Chapter 4:

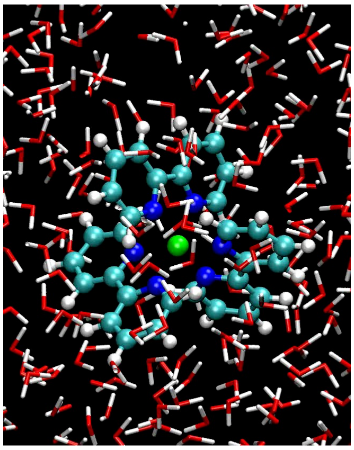
Molecular Dynamics Simulations

Monte Carlo versus Molecular Dynamics

MC	MD
Stochastic sampling	deterministic sampling
Thermodynamic properties	thermodynamic and dynamic properties
Easy to generalize to other ensembles e.g. grand-canonical MC	special algorithms for different ensembles
Difficult to impose constraints	easy to impose constraints
No force calculations needed	force calculations needed, i.e. potential has to be differentiable
Random moves can be efficient to overcome energy barriers	barriers can only be overcome by thermal energy kT
Less efficient for collective moves	makes use of natural dynamics => efficient collective moves
dense systems difficult	no special problems for dense systems

Ensemble Properties via MD

Ru-tris(bipy) in water



=> use intrinsic dynamics to generate thermally relevant configurations

Basic Assumptions:

- Born-Oppenheimer approximation, dynamics on a single potential energy surface V(**R**)
- Ergodic theorem

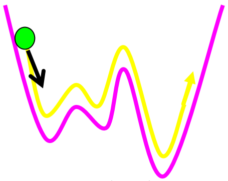
$$\boxed{\langle A\rangle_{ens} = \langle A\rangle_{time}} \qquad \boxed{\langle A\rangle_{ens} = \sum_{i=1}^{N_{tot}} w_i A_i\left(\vec{R}_i\right) = \sum_{i=1}^{N_{tot}} A_i\left(\vec{R}\left(t_i\right)\right)}$$

- Atomic motion described by classical point particle dynamics

Newton's equation of motion (EOMs):

$$\boxed{\vec{f}_I\left(t\right) = m_I \vec{a}_I\left(t\right)}$$

$$\boxed{\vec{f}_I\left(t\right) = -\nabla_I V\left(\vec{R}\left(t\right)\right)}$$



R(t_0),**v**(t_0) => **R**(t)

$$\vec{R}\left(t\right) = \vec{R}\left(t_0\right) + \int_{t_0}^{t} \vec{v}(t)\,dt = \vec{R}\left(t_0\right) + \vec{v}(t_0)(t-t_0) + \frac{1}{2}\int_{t_0}^{t} dt \int_{t_0}^{t} \vec{a}(t)\,dt$$

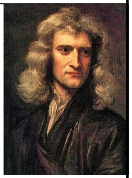
=> Solved by numerical integration!

⇒ Thermodynamic properties

⇒ dynamic properties!

Different Formulations of Classical Mechanics

Newtonian Mechanics $(\vec{R}, \vec{v} = \frac{d\vec{R}}{dt} = \dot{\vec{R}})$



Sir Isaac Newton
1643-1727

2nd law $\boxed{M_I \frac{d^2\vec{R}_I}{dt^2} = -\nabla_I V\left(\vec{R}\right)}$ 3N 2nd order differential equations

Lagrangian Mechanics $(\vec{q}, \dot{\vec{q}})$

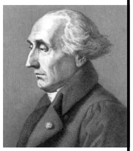
generalized coordinates & their time derivatives

Lagrangian $L = T(\dot{\vec{q}}) - V(\vec{q})$ Kinetic energy – potential energy

Euler-Lagrange equations

$$\boxed{\frac{\partial L}{\partial \vec{q}_j} - \frac{d}{dt}\frac{\partial L}{\partial \dot{\vec{q}}_j} + \sum_{i=1}^{C} \lambda_i \frac{\partial c_i}{\partial \vec{q}_j} = 0}$$

3N(+C) 2nd order differential equations
C: number of (holonomic) constraints



Joseph-Louis Lagrange
1738-1813

Hamiltonian Mechanics $(\vec{q}, \vec{p})$

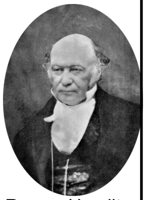
Canonical coordinates **r** = (**q**, **p**)

Hamiltonian $H = T(\vec{p}) + V(\vec{q})$ Kinetic energy + potential energy

Hamilton's equations

$$\boxed{\frac{\partial \vec{p}}{\partial t} = -\frac{\partial H}{\partial \vec{q}}} \boxed{\frac{\partial \vec{q}}{\partial t} = +\frac{\partial H}{\partial \vec{p}}}$$

6N 1st order differential equations



William Rowan Hamilton
1805-1865

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Quiz VI: Newtonian vs Lagrangian Dynamics

1) Show that for $\vec{R} = \vec{q}$ and $\vec{v} = \dot{\vec{q}}$ and no additional constraints C, the Euler-Lagrange equations become identical to Newton's equations.

Numerical Integration of EOMs

Idea: integrate EOMs in small discrete time steps Δt during which **f**(Δt) ≈ constant

Position Verlet   Initial conditions: **R**(t=0), **v**(t=0)

Taylor expansion of **R**(t+Δt) $\vec{R}_I(t+\Delta t) = \vec{R}_I(t) + \vec{v}_I(t)\Delta t + \frac{1}{2}\vec{a}_I(t)\Delta t^2 + \frac{1}{6}\vec{b}_I(t)\Delta t^3 + O(\Delta t^4)$

Taylor expansion of **R**(t-Δt) $\vec{R}_I(t-\Delta t) = \vec{R}_I(t) - \vec{v}_I(t)\Delta t + \frac{1}{2}\vec{a}_I(t)\Delta t^2 - \frac{1}{6}\vec{b}_I(t)\Delta t^3 + O(\Delta t^4)$

Sum $\vec{R}_I(t+\Delta t) + \vec{R}_I(t-\Delta t) = 2\vec{R}_I(t) + \vec{a}_I(t)\Delta t^2 + O(\Delta t^4)$

Position propagation $\boxed{\vec{R}_I(t+\Delta t) = 2\vec{R}_I(t) - \vec{R}_I(t-\Delta t) + \vec{a}_I(t)\Delta t^2 + O(\Delta t^4)}$

⇒ Need positions at previous and current time steps and forces at current time
⇒ No information on velocities needed!!
⇒ But: velocities needed to calculate e.g. total energy!

Velocities from finite differences $\boxed{\vec{v}_I(t) = \frac{\vec{R}_I(t+\Delta t) - \vec{R}_I(t-\Delta t)}{2\Delta t} + O(\Delta t^2)}$

Or even: $\boxed{\vec{v}_I(t) = \frac{\vec{R}_I(t) - \vec{R}_I(t-\Delta t)}{\Delta t} + O(\Delta t)}$

=> Velocities not directly available and can only be calculated with less accuracy (O(Δt^2))

More Time Propagation Algorithms

Leap Frog Initial conditions: **R**(t=0), **v**(t=0)

$$\boxed{\vec{v}_I(t+\frac{1}{2}\Delta t)=\vec{v}_I(t-\frac{1}{2}\Delta t)+\vec{a}_I(t)}$$

$$\boxed{\vec{R}_I(t+\Delta t)=\vec{R}_I(t)+\vec{v}_I(t+\frac{1}{2}\Delta t)\Delta t}$$

⇒ Need velocities at previous mid-step and position and forces at current time step
⇒ Velocities always ½ time step behind/in advance => ‘leap frog’ = ‘saute mouton’
⇒ Local error also Δt^4, global Δt^2 (like position Verlet)

Velocity Verlet Initial conditions: **R**(t=0), **v**(t=0)

$$\boxed{\vec{R}_I(t+\Delta t)=\vec{R}_I(t)+\vec{v}_I(t)\Delta t+\frac{1}{2}\vec{a}_I(t)\Delta t^2}$$

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

1) Calculate velocities at mid time step

$$\vec{v}_I(t+\frac{1}{2}\Delta t)=\vec{v}_I(t)+\frac{1}{2}\vec{a}_I(t)\Delta t$$

2) Calculate positions at full time step

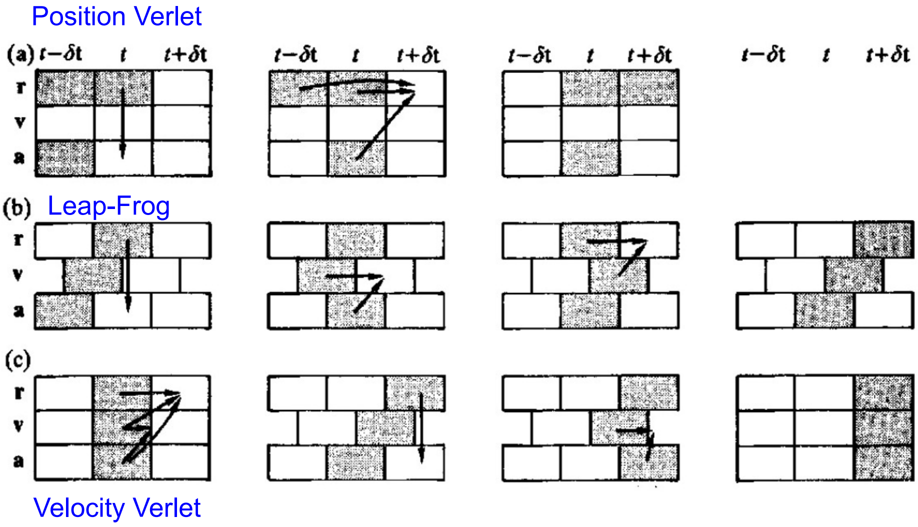
$$\vec{R}_I(t+\Delta t)=\vec{R}_I(t)+\vec{v}_I(t+\frac{1}{2}\Delta t)\Delta t$$

3) Propagate velocities to full time step

$$\vec{v}_I(t+\Delta t)=\vec{v}_I(t+\frac{1}{2}\Delta t)+\frac{1}{2}\vec{a}_I(t+\Delta t)$$

Higher Order Integrators: Gear Predictor-Corrector, Yoshida, Runge-Kutta etc
=> Not much used for MD

Graphical Summary



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Quiz VII: Energy Conservation

1) Show that for systems with time independent potentials, the Newton (or equivalently the Lagrange or Hamilton) equations of motion conserve total energy: dE/dt = 0.

2) What does this imply for MD simulations in the microcanonical ensemble?

3) How could you make use of this property in choosing the appropriate numerical integration scheme?

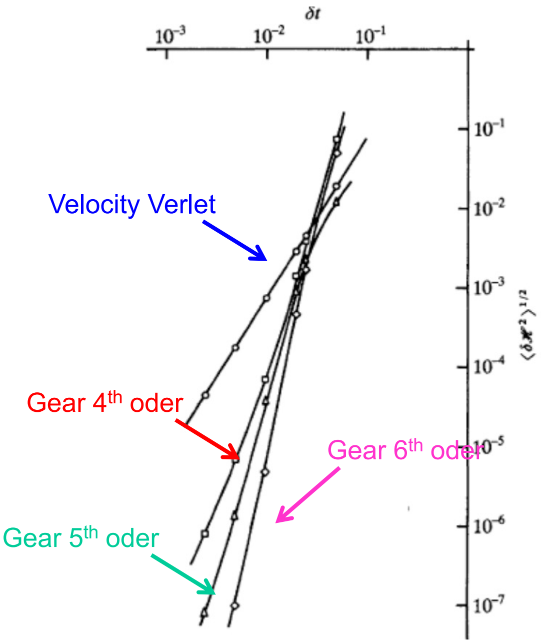
Constants of Motion dA/dt = 0

Noether's theorem
If a system has a symmetry property (i.e. Hamiltonian remains invariant upon changes) then there is a corresponding quantity that is conserved in time.

Symmetry property		*Constant of motion*
coordinate translations	⇔	linear momentum
coordinate rotations	⇔	angular momentum
time translations	⇔	energy

Emmy Noether
1882-1935
© image from wikipedia

Energy Conservation during Numerical Integration



Why no higher-order integrators?

=> Only more accurate at small time steps

Properties of an Ideal Propagator

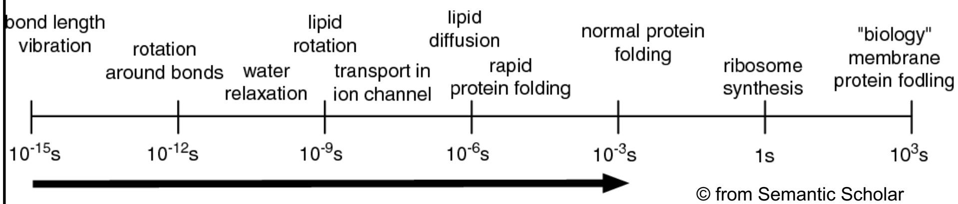
- Accurate
- Conserve energy & momentum
- Long time step
- Low CPU and memory cost
- Error bound
- Time reversible
- Symplectic (phase space volume is preserved under time evolution)

© graph from Tildesley & Allen

Choice of Time Step

- Usually single time step of constant size
- Force has to be roughly constant during Δt
- => Time step has to be ca. 10-100 times smaller than fastest motion in the system

What is the fastest motion?



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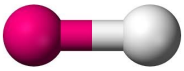
Harmonic oscillator:



$$\boxed{\omega = \sqrt{\frac{k}{m}}}$$

k: force constant
m: reduced mass

$$\boxed{m = \frac{m_1 m_2}{m_1 + m_2}}$$

⇒ Fastest frequencies: covalent bonds with light atoms
⇒ H-X bonds

e.g. O-H stretch vibrations 3600cm^{-1} ⇔ 108THz ⇔ 10fs => $\Delta t \approx$ 0.1-1fs

How can we use a maximal Δt?

- Multiple time step integrators => different Δt's for different force components
- Constraints: keep H-X bonds fixed at their equilibrium value

Constraint Algorithms

e.g. bond distance constraint

$$\sigma_k(t) = \left|\vec{R}_A(t) - \vec{R}_B(t)\right|^2 - d_{AB}^2 = 0$$

Holonomic constraints $\sigma = \sigma_k(\vec{R},t)$

- Dynamics in internal coordinates
- Lagrange multipliers λ

Extended Lagrangian

$$L = T - V - \sum_{k=1}^{c} \lambda_k \sigma_k(\vec{R},t)$$

Force on atom I

$$\vec{f}_I(t) = -\nabla_I V(\vec{R}) - \nabla_I \sum_{k=1}^{c} \lambda_k \sigma_k(\vec{R},t) = \vec{f}_I^{uc} + \vec{f}_I^{c}$$

$$\vec{R}_I(t+\Delta t) = \vec{R}_I^{uc}(t+\Delta t) + \sum_{k=1}^{c} \lambda_k \frac{\partial \sigma_k(\vec{R},t)}{\partial R_I m_I} (\Delta t)^2$$

$$\sigma_k(t+\Delta t) = \left|\vec{R}_A(t+\Delta t) - \vec{R}_B(t+\Delta t)\right|^2 - d_{AB}^2 = 0$$

System of c nonlinear coupled equations

$$\sigma_j(t+\Delta t) = \left|\vec{R}_A^{uc}(t+\Delta t) - \vec{R}_B^{uc}(t+\Delta t) + \sum_{k=1}^{c} \lambda_k (\Delta t)^2 \left[\frac{\partial \sigma_k(\vec{R},t)}{\partial \vec{R}_A m_A} - \frac{\partial \sigma_k(\vec{R},t)}{\partial \vec{R}_B m_B}\right]\right|^2 - d_{AB}^2 = 0$$

solved iteratively till σ_k < tol

=> Newton-Raphson, SHAKE, RATTLE

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Chapter 5:

Molecular Dynamics Simulations (2)

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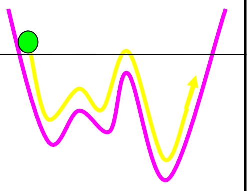
Determination of V(R)



First-Principles Surfaces:

- Pointwise QM determination of the full 3N dim PES
  ⇒ only practicable for very small molecules

- PES determined on the fly where it is needed: Car-Parrinello MD
  ⇒ <1000 atoms

Empirical Interaction Potentials:

- Choice of functional form:

$$V(\{R_I\}) \cong \sum_I V_1\left(R_I\right) + \sum_I \sum_{J>I} V_2\left(R_I, R_J\right) + \sum_I \sum_{J>I} \sum_{K>J} V_3\left(R_I, R_J, R_K\right) + \dots$$

- most of the time truncated after pair-potential term
- few many-body force fields (3-body: Axilrod-Teller, n-body: Tersoff, glue potential, embedded atom method (EAM) => especially for metals)

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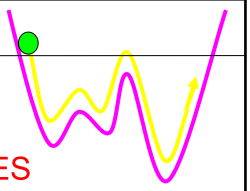
Determination of V(R)



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- Pointwise QM determination of the full 3N dim PES
  ⇒ only practicable for very small molecules

- PES determined on the fly where it is needed: Car-Parrinello MD
  ⇒ <1000 atoms

Empirical Interaction Potentials:

- Choice of functional form
  (2-body? Many-body? Nonpolarizable/Polarizable ? All atom/united atom?)
- Parameterized with experimental or QC data on small gas phase molecules (plus adaption to condensed phase environment)

Exp. Dipole moment H_2O 1.85D (gas phase)
~3 D (water)

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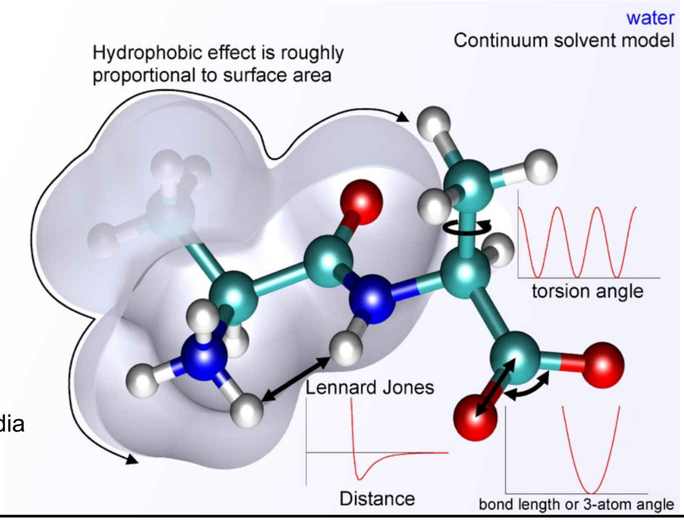
Materials: Interatomic potentials

https://www.ctcms.nist.gov/potentials

(Bio)Molecular Force Fields

- molecules modeled as classical mechanical objects with electrostatic charge interactions
- no explicit electrons only set of classical particles or interaction sites
- no quantum effects



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from wikipedia

Standard (Bio)molecular Force Field

$$H_{MM} = \sum_b \frac{1}{2} k_b (r_{ij} - b_0)^2 + \sum_\theta \frac{1}{2} k_\theta (\theta_{ijk} - \theta_0)^2$$

Bond term angle term

$$+\sum_\varphi \sum_n k_n \left[1 + \cos(n\varphi_{ijkh} - \varphi_0)\right]$$

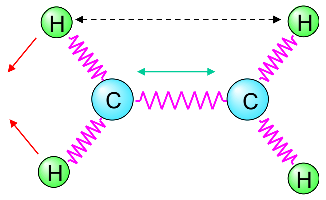
Torsional term

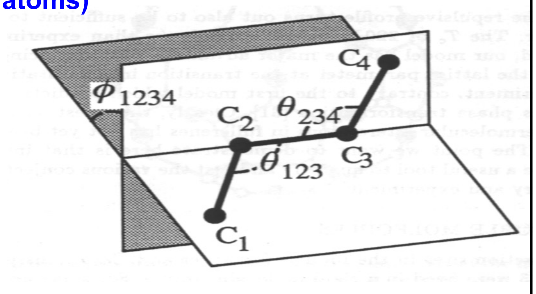
$$+\sum_{lm} \frac{q_l q_m}{4\pi\varepsilon_0 r_{lm}} + \sum_{op} 4\varepsilon \left(\left(\frac{\sigma}{r_{op}}\right)^{12} - \left(\frac{\sigma}{r_{op}}\right)^{6} \right)$$

electrostatics Lennard-Jones 12-6

- GROMOS, AMBER, CHARMM, OPLS-AA, MM3, SYBIL, UFF, SPC, SPC/E, TIP3P, TIP4P, TIP5P etc..

chemical bonds (2 adjacent atoms):
-> described by mechanical springs: bond potential (harmonic, anharmonic, Morse etc..)
force constants e.g. from stretching modes
bond angles (3 adjacent atoms): ditto (harmonic, anharmonic etc..),
→ force constants e.g. from bending modes
Torsional Potentials (4 adjacent atoms)





- **electrostatic interactions:** Coulomb interaction between effective (atom centered or off-site) point charges

- **van der Waals interactions (Pauli repulsion & dispersion):** Lennard-Jones 12-6, n-m, Williams exponential

MOLECULAR DYNAMICS PACKAGES

OpenMM	http://openmm.org
AMBER	http://ambermd.org
CHARMM	https://www.charmm.org/charmm/
GROMOS	http://www.gromos.net
GROMACS	http://www.gromacs.org free (incl. source)
NAMD	http://www.ks.uiuc.edu/Research/namd/ free (incl. source)
TINKER	https://dasher.wustl.edu/tinker free (incl. source)
X-PLOR	ahttp://www.csb.yale.edu/userguides/datamanip/xplor
DL-POLY	https://www.scd.stfc.ac.uk/Pages/DL_POLY.aspx
LAMMPS	https://lammps.sandia.gov

Limitations of Empirical Force Fields

⇒ **Transferability Problem**
empirical force fields are only parameterized for a given electronic environment, cannot adjust to large changes in the electron distribution
(e.g. different types of chemical bonding)

⇒ **cannot treat breaking and forming of chemical bonds**
⇒ **no chemical reactions!**

⇒ **many-body effects (polarization)!**

⇒ **transition metals difficult to treat!**

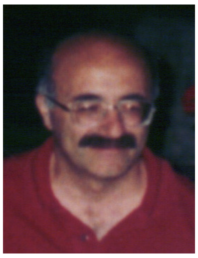
⇒ **parameter-free first-principles MD**

Car - Parrinello Molecular Dynamics

$$L = \sum_I 1/2 M_I \dot{R}_I^2 + \sum_i \mu \langle \dot{\phi}_i | \dot{\phi}_i \rangle - E[\{\phi_i\},\{R_I\}] + \sum_{ij} \Lambda_{ij} \left[\left\{ \int \phi_i(r) \phi_j(r) dr \right\} - \delta_{ij} \right]$$

Roberto
Car

Michele
Parrinello



$$M_I \ddot{R}_I = -\frac{\delta E}{\delta R_I}$$

$$\mu \ddot{\phi}_i = -H\phi_i + \sum_j \Lambda_{ij} \phi_j$$

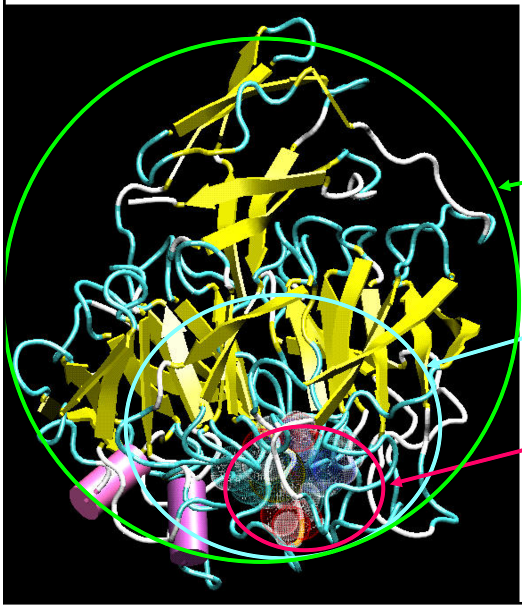
Does this fictitious dynamics have anything to do with the real physical dynamics???

- if $\mu << M_I\text{'s} \rightarrow K_e \approx 0$

the total energy of the system is ≈ the real physical total energy:

$$K_e + K_I + E_{pot} \approx K_I + E_{pot}$$

Mixed Quantum Mechanical / Molecular (QM/MM) Mechanical Methods



MM part

> 1000 solute atoms
> 10000 solvent atoms

Interface region

QM part

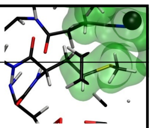
~ 100-1000 atoms
~ 400 electrons

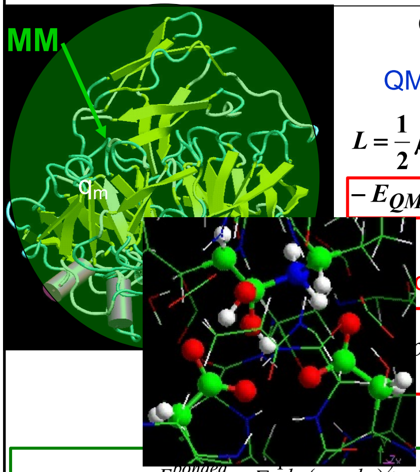
Nobelprize in Chemistry 2013

Martin Karplus **Michael Levitt** **Arieh Warshel**

"for the development of multiscale models for complex chemical systems": mixed quantum mechanical/molecular mechancial (QM/MM) simulations

Mixed QM/MM Car-Parrinello Simulations





CPMD (www.cpmd.org)

QM/MM Extended CP Lagrangian:

$$L = \frac{1}{2}\mu \sum_i \int d\vec{r}\, \dot{\psi}_i^*(\vec{r})\dot{\psi}_i(\vec{r}) + \frac{1}{2}\sum_I M_I \dot{\vec{R}}_I^2 - \boxed{E_{MM}} - \boxed{E_{QM/MM}}$$
$$\boxed{-E_{QM}} + \sum_{i,j} \Lambda_{i,j}\left(\int d\vec{r}\, \psi_i^*(\vec{r})\psi_j(\vec{r}) - \delta_{i,j}\right)$$

ctronic ground state $E_{QM} = E^{DFT}$ (ps, pw, GGA)

$$\rho] + \int_\Omega V^{ex}(\vec{r})\rho(\vec{r})dr + \frac{1}{2}\iint \frac{\rho(\vec{r}_1)\rho(\vec{r}_2)}{r_{12}} d\vec{r}_1 d\vec{r}_2 + E_{xc}[\rho] + \frac{1}{2}\sum_I \sum_J \frac{Z_I Z_J}{R_{IJ}}$$

$$\Updownarrow$$

$$E_{MM}^{bonded} = \sum_b \frac{1}{2} k_b (r_{ij} - b_0)^2 + \sum_\theta \frac{1}{2} k_\theta (\theta_{ijk} - \theta_0)^2 + \sum_\varphi \sum_n k_n \left[1 + \cos(n\varphi_{ijkl-}\varphi_0)\right]$$

$$E_{MM}^{non-bonded} = \sum_{lm} \frac{q_l q_m}{4\pi\varepsilon_0 r_{lm}} + \sum_{op} 4\varepsilon_{op}\left(\left(\frac{\sigma_{op}}{r_{op}}\right)^{12} - \left(\frac{\sigma_{op}}{r_{op}}\right)^{6}\right)$$

E_{MM}: AMBER or GROMOS
Non-polarizable

JCP 116, 6941 (2002); JPCB 106, 7300 (2002); JPCB 108,7963 (2004); reviews in: CHIMIA 56, 11 (2002); CHIMIA 59, 493 (2005); CHIMIA ***9****, 667-671 (2011); CHIMIA 65, 330-333 (2011)*