# Molecular Dynamics

# Numerical Integration and Position/Velocity update

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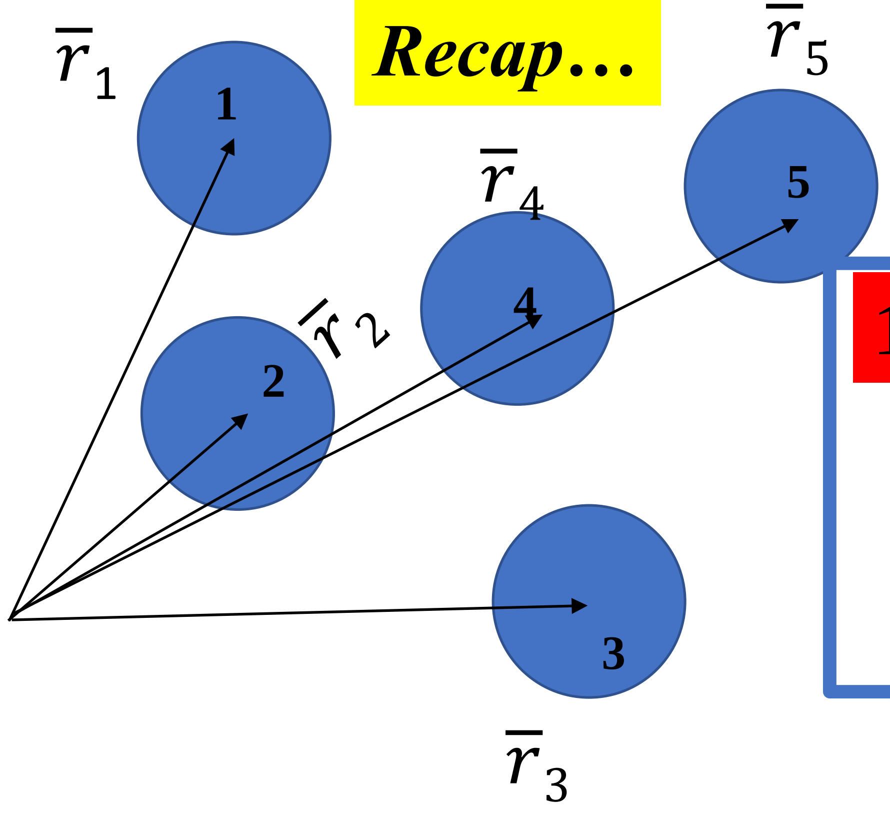
**Recap…**




# MD cycle (Four Steps)

**1**

$\{\bar{r}_i\}(0)$ $\{\bar{r}_i\}(\mathrm{dt})$

$\{\bar{v}_i\}(0)$ $\{\bar{v}_i\}(\mathrm{dt})$

$i \in [1, \mathrm{N}]$

**2**

$\mathrm{U}_{ij}(r_{ij})$

$$\mathrm{U}_{total} = \sum_{i>j} \mathrm{U}_{ij}(r_{ij})$$

**3**

$$\bar{F}_{j \to i} = -\frac{\partial \mathrm{U}_{ij}}{\partial r_{ij}} \vec{r}$$

$$\bar{F}_i = \sum_{i \neq j} \bar{F}_{j \to i}$$

**4**

**Newtons Law**

$$\mathrm{a}_\mathrm{i} = \frac{\bar{F}_i}{m_i}$$

*acceleration*

*Mass of "i" particle*

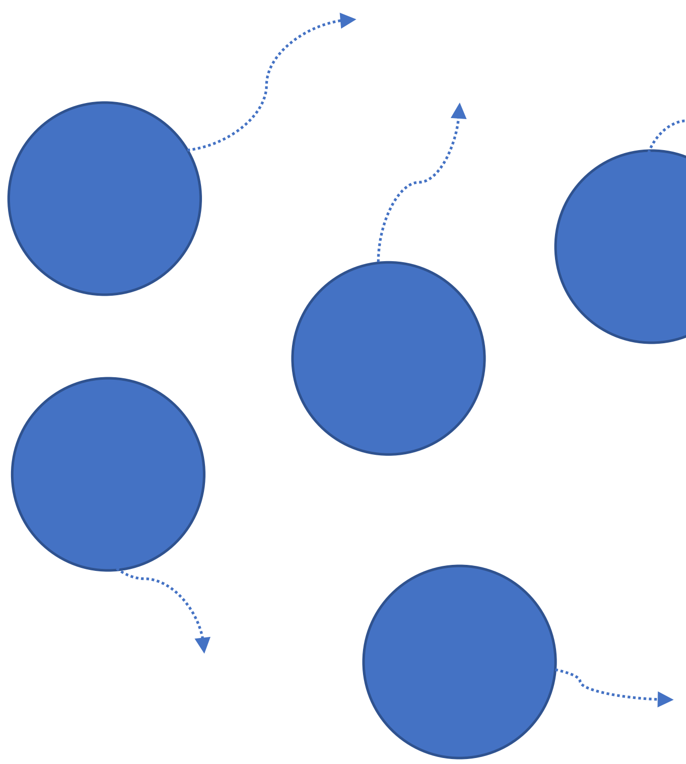
**Numerical integration**

**Time Step = dt**

***Recap…***

MD cycle (Four Steps)

0 → dt → 2 dt → 3dt ….



Outcome = Trajectory

# We will discuss the Green box

1

$\{\bar{r}_i\}(0)$ $\{\bar{r}_i\}(\mathrm{dt})$

$\{\bar{v}_i\}(0)$ $\{\bar{v}_i\}(\mathrm{dt})$

$i \in [1, \mathrm{N}]$

2

$\mathrm{U}_{ij}(r_{ij})$

$$\mathrm{U}_{total} = \sum_{i>j} \mathrm{U}_{ij}(r_{ij})$$

3

$$\bar{F}_{j \to i} = -\frac{\partial \mathrm{U}_{ij}}{\partial r_{ij}} \vec{r}$$

$$\bar{F}_i = \sum_{i \neq j} \bar{F}_{j \to i}$$

**Numerical integration**
**Time Step = dt**

4

**Newtons Law**

$$\mathrm{a}_i = \frac{\bar{F}_i}{m_i}$$

## Newtons Law

$$F_i = m_i a_i = m_i \frac{dv_i}{dt} = \frac{d(m_i v_i)}{dt} = \frac{dp_i}{dt} \quad \ldots(1)$$

F = Force, m = Mass, a = Acceleration
*v* = velocity, *t* = Time, P = m*v* = momentum
*i* = level of the particle

$$F_i = -\frac{dU}{dq_i} \quad \ldots.\ (2)$$

U = Energy, *q* = position of the particle

Equating above two equations:

$$\boxed{\frac{dp_i}{dt} = -\frac{dU}{dq_i}}$$

## Kinetic Energy

$$KE_i = \frac{1}{2} m_i v_i^2 = \frac{1}{2}\frac{m_i^2 v_i^2}{m_i} = \frac{P_i^2}{2\,m_i}$$

KE = Kinetic Energy

Differentiating with respect to time

$$\frac{d\,KE_i}{d\,P_i} = \frac{2.\,P_i}{2\,m_i} = \frac{P_i}{m_i} = \frac{m_i v_i}{m_i} = v_i = \frac{dq_i}{dt} \longrightarrow \boxed{\frac{d\,KE_i}{d\,P_i} = \frac{dq_i}{dt}}$$

# Hamilton's Equation of motion

$$\boxed{\frac{dp_i}{dt} = -\frac{dU}{dq_i}} \quad \text{.....} \quad (1)$$

$$\boxed{\frac{dq_i}{dt} = \frac{d\,KE_i}{d\,P_i}} \quad \text{.....} \quad (2)$$

- No exact solutions of equation (1) and (2)
- SOLVED NUMBERICALLY

***How ?***

## Taylor Series expansion in ‘position’

$$q(t+\Delta t) = q(t) + \Delta t \frac{d\,q(t)}{dt} + \frac{\Delta t^2}{2!}\frac{d^2 q(t)}{dt^2} + \frac{\Delta t^3}{3!}\frac{d^3 q(t)}{dt^3} + \frac{\Delta t^4}{4!}\frac{d^4 q(t)}{dt^4} + \dots$$

**Difficulty:**

- All the derivatives at $q_i$ are known (Infinite number).
- The function and all its derivatives are continuous and well defined.

Neglecting the higher order terms.

$$q(t+\Delta t) = q(t) + \Delta t \frac{d\,q(t)}{dt} + \frac{\Delta t^2}{2!}\frac{d^2 q(t)}{dt^2} + \cancel{\frac{\Delta t^3}{3!}\frac{d^3 q(t)}{dt^3}} + \cancel{\frac{\Delta t^4}{4!}\frac{d^4 q(t)}{dt^4}} + \cancel{\dots}$$

$$q(t+\Delta t) = q(t) + \Delta t \frac{dq(t)}{dt} + \frac{\Delta t^2}{2!}\frac{d^2 q(t)}{dt^2}$$

***v = velocity***

***a = Acceleration***

$$q(t+\Delta t) = q(t) + \Delta t \frac{dq(t)}{dt} + \frac{\Delta t^2}{2!}\frac{d^2q(t)}{dt^2}$$

$$=) \; q(t+\Delta t) = q(t) + \Delta t \, v(t) + \frac{\Delta t^2}{2!} a(t)$$

$$=) \; q(t+\Delta t) = q(t) + \Delta t \, v(t) + \frac{\Delta t^2}{2!}\frac{F(t)}{m}$$

Newtons Law: $a(t) = \frac{F(t)}{m}$

$$=) \; q(t+\Delta t) = q(t) + \Delta t \, v(t) + \frac{\Delta t^2}{2\,m}\left(-\frac{dU}{dq}\right)$$

$$\boxed{F = -\frac{dU}{dq}}$$

$$\boxed{q(t+\Delta t) = q(t) + \Delta t \, v(t) - \frac{\Delta t^2}{2\,m}\frac{dU}{dq}} \quad \text{….. (3)}$$

## Taylor Series expansion in ‘velocity’

$$v(t+\Delta t) = v(t) + \Delta t \frac{d\,v(t)}{dt} + \frac{\Delta t^2}{2!}\frac{d^2 v(t)}{dt^2} + \frac{\Delta t^3}{3!}\frac{d^3 v(t)}{dt^3} + \frac{\Delta t^4}{4!}\frac{d^4 v(t)}{dt^4} + \dots$$

If the “$\Delta t$” is small then I can neglect the higher order terms.

$$v(t+\Delta t) = v(t) + \Delta t \frac{d\,v(t)}{dt} + \frac{\Delta t^2}{2!}\frac{d^2 v(t)}{dt^2}$$

***a* = *Acceleration***

What is this term ?

**I need to replace this RED term with known !**

**Lets do a Taylor Series expansion in '$\frac{d\,v(t)}{dt}$'**

$$\frac{d\,v(t+\Delta t)}{dt} = \frac{d\,v(t)}{dt} + \Delta t\,\frac{d}{dt}\frac{d\,v(t)}{dt} + \frac{\Delta t^2}{2!}\frac{d^2}{dt^2}\frac{d\,v(t)}{dt} + \frac{\Delta t^3}{3!}\frac{d^3}{dt^3}\frac{d\,v(t)}{dt} + \frac{\Delta t^4}{4!}\frac{d^4}{dt^4}\frac{d\,v(t)}{dt} + \ldots$$

If the "$\Delta t$" is small then I can neglect the higher order terms.

$$\Rightarrow \frac{d\,v(t+\Delta t)}{dt} = \frac{d\,v(t)}{dt} + \Delta t\,\frac{d^2 v(t)}{dt^2} + \cancel{\frac{\Delta t^2}{2!}\frac{d^3 v(t)}{dt^3}} + \cancel{\frac{\Delta t^3}{3!}\frac{d^4 v(t)}{dt^4}} + \cancel{\frac{\Delta t^4}{4!}\frac{d^5 v(t)}{dt^5}} + \ldots$$

$$\Rightarrow \frac{d\,v(t+\Delta t)}{dt} = \frac{d\,v(t)}{dt} + \Delta t\,\frac{d^2 v(t)}{dt^2}$$

Multiple $\frac{\Delta t}{2}$ both sides: $\frac{\Delta t}{2}\frac{d\,v(t+\Delta t)}{dt} = \frac{\Delta t}{2}\frac{d\,v(t)}{dt} + \frac{\Delta t}{2}.\Delta t\,\frac{d^2 v(t)}{dt^2}$

$$\Rightarrow \frac{\Delta t}{2}\frac{d\,v(t+\Delta t)}{dt} = \frac{\Delta t}{2}\frac{d\,v(t)}{dt} + \frac{\Delta t^2}{2}\frac{d^2 v(t)}{dt^2}$$

Term needs to be replaced

$$\frac{\Delta t^2}{2}\frac{d^2 v(t)}{dt^2} = \frac{\Delta t}{2}\frac{d\,v(t+\Delta t)}{dt} - \frac{\Delta t}{2}\frac{d\,v(t)}{dt}$$

Substituting the above term in "Equation 3"

$$v(t+\Delta t) = v(t) + \Delta t\,\frac{d\,v(t)}{dt} + \frac{\Delta t^2}{2!}\frac{d^2 v(t)}{dt^2}$$

$$=)\ v(t+\Delta t) = v(t) + \Delta t\,\frac{d\,v(t)}{dt} + \frac{\Delta t}{2}\frac{d\,v(t+\Delta t)}{dt} - \frac{\Delta t}{2}\frac{d\,v(t)}{dt}$$

$$=)\ v(t+\Delta t) = v(t) + \frac{\Delta t}{2}\frac{d\,v(t)}{dt} + \frac{\Delta t}{2}\frac{d\,v(t+\Delta t)}{dt}$$

$a(t)$ = *Acceleration*

$a(t+\Delta t)$ = *Acceleration*

$$=)\ v(t+\Delta t) = v(t) + \frac{\Delta t}{2}\ a(t) + \frac{\Delta t}{2}\ a(t+\Delta t)$$

$$=)\ v(t+\Delta t) = v(t) + \frac{\Delta t}{2}\ [\ a(t) + \ a(t+\Delta t)\ ]$$

$$=)\ v(t+\Delta t) = v(t) + \frac{\Delta t}{2}\ [\ \frac{F(t)}{m} + \frac{F(t+\Delta t)}{m}]$$

Newtons Law:

$a(t) = \frac{F(t)}{m}$

$$=)\ v(t+\Delta t) = v(t) + \frac{\Delta t}{2}\ [\ \frac{F(t)}{m} + \frac{F(t+\Delta t)}{m}]$$

$$F\ = -\ \frac{dU}{dq}$$

$$=)\ v(t+\Delta t) = v(t) + \frac{\Delta t}{2\ m}\ [-\ \frac{dU(t)}{dq}\ - \frac{dU(t+\Delta t)}{dq}]$$

$$=)\ v(t+\Delta t) = v(t) - \frac{\Delta t}{2\ m}\ [\frac{dU(t)}{dq}\ + \frac{dU(t+\Delta t)}{dq}] \quad \text{..... (4)}$$

# Velocity Verlet algorithm

*time-step*

*Positions of Previous time-step*

*Velocities of Previous time-step*

*Gradient of energy at Previous time-step*

$$q(t+\Delta t) = q(t) + \Delta t\, v(t) - \frac{\Delta t^2}{2\,m}\frac{dU(t)}{dq} \quad \text{..... (3)}$$

$$v(t+\Delta t) = v(t) - \frac{\Delta t}{2\,m}\left[\frac{dU(t)}{dq} + \frac{dU(t+\Delta t)}{dq}\right] \quad \text{..... (4)}$$

*Gradient of energy at next time-step*

# Velocity Verlet algorithm

$$q(t+\Delta t) = q(t) + \Delta t\, v(t) - \frac{\Delta t^2}{2\,m}\frac{dU(t)}{dq} \quad \text{....(3)}$$

$$v(t+\Delta t) = v(t) - \frac{\Delta t}{2\,m}\left[\frac{dU(t)}{dq} + \frac{dU(t+\Delta t)}{dq}\right] \quad \text{....(4)}$$

1. Given initial positions [ q(t) ] and velocities [ v(t)] at time ‘t’
2. Calculate $\frac{dU(t)}{dq}$
3. Calculate q($t$+Δ$t$) from equation 3
4. Calculate $\frac{dU(t+\Delta t)}{dq}$
5. Calculate $v$($t$+Δ$t$) from equation 4.
6. Repeat (2 → 5)

# Molecular Dynamics

## Velocity Verlet algorithm

1. Given initial positions [ q(t) ] and velocities [ v(t)]  at time ‘t’

2. Calculate $\frac{dU(t)}{dq}$

3. Calculate q($t$+Δ$t$) from equation 3

4. Calculate $\frac{dU(t+\Delta t)}{dq}$

5. Calculate $v$($t$+Δ$t$) from equation 4.

6. Repeat (2 →5)

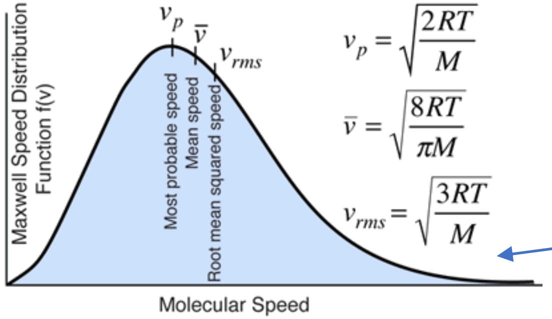
- **Initial coordinates q(t=0) :**

**PDB,   Theoretical Model (e.g, Homology Model).**

- **Initial velocities $v$(t=0) :**

**Maxwell-Boltzmann distribution at a given temperature (Require THERMAL EQUILIBRIUM)**

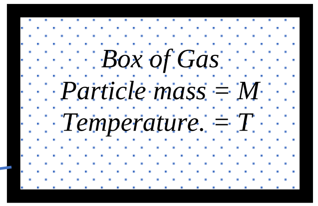
$$f(v) = 4\pi\left[\frac{M}{2\pi RT}\right]^{\frac{3}{2}} v^2 \exp\left[\frac{-Mv^2}{2RT}\right]$$




$$v_p = \sqrt{\frac{2RT}{M}}$$

$$\bar{v} = \sqrt{\frac{8RT}{\pi M}}$$

$$v_{rms} = \sqrt{\frac{3RT}{M}}$$

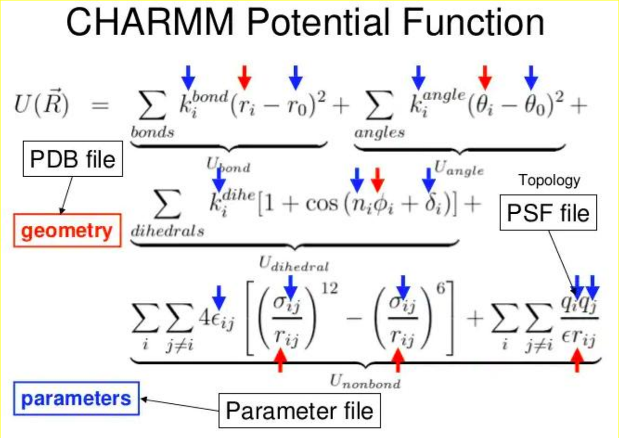



https://socratic.org/questions/5a3da9a0b72cff0f5f5840ed

# Molecular Dynamics (MD)

**CALCULATION OF Energy Gradient $\frac{dU}{dq}$**

- Using Classical Force-field ➔ Classical MD




- Using Quantum Mechanics “Schrodinger equation” ➔ Abinito MD

- Combining Quantum Mechanics & Classical Force-field ➔ QM/MM MD

## What Time – Step "$\Delta t$" one should use ?

- ❖ No hard and fast rule.
- ❖ "$\Delta t$" too small ➔ Limited Sampling
- ❖ "$\Delta t$" too Large ➔ error in Velocity-verlet algorithm (Taylor series truncation)

- ➢ Appropriate time-step "$\Delta t$" ➔ Efficient Sampling + Collision occur smoothly
  - ➢ Liquid Simulations: "$\Delta t$" should be small compared to <collision time>
  - ➢ Biomolecules: $\Delta t$ should be ($1/10^{th}$) of the fastest motion

e.g, C-H bond vibrate with 10 fs repeat period

Thus, use $\Delta t = 1$ fs

High frequency motions are usually of relatively less interest and have a minimal effect on the overall behavior of the system

(Solution: Constrain covalent bonds involving hydrogens)

$\Delta t = 2$ fs (**SHAKE algorithm, LINCS algorithm)**

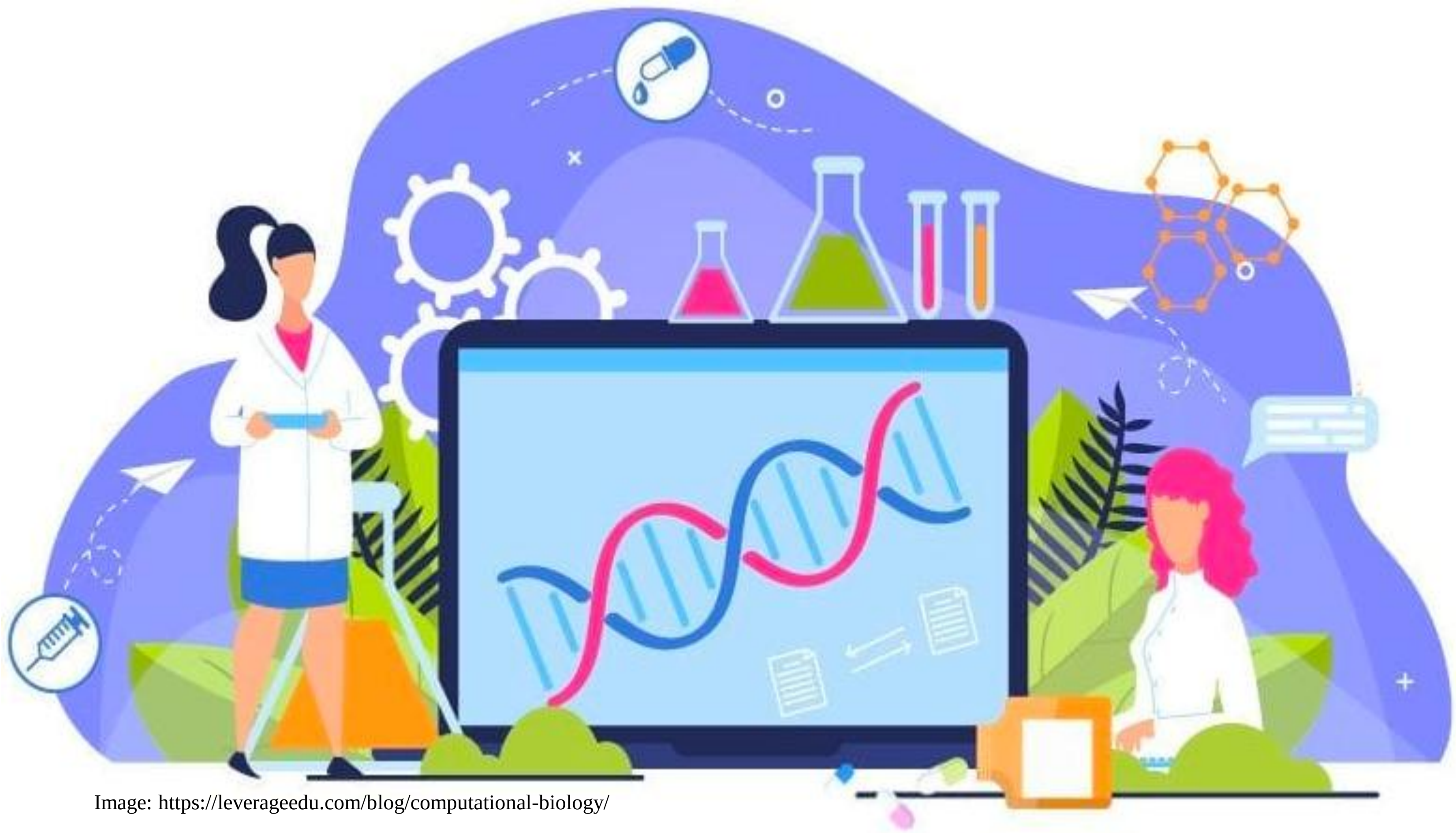


Image: https://leverageedu.com/blog/computational-biology/

# Next :Boundary Conditions, Cut-off, Temperature and Pressure control