

# Lecture 10 - The Molecular Dynamics method

## Lecture 10 - The Molecular Dynamics method

Newtonian  
dynamics

MD Potentials

MD  
Applications

Summary

- Can properties be computed from MD?
- Newtonian dynamics.
- Potentials.
- Some typical applications of MD.

# Ergodic hypothesis

- Original statistical sampling expression  
( $Q = \int e^{-E(q)/k_B T} dq$ ):

$$\langle A \rangle = \int A(q) Q^{-1} e^{-E(q)/k_B T} dq$$

- Metropolis with a weighted choice of configurations  $q_i$

$$\langle A \rangle = \frac{1}{X} \sum_i^X A(q_i)$$

- Properties sampled over a trajectory: ergodic hypothesis

$$\langle A \rangle = \frac{1}{X} \sum_i^X A(t_i) \Rightarrow \langle A \rangle = \lim_{t \rightarrow \infty} \frac{1}{t} \int_{t_0}^{t_0+t} A(\tau) d\tau$$

# Newton Equations

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- Newton equations of motion:

$$m_i \frac{d^2 r_i(t)}{dt^2} = F_i = -\nabla V$$

- Can be solved analytically for some potentials  $V$  (eg. harmonic potential).
- Arbitrary potential require a numerical trajectory integration.

# Time Discretization

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Summary

- Solve coupled set of equations:
- **Euler approximation** – exact in the limit  $\Delta t \rightarrow 0$ :

$$\begin{cases} r(t + \Delta t) = q(t) + \frac{p(t)}{m} \Delta t \\ p(t + \Delta t) = p(t) + ma(t) \Delta t \end{cases}$$

- Instable in all non-trivial cases.

# Time Discretization in Practice

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Summary

- Various schemes exist based on the Taylor expansions of  $r(t + \Delta t)$
- **Verlet step** (1967) considers the sum of the Taylor expansion corresponding to forward and reverse time steps  $\Delta t$  – odd derivatives disappear:

$$r(t + \Delta t) = 2r(t) - r(t - \Delta t) + a(t)(\Delta t)^2$$

- Accurate up to fourth order.
- Still requires Euler to bootstrap the first step.

# Leapfrog Algorithm

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Summary

- Verlet does not use momentum explicitly: no means to adjust the kinetic energy/temperature.
- **Leapfrog algorithm:**

$$\begin{aligned}r(t + \Delta t) &= r(t) + v(t + \frac{1}{2}\Delta t)\Delta t \\v(t + \frac{1}{2}\Delta t) &= v(t - \frac{1}{2}\Delta t) + a(t)\Delta t\end{aligned}$$

- Forces computed only at integer times (not between steps).
- Ignores third-order terms in the Taylor expansions – decreased stability.

# More Advanced Algorithms

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- **Runge-Kutta** (1986) of various orders: gradient of a function evaluated at a number of different intermediate points.
- Gear **predictor-corrector** (1971): higher-order terms in the Taylor expansion used to predict steps along the trajectory, actual particle *accelerations* computed are compared. Differences used to correct the *position*.
- Considered expensive for MD applications.

# Step-length Increasing Methods

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Summary

- Step-length used dependent on the frequencies appearing in the system.
- Solution: **remove high-frequency motion** from the system.
  - Freeze heavy-atom – hydrogen bond stretching modes.
  - Freeze some of all the degrees of freedom within the solvent molecules.

# Freezing Methods

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Summary

- SHAKE algorithm (Ryckaert, Ciccotti and Berendsen 1977).

- 1 Take unconstrained Verlet step  $r_i^0(t + \Delta t)$  for  $i$ th particle.
- 2 Correct the positions so that  $r_{ij} = r_i - r_j$  is frozen to be  $d_{ij}$ :

$$\begin{aligned}r_i(t + \Delta t) &= r_i^0(t + \Delta t) + \Delta r_i(t) \\ \Delta r_i(t) &= \frac{2(\Delta t)^2}{m_i} \sum \lambda_{ij} r_{ij}(t)\end{aligned}$$

- 3 Lagrange multipliers  $\lambda_{ij}$  determined from the constraints added to the Verlet step equation:

$$|\vec{r}_{ij}|^2 - d_{ij}^2 = 0$$

# Force/Potential Calculation

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Summary

- Force/potential calculation is the time consuming part: it scales formally as a square of the number of particles.
- use Newton's Third Law:  $F_{ij} = -F_{ji}$
- Use space partitioning techniques to quickly select nonvanishing interactions (for short range potentials).

# Potentials

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Short-range potentials:

stretching: 
$$U_{ab}^{\text{ST}}(R_{ab}) = \frac{k_{AB}}{2}(R_{ab} - R_{AB})^2$$

bending: 
$$U_{abc}^{\text{BN}}(\theta_{abc}) = \frac{k_{ABC}}{2}(\theta_{abc} - \theta_{ABC})^2$$

torsion: 
$$U_{abcd}^{\text{TR}}(\phi_{abcd}) = \frac{V_{BC}}{2}(1 - \cos 2\phi_{abcd})$$

- $k_{AB}$ ,  $R_{AB}$ ,  $k_{ABC}$ ,  $\theta_{ABC}$ ,  $V_{BC}$  are force field parameters.
- The parameters depend on the types of atoms involved.
- Other terms: van der Waals, electrostatic energy, cross terms.

# Potential Representation

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Summary

- Harmonic potential works only for small displacements:

$$U_h(r) = \frac{1}{2}k(r - R_0)^2$$

- Anharmonic terms needed in general.
- Morse describes dissociation ( $\alpha$  related to the force constant  $k$ ):

$$U_M(r) = D(1 - e^{-\alpha(r-R_0)})^2$$

**Exercise:** find the relation between  $\alpha$  and  $k$  by comparing derivatives of  $U_h$  and  $U_M$ .

# Van der Waals energy

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Summary

- VdW is zero for large distances.
- Strongly repulsive for small  $r$  (electron cloud repulsion).
- weak attraction  $R^{-6}$  at intermediate distances due to electron correlation (induced dipole-dipole interaction).
- Called also *dispersion force*.
- Higher order ( $R^{-8}$  etc) terms associated with induced dipole-quadrupole interactions.
- Popular representation: Lennard-Jones:

$$E_{LJ} = \frac{C_1}{r^{12}} - \frac{C_2}{r^6}$$

$$E_{LJ} = \varepsilon \left( \frac{R_0}{r^{12}} - 2 \frac{R_0}{r^6} \right)$$

$R_0$  – minimum distance;  $\varepsilon$  – minimal energy.

- Another form: Buckingham potential. Morse potential.

# Comparison of various VdW potentials

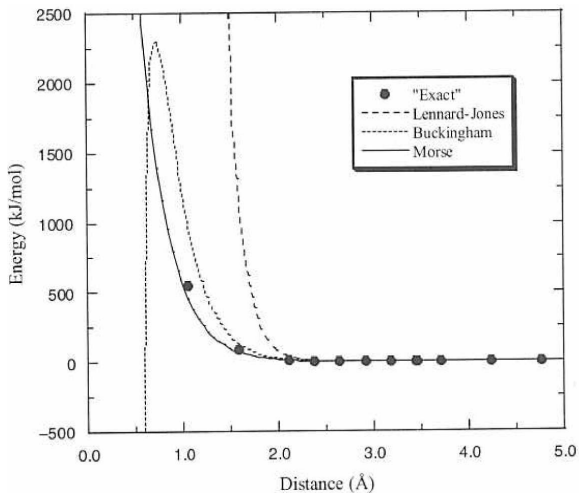
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Comparison of  $E_{\text{vdw}}$  functionals for the  $\text{H}_2$ —He potential

# Traditional MD Potentials

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Summary

- Typical atom types parametrized.
- Well known force field types: Merck Molecular Force Field (MMFF94), Amber.
- Very good for “typical systems”.
- ... but transferability problems.

# Other MD Potentials

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Summary

- Quantum mechanical polarizable force field (eg. QMPFF3).
- Introduces additional terms: electrostatic between charge clouds, exchange and dispersion.
- More time-consuming to evaluate.
- Limited improvement for “typical systems” ...
- ... but better transferability.

# Is Molecular Dynamics deterministic?

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Summary

- Molecular Dynamics expected to be deterministic!
- Small differences in the force field evaluation may introduce a chaotic behavior.
- Even the same program on different architectures may generate different trajectories.
- Observables unaffected (with exception for pathologic cases).

# MD Applications

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Summary

- Several thousands atoms.
- Time evolution for  $\mu s$ .
- Calculations of temperature-dependent effects.
- Folding processes.

## Deficiencies

- The part of the phase space sampled depends on the temperature and the starting point.
- Chemical reactions difficult to handle: eg. protonation state changes.

# MD Methodology

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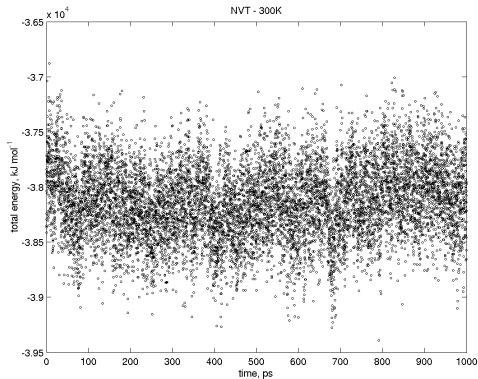
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Summary

- Start a calculation with a **equilibration phase**.
- Collect statistics.
- Stop when the properties converge.



# Molecular Dynamics: Summary

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Summary

- Properties as Time averages.
- Newtonian dynamics: propagation methods.
- Potentials determine the quality.
- Applications and Methodology.