Python PsudoCode

Step 1: Universe

- Loading the universe using the md.tpr and md.trr files.
- Output: An object that allows to access of simulation data, atoms, residues…

Step 2: **Distance Matrix**

- Calculate the distances between the center of mass of the residues.
- Output: A symmetric Matrix with elements ij.

Step 3: Energy Interaction Matrix

- Calculate the Vanderwaals potential using the distance between residues.
- Calculate Coulombic interaction using the distance between residues.
- Add them
- Output: Symmetric matrix shape (20, 20) with stored energy sums values.

Step 4: **Diagonalize the matrix**

- Np.linalg.eigh
- Output:
    - Eigenvalues: Represent energy modes.
    - Eigenvectors: Indicates residues with their contributions.

Step 5: Calculate the Energy Gap

- Based on the spectral between the first two lowest eigenvalues.

Step 6: Identify strong interaction residues.

- Define a threshold to filter out residues with strong interactions based on their eigenvector component values.

Performing the MD simulation

Step 1: Prepare the topology file using:

- Module: pdb2gmx.
- Force field: amber99sb-ildn.
- Water: spce.
- Output file: topol.top

Step 2:

i) Create a simulation box and put the protein in it.

- Box: cubic d=1.
- Module: editconf.
- Output file: trpcagebox.gro.

ii) Add water to the box (Solvate).

- Output file: trpcage_solvated.gro
- Updated file: topol.top
- Output configuration contains
    - 8341 atoms in 2699 residue.
    - Volume 84.737 nm3.
    - Density 991.162 g/l
    - Number of solvent molecules 2679

Step 3: Add ions to neutralize the environment of the protein NOT the protein.

i) Prepare molecular dynamics parameters file (mdp) for energy minimization.
Output: ion.mdp

ii) Create a trajectory file (tpr)

- Output: ions.tpr
- Update: topol.top

iii) Add the ions Na and Cl, gromax will add as needed.

Step4: Energy minimization

i) Create em.mdp file
ii) Create em.tpr file
iii) Run the minimization
iv) Updated file: topol.top

Step 5: System Equalization

i) NVT

- Output: nvt.tpr
- Updated file: topol.top

ii) NPT

- Output: npt.tpr
- Updated file: topol.top

Step 6: Prepare and Run the md.mdp file

- Output: md.tpr
- Updated file: topol.top