Prerequisite:

- ➢ MOE installed on your PC.
- ➢ JavaScript or JasMol installed on your PC.
- ➢ 7-zip or winRAR installed on your PC.

Prerequisite terminologies:

In order to have a thorough understanding of our main topic, you should have the basic concept of the following terminologies:

- ➢ Drug Designing.
- ➢ Molecular Docking.
- ➢ Information retrieval from PDB.
- ➢ Protein-Protein docking using MOE.

Introduction:

MDockPep is an online web server available publicly for the users to dock a receptor protein against a peptide (ligand) molecule to predict a protein-peptide complex structure. It completes this process in the following 3 steps:

1. Modeling peptide conformers;

2. Globally and flexibly sampling protein-peptide binding modes;
3. Scoring and ranking the sampled binding modes.

Steps:

- Click on the following link to visit the homepage of MDockPeP server: http://zougrouptoolkit.missouri.edu/mdockpep/index.html
- On the homepage of the MDockPeP server, it provides the basic information about the working of the server.
    - Then in the menu bar, it provides the following buttons:
        - **Queue-** where the docking results will be displayed.
        - **About-** additional details about the working of MDockPep server.
        - **Tutorial-** how to enter a query and get the results back.
        - **Zou lab-** to learn about the organization hosting this server.
- Before moving on, 1st you need to prepare the receptor protein for docking to fix the protonation and minimize the energy.
  [You can use any online server to perform this job. We would recommend using MOE.]
- Open your MOE interface and go to ‘File’ and then ‘Open’ and then select the file of your receptor molecule.
    - Click on the ‘SEQ’ button and select extra ligand, chains, and water molecules to remove them from the receptor molecule.
    - Then click on the ‘Minimize’ button to perform the energy minimization process.
    - Then click on the ‘QuickPrep’ button from the right hand side tab and complete this process.
    - After completing the ‘QuickPrep’ process, go to ‘File’ and then click on ‘Save’ and then select the location on your PC to save the file, enter the name of the file and then select the format of your file (must be .pdb) and then click ‘OK’.
- Then go to the homepage of the server, then go to the “Job Submission” section to enter your query:

- In the first box, paste your peptide (ligand) sequence in .txt format or upload the file from your system in FASTA format.
- Then in the next box, click on the ‘Choose file’ button to upload the protein receptor file (in .pdb format).
- Then enter the ‘Job Name’ for your docking process, or leave it by default.
- Then provide your email ID to get the results link via email.
- If you want to keep your results private, click on the check box present against the “Do not show my job on the queue page” option.
- Then click on the drop down button present against the “Advanced options” section to set some advanced parameters (or leave them by default).
    - Select the number of initial peptide models that you want to dock against the receptor protein.
    - Then you can upload the structure of your peptide, if you have any, in the .pdb format.

Note: You must not confuse the peptide structure with any homologous structure of the peptide, it must be the structure of the exact same peptide molecule you entered in the query.

    - Then enter the cutoff of bRMSD value for peptide conformation or leave it by default.
      [We would recommend using 4.0 Angstrom value for bRMSD of peptide conformations.]
    - Then enter the value for the exhaustiveness of the sample or leave it by default.
    - Then enter the x,y,z-coordinates values (if you want to restrict your docking at some specific positions) otherwise leave it by default.
    - Then enter the size of the search box in the Angstrom unit or leave it by default.
- Then click on the ‘Submit’ button to start the docking process.
  [It’ll take 8-10 hours or may be more to provide the results.]

- Then it'll take you to the "Job Submission" page, where it'll provide you the query parameters you've selected, your job ID and the link of the webpage on which the results will be displayed.
  [Copy the link and paste it on your Notepad or make a .docx file, so that you can visit the results page if you didn't enter your email address there.]

➢ **Results:**

- Click on the link you pasted on your Notepad or .docx file or the link you received via email in your inbox to get to the results page.
- On the results page, it'll provide your Job submission details on the top.
- Then it'll provide the list of 'Top 10 predicted models' in a tabular form.
  - On the left hand side of the table, it'll provide you the 3D structure of the models.
  - Then on the right hand side of the table, it provides the list of the models, by clicking on the 'View' button present against any specific model, you will be able to observe the 3D structure of that docking complex model.
  - Then it proved the 'ITScorePeP' values for each of the predicted models.
    [The lower the 'ITScorePeP' score is, the higher will be the binding energies of the complex.]
  - If you want to download the models individually, click on the 'Download' hyperlink present against each model in the table and save it in the folder you want.
- Then below the table, it provides the 'Download' hyperlink to download all the resulting docked complexes in compressed form and save it on your system.
- Uncompress the results file using the winRAR or 7zip tool to open the docking complex models.

- You can open the downloaded models in MOE, PyMol, Chimera or any other structure visualization tool and apply multiple parameters on the structure to analyze the results in a much better way.

Summary:

In this video tutorial of Molecular Docking, we learned to dock a receptor protein molecule against the ligand peptide molecule (Protein-Peptide docking) using the MDockPeP server. We also got to know how to prepare the receptor file for the docking process and analyzed the results we got.