Ab initio molecular dynamics: ground and excited states

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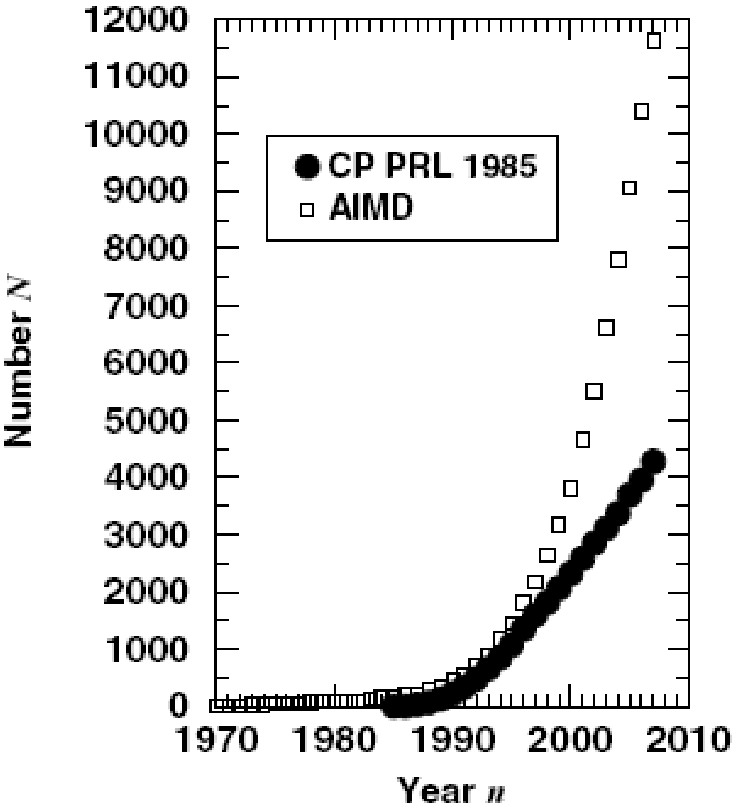
About 25 years ago…

Roberto Car and Michele Parrinello, *Phys. Rev. Lett.* **55**, 2471 (1985): Unified Approach for Molecular Dynamics and Density Functional Theory

References

- R. Car, M. Parrinello , *Unified Approach for Molecular Dynamics and Density Functional Theory*. Phys. Rev. Lett. **55** , 2471 (1985)
- G. Pastore, E. Smargiassi and F. Buda, *Theory of ab initio molecular dynamics calculations*. Phys. Rev. A **44** ,6334 (1991)
- Review paper: D. Marx and J. Hutter, *Ab initio molecular dynamics: Theory and Implementation.* NIC series, Volume 1 (2000). Available online at **http://www.fz-juelich.de/nic-series/Volume1**
- *Ab initio Molecular Dynamics: Basic Theory and Advanced Methods*, D. Marx and J. Hutter, Cambridge University Press, 2009
- CPMD code distributed at: www.cpmd.org

Publication and citation analysis up to the year 2007



Outline

- Introduction
- Molecular Dynamics
- Density Functional Theory
- Born-Oppenheimer MD
- Car-Parrinello MD: Extended Lagrangian approach
- Beyond microcanonic ensemble
- Beyond ground state

The Hamilton operator for a general system with n nuclei and N electrons

- The time-dependent Schrödinger equation is:

$$\hat{H}\Psi(r,R,t) = i\hbar\frac{\partial}{\partial t}\Psi(r,R,t)$$

with the Hamiltonian

nucleus-nucleus
interaction

$$\left[-\frac{\hbar^2}{2m_e}\sum_i \nabla^2_{r_i} - \frac{\hbar^2}{2M_I}\sum_I \nabla^2_{R_I} + \frac{1}{2}\sum_{i\neq j}\frac{e^2}{4\pi\varepsilon_0\left|r_i-r_j\right|} - \sum_{i,I}\frac{Z_I e^2}{4\pi\varepsilon_0\left|r_i-R_I\right|} + \frac{1}{2}\sum_{I\neq J}\frac{Z_I Z_J e^2}{4\pi\varepsilon_0\left|R_I-R_J\right|}\right]$$

Electron
kinetic energy

Nuclear
kinetic energy

electron-electron interaction

electron-nucleus interaction

I,J label atoms with positions R_I, R_J

i,j label electrons with positions r_i, r_j

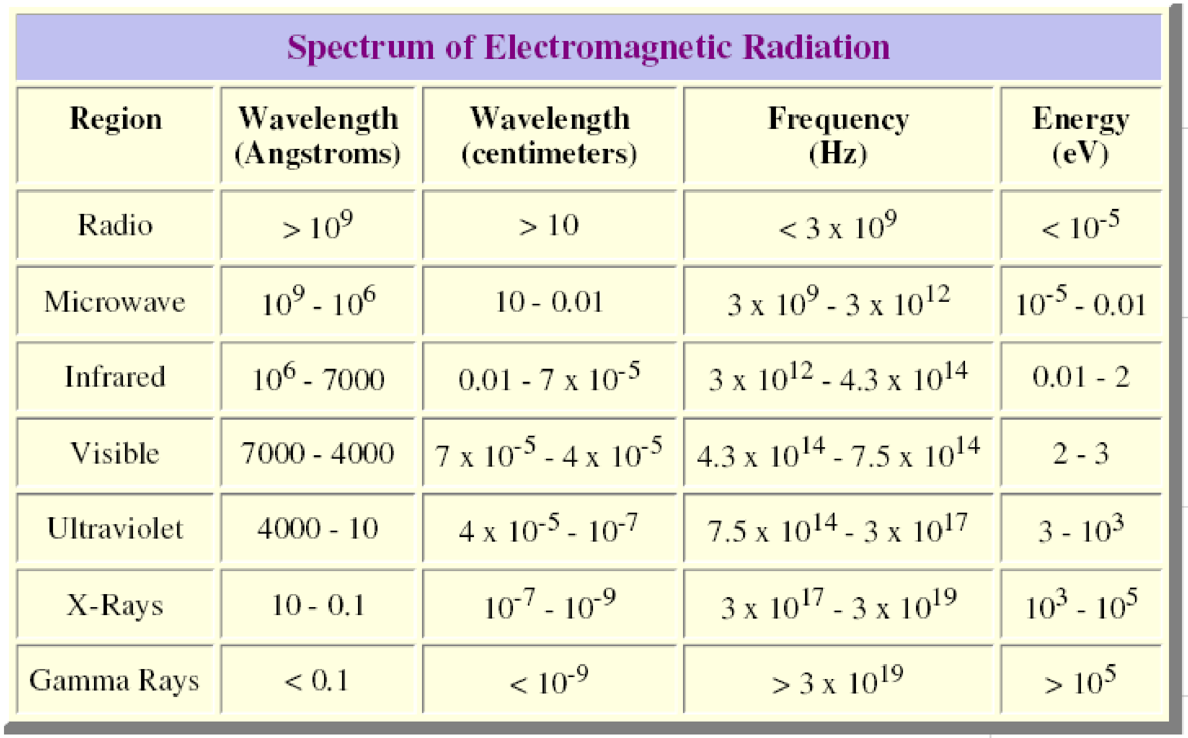
The Born-Oppenheimer approximation

Large difference between electronic and nuclear mass allows to separate the electronic from the nuclear motion:

$$m_e << m_I$$

=> different time scales

=> different energy scales



Spectrum of Electromagnetic Radiation

Region	Wavelength (Angstroms)	Wavelength (centimeters)	Frequency (Hz)	Energy (eV)
Radio	$> 10^9$	> 10	$< 3 \times 10^9$	$< 10^{-5}$
Microwave	$10^9 - 10^6$	$10 - 0.01$	$3 \times 10^9 - 3 \times 10^{12}$	$10^{-5} - 0.01$
Infrared	$10^6 - 7000$	$0.01 - 7 \times 10^{-5}$	$3 \times 10^{12} - 4.3 \times 10^{14}$	$0.01 - 2$
Visible	$7000 - 4000$	$7 \times 10^{-5} - 4 \times 10^{-5}$	$4.3 \times 10^{14} - 7.5 \times 10^{14}$	$2 - 3$
Ultraviolet	$4000 - 10$	$4 \times 10^{-5} - 10^{-7}$	$7.5 \times 10^{14} - 3 \times 10^{17}$	$3 - 10^3$
X-Rays	$10 - 0.1$	$10^{-7} - 10^{-9}$	$3 \times 10^{17} - 3 \times 10^{19}$	$10^3 - 10^5$
Gamma Rays	< 0.1	$< 10^{-9}$	$> 3 \times 10^{19}$	$> 10^5$

The Born-Oppenheimer approximation

Ansatz for the total wave function:

Electron wavefunction for given nuclear positions *R*

Nuclear wavefunction

$$\Psi(\mathbf{R},\mathbf{r},t)=\sum_i \psi_i(\mathbf{r};\mathbf{R})\chi_i(\mathbf{R},t)$$

Where the ψ_i are a complete set of electronic eigenfunctions:

$$\left(\hat{T}_{el}+\hat{V}_{nuc,nuc}+\hat{V}_{el,el}+\hat{V}_{nuc,el}\right)\psi_i(\mathbf{r};\mathbf{R})=\boxed{E_i(\mathbf{R})}\psi_i(\mathbf{r};\mathbf{R})$$

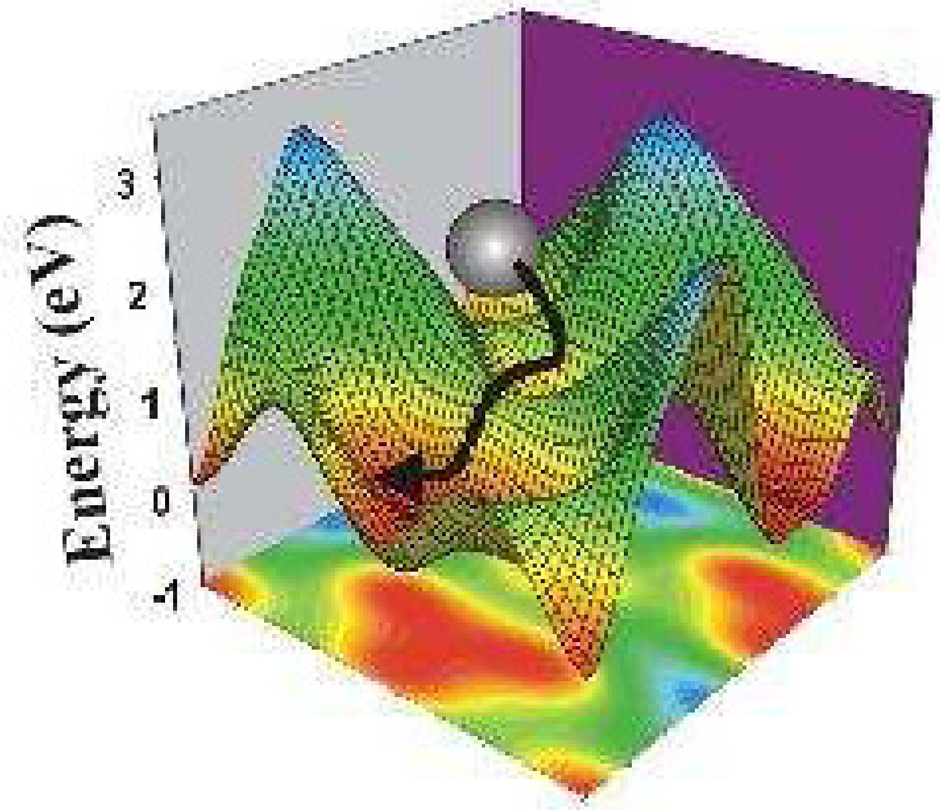
Then the nuclei are described by:

Potential energy surface (PES)

$$i\hbar\frac{\partial\chi_i(\mathbf{R},t)}{\partial t}=\left[\hat{T}_{nuc}+\boxed{E_i(\mathbf{R})}\right]\chi_i(\mathbf{R},t)$$

Or in the classical limit by:

$$m_I\frac{d^2\mathbf{R}_I(t)}{dt^2}=-\nabla_I E_i(\mathbf{R})$$



A cartoon of a potential energy surface (PES).
The sphere represent the position of the system (in the 2-dim. coordinate space). The arrow shows the path followed during the dynamics.

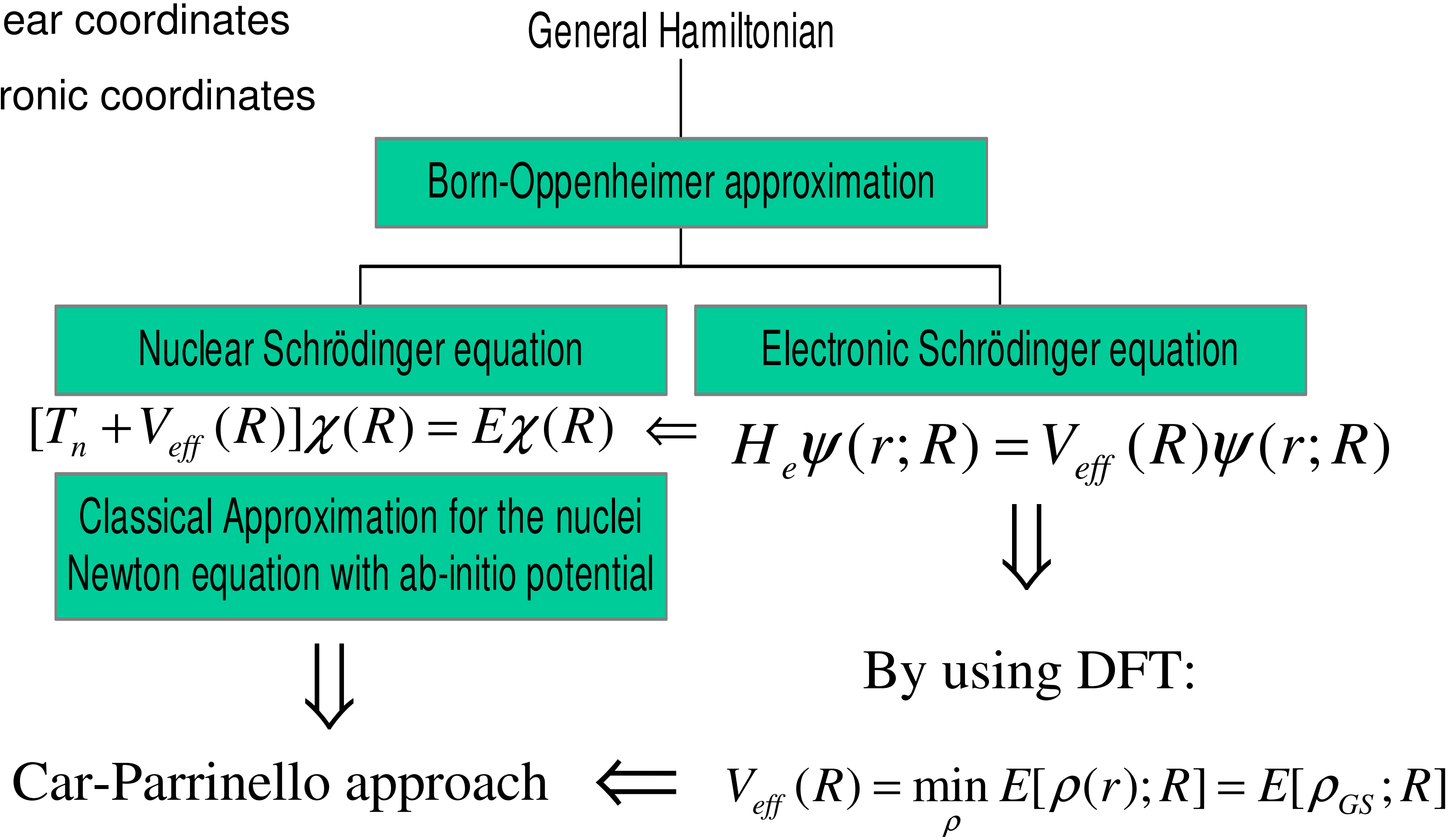
The Born-Oppenheimer Approximation

- The large difference between the electronic mass and the nuclear mass allows one to separate the electronic and the nuclear problem
- The interatomic forces and potential energy are determined by the behaviour of the bonding electrons, which itself depends parametrically on the atomic structure
- In the B-O approximation we neglect coupling terms involving different electronic eigenfunctions. This implies that the motion of the nuclei proceeds without changing the electronic state during time evolution.

$$\hat{H}\Psi(r,R) = E\Psi(r,R)$$

R: nuclear coordinates

r: electronic coordinates



General Hamiltonian

Born-Oppenheimer approximation

Nuclear Schrödinger equation

Electronic Schrödinger equation

$$[T_n + V_{eff}(R)]\chi(R) = E\chi(R) \Leftarrow H_e\psi(r;R) = V_{eff}(R)\psi(r;R)$$

Classical Approximation for the nuclei
Newton equation with ab-initio potential

$$\Downarrow$$

By using DFT:

$$\text{Car-Parrinello approach} \Leftarrow V_{eff}(R) = \min_{\rho} E[\rho(r);R] = E[\rho_{GS};R]$$

Why *ab initio* Molecular Dynamics ?

Molecular Dynamics:

Classical approximation for the nuclear motion

- Assume the nuclei are heavy enough to be described with classical mechanics
  - ➔ The quantum aspects of the nuclear motion, such as tunneling and zero-point motion, are neglected.
- Instead of solving the Schrödinger equation for the nuclei we solve the Newton equation for N particles moving on the *Potential Energy Surface* (PES) $V_{eff}(R)$

$$M_I \frac{d^2 R_I}{dt^2} = -\nabla_I V_{eff}(\{R\})$$

Force Field Methods: empirical potentials

- Capture very simple interactions between atoms
- Predefined functional form for the interatomic potential
- Contain many parameters to be fixed according to experimental data or theoretical calculations
- Usually work in situations where it is easy to identify individual `atomic' charge distributions, and these do not vary strongly as the atoms move around
- Some popular Force Fields for treating (bio)-molecules:
  - AMBER
  - CHARMM
  - GROMOS
  - SYBYL

Force Field Energy

The force field energy (PES) is written as a sum of terms describing bonded and non-bonded interatomic interactions

$$V = E_{bonded} + E_{non-bonded}$$

- bonded terms

$$E_{bonded} = E_{stretch} + E_{bend} + E_{torsion}$$

- non-bonded terms (van der Waals and electrostatic)

$$E_{non-bonded} = E_{vdw} + E_{electrostatic}$$

Each term contains a number of empirical fitting parameters

The Stretching Energy

- The energy function for stretching a bond between two atoms A and B can be written as a Taylor expansion around the equilibrium bond length

$$E_{stretch} = E_0 + \left.\frac{dE}{dR}\right|_{R_0} (R^{AB} - R_0^{AB}) + \frac{1}{2}\left.\frac{d^2E}{dR^2}\right|_{R_0} (R^{AB} - R_0^{AB})^2 + \ldots$$

- In the harmonic approximation

$$E_{stretch}(R^{AB}) = \tfrac{1}{2} k^{AB} (R^{AB} - R_0^{AB})^2$$

- Fitting parameters:

$$k^{AB}, R_0^{AB}$$

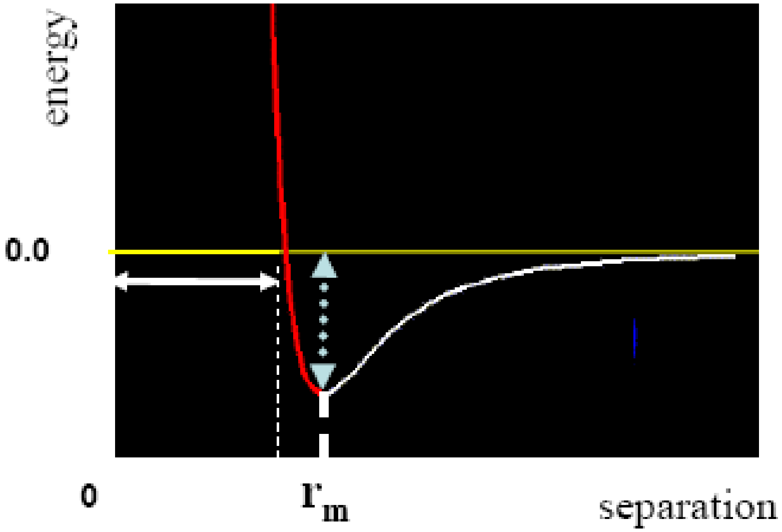
Non-bonded energy terms

Van der Waals term: often modeled as a Lennard-Jones potential
- attractive term due to instantaneous dipoles
- repulsive term due to electron cloud overlap (Pauli repulsion)

$$E_{vdw} = 4\varepsilon_{AB}\left[\left(\frac{\sigma_{AB}}{R_{AB}}\right)^{12} - \left(\frac{\sigma_{AB}}{R_{AB}}\right)^{6}\right]$$

σ: distance for which E=0

ε: well depth



Non-bonded energy terms

Electrostatic energy: Coulomb potential

$$E_{electrostatic} = \frac{q^A q^B}{4\pi\varepsilon_0 R_{AB}}$$

where q^A and q^B are centered on the nuclei A and B, respectively, and are called partial atomic charges.

The electrostatic interactions are effective also at long range since they decay as R^{-1}

Molecular Dynamics

- Basic idea: simply follow the dynamical evolution according to Newton’s equations of motion for the atoms
- Break time into discrete `steps’ Δt, compute forces on atoms from their positions at each timestep
- Evolve positions by, for example, Verlet algorithm (1967):

$$R(t+\Delta t) = R(t) + [R(t) - R(t-\Delta t)] + \frac{(\Delta t)^2}{M} F(t)$$

- or the equivalent `velocity Verlet’ scheme

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

$$R(t+\Delta t) = R(t) + v(t)\Delta t + \frac{\Delta t^2}{2M} F(t)$$

Molecular Dynamics

- Follow the `trajectory’ and use it to sample the states of the system: The system samples the ‘microcanonical’ (constant-energy) thermodynamic ensemble, provided that the trajectory eventually passes through all states with a given energy (ergodicity)

Ensemble Averages and Time Averages (ergodic hypothesis)

Ensemble average of a property *A* at equilibrium

$$\langle A \rangle = \int A(q,p)P(q,p)\,dq\,dp$$

where the probability *P(q,p)* in the canonical ensemble [T,V,N] is given by

$$P(q,p) = \frac{e^{-E(q,p)/k_B T}}{\int e^{-E(q,p)/k_B T}\,dq\,dp}$$

The time average, defined as

$$\langle A \rangle = \lim_{t\to\infty} \frac{1}{t} \int_{t_0}^{t_0+t} A(\tau)\,d\tau$$

is equivalent to the ensemble average in the ergodic hypothesis

Time-correlation functions and transport coefficient

- They give a clear picture of the dynamics in a fluid
- Their time integral may be related directly to macroscopic transport coefficients (e.g. the diffusion coefficient)
- Their Fourier transform may be related to experimental spectra (e.g., vibrational DOS, infrared spectra)

Molecular Dynamics

- Assuming forces are conservative, the total energy will be conserved with time (to order $(\Delta t)^2$ in the case of Verlet)

$$E = K + V = \sum_I \frac{1}{2} M_I \dot{R}_I(t)^2 + V(\{R(t)\}) = \text{constant}$$

- Note: the energy conservation along the dynamics is also a test on the accuracy and stability of the numerical integration

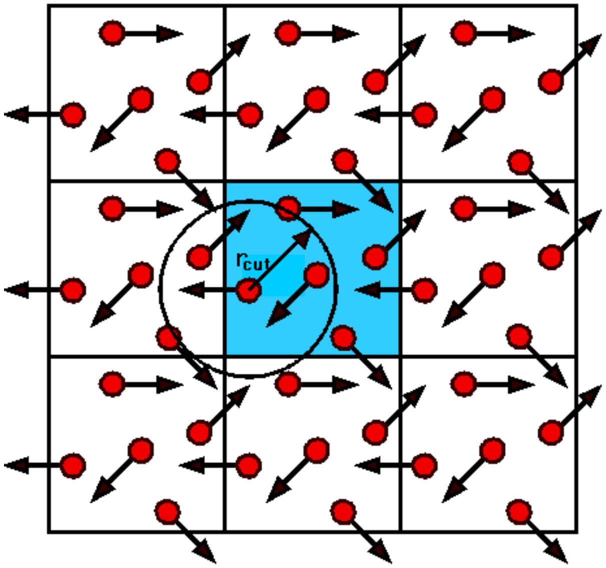
Technical details

Choice of time step:

- The time step Δt must be ~one order of magnitude smaller than the shortest oscillation period of the normal modes of the system

Periodic boundary conditions (to overcome surface effects):

- The box is replicated throughout space to form an infinite lattice
- Forces are computed according to the 'minimum image convention'



How to simulate ‘rare events’?

- Low probability regions of the PES will not be visited during the ‘short’ time scale of a typical MD simulation (particularly critical for chemical reactions)
- Different schemes are being developed to overcome this problem:
  - Biasing potential added to the PES (umbrella sampling) [Torrie, Vallieau 1974]
  - Constrained Molecular Dynamics [Sprik, Ciccotti 1998]
  - Metadynamics approach (dynamically adjustable biasing potential) [Laio, Parrinello 2002]

Molecular Dynamics: beyond microcanonics

- Refinements exist to allow simulations with
  - Constant temperature (an additional variable is connected to the system which acts as a ‘heat bath’)
  - Constant pressure (the volume of the system is allowed to fluctuate)
  - Constant stress (the shape, as well as the volume, of the system is allowed to fluctuate)
  - Geometrical constraints

Advantages and Limitations of Force Field Methods

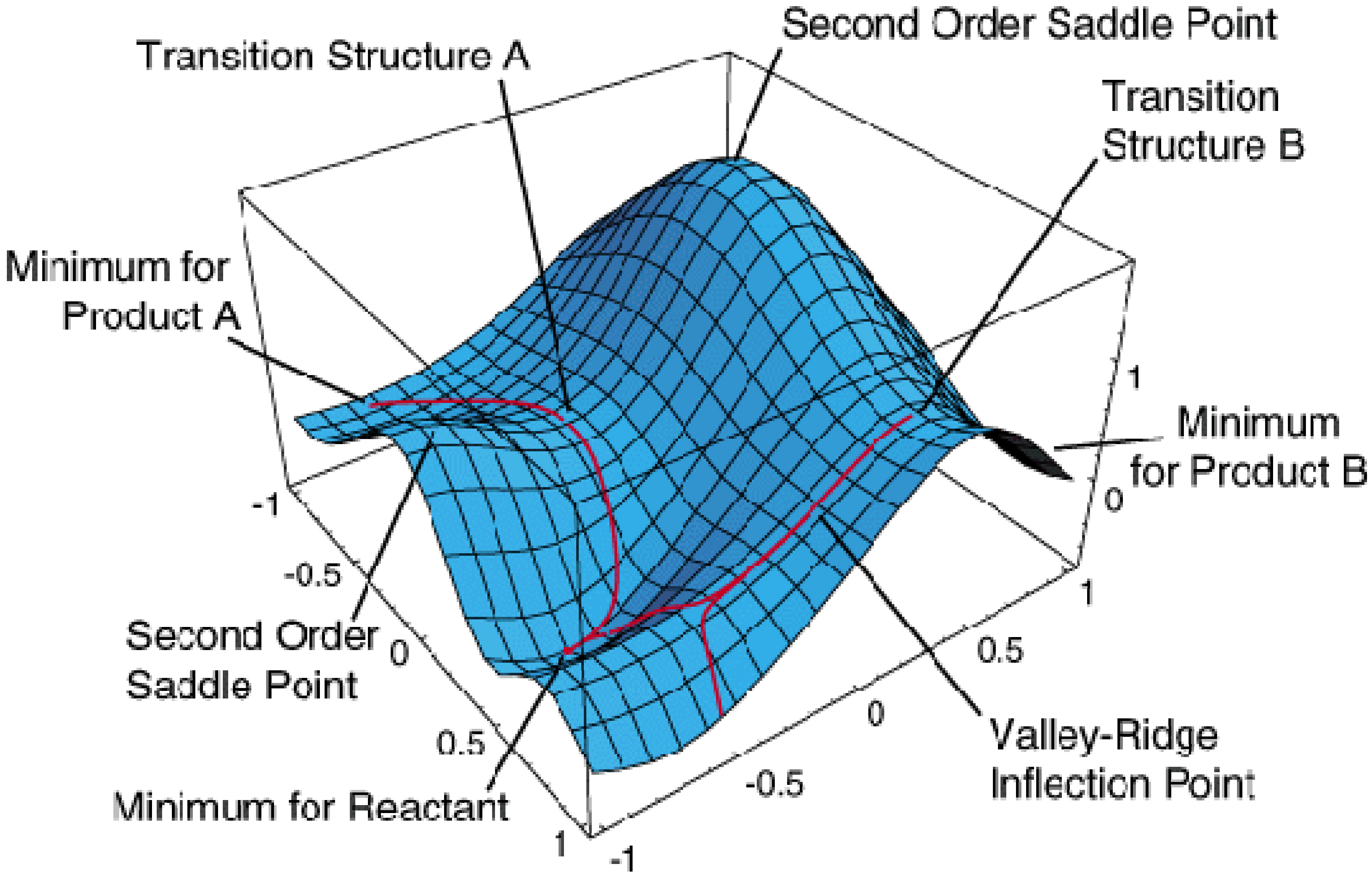
- Advantages
  - speed of calculations
  - large systems can be treated (several thousands atoms with a PC)
  - easy to include solvent effects and crystal packing
- Limitations
  - Lack of good parameters (for molecules which are out of the ordinary)
  - The predicting power is very limited
  - Transferability limited
  - Cannot simulate bond breaking and forming

References on classical MD

- Allen MP and Tildesley DJ (1987) Computer Simulation of Liquids, Clarendon Press, Oxford
- Frenkel D and Smit B (1996) Understanding Molecular Simulation – From Algorithms to Applications, Academic Press, San Diego

Ab initio Molecular Dynamics

- Use a Potential Energy Surface obtained by solving the electronic structure.
- Why AIMD ? Overcome limitations of (force-field) MD, specifically in simulating bond breaking and forming.
- How can we obtain the *Potential Energy Surface* (V_{eff}) ?
  - By fitting *ab initio* results to a suitable functional form. This is very demanding and can be done only for extremely small systems; furthermore it is difficult to design a well-behaved fitting function
  - The fitting step can be bypassed and the dynamics performed directly by calculating the interatomic forces (obtained from the electronic structure calculated *on-the-fly*) at each time-step of an MD simulation


Second Order Saddle Point
Transition Structure A
Transition Structure B
Minimum for Product A
Minimum for Product B
Second Order Saddle Point
Minimum for Reactant
Valley-Ridge Inflection Point
-1
-0.5
0
0.5
1
-1
-0.5
0
0.5
1
0
1

Born-Oppenheimer Molecular Dynamics

- Calculate interatomic forces in Molecular Dynamics by solving the electronic structure problem for each nuclear configuration in the MD trajectory:

$$M_I \frac{d^2 R_I}{dt^2} = -\nabla_I \min_{\Psi_0} \{ \langle \Psi_0 | H_e | \Psi_0 \rangle \}$$

$$H_e \Psi_0 = E_0(R) \Psi_0$$

- Density Functional Theory is mostly used to solve the electronic structure (self-consistent solution of the Kohn-Sham equations). However, in principle other methods can be used (HF, MCSCF, …)
- the direct BO-MD involves a SCF calculation of the wave functions at each time step ➔computationally very demanding

Density Functional Theory
(Hohenberg and Kohn, 1964)

- The ground-state electronic energy (E) of a N-electron system can be uniquely determined by the electron charge density $\rho(r)$

$$E = E\left[\rho(r)\right]$$

- Given an external potential (due to the nuclei) there is only one ground state wavefunction and thus only one ground state charge density
- A variational principle holds for the energy functional:

$$E\left[\rho\right] \geq E_{GS} \quad \text{for any electron density} \quad \rho \neq \rho_{GS}$$

$$E\left[\rho_{GS}\right] = E_{GS}$$

Walter Kohn: Nobel Prize in Chemistry, 1998

Density Functional Theory

(Kohn and Sham, 1965)

$$E[\rho;R] = T_{\text{single-particle}}[\rho] + E_{\text{ext}}[\rho;R] + E_{\text{Hartree}}[\rho] + E_{\text{Exchange-correlation}}[\rho]$$

$$T = \sum_i f_i \int dr \phi_i^* \left(-\frac{\nabla^2}{2} \right) \phi_i$$

K.E. of noninteracting particles at this density

$$E_{ext} = \sum_I \int dr \frac{\rho(r) Z_I}{|r - R_I|}$$

Interaction with external potential: nuclei-electrons term

$$E_H[\rho] = \frac{1}{2} \iint dr_1 dr_2 \frac{\rho(r_1)\rho(r_2)}{|r_1 - r_2|}$$

Interaction with Hartree potential (Coulomb energy)

E_{xc} contains the exchange energy, the correlation energy and the kinetic terms not included in T

Usually also the nuclear-nuclear term $U\{R_I\}$ is added in the total energy functional

Electron density written in terms of a set of auxiliary one-electron functions:

$$\rho(r) = \sum_{i=1}^{N} |\varphi_i(r)|^2$$

Density Functional Theory

(Kohn and Sham, 1965)

- By applying the variational principle for the functional with the constraint on the total number of electrons we obtain a set of *self-consistent* single-particle (Kohn-Sham) equations

$$\left(-\frac{1}{2}\nabla^2 + V^{KS}(r)\right)\varphi_i(r) = \varepsilon_i \varphi_i(r)$$

- where the effective ***local*** potential is given by

$$V^{KS}(r) = V_{ext}(r) + \int \frac{\rho(r')}{|r-r'|}dr' + V_{xc}(r)$$

- with the exchange-correlation potential defined as

$$V_{xc}(r) \equiv \frac{\partial E_{xc}[\rho(r)]}{\partial \rho(r)}$$

Basis Set approximation

- All calculations use a basis set expansion to express the unknown Kohn-Sham (Molecular) Orbitals
- Mostly used basis set are atom-centered functions that resemble atomic orbitals (Linear Combination of Atomic Orbitals)
- basis set used in practical calculations are
  - STO (exponential: Slater-type orbitals)
  - GTO (Gaussian-type orbitals)
  - Plane waves

Local Density Approximation (LDA)

- The Kohn-Sham approach enables one to derive an *exact* set of one-electron equations
- Problem: all the nasty bits (including exchange) are now included into the unknown exchange-correlation energy
- A simple approximation, the *Local Density Approximation*, is surprisingly good: approximate exchange-correlation energy per electron at each point by its value for a homogeneous electron gas of the same density (known from QMC results)

$$E_{XC}^{LDA} = \int \rho(r)\varepsilon_{\mathrm{XC,\ homogeneous}}(\rho(r))dr$$

- Can be generalized to include spin polarization (LSDA)

Generalized Gradient Approximation (GGA)

- Though Local Density Approximation works quite well in many cases (metals and semiconductors), in general underestimates the exchange energy and gives poor results for molecules.
- To improve over the LSDA, the exchange-correlation energy should depend not only on the density, but also on derivatives of the density (gradient corrections) :

$$E_{xc}^{GGA} = \int \rho(r) f(\rho(r), \nabla \rho(r)) dr$$

- GGA, as e.g. the BP (Becke-Perdew) or the BLYP (Becke-Lee-Yang-Parr) functional, can give accuracy of the same or better quality than MP2.
- Hybrid functionals (such as B3LYP), which include part of the exact HF exchange, are also broadly used.
- The search for increasingly accurate functionals is a current hot topic in the field:
  - Meta-GGA have been also recently developed

$$E_{xc}^{meta-GGA} = \int f(\rho(r), \nabla\rho(r), \nabla^2\rho(r))dr$$

Why DFT is the preferred choice for *ab initio* MD?

- Advantages
  - General accuracy for geometries and vibrational frequencies similar or better than MP2
  - Computational cost scales at most as N^3 (N = number of basis functions)
- Limitations
  - Weak interactions (vdW) are poorly described
  - Lack of a systematic improvability

Born-Oppenheimer Molecular Dynamics

- Molecular Dynamics with interatomic forces obtained using DFT for each nuclear configuration in the MD trajectory:

$$M_I \frac{d^2 R_I}{dt^2} = -\nabla_I V_{eff}(R)$$

$$V_{eff}(R) \equiv E^{KS}[\rho;\{R\}]$$

$$\frac{\partial E^{KS}}{\partial \rho} = 0 \Rightarrow \left(-\frac{1}{2}\nabla^2 + V^{KS}(r) \right)\varphi_i(r) = \varepsilon_i \varphi_i(r)$$

- the direct BO-MD involves a SCF solution of the Khon-Sham equations at each step ➔computationally very demanding

Car-Parrinello Molecular Dynamics

- Car and Parrinello (1985) proposed an approach in which the electronic self-consistent problem has to be solved only for the initial nuclear configuration in the MD
- CPMD evolves in time the nuclear positions and the electronic degrees of freedom using an extended Lagrangian:

$$L_{eI} = K_e + K_I - E^{KS}\left[\{\phi_i\},\{R_I\}\right] + \sum_{i,j} \lambda_{ij}\left(\langle \phi_i \mid \phi_j \rangle - \delta_{ij}\right)$$

Orthogonalization constraint

$$K_e = \mu \sum_i \int dr \mid \dot{\phi}_i \mid^2$$

Fictitious Elec. Kinetic energy

- This dynamics generates *at the same time* the nuclear trajectory and the corresponding electronic ground state.

Car-Parrinello Molecular Dynamics

- The corresponding Newtonian equations of motion are obtained from the associated Euler-Lagrange equations:

$$M_I \frac{d^2 R_I}{dt^2} = -\nabla_{R_I} E^{KS}[R,\phi]$$

$$\mu \frac{d^2 \phi_i}{dt^2} = -\frac{\delta E^{KS}}{\delta \phi_i^*} + \sum_j \lambda_{ij} \phi_j$$

- which can be solved numerically using, for example, the Verlet algorithm

Initial conditions

- The electrons must be in the ground state corresponding to the initial nuclear configuration
- Electron velocities and accelerations are set to zero
- The equations of motion for the electrons are equivalent to the Kohn-Sham equations after a unitary transformation
- The nuclei can have also zero velocities or a distribution of velocities consistent with the required temperature

Why does the Car-Parrinello method work ?

- CPMD exploits a classical adiabatic energy scale separation between the nuclear and electronic degrees of freedom: By choosing the parameter $\mu << M$ the evolution of the ϕ_i can be decoupled from that of R_I

$$\omega_e >> \omega_I$$

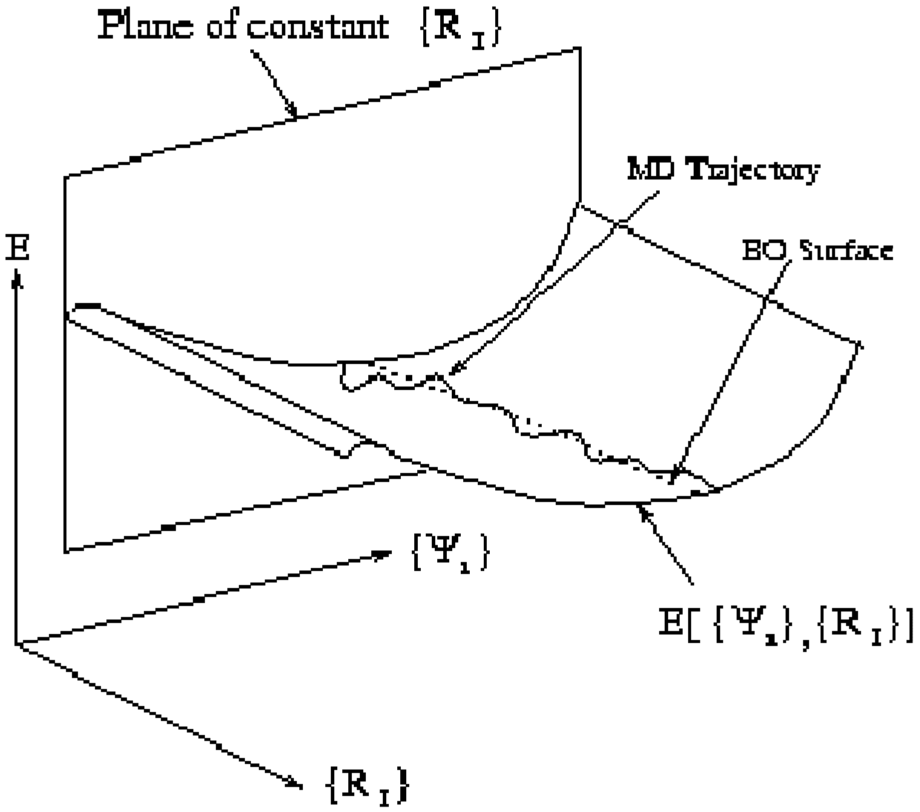
- The electrons oscillate around the instantaneous ground-state BO surface with very low kinetic energy

$$K_e << K_I$$

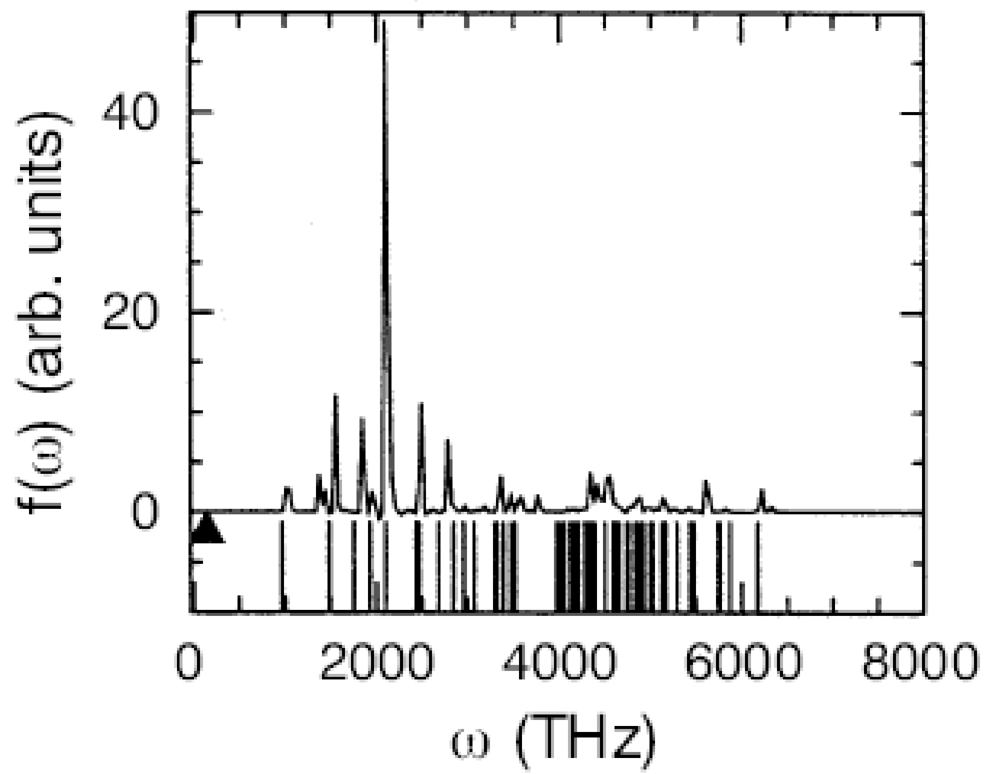
$$U_I' = K_I + E^{KS} \cong const$$

- The physical total energy U_I' behaves approximately like the strictly conserved total energy in classical MD

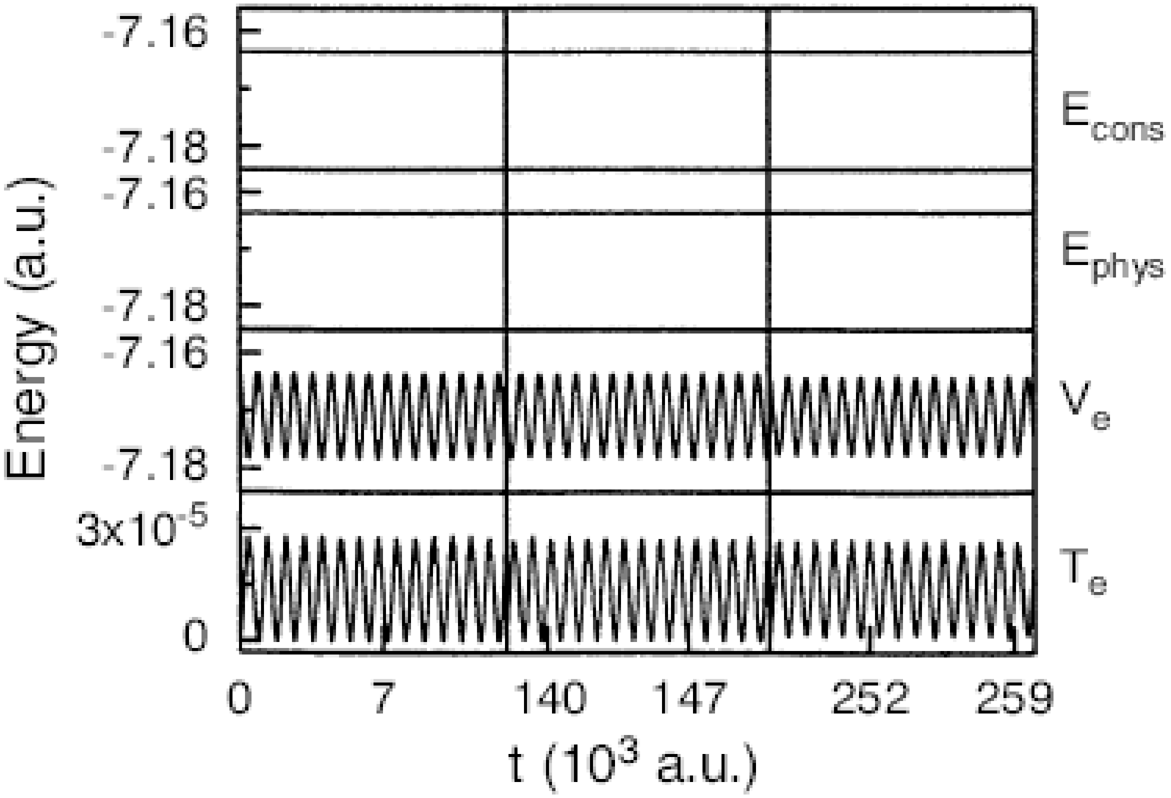
- Under these conditions the CPMD trajectories derived from the extended Lagrangian
  - reproduce very closely the *true* (Born-Oppenheimer) nuclear trajectories
  - approximates very closely the microcanonical dynamics


Plane of constant $\{R_I\}$
MD Trajectory
BO Surface
E
$\{\Psi_i\}$
$E[\{\Psi_i\},\{R_I\}]$
$\{R_I\}$

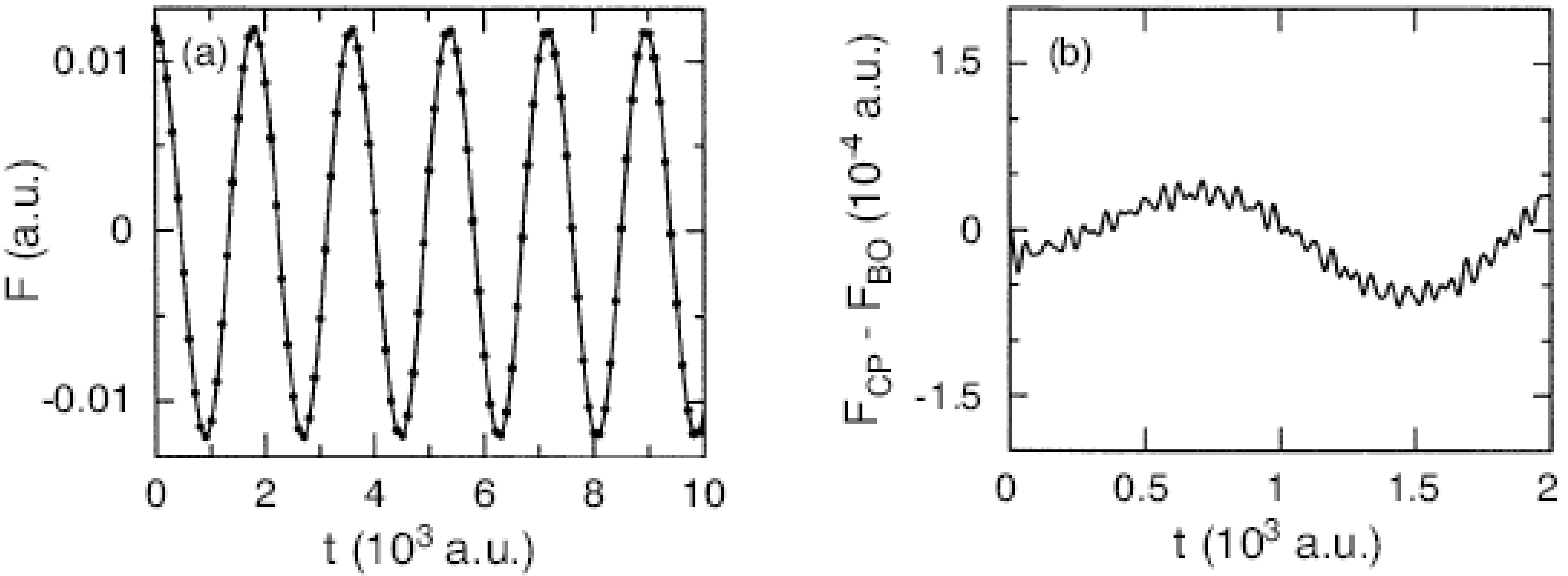
Vibrational density of states



Various energy terms for a model system



Comparison between Born-Oppenheimer and Car-Parrinello forces



How to control adiabaticity ?

- The electronic frequencies depend also on the electronic structure:

$$\omega_{ij}^{e} = \sqrt{\frac{2\left(\varepsilon_i - \varepsilon_j\right)}{\mu}}$$

$$\omega_{\min}^{e} \propto \sqrt{\frac{E_{HOMO-LUMO}}{\mu}}$$

- warning: adiabaticity is broken when the gap between occupied and virtual orbitals is too small (problems with metals)

Practical solution to broken adiabaticity

- Couple the electronic subsystem with a thermostat keeping the electron at low temperature
- Couple the nuclear subsystem with a thermostat at the desired physical temperature of the system

Technical details

- Time step Δt
  - Limited by the fast electronic motion
  - Typical value $\Delta t \approx 0.1$ fsec
- Electronic mass μ:
  - Adiabatic evolution if $\mu/M << 1$
  - Typical value $\mu/M = 1/100$

Technical details

- Supercell geometry
  - Periodic boundary conditions
- Plane wave expansion of electronic states

$$\phi_i(r) = \sum_G c_G^i \exp(iG \cdot r)$$

  - more suitable for extended systems: solids, liquids
  - Only one parameter controls the accuracy

$$\frac{1}{2}\left|k+G\right|^2 \leq E_{cut}$$

  - Fast Fourier transform (FFT) can be used
  - Evaluation of nuclear forces easy (no Pulay forces)

The Hellman-Feynman theorem

- For a general electron state ψ the electronic energy depends on the state, as well as explicitly on the atomic positions
- In order to find the force on any particular atom, we would therefore have use the chain rule to write

$$\frac{dE_{\mathrm{el}}(R)}{dR_I} = \langle\psi|\frac{\partial \hat{H}_{\mathrm{el}}(R)}{\partial R_I}|\psi\rangle + \frac{\delta\langle\psi|\hat{H}_{\mathrm{el}}|\psi\rangle}{\delta\langle\psi|}\frac{\partial\langle\psi|}{\partial R_I}$$

Explicit dependence of *H* on *R*

Implicit dependence of *E* on *R* via the change in wavefunction as atoms move

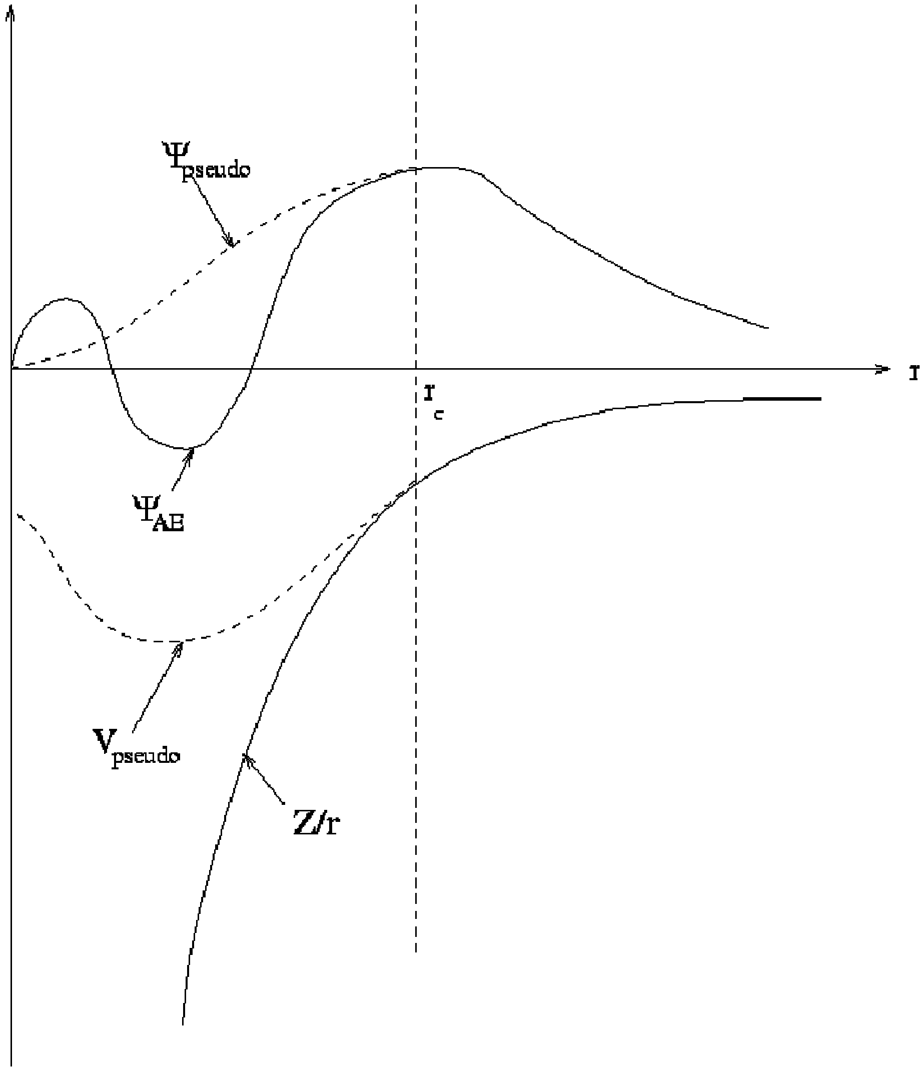
- For the ground state (or indeed any electronic eigenstate) the electronic energy is stationary with respect to variations in ψ and we can therefore ignore the second term.

The Hellman-Feynman theorem

- This theorem is true also for variational wavefunctions such as Hartree-Fock or DFT provided that *complete basis sets* are used.
- In practical calculations this is never the case and the second term needs to be computed explicitly:
  - If the one-particle orbitals are expanded in atom-centered functions (Gaussian, STO), this term gives rise to the so-called “Pulay force”
  - If we use plane waves the Pulay force vanishes exactly

Pseudopotentials

- To minimize the size of the plane wave basis
  - only valence electrons are included explicitly
  - core electrons are replaced by pseudopotentials
- First-principles pseudopotentials are built to
  - correctly represent the long range interactions of the core
  - produce pseudo-wavefunctions that approach the full wavefunction outside a core radius r_c


Ψ_{pseudo}
Ψ_{AE}
V_{pseudo}
Z/r
r_c
r

Car-Parrinello Molecular Dynamics

- Advantages:
  - More general applicability and predictive power compared to MD using “predefined potentials”
  - In comparison with static quantum chemistry approaches allows for the inclusion of dynamical, entropic effects, and the possibility of treating disordered systems (e.g. chemical reactions in solution)
- Limitations:
  - approximation in the exchange-correlation functional
  - size: 100-1000 atoms
  - time scale : 10-100 ps

Advanced techniques (recent developments)

- QM/MM extension
- Excited state Molecular Dynamics
- Extension to localized basis set (Gaussians): more suitable for molecules, clusters

Phenylalanine hydroxylase

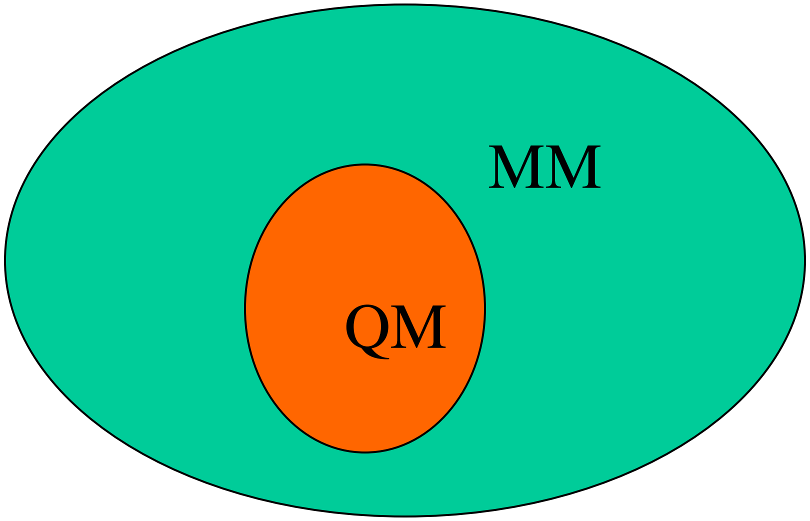
Hybrid QM/MM approaches:
quantum-mechanics/molecular-mechanics

- Systems of interest in computational biology are too large for a full quantum-mechanical treatment
- Need to integrate various computational chemistry methodologies with differing accuracies and cost.
- In QM/MM approaches this is done by embedding a QM calculation in a classical MM model of the environment

- Review paper: P. Sherwood, (2000), in
  - http://www.fz-juelich.de/nic-series/Volume1

QM/MM scheme

- The system is divided in two subsystems: an inner region (QM) where quantum-mechanics is used and an outer region (MM) where a classical field is used, interacting with each other



Why and when QM/MM ?

- Interest in active sites of proteins / enzymes or drug-DNA interaction
- Geometry and Functionality of active site influenced by the protein environment
- Proteins still too large to be handled completely by quantum chemistry &
  high quality (QM) description only needed for a usually small region of interest (*active site*)
- QM/MM schemes aim to incorporate environmental effects at an atomistic level, including mechanical constraints, electrostatic perturbations and dielectric screening

QM-MM Hamiltonian

- We can in general write a total Hamiltonian of the QM-MM system as follows:

$$H=H_{QM}+H_{MM}+H_{QM/MM}$$

- H_{QM} includes all the interactions between the particles treated with QM
- H_{MM} includes all the interactions between the classical particles
- $H_{QM/MM}$ accounts for all the interactions between one quantum particle and one classical particle

The choice of the QM method

- The choice of the QM method within a hybrid approach depends on the accuracy required and on the size of the QM region.
- Implementation of QM-MM methods have been reported with almost any QM approach:
  - The first application of Warshel and Levitt (1976) employed a semiempirical method.
  - More recently several implementation involving DFT and Car-Parrinello MD have been reported. This is a very interesting development since DFT can deal with relatively large QM regions and can be used also in combination with Molecular Dynamics.

The choice of the MM model

- The H_{MM} term is determined by the specific classical force field used to treat the MM part.
- The most popular force fields for hybrid QM-MM simulations are the same force fields mostly used for biomolecules:
  - CHARMM
  - AMBER
  - GROMOS96

Handling the hybrid term

- The third term of the Hamiltonian, $H_{QM\text{-}MM}$, is the most critical and the details of this interaction term may differ substantially in different implementations.
- In terms of classification, we can distinguish two possibilities:
  - (i) the boundary separating the QM and MM region, does not cut across any chemical bond
  - (ii) the boundary cuts across at least one chemical bond

Handling the hybrid term:

(i) the QM/MM boundary does not cut chemical bonds

- the QM-MM coupling term in the Hamiltonian contains the non-bonded interactions, i.e., electrostatic and short-range (van der Waals) forces.
- The treatment of the electrostatic interactions varies for different implementations, but the most common is the **electrostatic embedding**, in which the classical part appears as an external charge distribution (e.g. a set of point charges) in the QM Hamiltonian.
- The van der Waals interactions are usually described by a Lennard-Jones potential between QM and MM atoms with values of the parameters characteristic for their atomic type.

Handling the hybrid term:

(ii) the QM/MM boundary cuts chemical bonds

- If there are bonds between the QM and MM regions, it is necessary to introduce some termination of the QM part.
- For termination of sites where a covalent bond has been broken, addition of a so-called **link atom** is the most common approach: An extra nuclear centre is introduced together with the electrons required to form a covalent bond to the QM dangling valences that will mimic the bond to the MM region.
- The simplest and most used choice is to add a hydrogen atom as link atom. Of course there are chemical differences between hydrogen and the chemical group it replaces. One possible approach to adjust the link atom interaction is to place a pseudopotential at the MM site to mimic the electronic properties of the replaced bond.

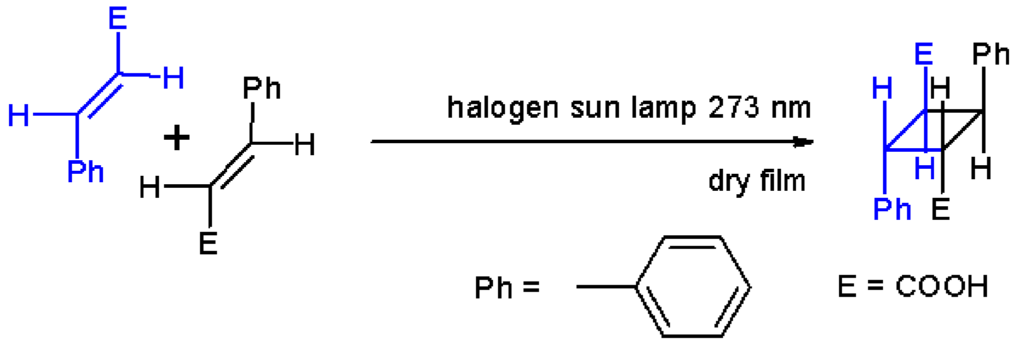
Why excited states?

- Microscopic understanding of photo-induced reactions in photoactive molecules and proteins
- Complementary to experiment in the interpretation of spectroscopic data
- Use the knowledge about mechanisms and predictive power of computational tools to assist in the engineering process of photoactive devices

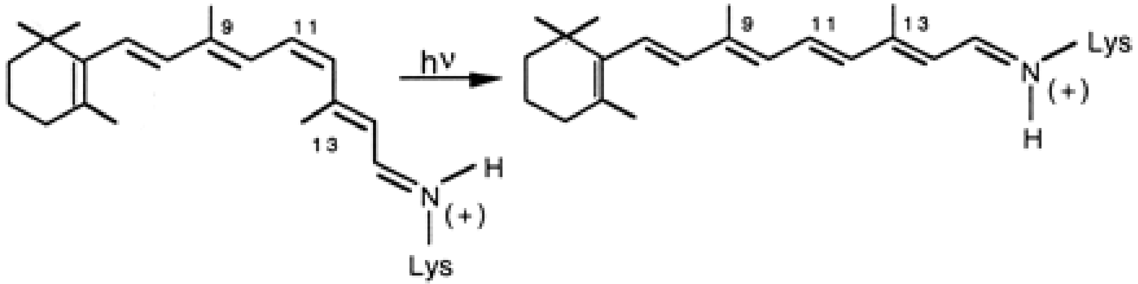
Basic concepts

- When light is absorbed by a molecule, this is promoted to an electronic excited state
- As a consequence of the excitation a rearrangement or photochemical reaction is observed:
  - Isomerization
  - Bond breaking
  - Cycloaddition
  - …

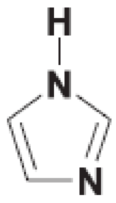
- Cinnamic acid cycloaddition



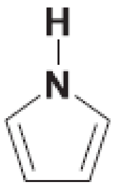
- Retinal photoisomerization



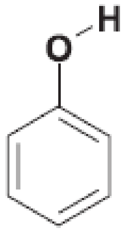
- Photodissociation of heteroaromatic molecules



Imidazole



Pyrrole

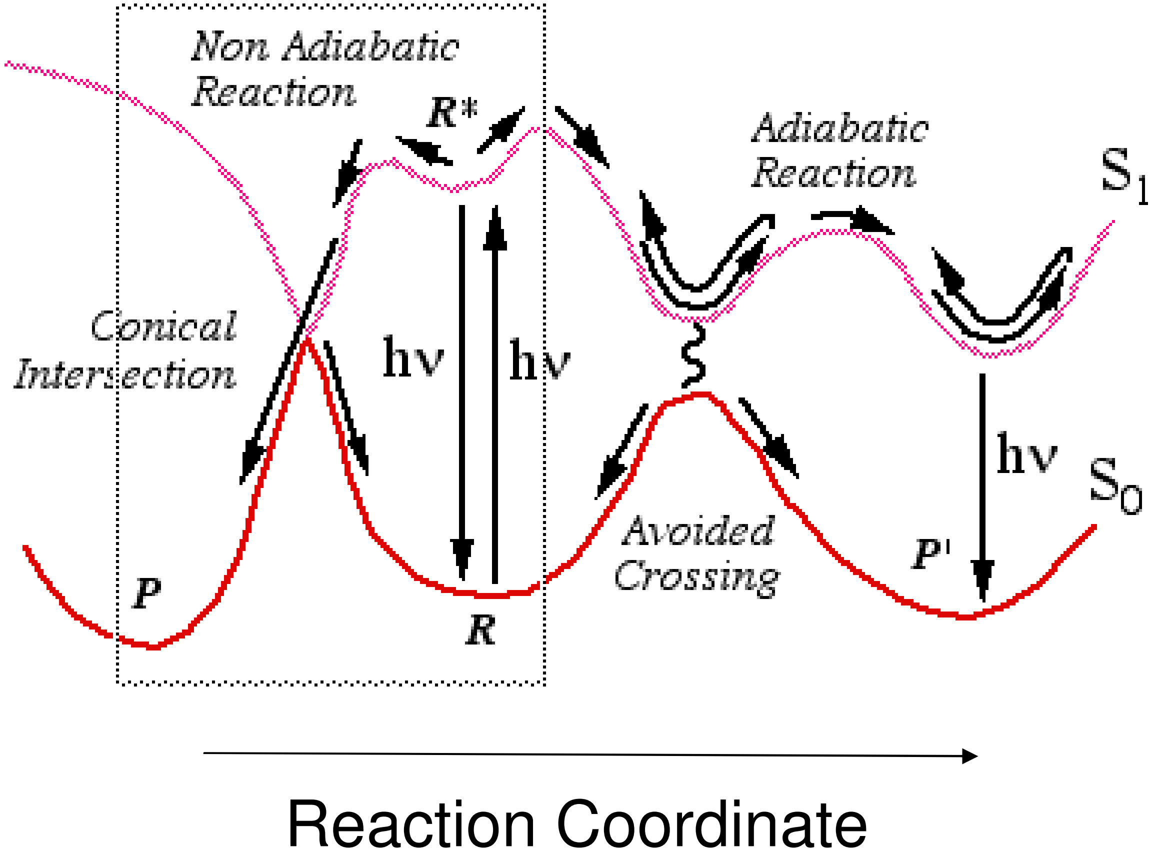


Phenol

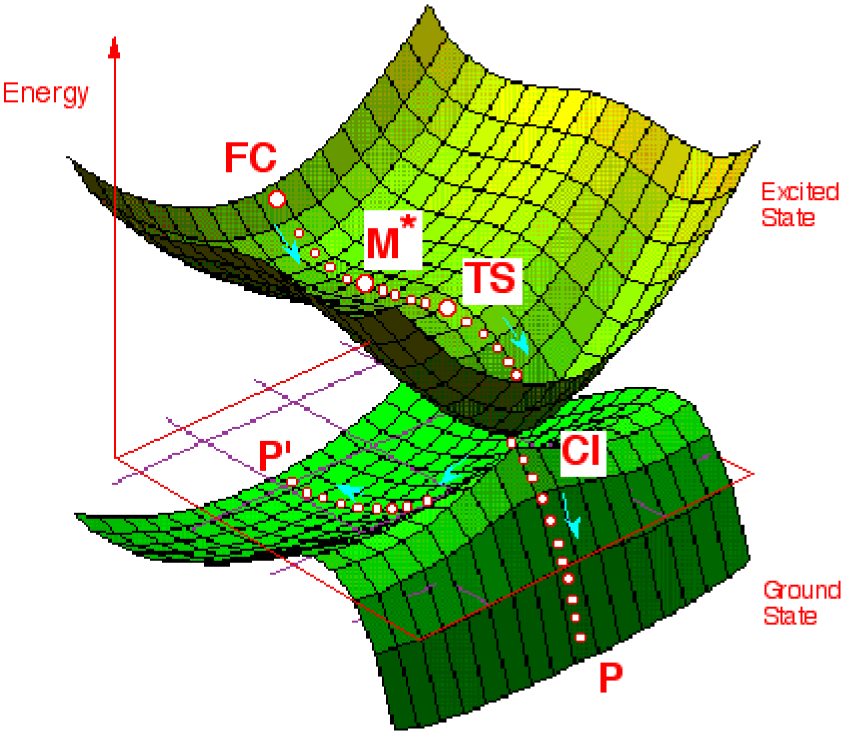
Potential Energy Surfaces (PES)

S_0 : ground state PES

S_1 : first excited state PES



Static vs. dynamical approaches



Static:

stationary points (M*)

transition states (TS)

conical intersection (CI)

minimum energy path

Dynamics:

relaxation time

kinetic effects

thermal fluctuations

Validity of the BO approximation

- The BO approximation holds as long as the excited and ground state PES are not too close to each other
- When S_0 and S_1 approach each other, we have to consider explicitly the probability of electron hopping from one PES to the other

=> Non-adiabatic dynamics

(see e.g., J. Tully, J. Chem. Phys. **93**, 1061, 1990)

Methods for excited state energy and gradient computations

- Wave function based methods (ab initio)
  - Hartree-Fock (HF), Configuration Interaction (CI), MCSCF, CASSCF, CASPT2, CC

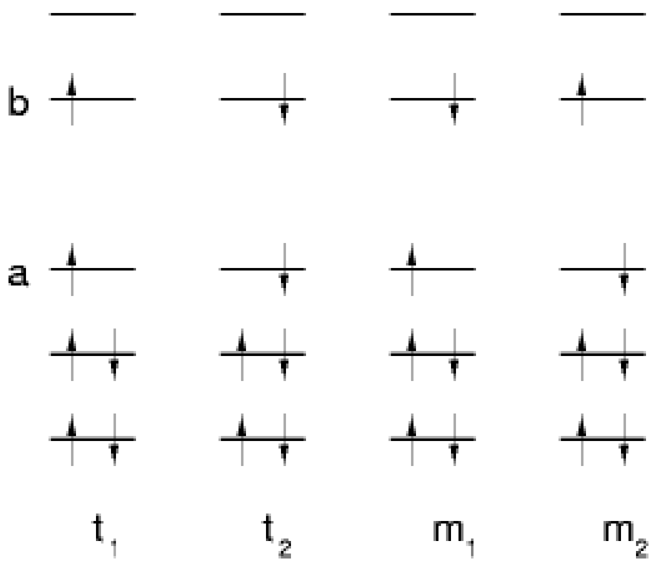
- DFT methods
  - ROKS (restricted open-shell Kohn-Sham)
  - TD-DFT (time dependent Density Functional Theory)

Restricted open-shell Kohn-Sham (ROKS)

[Frank,Hutter,Marx,Parrinello, JCP (1998), 108, 4060]

- Kohn-Sham-like formalism for the treatment of excited singlet states.
- This scheme is suited to perform molecular dynamics simulation in the excited state.
- Suitable for large gap systems with well separated states. The nuclei move on one excited state PES
- A spin-adapted function is constructed and the corresponding energy expression minimized.
- Inspired to the sum method for the calculation of multiplet splittings (Ziegler, Rauk, Baerends, 1977)
- Calculation of forces is easy: successfully applied to the dynamical simulation of the *cis-trans* isomerization of formaldimine.

ROKS



Four possible determinants t_1, t_2, m_1 and m_2 as a result of the promotion of a single electron from the HOMO to the LUMO of a closed shell system. Suitable Clebsch-Gordon projections of the mixed states m_1 and m_2 yield another triplet state t_3 and the desired first excited singlet S1 state.

ROKS

- The total energy of the S1 state is given by

$$E_{S_1}\left[\{\phi_i\}\right] = 2E_m^{\mathrm{KS}}\left[\{\phi_i\}\right] - E_t^{\mathrm{KS}}\left[\{\phi_i\}\right]$$

where the energies of the mixed and triplet determinants

$$E_m^{\mathrm{KS}}[\{\phi_i\}] = T_{\mathrm{s}}[n] + \int d\mathbf{r}\ \ V_{\mathrm{ext}}(\mathbf{r})n(\mathbf{r}) + \frac{1}{2}\int d\mathbf{r}\ \ V_{\mathrm{H}}(\mathbf{r})n(\mathbf{r}) + E_{\mathrm{xc}}[n_m^{\alpha}, n_m^{\beta}]$$
$$E_t^{\mathrm{KS}}[\{\phi_i\}] = T_{\mathrm{s}}[n] + \int d\mathbf{r}\ \ V_{\mathrm{ext}}(\mathbf{r})n(\mathbf{r}) + \frac{1}{2}\int d\mathbf{r}\ \ V_{\mathrm{H}}(\mathbf{r})n(\mathbf{r}) + E_{\mathrm{xc}}[n_t^{\alpha}, n_t^{\beta}]$$

are expressed in terms of (restricted) Kohn-Sham spin-density functionals constructed from the set $\{\phi_i\}$

Nonadiabatic Car-Parrinello Molecular Dynamics

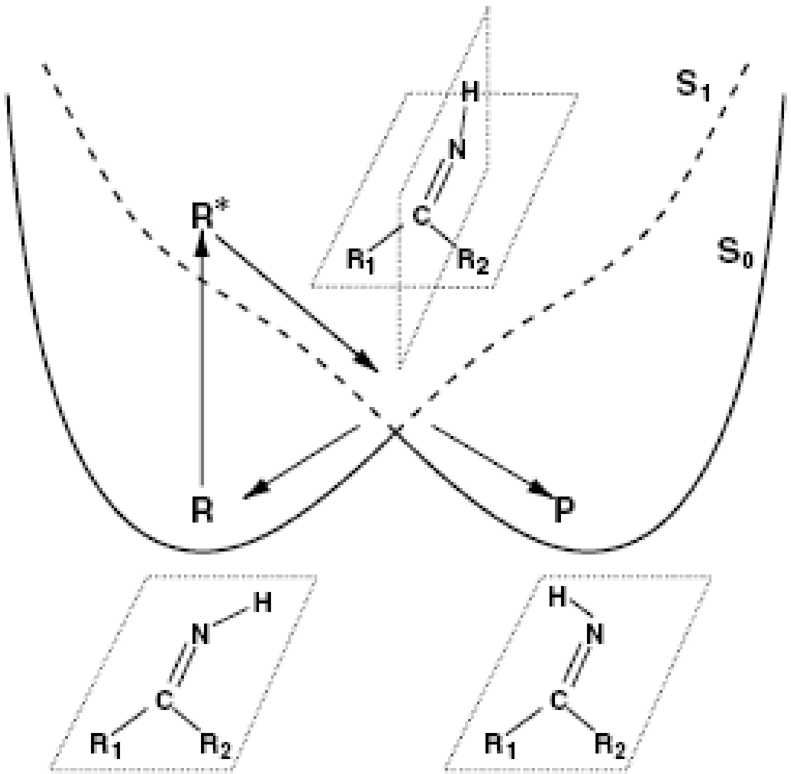


FIG. 1. Schematic view of the photoreaction pathways of formaldimine ($R_1 = R_2 = H$). S_0 (solid line) and S_1 (dashed line) energy curves are plotted qualitatively against a hypothetical reaction coordinate whose main contributor is the NH twist angle (defined here as the angle between the planes containing R_1CR_2 and HNC, respectively).

(N. Doltsinis, D. Marx, PRL, **88,** 166402, 2002)

Time-dependent Density Functional Theory (TD-DFT)

(Runge and Gross, 1984)

- Time-dependent analogue of the HK theorem
- TD-DFT allows to calculate properties like **polarizability** and **excitation energies** through the linear density response of the system to the external time dependent field.
- Efficiently implemented in various packages
- Calculation of forces within TD-DFT have been recently implemented
    - MD simulations in the excited state using the TD-DFT forces are becoming feasible

LR-TDDFT

- The basic quantity in the LR-TDDFT is the density-density response function

$$\chi(\mathbf{r},t,\mathbf{r}',t') = \left.\frac{\delta\rho(\mathbf{r},t)}{\delta v_{ext}(\mathbf{r}',t')}\right|_{v_0}$$

- which relates the first order density response δρ(r, t) to the applied perturbation δv(r, t)

$$\delta\rho(\mathbf{r},t) = \int d^3\mathbf{r}'\,dt'\,\chi(\mathbf{r},t,\mathbf{r}',t')\,\delta v(\mathbf{r}',t')$$

- The response function for the physical system of interacting electrons, χ(r, t, r′, t′), can be related to the computationally more advantageous Kohn-Sham response, χ_s(r, t, r′, t′)
- $$\chi^{-1}(\mathbf{r},\mathbf{r}',\omega) = \chi_s^{-1}(\mathbf{r},\mathbf{r}',\omega) - \frac{1}{|\mathbf{r}_1-\mathbf{r}_2|} - f_{xc}(\mathbf{r}_1,\mathbf{r}_2,\omega)$$
- where

$$\chi_s(\mathbf{r},\mathbf{r}',\omega) = \sum_{k,j}(f_k - f_j)\frac{\psi_k^*(r)\psi_j(r)\psi_j(r')\psi_k^*(r')}{\omega-(\epsilon_j-\epsilon_k)+i\eta}$$

Performance of TD-DFT

- Usually TD-DFT results are reliable for low-energy excitations, specifically for energies lower than the ionization potential
- Tests on small organic molecules show average errors of about 0.2 eV using BP or B3LYP functionals

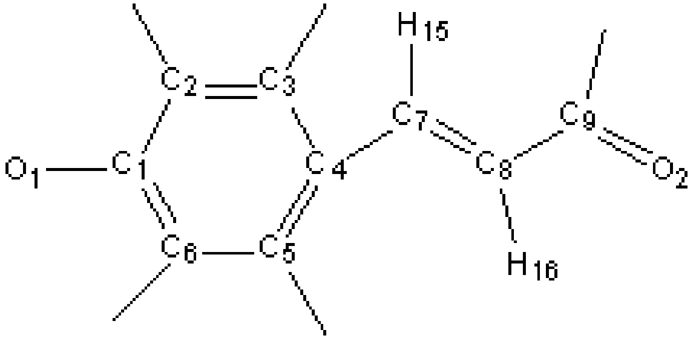
  => usually better than CIS

(Marques, Gross: Annu. Rev. Phys. Chem. 2004, 55, 427–55)

- however TD-DFT does not provide information on the wavefunctions

The Photoactive Yellow Protein (PYP)

blue light photoreceptors isolated in 1985 from *Halorhodospira halophila*

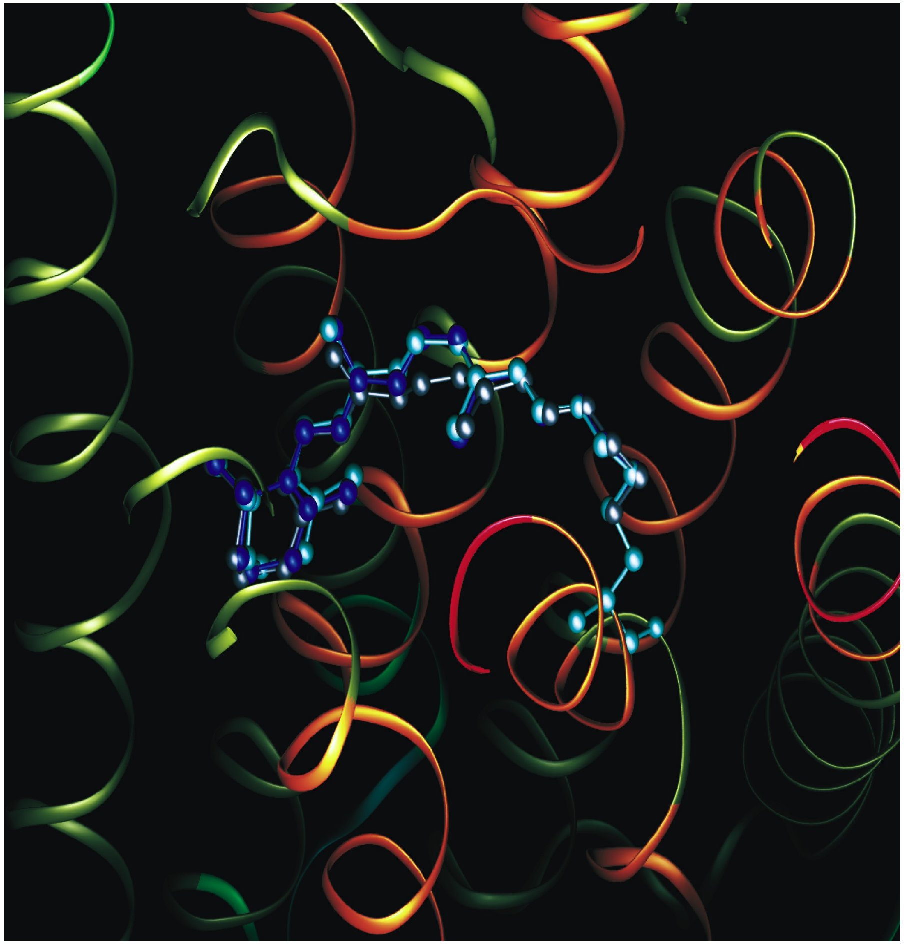


4-hydroxycinnamic acid (pCA) chromophore (Hoff et al., *Biochemistry* **33**, 13959 (1994)

Borgstahl,Williams,Getzoff, *Biochemistry* **34**, 6278 (1995)

Structure, Initial Excited-State Relaxation and Energy Storage of Rhodopsin at the CASPT2//CASSCF/AMBER level of Theory.

T. Andruniow, N. Ferré and M. Olivucci (PNAS) USA , 2004



Applications:
From Materials Science to Biochemistry

- Semiconductors: silicon in crystalline and disordered phases
- Structural phase transitions of materials under pressure
- Diffusion of atoms in solids
- Surface reconstruction, chemisorption on surfaces
- Simulations of liquids, water, ions in water
- Clusters, fullerenes, nanostructures
- Chemical reactions (in gas phase or in solution)
- Polymerization reactions – Ziegler-Natta catalysts
- Zeolites, metallocenes
- Rhodopsin, enzymatic reactions, drug-DNA interactions