Molecular Dynamics

Analysis of MD trajectory (Part 1)

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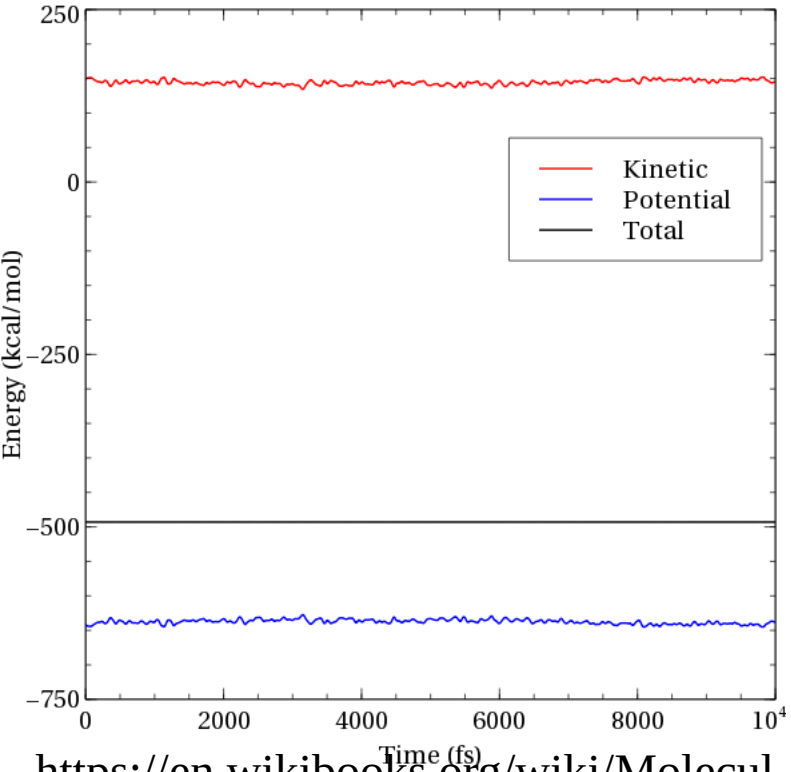
Why Temperature changes of MD simulation ?

Total Energy (U) = Kinetic Energy + Potential Energy **= CONSTANT**

Positive *Usually negative*



https://en.wikibooks.org/wiki/Molecular_Simulation/Molecular_Dynamics

1. ***At the start of simulation***

Maxwell-Boltzmann distribution Temperature is fixed (say, 300K)

Kinetic energy is fixed.

If the initial structure is bad => Starting Potential Energy (**Less negative**)

2. During simulation Structure will be better => Potential Energy is **more negative**

Energy conservation => Kinetic energy should go up ➔ Temperature will increase

- THERMOSTAT fix "Temperature.
- But if you use thermostat energy not longer is conserved.

MD trajectory

Time-step = Δt = 1 fs = 10^{-15} sec

Total Simulation time/ Trajectory = 1 ns= 10^{-9} sec

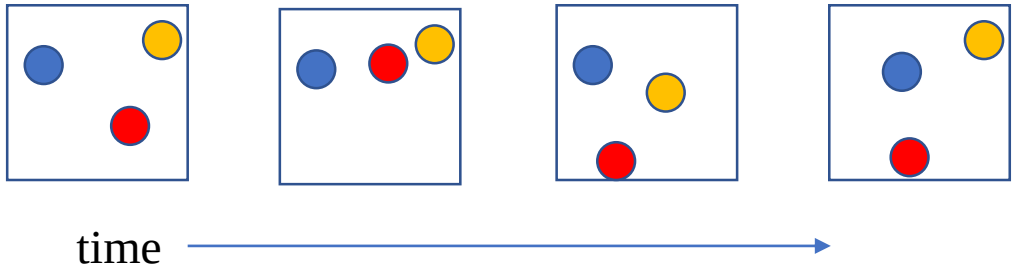
If you want to save frame/snapshot after every time-step = 10^6 fames (1 ns trajectory)

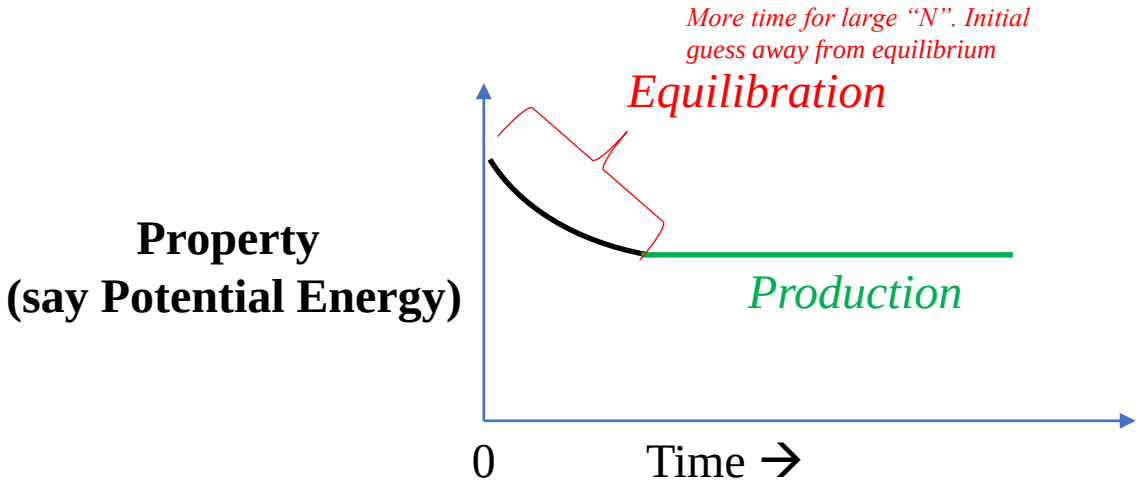
Every Fame = position and velocities of 'N' particles of the system

Every particle = 3 positions (x, y, z) + 3 velocities (v_x, v_y, y_z)
Single frame = 3N positions + 3N velocities = 6N information's
1 ns Trajectory (frames at every 1fs) = 10^6 x 6N information's
= 10^6 x 6 x 10^6 information's
= 6 x 10^{12} information's

Trajectory file (Too much information) ➔ Storage Issue + Post-processing issue

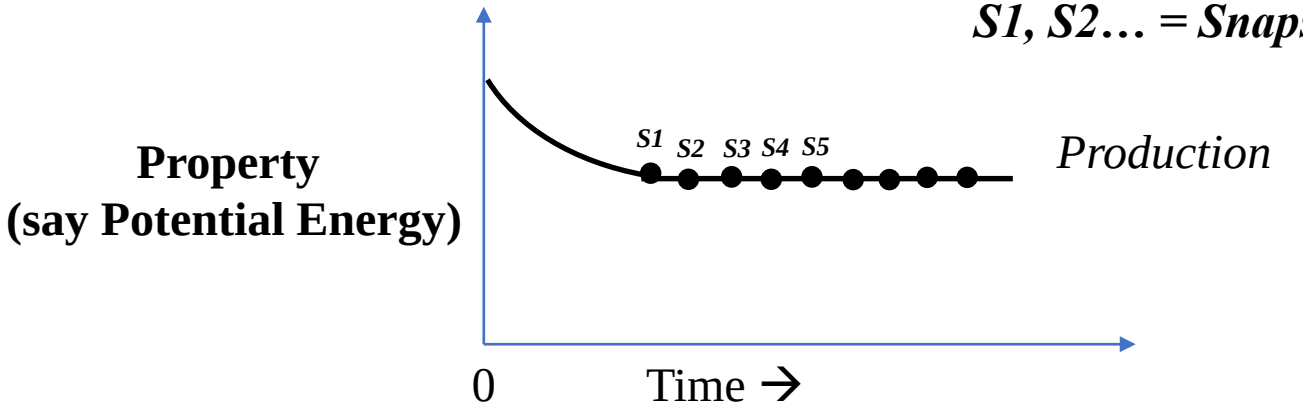
Monitor the MD trajectory





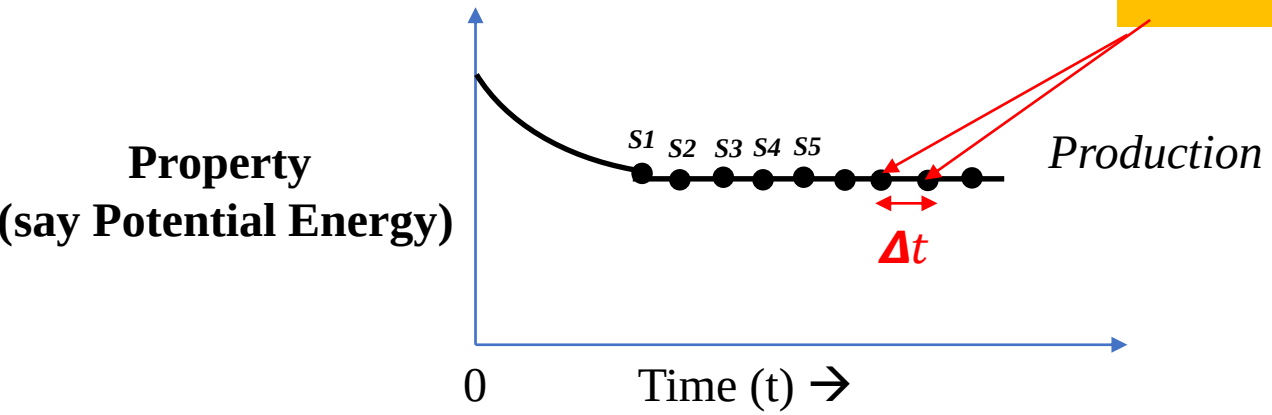
AVERAGE PROPERTIES WILL BE CALCULATED FROM THE SNAPS (*S1, S2…*)

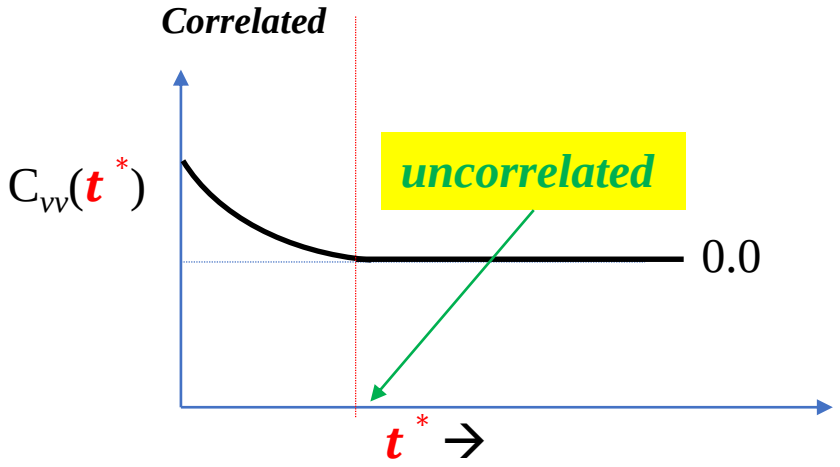
S1, S2… = Snapshot/Frame



Do we need all the Snaps ?

1. We need uncorrelated Snaps($\Delta t = t^*$?)
2. Simulation Time >> Δt





How to get uncorrelated snaps (t^*) ?

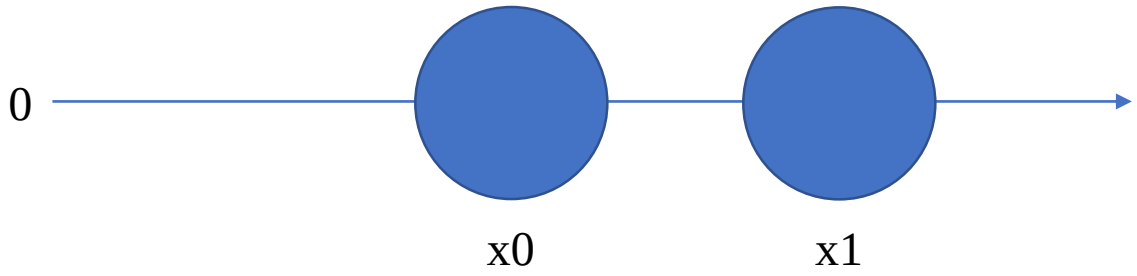
Answer: Autocorrelation function

Velocity autocorrelation function

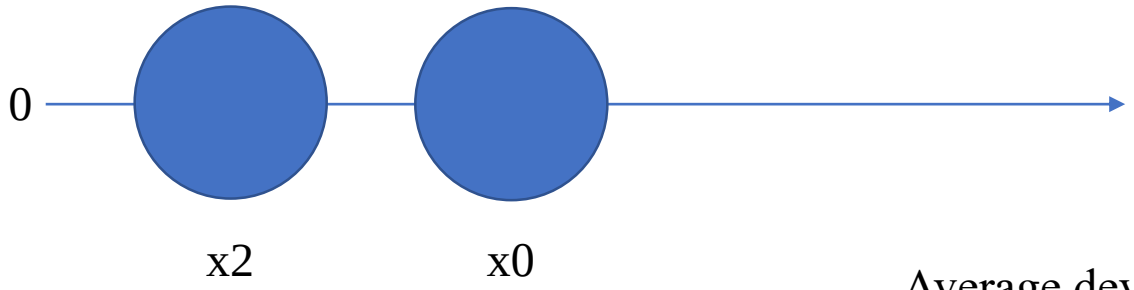
$$C_{vv}(t^*) = < v(t+t^*).\, v(t) > = < \frac{1}{N} \sum_{i=1}^{N} v_i(t+t^*).\, vi\,(t) >$$

Use uncorrelated snaps for estimating average properties (Biomolecular simulations typically: t* > 1 ps / 10^{-12} sec)

Compare two structures.



Deviation: D(t1) = (x1 –x0) = +ve



Deviation: D(t2) = (x2 –x0) = -ve

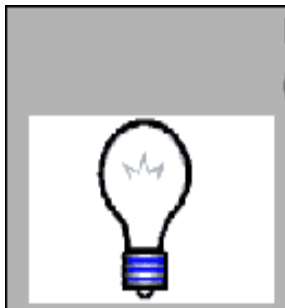
Average deviation= [D(t1)+D(t2)+….]/total no of snaps
= 0.0

How to compare estimate the difference ?

Deviation: D*(t1)= $\sqrt{(x1 - x0)2}$ $= Always\ positive\ number$

Average deviation for N-number of particles: $RMSD = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(x_i(t) - x_i(0)^2}$

Root Mean Square deviation (RMSD)

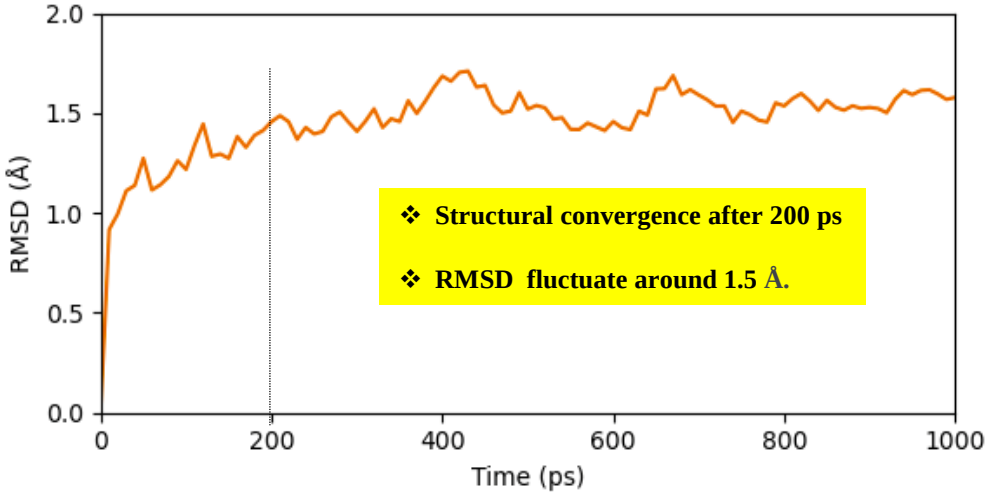


Root Mean Square Deviation. The Root Mean Squared Deviation (RMSD) is defined as :

$$RMSD = \sqrt{\frac{\sum_{i=1}^{N_{atoms}} (r_i(t_1) - r_i(t_2))^2}{N_{atoms}}} \quad (1)$$

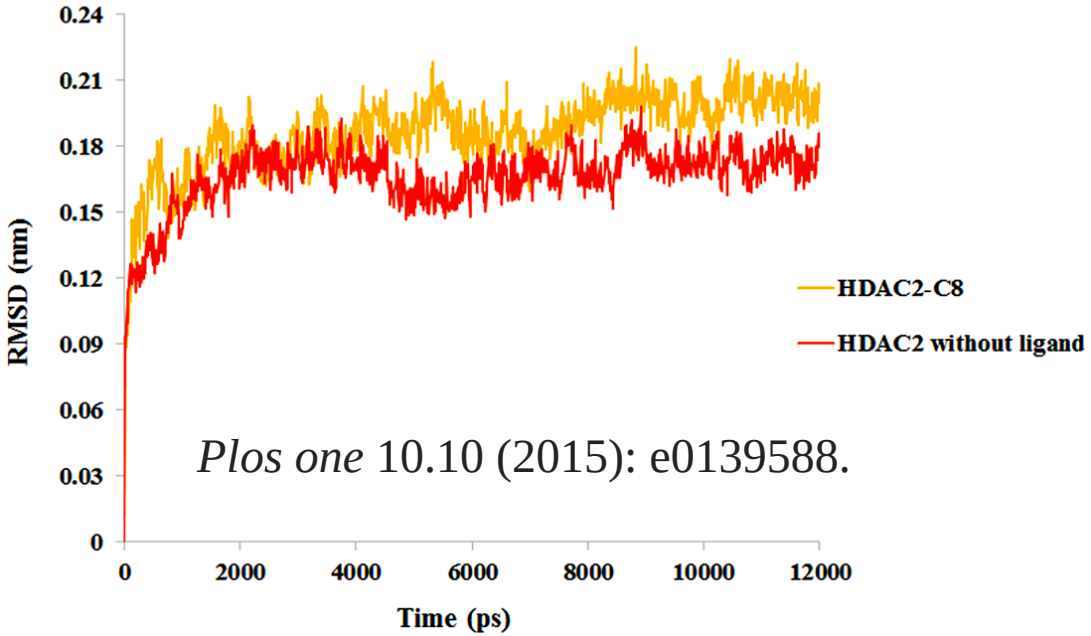
where N_{atoms} is the number of atoms whose positions are being compared, and $r_i(t)$ is the position of atom i at time t.

https://www.ks.uiuc.edu/Training/Tutorials/vmd/tutorial-html/node5.html



https://www.biotite-python.org/examples/gallery/structure/md_analysis.html

a



Plos one 10.10 (2015): e0139588.

- Measure of structural Similarity between two structures
- Indicate structural convergence

Root Mean Square fluctuation (RMSF)

$$RMSF = \sqrt{\frac{1}{T}\sum_{t_j=1}^{T}(r_i(tj) - \tilde{r}_i)^2}$$

$\tilde{r}_i$ = Average position of particle "i" from trajectory 'T'
$r_i(t_j)$ = position of particle "i" at time/snap 't_j'
T = Trajectory/snapshots

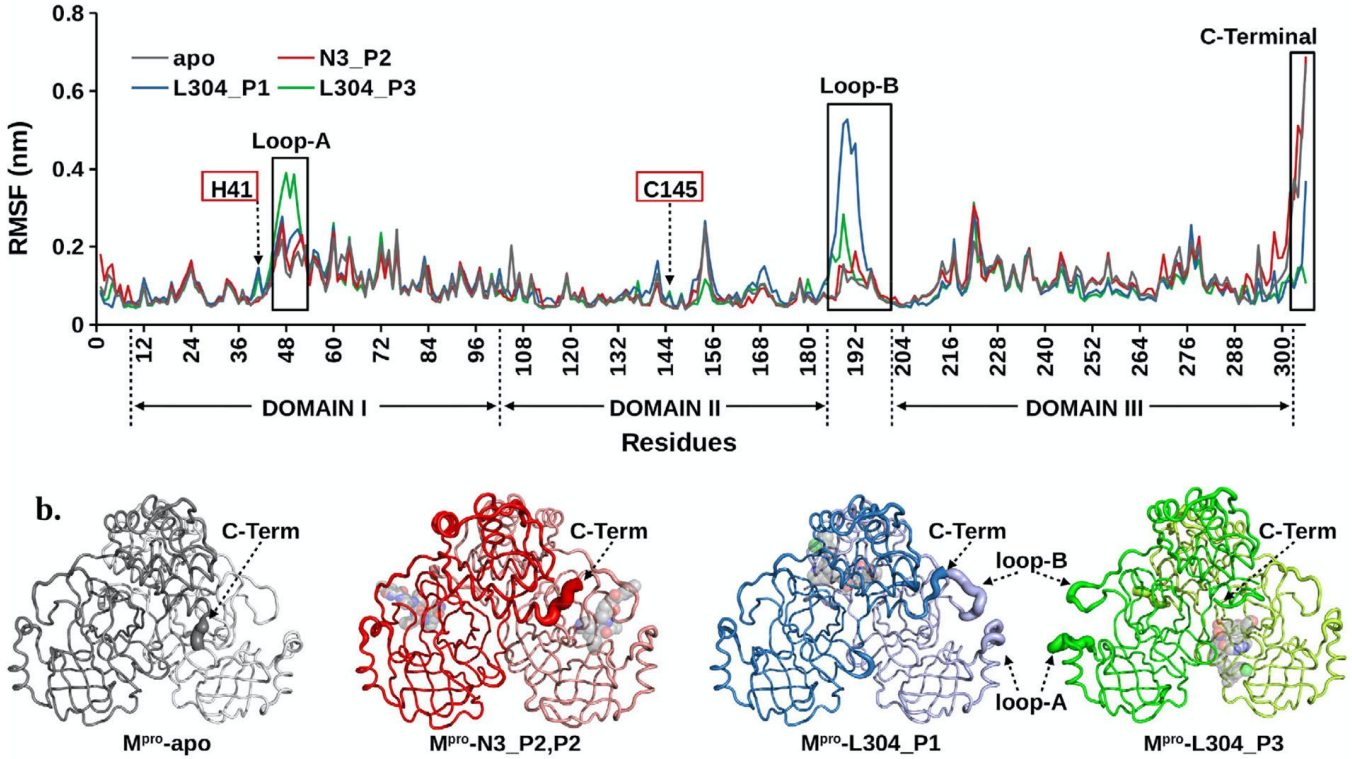


Figure 6. Residue-wise RMSF (averaged from the last 50 ns of the 150 ns trajectory) of protein-heavy atoms. (a) M^{pro}-apo and M^{pro}-holo. The C-terminal region, Loop-A and Loop-B are shown in the rectangular box. H41, C154 (catalytic dyad) is highlighted in the red box. (b) RMSF-based putty representations of M^{pro} protein is shown for visual analysis of protein flexibility. N3 and L304 are represented with van der Waals spheres.

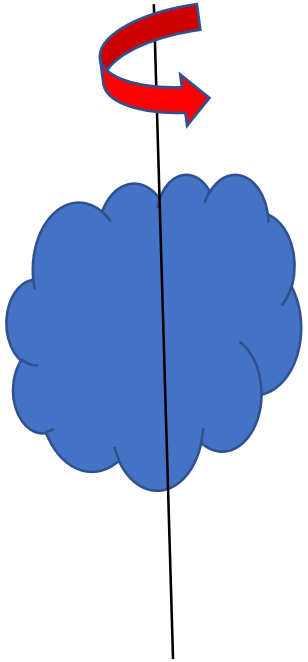
- Porcupine plot
- Flexibility as a function of residue number
- Flexibility = RMSF = averaged over MD snaps

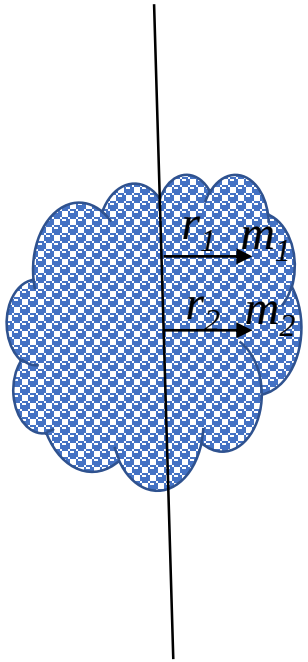
Measure of "FLEXIBILITY" at different region of the protein during a MD trajectory segment

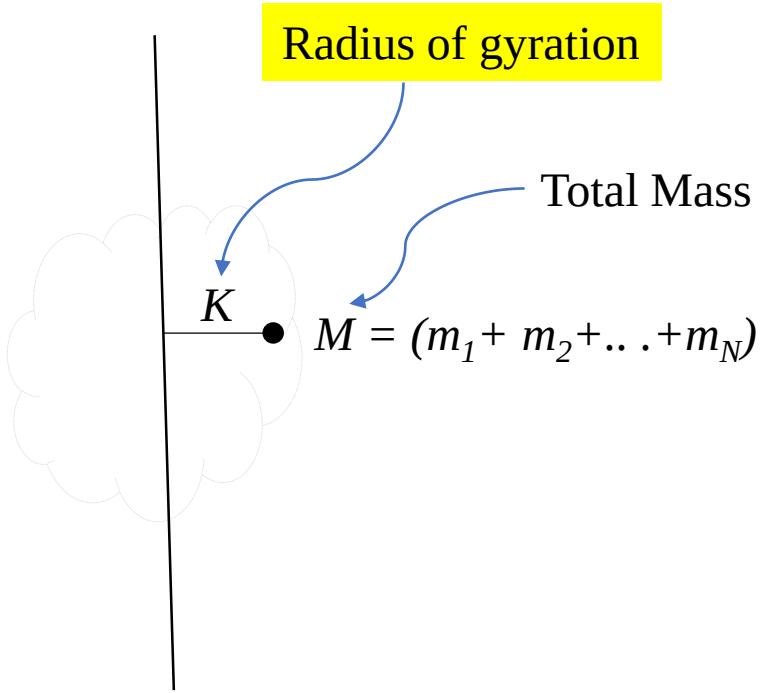
Ghosh S. et al. Journal of Biomolecular Structure & Dynamics. 2021 Aug:1-12.
DOI: 10.1080/07391102.2021.1967786. PMID: 34424151.

Radius of gyration

Axis of rotation







Moment of inertia $= \sum_{i=1}^{N} m_i r_i^2$

Moment of inertia $= MK^2$

$$MK^2 = \sum_{i=1}^{N} m_i r_i^2$$

K = Radius of gyration = ***Effective distance of the total mass from the axis of rotation***

Radius of gyration (From MD simulation)

A radius of gyration in general is **the distance from the center of mass of a body at which the whole mass could be concentrated without changing**

Radius of gyration as an indicator of protein structure compactness

•Physical Chemistry Research, 2016. 5(2):205-219
DOI: 10.22036/pcr.2017.40480

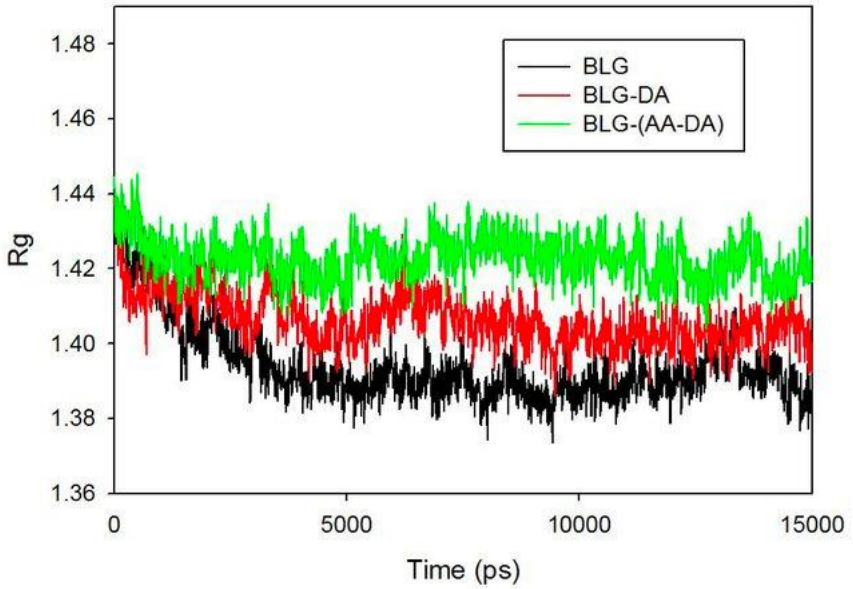
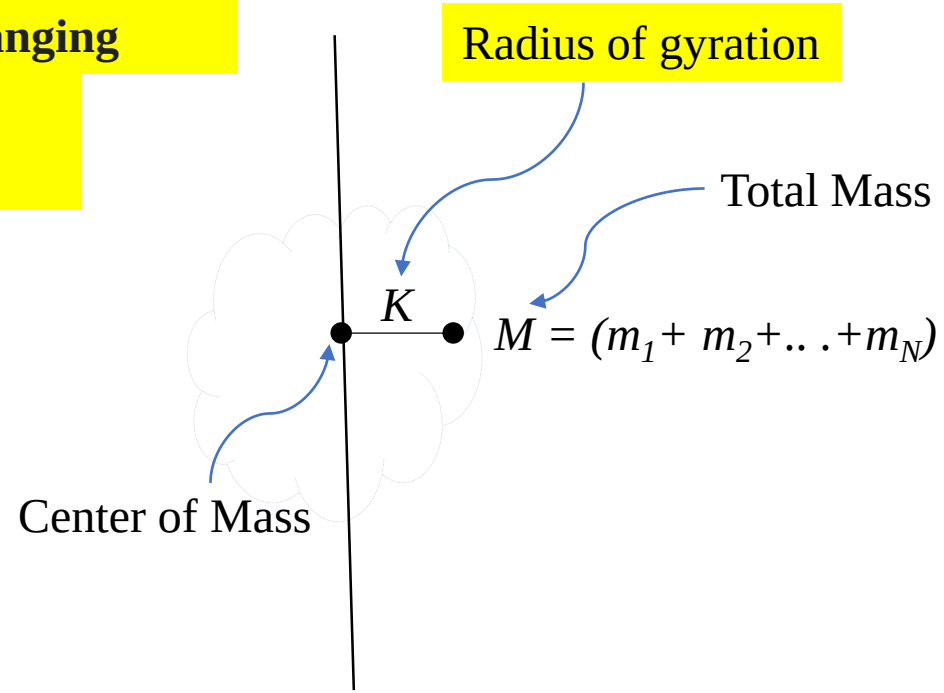


Fig. 4. RMSF of BLG residues with respect to their time-averaged positions for free and bound BLG. RMSF reductions in regions that directly in contact with ligands are shown with arrows.



Moment of inertia $= MK^2$

Molecular BioSystems 11.3 (2015): 958-968.

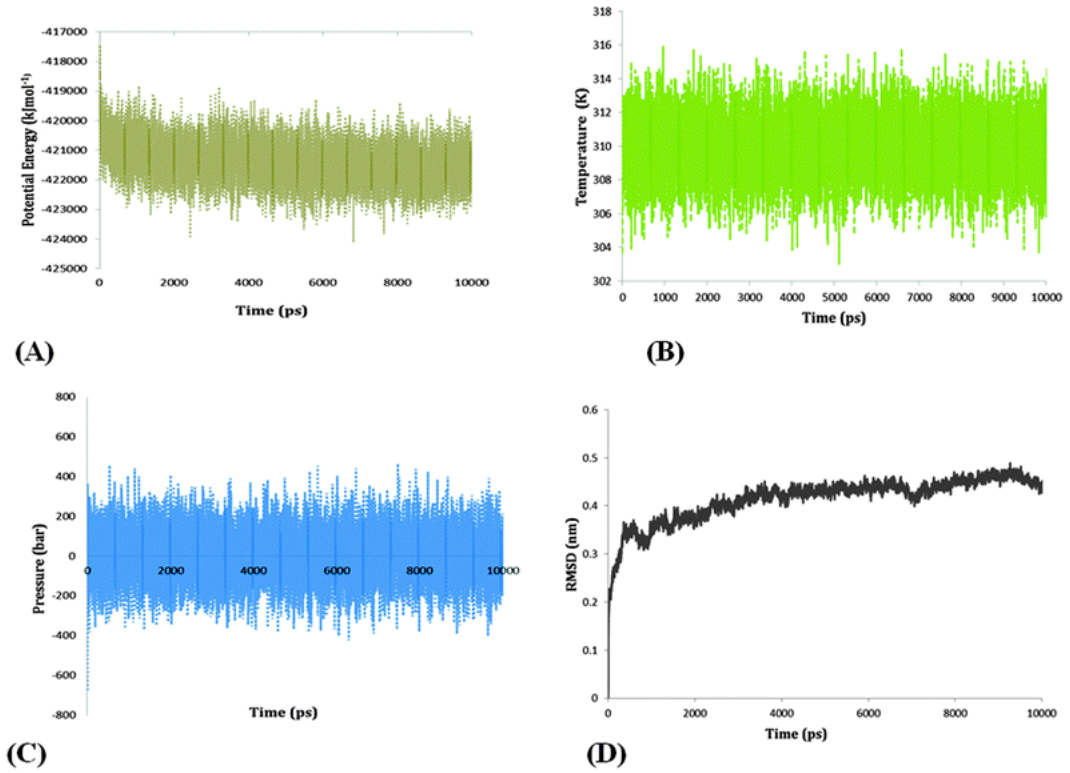


Fig. 5 Molecular dynamics simulation (A) potential energy (B) temperature 310 K (C) pressure of 1 bar (D) RMSD of the protein with respect to time and the protein structure.

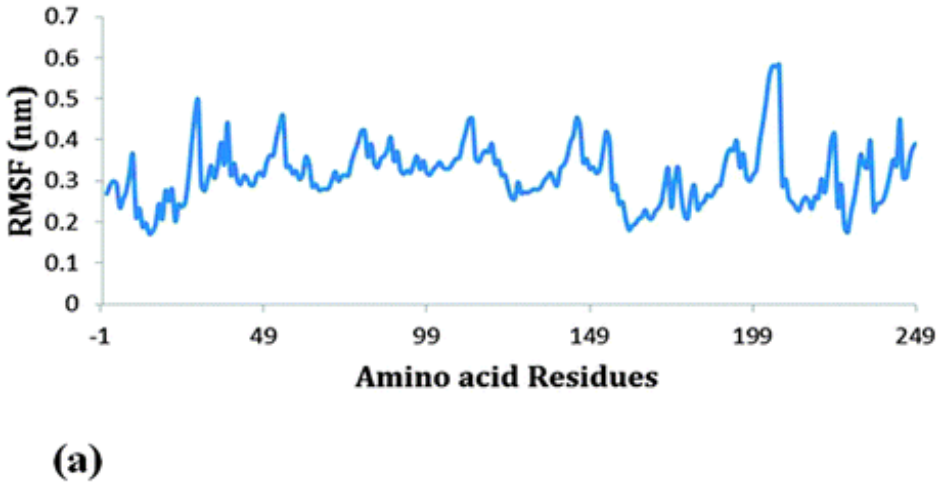


Fig. 6 (a) Root mean square fluctuation

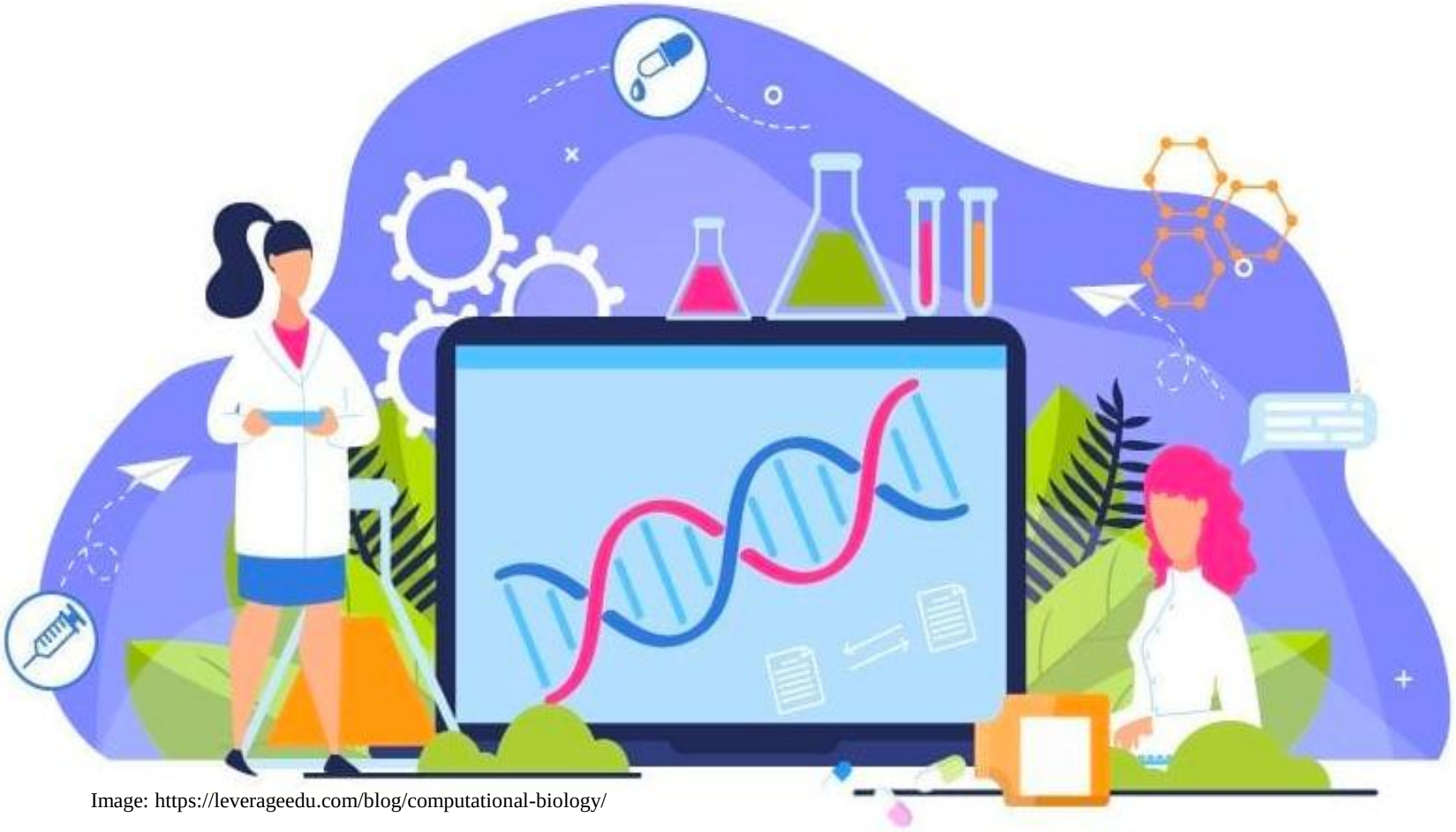


Image: https://leverageedu.com/blog/computational-biology/

Next : Analysis of MD trajectory (Part 2)