0. Disclaimer:

1. This set of materials was designed to cover the fundamental knowledge required for this project, not necessarily comprehensive.
2. We are not responsible for any potential data lost or hardware damage for using the software recommended here.
3. We have tried our best to ensure that the links provided here are safe but it's the user's responsibility to be cautious when using the links.

I. Objectives

- Equip the user/mentee/student/trainee from different theoretical backgrounds with the fundamental knowledge for performing computer-aid drug design though question-guided self-study and hands-on activities.
- Through a modular approach
    - allowing flexible adaptation including week-based workshop, month-based internship, or a year-based undergraduate research training.
    - Can be fine-tuned for students of different level
    - Recommended to combine with experimental modules according to available resource for a better understanding of the "real" drug-design pipeline.
- The simplified workflow of quick evaluation of designed inhibitors applied in this plan was inspired by the blogpost at [https://www.cheminformania.com/ligand-docking-with-smina/], aiming to further lower the technical barrier for novice users to use molecular docking techniques, especially for researchers from experimental groups of related fields, allow them to focus more on the design process instead of software installation and command-line usage.

II. Question-guided materials for self-paced study

Outline of the mentoring plan with materials separated into two categories:

- Handouts (docx) with questions to guide self-paced study
    - with links to software download pages or web services
    - links to (hopefully) mobile-friendly recommended readings of this project
    - remarks on each handout:
        - No more than 100 words per answer!!!
        - Use your own words or drawings to answer the questions
        - Insert picture(s) in the space provided for hand-drawn figures (either pictures of pencil-and-paper drawings or digital drawings are ok)
        - Submit the e-copy of your answer via electronic means
- Tutorials with worked examples (demo, exercise)

Content	Progress
1. Minimal biochemistry	Handout [done] (1-minimal-biochem.docx)
1.1. variety of protein functions	
1.2. protein structures 1.2.1. building block of protein: amino acids and their standard states 1.2.2. Primary, secondary and tertiary protein structures (details of 3D representations will be discussed in the next handout)	

	1.3. Nucleic acid structures 1.3.1. Nucleotides (introduction section only) 1.3.2. RNA capping (general), project specific question	
	1.4. biochemical interactions 1.4.1. Types of interactions (general)	
	1.5. Competitive inhibition of proteins (1st section)	
	1.6. [Bonus]Minimal pharmacology and importance of selectivity	
2.	Interpretation of 3D molecular models 2.1. 3D representations of protein structure 2.2. Protein-ligand binding	Handout [done] (2-molstruc-3D.docx)
3.	Practical usage of free computational chemistry-related online resources or offline tools for academic usage 3.1. Reason of small-molecule inhibitor design: 3.1.1. Function of target protein: Why should we inhibit this protein? 3.1.1.1. journal article 3.1.1.2. Uniprot 3.2. The protein databank 3.2.1. Search on uniprot and RCSB PDB [also ex1] 3.2.2. Selection of experimental structure 3.3. Software download links and installation (demo0) 3.3.1. Installation of computational chemistry programs 3.3.1.1. Anaconda/miniconda 3.3.1.2. Install everything in the same conda environment 3.3.1.3. Optional manual install 3.4. Other resources that will be discussed later 3.4.1. pubchem [ex2-3] 3.4.2. PDB2PQR server [ex1] 3.4.3. (pdb quick screen/swisssimilarity/pharmit/zinc) [ex3]	Demo0 [done] (demo0-install.pdf) Handout [done] (3-free-compchem-resources.docx)
4.	Exercise 1: warm-up exercise and limits of quick computational model. 4.1. Fundamental of science: control test to validate your protocol 4.2. Demo1-manual-fit-eval	Demo1 [done] (demo1-manual-fit-eval.pdf) Handout [done] (4-quick-eval-ex1-and-limit.docx) Scripts [done] (in "scripts/box-local")
5.	(optional 2022) Exercise 2: application of the "standard" protocol 5.1. Workflow 5.2. Demo2-common-protocol	Work in progress: Demo and handout Scripts done
6.	(optional 2022) Exercise 3: virtual screening, another direction of structure based drug design 6.1. Workflow 6.2. Demo3-virtual-screening	All pending
7.	Optional: Molecular Dynamics	
8.	Optional: QSAR and Machine learning-based optimization	

III. Free reference materials and remarks

- Notes:
    - Libretext materials have many typos but could be ok as introductory text under creative commons license.
    - When "standard" textbook-like articles are too advanced for our purpose, more generic information from Wikipedia would be used.
- Selected chapters in
    - Selected https://chem.libretexts.org/Bookshelves/Biological_Chemistry/Supplemental_Modules_(Biological_Chemistry)/Proteins
    - Selected (still many typos) https://bio.libretexts.org/Bookshelves/Biochemistry/Fundamentals_of_Biochemistry_(LibreTexts)
    - Selected *https://www.ncbi.nlm.nih.gov/books/NBK26911*
    - https://chem.libretexts.org/Bookshelves/Biological_Chemistry/Book%3A_Biochemistry_Online_(Jakubowski)
    - https://bio.libretexts.org/Bookshelves/Biochemistry/Book%3A_Biochemistry_Free_For_All_(Ahern_Rajagopal_and_Tan)
    - (Reason: open access and mobile friendly)
- Some general information from wiki
- Uniprot data of target protein
- The RCSB PDB
- pubchem
- Swiss-target or UCSF Sea off-target prediction

IV. Further readings

- Basic PharmChem (MIT course?)
- Advanced drug design workflow recommended only for advanced final year project students who'd like to learn some programming (TeachOpenCADD, mainly jupyter notebooks written in python)
- Dated, now buggy, but still very comprehensive drug design tutorial with OPEN3DQSAR
-