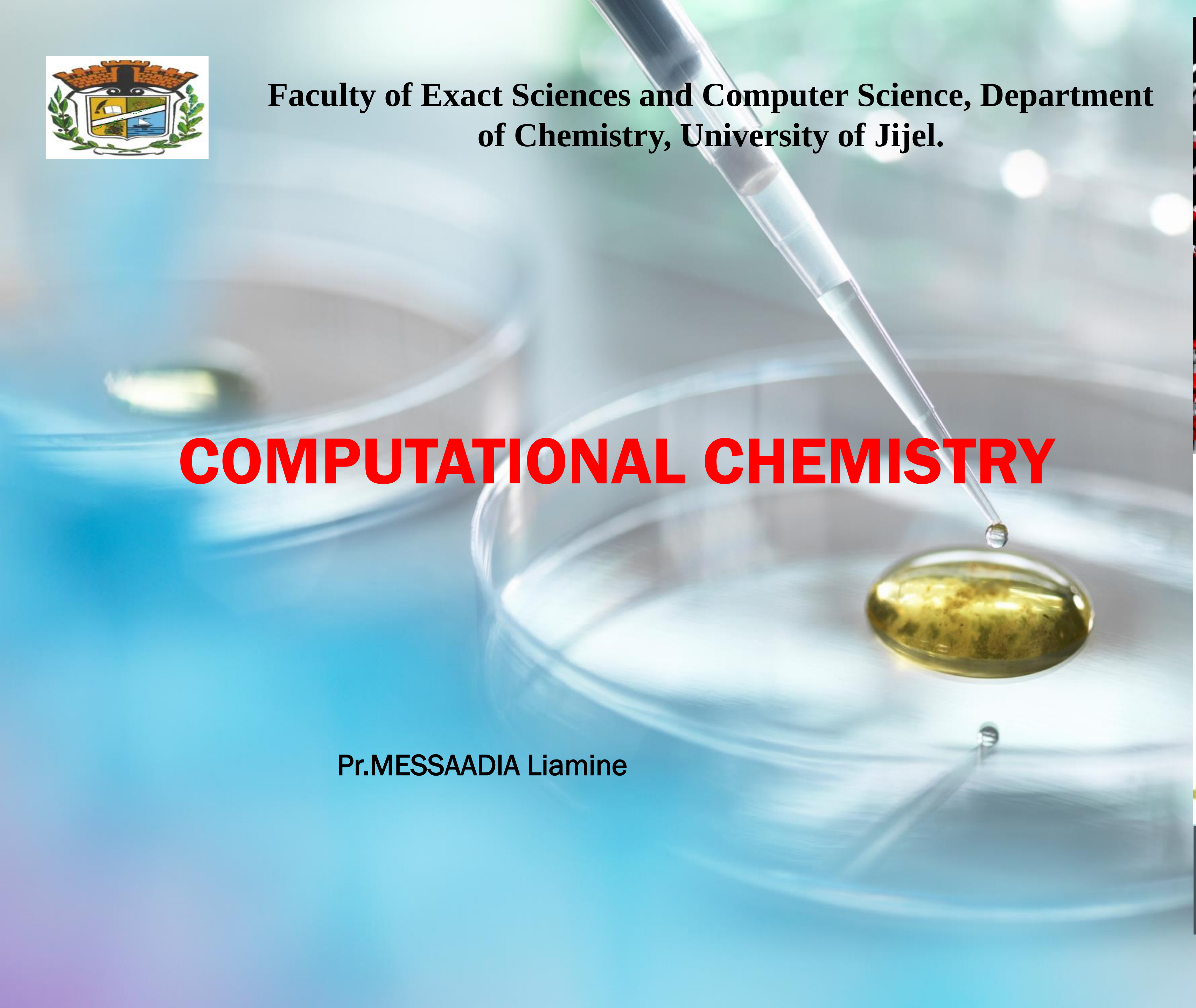
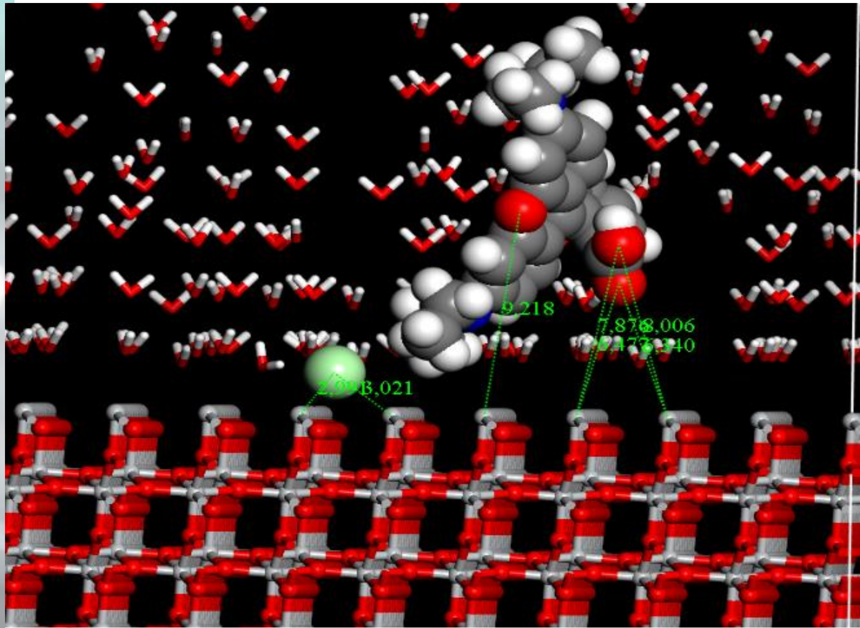
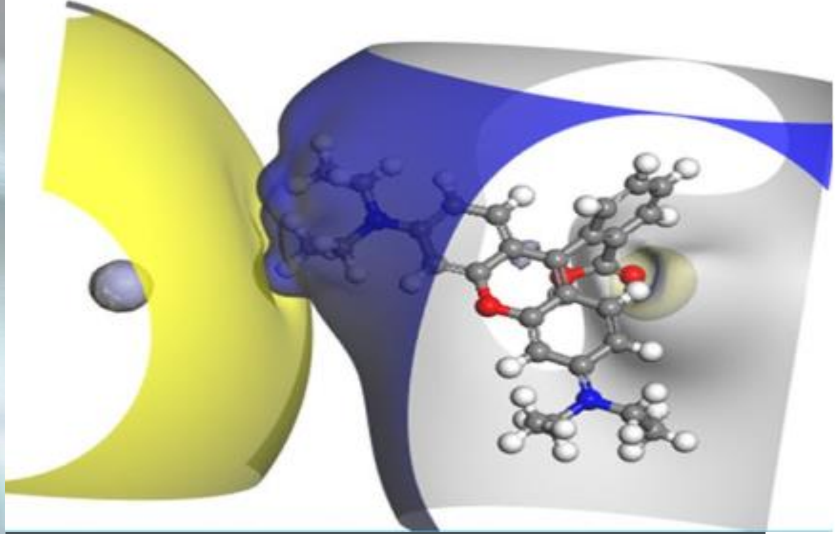


Faculty of Exact Sciences and Computer Science, Department of Chemistry, University of Jijel.

COMPUTATIONAL CHEMISTRY

Pr.MESSAADIA Liamine





Outline

- What does computational chemistry mean ?
- The main goal of computational chemistry
- What you can do with computational chemistry?
- The tools of computational chemistry.

What does computational chemistry mean ?

- Computational Chemistry is a branch of chemistry that uses computer simulation to *assist* in solving complex *chemical problems.*
- It exploits methods of theoretical chemistry, *incorporated into efficient* computer programs, to calculate the structures, the interactions, and the properties of molecules.

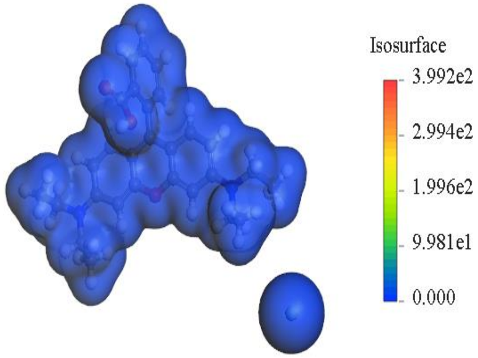
- Coupled-Cluster techniques for Computational Chemistry: is a program package for performing high-level quantum chemical calculations on atoms and molecules.

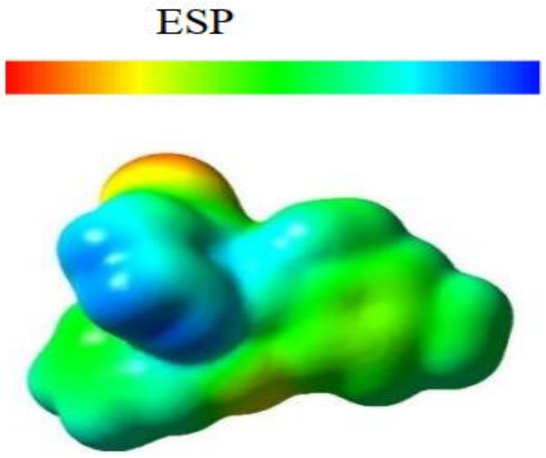
https://cfour.uni-mainz.de/cfour/index.php?n=Main.HomePage.

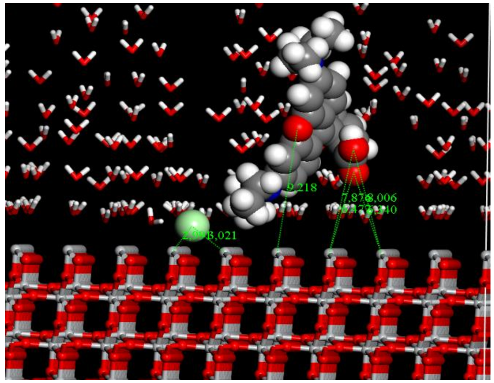
- Some Program Package of the quantum chemical : Gaussian, molpro, ADF and GAMESS…

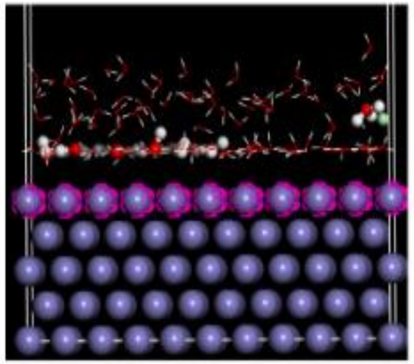
http://www3.uva.es/ccg/facilities.html

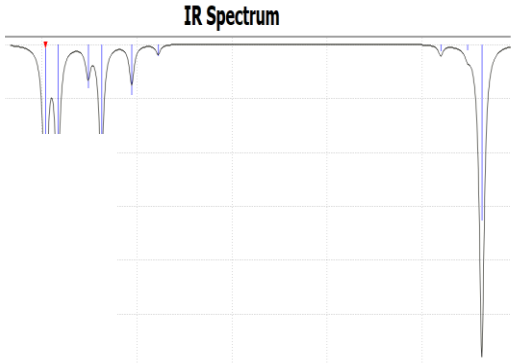
Some chemical problems

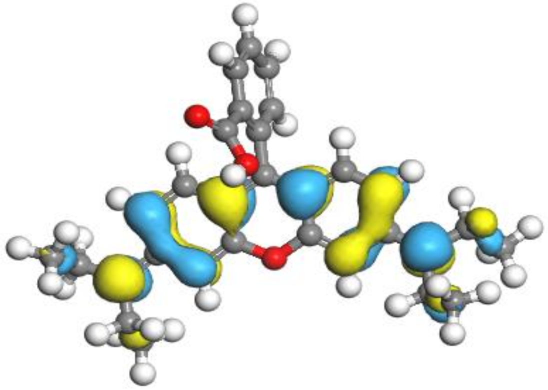




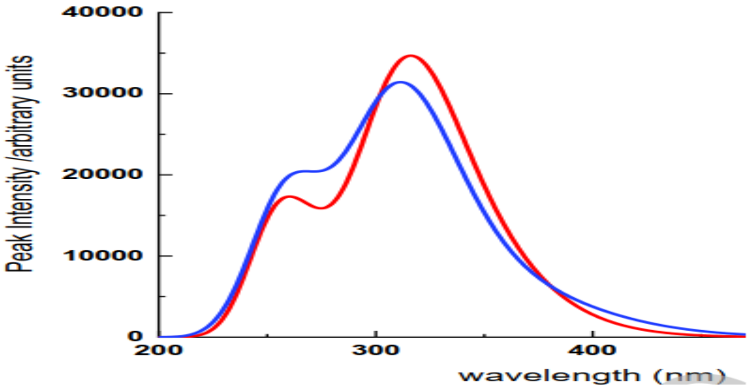


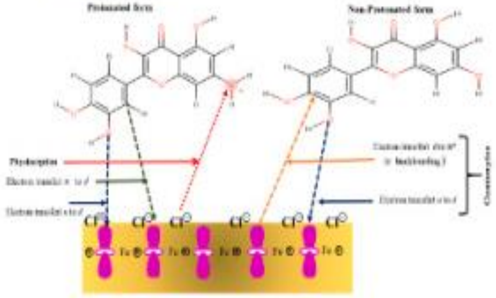






Fukui functions





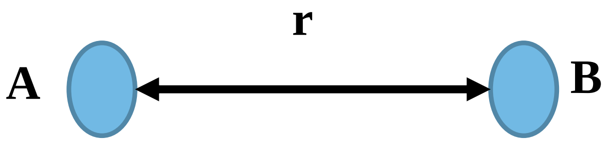
○ The main goal of computational chemistry

- The main goal of *computational chemistry* is to **solve chemical problems** by simulating chemical systems (**molecular**, **biological**, **materials**) in order to *provide reliable*, *accurate* and *comprehensive* information at an atomic level.

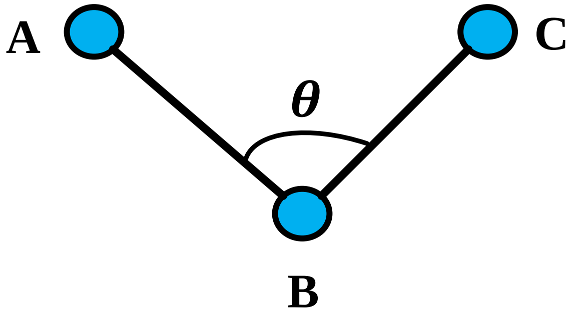
What you can do with computational chemistry?

❑ Questions commonly investigated computationally are:

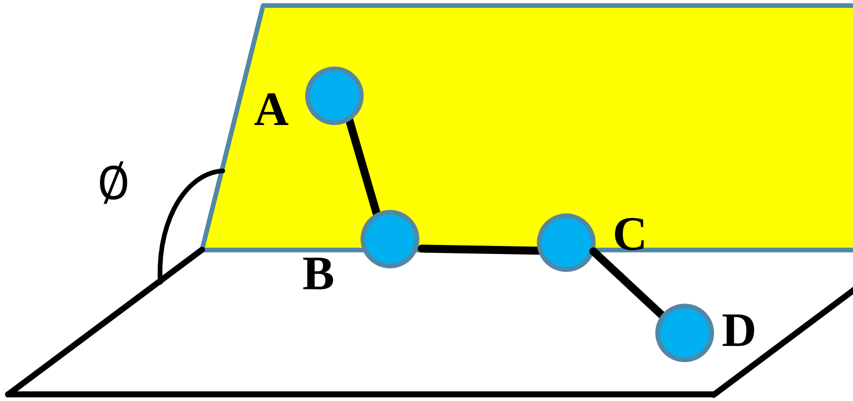
- ✓ **Computational chemistry**: (also called molecular modelling) is a set of techniques for investigating chemical problems on a computer.
- ✓ **Molecular geometry**: The ***shapes*** of molecules – bond ***lengths***, **angles**, and ***dihedrals*** (***torsion***).



bond lengths



bond *angle*



Dihedral **(*torsion*) angle**

Dihedrals: an angle formed by two plane faces.

- ✓ **Chemical reactivity:** For example, knowing where the electrons are concentrated (**nucleophilic sites**) and where they want to go (**electrophilic sites**) *enables* us to predict where various kinds of reagents will attack a molecule.
- ✓ **Energies of molecules and transition states:** This tells us which *isomer* is favoured, and (from transition state and reactant energies) how fast a reaction should go.
- ✓ **IR, UV, and NMR spectra**: These can be calculated.
- ✓ **The physical properties of substances:** These depend on the properties of individual molecules and on how the molecules interact in the *bulk* material.
- ✓ **The interaction of a substrate with an enzyme**: Seeing how a molecule fits into the active site of an enzyme is one approach to *designing* better *drugs*.

○ The tools of Computational chemistry

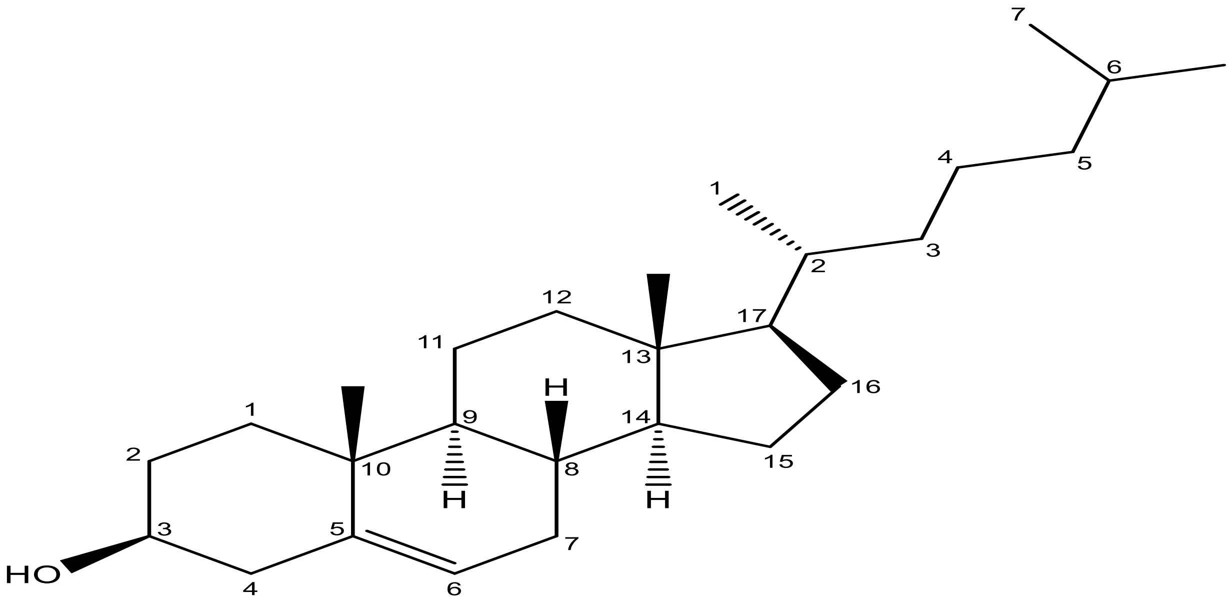
❖ The main tools available *belong* to five *broad* classes:

1. **Molecular mechanics (MM)**
2. **Ab initio calculations**
3. **Semiempirical (SE) calculations**
4. **Density functional theory (DFT) calculations**
5. **Molecular dynamics calculations (MD)**

1. Molecular mechanics (MM)

- ✓ **Molecular mechanics (MM):** is based on a model of a molecule as a *collection* of *balls* (atoms) *held* together by *springs* (bonds).
- ✓ If we know the normal **spring lengths** and the **angles** between them, and how much **energy** it takes to *stretch* and *bend* the springs, we can calculate the **energy of a given collection of balls** and springs, i.e. of a given **molecule**;
- ✓ Changing the geometry *until* the *lowest* energy is found enables us to do a **geometry optimization**, i.e. to calculate a geometry for the molecule.

Molecular mechanics is fast: a fairly large molecule like a steroid (e.g. **cholesterol**, C27H46O) can be optimized in seconds on a personal computer.



cholesterol

2. Ab initio calculations

- *Ab initio* is from the Latin: “From first principles” are based on the Schrödinger equation.
- This is a one of the fundamental equations of modern physics and describes, *among* other things, *how the electrons in a molecule behave.*
- The *ab initio* method solves the *Schrödinger equation* for a molecule and gives us the molecule’s energy and *wavefunction*.
- The wavefunction is a mathematical function that can be used to calculate the electron distribution.
- From the electron distribution we can tell things like how **polar** the molecule is, and which parts of it are likely to be attacked by **nucleophiles** or **electrophiles**.

- The Schrödinger equation cannot be solved exactly for any molecule with more thane one electron.
- Thus approximations are used.
- ab initio calculation is based only on basic physical theory (quantum mechanics) and is in this sense “from first principles”.
- ab initio calculations are **relatively slow**: the geometry and IR spectra (= the vibrational frequencies) of **propane** can be calculated at a reasonably **high level** in **minutes** on a personal computer, but a fairly **large molecule**, like a **steroid**, could take perhaps **weeks**.

3. Semiempirical (SE) calculations

- Semiempirical (SE) calculations are, like ab initio, based on the Schrödinger equation.
- However, more approximations are made in solving it, and the very complicated integrals that must be calculated in the ab initio method are **not actually evaluated** in SE calculations.
- The program **draws** on a kind of **library of integrals** that was compiled by finding the best fit of some calculated entity like **geometry or energy** (heat of formation) to the experimental values.
- This plugging of experimental values into a mathematical procedure to get the best calculated values is called **parameterization**.
- It is the **mixing** of **theory** and **experiment** that makes the method "**semiempirical**":

- it is based on the **Schrödinger equation**, but parameterized with experimental values (empirical means experimental)
- Semiempirical calculations are slower than MM but much faster than ab initio calculations.
- SE calculations take roughly 100 times as long as MM calculations, and ab initio calculations take roughly 100–1000 times as long as SE.

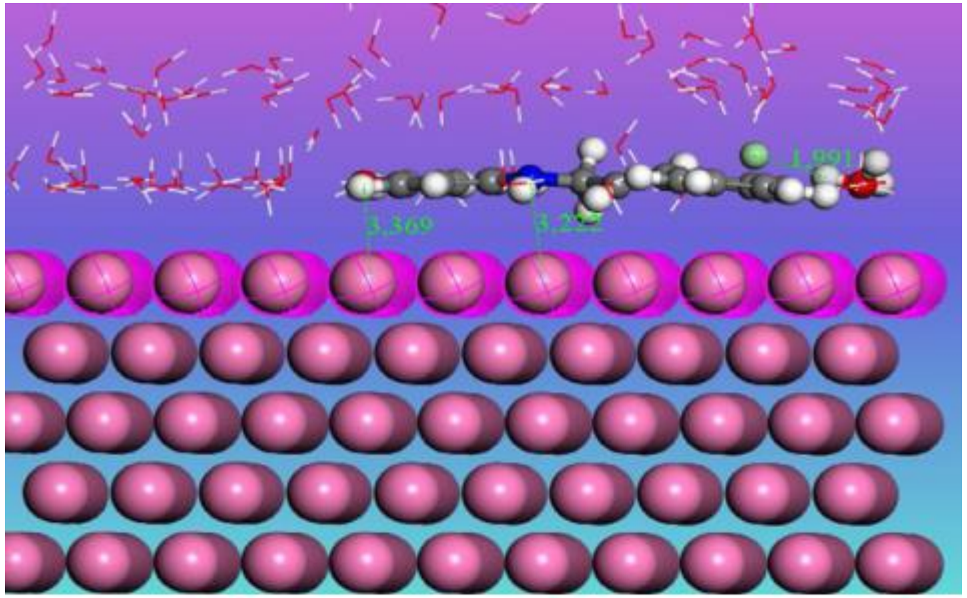
4. Density functional calculations

- **Density functional theory (DFT)** calculations are, like ***ab initio*** and **SE** calculations, based on **the Schrödinger equation**.
- However, **unlike** the other **two methods**, DFT does not calculate a **wavefunction**, but rather derives the electron distribution (electron *density* function) directly.
- A **functional** is a mathematical entity related to a **function**.
- Density functional calculations are usually **faster** than ***ab initio***, but **slower** than **SE**.
- DFT is relatively **new** (serious DFT computational chemistry goes back to the 1980’s, while computational chemistry with the *ab initio* and SE approaches was being done in the 1960’s).

4. Molecular dynamics calculations

- Molecular dynamics calculations apply the **laws** of **motion** to molecules.

✓ Thus one can simulate the **motion** of an **enzyme** as it changes **shape** on **binding** to a substrate, or the motion of a **swarm** of water molecules around a molecule of solute.



Boughoues, Y., Benamira, M., **Messaadia, L.**,**(2020).** https://doi.org/10.1016/j.colsurfa.2020.124610

Putting It All Together

- Very **large molecules** can be studied only with **MM**, because other methods (quantum mechanical methods, based on the Schrödinger equation: SE, ab initio and DFT) would **take too long**.
- Calculations on the structure of large molecules like **proteins** or **DNA** are done with MM (does not give information on **electron distribution**).
- The motions of these large **biomolecules** (protein, lipids, and nucleic acids **)** can be studied with molecular dynamics (MD).
- Key portions of a large molecule, like the **active site** of an **enzyme**, can be studied with **SE** or **even ab initio methods**.
- The energies of molecules can be calculated by **MM, SE, ab initio or DFT**.

- The **method chosen** depends very much on **the particular problem**.
- **Reactivity**, which depends largely on electron distribution, must usually be studied with a quantum-mechanical method (SE, ab initio or DFT).
- **Spectra** are most reliably calculated by ab initio methods, but useful results can be obtained with SE methods, and some MM programs will calculate fairly good IR spectra.
- Docking a molecule into the active site of an enzyme to see how it fits is an extremely important application of computational chemistry.
- This work is usually done with MM, because of the large molecules involved.
- Although selected portions of the biomolecules could be studied by one of the quantum mechanical methods.

- Computational chemistry is fairly **cheap**, it is **fast** compared to *experiment*, and it is **environmentally safe**.
- It does not replace **experiment**, which remains the **final arbiter** of truth about **Nature**.
- Furthermore, to make something – new drugs, new materials – one has to go into the lab.
- However, **computation** has become so **reliable** in some respects that, more and more, scientists in general are employing it before **embarking** on an experimental project.
- Computational chemistry is widely used in the pharmaceutical industry to explore the interactions of potential drugs with **biomolecules**, for example by **docking** a candidate drug into the active site of an enzyme.

Summary

- ✓ Computational chemistry *allows* one to calculate **molecular geometries**, **reactivities**, **spectra**, and other properties. em
- ✓ **Molecular mechanics** – based on a ball-and-springs model of molecules.
- ✓ Ab initio methods : based on approximate solutions of the Schrödinger equation without appeal to fitting to experiment.

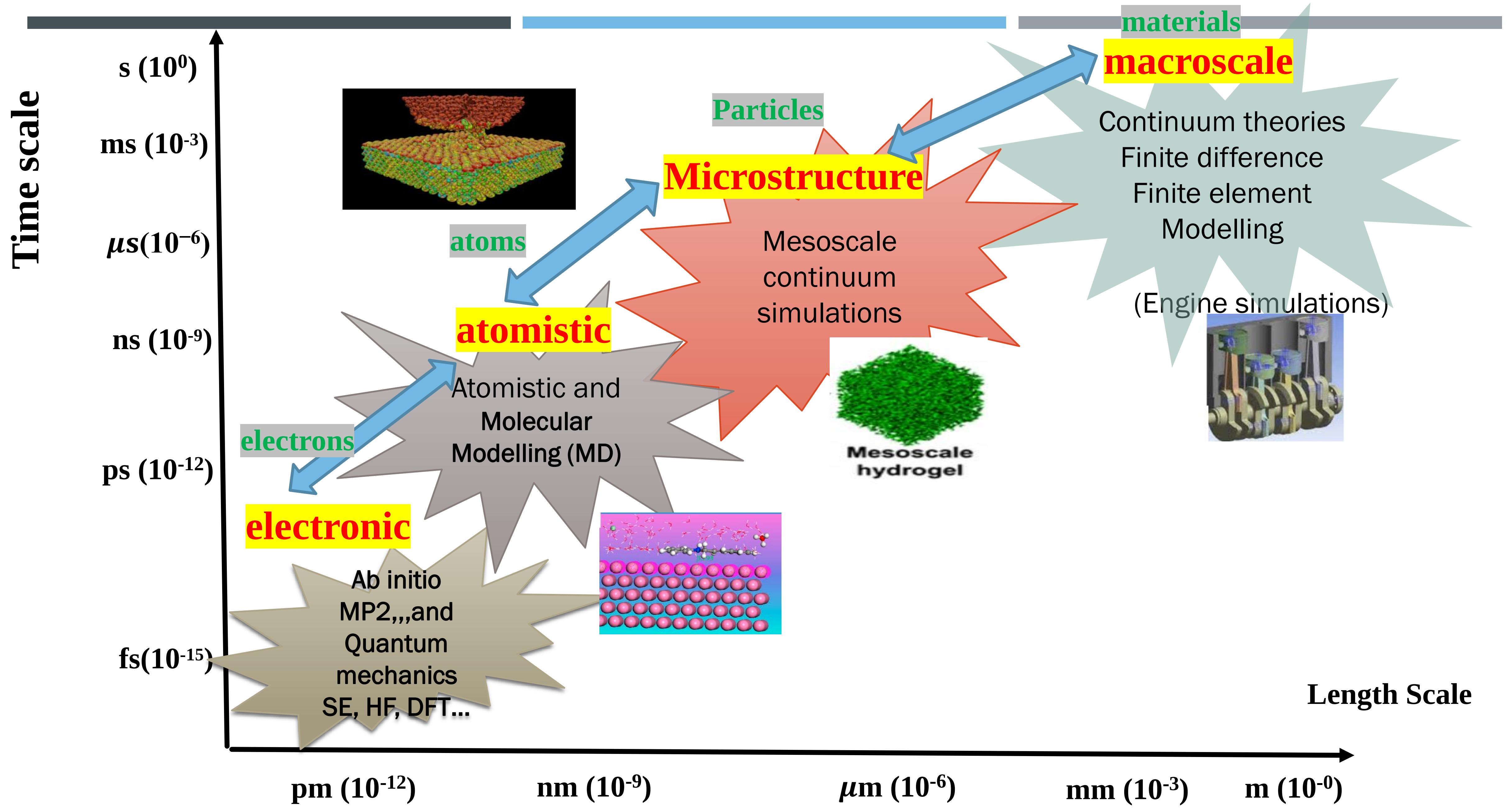
Semiempirical methods: based on approximate solutions of the Schrödinger equation with appeal to fitting to experiment (using parameterization). it is also used to investigate the properties of solids.

- ✓ **DFT methods** : based on approximate solutions of the Schrödinger equation, bypassing the wavefunction that is a central feature of ab initio and semiempirical methods.
- ✓ **Molecular dynamics** methods study molecules in motion.
- ✓ **Ab initio** and the faster DFT *enable* novel molecules of theoretical interest to be studied, provided they are not too big.
- ✓ **Semiempirical methods**, which are much **faster** than ab initio or even DFT, can be applied to fairly large molecules.
- ✓ **MM** will calculate geometries and energies of very large molecules such as proteins and nucleic acids.
- ✓ it is also used to investigate the properties of solids (e.g. plastics) in materials science.
- ✓ MM does not give information on electronic properties.

- ✓ **Computational chemistry** is widely used in the **pharmaceutical industry** to explore the interactions of potential **drugs** with **biomolecules**, for example by **docking** a candidate drug into the active site of an enzyme.
- ✓ It is also used to investigate the properties of solids (e.g. plastics) in materials science.

❑ QUESTIONS

1. What does the term computational chemistry mean?
2. What kinds of questions can computational chemistry answer?
3. Name the main tools available to the computational chemist. Outline (a few sentences for each) the characteristics of each.
4. Generally speaking, which is the fastest computational chemistry method (tool), and which is the slowest?
5. Why is computational chemistry useful in industry?
6. Basically, what does the Schrödinger equation describe, from the chemist's viewpoint ?
7. What is the limit to the kind of molecule for which we can get an exact solution to the Scherzinger equation?
8. What is parameterization ?



Time scale

s (10^0)

ms (10^{-3})

$\mu s(10^{-6})$

ns (10^{-9})

ps (10^{-12})

fs(10^{-15})

materials

macroscale

Continuum theories
Finite difference
Finite element
Modelling

(Engine simulations)

Particles

Microstructure

Mesoscale
continuum
simulations

Mesoscale
hydrogel

atoms

atomistic

Atomistic and
Molecular
Modelling (MD)

electrons

electronic

Ab initio
MP2,,,and
Quantum
mechanics
SE, HF, DFT…

Length Scale

pm (10^{-12})

nm (10^{-9})

μm (10^{-6})

mm (10^{-3})

m (10^{-0})

- A graph of the different modelling techniques developed in the computational modelling at different **scales.**

Electronic models (10^{-10}–10^{-9} m and 10^{-12} s)

- ✓ These models explicitly consider **nuclei** and **electrons**, and their quantum-mechanical state commands the interactions among atoms.
- ✓ Models and theories working at the **quantum scale** allow **information** about e.g., **electronic** band **structure** giving **conductive/dielectric** and **optical properties**, (magnetic) **anisotropy**, **diffusion coefficient**, **activation energies**, **thermodynamic stability** and **kinetic elementary processes** for atomic defects and dopants, and chemical reaction coefficients to be obtained.

2. Atomistic models (10^{-10}–10^{-7} m and 10^{-12}–10^{-6} s)

- ✓ At this scale, all atoms are explicitly represented or, in some cases, small groups of atoms are grouped in single sites referred to as pseudo or united atoms.
- ✓ The potential energy in the system is estimated using different classes of interactions (collectively known as force fields), typically consisting of:
- ✓ (i) bonded interactions, including bond-length (stretch) potentials, bond-angle (bend) potentials, torsion (twist) potentials and cross-terms, and
- ✓ (ii) non-bonded interactions, mostly comprising Coulomb interactions and dispersion forces. Examples of direct atomistic model results include, among others: molecular trajectories, packing, stiffness, surface and interface energies, constitutive equation parameters, mechanical properties, and heat and mass transfer data.

3. Mesoscopic models (10-9–10-1 m and 10-6–101 s)

- In these models, a molecule is represented either by a field description (field-based models) or by microscopic particles (particle-based models): in both cases, molecular details are amalgamated implicitly. Therefore, they are able to describe phenomena on length and time scales currently nonaccessible by classical atomistic approaches, such as system morphology, domain formation and growth kinetics, thermal stability, rheological and magnetic behaviour.

4. **Continuum models (10-3–101 m and 101–103 s)**

- ✓ Constitutive laws govern the behaviour of the physical system at these length/time levels, the material is assumed to be continuously distributed throughout its volume, and the models disregard atomic and molecular structures and their influence on the overall system behaviour. Prototypical properties predicted by this model category are macroscopic structural and mechanical data, heat and mass transport coefficients, and chemical reaction kinetics

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2. **F. Jensen, Introduction to Computational Chemistry, Wiley, Hoboken, NJ, (2007).**
3. **Fermeglia, M., Mio, A., Aulic, S., Marson, D., Laurini, E., & Pricl, S. (2020). Multiscale molecular modelling for the design of nanostructured polymer systems: industrial applications. Molecular Systems Design & Engineering, 5(9), 1447-1476**.

Chapter 2

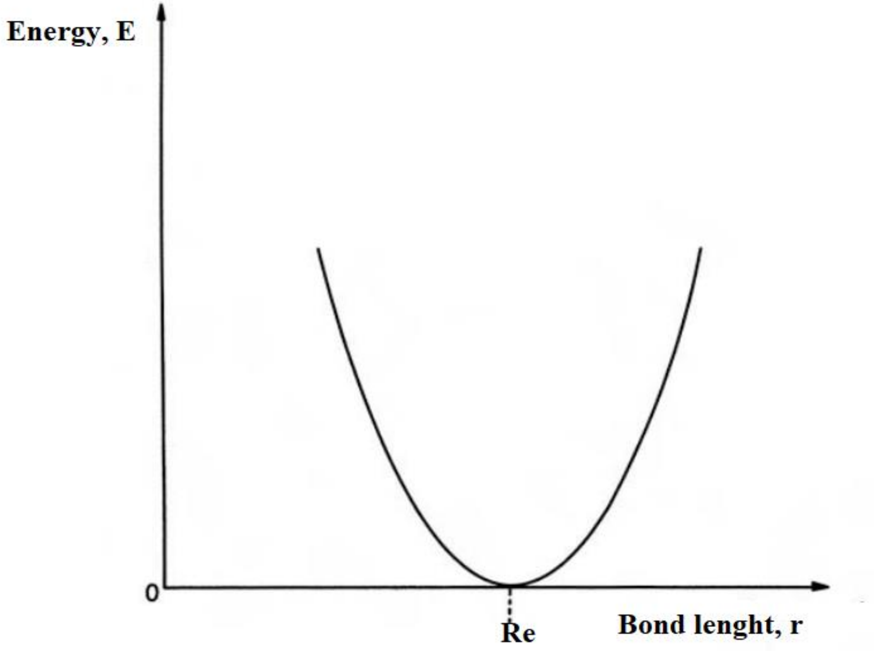
Everything should be made as simple as possible, but not simpler.
Albert Einstein

❑ The Concept of the Potential Energy Surface

- ✓ The potential energy surface (PES) is **central to computational** chemistry.
- ✓ Potential energy surfaces are **important** because they aid us in visualizing.
- ✓ understanding the **relationship** between potential energy and molecular geometry
- ✓ In understanding how computational chemistry programs locate and characterize structures of interest.
- ✓ The fact that a molecule is never actually stationary with zero kinetic energy (it always has zero-point energy (ZPE).

▪ Consider a diatomic molecule AB

- ✓ In some ways a molecule behaves like balls (atoms) held together by springs (chemical bonds), this simple picture is the basis of the important method molecular mechanics.
- ✓ The potential energy increases if the bond length $\boldsymbol{r}$ is stretched or compressed away from its equilibrium value $\boldsymbol{R_e}$.
- ✓ The potential energy at R_e (Zero distortion of bond length) has been chosen as the zero of energy.



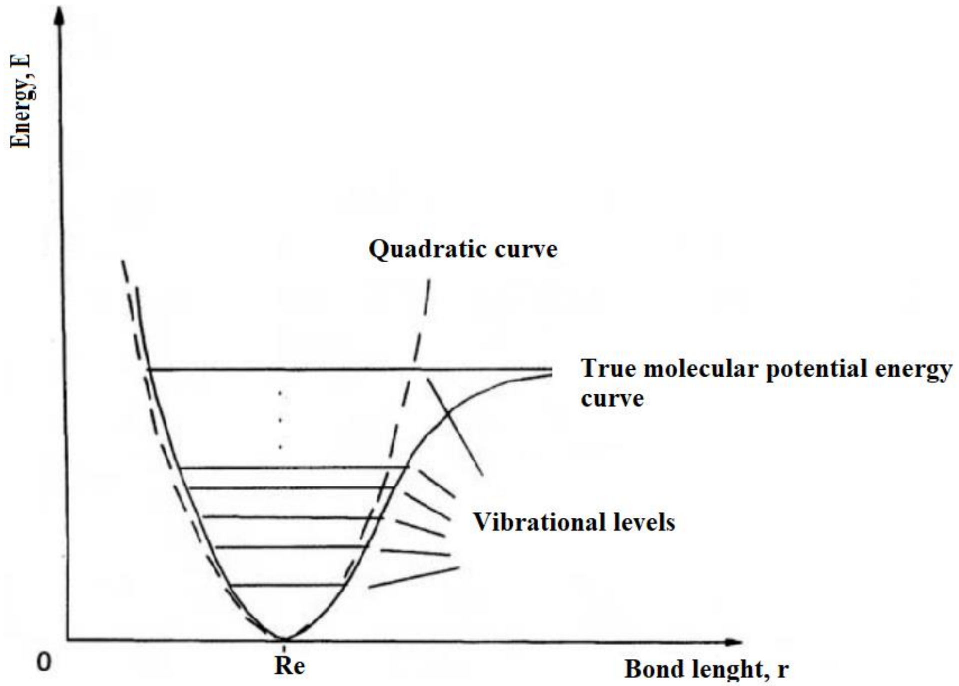
- The graph of potential energy against bond length is an example of a PES.

- The PES of diatomic molecule

- ✓ The curve to indicate the possible amounts of vibrational energy the molecule can have (the *vibrational levels* it can occupy).
- ✓ A molecule never sits at the bottom of the curve, but rather occupies one of the vibrational levels.
- ✓ A real molecule is described fairly well by a **quadratic equation**, that of the simple harmonic oscillator. E== $\frac{1}{2}\boldsymbol{K}(r-R_0)^2$,

  where **k** is the force constant of the spring.

- ✓ the minimum potential energy geometry is the point at which $\frac{dE}{dr}=0$.



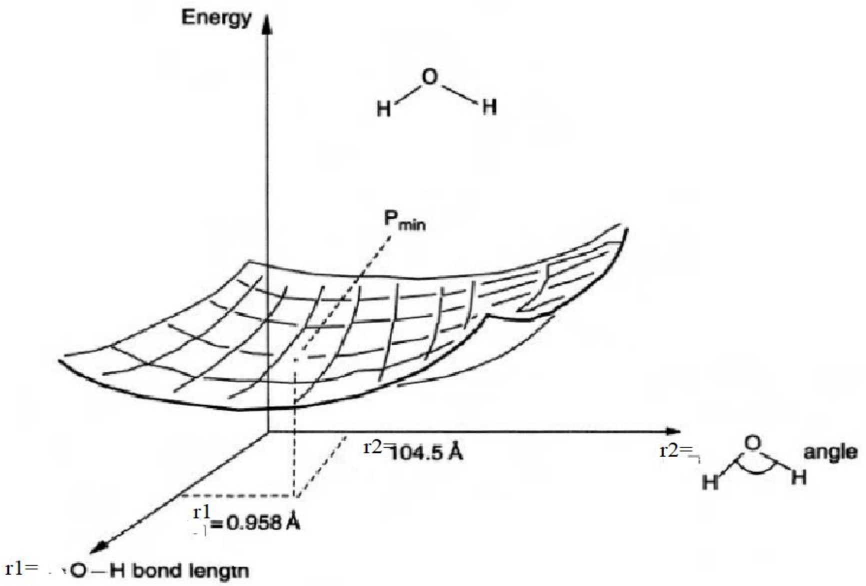
- ✓ the geometry is defined by two bond lengths and a bond angle.
- ✓ then the PES for this **triatomic molecule** is a graph of E vs. two **geometric parameters**,

$r_1 =$ the O-H, bond length, and $\qquad r_2 = \text{the H} - \text{O} - \text{H}$, bond angle

- ✓ The Pmin corresponds to the minimum energy geometry for 3 atoms.

- ✓ On the PES, the **minimum energy geometry** is defined by the point $\boldsymbol{P_m}$, corresponding to the equilibrium values of and at this point.

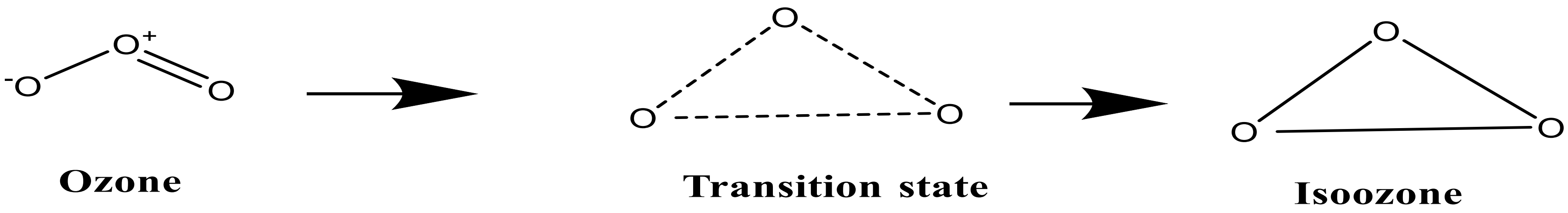
$$\frac{dE}{dr_1} = 0, \frac{dE}{dr_2} = 0$$



- **The water PES.**

❑ Stationary points

- ✓ **Potential energy surfaces** are important because they aid us in **visualizing** and **understanding** the relationship between **potential energy** and **molecular geometry**.
- ✓ Understanding how computational chemistry programs locate and characterize structures of interest.
- ✓ Among the main **tasks** of computational chemistry are to determine the structure and energy of molecules and of the **transition** states involved in chemical a priori.



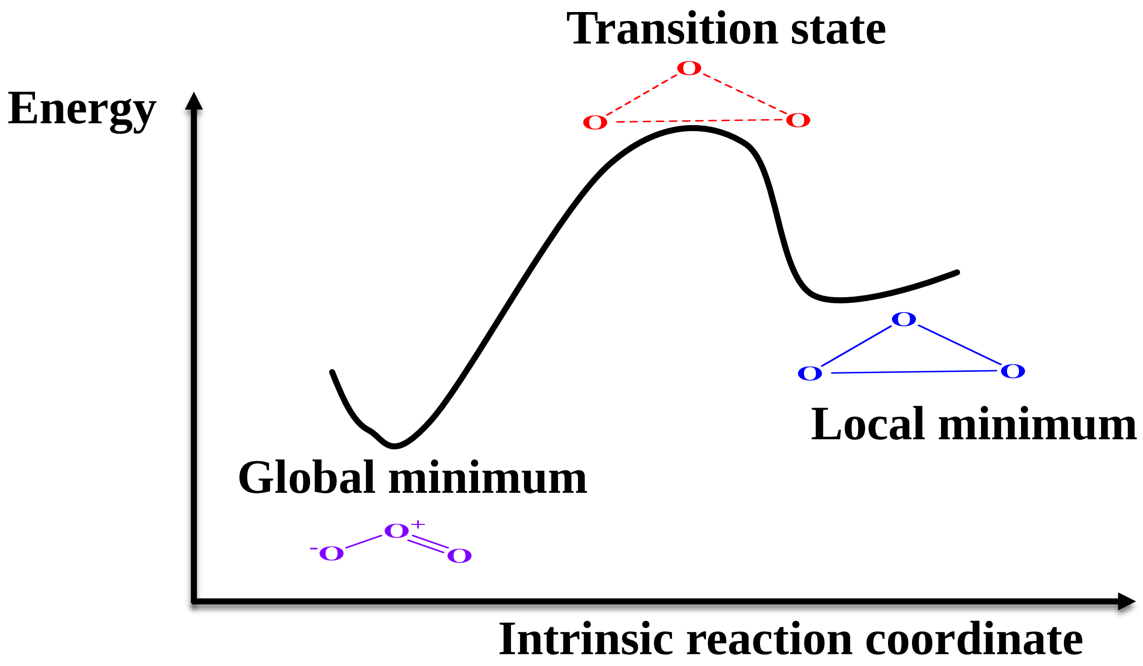
- The PES shown makes the point

✓ The potential energy E must be plotted against only two geometric parameters, the **bond length** (O–O) of ozone, and the O–O–O **bond angle**.

✓ The three species of interest, *ozone*, *isoozone*, and the *transition state* linking these two, are called **stationary points**.

✓ A **stationary point** on a PES is a point at which the **surface is flat**.

✓ For a transition state: $\frac{\partial^2 E}{\partial x^2} > 0$



- The ozone/isoozone PES (calculated by the AM1 method)

- ✓ Mathematically, a **stationary point** is one at which the first derivative of the potential energy with respect to each geometric parameter is zero:

$$\frac{\partial E}{\partial r_1} = \frac{\partial E}{\partial r_2} = \ldots = 0$$

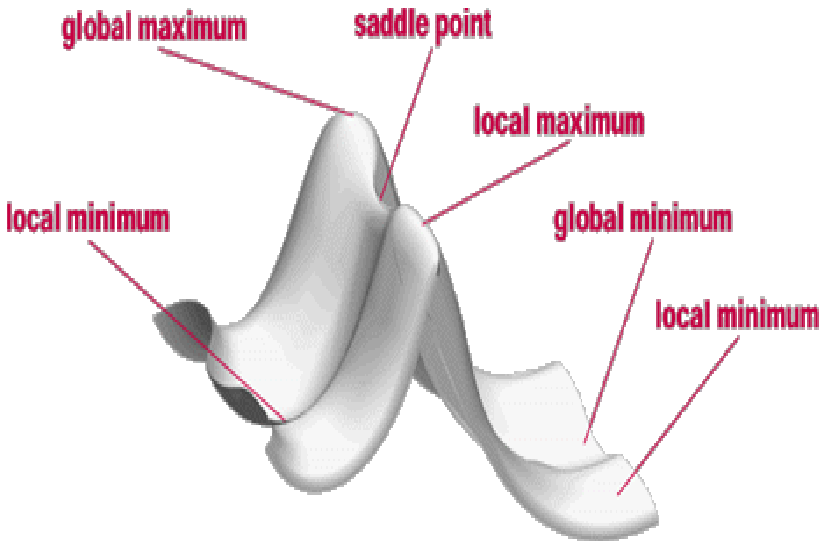
- ✓ *Ozone* is a **global minimum**, since it is the **lowest-energy minimum** on the whole PES, while *isoozone* is a **relative minimum,** a minimum compared only to nearby points on the surface.

- ✓ The lowest-energy pathway linking the two minima, the reaction coordinate or intrinsic reaction coordinate (**IRC**; dashed line).

- ✓ Is the **path** that would be followed by a molecule in going from one minimum to another should it acquire just **enough energy** to overcome the **activation barrier**, pass through the transition state, and reach the other minimum.

- ✓ A **saddle point**, the point on a PES where the **second derivative of energy** with respect to one and only geometric coordinate **is negative, corresponds to a transition state** $\frac{\partial^2 E}{\partial x^2} < 0$.

- ✓ Locating a **minimum** is often called an energy minimization or simply a minimization.
- ✓ locating a **transition** state is often referred to specifically as a transition state optimization.



https://studynights.blogspot.com/2015/03/geometry-optimization-potential-energy.html

❑ The born–oppenheimer approximation

✓ A **PES** is a plot of **the energy of a collection** of nuclei and electrons against the geometric coordinates of the nuclei.

✓ **Molecular geometry :** it may be regarded as the mathematical equation that gives the energy as a function of the nuclear coordinates.

➢ But if a molecule is a collection of nuclei and electrons

- why plot energy vs nuclear coordinates ?
- why not against electron coordinates ?
- why are nuclear coordinates the parameters that define molecular geometry ?

✓ The answer to this question lies in the **Born–Oppenheimer approximation**.

- ✓ **Born and Oppenheimer** showed in 1927 that to a very good approximation the **nuclei in a molecule** are **stationary** with respect to **the electrons**.
- ✓ Mathematically, the approximation states that the **Schrödinger equation** for a molecule may be separated into an electronic and a nuclear equation.
- ✓ calculate the **energy** of a molecule is to solve the **electronic Schrödinger** equation and then **add** the **electronic energy** to the internuclear repulsion to get the **total internal energy.**
- ✓ The **nuclei** see the **electrons** as a smeared-out cloud of **negative charge** which binds them in fixed relative positions.
- ✓ The mutual attraction between **electrons** and **nuclei** in the internuclear region and which defines the surface of the molecule.
- ✓ The nuclei are relatively stationary, since they are much more massive.

- ✓ Because of the rapid motion of the electrons compared to the nuclei.
- ✓ geometric parameters of the molecule are the nuclear coordinates.
- ✓ The **energy** (and the other properties) of a molecule is a function of the electron coordinates.

$$E = \boldsymbol{\psi}(\, x, y, z \ldots \text{of each electron}\,)$$

- ✓ Actually, the nuclei are not stationary, but execute **vibrations** of small amplitude about equilibrium positions.
- ✓ The **nuclei** are much more **sluggish** than the **electrons** because they are **much more massive** (a hydrogen **nucleus** is about 2000 times more massive than an **electron**).

Geometry optimization

- ✓ The characterization (the location) of a **stationary point** on a PES, i.e. demonstrating that the point in question exists and calculating its geometry and energy, is a ***geometry optimization***.
- ✓ The **stationary point** of interest might be a minimum, a transition state, or, occasionally, a higher-order saddle point.
- ✓ Locating a **minimum** is often called an energy minimization or simply a minimization.
- ✓ locating a **transition** state is often referred to specifically as a transition state optimization.

Self-consistent Field Molecular Orbital Theory