

# Program

## I. OVERVIEW

1. Modern methods of computational chemistry (MM, ab initio, DFT and Hybrid methods).
2. Introduction to the Emerson Center's facilities
3. Intro (cont.)

## II. Molecular mechanics and Molecular Dynamics

### 4. Molecular Mechanics and Molecular Dynamics methods

5. Applications and Practical sessions on Problem solving

## III. Transition Metal Chemistry and Catalysis

6. Computational approaches to the Transition Metal Chemistry
7. Computational Catalysis (including Organic, Inorganic and Enzymatic)
8. Practical sessions on Problem solving.

## IV. PhotoChemistry and Excited State Studies

9. Introduction, Overview of Methodology, and some Typical Examples
10. A problem solving session on Spectroscopy, Radicals and PhotoChemistry

# Lecture 4:

## Molecular Mechanics, Force Fields, and Principles of Molecular Dynamics

# Outline

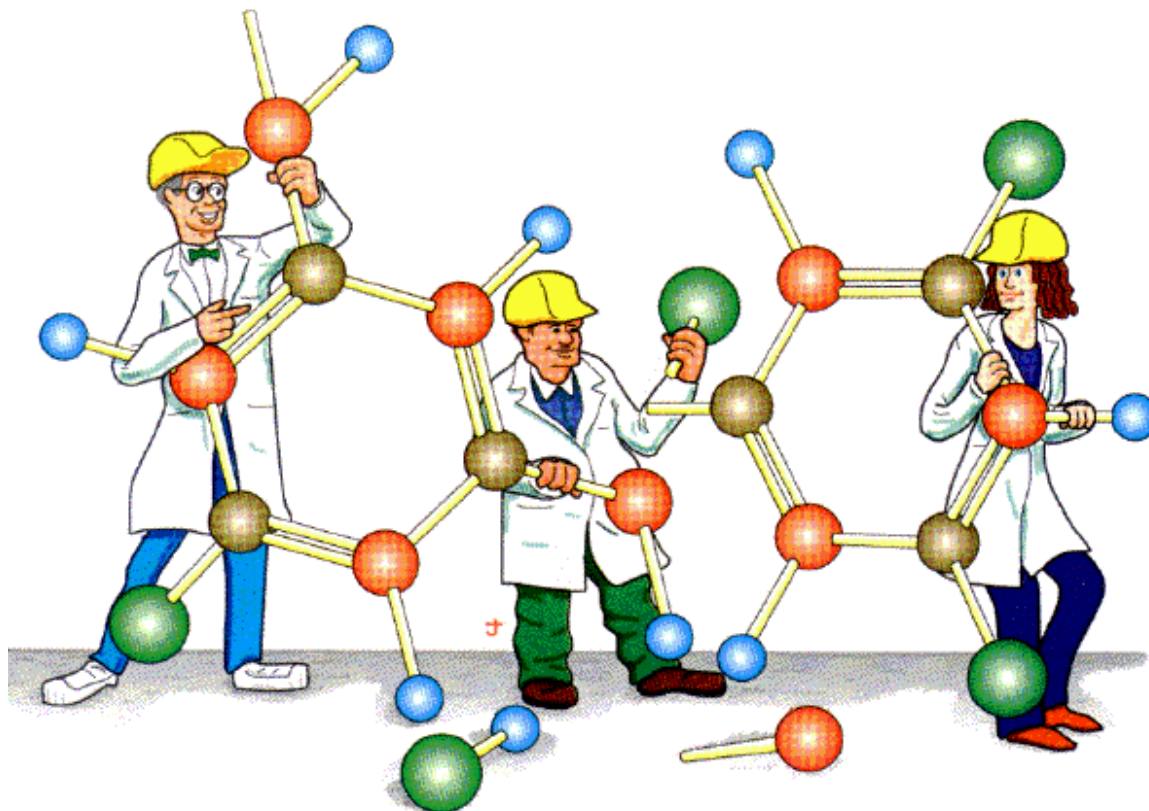
- **the basic premises of MM**
  - standard FF definitions & parameters
  - popular Force Field libraries
  - some illustrative examples
- **principles of MD simulations**
  - trajectory propagation
  - ensemble types
  - examples

# Basics of MM

- electronic SE:  $H(\mathbf{r};\mathbf{R})\Psi(\mathbf{r};\mathbf{R})=E(\mathbf{R})\Psi(\mathbf{r};\mathbf{R})$
- $E(\mathbf{R}) = \langle \Psi | H | \Psi \rangle$  the eigenvalue  $E$  is also called the “Force Field”  
(electron coordinates  $\mathbf{r}$  are averaged out)
- the aim of MM is to provide a value for the Force Field  $E$ , given  $\mathbf{R}$ , **without explicitly solving the electronic SE**
- in fact, MM uses basic chemical knowledge, and a good deal of empirical data, to approximate or **model** a molecule’s energy as a function of  $\mathbf{R}$ :

$$E_{\text{MM}}(\mathbf{R}) \Rightarrow E(\mathbf{R})$$

# Molecular Modeling



<https://dasher.wustl.edu/tinker/>

- i) what do we know about a molecule's structure?
- ii) bonding interactions?
- iii) non-bonding interactions?
- iv) charge distribution?

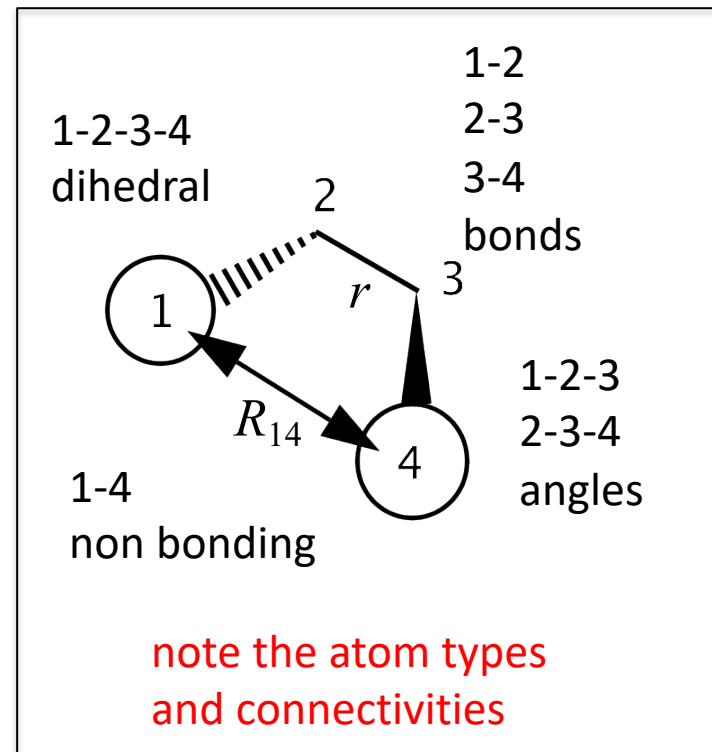
# A Generic Force Field

$$\begin{aligned}
 E_{total} = & \sum_{bonds} k_b (r - r_0)^2 \\
 & + \sum_{angles} k_\theta (\theta - \theta_0)^2 \\
 & + \sum_{dihedrals} V_n [1 + \cos(n\phi - \gamma)] \\
 & + \sum_{i=1}^{N-1} \sum_{j=i+1}^N \left[ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]
 \end{aligned}$$

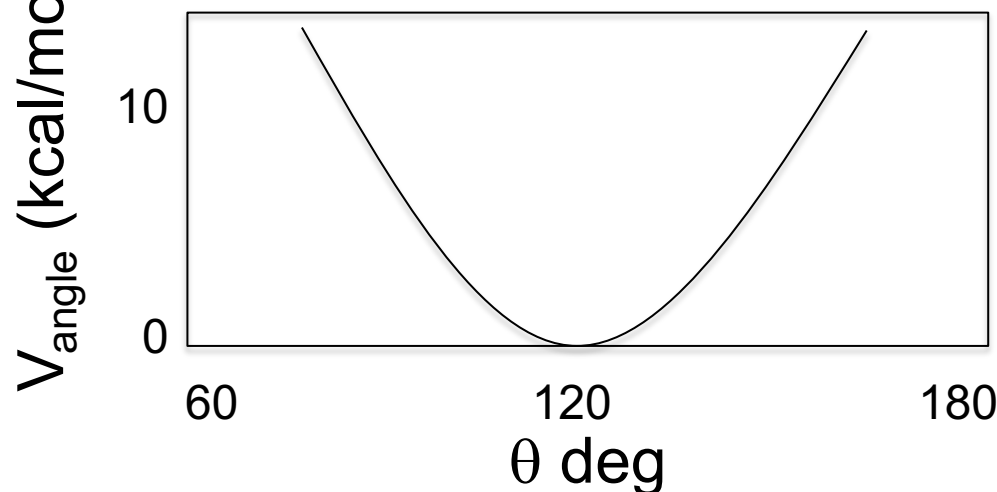
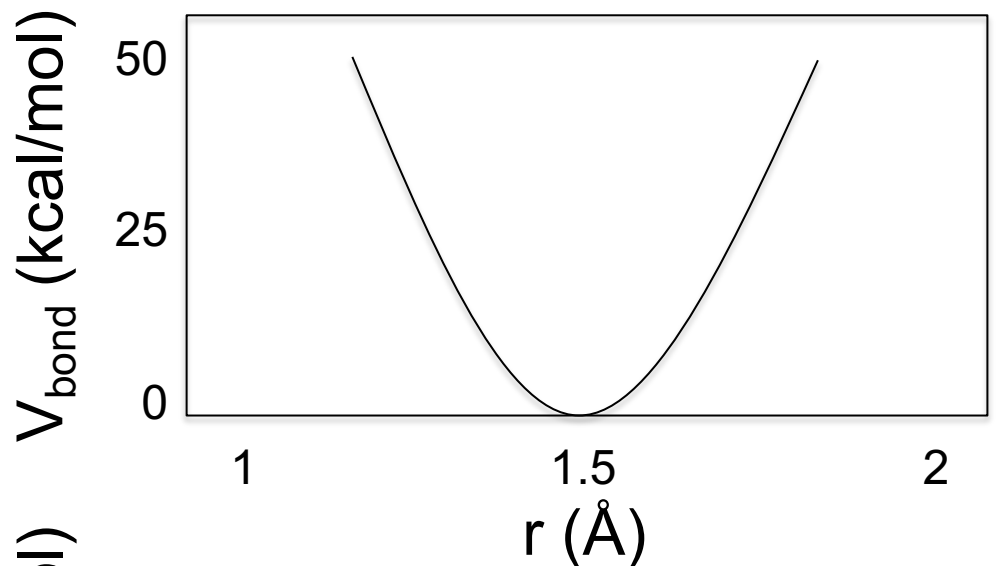
close-range repulsion

long-range VDW energy

electrostatic energy in a dielectric medium

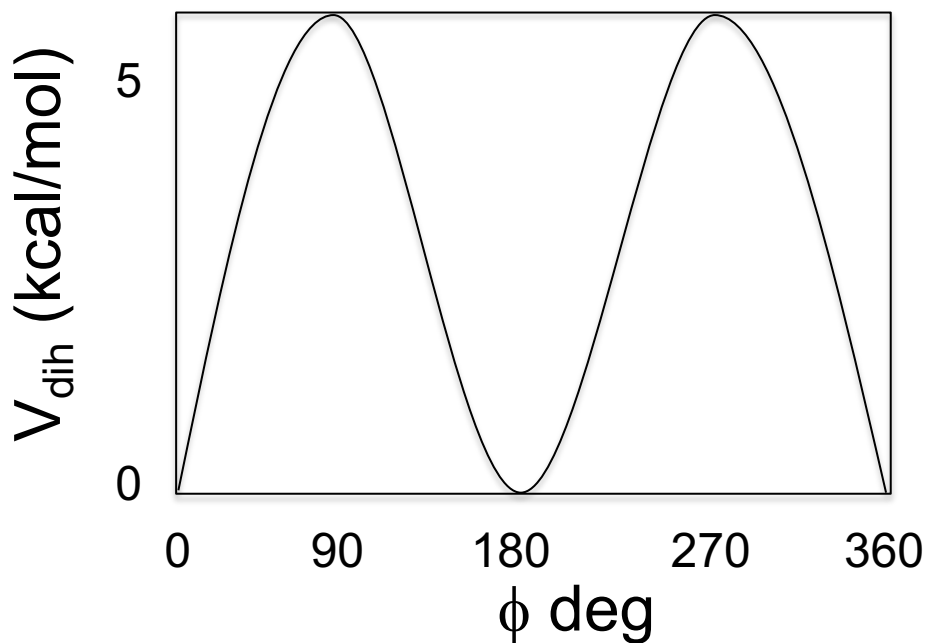


# Bonded interactions: bonds (stretch) & bond angles (bend)



- a) the bonds and angles are inflexible;
- b) the bonds cannot be broken, and
- c) no new bonds can be formed

# Bonded interactions: dihedral angles (torsion)

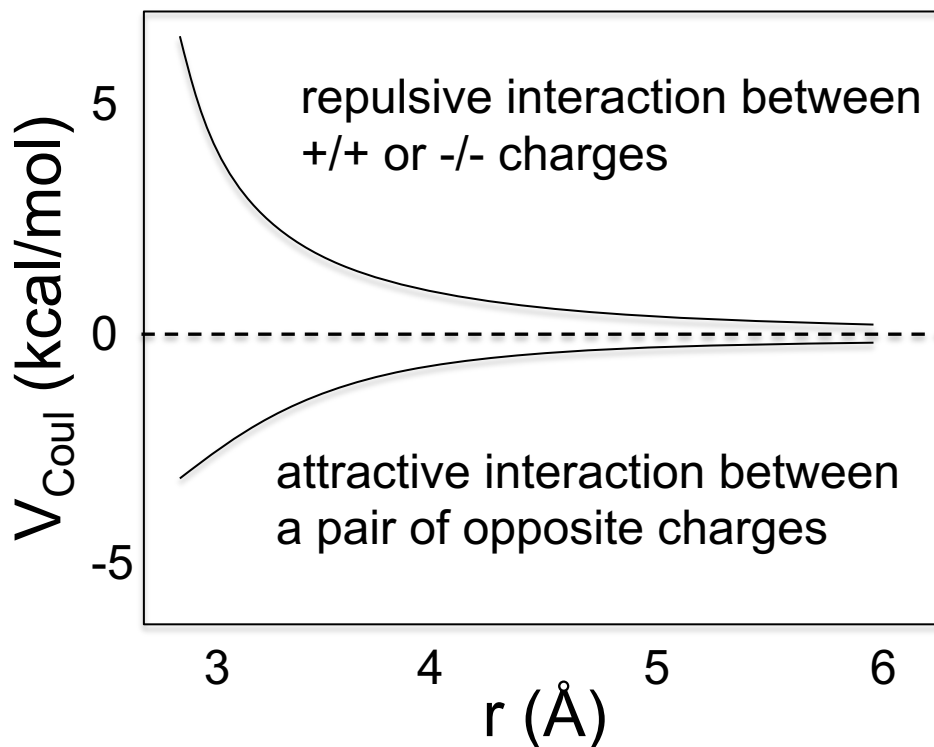


the torsional motion is described  
by sinusoidal “hindered rotor”  
potentials

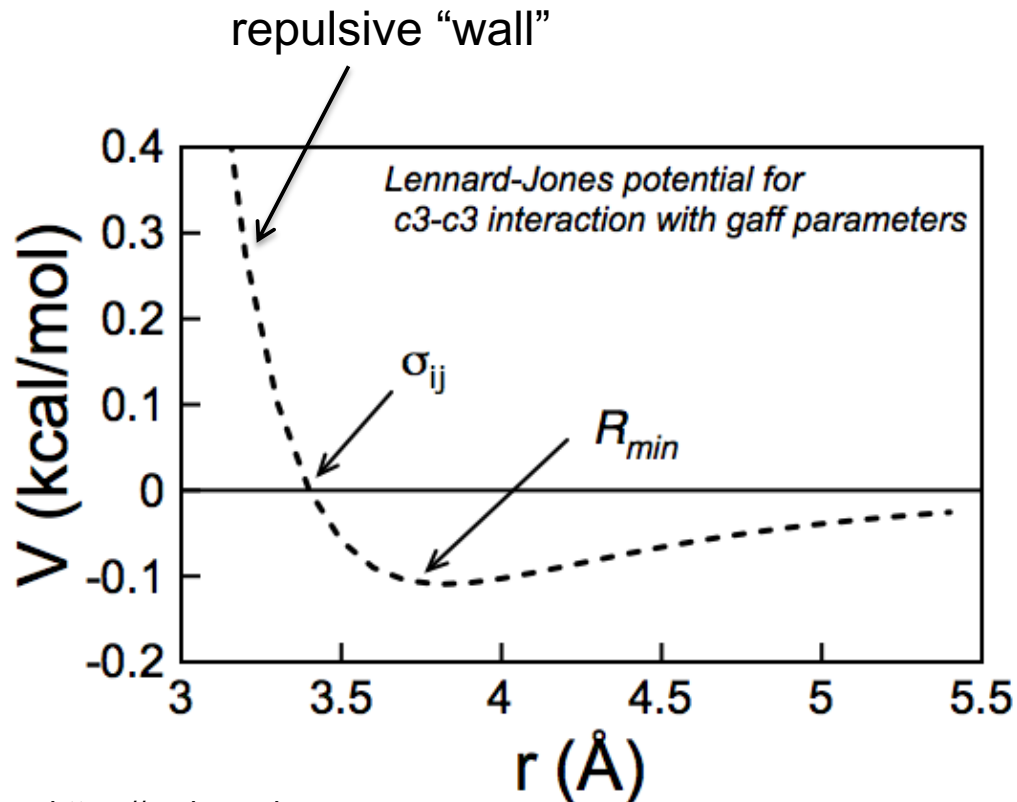




# Coulombic interactions



# Standard form of Van Der Waals interactions



$$V_{i,j} = \epsilon_{i,j} \left[ \left( \frac{R_{min}}{r_{i,j}} \right)^{12} - 2 \left( \frac{R_{min}}{r_{i,j}} \right)^6 \right]$$

$\epsilon_{i,j}$  is the long-range attraction energy between the  $i$ - $j$  pair

$R_{min}$  is the "range" of interaction

<https://ambermd.org>

# General Force Field considerations

- atom types are automatically assigned for all atoms
- force constants  $\mathbf{k}_r$   $\mathbf{k}_q$   $\mathbf{V}_n$  are tabulated for molecules containing 1st and 2nd row elements
- non-bonding  $\mathbf{A}_{ij}$   $\mathbf{B}_{ij}$  parameters are also available from the databases or *ab initio*/DFT calculations of diatomics
- fixed partial charges  $\mathbf{q}_i$  are tabulated, or derived from *ab initio*/DFT calculations: Electrostatic Potential (ESP) fitting
- any missing non-standard parameters are to be provided by user, for instance, those involving hypervalent elements, metal ions, heavy elements

# Popular Force Fields

**CHARMM** Chemistry HARvard Molecular Mechanics (M. Karplus)

**AMBER** UCSF/Scripps Research Institute (P. Kollman/D. Case)

**MM2/MM3** UGA (N. Allinger)

**OPLSA** Yale (W. Jorgensen)

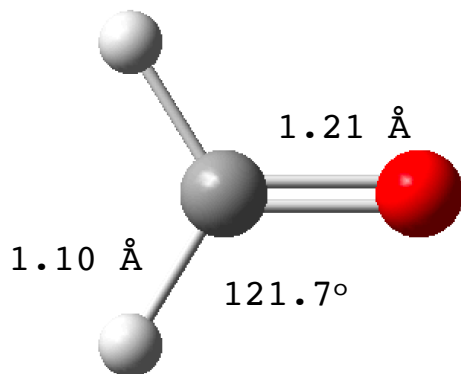
**GROMOS** U. of Groningen and others from EU

**AMOEBA** U. of Washington St. Louis (J. Ponder)

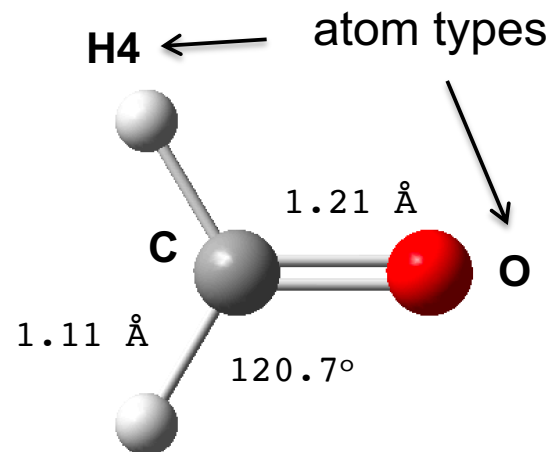
**+ many others**

# Simple Example 1: H<sub>2</sub>CO

Schrödinger Equation: MP2

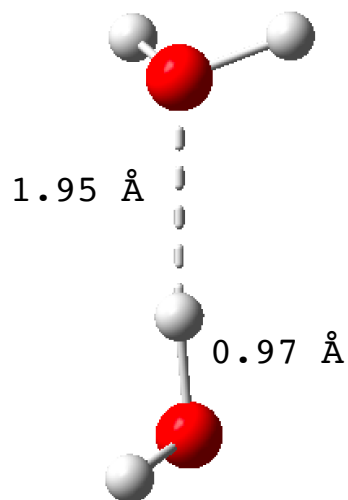


MM: AMBER

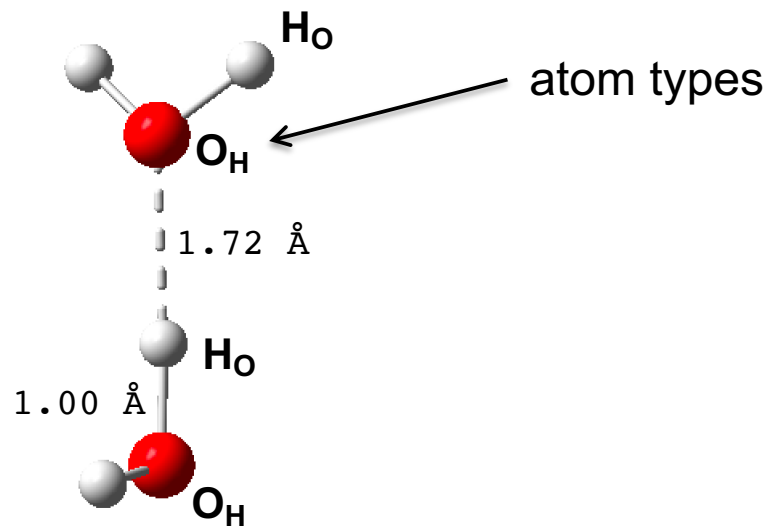


## Simple Example 2: $(\text{H}_2\text{O})_2$

Schrödinger Equation: MP2



MM: AMBER



# Basics of MD simulation: the Hamiltonian

System's ( $N$ -atom molecule) total energy, kinetic + potential, is called the Hamiltonian, after W. R. Hamilton (1805-1865)

$$H(v, R) = \sum_{i=1}^N \frac{m_i \vec{v}_i^2}{2} + V(R) = \text{const}$$

kinetic                      potential


$H$  is a conservative quantity, that is, it does not change with time.

# Basics of MD simulation: equations of motion (EOM)

Hamilton's classical EOM for an  $N$ -atom system

$$\dot{\vec{R}}_i = \vec{v}_i \quad \text{time rate of change of the position of atom } i$$

$$\dot{\vec{v}}_i = \frac{\vec{f}_i}{m_i} \quad \text{time rate of change of the velocity of atom } i$$


$$\ddot{\vec{R}}_i = \frac{\vec{f}_i}{m_i} = \vec{a}_i \quad \text{acceleration is proportional to the force}$$

aka **Newton's 2nd law**, discovered separately by I. Newton ca. 1680



# Basics of MD simulation: propagation of trajectories

1) Let  $R_0$  and  $v_0$  be the given initial conditions at time  $t = 0$ .

2) Let us choose a small enough time step  $\Delta t$

in real life  $\Delta t = 1 \text{ fs} = 10^{-15} \text{ s}$

3) Can we calculate  $R(t_n)$  and  $v(t_n)$  for a time sequence

$$t_n = n\Delta t, n = 0, 1, 2, \dots ?$$

# Basics of MD simulation: propagation of trajectories

4) We know that small changes in  $R$  and  $v$  are given by

$$\Delta R = v\Delta t \quad \Delta v = \frac{f}{m} \Delta t$$

5) Thus, the initial step takes the “system” to

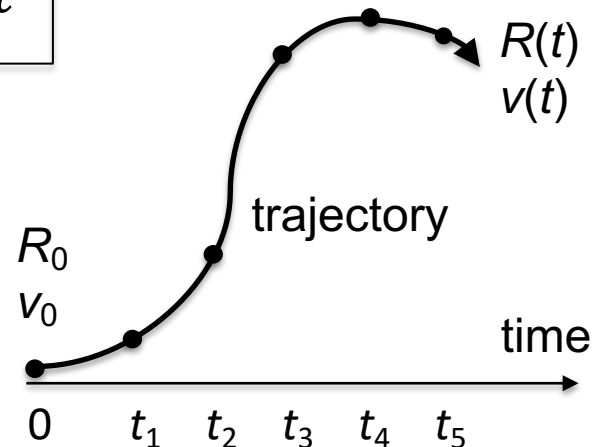
$$R(t_1) = R_0 + v_0 \Delta t \quad \text{and} \quad v(t_1) = v_0 + f_0 \Delta t / m$$

# Basics of MD simulation: propagation of trajectories

Euler's method (L. Euler 1707-1783)

$$R(t_{n+1}) = R(t_n) + v(t_n)\Delta t$$

$$v(t_{n+1}) = v(t_n) + \frac{f(t_n)}{m} \Delta t$$



# Basics of MD simulation: standard propagators

Euler (1st order);  
Taylor series to  $n$ -th order

unstable, never used  
(textbook material)

Verlet (3rd order);  
**Velocity-Verlet (3rd order)**

stable, efficient;  
often used

Predictor-Corrector family  
(4th order and higher)

stable, but expensive;  
used in very specific  
applications

Runge-Kutta (4th order)

stable, but expensive;  
seldom used in MD

Symplectic family  
(4th order)

stable, but expensive;  
used in matrix  
propagation MD apps.

# Basics of MD simulation: ensemble types by constants of motion

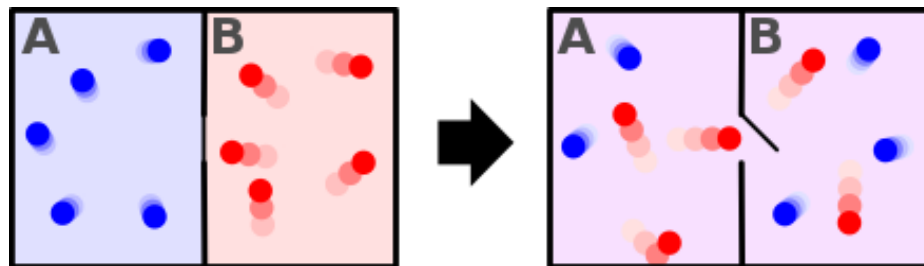
**NVE** -- **N** particles/**V**olume/**E**nergy (aka *Microcanonical* ensemble)

**NVT** -- **N** particles/**V**olume/**T**emperature (*Canonical*)

**NPT** -- **N** particles/**P**ressure/**T**emperature (*Isothermal-Isobaric*)

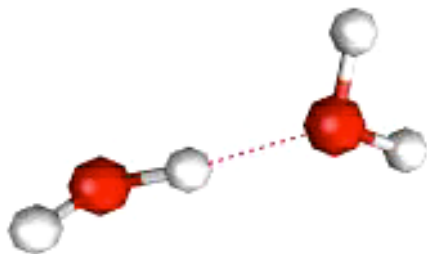
**NPH** -- **N** particles/**P**ressure/**H**elmholtz (*Isoenthalpic-Isobaric*)

$\mu$ **VT** -- Chemical Potential/**V**olume/**T**emperature (*Grand-Canonical*)





# visualization of MD trajectories using VMD: a water dimer



$T = 300\text{K}$

$\Delta t = 1\text{ fs}$

total time = 10 ps

method = velocity-verlet

FF = Amber

What ensemble is this?

# a summary

- simple FF definitions allow to carry out calculations on general molecular systems
- Standard MD simulation methods are available within all commercial and free packages
- simulations of proteins, bulk materials, in gas phase and in solution can be readily performed
- **can chemical reactions be modeled? (*to be continued*)**