



---

## **Quantum Computing for Quantum Chemistry**

**Axel Courtat<sup>1</sup>   Daniele Loco<sup>1</sup> and Jerome Foret<sup>1</sup>**

**November 15, 2023**

# Table of contents

---

## Quantum computing for Drug Discovery [30min]

Drug Discovery Pipeline

Where is Quantum Chemistry in the Drug Discovery Pipeline?

## Quantum Chemistry [2h]

Quantum Chemistry : Overview

Schrödinger equation for multi-electron atoms

Schrödinger equation solutions for the Hydrogen atom

Approximations and Slater determinants

Schrödinger equation solutions for multi-electron atoms

Self-consistent field equations (Hartree-Fock)

Second Quantization

Hartree-Fock in Second Quantization

## Bibliography

## Quantum computing for Drug Discovery [30min]

Drug Discovery Pipeline

Where is Quantum Chemistry in the Drug Discovery Pipeline?

## Quantum Chemistry [2h]

Quantum Chemistry : Overview

Schrödinger equation for multi-electron atoms

Schrödinger equation solutions for the Hydrogen atom

Approximations and Slater determinants

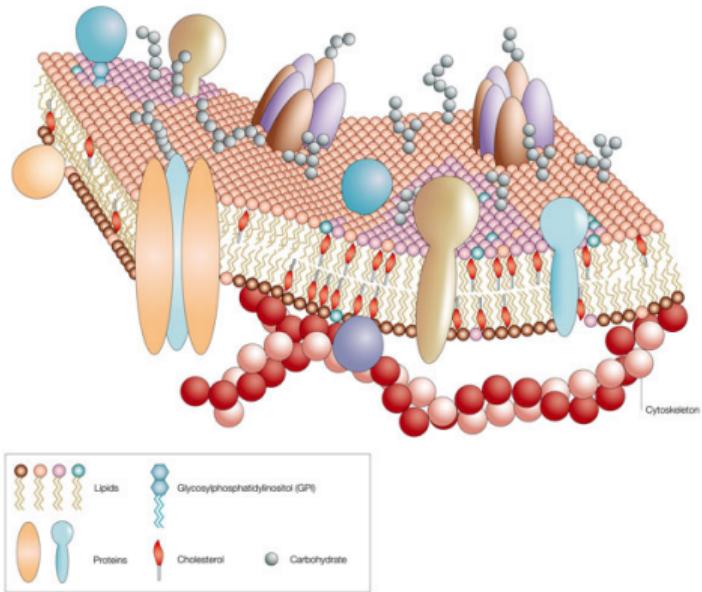
Schrödinger equation solutions for multi-electron atoms

Self-consistent field equations (Hartree-Fock)

Second Quantization

Hartree-Fock in Second Quantization

## Bibliography



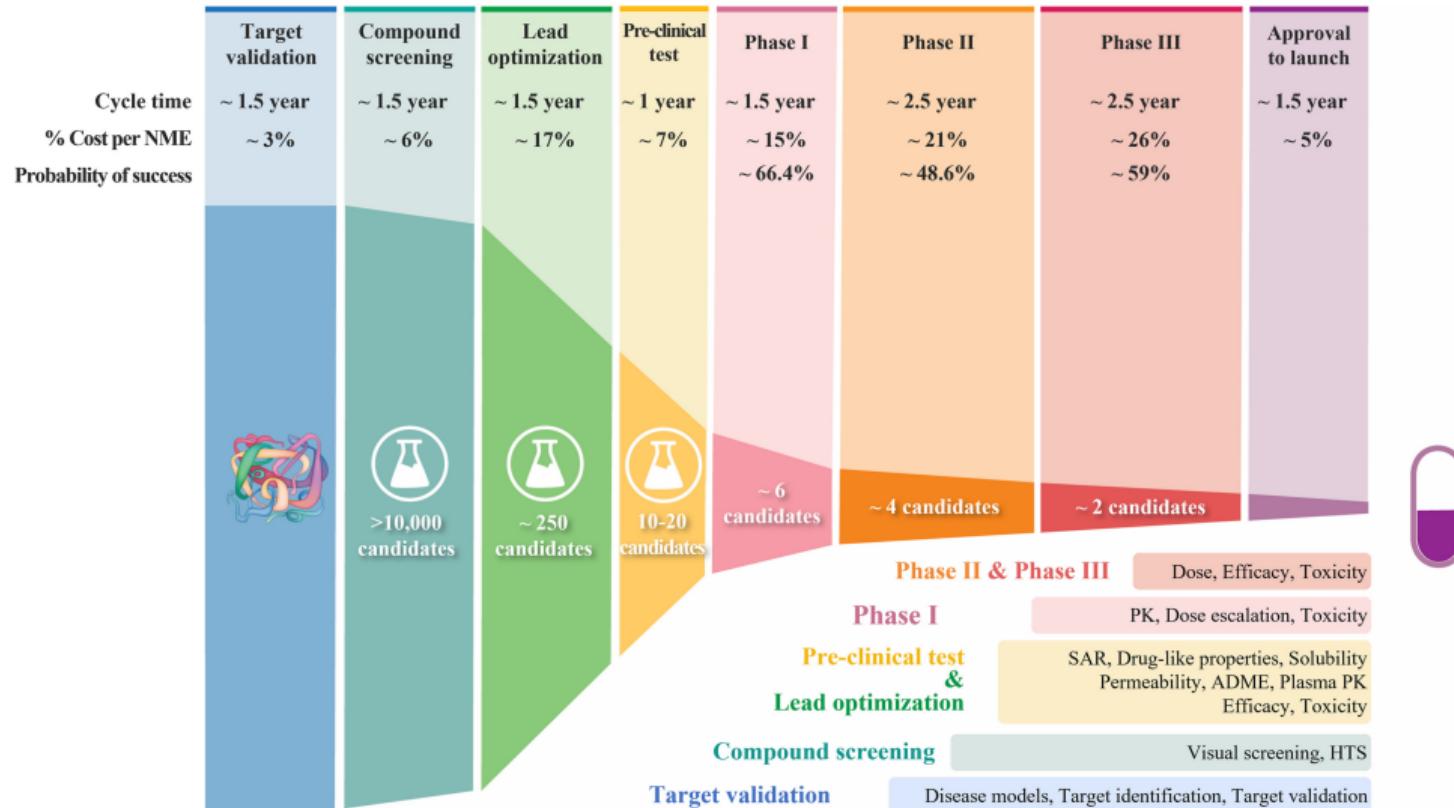
Human body is composed of organs, each of which is composed of cells, each cell is composed of a lipidic membrane encasing the nucleus and a variety of biological molecules, among which several types of proteins. One of the main cause for a disease is a **malfunctioning protein**: a protein that either doesn't work as expected, or shall be stopped to do something wrong.

**Drug Discovery** is the process of searching (and hopefully finding) for a small molecule (namely a drug) that **enables** or **inhibits** the malfunctioning protein.

The drug discovery process is the beginning of a much broader process aimed at putting a drug on the market:

1. Target assessment: RD level (usually academic labs) to understand what is the *pathway* (proteins interactions) responsible for the disease and what protein should be targeted and in the protein what part (pocket) of the protein should be enabled/inhibited.
2. Drug Discovery: given a protein find a drug
3. Pre-clinical trials: tests of the drug on small animals
4. Clinical phases:
  - 4.1 Phase 1: test if a new treatment is safe (Dose-ranging). 20-100 healthy volunteers.
  - 4.2 Phase 2: test treatment efficiency and side effects. 100-300 participants with specific disease.
  - 4.3 Phase 3: test treatment effectiveness (i.e. efficiency compared to other existing treatments) and safety. 300-3,000 people with a specific disease.
  - 4.4 Phase 4: market access approval.

# Drug Discovery Pipeline



In a standard pharmaceuticals industry the DD process consists in following these steps:

- **Input:** targeted protein
- **Process:** Repeat until a good **activity** is found

**Design** Create a batch (around 10) of new molecules "on the paper"

**Synthesize** Concretely create these molecules: design and implement chemical processes (named synthesis pathway) to produce the desired molecule.

**Test** Create assays to test the **activity** of the molecule on the cell

**Analyze** Analyze the results

- **Output: 1 or 2 molecules** that inhibits (enables) the protein

In a **Computer Aided** DD (CADD) company we prefer these steps:

- **Input:** 3D structure of the targeted protein
- **Process:** Iterate until a good **activity** is found

**Design** Start from millions of digital clones of molecules available in vendors database, picked in order to cover a "broad" part of the chemical space

**Analyze** Make each molecule (their digital clone) undergo a complex process to analyse its activity. This process is a **funnel**: starting from millions of molecules down to few:

**VSHT** Virtual Screening High Throughput

**VSLT** Virtual Screening Low Throughput

**MD** Molecular Dynamics.

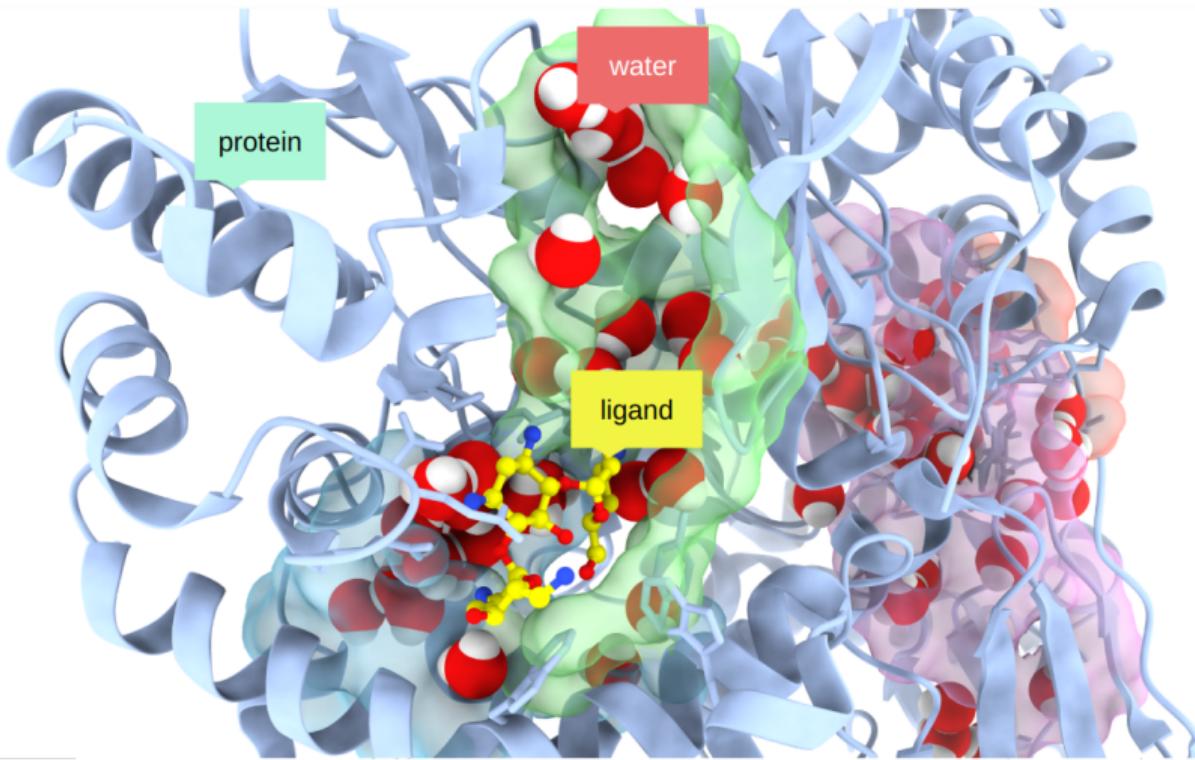
**Synthesize** Same as in the standard process

**Test** Create assays to test the **activity** of the molecule on the cell

- **Output:** 1 or 2 molecules that inhibits (enables) the protein

In a **Computer Aided** DD (CADD) company we prefer these steps:

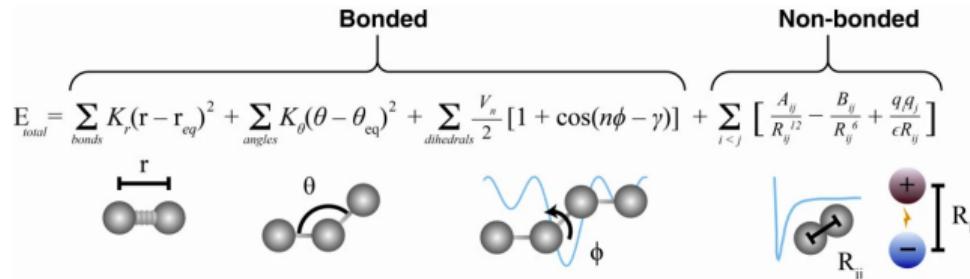
- VSHT Virtual Screening High Throughput : from millions of molecules keep 1-10% that **dock** in the protein **pocket**. Docking, at this stage, is the *geometrical* placement of the molecule into the protein cavity.
- VSLT Virtual Screening Low Throughput : From selected molecules keep 1 to 10% of those with highest docking score. Docking, at this stage, not only involves geometrical constraints but also chemical and physical ones (Coulomb interaction, different 3D conformation of the molecules etc ...)
- MD Molecular Dynamics: create a digital complex [**solvent+protein+molecule**] and simulate the dynamics of the system when subject to complex atomic interactions to see if the molecule "sticks" inside the pocket. The activity is measured by the so called **Binding Free Energy** (BFE). The more negative the energy is, better the affinity.



To evaluate the affinity of the **small molecule** with the **protein** we need to compute their interaction energy.

The Quantum Physics is intractable at this scale

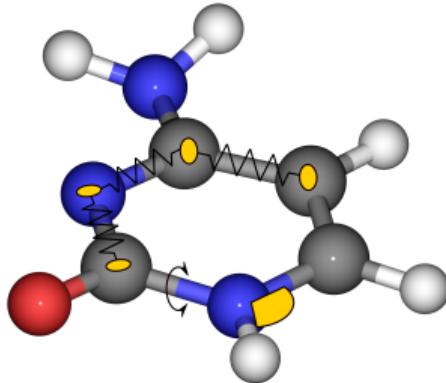
A classical mechanics approximation is introduced, where the interaction energy is a function depending on a **set of parameters** to "mimic" the behaviour of quantum particles: **Molecular Mechanics approximation**

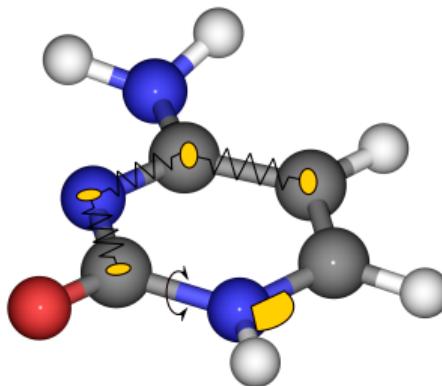


# Where is Quantum in the Drug Discovery Pipeline?

Based on this approximation, the behaviour of the molecules' dynamics is approximated, for each atom  $i = 1, \dots, N$ , according to

$$m_i \frac{\partial v_i}{\partial t} = -\nabla \mathbf{V} = -\underbrace{\sum_{j \neq i}^N \nabla (U_{ele} + U_{VdW} + U_{bond} + U_{tor} + \dots)_{ij}}_{\text{Force felt by the } i^{\text{th}} \text{ atom due to the potential field } \mathbf{V}}$$





Consider, as an example

$$U_{bond} = \kappa(r_{ij} - r_{ij}^{eq})^2$$

the energy of a chemical bond between two atoms is approximated by a spring force where  $\kappa$  is the stiffness and  $r_{ij}^{eq}$  the optimal bond length. Here is where Quantum Mechanics comes in action!

Quantum computing for Drug Discovery [30min]

Drug Discovery Pipeline

Where is Quantum Chemistry in the Drug Discovery Pipeline?

## Quantum Chemistry [2h]

Quantum Chemistry : Overview

Schrödinger equation for multi-electron atoms

Schrödinger equation solutions for the Hydrogen atom

Approximations and Slater determinants

Schrödinger equation solutions for multi-electron atoms

Self-consistent field equations (Hartree-Fock)

Second Quantization

Hartree-Fock in Second Quantization

Bibliography

# Quantum Chemistry : Overview

Starting point of everything: Schrödinger equation

$$\left( -\frac{\hbar^2}{2m} \Delta + V \right) \psi(r_1, \dots, r_n, t) = i\hbar \frac{\partial}{\partial t} \psi(r_1, \dots, r_n, t)$$

Time independent Schrödinger equation

$$\mathbf{H}\psi(r_1, \dots, r_n) = E\psi(r_1, \dots, r_n), E \in \mathbb{R}$$

Schrödinger equation in Quantum Chemistry

$$\left( -\sum_{A=1}^N \frac{\hbar^2}{2m_A} \Delta_A - \sum_{i=1}^n \frac{\hbar^2}{2m_e} \Delta_i + \sum_{B=2}^N \sum_{A=1}^{B-1} \frac{Z_A Z_B e^2}{4\pi\epsilon_0 r_{AB}} - \sum_{A=1}^N \sum_{i=1}^n \frac{Z_A e^2}{4\pi\epsilon_0 r_{Ai}} - \sum_{j=2}^n \sum_{l=1}^{j-1} \frac{e^2}{4\pi\epsilon_0 r_{lj}} \right) |\psi\rangle = E |\psi\rangle$$

Dirac notation of the Schrödinger equation in QC

$$\mathbf{H} |\phi(r_{nuc}, r_{el}, spin)\rangle = E |\phi(r_{nuc}, r_{el}, spin)\rangle$$

Born-Oppenheimer approximation

$$E_n = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle = \langle \Phi_n | \sum_i h(i) | \Phi_n \rangle + \langle \Phi_n | \sum_{i < j} r_{ij}^{-1} | \Phi_n \rangle + \langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle$$

Energy as a function of Molecular Orbitals wave functions

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_j \varphi_i \rangle$$

Mean field approximation

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_j \varphi_i \rangle$$

Problem to solve

$$\min_{\varphi_i} E_n, \int |\varphi_i|^2 dr = 1 \iff \delta \left( E_n - \sum_i \epsilon_i \int |\varphi_i|^2 dr \right) = 0$$

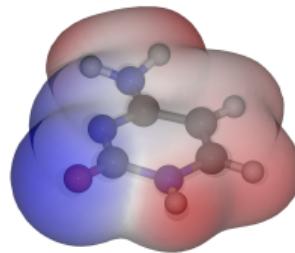
The Hartree-Fock equations are given for each Molecular Orbitals

$$F|\varphi_k\rangle = \epsilon_k |\varphi_k\rangle \quad \forall k = 1, \dots, M$$

## Goal of Quantum Chemistry

To study the intrinsic properties of *molecules* and *atoms*

These properties can only be understood with **Quantum Mechanics**, that provides us the necessary physical and mathematical tools to understand the structure and the dynamical interactions inside a molecule.



## Goal of Quantum Chemistry

To study the intrinsic properties of *molecules* and *atoms*

A molecule is a system made such as:

1. a stable structure of interacting atoms through attractive *Coulomb interaction*, called a **bound state**
2. the interactions, called **chemical bonds**, rely on some **valence electrons** being "physically attached" to two atoms at the same time
3. quantum properties are inherent : discretized energy levels, indistinguishable electrons, probabilistic description ...

In the framework of Quantum Chemistry, we seek to obtain precise results on molecular properties, such as :

1. the **energy** of the physical state of the molecule, completely described by the corresponding **wave-function**  $\Rightarrow$  Potential Energy Study
2. the **intramolecular forces** corresponding to all interactions inside the molecule  $\Rightarrow$  Structural and Stability Study
3. the electrostatic multipoles of the molecule, to explain possible interactions between molecular aggregates  $\Rightarrow$  Condensed Phase Study

As we are studying quantum systems, we are going to use the **time-independent Schrödinger equation**, because we do not care about the dynamics of the system but its internal properties !

# Quantum Chemistry : Overview

Starting point of everything: Schrödinger equation

$$\left( -\frac{\hbar^2}{2m} \Delta + V \right) \psi(r_1, \dots, r_n, t) = i\hbar \frac{\partial}{\partial t} \psi(r_1, \dots, r_n, t)$$

Time independent Schrödinger equation

$$\mathbf{H}\psi(r_1, \dots, r_n) = E\psi(r_1, \dots, r_n), E \in \mathbb{R}$$

Schrödinger equation in Quantum Chemistry

$$\left( -\sum_{A=1}^N \frac{\hbar^2}{2m_A} \Delta_A - \sum_{i=1}^n \frac{\hbar^2}{2m_e} \Delta_i + \sum_{B=2}^N \sum_{A=1}^{B-1} \frac{Z_A Z_B e^2}{4\pi\epsilon_0 r_{AB}} - \sum_{A=1}^N \sum_{i=1}^n \frac{Z_A e^2}{4\pi\epsilon_0 r_{Ai}} - \sum_{j=2}^n \sum_{l=1}^{j-1} \frac{e^2}{4\pi\epsilon_0 r_{lj}} \right) |\psi\rangle = E |\psi\rangle$$

Dirac notation of the Schrödinger equation in QC

$$\mathbf{H} |\phi(r_{nuc}, r_{el}, spin)\rangle = E |\phi(r_{nuc}, r_{el}, spin)\rangle$$

Born-Oppenheimer approximation

$$E_n = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle = \langle \Phi_n | \sum_i h(i) | \Phi_n \rangle + \langle \Phi_n | \sum_{i < j} r_{ij}^{-1} | \Phi_n \rangle + \langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle$$

Energy as a function of Molecular Orbitals wave functions

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_j \varphi_i \rangle$$

Mean field approximation

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_j \varphi_i \rangle$$

Problem to solve

$$\min_{\varphi_i} E_n, \int |\varphi_i|^2 dr = 1 \iff \delta \left( E_n - \sum_i \epsilon_i \int |\varphi_i|^2 dr \right) = 0$$

The Hartree-Fock equations are given for each Molecular Orbitals

$$F|\varphi_k\rangle = \epsilon_k |\varphi_k\rangle \quad \forall k = 1, \dots, M$$

The main objective is to find suitable approximation for computing a wave function  $\Psi_k$  and the associated levels of energy  $E_k$ , formally related by:

$$\mathbf{H}_{mol}(\mathbf{r}, \mathbf{R})\Psi_k(\mathbf{r}, \mathbf{R}) = E_k\Psi_k(\mathbf{r}, \mathbf{R}), \quad k \in \mathbb{N}^+$$

$$\mathbf{H}_{mol} = T_{nuc} + T_{el} + V_{nuc-nuc} + V_{nuc-el} + V_{el-el}$$

$$E_k \in \mathbb{R}$$

$$\Psi_k : \mathbb{R}^{3(N+n)} \rightarrow \mathbb{C}$$

$$\mathbf{r} := (\vec{r}_1, \dots, \vec{r}_n)$$

$$\mathbf{R} := (\vec{r}_1, \dots, \vec{r}_N)$$

The  $T_{...}$  operators correspond to the kinetic operators while the  $V_{...}$  ones are the potential operators (derived from Coulomb attraction law).

# Schrödinger equation for multi-electron atoms

$$T_{nuc} = - \sum_{A=1}^N \frac{\hbar^2}{2m_A} \Delta_A$$

$$T_{el} = - \sum_{i=1}^n \frac{\hbar^2}{2m_e} \Delta_i$$

$$V_{nuc-nuc} = \sum_{B=2}^N \sum_{A=1}^{B-1} \frac{Z_A Z_B e^2}{4\pi\epsilon_0 r_{AB}}$$

$$V_{nuc-el} = - \sum_{A=1}^N \sum_{i=1}^n \frac{Z_A e^2}{4\pi\epsilon_0 r_{Ai}}$$

$$V_{el-el} = \sum_{j=2}^n \sum_{i=1}^{j-1} \frac{e^2}{4\pi\epsilon_0 r_{ij}}$$

where the following notations were adopted :

$$\Delta = \left( \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2} \right) \quad (\text{Laplacian})$$

$$r_{ab} = |\vec{r}_a - \vec{r}_b|$$

(relative distance between particles  $a$  and  $b$ )

# Schrödinger equation for multi-electron atoms

Starting point of everything: Schrödinger equation

$$\left( -\frac{\hbar^2}{2m} \Delta + V \right) \psi(r_1, \dots, r_n, t) = i\hbar \frac{\partial}{\partial t} \psi(r_1, \dots, r_n, t)$$

Time independent Schrödinger equation

$$\mathbf{H}\psi(r_1, \dots, r_n) = E\psi(r_1, \dots, r_n), E \in \mathbb{R}$$

Schrödinger equation in Quantum Chemistry

$$\left( -\sum_{A=1}^N \frac{\hbar^2}{2m_A} \Delta_A - \sum_{i=1}^n \frac{\hbar^2}{2m_e} \Delta_i + \sum_{B=2}^N \sum_{A=1}^{B-1} \frac{Z_A Z_B e^2}{4\pi\epsilon_0 r_{AB}} - \sum_{A=1}^N \sum_{i=1}^n \frac{Z_A e^2}{4\pi\epsilon_0 r_{Ai}} - \sum_{j=2}^n \sum_{l=1}^{j-1} \frac{e^2}{4\pi\epsilon_0 r_{lj}} \right) |\psi\rangle = E|\psi\rangle$$

Dirac notation of the Schrödinger equation in QC

$$\mathbf{H}|\phi(r_{nuc}, r_{el}, spin)\rangle = E|\phi(r_{nuc}, r_{el}, spin)\rangle$$

Born-Oppenheimer approximation

$$E_n = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle = \langle \Phi_n | \sum_i h(i) | \Phi_n \rangle + \langle \Phi_n | \sum_{i < j} r_{ij}^{-1} | \Phi_n \rangle + \langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle$$

Energy as a function of Molecular Orbitals wave functions

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_j \varphi_i \rangle$$

Mean field approximation

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_j \varphi_i \rangle$$

Problem to solve

$$\min_{\varphi_i} E_n, \int |\varphi_i|^2 dr = 1 \iff \delta \left( E_n - \sum_i \epsilon_i \int |\varphi_i|^2 dr \right) = 0$$

The Hartree-Fock equations are given for each Molecular Orbitals

$$F|\varphi_k\rangle = \epsilon_k |\varphi_k\rangle \quad \forall k = 1, \dots, M$$

To understand the complexity of the former equation let's consider a simple Hydrogen atom. In this case only one electron interacts with one nucleus. The Schrödinger equation simplifies to:

$$\left( -\frac{\hbar^2}{2m_A} \Delta_A - \frac{\hbar^2}{2m_e} \Delta_1 - \frac{Z_A e^2}{4\pi\epsilon_0 r_{A1}} \right) \psi(\vec{r}_A, \vec{r}_1) = E\psi(\vec{r}_A, \vec{r}_1)$$

To understand the complexity of the former equation let's consider a simple Hydrogen atom. In this case only one electron interacts with one nucleus. The Schrödinger equation simplifies to:

$$\left( -\frac{\hbar^2}{2m_A} \Delta_A - \frac{\hbar^2}{2m_e} \Delta_1 - \frac{Z_A e^2}{4\pi\epsilon_0 r_{A1}} \right) \psi(\vec{r}_A, \vec{r}_1) = E\psi(\vec{r}_A, \vec{r}_1)$$

Usually to solve this equation, we restrict the study to the Schrödinger equation for the electron only, with the splitting  $\psi(\vec{r}_A, \vec{r}_1) = \phi(\vec{r}_1)\zeta(\vec{r}_A)$ . This further simplifies to :

$$-\frac{\hbar^2}{2m_e} \Delta \phi(\vec{r}) - \frac{Z_A e^2}{4\pi\epsilon_0 r} \phi(\vec{r}) = E\phi(\vec{r}) \quad (1)$$

where we relabelled  $\vec{r}_1 \rightarrow \vec{r}$

In spherical coordinates, the expression of the Hydrogen wave-function is then :

$$\phi_{n,m,l}(r, \theta, \varphi) = \sqrt{\left(\frac{2}{na_0^*}\right)^{-3} \frac{(n-l-1)!}{2n(n+l)!}} e^{-\frac{2r}{na_0^*}} \left(\frac{2r}{na_0^*}\right)^l L_{n-l-1}^{2l+1} \left(\frac{2r}{na_0^*}\right) Y_l^m(\theta, \varphi)$$

where :

- $n, l, m$  are the principal, azimuthal and magnetic quantum numbers
- $a_0^*$  is the reduced Bohr radius
- $L_{n-l-1}^{2l+1}$  is a generalized Laguerre polynomial of degree  $n - l - 1$
- $Y_l^m$  is a spherical harmonic function of degree  $l$  and order  $m$

In spherical coordinates, the expression of the Hydrogen wave-function is then :

$$\phi_{n,m,l}(r, \theta, \varphi) = \sqrt{\left(\frac{2}{na_0^*}\right)^{-3} \frac{(n-l-1)!}{2n(n+l)!}} e^{-\frac{2r}{na_0^*}} \left(\frac{2r}{na_0^*}\right)^l L_{n-l-1}^{2l+1} \left(\frac{2r}{na_0^*}\right) Y_l^m(\theta, \varphi)$$

where :

- $n, l, m$  are the principal, azimuthal and magnetic quantum numbers
- $a_0^*$  is the reduced Bohr radius
- $L_{n-l-1}^{2l+1}$  is a generalized Laguerre polynomial of degree  $n - l - 1$
- $Y_l^m$  is a spherical harmonic function of degree  $l$  and order  $m$

This equation can be solved analytically and numerically. However for atoms with more electrons (and nuclei) it becomes very quickly impossible to solve this equation analytically.

Indeed, consider we have an atom with  $n$  electrons. Then we shall have one equation for each electron, thus  $n$  equations.

But the electrons are also interacting with each other, so all of these equations shall be modified in such a way that they become all intrinsically related.

Rapidly such an expression is **not feasible**, and **only approximations and numerical methods** are efficient for obtaining results.

Indeed, consider we have an atom with  $n$  electrons. Then we shall have one equation for each electron, thus  $n$  equations.

But the electrons are also interacting with each other, so all of these equations shall be modified in such a way that they become all intrinsically related.

Rapidly such an expression is **not feasible**, and **only approximations and numerical methods** are efficient for obtaining results.

Now consider a molecule, made of at least two atoms, usually of different type (i.e. different number of nuclei and electrons).

We shall have for each atom its corresponding collection of equations, to which we also need to add modifications in order to retain all the bondings that make the molecule a stable structure.

Indeed, consider we have an atom with  $n$  electrons. Then we shall have one equation for each electron, thus  $n$  equations.

But the electrons are also interacting with each other, so all of these equations shall be modified in such a way that they become all intrinsically related.

Rapidly such an expression is **not feasible**, and **only approximations and numerical methods** are efficient for obtaining results.

Now consider a molecule, made of at least two atoms, usually of different type (i.e. different number of nuclei and electrons).

We shall have for each atom its corresponding collection of equations, to which we also need to add modifications in order to retain all the bondings that make the molecule a stable structure.

Clearly we **need new methods and approximations** to provide expressions that **will be only solvable** through numerical computations.

Conventionally, several approximations are introduced

- we choose a system of units where

$$\hbar = m_e = e = 4\pi\epsilon_0 = 1$$

- we switch to relative coordinates to eliminate the dependence of the wave-function on *centre-of-mass (COM)*

$$\Psi_{k,\text{total}} = \Psi_{k,\text{relative}} \xi_{COM}$$

- We'll only focus on the *relative* part to have **bound-state solutions**. To do so, we measure all of the coordinates relative to one of the nuclei, say  $\vec{r}_X$  :

$$\vec{q}_A = \vec{r}_A - \vec{r}_X, \quad \vec{q}_i = \vec{r}_i - \vec{r}_X$$

From that we make an adiabatic approximation, the so-called **Born-Oppenheimer approximation**.

It consists on **separating** the nuclear wave-function from the electronic wave-function by considering that the dynamics of the nucleus is very slow compared to the dynamics of the electrons :

$$\Psi_k \approx \chi_k(\vec{q}_A, \text{nuclear spins}) \times \Phi_k(\vec{q}_e, \text{electronic spins}; \vec{q}_A) = \chi_k \Phi_k \quad (2)$$

where  $\vec{q}_A \in \mathbb{R}^{3(N-1)}$  and  $\vec{q}_e \in \mathbb{R}^{3n}$ .

From that we make an adiabatic approximation, the so-called **Born-Oppenheimer approximation**.

It consists on **separating** the nuclear wave-function from the electronic wave-function by considering that the dynamics of the nucleus is very slow compared to the dynamics of the electrons :

$$\Psi_k \approx \chi_k(\vec{q}_A, \text{nuclear spins}) \times \Phi_k(\vec{q}_e, \text{electronic spins}; \vec{q}_A) = \chi_k \Phi_k \quad (3)$$

where  $\vec{q}_A \in \mathbb{R}^{3(N-1)}$  and  $\vec{q}_e \in \mathbb{R}^{3n}$ .

In the BO approximation we can thus separate the electronic and nuclear problem and from now on we will **focus only on the electronic problem** :

$$\mathbf{H}_e \Phi_k(\vec{q}_e; \vec{q}_A) = E_k \Phi_k(\vec{q}_e; \vec{q}_A)$$

$$\mathbf{H}_e = T_{el} + V_{nuc-nuc} + V_{nuc-el} + V_{el-el}$$

# Approximations and Slater determinants

Starting point of everything: Schrödinger equation

$$\left( -\frac{\hbar^2}{2m} \Delta + V \right) \psi(r_1, \dots, r_n, t) = i\hbar \frac{\partial}{\partial t} \psi(r_1, \dots, r_n, t)$$

Time independent Schrödinger equation

$$\mathbf{H}\psi(r_1, \dots, r_n) = E\psi(r_1, \dots, r_n), E \in \mathbb{R}$$

Schrödinger equation in Quantum Chemistry

$$\left( -\sum_{A=1}^N \frac{\hbar^2}{2m_A} \Delta_A - \sum_{i=1}^n \frac{\hbar^2}{2m_e} \Delta_i + \sum_{B=2}^N \sum_{A=1}^{B-1} \frac{Z_A Z_B e^2}{4\pi\epsilon_0 r_{AB}} - \sum_{A=1}^N \sum_{i=1}^n \frac{Z_A e^2}{4\pi\epsilon_0 r_{Ai}} - \sum_{j=2}^n \sum_{l=1}^{j-1} \frac{e^2}{4\pi\epsilon_0 r_{lj}} \right) |\psi\rangle = E |\psi\rangle$$

Dirac notation of the Schrödinger equation in QC

$$\mathbf{H} |\phi(r_{nuc}, r_{el}, spin)\rangle = E |\phi(r_{nuc}, r_{el}, spin)\rangle$$

Born-Oppenheimer approximation

$$E_n = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle = \langle \Phi_n | \sum_i h(i) | \Phi_n \rangle + \langle \Phi_n | \sum_{i < j} r_{ij}^{-1} | \Phi_n \rangle + \langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle$$

Energy as a function of Molecular Orbitals wave functions

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_j \varphi_i \rangle$$

Mean field approximation

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_j \varphi_i \rangle$$

Problem to solve

$$\min_{\varphi_i} E_n, \int |\varphi_i|^2 dr = 1 \iff \delta \left( E_n - \sum_i c_i \int |\varphi_i|^2 dr \right) = 0$$

The Hartree-Fock equations are given for each Molecular Orbitals

$$F|\varphi_k\rangle = \epsilon_k |\varphi_k\rangle \quad \forall k = 1, \dots, M$$

To solve our electronic problem, we need to further simplify our molecular wave-function. For that purpose, we are going to **decompose** our wave-function into the so-called *molecular orbitals (MO)* basis  $\{\varphi_i(\vec{r})\}_{i \in I}$ , such that :

$$\Phi_k(\vec{r}_1, \vec{r}_2, \dots, \vec{r}_n) = \mathcal{A} \varphi_1(\vec{r}_1) \varphi_2(\vec{r}_2) \cdots \varphi_n(\vec{r}_n)$$

The molecular orbitals are defined as **one-electron functions**  $\varphi_i(\vec{r})$ , thus we have at least as many elements than electrons in the molecule, i.e.  $I = \{1, \dots, M\}$ ,  $M > n$ .

To solve our electronic problem, we need to further simplify our molecular wave-function. For that purpose, we are going to **decompose** our wave-function into the so-called *molecular orbitals (MO)* basis  $\{\varphi_i(\vec{r})\}_{i \in I}$ , such that :

$$\Phi_k(\vec{r}_1, \vec{r}_2, \dots, \vec{r}_n) = \mathcal{A} \varphi_1(\vec{r}_1) \varphi_2(\vec{r}_2) \cdots \varphi_n(\vec{r}_n)$$

The molecular orbitals are defined as **one-electron functions**  $\varphi_i(\vec{r})$ , thus we have at least as many elements than electrons in the molecule, i.e.  $I = \{1, \dots, M\}$ ,  $M > n$ .

However, you can see that the above product is not a simple one, but it intervenes an operator  $\mathcal{A}$ .

Indeed, since we are treating the molecule in an electronic point-of-view (only dealing with electrons), the molecular wave-function shall respect the **Pauli exclusion principle** : it shall be **anti-symmetrized** !

Thus the molecular wave-function is an **anti-symmetrized product** of MOs, and  $\mathcal{A}$  corresponds to the so-called *anti-symmetrization operator*.

It is integrating all possible permutations of the indices to generate the right normalization.

Hence,

$$\Phi_k(\vec{r}_1, \vec{r}_2, \dots, \vec{r}_n) = \frac{1}{\sqrt{n!}} \begin{vmatrix} \varphi_1(\vec{r}_1) & \varphi_1(\vec{r}_2) & \cdots & \varphi_1(\vec{r}_n) \\ \varphi_2(\vec{r}_1) & \varphi_2(\vec{r}_2) & \cdots & \varphi_2(\vec{r}_n) \\ \vdots & & & \\ \varphi_n(\vec{r}_1) & \varphi_n(\vec{r}_2) & \cdots & \varphi_n(\vec{r}_n) \end{vmatrix} \quad (4)$$

Thus the molecular wave-function is an **anti-symmetrized product** of MOs, and  $\mathcal{A}$  corresponds to the so-called *anti-symmetrization operator*.

It is integrating all possible permutations of the indices to generate the right normalization.

Hence,

$$\Phi_k(\vec{r}_1, \vec{r}_2, \dots, \vec{r}_n) = \frac{1}{\sqrt{n!}} \begin{vmatrix} \varphi_1(\vec{r}_1) & \varphi_1(\vec{r}_2) & \cdots & \varphi_1(\vec{r}_n) \\ \varphi_2(\vec{r}_1) & \varphi_2(\vec{r}_2) & \cdots & \varphi_2(\vec{r}_n) \\ \vdots & & & \\ \varphi_n(\vec{r}_1) & \varphi_n(\vec{r}_2) & \cdots & \varphi_n(\vec{r}_n) \end{vmatrix} \quad (5)$$

$\Phi_k(\vec{r}_1, \vec{r}_2, \dots, \vec{r}_n)$  is called a **Slater determinant**. In the Dirac notation :

$$|\Phi_k\rangle = |\varphi_1 \varphi_2 \dots \varphi_n\rangle \equiv \frac{1}{\sqrt{n!}} |det(\varphi_1 \dots \varphi_n)\rangle \quad (6)$$

A basis set made of molecular orbitals is a very convenient basis for analytical definition and computations. However, it is neither well-defined nor practical for numerical computations.

MO are as we know one-electron functions. But we already know well-defined, both mathematically and physically, one-electron functions : the **atomic orbitals (AO)**!

Thus, every molecular orbital shall be constructed from **linear combination of atomic orbitals** :

$$\varphi_i(\vec{r}) = \sum_{\rho} c_{\rho i} \chi_{\rho}(\vec{r}), \quad \chi_{\rho}(\vec{r}) \text{ atomic orbital (AO)}$$

There exists many different molecular basis sets, with very simple ones (currently the more used in quantum computing methods) to very complicated ones.

Oftently, the more complete and complicated the basis set is, more precise the results will be.

From now on we'll switch to the Dirac notation.

Let us write the electronic Hamiltonian in a more useful explicit form :

$$\mathbf{H}_e = T_{el} + V_{nuc-nuc} + V_{nuc-el} + V_{el-el} = \sum_i h(\vec{r}_i) + \sum_{i < j} r_{ij}^{-1} + V_{nuc-nuc} \quad (7)$$

where we introduce the *one-electron hamiltonian* :

$$h(\vec{r}_i) \equiv h(i) = -\frac{1}{2}\Delta_i - \sum_A \frac{Z_A}{r_{Ai}}$$

From now on we'll switch to the Dirac notation.

Let us write the electronic Hamiltonian in a more useful explicit form :

$$\mathbf{H}_e = T_{el} + V_{nuc-nuc} + V_{nuc-el} + V_{el-el} = \sum_i h(\vec{r}_i) + \sum_{i < j} r_{ij}^{-1} + V_{nuc-nuc} \quad (8)$$

where we introduce the *one-electron hamiltonian* :

$$h(\vec{r}_i) \equiv h(i) = -\frac{1}{2}\Delta_i - \sum_A \frac{Z_A}{r_{Ai}}$$

The molecular energy is then defined as :

$$E_n = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle = \langle \Phi_n | \sum_i h(i) | \Phi_n \rangle + \langle \Phi_n | \sum_{i < j} r_{ij}^{-1} | \Phi_n \rangle + \langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle \quad (9)$$

# Schrödinger equation solutions for multi-electron atoms

Starting point of everything: Schrödinger equation

$$\left( -\frac{\hbar^2}{2m} \Delta + V \right) \psi(r_1, \dots, r_n, t) = i\hbar \frac{\partial}{\partial t} \psi(r_1, \dots, r_n, t)$$

Time independent Schrödinger equation

$$\mathbf{H}\psi(r_1, \dots, r_n) = E\psi(r_1, \dots, r_n), E \in \mathbb{R}$$

Schrödinger equation in Quantum Chemistry

$$\left( -\sum_{A=1}^N \frac{\hbar^2}{2m_A} \Delta_A - \sum_{i=1}^n \frac{\hbar^2}{2m_e} \Delta_i + \sum_{B=2}^N \sum_{A=1}^{B-1} \frac{Z_A Z_B e^2}{4\pi\epsilon_0 r_{AB}} - \sum_{A=1}^N \sum_{i=1}^n \frac{Z_A e^2}{4\pi\epsilon_0 r_{Ai}} - \sum_{j=2}^n \sum_{l=1}^{j-1} \frac{e^2}{4\pi\epsilon_0 r_{lj}} \right) |\psi\rangle = E |\psi\rangle$$

Dirac notation of the Schrödinger equation in QC

$$\mathbf{H} |\phi(r_{nuc}, r_{el}, spin)\rangle = E |\phi(r_{nuc}, r_{el}, spin)\rangle$$

Born-Oppenheimer approximation

$$E_n = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle = \langle \Phi_n | \sum_i h(i) | \Phi_n \rangle + \langle \Phi_n | \sum_{i < j} r_{ij}^{-1} | \Phi_n \rangle + \langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle$$

Energy as a function of Molecular Orbitals wave functions

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_j \varphi_i \rangle$$

Mean field approximation

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_j \varphi_i \rangle$$

Problem to solve

$$\min_{\varphi_i} E_n, \int |\varphi_i|^2 dr = 1 \quad \Leftrightarrow \quad \delta \left( E_n - \sum_i \epsilon_i \int |\varphi_i|^2 dr \right) = 0$$

The Hartree-Fock equations are given for each Molecular Orbitals

$$F|\varphi_k\rangle = \epsilon_k |\varphi_k\rangle \quad \forall k = 1, \dots, M$$

Let us compute each term :

$$\langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle = \langle \Phi_n | \Phi_n \rangle V_{nuc-nuc} = V_{nuc-nuc}$$

The nuclei-nuclei interaction term is just a constant term in the electronic problem.

Let us compute each term :

$$\langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle = \langle \Phi_n | \Phi_n \rangle V_{nuc-nuc} = V_{nuc-nuc}$$

The nuclei-nuclei interaction term is just a constant term in the electronic problem !

$$\langle \Phi_n | \sum_i h(i) | \Phi_n \rangle = \sum_i \langle \Phi_n | h(i) | \Phi_n \rangle = \sum_i \langle \varphi_i | h(i) | \varphi_i \rangle \equiv \sum_i h_{ii}$$

The expectation values of the one-electron Hamiltonians with respect to each orbital only are considered !

Let us compute each term :

$$\langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle = \langle \Phi_n | \Phi_n \rangle V_{nuc-nuc} = V_{nuc-nuc}$$

The nuclei-nuclei interaction term is just a constant term in the electronic problem !

$$\langle \Phi_n | \sum_i h(i) | \Phi_n \rangle = \sum_i \langle \Phi_n | h(i) | \Phi_n \rangle = \sum_i \langle \varphi_i | h(i) | \varphi_i \rangle \equiv \sum_i h_{ii}$$

The expectation value of the one-electron Hamiltonians with respect to each orbital only are considered !

$$\langle \Phi_n | \sum_{i < j} r_{ij}^{-1} | \Phi_n \rangle = \sum_{i < j} \langle \Phi_n | r_{ij}^{-1} | \Phi_n \rangle = \sum_{i < j} \left( \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_j \varphi_i \rangle \right)$$

The expectation value of the Coulombian interaction generates native and permuted 2-point interactions between orbitals.

# Self-consistent field equations (Hartree-Fock)

Starting point of everything: Schrödinger equation

$$\left( -\frac{\hbar^2}{2m} \Delta + V \right) \psi(r_1, \dots, r_n, t) = i\hbar \frac{\partial}{\partial t} \psi(r_1, \dots, r_n, t)$$

Time independent Schrödinger equation

$$\mathbf{H}\psi(r_1, \dots, r_n) = E\psi(r_1, \dots, r_n), E \in \mathbb{R}$$

Schrödinger equation in Quantum Chemistry

$$\left( -\sum_{A=1}^N \frac{\hbar^2}{2m_A} \Delta_A - \sum_{i=1}^n \frac{\hbar^2}{2m_e} \Delta_i + \sum_{B=2}^N \sum_{A=1}^{B-1} \frac{Z_A Z_B e^2}{4\pi\epsilon_0 r_{AB}} - \sum_{A=1}^N \sum_{i=1}^n \frac{Z_A e^2}{4\pi\epsilon_0 r_{Ai}} - \sum_{j=2}^n \sum_{l=1}^{j-1} \frac{e^2}{4\pi\epsilon_0 r_{lj}} \right) |\psi\rangle = E |\psi\rangle$$

Dirac notation of the Schrödinger equation in QC

$$\mathbf{H} |\phi(r_{nuc}, r_{el}, spin)\rangle = E |\phi(r_{nuc}, r_{el}, spin)\rangle$$

Born-Oppenheimer approximation

$$E_n = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle = \langle \Phi_n | \sum_i h(i) | \Phi_n \rangle + \langle \Phi_n | \sum_{i < j} r_{ij}^{-1} | \Phi_n \rangle + \langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle$$

Energy as a function of Molecular Orbitals wave functions

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_j \varphi_i \rangle$$

Mean field approximation

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_j \varphi_i \rangle$$

Problem to solve

$$\min_{\varphi_i} E_n, \int |\varphi_i|^2 dr = 1 \iff \delta \left( E_n - \sum_i \epsilon_i \int |\varphi_i|^2 dr \right) = 0$$

The Hartree-Fock equations are given for each Molecular Orbitals

$$F|\varphi_k\rangle = \epsilon_k |\varphi_k\rangle \quad \forall k = 1, \dots, M$$

If we summarize, we have proven that :

$$E_n \equiv E[\Phi_n] = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} (\langle ij|ij\rangle - \langle ij|ji\rangle) \quad (10)$$

where we use the short notation  $\langle ij|ij\rangle = \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle$ .

If we summarize, we have proven that :

$$E_n \equiv E[\Phi_n] = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} (\langle ij | ij \rangle - \langle ij | ji \rangle) \quad (11)$$

where we use the short notation  $\langle ij | ij \rangle = \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle$ .

From the Pauli principle, we now that electrons are **indistinguishable**. Hence the two-electrons integrals are **all equals**, so for the following will we use the following notation :

$$\langle ij | r_{ij}^{-1} | ij \rangle \equiv \langle ij | r_{12}^{-1} | ij \rangle = \int d\vec{r}_1 \int d\vec{r}_2 \varphi_i^*(\vec{r}_1) \varphi_j^*(\vec{r}_2) r_{12}^{-1} \varphi_i(\vec{r}_1) \varphi_j(\vec{r}_2)$$

If we summarize, we have proven that :

$$E_n \equiv E[\Phi_n] = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} (\langle ij | ij \rangle - \langle ij | ji \rangle) \quad (12)$$

where we use the short notation  $\langle ij | ij \rangle = \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle$ .

From the Pauli principle, we now that electrons are **indistinguishable**. Hence the two-electrons integrals are **all equals**, so for the following will we use the following notation :

$$\langle ij | r_{ij}^{-1} | ij \rangle \equiv \langle ij | r_{12}^{-1} | ij \rangle = \int d\vec{r}_1 \int d\vec{r}_2 \varphi_i^*(\vec{r}_1) \varphi_j^*(\vec{r}_2) r_{12}^{-1} \varphi_i(\vec{r}_1) \varphi_j(\vec{r}_2)$$

Thus a Slater determinant seems to be a **reasonable approximation** for the molecular wave-function.

# Self-consistent field equations (Hartree-Fock)

Starting point of everything: Schrödinger equation

$$\left( -\frac{\hbar^2}{2m} \Delta + V \right) \psi(r_1, \dots, r_n, t) = i\hbar \frac{\partial}{\partial t} \psi(r_1, \dots, r_n, t)$$

Time independent Schrödinger equation

$$\mathbf{H}\psi(r_1, \dots, r_n) = E\psi(r_1, \dots, r_n), E \in \mathbb{R}$$

Schrödinger equation in Quantum Chemistry

$$\left( -\sum_{A=1}^N \frac{\hbar^2}{2m_A} \Delta_A - \sum_{i=1}^n \frac{\hbar^2}{2m_e} \Delta_i + \sum_{B=2}^N \sum_{A=1}^{B-1} \frac{Z_A Z_B e^2}{4\pi\epsilon_0 r_{AB}} - \sum_{A=1}^N \sum_{i=1}^n \frac{Z_A e^2}{4\pi\epsilon_0 r_{Ai}} - \sum_{j=2}^n \sum_{l=1}^{j-1} \frac{e^2}{4\pi\epsilon_0 r_{lj}} \right) |\psi\rangle = E |\psi\rangle$$

Dirac notation of the Schrödinger equation in QC

$$\mathbf{H} |\phi(r_{nuc}, r_{el}, spin)\rangle = E |\phi(r_{nuc}, r_{el}, spin)\rangle$$

Born-Oppenheimer approximation

$$E_n = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle = \langle \Phi_n | \sum_i h(i) | \Phi_n \rangle + \langle \Phi_n | \sum_{i < j} r_{ij}^{-1} | \Phi_n \rangle + \langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle$$

Energy as a function of Molecular Orbitals wave functions

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_j \varphi_i \rangle$$

Mean field approximation

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_j \varphi_i \rangle$$

Problem to solve

$$\min_{\varphi_i} E_n, \int |\varphi_i|^2 dr = 1 \iff \delta \left( E_n - \sum_i \epsilon_i \int |\varphi_i|^2 dr \right) = 0$$

The Hartree-Fock equations are given for each Molecular Orbitals

$$F|\varphi_k\rangle = \epsilon_k |\varphi_k\rangle \quad \forall k = 1, \dots, M$$

Now we seek to find the best Slater determinant, and for that we compute the energy change from a little variation of the basis orbitals :

$$\begin{aligned}\delta E[\Phi_n] &= \delta \left[ \langle \Phi_n | \mathbf{H} | \Phi_n \rangle - \sum_i \epsilon_i \int d\vec{r} |\varphi_i|^2 \right] = 0 \\ &= \delta \sum_i h_{ii} + \delta \frac{1}{2} \sum_{i,j} (\langle ij | ij \rangle - \langle ij | ji \rangle)\end{aligned}$$

where the term  $\sum_i \epsilon_i \int d\vec{r} |\varphi_i|^2$  plays the role of a *Lagrangian multiplier* to enforce the constraints.

Let us do it again for each term :

Two terms are very simple to vary :

$$\delta \sum_i h_{ii} = \int d\vec{r} h(\vec{r}) \varphi_k(\vec{r}) \delta \varphi_k^*(\vec{r})$$

$$\delta \sum_i \epsilon_i \int d\vec{r} |\varphi_i|^2 = \int d\vec{r} \epsilon_k \varphi_k(\vec{r}) \delta \varphi_k^*(\vec{r})$$

Two terms are very simple to vary :

$$\delta \sum_i h_{ii} = \int d\vec{r} h(\vec{r}) \varphi_k(\vec{r}) \delta \varphi_k^*(\vec{r})$$

$$\delta \sum_i \epsilon_i \int d\vec{r} |\varphi_i|^2 = \int d\vec{r} \epsilon_k \varphi_k(\vec{r}) \delta \varphi_k^*(\vec{r})$$

Then for the Coulombian interaction terms :

$$\delta \sum_{i,j} \langle ij | r_{12}^{-1} | ij \rangle = 2 \int d\vec{r}_1 d\vec{r}_2 \left[ \sum_j \varphi_j^*(\vec{r}_2) r_{12}^{-1} \varphi_j(\vec{r}_1) \right] \varphi_k(\vec{r}_2) \delta \varphi_k^*(\vec{r}_1)$$

$$\delta \sum_{i,j} \langle ij | r_{12}^{-1} | ji \rangle = 2 \int d\vec{r}_1 d\vec{r}_2 \left[ \sum_j \varphi_j^*(\vec{r}_2) r_{12}^{-1} \varphi_j(\vec{r}_1) \right] \varphi_k(\vec{r}_2) \delta \varphi_k^*(\vec{r}_1)$$

Summing everything up, we have :

$$\begin{aligned}
 0 &= \int d\vec{r} [h(\vec{r}) - \epsilon_k] \varphi_k(\vec{r}) \delta \varphi_k^*(\vec{r}) \\
 &\quad + \int d\vec{r}_1 d\vec{r}_2 \left[ \sum_j \varphi_j^*(\vec{r}_2) r_{12}^{-1} \varphi_j(\vec{r}_2) \right] \varphi_k(\vec{r}_1) \delta \varphi_k^*(\vec{r}_1) \\
 &\quad - \int d\vec{r}_1 d\vec{r}_2 \left[ \sum_j \varphi_j^*(\vec{r}_2) r_{12}^{-1} \varphi_j(\vec{r}_1) \right] \varphi_k(\vec{r}_2) \delta \varphi_k^*(\vec{r}_1) \\
 &= \int d\vec{r} [h(\vec{r}) + J(\vec{r}) + K(\vec{r}) - \epsilon_k] \varphi_k(\vec{r}) \delta \varphi_k^*(\vec{r})
 \end{aligned} \tag{13}$$

where we introduce two operators  $J(\vec{r})$  and  $K(\vec{r})$ .

The operator  $J(\vec{r})$  is known as the **Coulomb operator**, corresponding to the electrostatic potential from the total electron distribution in the molecule. In other words, it represents the *self-interaction* that each electron suffers.

It is defined as :

$$J(\vec{r}) = \sum_j \int \varphi_j^*(\vec{r}') |\vec{r} - \vec{r}'|^{-1} \varphi_j(\vec{r}') d\vec{r}' \quad (14)$$

The operator  $J(\vec{r})$  is known as the **Coulomb operator**, corresponding to the electrostatic potential from the total electron distribution in the molecule. In other words, it represents the *self-interaction* that each electron suffers.

It is defined as :

$$J(\vec{r}) = \sum_j \int \varphi_j^*(\vec{r}') |\vec{r} - \vec{r}'|^{-1} \varphi_j(\vec{r}') d\vec{r}' \quad (15)$$

The operator  $K(\vec{r})$  is known as the **Exchange operator**, corresponding to the indistinguishability of the electrons in the anti-symmetric wave-function.

It is a non-local operator, defined by its action on an arbitrary function  $f(\vec{r})$  as :

$$K(\vec{r}) f(\vec{r}) = \sum_j \left[ \int \varphi_j^*(\vec{r}') |\vec{r} - \vec{r}'|^{-1} f(\vec{r}') d\vec{r}' \right] \varphi_j(\vec{r}) \quad (16)$$

Returning to (13), we see that the term in the braket shall be 0, thus we get :

$$0 = [h(\vec{r}) + J(\vec{r}) - K(\vec{r}) - \epsilon_k] \varphi_k \implies [h(\vec{r}) + J(\vec{r}) - K(\vec{r})] \varphi_k = \epsilon_k \varphi_k$$

Or in the most common form :

$$F(\vec{r})\varphi_k(\vec{r}) = \epsilon_k \varphi_k(\vec{r}) \quad (\text{Hartree-Fock equations})$$

where  $F(\vec{r})$  is the so-called **Fock operator**, defined as :

$$F(\vec{r}) = h(\vec{r}) + J(\vec{r}) - K(\vec{r}) \quad (17)$$

Returning to (13), we see that the term in the braket shall be 0, thus we get :

$$0 = [h(\vec{r}) + J(\vec{r}) - K(\vec{r}) - \epsilon_k] \varphi_k \implies [h(\vec{r}) + J(\vec{r}) - K(\vec{r})] \varphi_k = \epsilon_k \varphi_k$$

Or in the most common form :

$$F(\vec{r})\varphi_k(\vec{r}) = \epsilon_k \varphi_k(\vec{r}) \quad (\text{Hartree-Fock equations})$$

where  $F(\vec{r})$  is the so-called **Fock operator**, defined as :

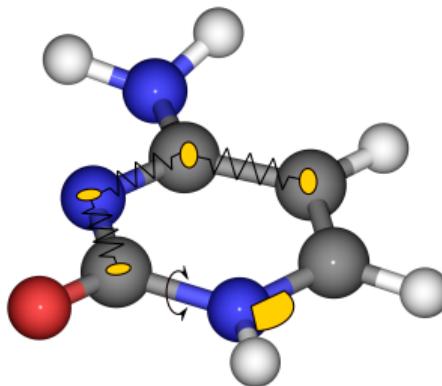
$$F(\vec{r}) = h(\vec{r}) + J(\vec{r}) - K(\vec{r}) \quad (18)$$

In the Dirac notation, that we will use in all the following works :

$$F|\varphi_k\rangle = \epsilon_k |\varphi_k\rangle \quad \forall k = 1, \dots, M \quad (19)$$

$\epsilon_k$  represents the *molecular orbital energies*.

Going back to the question "Where is Quantum in the Drug Discovery Pipeline?" with the example of  $U_{bond}(\kappa, r_{ij})$



- Solve  $F|\varphi_k\rangle(\mathbf{R}) = \epsilon_k |\varphi_k\rangle(\mathbf{R})$  for all orbitals and then get the total energy  $E(\mathbf{R})$
- apply a minimization algorithm so to find  $E(\mathbf{R}^{eq}) := E^{min}$
- Extract  $(r_{ij}^{eq}, \kappa)$  for atom pair  $(i, j)$

As we have shown, to treat molecular system we need to take into account the quantum nature of electrons. This requires, for fundamental reasons, to anti-symmetrized our global wave-function, which is **painful and not practical**.

As we have shown, to treat molecular system we need to take into account the quantum nature of electrons. This requires, for fundamental reasons, to anti-symmetrized our global wave-function, which is **painful and not practical**.

To make this mathematically, physically and practically better, we are going into a new formalism : **Second Quantization**.

The Second Quantization relies on considering the matter wave-functions, called *fields*, as "fields operators". For us it means switching the question of :

As we have shown, to treat molecular system we need to take into account the quantum nature of electrons. This requires, for fundamental reasons, to anti-symmetrized our global wave-function, which is **painful and not practical**.

To make this mathematically, physically and practically better, we are going into a new formalism : **Second Quantization**.

The Second Quantization relies on considering the matter wave-functions, called *fields*, as "fields operators". For us it means switching the question of :

*“Which electrons are in which orbitals?”*

into

*“How many electrons are in which orbital?”*

Why switching formalism? The reasons are simple :

- electrons are indistinguishable, thus the first question is somehow irrelevant
- we know the answer of the second question : a maximum of 2, one with spin  $+\frac{1}{2}$ , the other with spin  $-\frac{1}{2}$

## Objective

We seek to pass from wave-function based formalism to field operators formalism

Let us recall that the wave-function is interpreted as a **probability amplitude** and

$$\int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r} = 1$$

# Second Quantization

## Quantum Chemistry Second Quantization

- $\int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r} = 1$

$$\Psi(\vec{r}) = \sum_p \varphi_p(\vec{r}) a_p \implies a_p = \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r}$$

$$\Psi^\dagger(\vec{r}) = \sum_p \varphi_p^\dagger(\vec{r}) a_p^\dagger \implies a_p^\dagger = \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \varphi_p(\vec{r}) d^3\vec{r}$$

- $a_p$  is an *annihilation operator*, annihilating an electron in the orbital  $p$

- $a_p^\dagger$  is a *creation operator*, creating an electron in the orbital  $p$

- $|\varphi_1 \dots \varphi_M\rangle \rightarrow |f_1 \dots f_M\rangle, f_i = \begin{cases} 0, & \text{if unoccupied} \\ 1, & \text{if occupied} \end{cases}$

- $\mathbf{H} = \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s + V_{nuc-nuc}$

## Hartree-Fock in Second Quantization

- $|HF\rangle = a_1^\dagger \dots a_m^\dagger |\Omega\rangle = |\underbrace{1 \dots 1}_m \underbrace{0 \dots 0}_{M-m}\rangle$

- $E^{HF} = \langle HF | \mathbf{H} | HF \rangle = \langle HF | \left[ \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s \right] | HF \rangle + V_{nuc-nuc}$

Why switching formalism? The reasons are simple :

- electrons are indistinguishable, thus the first question is somehow irrelevant
- we know the answer of the second question : a maximum of 2, one with spin  $+\frac{1}{2}$ , the other with spin  $-\frac{1}{2}$

### Objective

We seek to pass from wave-function based formalism to field operators formalism

Let us recall that the wave-function is interpreted as a **probability amplitude** and

$$\int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r} = 1$$

Thus what if we interpret  $\Psi^\dagger(\vec{r})$  and  $\Psi(\vec{r})$  to be respectively *creation* and *annihilation operators* of an electron at the position  $\vec{r}$ ?

## Validation of the field interpretation

First we must respect the Pauli Exclusion Principle

It translate into **anti-commutation relations for the electron field operators :**

$$[\Psi^\dagger(\vec{r}), \Psi^\dagger(\vec{r}')]_+ = 0 = [\Psi(\vec{r}), \Psi(\vec{r}')]_+ \quad (20)$$

$$[\Psi(\vec{r}), \Psi^\dagger(\vec{r}')]_+ = \Psi(\vec{r})\Psi^\dagger(\vec{r}') + \Psi^\dagger(\vec{r}')\Psi(\vec{r}) = \delta(\vec{r} - \vec{r}') \quad (21)$$

Moreover, we know that the wave-functions can always be written as a linear combination of an orthonormal orbital basis  $\{\varphi_p(\vec{r})\}_{p=1}^M$ . More explicitly, we have the following expansion :

$$\begin{aligned} \Psi(\vec{r}) &= \sum_p \varphi_p(\vec{r}) a_p \implies a_p = \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r} \\ \Psi^\dagger(\vec{r}) &= \sum_p \varphi_p^\dagger(\vec{r}) a_p^\dagger \implies a_p^\dagger = \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \varphi_p(\vec{r}) d^3\vec{r} \end{aligned} \quad (22)$$

# Second Quantization

## Quantum Chemistry Second Quantization

- $\int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r} = 1$

$$\Psi(\vec{r}) = \sum_p \varphi_p(\vec{r}) a_p \implies a_p = \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r}$$

$$\Psi^\dagger(\vec{r}) = \sum_p \varphi_p^\dagger(\vec{r}) a_p^\dagger \implies a_p^\dagger = \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \varphi_p(\vec{r}) d^3\vec{r}$$

- $a_p$  is an *annihilation operator*, annihilating an electron in the orbital  $p$

- $a_p^\dagger$  is a *creation operator*, creating an electron in the orbital  $p$

- $|\varphi_1 \dots \varphi_M\rangle \rightarrow |f_1 \dots f_M\rangle, f_i = \begin{cases} 0, & \text{if unoccupied} \\ 1, & \text{if occupied} \end{cases}$

- $\mathbf{H} = \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s + V_{nuc-nuc}$

## Hartree-Fock in Second Quantization

- $|HF\rangle = a_1^\dagger \dots a_m^\dagger |\Omega\rangle = |\underbrace{1 \dots 1}_m \underbrace{0 \dots 0}_{M-m}\rangle$

- $E^{HF} = \langle HF | \mathbf{H} | HF \rangle = \langle HF | \left[ \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s \right] | HF \rangle + V_{nuc-nuc}$

We have our wanted operators !

- $a_p$  is an *annihilation operator*, annihilating an electron in the orbital  $p$
- $a_p^\dagger$  is a *creation operator*, creating an electron in the orbital  $p$

We have our wanted operators !

- $a_p$  is an *annihilation operator*, annihilating an electron in the orbital  $p$
- $a_p^\dagger$  is a *creation operator*, creating an electron in the orbital  $p$

Their algebra directly follows from that of the field operators :

$$\begin{aligned}
 [a_p, a_q^\dagger]_+ &= \left[ \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r}, \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}') \varphi_q(\vec{r}') d^3\vec{r}' \right]_+ \\
 &= \int_{\mathbb{R}^3} \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \varphi_q(\vec{r}') [\Psi(\vec{r}), \Psi^\dagger(\vec{r}')]_+ d^3\vec{r} d^3\vec{r}' \\
 &= \int_{\mathbb{R}^3} \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \varphi_q(\vec{r}') \delta(\vec{r} - \vec{r}') d^3\vec{r} d^3\vec{r}' \\
 &= \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \varphi_q(\vec{r}) d^3\vec{r} = \delta_{pq}
 \end{aligned}$$

# Second Quantization

## Quantum Chemistry Second Quantization

- $\int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r} = 1$

- $\Psi(\vec{r}) = \sum_p \varphi_p(\vec{r}) a_p \implies a_p = \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r}$

- $\Psi^\dagger(\vec{r}) = \sum_p \varphi_p^\dagger(\vec{r}) a_p^\dagger \implies a_p^\dagger = \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \varphi_p(\vec{r}) d^3\vec{r}$

- $a_p$  is an *annihilation operator*, annihilating an electron in the orbital  $p$

- $a_p^\dagger$  is a *creation operator*, creating an electron in the orbital  $p$

- $|\varphi_1 \dots \varphi_M\rangle \rightarrow |f_1 \dots f_M\rangle, f_i = \begin{cases} 0, & \text{if unoccupied} \\ 1, & \text{if occupied} \end{cases}$

- $\mathbf{H} = \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s + V_{nuc-nuc}$

## Hartree-Fock in Second Quantization

- $|HF\rangle = a_1^\dagger \dots a_m^\dagger |\Omega\rangle = |\underbrace{1 \dots 1}_m \underbrace{0 \dots 0}_{M-m}\rangle$

- $E^{HF} = \langle HF | \mathbf{H} | HF \rangle = \langle HF | \left[ \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s \right] | HF \rangle + V_{nuc-nuc}$

To sumup, the algebra of the creation and annihilation operators is :

$$[a_p^\dagger, a_q^\dagger]_+ = 0 = [a_p, a_q]_+ \quad (23)$$

$$[a_p, a_q^\dagger] = \delta_{pq} \quad (24)$$

To sumup, the algebra of the creation and annihilation operators is :

$$[a_p^\dagger, a_q^\dagger]_+ = 0 = [a_p, a_q]_+ \quad (25)$$

$$[a_p, a_q^\dagger] = \delta_{pq} \quad (26)$$

One great thing is that we have previously worked all of our equations with Slater determinants. And Slater determinants are constructed from an orthonormal orbital basis.

Hence, the action of the operators  $a_p$  and  $a_q^\dagger$  on the Slater determinants are simple :

To sumup, the algebra of the creation and annihilation operators is :

$$[a_p^\dagger, a_q^\dagger]_+ = 0 = [a_p, a_q]_+ \quad (27)$$

$$[a_p, a_q^\dagger] = \delta_{pq} \quad (28)$$

One great thing is that we have previously worked all of our equations with Slater determinants. And Slater determinants are constructed from an **orthonormal orbital basis**.

Hence, the action of the operators  $a_p$  and  $a_q^\dagger$  on the Slater determinants are simple :

$$a_p |\varphi_1 \dots \varphi_p \dots \varphi_M\rangle = |\varphi_1 \dots \varphi_{p-1} \varphi_{p+1} \dots \varphi_M\rangle \quad (29)$$

$$a_p^\dagger |\varphi_1 \dots \varphi_{p-1} \varphi_{p+1} \dots \varphi_M\rangle = |\varphi_i \dots \varphi_p \dots \varphi_M\rangle \quad (30)$$

For more efficiency, we will slightly modify the definition of the Slater determinants and use some specific denominations.

For more efficiency, we will slightly modify the definition of the Slater determinants and use some specific denominations.

Consider we have an orthonormal orbital basis  $\{\varphi_p\}_{p=1}^M$ . Then a Slater determinant is mapped to a vector defining the (non)-occupancy of the  $n$  orbitals. In other words :

$$|\varphi_1 \dots \varphi_M\rangle \rightarrow |f_1 \dots f_M\rangle, \quad f_i = \begin{cases} 0, & \text{if unoccupied} \\ 1, & \text{if occupied} \end{cases} \quad (31)$$

This "occupancy" Slater determinant leaves in a  $2^n$  dimensional space called the **Fock space** of the many-body system.

For more efficiency, we will slightly modify the definition of the Slater determinants and use some specific denominations.

Consider we have an orthonormal orbital basis  $\{\varphi_p\}_{p=1}^M$ . Then a Slater determinant is mapped to a vector defining the (non)-occupancy of the n orbitals. In other words :

$$|\varphi_1 \dots \varphi_M\rangle \rightarrow |f_1 \dots f_M\rangle, \quad f_i = \begin{cases} 0, & \text{if unoccupied} \\ 1, & \text{if occupied} \end{cases} \quad (32)$$

This "occupancy" Slater determinant leaves in a  $2^n$  dimensional space called the **Fock space** of the many-body system.

A Fock space possesses a very particular state, called the **vacuum state** :

$$|vac\rangle \equiv |\Omega\rangle = |0 \dots 0\rangle \quad (33)$$

For us it corresponds to state where all orbitals are unoccupied !

# Second Quantization

## Quantum Chemistry Second Quantization

- $\int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r} = 1$

- $\Psi(\vec{r}) = \sum_p \varphi_p(\vec{r}) a_p \implies a_p = \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r}$

- $\Psi^\dagger(\vec{r}) = \sum_p \varphi_p^\dagger(\vec{r}) a_p^\dagger \implies a_p^\dagger = \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \varphi_p(\vec{r}) d^3\vec{r}$

- $a_p$  is an *annihilation operator*, annihilating an electron in the orbital  $p$

- $a_p^\dagger$  is a *creation operator*, creating an electron in the orbital  $p$

- $|\varphi_1 \dots \varphi_M\rangle \rightarrow |f_1 \dots f_M\rangle, f_i = \begin{cases} 0, & \text{if unoccupied} \\ 1, & \text{if occupied} \end{cases}$

- $\mathbf{H} = \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s + V_{nuc-nuc}$

## Hartree-Fock in Second Quantization

- $|HF\rangle = a_1^\dagger \dots a_m^\dagger |\Omega\rangle = |\underbrace{1 \dots 1}_m \underbrace{0 \dots 0}_{M-m}\rangle$

- $E^{HF} = \langle HF | \mathbf{H} | HF \rangle = \langle HF | \left[ \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s \right] | HF \rangle + V_{nuc-nuc}$

Every Slater determinant can be constructed from the vacuum state :

$$|f_1 \dots f_M\rangle = \prod_{p=1}^n (a_p^\dagger)^{f_p} |\Omega\rangle \quad (34)$$

The inner-product associated with the Fock space is also quite simple :

$$\langle \vec{f} | \vec{g} \rangle = \delta_{\vec{f}, \vec{g}} = \prod_{p=1}^n \delta_{f_p, g_p}, \quad \vec{f} = f_1 \dots f_M \quad (35)$$

Every Slater determinant can be constructed from the vacuum state :

$$|f_1 \dots f_M\rangle = \prod_{p=1}^n (a_p^\dagger)^{f_p} |\Omega\rangle \quad (36)$$

The inner-product associated with the Fock space is also quite simple :

$$\langle \vec{f} | \vec{g} \rangle = \delta_{\vec{f}, \vec{g}} = \prod_{p=1}^n \delta_{f_p, g_p}, \quad \vec{f} = f_1 \dots f_M \quad (37)$$

### Example

Example of algebra use

$$a_1^\dagger |0100\rangle = |1100\rangle = a_1^\dagger a_2^\dagger |\Omega\rangle$$

$$a_2^\dagger |1000\rangle = a_2^\dagger a_1^\dagger |\Omega\rangle = -a_1^\dagger a_2^\dagger |\Omega\rangle = -|1100\rangle$$

Now that we have detailed the Second Quantization formalism, we shall express our molecular Hamiltonian in it.

We recall that the general form of the Hamiltonian is (8). Let us express each term in the Second Quantization formalism :

Now that we have detailed the Second Quantization formalism, we shall express our molecular Hamiltonian in it.

We recall that the general form of the Hamiltonian is (8). Let us express each term in the Second Quantization formalism :

For  $h(\vec{r}_i)$  :

$$\begin{aligned}\sum_i h(\vec{r}_i) &= \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}_i) h(\vec{r}_i) \Psi(\vec{r}_i) d^3\vec{r}_i = \sum_p \sum_q \left\{ \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}_i) h(\vec{r}_i) \varphi_q(\vec{r}_i) d^3\vec{r}_i \right\} a_p^\dagger a_q \\ &= \sum_{pq} h_{pq} a_p^\dagger a_q\end{aligned}$$

Now that we have detailed the Second Quantization formalism, we shall express our molecular Hamiltonian in it.

We recall that the general form of the Hamiltonian is (8). Let us express each term in the Second Quantization formalism :

For  $r_{ij}^{-1}$  :

$$\begin{aligned}
 \frac{1}{2} \sum_{i \neq j}^n r_{ij}^{-1} &= \frac{1}{2} \int_{\mathbb{R}^3} \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}_i) \Psi^\dagger(\vec{r}_j) r_{ij}^{-1} \Psi(\vec{r}_i) \Psi(\vec{r}_j) d^3 \vec{r}_i d^3 \vec{r}_j \\
 &= \frac{1}{2} \sum_{pq} \sum_{rs} \left\{ \int_{\mathbb{R}^3} \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}_i) \varphi_q^\dagger(\vec{r}_j) r_{ij}^{-1} \varphi_r(\vec{r}_i) \varphi_s(\vec{r}_j) d^3 \vec{r}_i d^3 \vec{r}_j \right\} a_p^\dagger a_q^\dagger a_r a_s \\
 &= \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s
 \end{aligned}$$

Thus the Second Quantization expression of the Hamiltonian is :

$$\mathbf{H} = \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s + V_{nuc-nuc} \quad (38)$$

with :

$$h_{pq} = \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) h(\vec{r}) \varphi_q(\vec{r}) d^3\vec{r} \quad (\text{one-electron Hamiltonian})$$

$$V_{pq,rs} = \int_{\mathbb{R}^3} \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}_1) \varphi_q^\dagger(\vec{r}_2) r_{12}^{-1} \varphi_r(\vec{r}_1) \varphi_s(\vec{r}_2) d^3\vec{r}_1 d^3\vec{r}_2 \quad (\text{two-electrons Potential})$$

# Second Quantization

## Quantum Chemistry Second Quantization

- $\int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r} = 1$

- $\Psi(\vec{r}) = \sum_p \varphi_p(\vec{r}) a_p \implies a_p = \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r}$

- $\Psi^\dagger(\vec{r}) = \sum_p \varphi_p^\dagger(\vec{r}) a_p^\dagger \implies a_p^\dagger = \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \varphi_p(\vec{r}) d^3\vec{r}$

- $a_p$  is an *annihilation operator*, annihilating an electron in the orbital  $p$

- $a_p^\dagger$  is a *creation operator*, creating an electron in the orbital  $p$

- $|\varphi_1 \dots \varphi_M\rangle \rightarrow |f_1 \dots f_M\rangle, f_i = \begin{cases} 0, & \text{if unoccupied} \\ 1, & \text{if occupied} \end{cases}$

- $\mathbf{H} = \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_p^\dagger a_r a_s + V_{nuc-nuc}$

### Hartree-Fock in Second Quantization

- $|HF\rangle = a_1^\dagger \dots a_m^\dagger |\Omega\rangle = |\underbrace{1 \dots 1}_m \underbrace{0 \dots 0}_{M-m}\rangle$

- $E^{HF} = \langle HF | \mathbf{H} | HF \rangle = \langle HF | \left[ \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_p^\dagger a_r a_s \right] | HF \rangle + V_{nuc-nuc}$

Now that we have detailed the Second Quantization formalism, we shall express the Hartree-Fock energy in it.

Before going into the calculation, we define the *Hartree-Fock* wave-function in the Second Quantization formalism. For an orbital basis of dimension  $M$ , we have  $m < M$  electrons and thus  $m$  occupied orbitals, thus :

$$|HF\rangle = a_1^\dagger \dots a_m^\dagger |\Omega\rangle = \left| \underbrace{1 \dots 1}_m \underbrace{0 \dots 0}_{M-m} \right\rangle \quad (39)$$

Now that we have detailed the Second Quantization formalism, we shall the Hartree-Fock energy in it.

Before going into the calculation, we define the *Hartree-Fock* wave-function in the Second Quantization formalism. For an orbital basis of dimension  $M$ , we have  $m < M$  electrons and thus  $m$  occupied orbitals, thus :

$$|HF\rangle = a_1^\dagger \dots a_m^\dagger |\Omega\rangle = \left| \underbrace{1 \dots 1}_m \underbrace{0 \dots 0}_{M-m} \right\rangle \quad (40)$$

We also introduce some **indices notation** specific to orbitals :

- occupied orbitals :  $i, j, k, l, \dots$
- unoccupied (virtual) orbitals :  $a, b, c, d, \dots$
- general orbitals :  $p, q, r, s, \dots$

# Second Quantization

## Quantum Chemistry Second Quantization

- $\int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r} = 1$

- $\Psi(\vec{r}) = \sum_p \varphi_p(\vec{r}) a_p \implies a_p = \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r}$

- $\Psi^\dagger(\vec{r}) = \sum_p \varphi_p^\dagger(\vec{r}) a_p^\dagger \implies a_p^\dagger = \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \varphi_p(\vec{r}) d^3\vec{r}$

- $a_p$  is an *annihilation operator*, annihilating an electron in the orbital  $p$

- $a_p^\dagger$  is a *creation operator*, creating an electron in the orbital  $p$

- $|\varphi_1 \dots \varphi_M\rangle \rightarrow |f_1 \dots f_M\rangle, f_i = \begin{cases} 0, & \text{if unoccupied} \\ 1, & \text{if occupied} \end{cases}$

- $\mathbf{H} = \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s + V_{nuc-nuc}$

### Hartree-Fock in Second Quantization

- $|HF\rangle = a_1^\dagger \dots a_m^\dagger |\Omega\rangle = |\underbrace{1 \dots 1}_m \underbrace{0 \dots 0}_{M-m}\rangle$

- $E^{HF} = \langle HF | \mathbf{H} | HF \rangle = \langle HF | \left[ \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s \right] | HF \rangle + V_{nuc-nuc}$

We recall that the general form of the Hartree-Fock energy is (12). Let us express each term in the Second Quantization formalism :

$$E^{HF} = \langle HF | \mathbf{H} | HF \rangle = \langle HF | \left[ \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_p^\dagger a_r a_s \right] | HF \rangle + V_{nuc-nuc}$$

We recall that the general form of the Hartree-Fock energy is (12). Let us express each term in the Second Quantization formalism :

$$E^{HF} = \langle HF | \mathbf{H} | HF \rangle = \langle HF | \left[ \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_p^\dagger a_r a_s \right] | HF \rangle + V_{nuc-nuc}$$

For the first term :

$$E_1^{HF} = \sum_{pq} h_{pq} \langle HF | a_p^\dagger a_q | HF \rangle = \sum_i h_{ii} \quad (41)$$

For the second term :

$$E_2^{HF} = \frac{1}{2} \sum_{pqrs} V_{pq,rs} \langle HF | a_p^\dagger a_q^\dagger a_r a_s | HF \rangle = \frac{1}{2} \sum_{i \neq j} (V_{ij,ij} - V_{ij,ji}) \quad (42)$$

We recall that orbitals indices  $i, j$  correspond to occupied orbitals !

To sumup, the Hartree-Fock energy is then :

$$E^{HF}[\{\varphi_i\}] = \sum_i \langle \varphi_i | \hat{h} | \varphi_i \rangle + \frac{1}{2} \sum_{ij} (\langle ij | ij \rangle - \langle ij | ji \rangle) + V_{nn} \quad (43)$$

where we used again the common notations in quantum chemistry, explicitely in terms of orbitals :

$$\hat{h}_{ii} \equiv \langle \varphi_i | \hat{h} | \varphi_i \rangle$$

$$\sum_{i \neq j} (V_{ij,ij} - V_{ij,ji}) \equiv \sum_{ij} (\langle ij | ij \rangle - \langle ij | ji \rangle)$$

Hartree-Fock theory is the starting point for all wave-function based correlation methods such that :

$$E^{\text{exact}} = E^{\text{HF}} + E^{\text{Corr}} \quad (44)$$

As a conclusion, we'll just quote the most known of such methods :

Hartree-Fock theory is the starting point for all wave-function based correlation methods such that :

$$E^{\text{exact}} = E^{\text{HF}} + E^{\text{Corr}} \quad (45)$$

As a conclusion, we'll just quote the most known of the such methods :

$$|CI\rangle = (\mathbb{I} + \mathbf{C}) |HF\rangle, \mathbf{C} = \sum_{ia} c_i^a a_a^\dagger a_i + \frac{1}{4} \sum_{ijab} c_{ij}^{ab} a_a^\dagger a_b^\dagger a_i a_j + \dots \text{ (Configuration Interaction)}$$

$$\mathbf{C} = \mathbf{C}_1 + \mathbf{C}_2 + \mathbf{C}_3 + \dots$$

CI methods correspond to compute **all possible interactions** between the orbitals, up to a specific order.

As such, last-order CI method with **complete basis sets**, i.e. sets tending to an infinite number of basis functions, ends up with exact quantum calculations. This is known as **Full Configuration Interaction (FCI)**.

Hartree-Fock theory is the starting point for all wave-function based correlation methods such that :

$$E^{\text{exact}} = E^{\text{HF}} + E^{\text{Corr}} \quad (46)$$

As a conclusion, we'll just quote the most known of the such methods :

$$|CC\rangle = e^{\mathbf{T}} |HF\rangle, \quad \mathbf{T} = \sum_{ia} t_i^a a_a^\dagger a_i + \frac{1}{4} \sum_{ijab} t_{ij}^{ab} a_a^\dagger a_b^\dagger a_i a_j \dots \quad (\text{Coupled Cluster})$$

$$e^{\mathbf{T}} = \mathbb{I} + \mathbf{T}_1 + \mathbf{T}_2 + \frac{1}{2!} \mathbf{T}_1^2 + \mathbf{T}_3 + \frac{1}{3!} \mathbf{T}_1^3 + \mathbf{T}_1 \mathbf{T}_2 + \dots$$

CC methods, derived from very successful particle physics methods, correspond to compute **all possible correlated interactions** between the orbitals, up to a specific order.

They are usually considered as **Golden standard methods** in Quantum Chemistry, especially the **CCSD(T) method**, standing for CC method up to fourth-order.

You may think that both CI and CC methods are equivalent by looking at the different expressions. And indeed you are right if you consider all orders!

$$\mathbb{I} + \mathbf{C} = e^{\mathbf{T}} \iff \mathbf{C}_1 + \mathbf{C}_2 + \dots = \underbrace{\mathbf{T}_1}_{\mathbf{C}_1} + \underbrace{\mathbf{T}_2 + \frac{1}{2!}\mathbf{T}_1^2}_{\mathbf{C}_2} + \underbrace{\mathbf{T}_3 + \frac{1}{3!}\mathbf{T}_1^3 + \mathbf{T}_1\mathbf{T}_2 + \dots}_{\mathbf{C}_3} \quad (47)$$

But in practice, we cannot go to the full order, and we are forced to **truncate** to a specific order. And in doing so, differences have been made between the two methods ! As an example, let us truncate at the order 2, considering only **single and double excitations**. We have then respectively :

$$|\Psi_{CISD}\rangle = (\mathbb{I} + \mathbf{C}_1 + \mathbf{C}_2) |HF\rangle$$

$$|\Psi_{CCSD}\rangle = e^{\mathbf{T}_1 + \mathbf{T}_2} |HF\rangle = \left( \mathbb{I} + \mathbf{T}_1 + \mathbf{T}_2 + \frac{1}{2!}\mathbf{T}_1^2 + \mathbf{T}_3 + \frac{1}{3!}\mathbf{T}_1^3 + \mathbf{T}_1\mathbf{T}_2 + \dots \right) |HF\rangle$$

# Quantum Chemistry at a glance

Starting point of everything:  
Schrödinger equation

$$\left( -\frac{\hbar^2}{2m} \Delta + V \right) \psi(r_1, \dots, r_n, t) = i\hbar \frac{\partial}{\partial t} \psi(r_1, \dots, r_n, t)$$

The wave function is split as the product of 2 terms. One space dependent the other time only dependent.

Time independent Schrödinger equation

$$\mathbf{H} \psi(r_1, \dots, r_n) = E \psi(r_1, \dots, r_n), E \in \mathbb{R}$$

In Quantum Chemistry the Hamiltonian for a molecule is:

$$\mathbf{H} = T_{nuc} + V_{el} + V_{nuc-nuc} + V_{nuc-el} + V_{el-el}$$

Schrödinger equation in Quantum Chemistry

$$\begin{aligned} & \left( -\sum_{A=1}^N \frac{\hbar^2}{2m_A} \Delta_A - \sum_{l=1}^n \frac{\hbar^2}{2m_e} \Delta_l + \sum_{B=2}^N \sum_{A=1}^{B-1} \frac{Z_A Z_B e^2}{4\pi\epsilon_0 r_{AB}} \right. \\ & \left. - \sum_{A=1}^N \sum_{l=1}^n \frac{Z_A e^2}{4\pi\epsilon_0 r_{Al}} - \sum_{j=2}^n \sum_{i=1}^{j-1} \frac{e^2}{4\pi\epsilon_0 r_{ij}} \right) |\psi\rangle = E |\psi\rangle \end{aligned}$$

Where *nuc* stands for Nucleus of the molecule atoms, and *el* for electrons. Additionally to the Schrödinger equation, a constraint on electron orbitals has to be fulfilled: the **Pauli exclusion principle** states that no more than 2 electron can occupy the same orbital and that 2 electrons on the same orbital must have opposite spins.

Born-Oppenheimer approximation

$$\mathbf{H} |\phi(r_{nuc}, r_{el}, spin)\rangle = E |\phi(r_{nuc}, r_{el}, spin)\rangle$$

Stated as is, the equation is intractable analytically or numerically for more than 2 particles. Several approximations will be made to make it computable in a finite time. **Born-Oppenheimer** approximation consists in assuming that nucleus dynamics are much slower than electrons one. Therefore the wave function is approximated as  $|\psi\rangle \approx |\chi(r_{nuc})\rangle \times |\phi(r_{nuc}, r_{el}, spin)\rangle$

With associated Hamiltonian

$$\mathbf{H} = T_{el} + V_{nuc-nuc} + V_{nuc-el} + V_{el-el}$$

$$\begin{aligned} E_n = \langle \Phi_n | \mathbf{H} | \Phi_n \rangle &= \langle \Phi_n | \sum h(i) | \Phi_n \rangle + \\ &\langle \Phi_n | \sum_{i < j} r_{ij}^{-1} | \Phi_n \rangle + \langle \Phi_n | V_{nuc-nuc} | \Phi_n \rangle \end{aligned}$$

Expanding the Hamiltonian  $\mathbf{H}$  with differential operator yields:

$$\sum_i h(\vec{r}_i) + \sum_{i < j} r_{ij}^{-1} + V_{nuc-nuc} \quad \text{where } h(\vec{r}_i) \equiv h(i) = -\frac{1}{2} \Delta_i - \sum_A \frac{Z_A}{r_{Ai}}$$

Is defined as the **one-electron Hamiltonian**. Replacing in the Schrödinger equation and multiplying both sides by  $\langle \phi_n |$  gives the expression of the energy.

$$E_n = V_{nuc-nuc} + \sum h_{ii} + \sum \langle \varphi_i | \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i | \varphi_j | r_{ij}^{-1} | \varphi_j \varphi_i \rangle$$

Applying the **Pauli exclusion principle**, allows substituting  $|\phi(r_{nuc}, r_{el}, spin)\rangle$

by:  $A |\varphi_1(r_1) \varphi_2(r_2) \dots \varphi_k(r_k)\rangle$  where  $A$  is the Slater determinant. The

wave function now reads  $|\phi_n\rangle = \frac{1}{\sqrt{n!}} |\det(\varphi_1, \dots, \varphi_k)\rangle$ . Replacing this expression in the energy and computing each term one by one yields the proposed expression.

# Quantum Chemistry at a glance

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_j \varphi_i \rangle$$

In this expression,  $\varphi_k(\vec{r}_k)$  are the Molecular Orbitals of the system. The number of such MO can be arbitrary large and not less than the number of electron (or nb electron / 2 when considering spins). The  $V_{nuc-nuc}$  we choose, the more precise will be the approximation. Notice that  $V_{nuc-nuc}$  is simply a constant. Each MO is computed as a linear combination of Atomic Orbitals (AO):  $\varphi_l(\vec{r}) = \sum_p c_{pl} \chi_p(\vec{r})$

By term identification we have:  $h_{ii} \equiv \langle \phi_n | h(i) | \phi_n \rangle$  where the  $\phi_n$  are function of the MO.

$$E_n = V_{nuc-nuc} + \sum_i h_{ii} + \sum_{i < j} \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_i \varphi_j \rangle - \langle \varphi_i \varphi_j | r_{12}^{-1} | \varphi_j \varphi_i \rangle$$

Stated as is the expression remains intractable. Yet, involving the Slater determinant not only allows a good approximation of the term  $\langle \varphi_i \varphi_j | r_{ij}^{-1} | \varphi_i \varphi_j \rangle$  but also allows involving the anti-symmetry constraint of the MO. Substituting by the Slater determinant bellow, gives an approximated expression of the energy.

$$\langle ij | r_{12}^{-1} | kl \rangle = \int d\vec{r}_1 \int d\vec{r}_2 \varphi_i^*(\vec{r}_1) \varphi_j^*(\vec{r}_2) r_{12}^{-1} \varphi_k(\vec{r}_1) \varphi_l(\vec{r}_2)$$

$$\min_{\varphi_i} E_n, \int |\varphi_i|^2 dr = 1$$

$$\Leftrightarrow \delta \left( E_n - \sum_i \epsilon_i \int |\varphi_i|^2 dr \right) = 0$$

We wish to find the MO that minimize the energy under the normalization constraint. Where  $\epsilon_j$  are Lagrange multiplier and are homogeneous to the energy of all MOs.

Developing each term, and solving leads to the **Hartree-Fock equation** where  $F = h + J - K$  is given by:

$$h(k) + \underbrace{\sum_j \int \varphi_j^*(r') |r - r'|^{-1} \varphi_j(r') dr'}_{J(r)} - \underbrace{\sum_j \left[ \int \varphi_j^*(r') |r - r'|^{-1} \varphi_j(r) dr' \right] \varphi_j(r)}_{K(r)}$$

Where  $r_1$  and  $r_2$  have been substituted by  $r$  and  $r'$  for sake of readability

The Hartree-Fock equations are given for each Molecular Orbitals

$$F|\varphi_k\rangle = \epsilon_k |\varphi_k\rangle \quad \forall k = 1, \dots, M$$

# Quantum Chemistry at a glance

## Quantum Chemistry Second Quantization

Hartree-Fock in Second Quantization

$$\begin{aligned}
 & \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r} = 1 \\
 & \Psi(\vec{r}) = \sum_p \varphi_p(\vec{r}) a_p \implies a_p = \int_{\mathbb{R}^3} \varphi_p^\dagger(\vec{r}) \Psi(\vec{r}) d^3\vec{r} \\
 & \Psi^\dagger(\vec{r}) = \sum_p \varphi_p^\dagger(\vec{r}) a_p^\dagger \implies a_p^\dagger = \int_{\mathbb{R}^3} \Psi^\dagger(\vec{r}) \varphi_p(\vec{r}) d^3\vec{r} \\
 & a_p \text{ is an annihilation operator, annihilating an electron in the orbital } p \\
 & a_p^\dagger \text{ is a creation operator, creating an electron in the orbital } p \\
 & |\varphi_1 \dots \varphi_M\rangle \rightarrow |f_1 \dots f_M\rangle, f_i = \begin{cases} 0, & \text{if unoccupied} \\ 1, & \text{if occupied} \end{cases} \\
 & \mathbf{H} = \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s + V_{nuc-nuc} \\
 & |HF\rangle = a_1^\dagger \dots a_m^\dagger |\Omega\rangle = \underbrace{|1 \dots 1\rangle}_{m} \underbrace{|0 \dots 0\rangle}_{M-m} \\
 & E^{HF} = \langle HF | \mathbf{H} | HF \rangle = \langle HF | \left[ \sum_{pq} h_{pq} a_p^\dagger a_q + \frac{1}{2} \sum_{pqrs} V_{pq,rs} a_p^\dagger a_q^\dagger a_r a_s \right] | HF \rangle + V_{nuc-nuc}
 \end{aligned}$$

Reinterpret the wave function as **creation** and **annihilation** operators to answer the question: "How many electrons in each orbitals?" instead of "Which electrons are in which orbital?" which is not so relevant since all electrons are the same. Besides, the first question is much simple since we know the answer thanks to the **Pauli exclusion principle**: at most 2 electrons on each orbital!

**Second Quantization** consists in replacing Hartree-Fock equation by an equivalent where the **creation/annihilation** of electron on each orbital is preferred to their very position.

By linearity of the wave function we have the expression of the wave function.

Where the **creation and annihilation** are naturally defined per orbitals with the following Pauli exclusion principle fulfilled by construction:

$$[a_p, a_q^\dagger]_+ = \delta_{pq}$$

The Slater determinant becomes an **occupancy Slater determinant** leaving in the **Fock space** of  $2^M$  dimensional space. In this space we denote the **vacuum state** by :  $|\Omega\rangle = |0 \dots 0\rangle$  where all orbitals are unoccupied. Then one

can prove that  $|f_1 \dots f_M\rangle = \prod_{p=1}^n (a_p^\dagger)^{f_p} |\Omega\rangle$  : all states can be built from the

vacuum one using the creation/annihilation operators

Using the **creation/annihilation** operators, the Hamiltonian is simplified and the **Hartree-Fock** wave function is expressed as a function of the vacuum state and the corresponding Hartree-Fock energy is deduced.

Quantum computing for Drug Discovery [30min]

Drug Discovery Pipeline

Where is Quantum Chemistry in the Drug Discovery Pipeline?

Quantum Chemistry [2h]

Quantum Chemistry : Overview

Schrödinger equation for multi-electron atoms

Schrödinger equation solutions for the Hydrogen atom

Approximations and Slater determinants

Schrödinger equation solutions for multi-electron atoms

Self-consistent field equations (Hartree-Fock)

Second Quantization

Hartree-Fock in Second Quantization

Bibliography

- [1] Sam McArdle, Suguru Endo, Alán Aspuru-Guzik, Simon C. Benjamin, and Xiao Yuan. Quantum computational chemistry. *Rev. Mod. Phys.*, 92:015003, Mar 2020.
- [2] Attila Szabo and Neil S. Ostlund. *Modern Quantum Chemistry: Introduction to Advanced Electronic Structure Theory*. Dover Publications, Inc., first edition, 1996.
- [3] Jack Simons. Why is quantum chemistry so complicated? *Journal of the American Chemical Society*, 145(8):4343–4354, 2023. PMID: 36787532.
- [4] T Helgaker, P Jørgensen, and J Olsen. *Molecular Electronic Structure Theory*. John Wiley & Sons, LTD, 2000.