most likely
   b. asking several persons to perform the same docking using the same software, to check if the predicted binding mode remains identical
   c. using a protein 3D structure modelled with AlphaFold

5. Virtual screening
   a. replaces experimental screening using *in silico* methods to retrieve all the actives from a large library of small molecules.
   b. applies structure-based or ligand-based approaches to a large collection of molecules, to establish a short list enriched in compounds likely to be active against the target and to be tested in priority.
   c. filters out all inactive and toxic molecules.

6. A molecule is considered druglike
   a. if it shows high similarity of chemical structure with known bioactive molecules
   b. if its physicochemical properties are within optimal ranges for oral bioavailability
   c. if it satisfies all criteria to enter clinical development

7. Which one is a database of bioactive molecules?
   a. the Protein DataBank (PDB)
   b. ChEMBL
   c. AutoDock Vina

8. Bioavailability is a measurement of
   a. how strong a small molecule binds to a protein
   b. the stability of a chemical compound
   c. the amount of unchanged active ingredient in the bloodstream

9. The goal of bioisosteric design is to:
   a. mimic a template molecule to correct one of its deficiencies
   b. enrich a chemical library with bioactive molecules
   c. filter a chemical library for druglike compounds only

10. What is the most probable human protein targeted by **molecule_1**, whose SMILES is given below?
`NC[C@H](N[C@@H](CCc1ccccc1)C(O)=O)C(=O)N1CCC[C@H]1C(O)=O`
    a. SwissTargetPrediction returns the Angiotensin-converting enzyme (ACE) with a probability of 1, thus it is not an actual prediction.
    b. SwissTargetPrediction predicts the Angiotensin-converting enzyme (ACE) with a probability of approximatively 0.6.
    c. SwissTargetPrediction predicts the Angiotensin-converting enzyme (ACE) by homology.
    d. SwissADME displays violations in some druglikeness filters, thus it is not a bioactive molecule.

11. Which drug molecule in DrugBank is most similar to **molecule_1** for 3D-shape ?
    a. Ligand-based screening with SwissSimilarity returned compound CHEMBL3989406 with an Electroshape score of 0.953
    b. Ligand-based screening with SwissSimilarity returned Lisinopril with a ECFP4 score of 0.823
    c. Ligand-based screening with SwissSimilarity returned ligand 9YK with an Electroshape score of 0.948
    d. Ligand-based screening with SwissSimilarity returned Enalaprilat with an Electroshape score of 0.928

12. What prediction about the absorption and distribution of **molecule_1** is given by the BOILED-Egg?
    a. This compound displays properties to be well absorbed by the gastrointestinal tract but it can't permeate through the blood-brain barrier.
    b. This compound displays properties to be well absorbed by the gastrointestinal tract but will not stay in high concentration in the brain because it is probably effluxed.
    c. This compound cannot be well absorbed by the gastrointestinal tract, because it is not druglike.
    d. This compound is too lipophilic to access the central nervous system.