



# Molecular simulation

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Gerald R. Kneller

Centre de Biophysique Moléculaire, CNRS  
Rue Charles Sadron; 45071 Orléans

<http://dirac.cnrs-orleans.fr>





# Content

1. Classical Molecular Dynamics
2. Monte Carlo simulation
3. *Ab initio* molecular dynamics
4. Annexe: Elements of quantum mechanics



# Chapter 1

# Classical Molecular Dynamics simulation





# Born-Oppenheimer approximation

Hamilton operator for nuclei and electrons :

$$\hat{H} = \hat{H}_{nn} + \hat{H}_{ee} + \hat{V}_{ne}$$

The components are

$$\hat{H}_{nn} = \sum_i \frac{-\hbar^2}{2M_i} \frac{\partial^2}{\partial \mathbf{R}_i^2} + \frac{1}{4\pi\epsilon_0} \sum_i \sum_{i < j} \frac{Z_i Z_j e^2}{|\mathbf{R}_i - \mathbf{R}_j|},$$

$$\hat{H}_{ee} = \sum_i \sum_{\alpha} \frac{-\hbar^2}{2m_e} \frac{\partial^2}{\partial \mathbf{r}_{i,\alpha}^2} + \frac{1}{4\pi\epsilon_0} \sum_{i,\alpha} \sum_{j < i,\beta} \frac{e^2}{|\mathbf{r}_{i,\alpha} - \mathbf{r}_{j,\beta}|} + \frac{1}{4\pi\epsilon_0} \sum_i \sum_{\alpha < \beta} \frac{e^2}{|\mathbf{r}_{i,\alpha} - \mathbf{r}_{i,\beta}|},$$

$$\hat{V}_{ne} = \frac{1}{4\pi\epsilon_0} \sum_i \sum_{j,\alpha} \frac{-Z_i e^2}{|\mathbf{R}_i - \mathbf{r}_{j,\alpha}|}.$$

Notation:  $n =$  nuclei ( $i, j, \dots$ ),  $e =$  electrons ( $\alpha, \beta, \dots$ ).



## Stationary problem for the electrons

Time scale separation between the time scales of the motions of the “light” and the “heavy” atoms ( $M_i \gg m_e$ ). The electron dynamics follows instantaneously the motions of the nuclei.

- *Electron wave function :*

$$\psi_e(\{\mathbf{r}_{i,\alpha}\}, t | \{\mathbf{R}_i\}) = u_e(\{\mathbf{r}_{i,\alpha}\} | \{\mathbf{R}_i\}) e^{-\frac{i}{\hbar} E_e t}.$$

- *Stationary Schrödinger equation :*

$$\left\{ \hat{H}_{ee} + \hat{V}_{ne} \right\} u_e = E_e(\{\mathbf{R}_i\}) u_e.$$

The eigenvalues are implicit functions of the configuration of the nuclei!



# Schrödinger Equation of the nuclei:

$$i\hbar \frac{\partial \psi_n}{\partial t} = \hat{H}_n \psi_n,$$
$$\hat{H}_n = \sum_i \frac{-\hbar^2}{2M_i} \frac{\partial^2}{\partial \mathbf{R}_i^2} + \underbrace{\hat{V}_{nn} + E_e(\{\mathbf{R}_i\})}_{V_n(\{\mathbf{R}_i\})}.$$

The potential of the nuclei is the superposition of the repulsive coulombic terms repulsive terms,  $V_{nn}$ , and the Born-Oppenheimer electronic energy,  $E_e(\{\mathbf{R}_i\})$ , which depends in a parametric way on the positions of the nuclei.





# Classical MD

## Concept

Instead of solving the Schrödinger equation with the potential  $V_n(\{\mathbf{R}_i\})$  for the nuclei, we solve the Newton equations,

$$M_i \ddot{\mathbf{R}}_i = -\frac{\partial U(\{\mathbf{R}_i\})}{\partial \mathbf{R}_i},$$

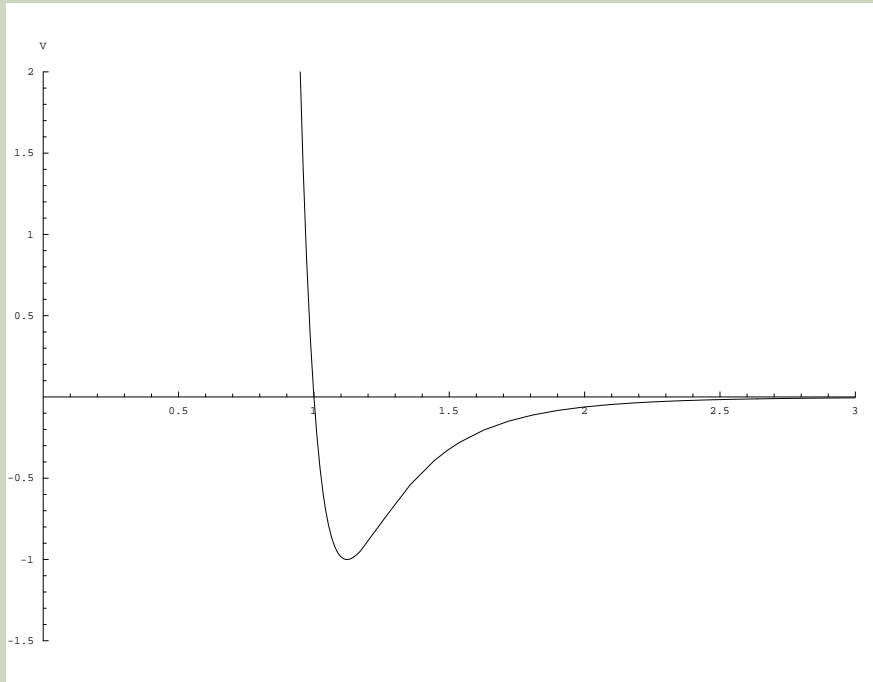
where  $U(\{\mathbf{R}_i\})$  is an *empirical potential* which is fitted to  $V_n(\{\mathbf{R}_i\})$ ,

$$U(\{\mathbf{R}_i\}) \approx V_n(\{\mathbf{R}_i\}).$$

The simplest example is the Lennard-Jones potential, which is used for simple liquids

$$U(r) = 4\epsilon \left( \frac{\sigma^{12}}{r^{12}} - \frac{\sigma^6}{r^6} \right).$$





*The Lennard Jones potential for  $\epsilon = 1$  and  $\sigma = 1$ . The minimum is at  $r_0 = 2^{1/6}\sigma$ .*





# Force field for a biological macromolecule:

$$\begin{aligned} U = & \sum_{\text{liaisons } ij} k_{ij} \left( r_{ij} - r_{ij}^{(0)} \right)^2 \\ & + \sum_{\text{angles } ijk} k_{ijk} \left( \phi_{ijk} - \phi_{ijk}^{(0)} \right)^2 \\ & + \sum_{\text{dièdres } ijkl} k_{ijkl} \cos \left( n_{ijkl} \theta_{ijkl} - \delta_{ijkl} \right) \\ & + \sum_{\text{paires } ij} 4\epsilon_{ij} \left( \frac{\sigma_{ij}^{12}}{r^{12}} - \frac{\sigma_{ij}^6}{r^6} \right) + \sum_{\text{paires } ij} \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}. \end{aligned}$$

The terms in red describe the resulting forces of **chemical bonds**, and the blue terms describe the effects of the interactions "non-bonded" (excluded volume, attractive interactions between induced dipoles, and electrostatic interactions).



## Coupled vibrations

- *Quadratic approximation of  $U$ :*

Near an equilibrium point,  $\mathbf{R}_0$ , we can approximate

$$U(\mathbf{R}) \approx U(\mathbf{R}_0) + \frac{1}{2}(\mathbf{R} - \mathbf{R}_0)^T \cdot \mathbf{K} \cdot (\mathbf{R} - \mathbf{R}_0),$$

where  $\mathbf{K}$  is the matrix of force constants

$$\mathbf{K} := \left. \frac{\partial^2 U(\mathbf{R})}{\partial \mathbf{R}^2} \right|_{\mathbf{R}_0} \quad \text{et} \quad \left. \frac{\partial U(\mathbf{R})}{\partial \mathbf{R}} \right|_{\mathbf{R}_0} = \mathbf{0}.$$

- *Matrix equation of motion:*

$$\mathbf{M} \cdot \ddot{\mathbf{x}} + \mathbf{K} \cdot \mathbf{x} = \mathbf{0}, \quad \text{où} \quad \mathbf{x} := \mathbf{R} - \mathbf{R}_0.$$

$\mathbf{M}$  is the (diagonal) mass matrix.



## ...Coupled vibrations

- *Diagonalisation:*

$$\ddot{\tilde{\mathbf{x}}} + \tilde{\mathbf{K}} \cdot \mathbf{x} = \mathbf{0}, \quad \text{où } \tilde{\mathbf{x}} := \mathbf{M}^{1/2} \cdot \mathbf{x}, \quad \tilde{\mathbf{K}} = \mathbf{M}^{-1/2} \cdot \mathbf{K} \cdot \mathbf{M}^{-1/2}.$$

- *Normal modes:*

$$\tilde{\mathbf{K}} \cdot \mathbf{u}_j = \omega_j^2 \mathbf{u}_j, \quad \mathbf{u}_i \cdot \mathbf{u}_j = \delta_{ij}.$$

Therefore

$$\tilde{\mathbf{x}}(t) = \sum_{j=1}^n \mathbf{u}_j \left\{ c_j \exp[i\omega_j t] + c_j^* \exp[-i\omega_j t] \right\},$$

where  $\omega_j > 0$ , assuming that  $\tilde{\mathbf{K}}$  is positive definite. The  $c_j$  are fixed by the initial conditions.





# Classical limit

- *Normal modes*: The classical approximation is valid if

$$\hbar\omega_j \ll k_B T.$$

In a macromolecule only modes with low frequencies can be described in the framework of classical mechanics.

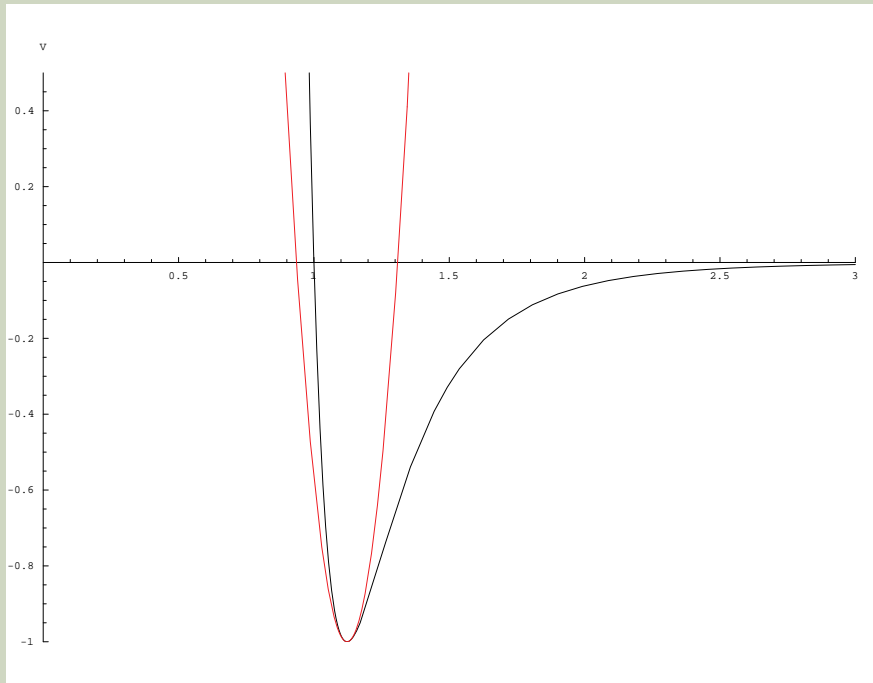
$$\nu_j \ll 200 \text{ cm}^{-1} \approx 6 \text{ THz}, \quad \text{où } \omega_j = 2\pi\nu_j \quad \text{et } T = 300 \text{ K}.$$

- *MD simulation*: We can estimate a frequency  $\omega_0$  by the *curvature* of the potential between two particles. For the LJ potential we get

$$U_{LJ}(r) \approx -\epsilon + \frac{18 \cdot 2^{2/3} \epsilon (r - 2^{1/6} \sigma)^2}{\sigma^2} \implies \omega_j = \sqrt{\frac{18 \cdot 2^{2/3} \epsilon}{\mu \sigma^2}},$$

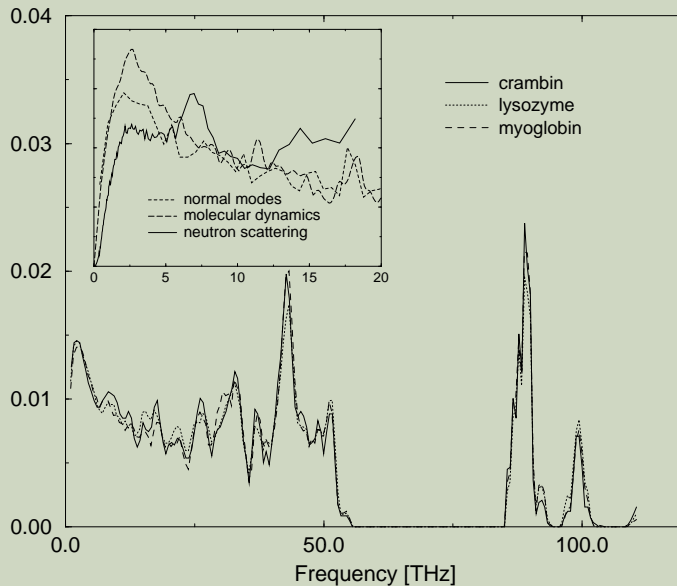
where  $\mu$  is the reduced mass.





Approximation of a Lennard-Jones potential by a harmonic potential ( $\epsilon = 1$ ,  $\sigma = 1$ ). For liquid argon we obtain  $\hbar\omega_0 = 2.15 \cdot 10^{-3} k_B T$  at  $T = 94.4K$ . The classical approximation is good.



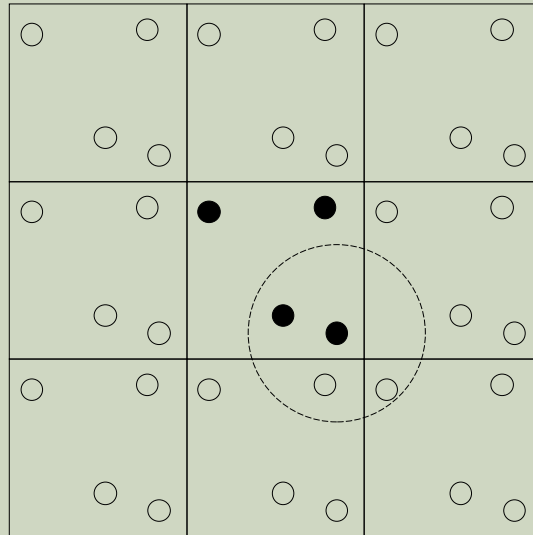


*Spectrum of normal modes for three proteins and  $T = 300\text{ K}$  as a function of  $\nu$ . The insertion concerns myoglobin only and shows a comparison between normal modes, MD simulation, and experimental data from inelastic neutron scattering. **The classical approximation is good for  $\nu \ll 6\text{ THz}$ .***





# Simulation of an infinite system



*Periodic conditions and “minimum image convention” in an MD simulation. If  $L$  is the length of the box, all interactions (except coulombic interactions) are computed within a radius within a radius  $L/2$ .*





# Integration algorithms

## Verlet:

Only the positions are used.

$$\mathbf{R}_i(t + \Delta t) \leftarrow 2\mathbf{R}_i(t) - \mathbf{R}_i(t - \Delta t) + \frac{\Delta t^2}{M_i} \mathbf{F}_i(t).$$

Accelerations and velocities are approximated by

$$\dot{\mathbf{R}}_i \approx \frac{\mathbf{R}_i(t + \Delta t) - \mathbf{R}_i(t - \Delta t)}{2\Delta t},$$
$$\ddot{\mathbf{R}}_i \approx \frac{\mathbf{R}_i(t + \Delta t) - 2\mathbf{R}_i(t) + \mathbf{R}_i(t - \Delta t)}{\Delta t^2}.$$





## “Leap-frog”:

Velocities and positions are used.

$$\mathbf{V}_i(t + \Delta t/2) \leftarrow \mathbf{V}_i(t - \Delta t/2) + \frac{\Delta t}{M_i} \mathbf{F}_i(t)$$

$$\mathbf{R}_i(t + \Delta t) \leftarrow \mathbf{R}_i(t) + \mathbf{V}_i(t + \Delta t/2)$$

## “Velocity-Verlet”:

Again velocities and positions are used.

$$\mathbf{R}_i(t + \Delta t) \leftarrow \mathbf{R}_i(t) + \mathbf{V}_i(t) \Delta t$$

$$\mathbf{V}_i(t + \Delta t) \leftarrow \mathbf{V}_i(t) + \frac{\Delta t}{M_i} \left( \frac{\mathbf{F}_i(t + \Delta t) + \mathbf{F}_i(t)}{2} \right)$$

Velocities and positions are available at the same time.





# Geometric constraints

Goal: "Freeze" the fastest movements, such as the vibrations of the bonds, in order to allow the use of longer integration steps.

## Holonomic constraints

It is required that

$$\sigma^\alpha(\mathbf{R}, t) = 0, \quad \alpha = 1 \dots l,$$

where  $\mathbf{R} = (\mathbf{R}_1^T, \dots, \mathbf{R}_N^T)^T$ . An example of a constraint is a fixed bond length:

$$\sigma(\mathbf{R}, t) := (\mathbf{R}_1 - \mathbf{R}_2)^2 - l_{12}^2 \equiv 0.$$



# Unconstrained Lagrangian Mechanics

With the *Lagrange function*

$$\mathcal{L} = \frac{1}{2} \dot{\mathbf{R}}^T \cdot \mathbf{M} \cdot \dot{\mathbf{R}} - \mathcal{V}(\mathbf{R}),$$

we obtain the equations of motion by postulating that the variation

$$\mathcal{S} = \int_{t_0}^{t_1} dt \mathcal{L}(\dot{\mathbf{R}}, \mathbf{R}, t) = \text{Min.}$$

for the true trajectory. This gives

$$\delta \mathcal{S} = \int_{t_0}^{t_1} dt \delta \mathbf{R}^T \left( \frac{d}{dt} \frac{\partial \mathcal{L}}{\partial \dot{\mathbf{R}}} - \frac{\partial \mathcal{L}}{\partial \mathbf{R}} \right) = 0.$$

Without constraints the variations  $\delta \mathbf{R}$  are arbitrary and

$$\frac{d}{dt} \frac{\partial \mathcal{L}}{\partial \dot{\mathbf{R}}} = \frac{\partial \mathcal{L}}{\partial \mathbf{R}} \quad \Longrightarrow \quad \mathbf{M} \cdot \ddot{\mathbf{R}} = -\frac{\partial \mathcal{V}}{\partial \mathbf{R}} \equiv \mathbf{f}.$$



# Lagrange mechanics with constraints

Since

$$\sigma^\alpha(\mathbf{R}_0 + \delta\mathbf{R}, t) - \sigma^\alpha(\mathbf{R}_0, t) = 0$$

for a differential variation, it follows that

$$\mathbf{A} \cdot \delta\mathbf{R} = \mathbf{0}, \quad A_i^\alpha = \frac{\partial \sigma^\alpha}{\partial r^i}.$$

The allowed variations are in the nullspace of  $\mathbf{A}$ ,  $\delta\mathbf{R} \in \mathbb{V}_\parallel$ . We know that

$$\delta\mathcal{S} = \int_{t_0}^{t_1} dt \underbrace{\delta\mathbf{R}^T}_{\in \mathbb{V}_\parallel} \cdot \underbrace{\left( \frac{d}{dt} \frac{\partial \mathcal{L}}{\partial \dot{\mathbf{R}}} - \frac{\partial \mathcal{L}}{\partial \mathbf{R}} \right)}_{\in \mathbb{V}_\perp} = 0.$$

Therefore

$$\mathbf{M} \cdot \ddot{\mathbf{R}} = \mathbf{f} + \mathbf{z}, \quad \mathbf{z} = \mathbf{A}^T \boldsymbol{\mu} \in V_\perp.$$

Here  $Mz$  is the *constraint force*, and  $\boldsymbol{\mu} = (\mu_1, \dots, \mu_l)^T$  contains the Lagrangian parameters.



## The SHAKE algorithm

For the computation of the  $\mu_k$  parameters J.-P. RYCKAERT *et al.* have proposed the SHAKE algorithm which guarantees that the constraints are verified in the presence of unavoidable numerical errors errors.<sup>1</sup>  
Dans le schéma de Verlet on écrit

$$\mathbf{R}_{n+1} = \mathbf{R}_{n+1}^{(0)} + \Delta t^2 \mathbf{M}^{-1} \cdot \mathbf{A}^T(\mathbf{R}_n) \cdot \boldsymbol{\mu}_n,$$

where  $\mathbf{R}_{n+1}^{(0)}$  is the new position *without* the presence of constraints

$$\mathbf{R}_{n+1}^{(0)} = 2\mathbf{R}_n - \mathbf{R}_{n-1} + \Delta t^2 \mathbf{M}^{-1} \cdot \mathbf{f}(\mathbf{R}_n).$$

We require that the constraints are exactly verified for the *new* positions,

$$\boldsymbol{\sigma}(\mathbf{R}_{n+1}) = \mathbf{0}, \quad \text{où } \boldsymbol{\sigma} := (\sigma^1, \dots, \sigma^l)^T.$$

Remark: In the Verlet scheme one should compute the  $\mu_\alpha$  from  $\boldsymbol{\sigma}(\mathbf{R}_n) = \mathbf{0}$ .

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<sup>1</sup>Ryckaert, J.-P., G. Ciccotti and H.J.C. Berendsen. *J. Comp. Phys.*, 23:327-341, 1977.



## Implementation of SHAKE:

1. Given  $\mathbf{R}_{n+1}^{(0)}$ , compute  $\sigma^\alpha(\mathbf{R}_{n+1}^{(0)})$ , and initialize  $j = 0$ .
2. Calcule  $d_\alpha^j = \Delta t^2 \left( \mathbf{A}(\mathbf{R}_{n+1}^{(j)}) \cdot \mathbf{M}^{-1} \cdot \mathbf{A}^T(\mathbf{R}_n) \right)_{\alpha\alpha}$
3. Compute the estimations  $\mu_\alpha^{(j)} = -\sigma^\alpha(\mathbf{R}_{n+1}^{(j)})/d_\alpha^j$
4. Compute corrected estimations  
$$\mathbf{R}_{n+1}^{(j+1)} = \mathbf{R}_{n+1}^{(j)} + \Delta t^2 \mathbf{M}^{-1} \cdot \mathbf{A}^T(\mathbf{R}_n) \cdot \boldsymbol{\mu}^{(j)}$$
5. Compute  $\sigma^\alpha(\mathbf{R}_{n+1}^{(j+1)})$  and verify that  $|\sigma^\alpha(\mathbf{R}_{n+1}^{(j+1)})| \leq \epsilon$  pour toutes les contraintes

for all the constraints. If the result is OK, stop. Otherwise, start over with 2

Here  $\epsilon$  is a tolerance parameter. We notice that the constraints are considered *independent* in the computation of  $\mu_\alpha^{(j)}$  estimates.





# Rigid molecules

## Positioning a rigid body

For each mass point we write

$$\mathbf{R}_i(t) = \mathbf{R}_0(t) + \mathbf{r}_i(t) \quad \text{où} \quad \mathbf{r}_i(t) = \mathbf{D}(\mathbf{x}(t)) \cdot \hat{\mathbf{r}}_i.$$

Here  $\mathbf{R}_0$  points to the center of mass, and  $\mathbf{r}_i = \mathbf{R}_i - \mathbf{R}_0$ . The matrix  $\mathbf{D}$  is orthogonal and parametrized by the coordinates  $\mathbf{x}$ .

## Angular velocities

Using  $\mathbf{D}^T \cdot \mathbf{D} = \mathbf{1}$  we deduce the relations

$$\dot{\mathbf{r}}_i = \boldsymbol{\omega} \wedge \mathbf{r}_i = \mathbf{D} \cdot (\hat{\boldsymbol{\omega}} \wedge \hat{\mathbf{r}}_i).$$

Here  $\boldsymbol{\omega} = \mathbf{D} \cdot \hat{\boldsymbol{\omega}}$ . The “hat” marks the reference frame related to the body. We have linear relations ( $\mathbf{A}$  and  $\hat{\mathbf{A}}$  depend on the choice of  $\mathbf{x}$ )

$$\boldsymbol{\omega} = \mathbf{A}(\mathbf{x}) \cdot \dot{\mathbf{x}}, \quad \hat{\boldsymbol{\omega}} = \hat{\mathbf{A}}(\mathbf{x}) \cdot \dot{\mathbf{x}}.$$



# Lagrange function

$$\mathcal{L} = \sum_{\alpha} \frac{1}{2} M_{\alpha} \dot{\mathbf{R}}_{\alpha,0}^2 + \sum_{\alpha,i} \frac{1}{2} m_{\alpha,i} \dot{\mathbf{r}}_{\alpha,i}^2 - \mathcal{V}(\{\mathbf{R}_{\alpha,0} + \mathbf{r}_{\alpha,i}\}).$$

For any molecule  $M_{\alpha} = \sum_i m_{\alpha,i}$ .

## Variation

$$\delta\mathcal{S} = \int_{t_0}^{t_1} dt \left\{ \sum_{\alpha} \delta\mathbf{R}_{\alpha,0}^T \cdot \left( \frac{d}{dt} \frac{\partial\mathcal{L}}{\partial\dot{\mathbf{R}}_{\alpha,0}} - \frac{\partial\mathcal{L}}{\partial\mathbf{R}_{\alpha,0}} \right) + \sum_{i,\alpha} \delta\mathbf{r}_{\alpha,i}^T \cdot \left( \frac{d}{dt} \frac{\partial\mathcal{L}}{\partial\dot{\mathbf{r}}_{\alpha,i}} - \frac{\partial\mathcal{L}}{\partial\mathbf{r}_{\alpha,i}} \right) \right\} = 0.$$

Here we pose ( $\eta_{\alpha}$  are quasi-coordinates)

$$\dot{\mathbf{r}}_{\alpha,i} = \boldsymbol{\omega}_{\alpha} \wedge \mathbf{r}_{\alpha,i}, \quad \delta\mathbf{r}_{\alpha,i} = \delta\boldsymbol{\eta}_{\alpha} \wedge \mathbf{r}_{\alpha,i}, \quad \delta\boldsymbol{\eta}_{\alpha} \propto \boldsymbol{\omega}_{\alpha}.$$





## Equations of motion for the center of mass:

The  $\delta \mathbf{R}_{\alpha,0}^T$  are arbitrary and we find

$$M_\alpha \ddot{\mathbf{R}}_{\alpha,0} = \sum_i \mathbf{F}_{\alpha,i}, \quad \mathbf{F}_{\alpha,i} = -\frac{\partial \mathcal{V}(\{\mathbf{R}_{\beta,j}\})}{\partial \mathbf{R}_{\alpha,i}}.$$

## Equations of motion for the rotation:

We find

$$\frac{d}{dt} [\Theta_\alpha \cdot \boldsymbol{\omega}_\alpha] \equiv \frac{d\mathbf{L}_\alpha}{dt} = \mathbf{N}_\alpha, \quad \mathbf{N}_\alpha = \sum_i \mathbf{r}_{\alpha,i} \wedge \mathbf{F}_{\alpha,i}.$$

For the  $\dot{\mathbf{x}}_\alpha$  we have the relations

$$\mathbf{A}(\mathbf{x}_\alpha) \cdot \dot{\mathbf{x}}_\alpha = \boldsymbol{\omega}_\alpha.$$

$\Theta_\alpha$  is the *inertia tensor* (index  $\alpha$  omitted)

$$\Theta = \begin{pmatrix} \sum_i (y_i^2 + z_i^2) & -\sum_i x_i y_i & -\sum_i x_i z_i \\ -\sum_i x_i y_i & \sum_i (x_i^2 + z_i^2) & -\sum_i y_i z_i \\ -\sum_i x_i z_i & -\sum_i y_i z_i & \sum_i (x_i^2 + y_i^2) \end{pmatrix}.$$



## Euler equations for the rotation:

We work in the reference of the principal axes  $\hat{\Sigma}$ :

$$\dot{\mathbf{r}}_{\alpha,i} = \mathbf{D}(\mathbf{x}_\alpha) \cdot (\hat{\boldsymbol{\omega}}_\alpha \wedge \hat{\mathbf{r}}_{\alpha,i}), \quad \delta \mathbf{r}_{\alpha,i} = \mathbf{D}(\mathbf{x}_\alpha) \cdot (\delta \hat{\boldsymbol{\eta}}_\alpha \wedge \hat{\mathbf{r}}_{\alpha,i}), \quad \delta \hat{\boldsymbol{\eta}}_\alpha \propto \hat{\boldsymbol{\omega}}_\alpha.$$

This gives ( $\hat{\mathbf{L}}_\alpha = \hat{\boldsymbol{\Theta}}_\alpha \cdot \hat{\boldsymbol{\omega}}_\alpha$  is the angular momentum in  $\hat{\Sigma}$ )

$$\frac{d}{dt} \left[ \hat{\boldsymbol{\Theta}}_\alpha \cdot \hat{\boldsymbol{\omega}}_\alpha \right] + \hat{\boldsymbol{\omega}}_\alpha \wedge \hat{\boldsymbol{\Theta}}_\alpha \cdot \hat{\boldsymbol{\omega}}_\alpha = \hat{\mathbf{N}}_\alpha, \quad \hat{\mathbf{N}}_\alpha = \sum_i \hat{\mathbf{r}}_{\alpha,i} \wedge \hat{\mathbf{F}}_{\alpha,i}.$$

For the  $\dot{\mathbf{x}}_\alpha$  we have the relations

$$\hat{\mathbf{A}}(\mathbf{x}_\alpha) \cdot \dot{\mathbf{x}}_\alpha = \hat{\boldsymbol{\omega}}_\alpha.$$

Here  $\hat{\boldsymbol{\Theta}}_\alpha$  is the inertia tensor in  $\hat{\Sigma}$  (constant and diagonal).

$$\hat{\boldsymbol{\Theta}} = \begin{pmatrix} \hat{\Theta}_{xx} & 0 & 0 \\ 0 & \hat{\Theta}_{yy} & 0 \\ 0 & 0 & \hat{\Theta}_{zz} \end{pmatrix}.$$



## Angular velocities and quaternions

We choose the components of a quaternion as angular coordinates coordinates,  $\mathbf{x} \leftarrow \mathbf{q} = (q_s, q_x, q_y, q_z)^T$ , tel que

$$\mathbf{D}(\mathbf{q}) = \begin{pmatrix} q_s^2 + q_x^2 - q_y^2 - q_z^2 & 2(-q_s q_z + q_x q_y) & 2(q_s q_y + q_x q_z) \\ 2(q_s q_z + q_x q_y) & q_s^2 + q_y^2 - q_x^2 - q_z^2 & 2(-q_s q_x + q_y q_z) \\ 2(-q_s q_y + q_x q_z) & 2(q_s q_x + q_y q_z) & q_s^2 + q_z^2 - q_x^2 - q_y^2 \end{pmatrix},$$

where  $q_s^2 + q_x^2 + q_y^2 + q_z^2 = 1$ . For  $\hat{\omega}$  one can write  $\dot{\mathbf{q}} = \hat{\mathbf{B}}(\mathbf{q}) \cdot \hat{\omega}$ ,

$$\begin{pmatrix} \dot{q}_s \\ \dot{q}_x \\ \dot{q}_y \\ \dot{q}_z \end{pmatrix} = \frac{1}{2} \begin{pmatrix} q_s & -q_x & -q_y & -q_z \\ q_x & q_s & -q_z & q_y \\ q_y & q_z & q_s & -q_x \\ q_z & -q_y & q_x & q_s \end{pmatrix} \cdot \begin{pmatrix} 0 \\ \hat{\omega}_x \\ \hat{\omega}_y \\ \hat{\omega}_z \end{pmatrix}.$$

If we choose the Euler angles  $\mathbf{x} \leftarrow (\alpha, \beta, \gamma)^T$  the relation  $\dot{x} \leftarrow \hat{\omega}$  can become singular:

$$\begin{pmatrix} \dot{\alpha} \\ \dot{\beta} \\ \dot{\gamma} \end{pmatrix} = \begin{pmatrix} -\frac{\cos \gamma}{\sin \beta} & \frac{\sin \gamma}{\sin \beta} & 0 \\ \sin \gamma & \cos \gamma & 0 \\ \cot \beta \cos \gamma & -\cot \beta \sin \gamma & 1 \end{pmatrix} \cdot \begin{pmatrix} \hat{\omega}_x \\ \hat{\omega}_y \\ \hat{\omega}_z \end{pmatrix}.$$



## An algorithm for the integration of Euler equations:

“Leap frog” scheme<sup>2</sup>:

$$\mathbf{L}(n + 1/2) = \mathbf{L}(n - 1/2) + \Delta t \mathbf{N}(n)$$

$$\mathbf{q}(n + 1) = \mathbf{q}(n) + \Delta t \hat{\mathbf{B}}(\mathbf{q}(n + 1/2)) \cdot (\hat{\boldsymbol{\omega}}(n + 1/2), 0)^T.$$

Realization with an auxiliary step (for each molecule  $\alpha$ ):

1.  $\mathbf{L}(n) = \mathbf{L}(n - 1/2) + \frac{\Delta t}{2} \mathbf{N}(n).$

2.  $\hat{\mathbf{L}}(n) = \mathbf{D}^T(\mathbf{q}(n)) \cdot \mathbf{L}(n).$

3.  $\hat{\boldsymbol{\omega}}(n) = \hat{\boldsymbol{\Theta}}^{-1} \cdot \hat{\mathbf{L}}(n).$

4.  $\mathbf{q}(n + 1/2) = \mathbf{q}(n) + \frac{\Delta t}{2} \hat{\mathbf{B}}(\mathbf{q}(n)) \cdot (\hat{\boldsymbol{\omega}}(n), 0)^T.$

5.  $\mathbf{L}(n + 1/2) = \mathbf{L}(n - 1/2) + \Delta t \mathbf{N}(n).$

6.  $\hat{\mathbf{L}}(n + 1/2) = \mathbf{D}^T(\mathbf{q}(n + 1/2)) \cdot \mathbf{L}(n + 1/2).$

7.  $\hat{\boldsymbol{\omega}}(n + 1/2) = \hat{\boldsymbol{\Theta}}^{-1} \cdot \hat{\mathbf{L}}(n + 1/2).$

8.  $\mathbf{q}(n + 1) = \mathbf{q}(n) + \Delta t \hat{\mathbf{B}}(\mathbf{q}(n + 1/2)) \cdot (\hat{\boldsymbol{\omega}}(n + 1/2), 0)^T.$

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<sup>2</sup>D. Fincham, Leapfrog rotational algorithms, *Molecular Simulation* **8**, 165-178 (1992).





# Simulations in the $NVT$ ensemble

## Extended system

We define a “virtual” dynamic system of  $N$  particles having positions  $\rho_i$  and speeds  $\dot{\rho}_i$ . The relation to the “real” system is given by

$$\begin{aligned}\mathbf{r}_i &= \rho_i, \\ \dot{\mathbf{r}}_i &= s\dot{\rho}_i.\end{aligned}$$

## Lagrange function

$$\mathcal{L}_e = \sum_i \frac{1}{2} m_i s^2 \dot{\rho}_i^2 - \mathcal{V}(\rho_1, \dots, \rho_N) + \frac{1}{2} M_s \dot{s}^2 - g k_B T \ln s.$$

$M_s$  is a fictitious “mass” for  $s$ , and  $g$  is still to be determined.



## Hamilton function

$$\mathcal{H}_e = \underbrace{\sum_i \frac{\pi_i^2}{2m_i s^2} + \mathcal{V}(\boldsymbol{\rho}_1, \dots, \boldsymbol{\rho}_N)}_{\mathcal{H}(\boldsymbol{\pi}, \boldsymbol{\rho})} + \frac{p_s^2}{2M_s} + gk_B T \ln s.$$

## Partition function

$$\begin{aligned}\omega_e(NVE) &= \frac{1}{N!} \int_{-\infty}^{+\infty} dp_s \int_0^{\infty} ds \int_{\mathbb{R}^{3N}} d^{3N} \pi \int_V d^{3N} \rho \delta(E - \mathcal{H}_e) \\ &= \frac{1}{g} \left( \frac{2\pi M_s}{k_B T} \right)^{1/2} \exp \left[ \frac{E}{k_B T} \right] \cdot Z_c(N, V, T).\end{aligned}$$

Here  $Z_c(N, V, T)$  is the partition function of the canonical ensemble:

$$Z_c(N, V, T) = \frac{1}{N!} \int_{\mathbb{R}^{3N}} d^{3N} \pi \int_V d^{3N} \rho \exp \left[ -\frac{\mathcal{H}(\boldsymbol{\pi}, \boldsymbol{\rho})}{k_B T} \right].$$



# Hamilton equations

$$\dot{\rho}_i = \frac{\partial \mathcal{H}_e}{\partial \pi_i} = \frac{\pi_i}{m_i s^2}$$

$$\dot{\pi}_i = -\frac{\partial \mathcal{H}_e}{\partial \rho_i} = -\frac{\partial \mathcal{V}}{\partial \rho_i}$$

$$\dot{s} = \frac{\partial \mathcal{H}_e}{\partial p_s} = \frac{p_s}{M_s}$$

$$\dot{\pi}_s = -\frac{\partial \mathcal{H}_e}{\partial s} = \sum_i \frac{\pi_i^2}{m_i s^3} - \frac{g k_B T}{s}$$



# Equations of motion for physical variables

We use that

$$s \frac{d}{d\tau} = \frac{d}{dt},$$

where  $\tau$  is the “virtual” time. This gives

$$\begin{aligned}\dot{\mathbf{r}}_i &= \frac{\mathbf{p}_i}{m_i} \\ \dot{\mathbf{p}}_i &= -\frac{\partial \mathcal{V}}{\partial \mathbf{r}_i} - \zeta \mathbf{p}_i \\ \dot{\zeta} &= \frac{1}{M_s} \left( \sum_i \frac{\mathbf{p}_i^2}{m_i} - g k_B T \right)\end{aligned}$$

We choose  $g = 3N$ . The variable  $\zeta$  plays the role of a “friction constant” which can be positive or negative.







# Simulations in the $NpT$ ensemble

## Extended system

virtuel	réel	relation
$Q$	$V$	$Q = V$
$\pi_Q$	$p_V$	$\frac{\pi_Q}{s} = p_V$
$s$	$S$	$s = S$
$\pi_s$	$p_S$	$\frac{\pi_s}{s} = p_s$
$\rho$	$\mathbf{r}$	$Q^{1/3} \rho = \mathbf{r}$
$\pi$	$\mathbf{p}$	$\frac{\pi}{Q^{1/3} s} = \mathbf{p}$
$d\tau$	$dt$	$\frac{d\tau}{s} = dt$



## Lagrange function

$$\mathcal{L}_e = \sum_i \frac{m_i Q^{2/3} s^2}{2} \dot{\rho}_i^2 - \mathcal{V}(Q^{1/3} \rho_1, \dots, Q^{1/3} \rho_N) + \frac{1}{2} M_Q s^2 \dot{Q}^2 - P_{ext} Q + \frac{1}{2} M_s \dot{s}^2 - g k_B T \ln s.$$

$M_Q$  and  $M_s$  are the fictitious "masses" for  $Q$  and  $s$ , respectively, and  $P_{ext}$  is the desired pressure.

## Hamilton function

$$\mathcal{H}_e = \sum_i \frac{\pi_i^2}{2Q^{2/3} m_i s^2} + \mathcal{V}(Q^{1/3} \rho_1, \dots, Q^{1/3} \rho_N) + \frac{1}{2M_Q s^2} p_Q^2 + P_{ext} Q + \frac{1}{2M_s} p_s^2 + g k_B T \ln s.$$



# Partition function

Here we have

$$\begin{aligned}\omega_e(NVE) &= \frac{1}{N!} \int_{-\infty}^{+\infty} dp_Q \int_0^\infty dQ \int_{-\infty}^{+\infty} dp_s \int_0^\infty ds \int_{\mathbb{R}_{3N}} d^{3N}\pi \int_V d^{3N}\rho \delta(E - \mathcal{H}_e) \\ &= \frac{1}{g} \left( \frac{4\pi^2 M_s M_Q}{k_B T} \right)^{1/2} \exp \left[ \frac{E}{k_B T} \right] \cdot Z_c(N, p, T).\end{aligned}$$

$Z_c(N, p, T)$  is the partition function of the  $NpT$  ensemble:

$$Z_c(N, p, T) = \frac{1}{N!} \int_0^\infty dV \int_{\mathbb{R}_{3N}} d^{3N}\pi \int_V d^{3N}\rho \exp \left[ -\frac{\mathcal{H}(\boldsymbol{\pi}, \boldsymbol{\rho}) + P_{ext}V}{k_B T} \right].$$



## Equations of motion for physical variables:

In the following we replace the indices “ $Q$ ” by “ $V$ ”.

$$\dot{\mathbf{r}}_i = \frac{\dot{V}}{3V} \mathbf{r}_i + \frac{\mathbf{p}_i}{m_i}$$

$$\dot{\mathbf{p}}_i = -\frac{\partial \mathcal{V}}{\partial \mathbf{r}_i} - \frac{\dot{V}}{3V} \mathbf{p}_i - \zeta \mathbf{p}_i$$

$$\dot{V} = \frac{p_V}{M_V}$$

$$\dot{p}_V = -P_{ext} + \frac{1}{3V} \left\{ \sum_i \left( \frac{\mathbf{p}_i^2}{m_i} - \mathbf{r}_i \cdot \frac{\partial \mathcal{V}}{\partial \mathbf{r}_i} \right) \right\}$$

$$\dot{\zeta} = \frac{1}{M_s} \left( \sum_i \frac{\mathbf{p}_i^2}{m_i} - g k_B T \right)$$





# Chapter 2

# The Monte Carlo method





# Master equation

## Définition:

- Let  $i$  be the index of  $N$  microstates of a system.
- Let  $p_i$  be the probability of finding the system in state  $i$ .
- Let  $w_{ji} \equiv w_{i \rightarrow j}$  be the transition rate  $i \rightarrow j$ .

With these definitions we have the balance

$$\frac{dp_i}{dt} = \sum_j w_{ij} p_j - \sum_j w_{ji} p_i.$$

We verify that

$$\frac{d}{dt} \left( \sum_i p_i \right) = 0.$$



## Matrix form:

With the definitions

$$\mathbf{A} = (A_{ij}), \quad A_{ij} = w_{ij} - \left( \sum_k w_{kj} \right) \delta_{ij},$$
$$\mathbf{p} = (p_1, \dots, p_N)^T,$$

the Master equation takes the form

$$\frac{d\mathbf{p}}{dt} = \mathbf{A} \cdot \mathbf{p},$$

with the formal solution

$$\mathbf{p}(t) = \exp(\mathbf{A}t) \cdot \mathbf{p}(0).$$

We see that the sum of the elements of a column of  $\mathbf{A}$  is zero:

$$\sum_i A_{ij} = \sum_i w_{ij} - \sum_k w_{kj} \sum_i \delta_{ij} = \sum_i w_{ij} - \sum_k w_{kj} = 0.$$



## Stationary state:

A stationary state is given by:

$$\frac{d\mathbf{p}_{eq}}{dt} = \mathbf{0} = \mathbf{A} \cdot \mathbf{p}_{eq}.$$

In components we have

$$\sum_j w_{ij} p_j^{eq} - \sum_j w_{ji} p_i^{eq} = 0.$$

## Detailed balance

We impose that for each pair of states  $i$  and  $j$

$$w_{ij} p_j^{eq} = w_{ji} p_i^{eq}.$$





# Attaining equilibrium

For  $p_{eq}$  to be an equilibrium state we must impose that

$$\mathbf{p}_{eq} = \lim_{t \rightarrow \infty} \exp(\mathbf{A}t) \cdot \mathbf{p}(0).$$

It is assumed that  $\mathbf{A}$  has a spectral decomposition of the form

$$\mathbf{A} = \sum_k \lambda_k \mathbf{u}_k \cdot \mathbf{v}_k^T, \quad \mathbf{v}_i^T \cdot \mathbf{u}_j = \delta_{ij}.$$

If we put  $\lambda_1 \equiv 0$ , it follows that

$$\exp(\mathbf{A}t) = \sum_k \exp(\lambda_k t) \mathbf{u}_k \cdot \mathbf{v}_k^T \xrightarrow{t \rightarrow \infty} \mathbf{u}_1 \cdot \mathbf{v}_1^T \equiv \mathbf{p}_{eq} \cdot \tilde{\mathbf{p}}_{eq}^T$$

if  $k > 1$  (necessary cond.). Since  $\sum_i A_{ij} = 0$ , it follows that  $\tilde{\mathbf{p}}_{eq} = (1, \dots, 1)^T$  and

$$\tilde{\mathbf{p}}_{eq}^T \cdot \mathbf{p}(0) = \sum_i p_i(0) = 1 \implies \lim_{t \rightarrow \infty} \exp(\mathbf{A}t) \cdot \mathbf{p}(0) = \mathbf{p}_{eq}.$$





# Canonical Monte Carlo

## State of equilibrium:

In the following  $i$  is a state in the configuration/phase space of a physical system,  $E_i$  the energy of  $i$ , and  $\beta = k_B T$ . We have

$$p_i^{eq} = \frac{\exp(-\beta E_i)}{Z}, \quad Z = \sum_i \exp(-\beta E_i).$$

## Decomposition of $w_{ij}$ :

We decompose  $w_{ij}$  as follows::

$$w_{ij} = \alpha_{ij} \pi_{ij},$$

where  $\alpha_{ij}$  is the *probability of proposal* for a move  $j$ , and  $\pi_{ij}$  is the *probability of acceptance*.





## Metropolis algorithm:

Here we put

$$\alpha_{ij} \equiv \alpha = \text{const.}$$

and we choose

$$\pi_{ij} = \min\left(1, \exp(-\beta[E_i - E_j])\right).$$

Verification:

$$\frac{w_{ij}}{w_{ji}} = \frac{\pi_{ij}}{\pi_{ji}} = \frac{\min\left(1, \exp(-\beta[E_i - E_j])\right)}{\min\left(1, \exp(-\beta[E_j - E_i])\right)} = \exp(-\beta[E_i - E_j]).$$

This is true regardless of  $E_i$  and  $E_j$ .





## Pseudo code:

1. Choose a particle in configuration  $j$  and calculate  $E_j$ .
2. Make a random movement of the chosen particle,

$$\mathbf{R} \longrightarrow \mathbf{R} + \Delta(\xi - 0.5),$$

where  $0 < \xi < 1$  is a random number (uniform distribution).

3. Compute the energy  $E_i$  of the new configuration  $i$ .
4. Accept  $i$  with probability  $\min\left(1, \exp(-\beta[E_i - E_j])\right)$ .





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# Chapter 3

## *Ab initio* Molecular Dynamics





# Motivation

MD simulation without the approximation of the electronic energy by an empirical potential.

## Reason:

Empirical potentials do not allow to consider physical processes that directly involve physical processes that directly involve electrons.

## Applications:

- Studies of chemical reactions.
- Simulations of spectroscopic observations that are directly coupled to coupled to the electronic degrees of freedom, such as Raman spectroscopy, and Raman spectroscopy, and chemical shift in NMR spectroscopy.

Remarque: The nuclei are always treated as classical particles.







# Solution of the electronic problem

## Variational method:

The solution of the stationary Schrödinger equation

$$\hat{H}_e u_e = E_e(\{\mathbf{R}_i\}) u_e,$$

can be formulated as a variational problem

$$(u_e, \hat{H}_e u_e) = \text{Min.}, \quad (u_e, u_e) = 1.$$

The wave function of the ground state,  $u_e(\mathbf{r}_{i,\alpha})$ , depends on all the electronic coordinates.

Here and in the following we suppress the parametric dependence of the electronic wave functions of positions  $\mathbf{R}_i$  of the nuclei.





## Equivalent minimization problem:

We choose  $u_e \equiv u_e(\mathbf{r}_{i,\alpha})$  as a superposition of appropriately chosen basis functions,

$$u_e(\{\mathbf{r}_{i,\alpha}\}) = \sum_n c_n \Phi_n(\{\mathbf{r}_{i,\alpha}\}).$$

This gives a constrained minimization problem for the coefficients  $\{c_i\}$ :

$$\sum_{n,m} c_m^* c_n (\Phi_m, \hat{H} \Phi_n) = \text{Min}(\{c_j\}), \quad \sum_n |c_n|^2 = 1.$$

Here  $m, n = 1, \dots, M$ , where  $M$  is the number of basis functions considered. **If  $M < \infty$ , we obtain an approximation of the variational problem.**



## Minimization with constraints:

We define the matrix  $M \times M$

$$\mathbf{H} = (H_{ij}), \quad H_{ij} = (\Phi_i, \hat{H} \Phi_j),$$

and the vector

$$\mathbf{c} = (c_1, \dots, c_M)^T,$$

and we look for a vector  $\mathbf{c}$  for which

$$f(\mathbf{c}, \lambda) = \mathbf{c}^T \cdot \mathbf{H} \cdot \mathbf{c} - \lambda \{ \mathbf{c}^T \cdot \mathbf{c} - 1 \} = \text{Min}.$$

Here  $\lambda$  is a Lagrange parameter for the constraint  $\mathbf{c}^T \cdot \mathbf{c} = 1$ . This gives

$$\mathbf{H} \cdot \mathbf{c} - \lambda \mathbf{c}, \quad \mathbf{c}^T \cdot \mathbf{c} = 1.$$

The optimal  $\mathbf{c}$  coefficients are given by the eigenvector of  $\mathbf{H}$  which corresponds to the smallest eigenvalue = minimum energy.





# Kohn - Sham Theorem

1. The electronic fundamental energy is a functional of the electronic density,

$$E_e(\{\mathbf{R}_i\}) = \mathcal{E}[\rho_e(\mathbf{r})].$$

2. The electronic density is a **function of three spatial coordinates**

$$\rho_e(\mathbf{r}) = \sum_{\alpha} e |\psi_{\alpha}(\mathbf{r})|^2,$$

where  $i$  is a sum over the orbitals occupied by a **only electron**.  
Reminder: The wave function  $u_e(\{mr_{i,\alpha}\})$  is a **function of  $3N_e$  coordinates**, if  $N_e$  is the total number of electrons.

The electronic fundamental energy can be obtained by the solution of a problem for an "effective particle".





# Ab initio MD

## Density functional:

$$\mathcal{E}[\rho_e(\mathbf{r})] = - \sum_{\alpha} \frac{\hbar^2}{2m} \int d^3r \psi_{\alpha}^*(\mathbf{r}) \frac{\partial^2}{\partial \mathbf{r}^2} \psi_{\alpha}(\mathbf{r}) \\ + \int d^3r \rho_e(\mathbf{r}) V_{ne}(\mathbf{r}, \{\mathbf{R}_i\}) + \int d^3r \rho_e(\mathbf{r}) V_H(\mathbf{r}) + \mathcal{E}_{xc}[\rho_e(\mathbf{r})].$$

Here  $V_H(\mathbf{r})$  is the Hartree energy (coulombic interaction interaction between the electrons),

$$V_H(\mathbf{r}) = \frac{1}{8\pi\epsilon_0} \int d^3r' \frac{\rho_e(\mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|},$$

and  $\mathcal{E}_{xc}[\rho_e(\mathbf{r})]$  is the correlation exchange density functional. It is not strictly known, and it contains all the hidden effects of many-body effects. There are approximations which "work well".



## Lagrangian for *ab initio* MD :

We construct the Lagrange function

$$\mathcal{L} = \sum_i \frac{1}{2} M_i \dot{\mathbf{R}}_i^2 - \left( \mathcal{E}[\{\rho(\mathbf{r}, t)\}] + V_{nn}(\{\mathbf{R}_i\}) \right) + \frac{\mu}{2} \sum_{\alpha} \int d^3r \psi_{\alpha}^*(\mathbf{r}, t) \dot{\psi}_{\alpha}(\mathbf{r}, t) + \sum_{\alpha, \beta} \lambda_{\alpha\beta} \left( \int d^3r \psi_{\alpha}^*(\mathbf{r}, t) \psi_{\beta}(\mathbf{r}, t) - \delta_{\alpha\beta} \right).$$

- The wave functions for the orbitals are expressed in

$$\psi_{\alpha}(\mathbf{r}, t) = \sum_{\alpha, i} c_{\alpha, i}(t) \phi_i(\mathbf{r}),$$

where the coefficients  $c_{\alpha, i}$  are dynamic variables. The idea is that the  $c_{\alpha, i}$  evolve such that  $\mathcal{E}[\{\psi_{\alpha}(\mathbf{r}, t)\}]$  always remains minimal

- The last term describes the normalization constraints of the  $\psi_{\alpha}(\mathbf{r}, t)$ .



## Plane wave bases

With  $\mathbf{q} = \frac{2\pi}{L}(l, m, n)$  (periodic conditions) we write  $\psi_\alpha(\mathbf{r}, t)$  as a plane wave superposition,

$$\psi_\alpha(\mathbf{r}, t) = \sum_{|\mathbf{q}| < q_{cut}} c_{\alpha, \mathbf{q}}(t) e^{i\mathbf{q} \cdot \mathbf{r}}.$$

## Equation of motion for the nuclei:

$$\frac{d}{dt} \frac{\partial \mathcal{L}}{\partial \dot{\mathbf{R}}_i} = \frac{\partial \mathcal{L}}{\partial \mathbf{R}_i}.$$

## Equation of motion for the coefficients:

With the definition

$$\mathbf{c}_\alpha = (c_{\alpha; \mathbf{0}}, \dots, c_{\alpha; \mathbf{q}_{max}})^T$$

we write

$$\frac{d}{dt} \frac{\partial \mathcal{L}}{\partial \dot{\mathbf{c}}_\alpha} = \frac{\partial \mathcal{L}}{\partial \mathbf{c}_\alpha}, \quad \mathbf{c}_\alpha^T \cdot \mathbf{c}_\beta = \delta_{\alpha\beta} \rightarrow \lambda_{\alpha\beta}.$$

