

The background of the slide features a complex molecular simulation visualization. It includes a light blue ribbon structure representing a protein or polymer chain, a yellowish-orange semi-transparent surface representing a molecular surface or electron density map, and a stick model of a molecule with orange and grey atoms. The elements are layered and semi-transparent, creating a sense of depth and scientific complexity.

BIOC404 Biochemical Methods

Introduction to Biomolecular Simulations

Dr. Erich Kuechler

erich.kuechler@msl.ubc.ca

My Office Doesn't Matter Anymore

Introduction to biomolecular simulation

Lecture 1:
Molecular Dynamics
& Ensembles

Lecture 2:
Force Fields &
Solvation Models

Lecture 3:
Enhanced Sampling
Methods

Assignment:
Analyze simulation output and relate the findings to concepts introduced by the course.

Introduction to biomolecular simulation: Lecture 2



Part 1: Introduction to force fields

Part 2: Common force field terms

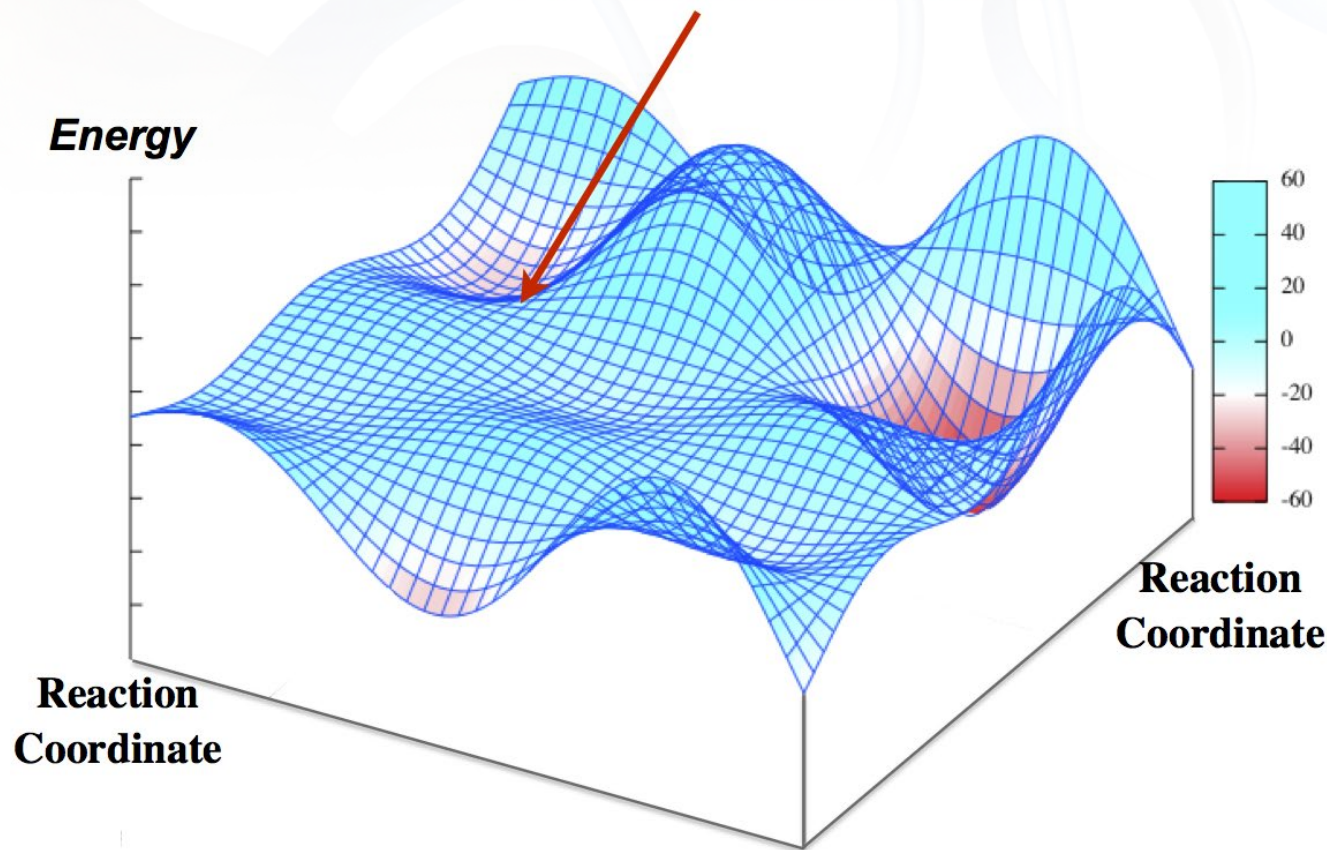
Part 3: Explicit and implicit solvation

Introduction to biomolecular simulation

Lecture 1: Molecular Dynamics & Ensembles

$$A_{obs} = \langle A \rangle_{\text{time}} = \langle A \rangle_{\text{ensemble}}$$

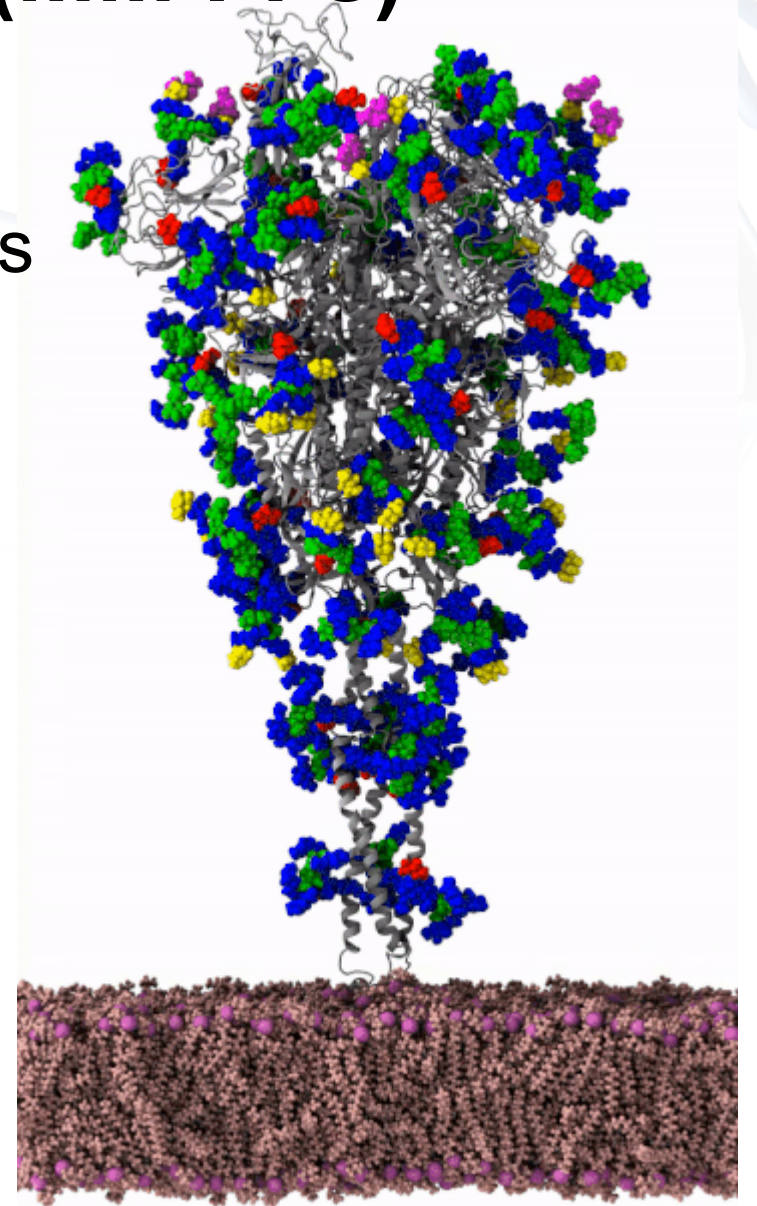
TS (Transition State)



Molecular Mechanics Force Fields (MM FFs)

“everything that living things do can be understood in terms of the jigglings and wigglings of atoms.” – Richard P. Feynman

$$\mathbf{F}_i = \dot{\mathbf{p}}_i - \frac{\partial U(\mathbf{r}^N)}{\partial \mathbf{r}_i}$$

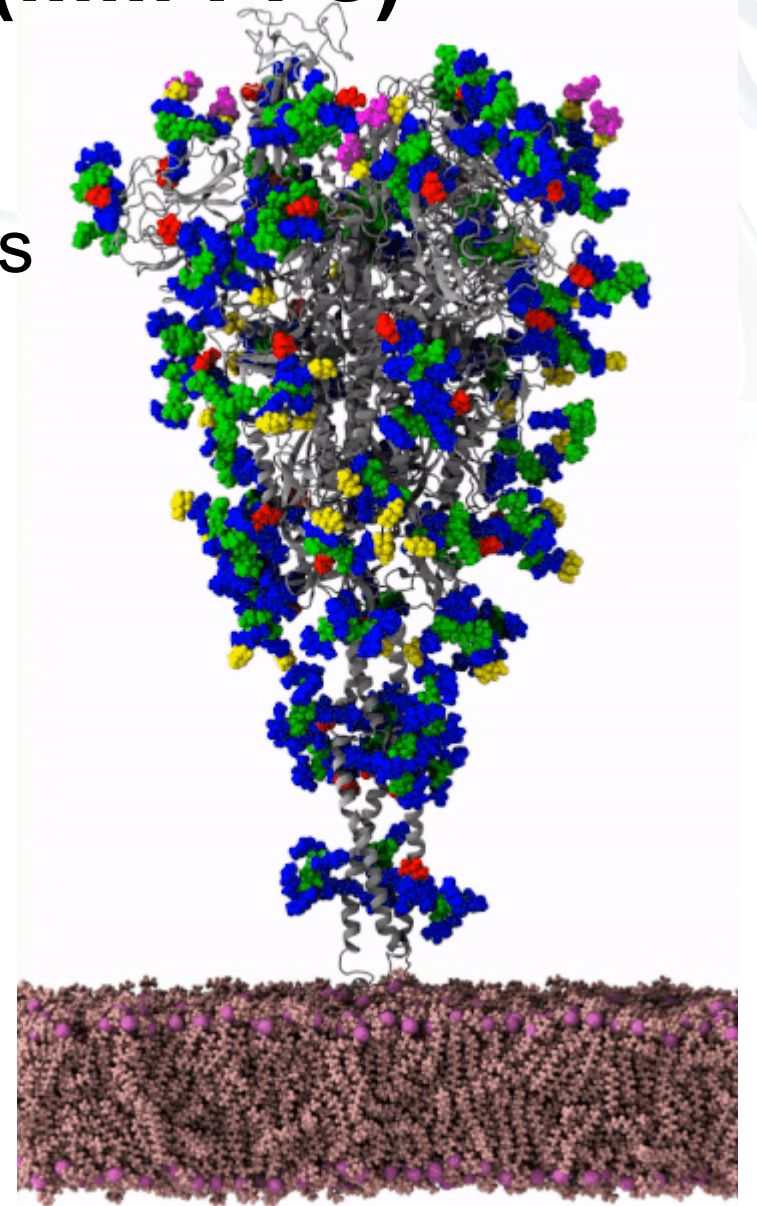


Molecular Mechanics Force Fields (MM FFs)

“everything that living things do can be understood in terms of the jiggings and wiggings of atoms.” – **Richard P. Feynman**

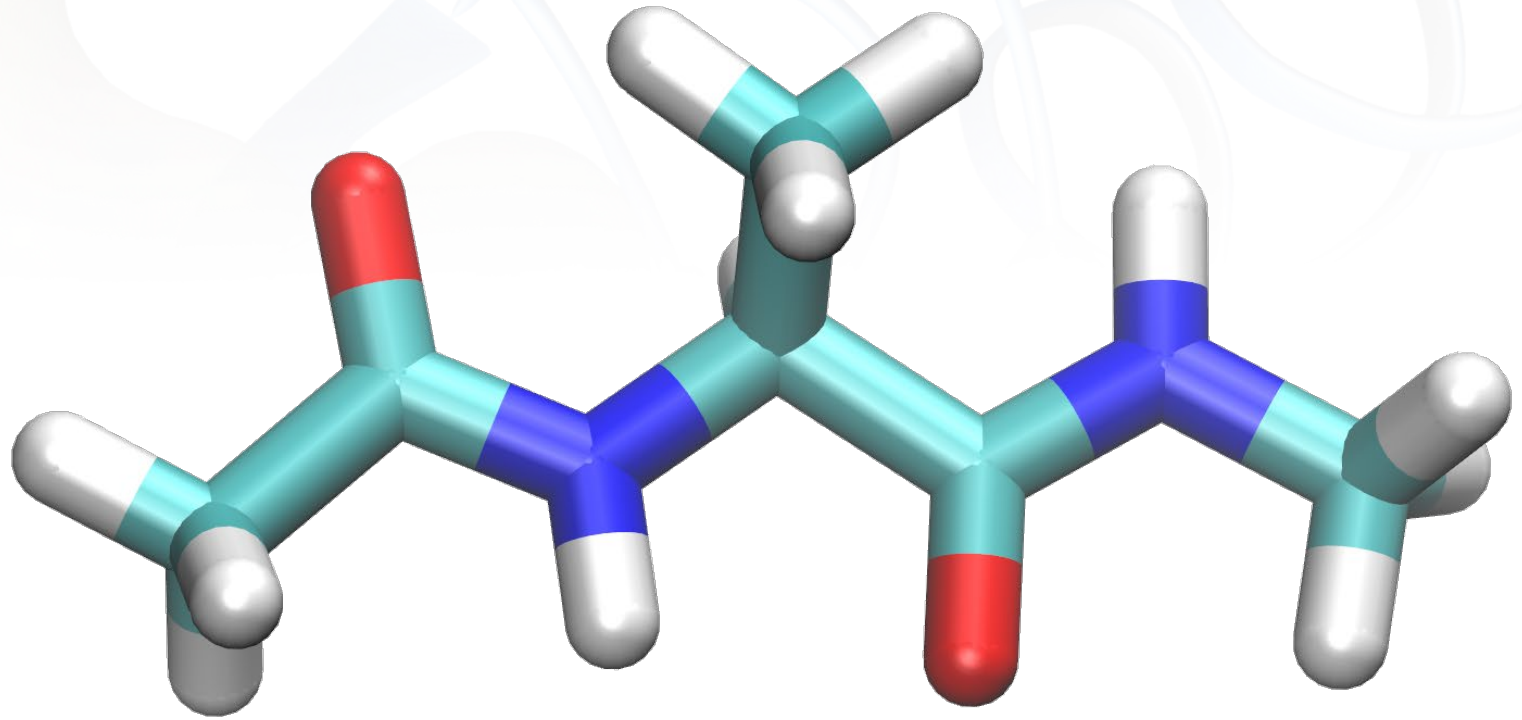
$$\mathbf{F}_i = \dot{\mathbf{p}}_i - \frac{\partial U(\mathbf{r}^N)}{\partial \mathbf{r}_i}$$

Force fields are a mathematical expression to define the **potential energy surface** in a simulation.



Molecular Mechanics Force Fields (MM FFs)

Force fields are a mathematical expression to define the **potential energy surface** in a simulation.

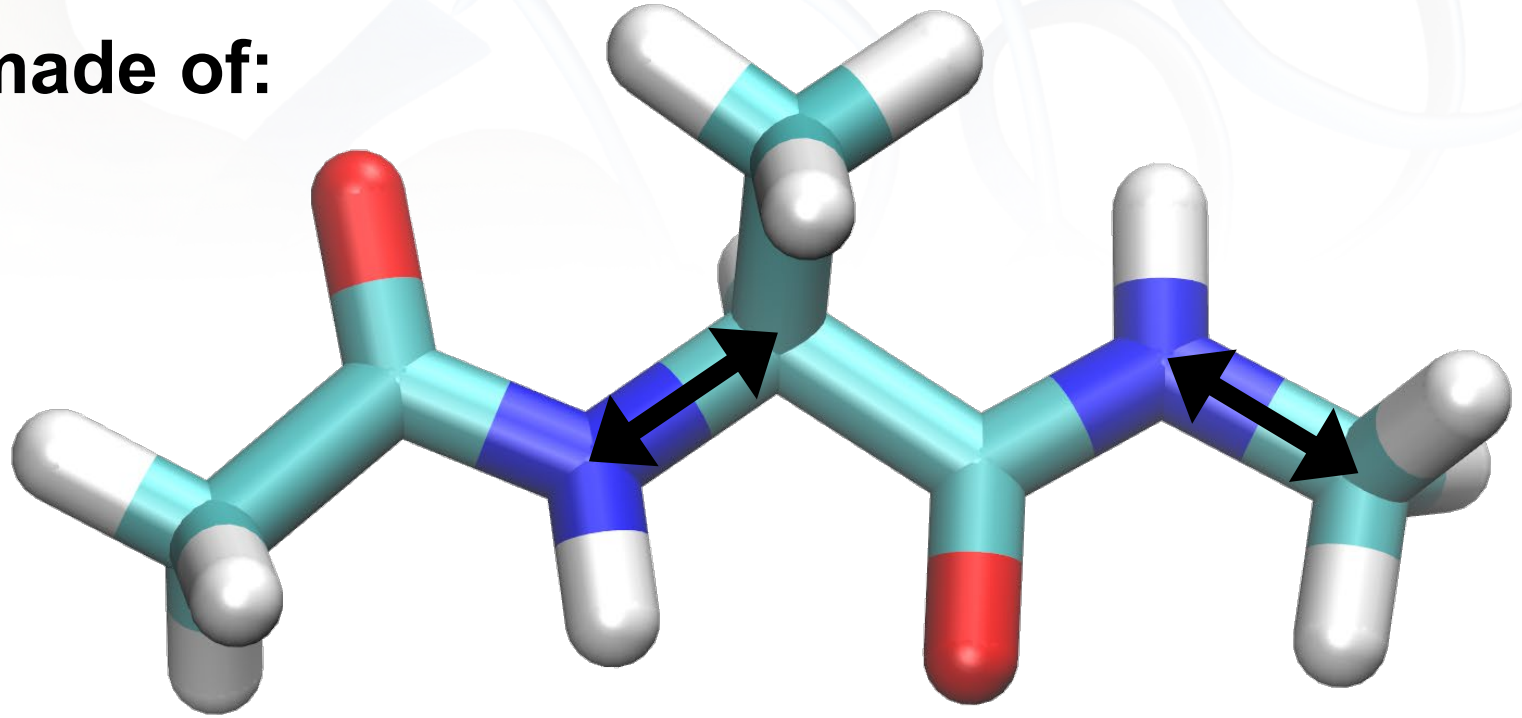


Molecular Mechanics Force Fields (MM FFs)

Force fields are a mathematical expression to define the **potential energy surface** in a simulation.

In MD, FFs are generally made of:

- Bond

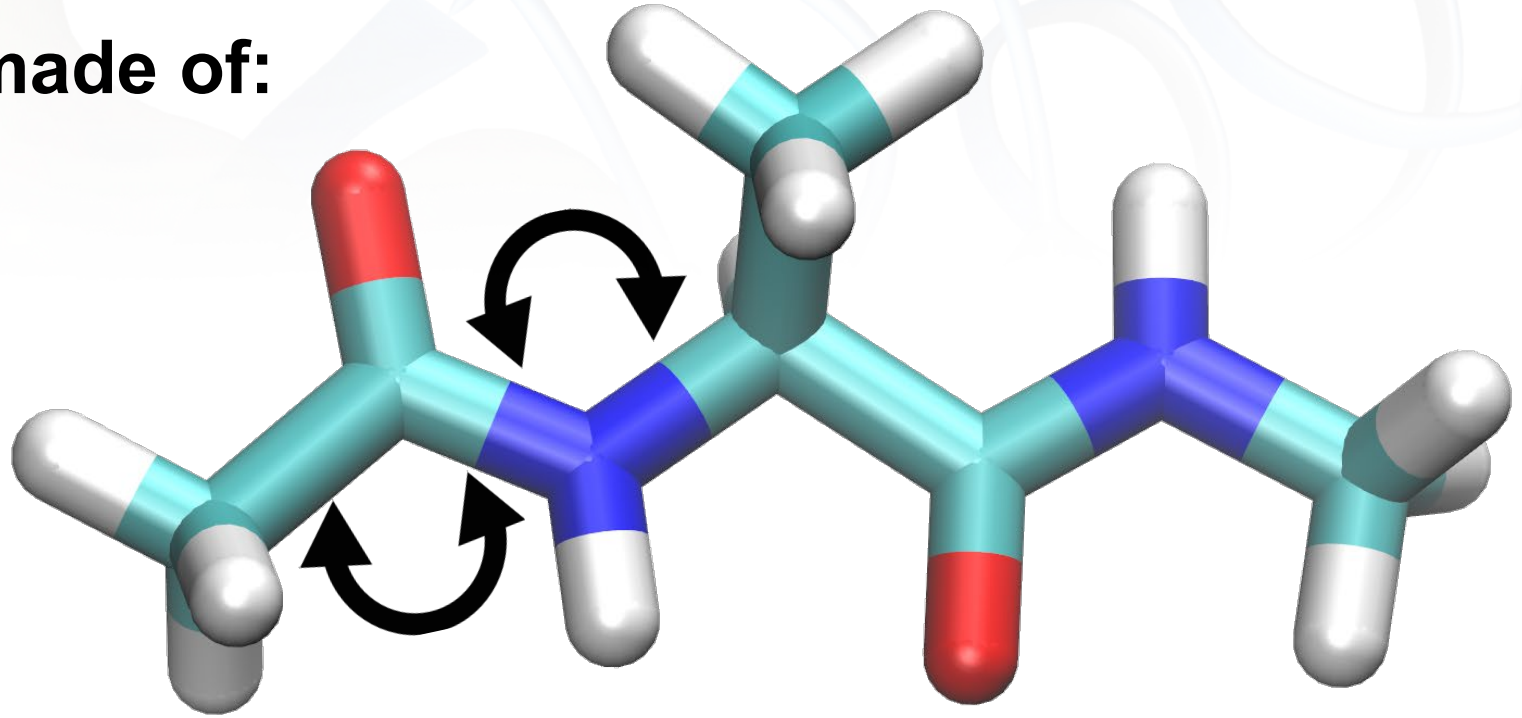


Molecular Mechanics Force Fields (MM FFs)

Force fields are a mathematical expression to define the **potential energy surface** in a simulation.

In MD, FFs are generally made of:

- Bond
- Angle

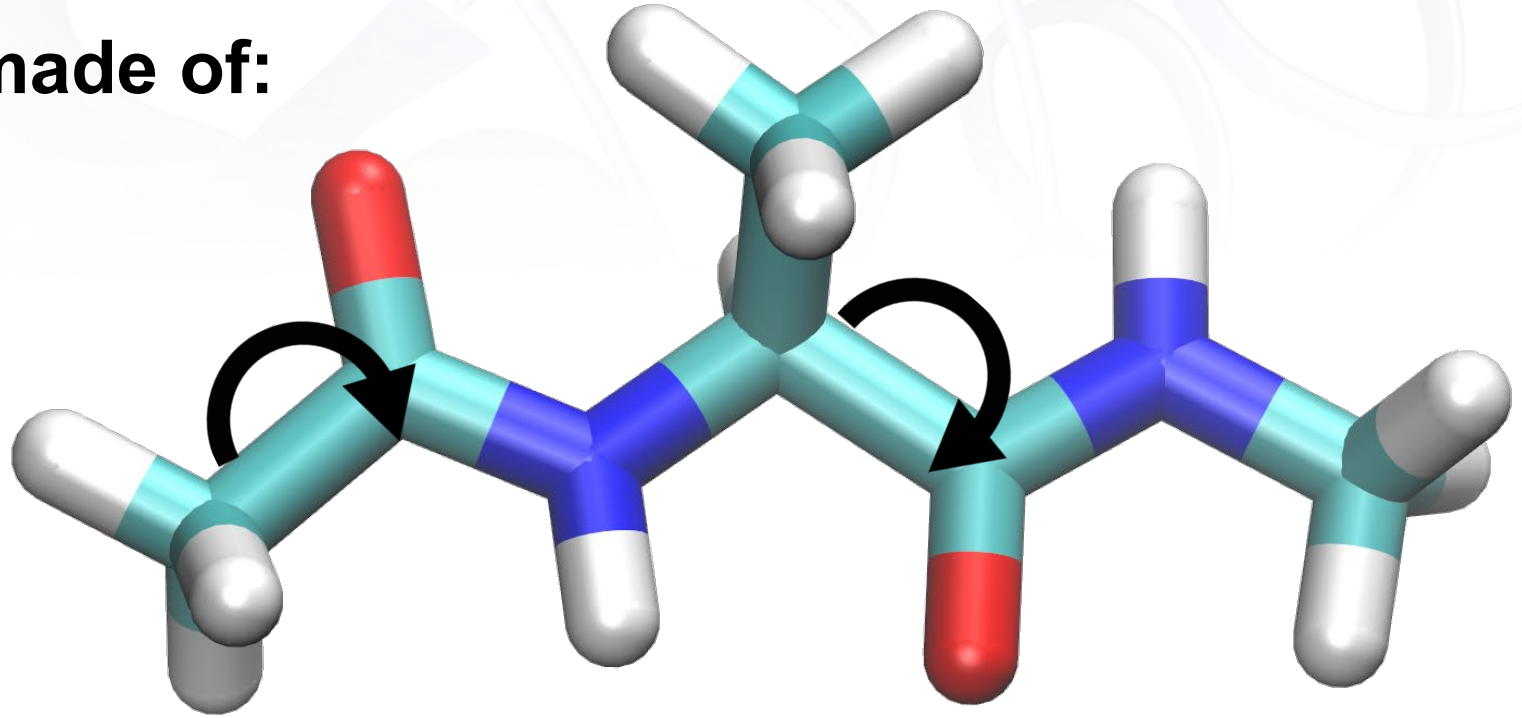


Molecular Mechanics Force Fields (MM FFs)

Force fields are a mathematical expression to define the **potential energy surface** in a simulation.

In MD, FFs are generally made of:

- Bond
- Angle
- Torsion

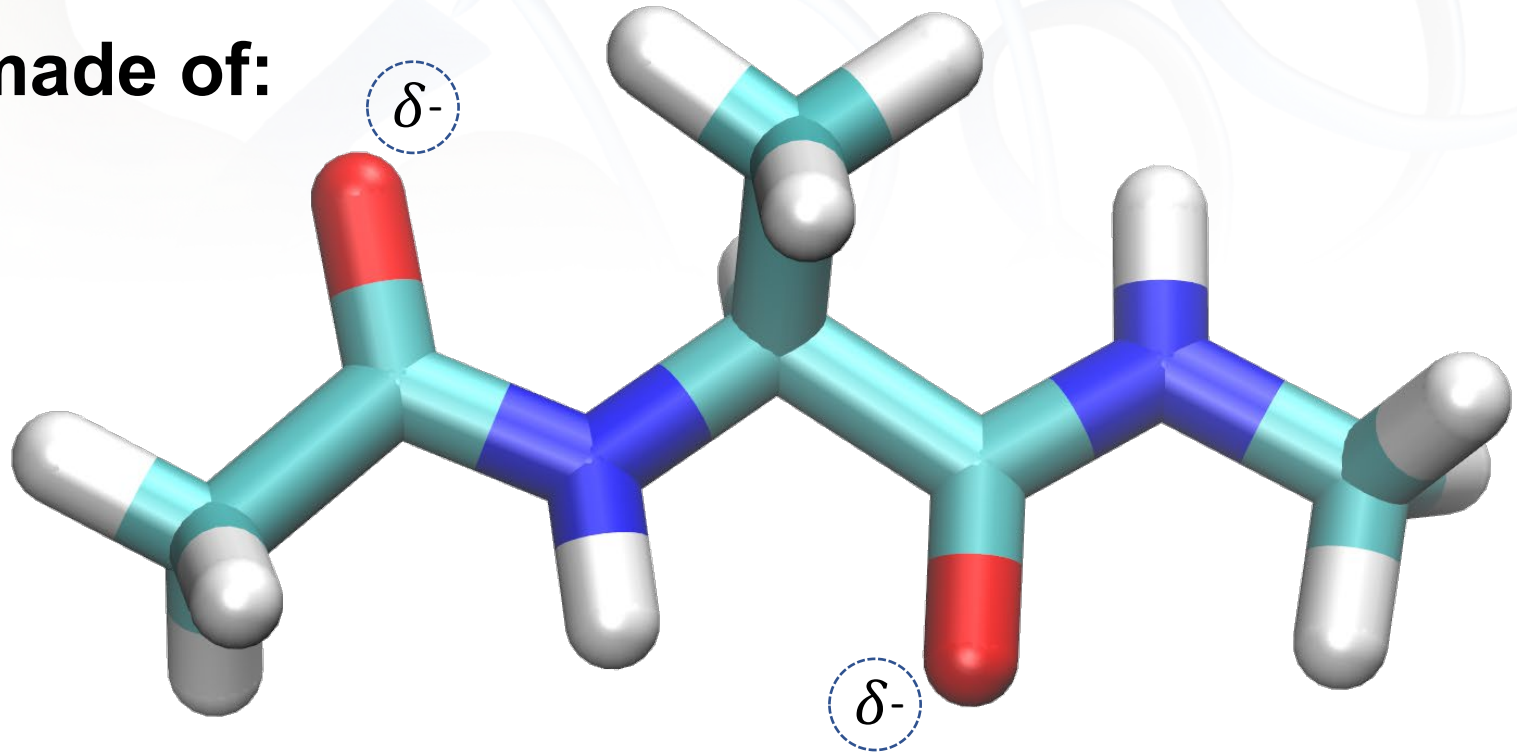


Molecular Mechanics Force Fields (MM FFs)

Force fields are a mathematical expression to define the **potential energy surface** in a simulation.

In MD, FFs are generally made of:

- Bond
- Angle
- Torsion
- Charge

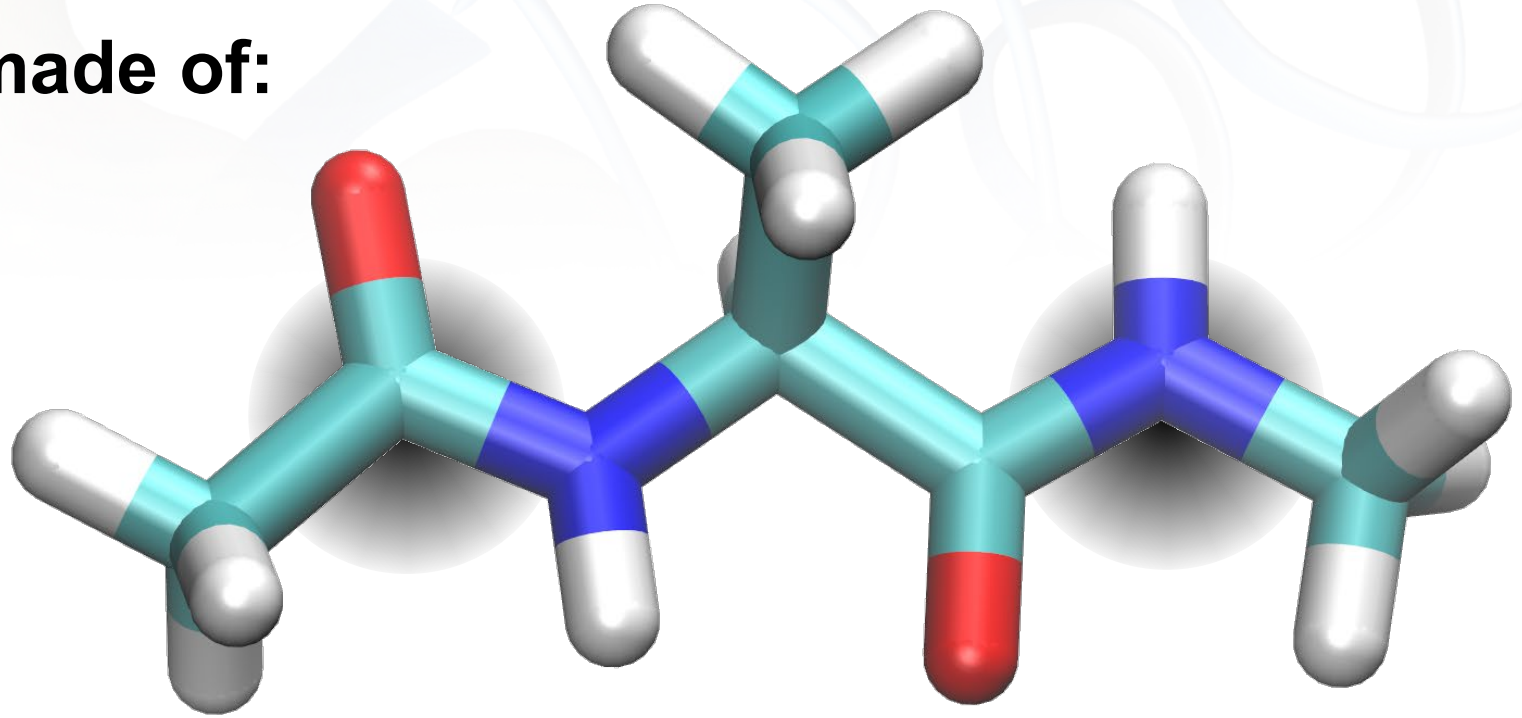


Molecular Mechanics Force Fields (MM FFs)

Force fields are a mathematical expression to define the **potential energy surface** in a simulation.

In MD, FFs are generally made of:

- Bond
- Angle
- Torsion
- Charge
- van der Waals

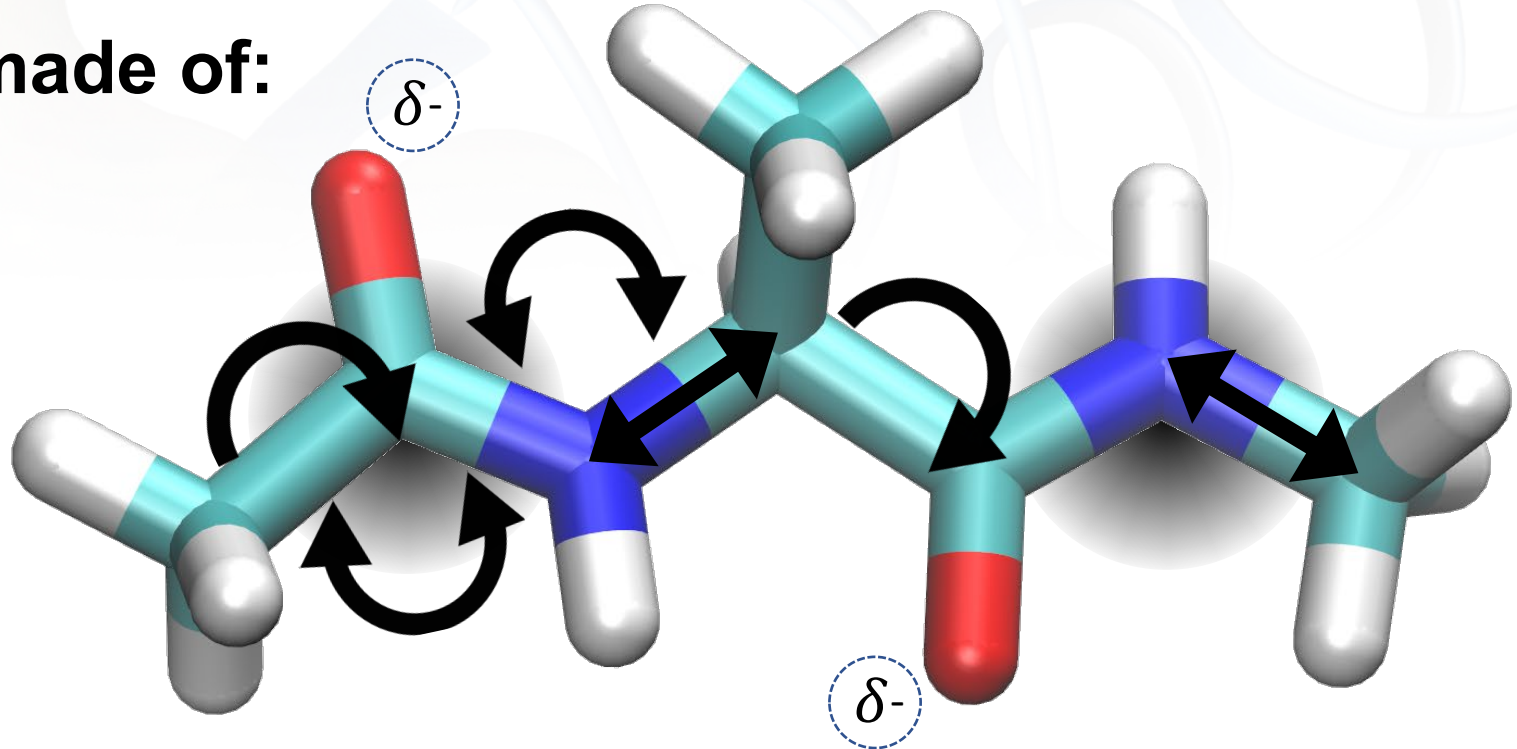


Molecular Mechanics Force Fields (MM FFs)

Force fields are a mathematical expression to define the **potential energy surface** in a simulation.

In MD, FFs are generally made of:

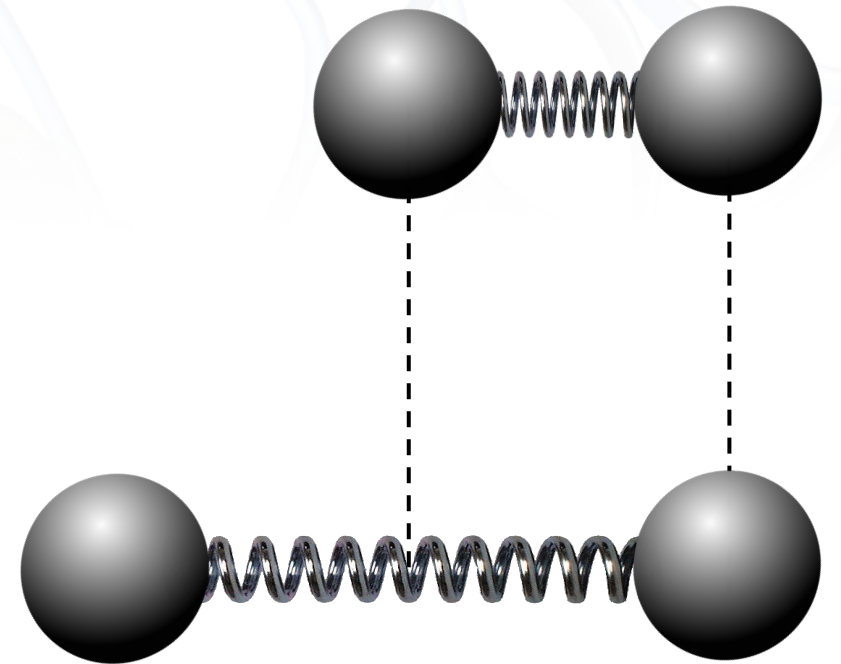
- Bond
- Angle
- Torsion
- Charge
- van der Waals



Force field parameters depend on **local electronic environment** and might be tuned for **specific properties**. Choice of force field can be **extremely** important!

Molecular Mechanics Force Fields (MM FFs)

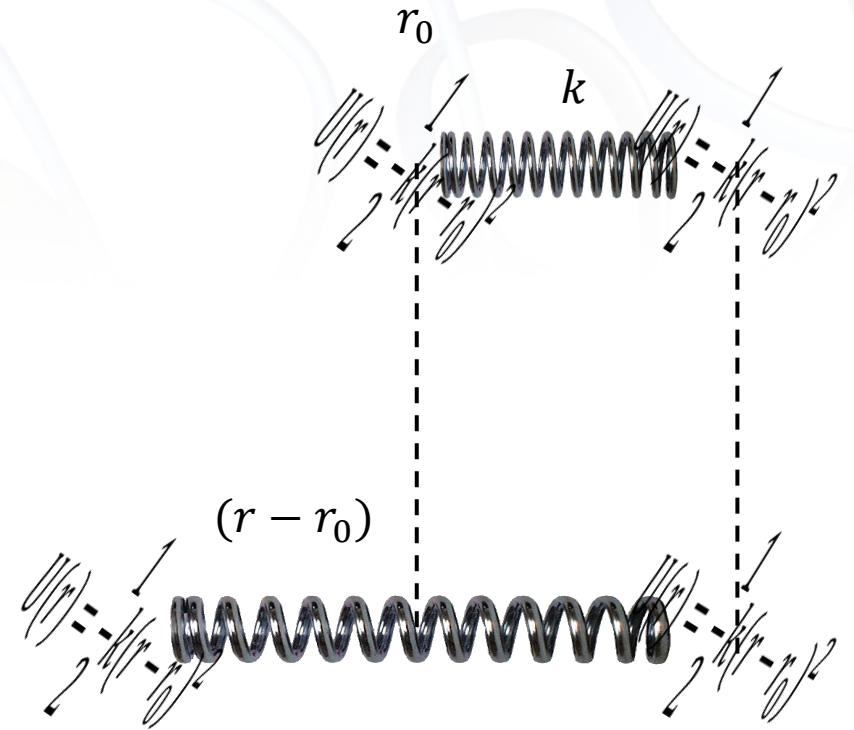
Chemical bonds are *most commonly* expressed through some variation of Hooke's Law.



Molecular Mechanics Force Fields (MM FFs)

Chemical bonds are *most commonly* expressed through some variation of Hooke's Law.

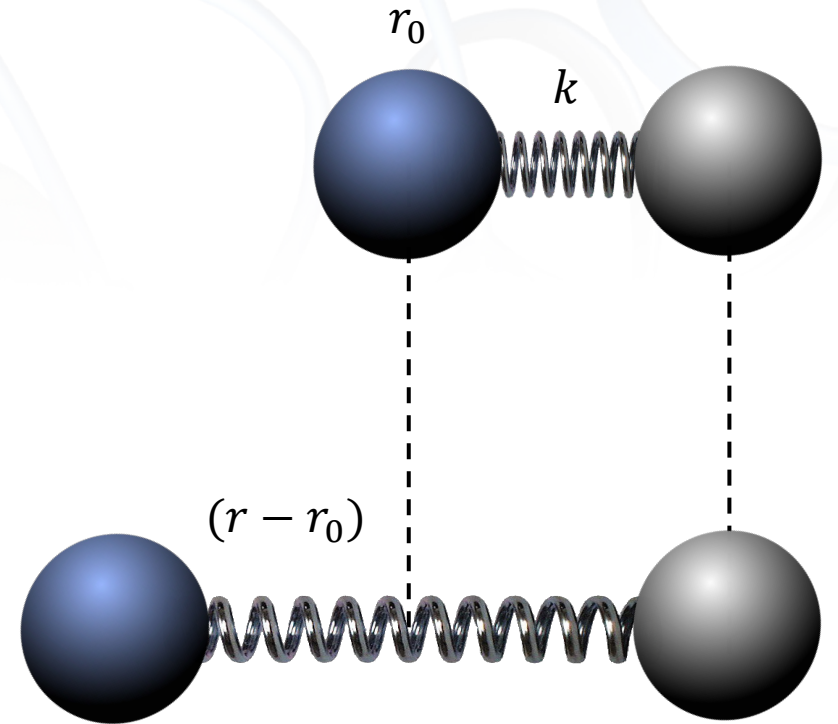
$$U(r) = \frac{1}{2} k (r - r_0)^2$$



Molecular Mechanics Force Fields (MM FFs)

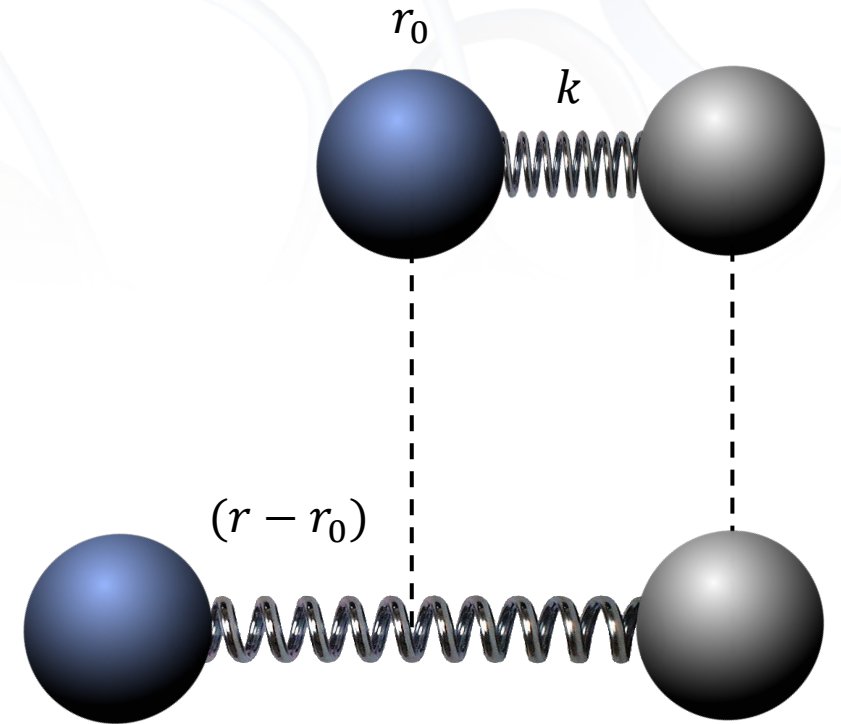
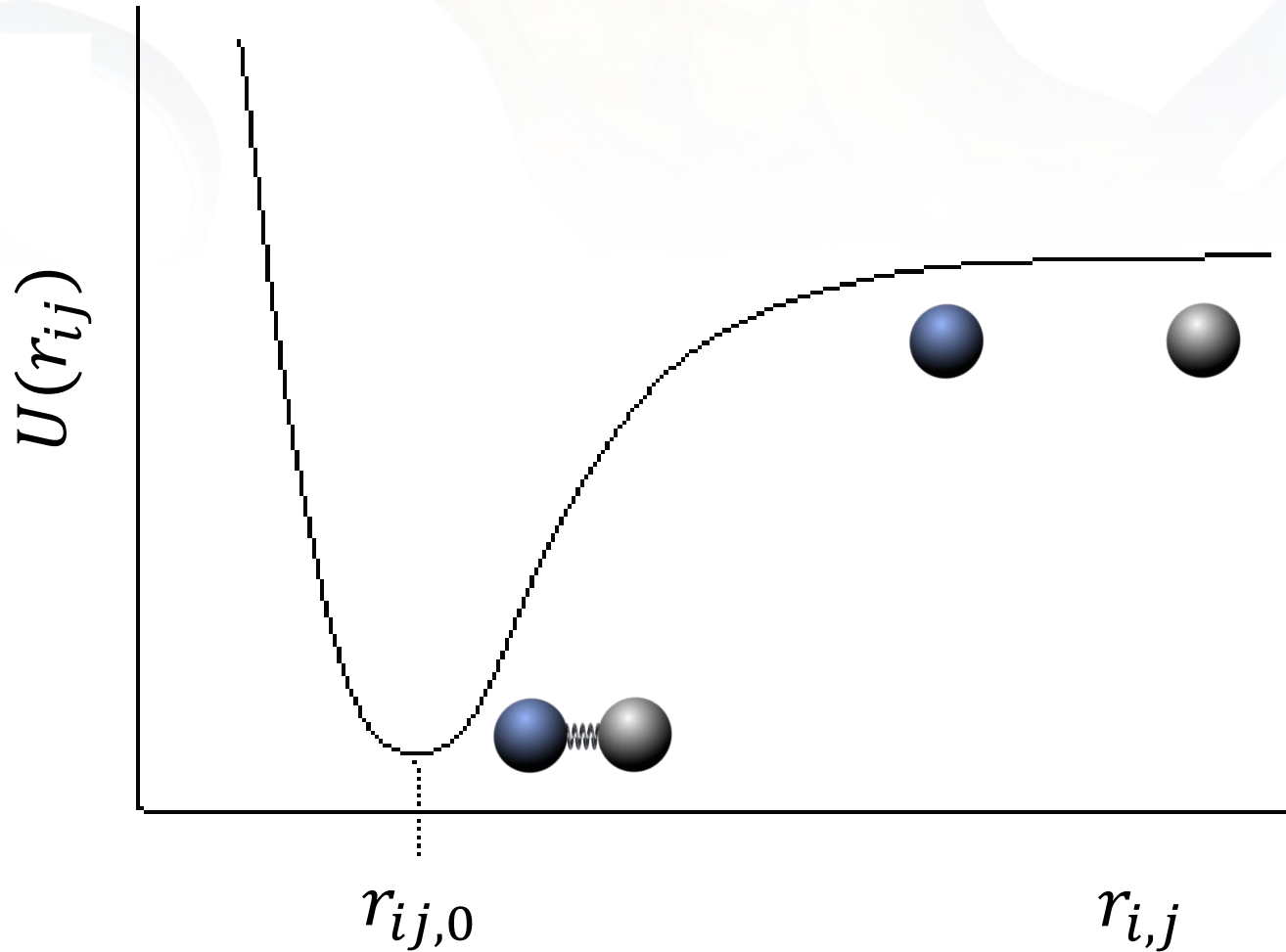
Chemical bonds are *most commonly* expressed through some variation of Hooke's Law.

$$U(r_{ij}) = \frac{1}{2} k_{ij} (r_{ij} - r_{ij,0})^2$$



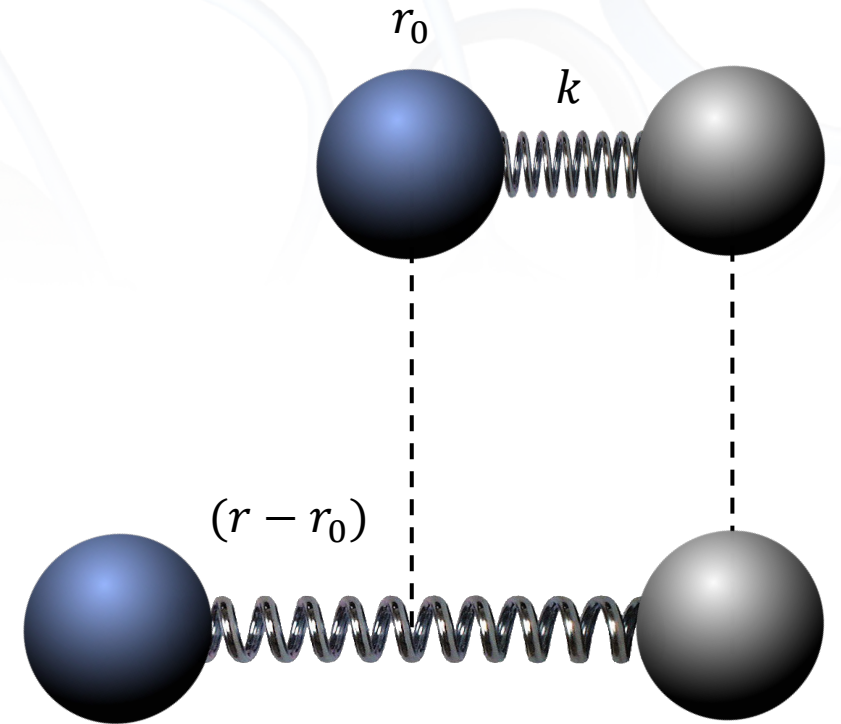
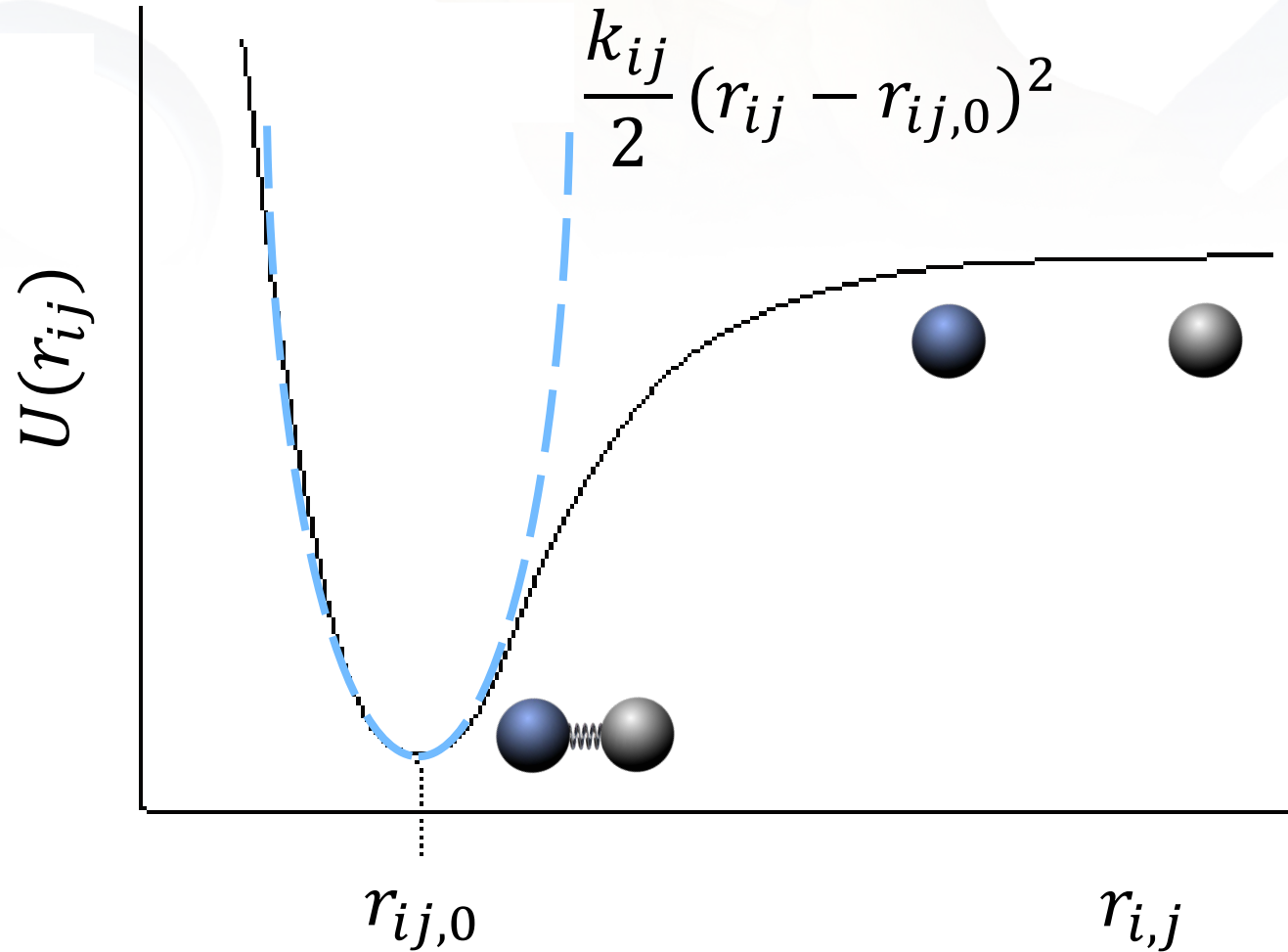
Molecular Mechanics Force Fields (MM FFs)

Chemical bonds are *most commonly* expressed through some variation of Hooke's Law.



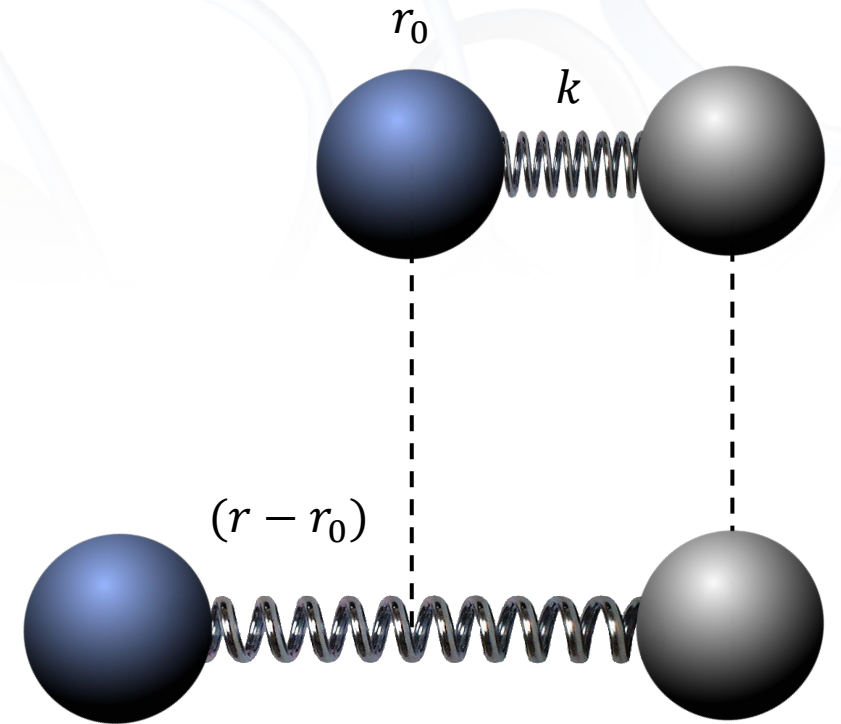
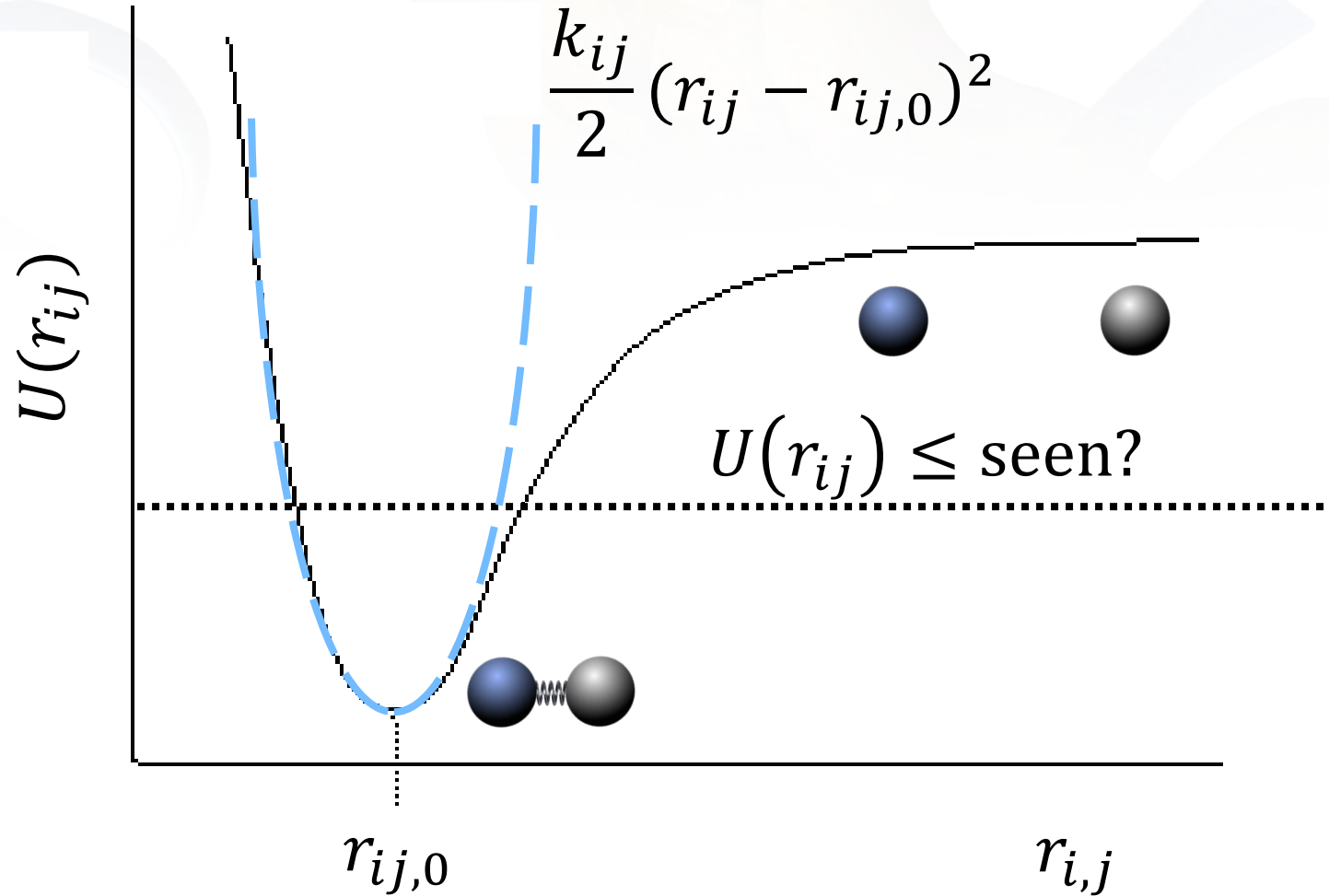
Molecular Mechanics Force Fields (MM FFs)

Chemical bonds are *most commonly* expressed through some variation of Hooke's Law.



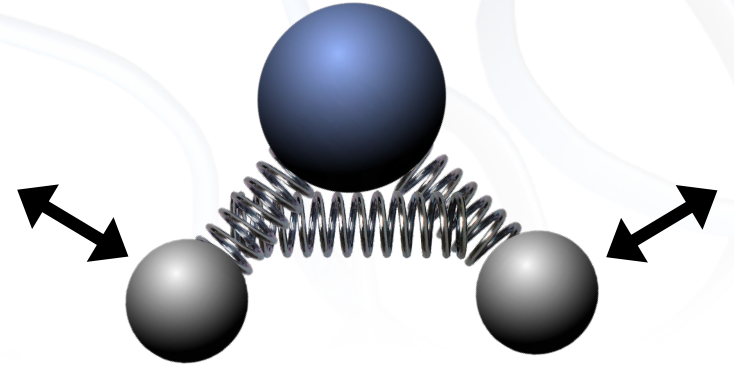
Molecular Mechanics Force Fields (MM FFs)

Chemical bonds are *most commonly* expressed through some variation of Hooke's Law.



Molecular Mechanics Force Fields (MM FFs)

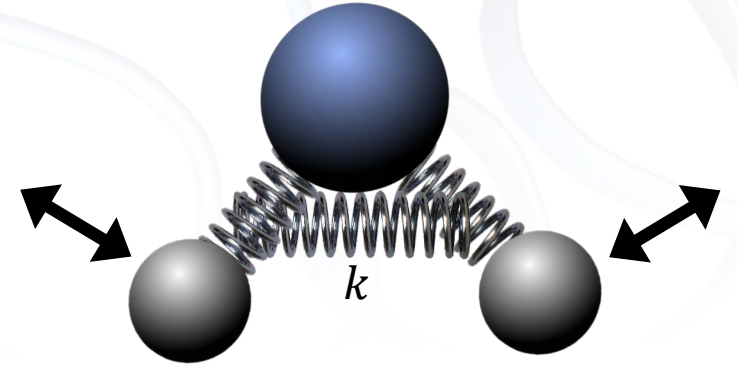
Bond angles are also expressed similarly.



Molecular Mechanics Force Fields (MM FFs)

Bond angles are also expressed similarly.

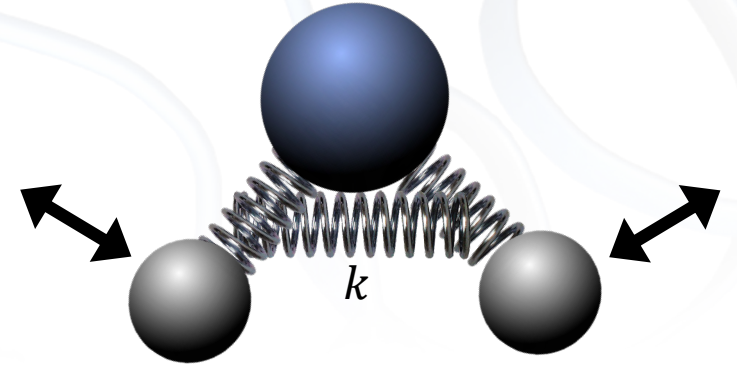
$$U(r) = \frac{1}{2} k (\theta - \theta_0)^2$$



Molecular Mechanics Force Fields (MM FFs)

Bond angles are also expressed similarly.

$$U(r) = \frac{1}{2} k (\theta - \theta_0)^2$$

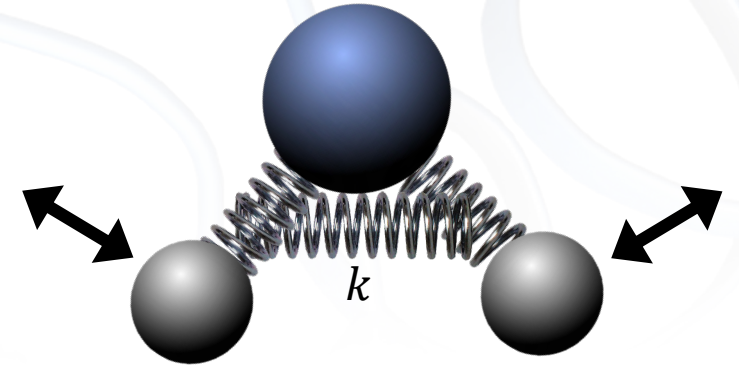


Bond distances and **angles** are sometimes called ‘hard’ degrees of freedom as compared to the remaining terms.

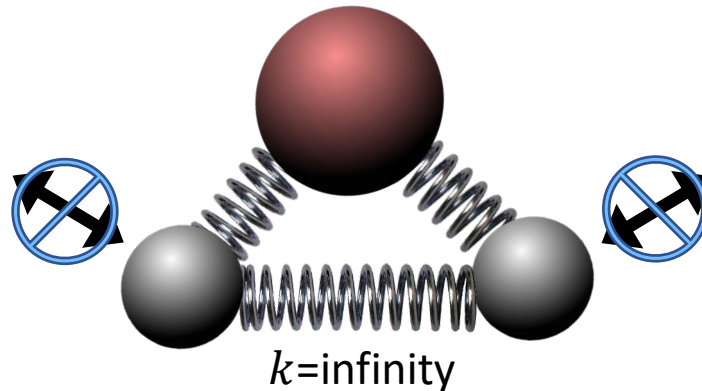
Molecular Mechanics Force Fields (MM FFs)

Bond angles are also expressed similarly.

$$U(r) = \frac{1}{2} k (\theta - \theta_0)^2$$



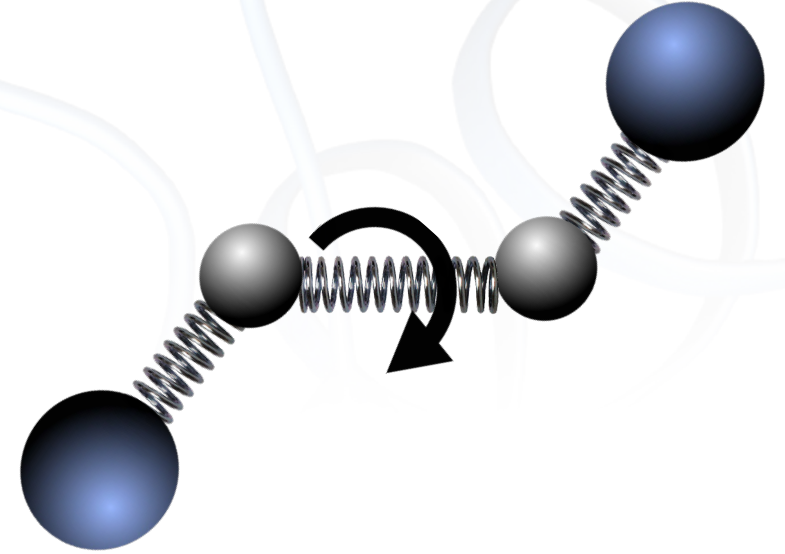
Special case: water



Molecular Mechanics Force Fields (MM FFs)

So are **dihedral angles**

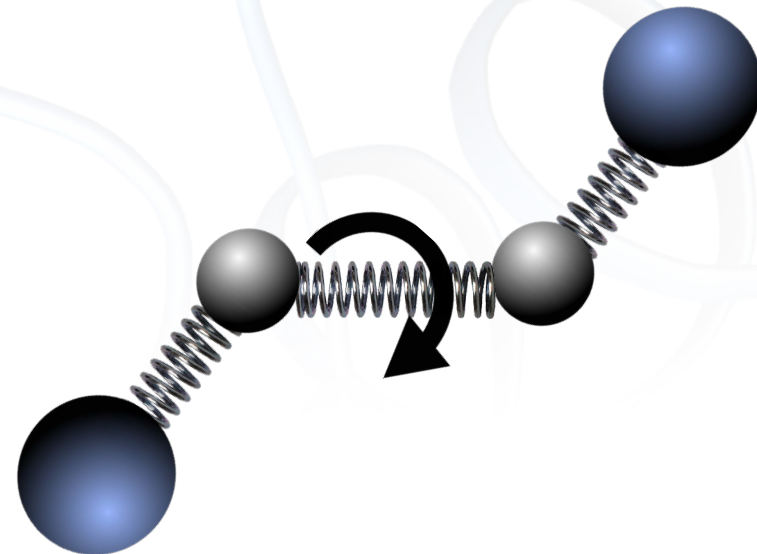
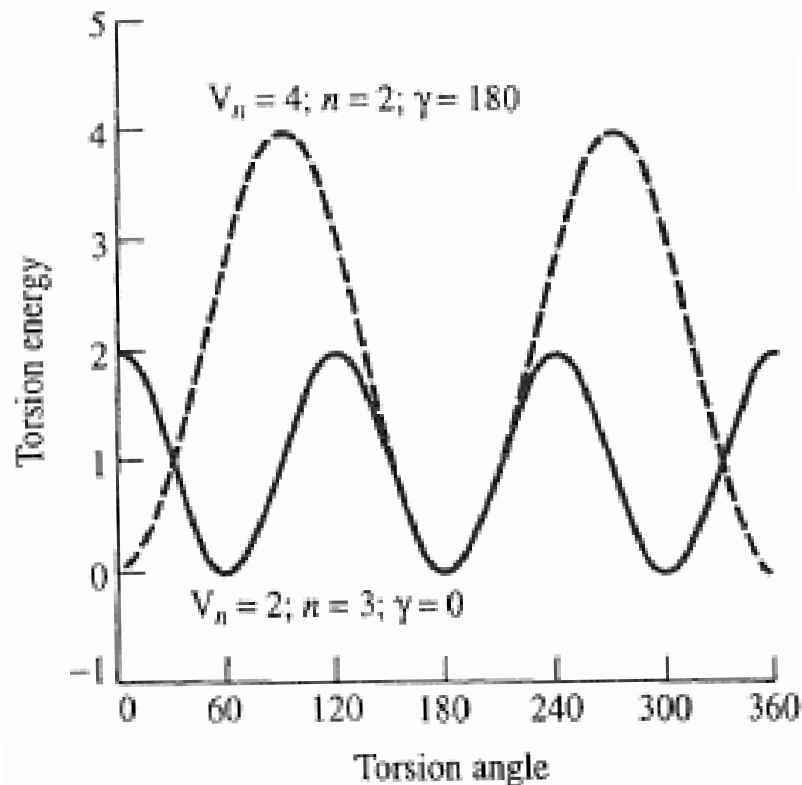
$$U(r) = \sum_{n=0}^N \frac{1}{2} V_n [1 + \cos(n\omega - \gamma)]$$



Molecular Mechanics Force Fields (MM FFs)

So are **dihedral angles**

$$U(r) = \sum_{n=0}^N \frac{1}{2} V_n [1 + \cos(n\omega - \gamma)]$$

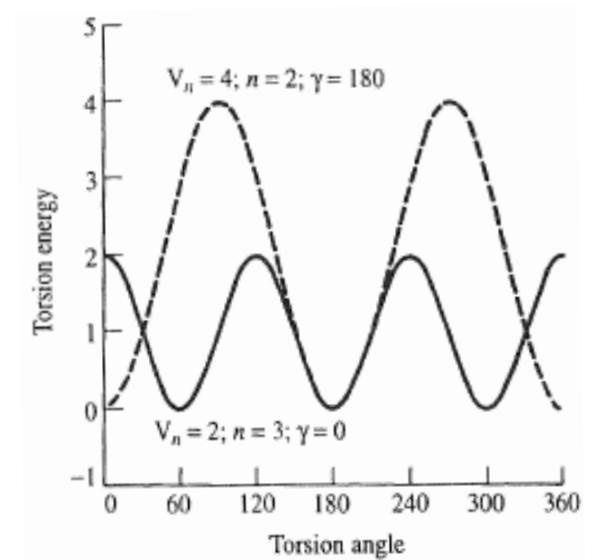
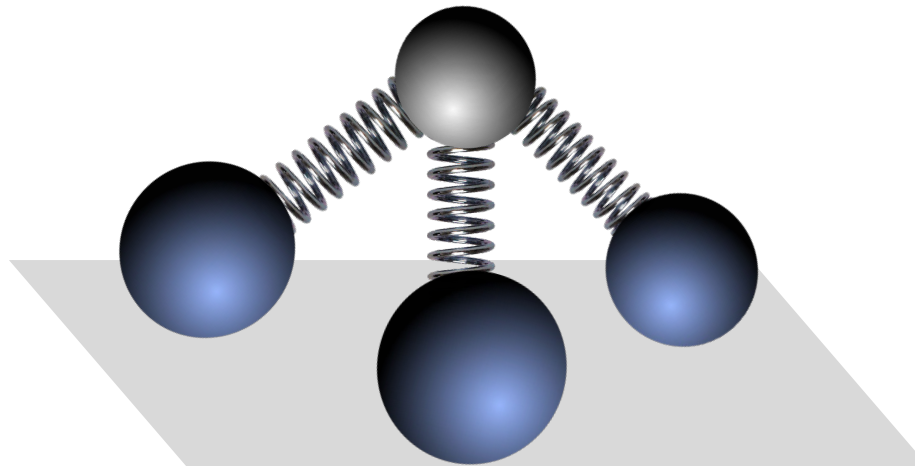
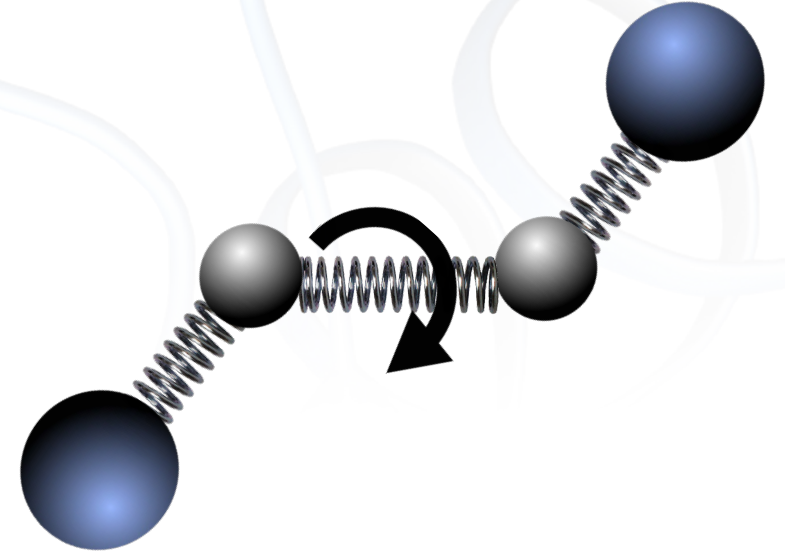


Molecular Mechanics Force Fields (MM FFs)

So are **dihedral angles**

$$U(r) = \sum_{n=0}^N \frac{1}{2} V_n [1 + \cos(n\omega - \gamma)]$$

Also, **improper dihedral angles** are included in force fields

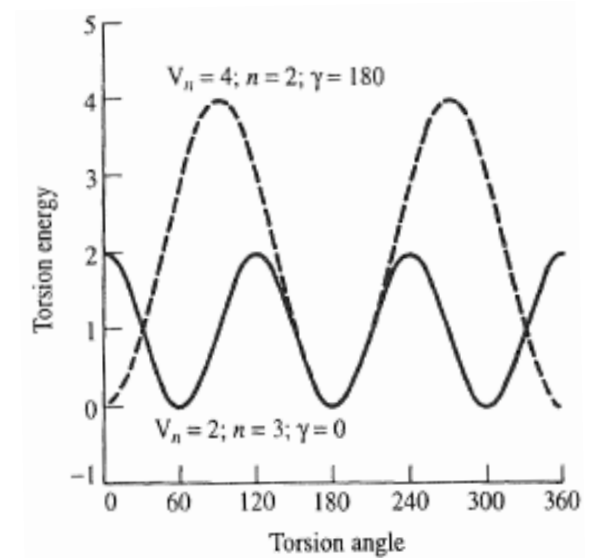
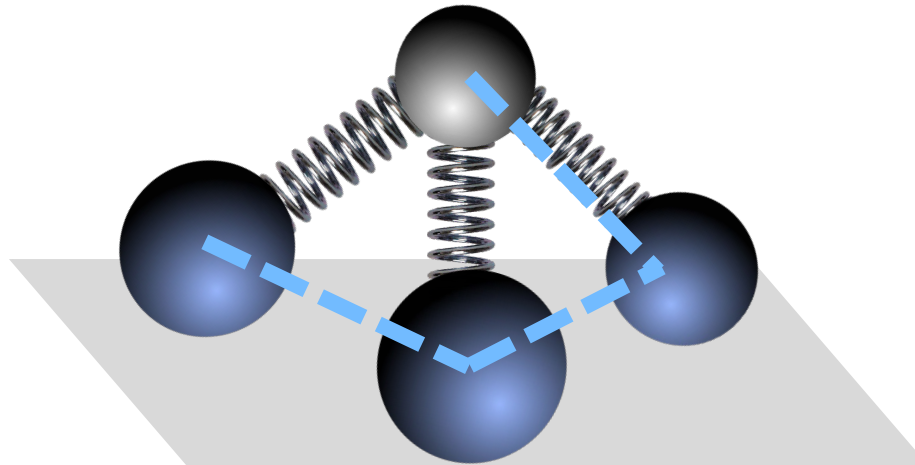
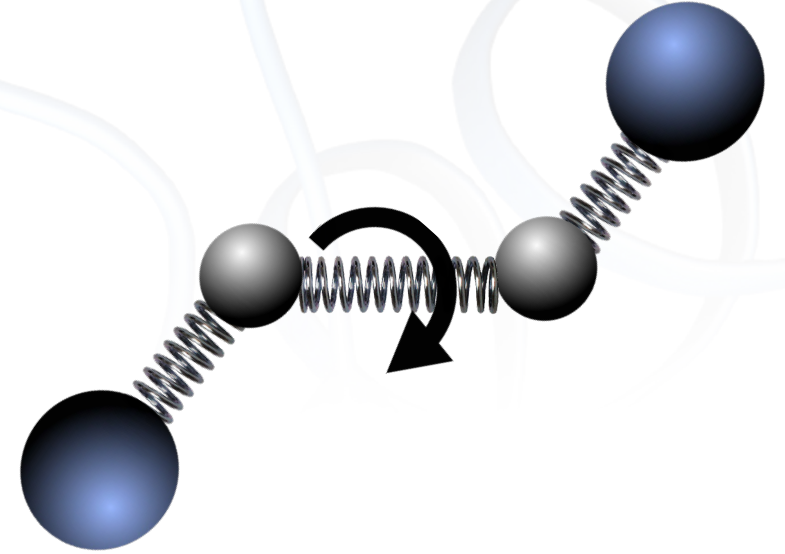


Molecular Mechanics Force Fields (MM FFs)

So are **dihedral angles**

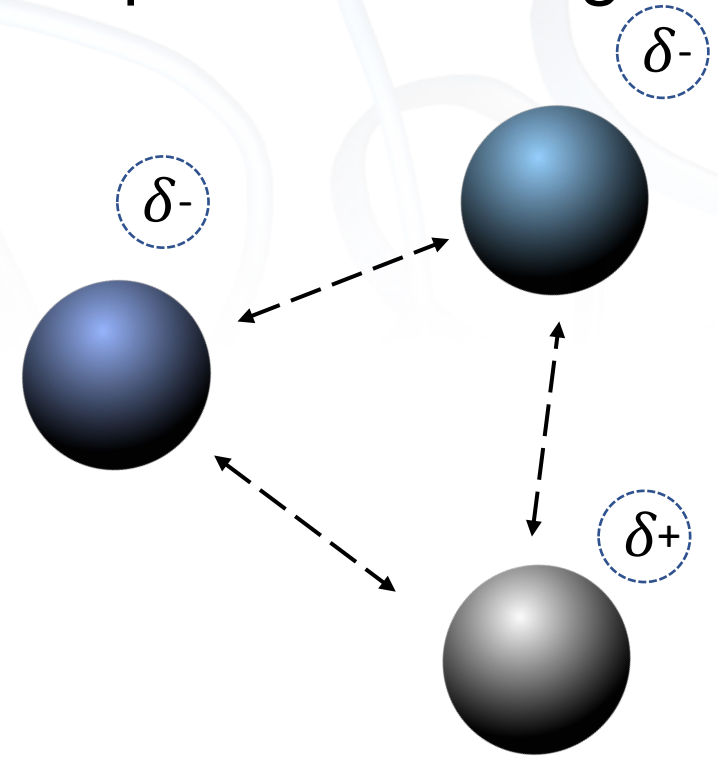
$$U(r) = \sum_{n=0}^N \frac{1}{2} V_n [1 + \cos(n\omega - \gamma)]$$

Also, **improper dihedral angles** are included in force fields



Molecular Mechanics Force Fields (MM FFs)

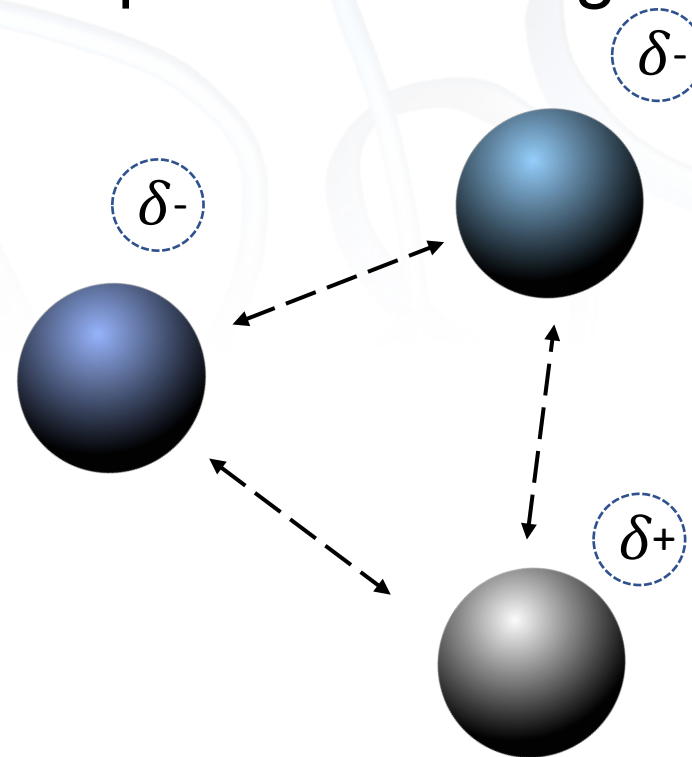
Electrostatic interactions are *most commonly* expressed through some variation of Coulomb's Law.



Molecular Mechanics Force Fields (MM FFs)

Electrostatic interactions are *most commonly* expressed through some variation of Coulomb's Law.

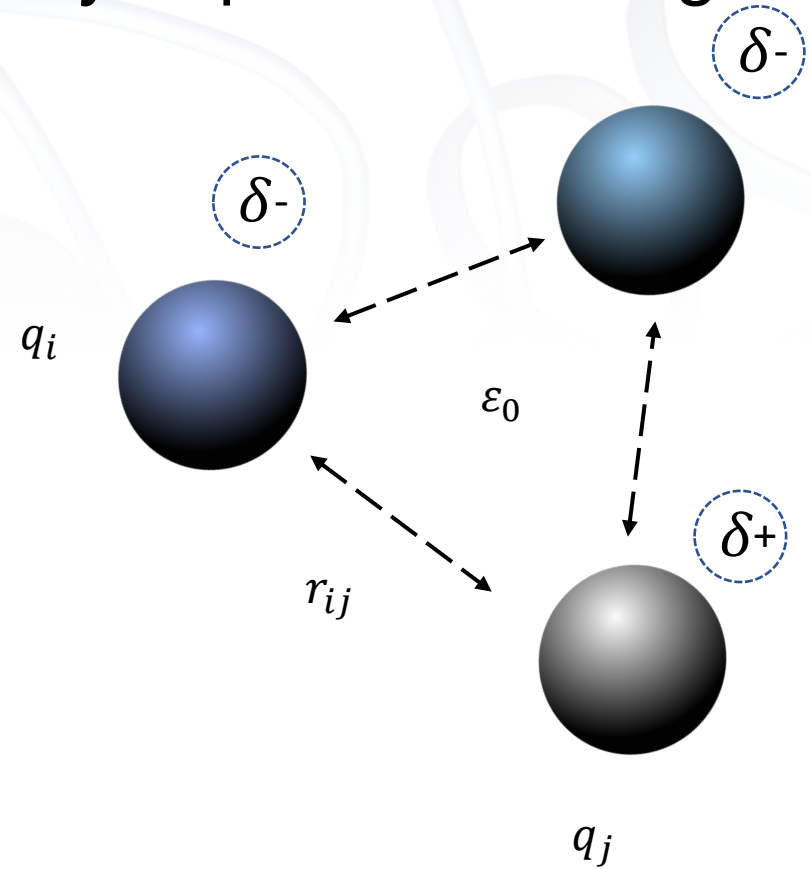
$$V(q, q') = \frac{1}{4\pi\epsilon_0} \left\{ \begin{aligned} &\frac{qq'}{r} \\ &+ \frac{1}{r^2} (q\mu' \cos \theta + q'\mu \cos \theta') \\ &+ \frac{\mu\mu'}{r^3} (2 \cos \theta \cos \theta' + \sin \theta \sin \theta' \cos \zeta) \\ &+ \frac{1}{2r^3} [q\Theta' (3 \cos^2 \theta' - 1) + q'\Theta (3 \cos^2 \theta - 1)] \\ &+ \frac{3}{2r^4} [\mu\Theta' \{ \cos \theta (3 \cos^2 \theta' - 1) + 2 \sin \theta \sin \theta' \cos \theta' \cos \zeta \} \\ &\quad + \mu'\Theta \{ \cos \theta' (3 \cos^2 \theta - 1) + 2 \sin \theta' \sin \theta \cos \theta \cos \zeta \}] \\ &+ \frac{3\Theta\Theta'}{4r^5} [1 - 5 \cos^2 \theta - 5 \cos^2 \theta' + 17 \cos^2 \theta \cos^2 \theta' \\ &\quad + 2 \sin^2 \theta \sin^2 \theta' \cos^2 \zeta + 16 \sin \theta \sin \theta' \cos \theta \cos \theta' \cos \zeta] \\ &+ \dots \end{aligned} \right\}$$



Molecular Mechanics Force Fields (MM FFs)

Electrostatic interactions are *most commonly* expressed through some variation of Coulomb's Law.

$$U(r_{ij}) = \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}$$

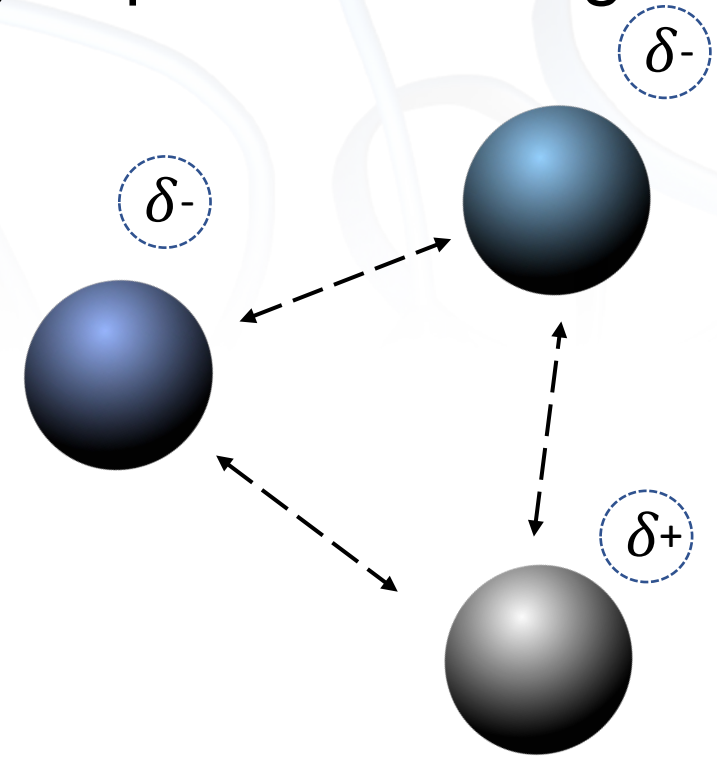


Molecular Mechanics Force Fields (MM FFs)

Electrostatic interactions are *most commonly* expressed through some variation of Coulomb's Law.

$$U(r_{ij}) = \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}$$

Note: Physics would demand that force fields include **many-bodied interactions**



$$U_{\text{tot}}(r_{(i,j,k)}) = U(r_{ij}) + U(r_{ik}) + U(r_{jk}) + U(r_{ijk})$$

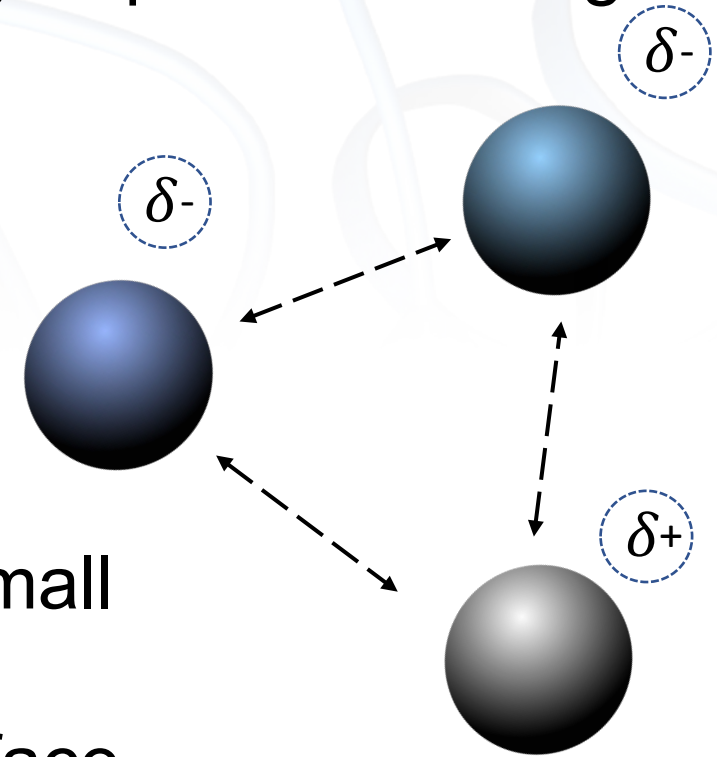
Molecular Mechanics Force Fields (MM FFs)

Electrostatic interactions are *most commonly* expressed through some variation of Coulomb's Law.

$$U(r_{ij}) = \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}$$

Assuming that many-bodied interactions are small and can be subsumed makes an **effective pairwise-potential** of the potential energy surface.

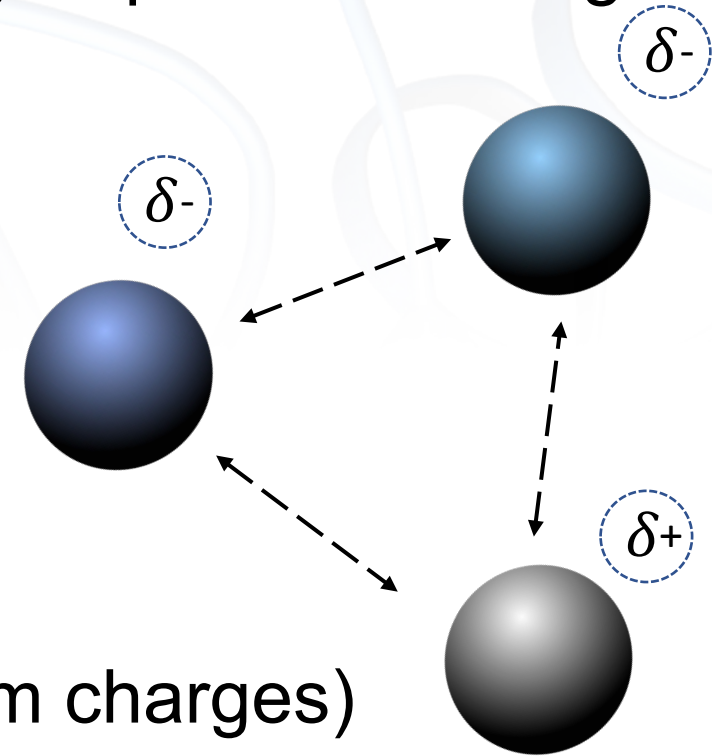
$$U_{\text{tot}}(r_{(i,j,k)}) \approx U(r_{ij}) + U(r_{ik}) + U(r_{jk})$$



Molecular Mechanics Force Fields (MM FFs)

Electrostatic interactions are *most commonly* expressed through some variation of Coulomb's Law.

$$U(r_{ij}) = \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}$$



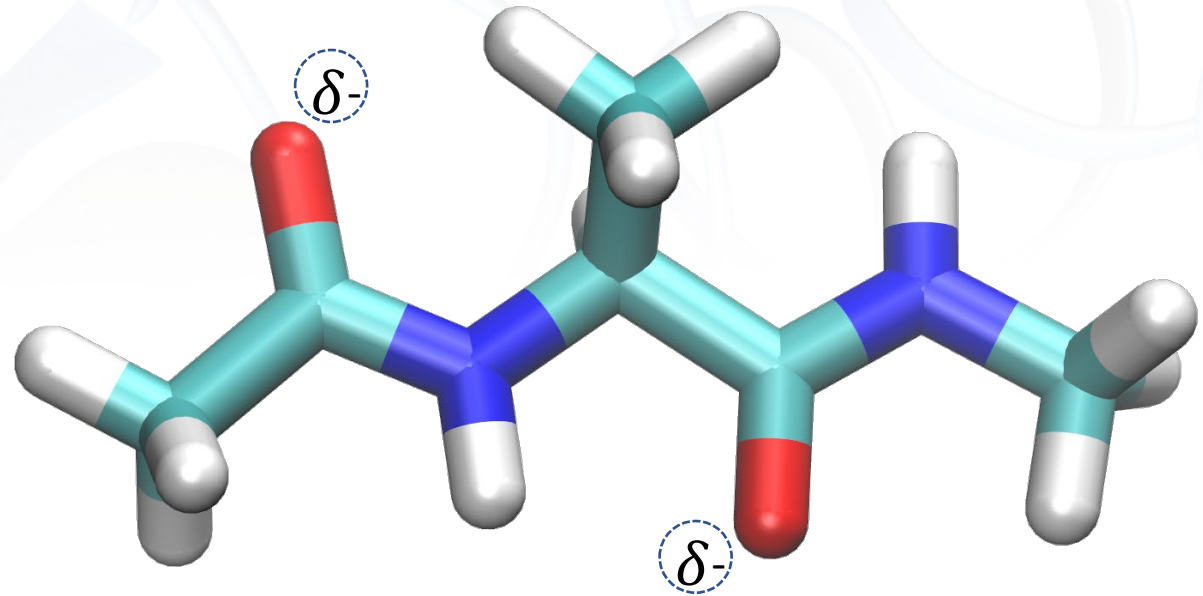
Approximation can have issues:

- Multipole moments are very hard (off-atom charges)
- Not good at very short ranges, no polarization
- Not good for very long ranges, creates more issues
- Condensed phase systems are very sensitive to electrostatics

Molecular Mechanics Force Fields (MM FFs)

Electrostatic interactions are *most commonly* expressed through some variation of Coulomb's Law.

$$U(r_{ij}) = \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}$$

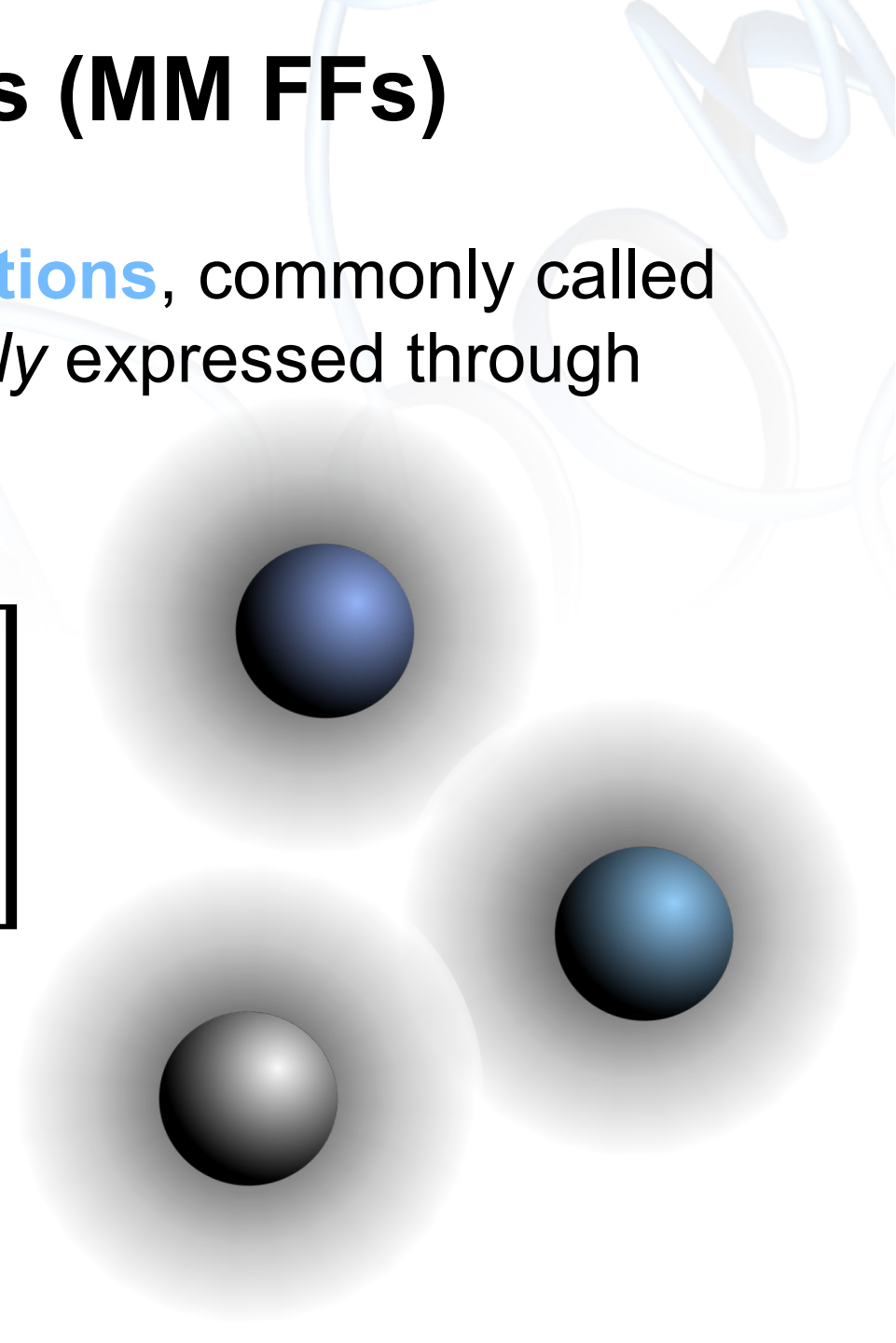


There are a number of ways to calculate charges but *most commonly* derived from **quantum chemical** calculation.

Molecular Mechanics Force Fields (MM FFs)

Election dispersion and correlation interactions, commonly called van der Waals interactions, are *most commonly* expressed through the Lennard-Jones (12-6) potential.

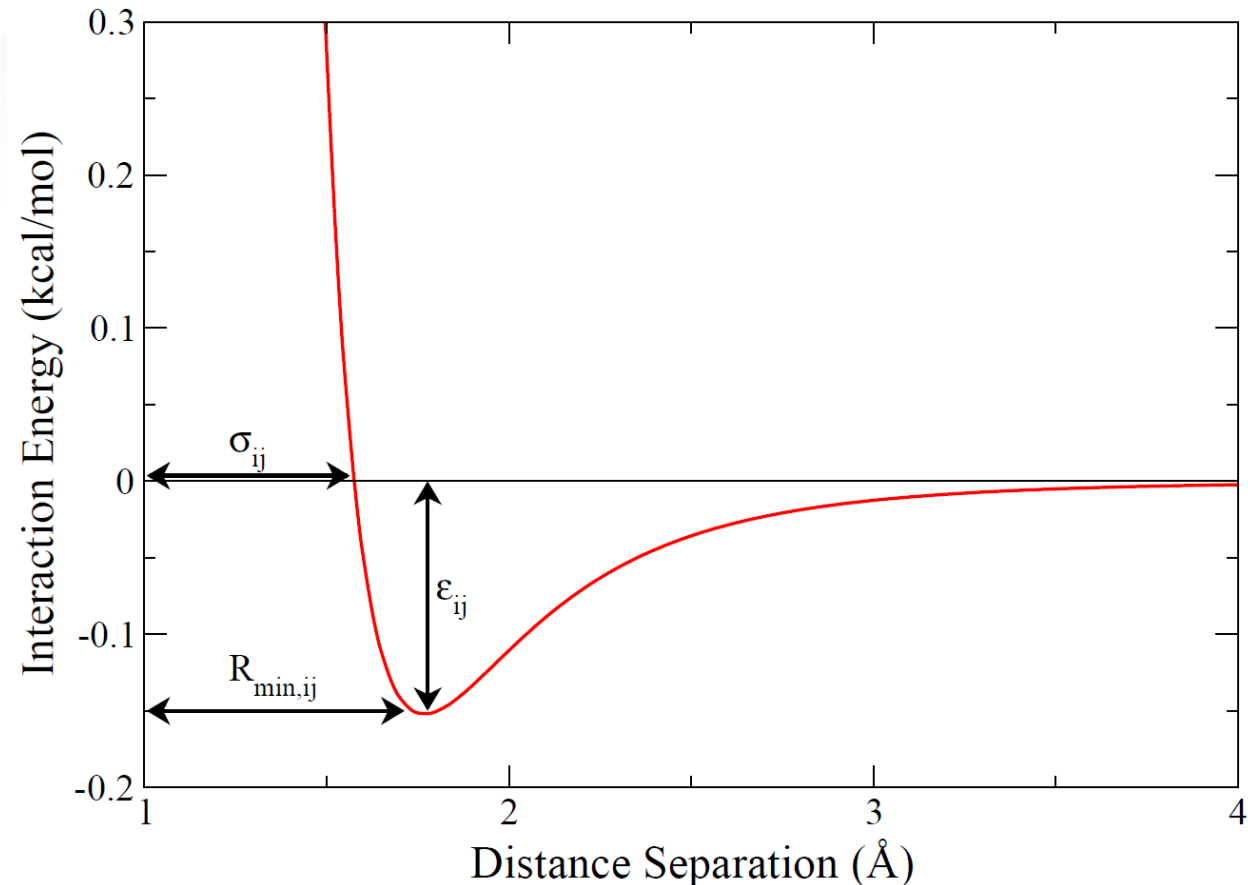
$$U(r_{ij}) = 4\varepsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right]$$



Molecular Mechanics Force Fields (MM FFs)

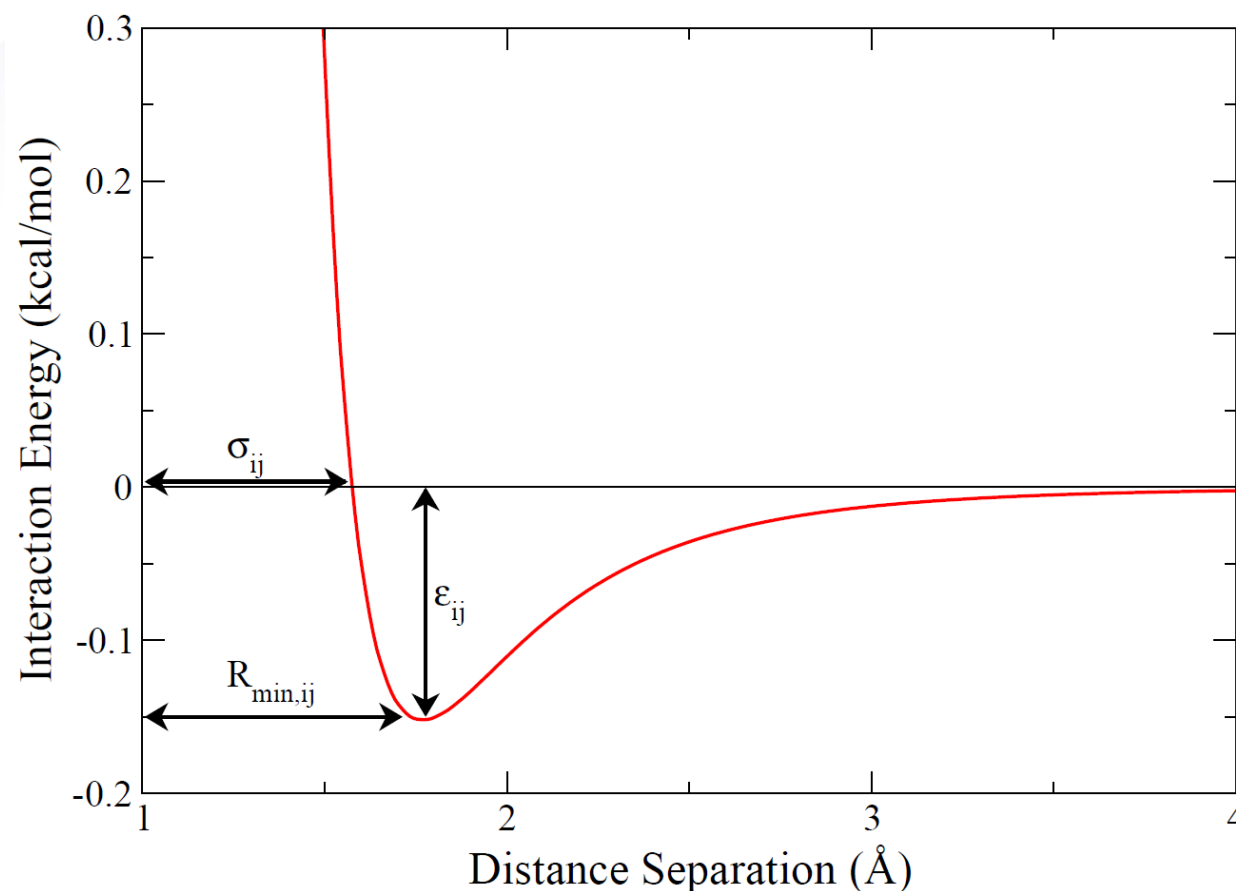
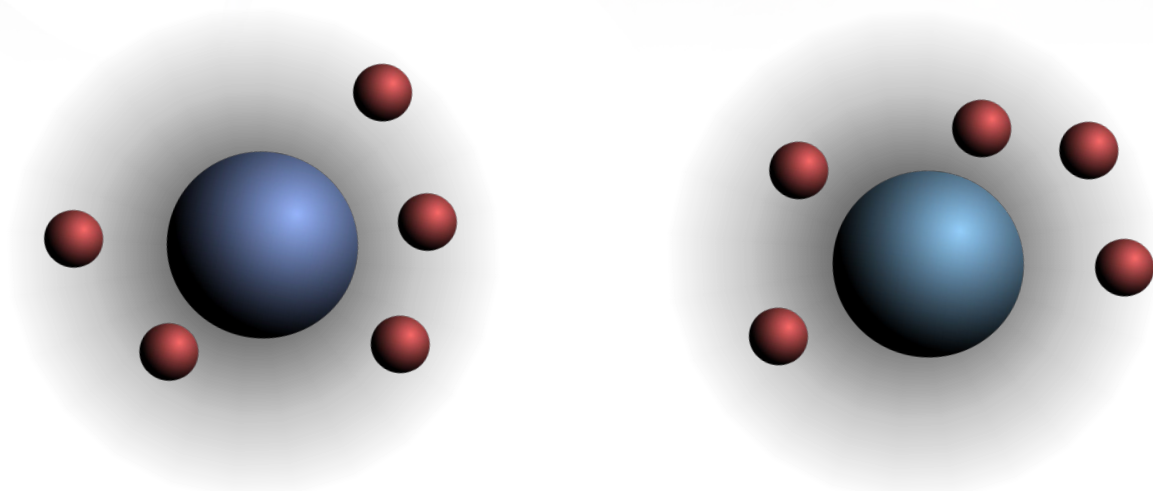
Election dispersion and correlation interactions, commonly called van der Waals interactions, are *most commonly* expressed through the Lennard-Jones (12-6) potential.

$$U(r_{ij}) = 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right]$$



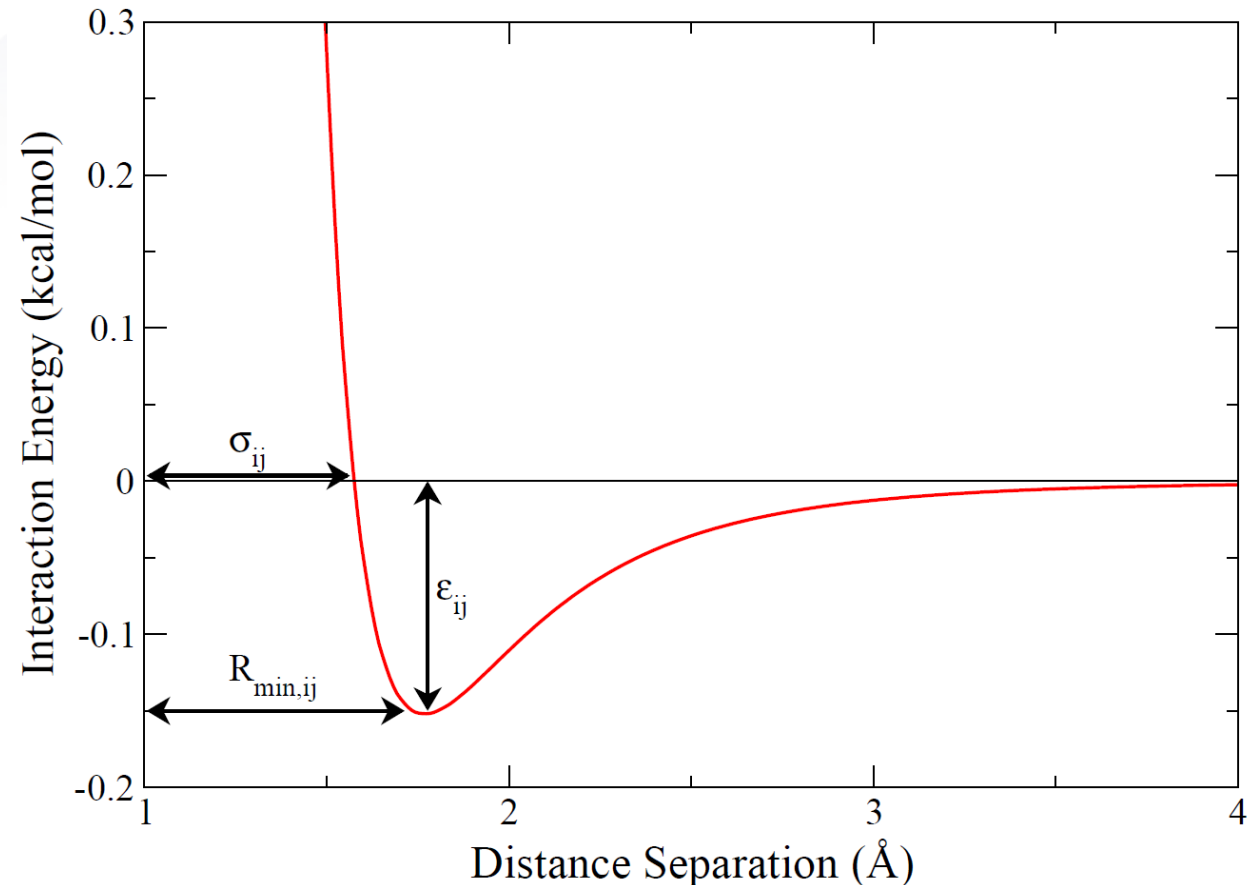
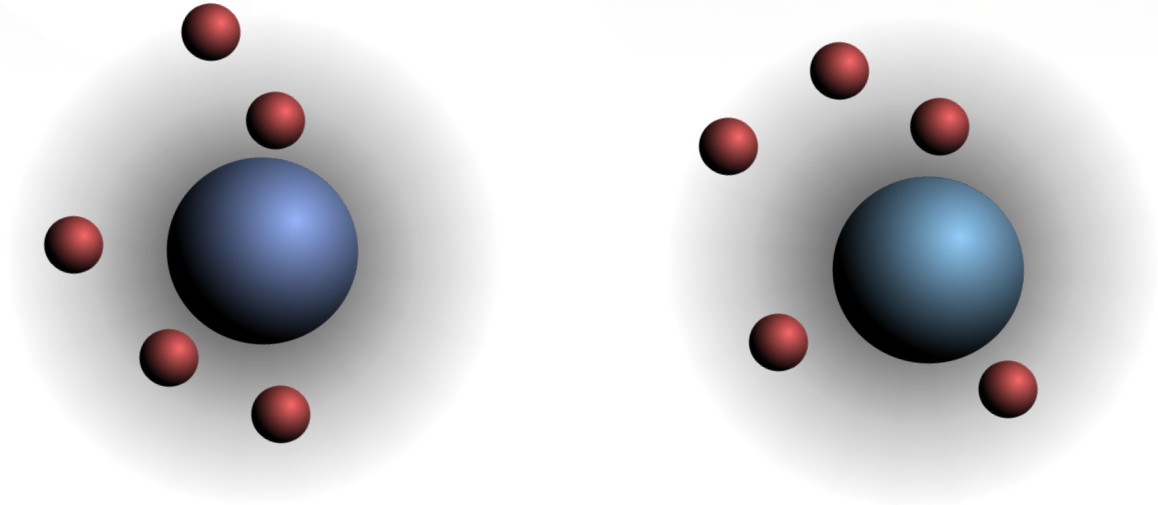
Molecular Mechanics Force Fields (MM FFs)

Election dispersion and correlation interactions, commonly called van der Waals interactions, are *most commonly* expressed through the Lennard-Jones (12-6) potential.



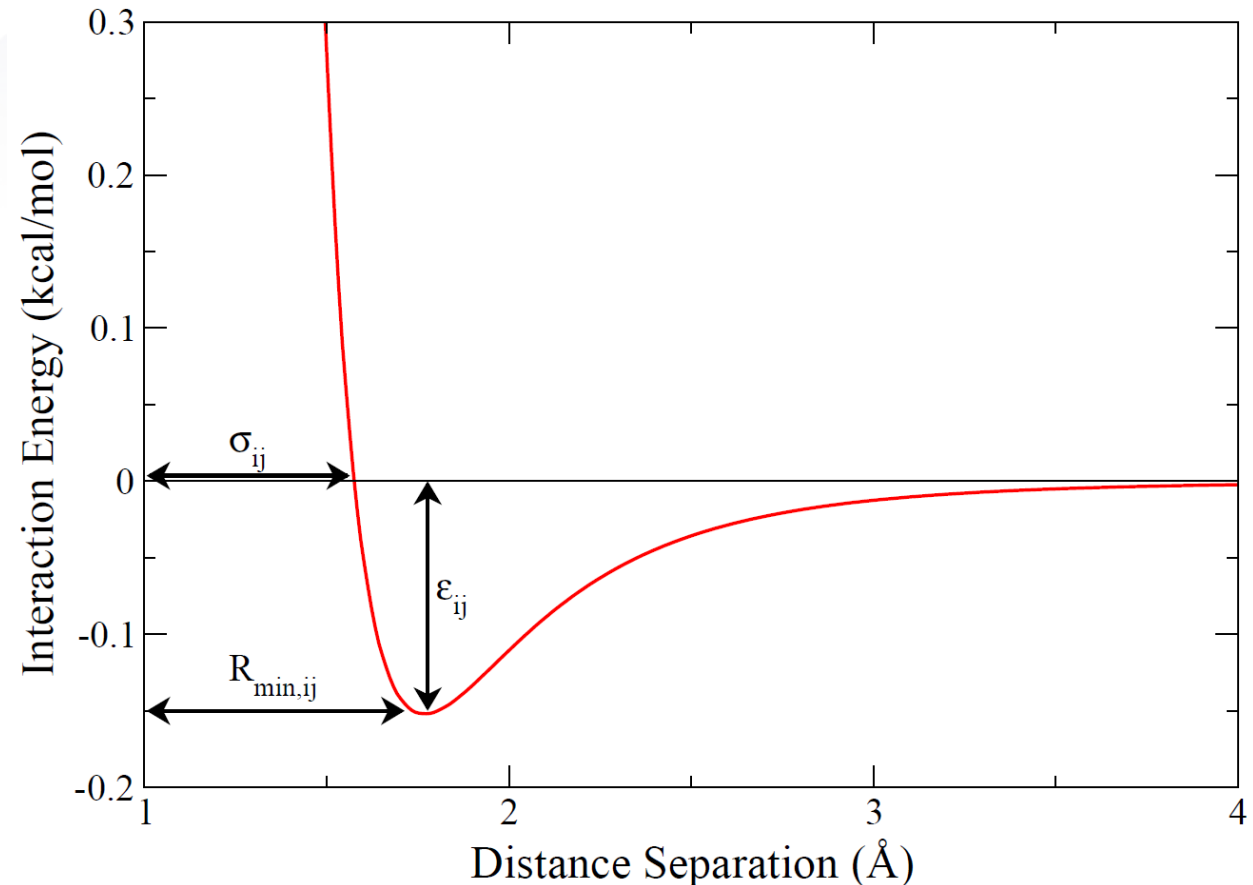
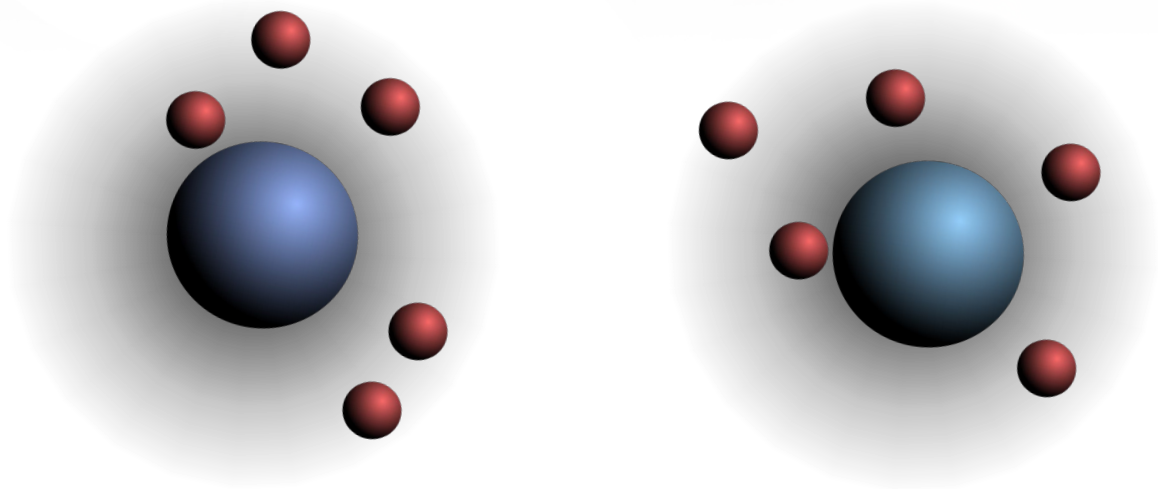
Molecular Mechanics Force Fields (MM FFs)

Election dispersion and correlation interactions, commonly called van der Waals interactions, are *most commonly* expressed through the Lennard-Jones (12-6) potential.



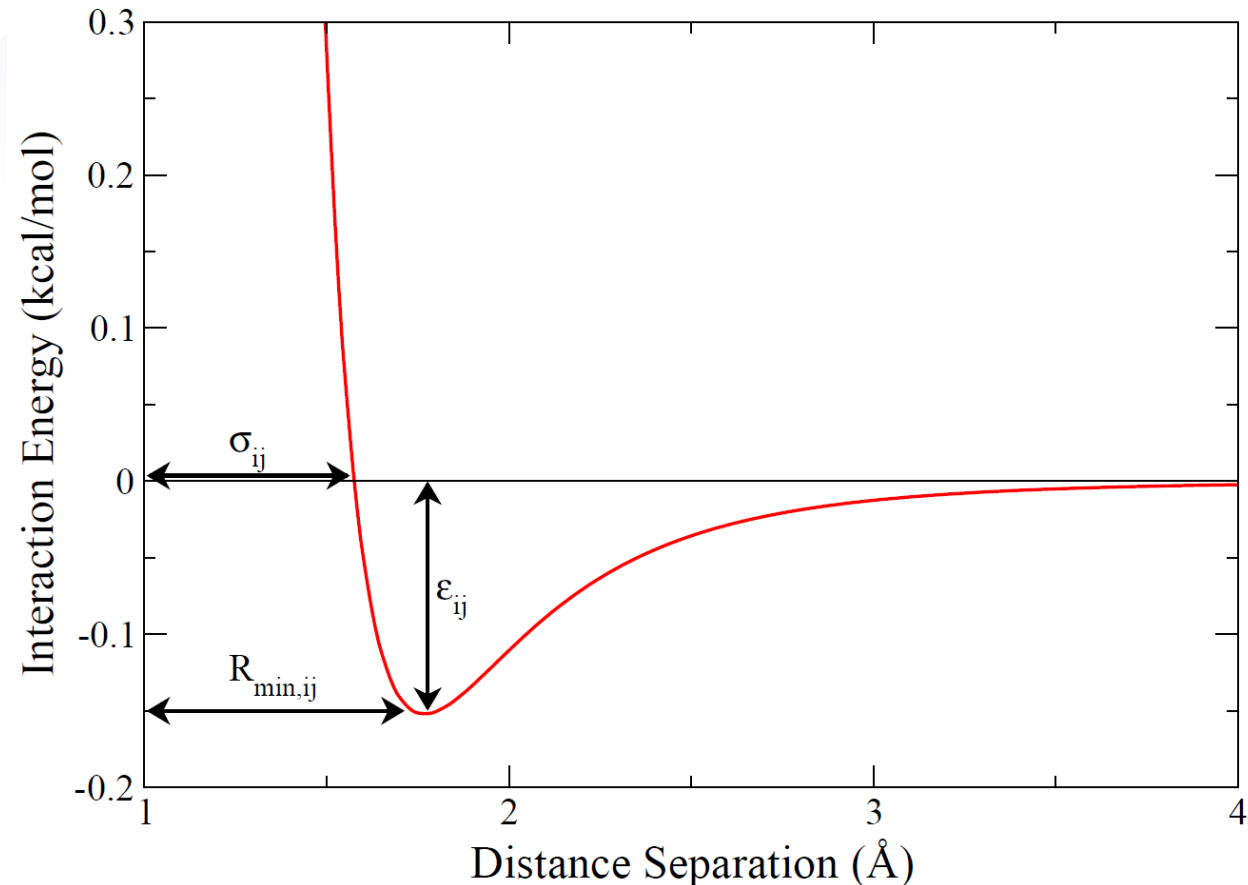
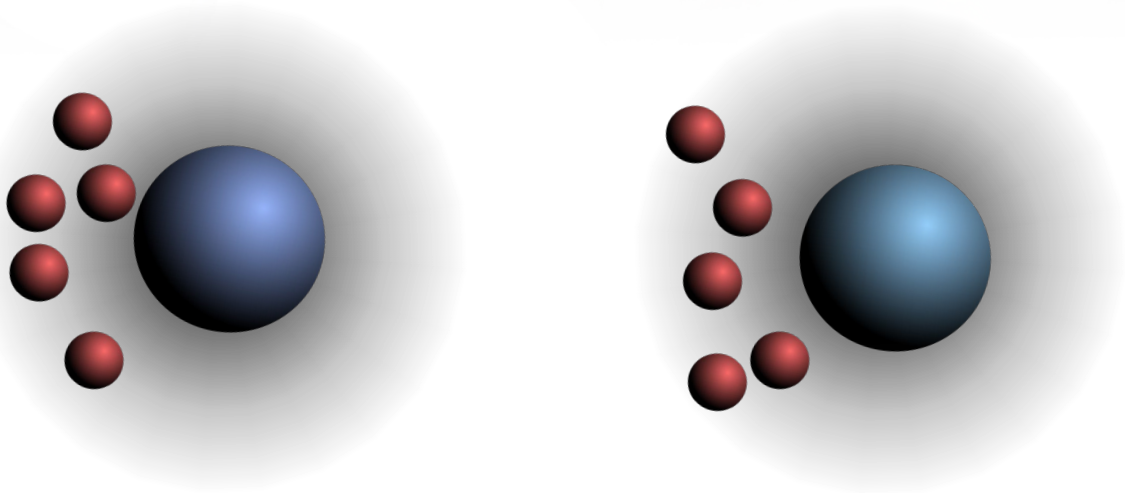
Molecular Mechanics Force Fields (MM FFs)

Election dispersion and correlation interactions, commonly called van der Waals interactions, are *most commonly* expressed through the Lennard-Jones (12-6) potential.



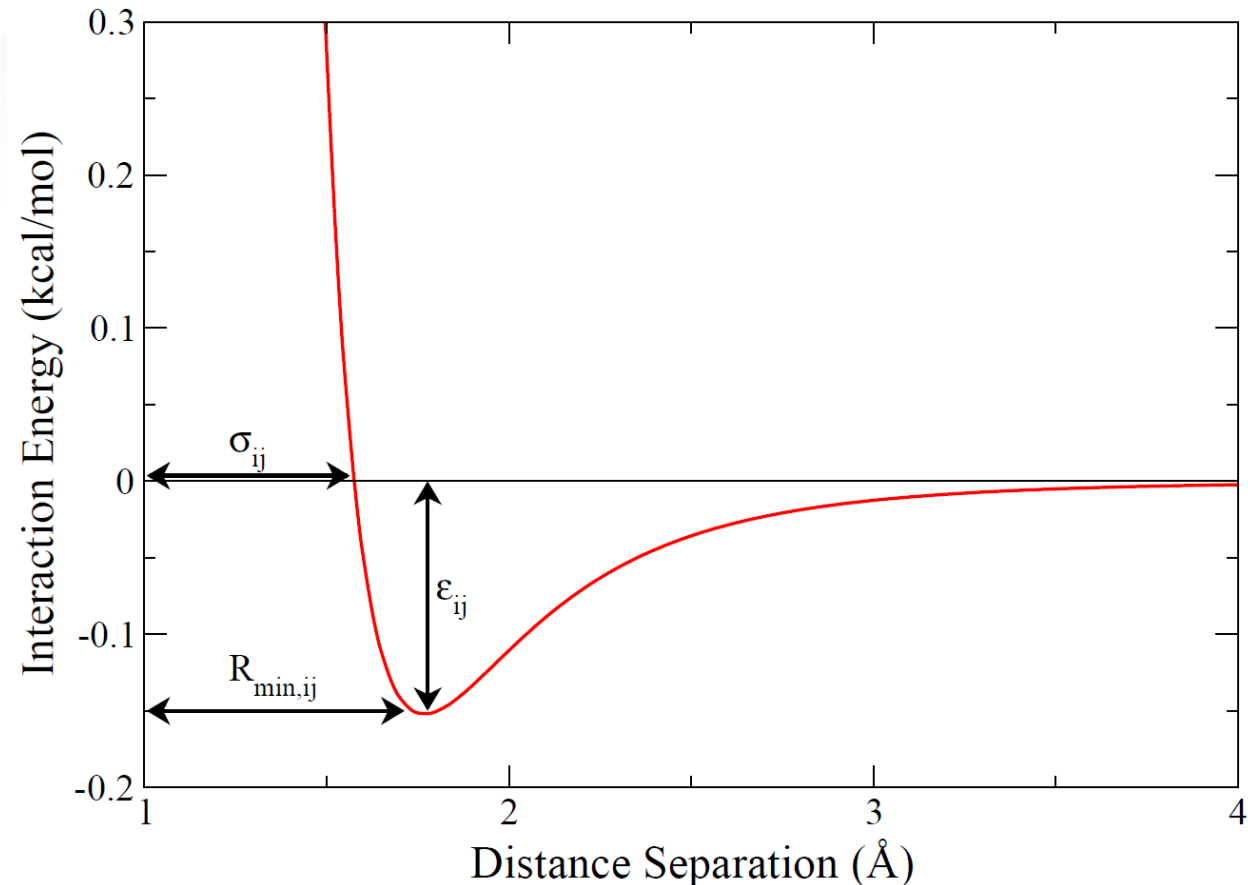
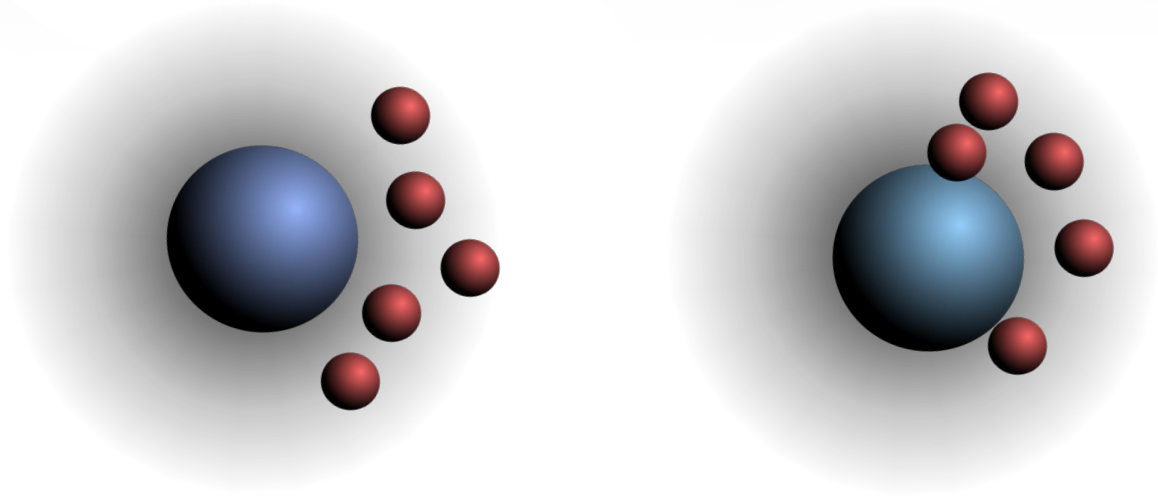
Molecular Mechanics Force Fields (MM FFs)

Election dispersion and correlation interactions, commonly called van der Waals interactions, are *most commonly* expressed through the Lennard-Jones (12-6) potential.



Molecular Mechanics Force Fields (MM FFs)

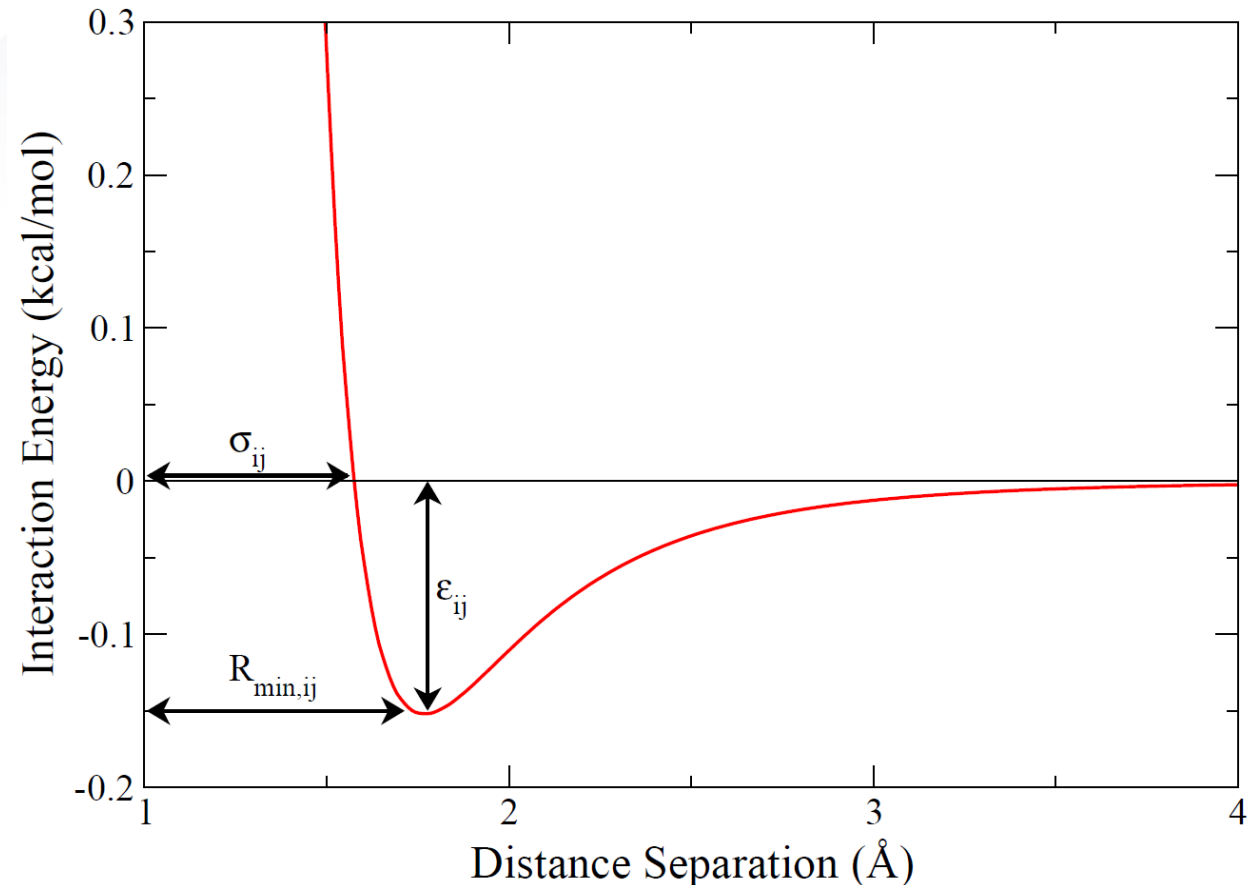
Election dispersion and correlation interactions, commonly called van der Waals interactions, are *most commonly* expressed through the Lennard-Jones (12-6) potential.



Molecular Mechanics Force Fields (MM FFs)

Election dispersion and correlation interactions, commonly called van der Waals interactions, are *most commonly* expressed through the Lennard-Jones (12-6) potential.

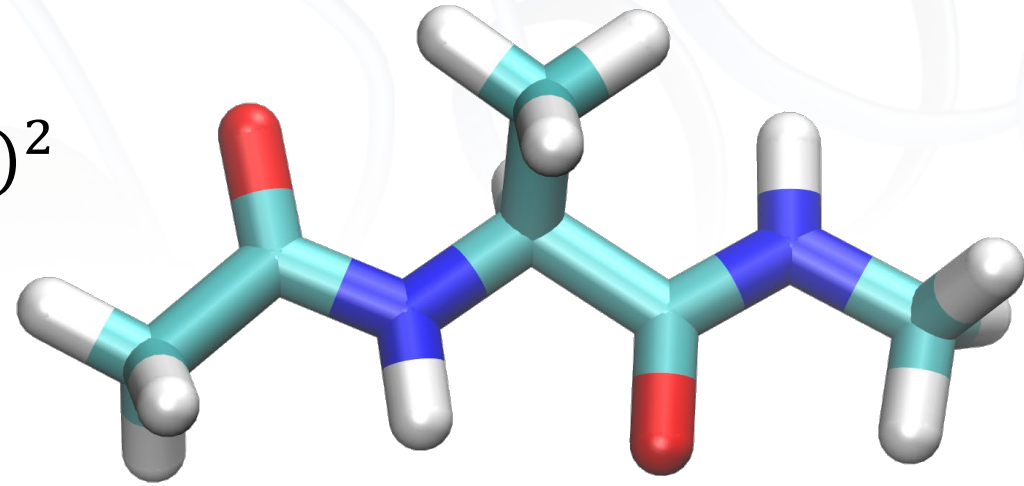
$$U(r_{ij}) = 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right]$$



Molecular Mechanics Force Fields (MM FFs)

Adding it all together:

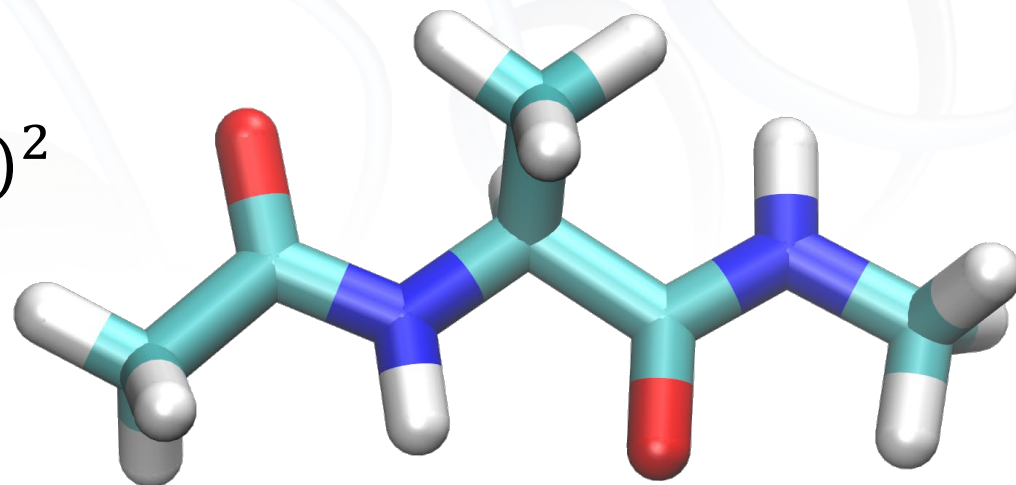
$$\begin{aligned} U(\mathbf{r}^N) &= \sum_{bonds} \frac{1}{2} k(r - r_0)^2 + \sum_{angles} \frac{1}{2} k(\theta - \theta_0)^2 \\ &+ \sum_{torsions} \frac{1}{2} V_n [1 + \cos(n\omega - \gamma)] \\ &+ \sum_{i=1}^N \sum_{j>i}^N \left\{ \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} + 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] \right\} \end{aligned}$$



Molecular Mechanics Force Fields (MM FFs)

Adding it all together:

$$\begin{aligned} U(\mathbf{r}^N) &= \sum_{\text{bonds}} \frac{1}{2} k(r - r_0)^2 + \sum_{\text{angles}} \frac{1}{2} k(\theta - \theta_0)^2 \\ &+ \sum_{\text{torsions}} \frac{1}{2} V_n [1 + \cos(n\omega - \gamma)] \\ &+ \sum_{i=1}^N \sum_{j>i}^N \left\{ \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} + 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] \right\} \end{aligned}$$

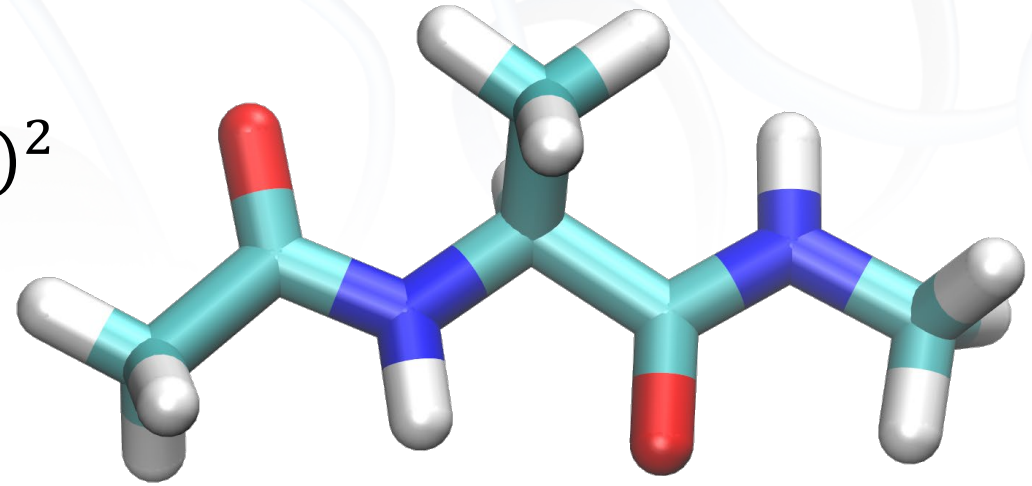


Non-bonded terms

Molecular Mechanics Force Fields (MM FFs)

Adding it all together:

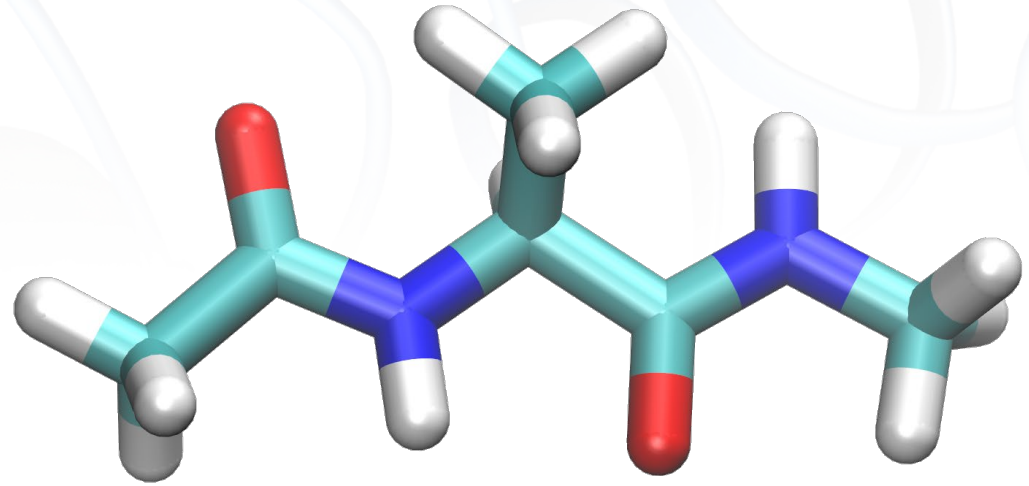
$$\begin{aligned} U(\mathbf{r}^N) &= \sum_{bonds} \frac{1}{2} k (r - r_0)^2 + \sum_{angles} \frac{1}{2} k (\theta - \theta_0)^2 \\ &+ \sum_{torsions} \frac{1}{2} V_n [1 + \cos(n\omega - \gamma)] \\ &+ \sum_{i=1}^N \sum_{j>i}^N \left\{ \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} + 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] \right\} \end{aligned}$$



System Parameters: $r_0, \theta_0, k, V, \sigma_{ij}$, etc

Molecular Mechanics Force Fields (MM FFs)

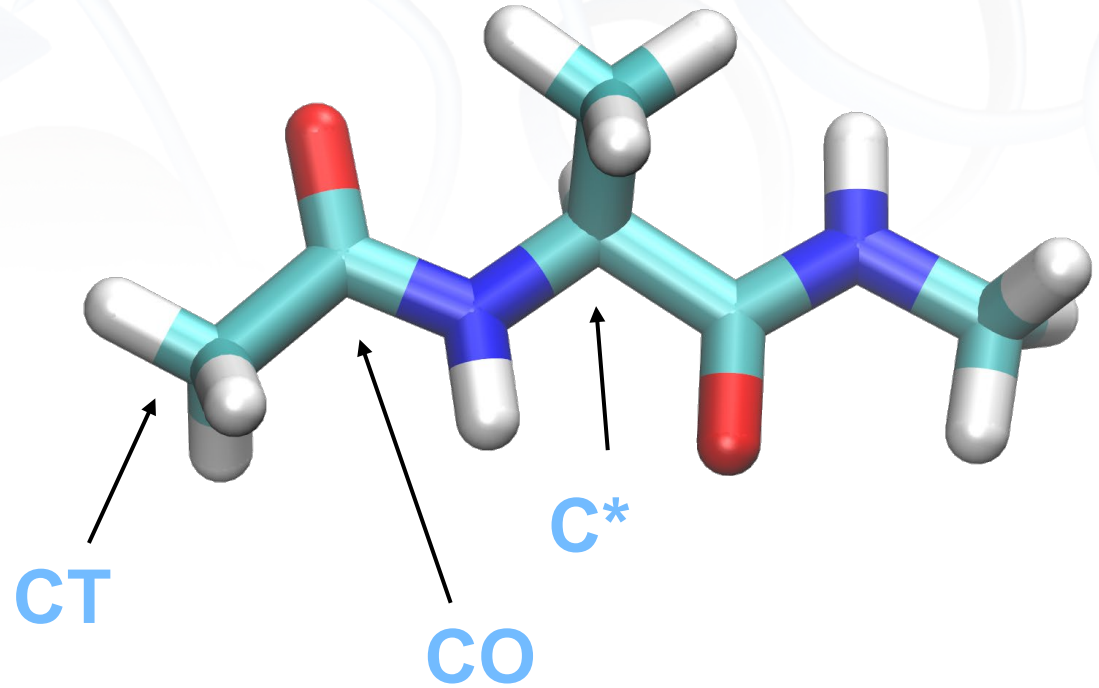
System Parameters: $r_0, \theta_0, k, V, q_i, \sigma_{ij}$, etc



Molecular Mechanics Force Fields (MM FFs)

System Parameters: $r_0, \theta_0, k, V, q_i, \sigma_{ij}$, etc

To define these parameters, **atom-types** are defined based on local information.



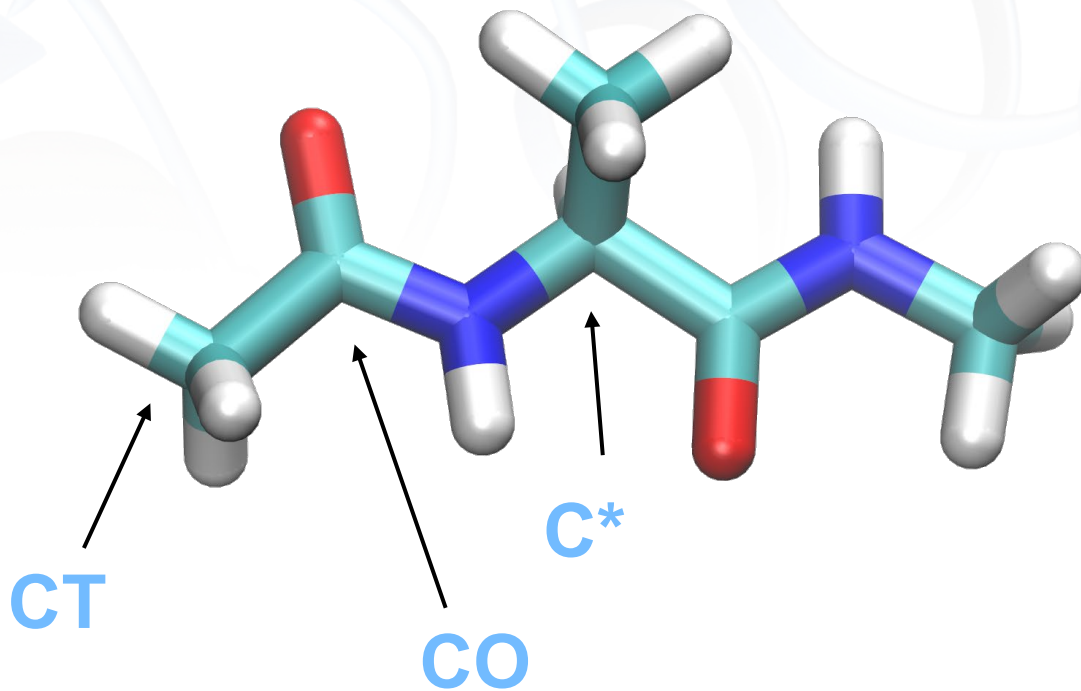
Molecular Mechanics Force Fields (MM FFs)

System Parameters: $r_0, \theta_0, k, V, q_i, \sigma_{ij}$, etc

To define these parameters, **atom-types** are defined based on local information.

Something to think about:

Are more or less atom-types better?



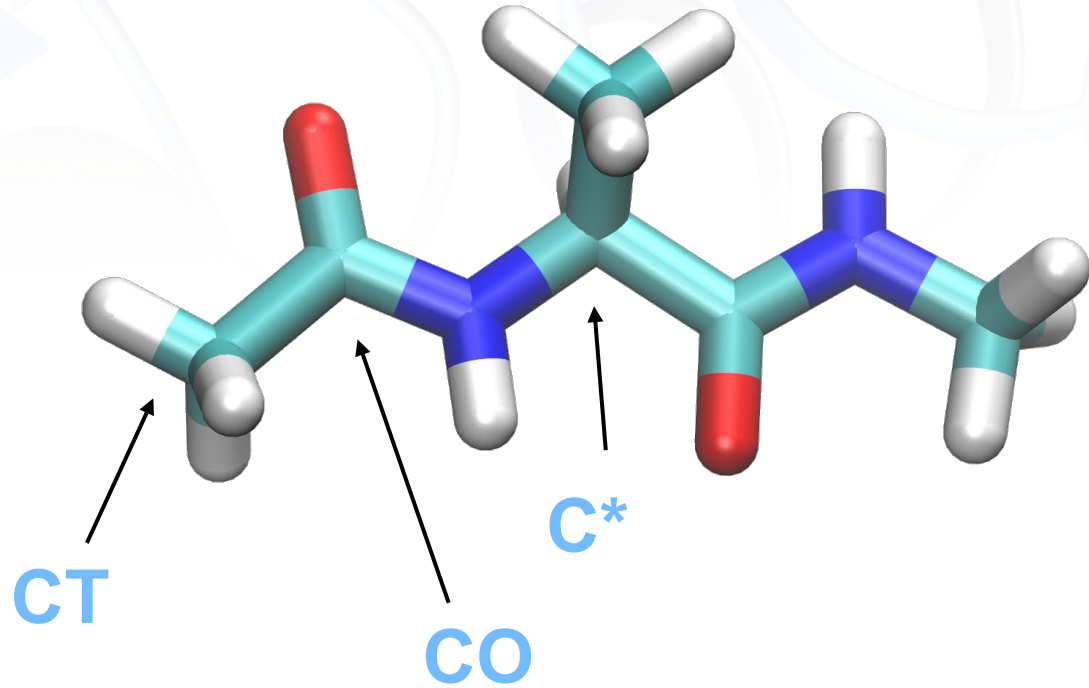
Molecular Mechanics Force Fields (MM FFs)

System Parameters: $r_0, \theta_0, k, V, q_i, \sigma_{ij}$, etc

To define these parameters, **atom-types** are defined based on local information.

Something to think about:

Are more or less atom-types better?
Specific interactions are more accurately modelled but the force field parameterization is harder with each one. The force field is less **transferable**.

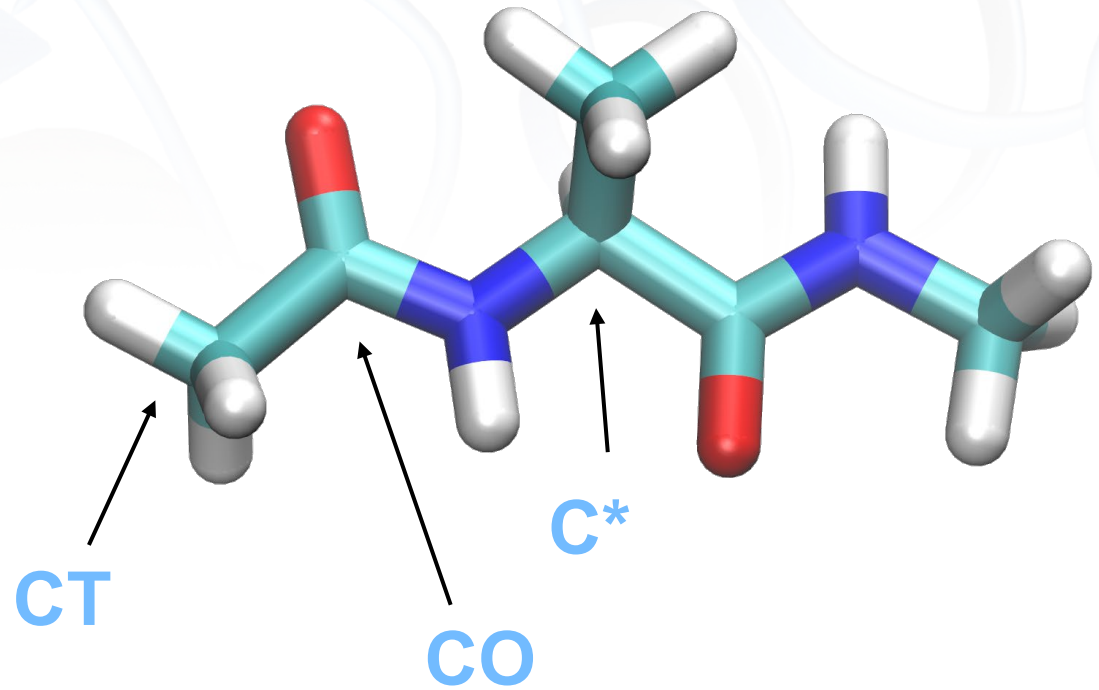


Molecular Mechanics Force Fields (MM FFs)

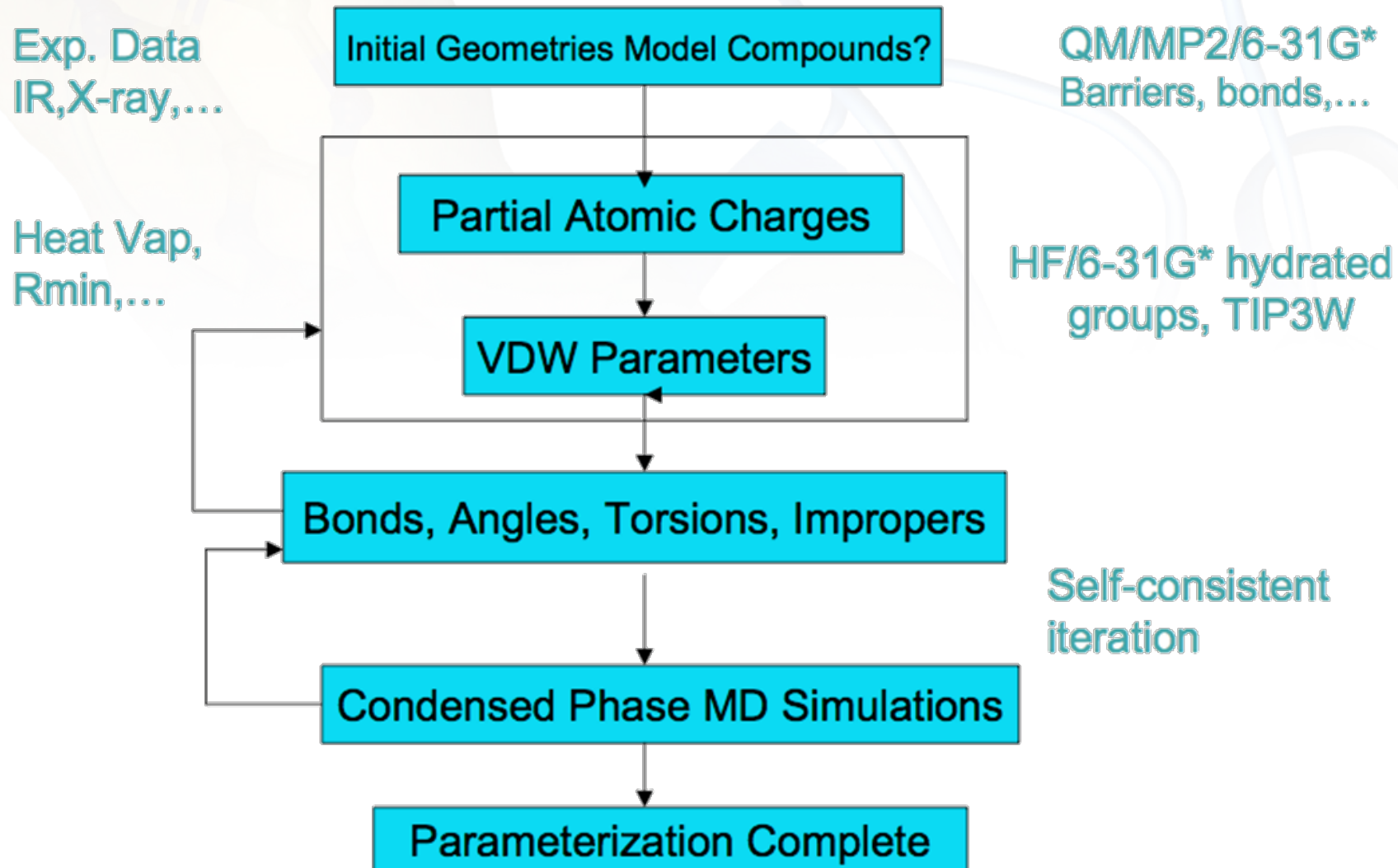
System Parameters: $r_0, \theta_0, k, V, q_i, \sigma_{ij}$, etc

To define these parameters, **atom-types** are defined based on local information.

Protein and nucleic acid structures are sensitive changes in these **parameters**.



Molecular Mechanics Force Fields (MM FFs)



* Summary of MacKerell, JCC v21, 86,105 (2000)

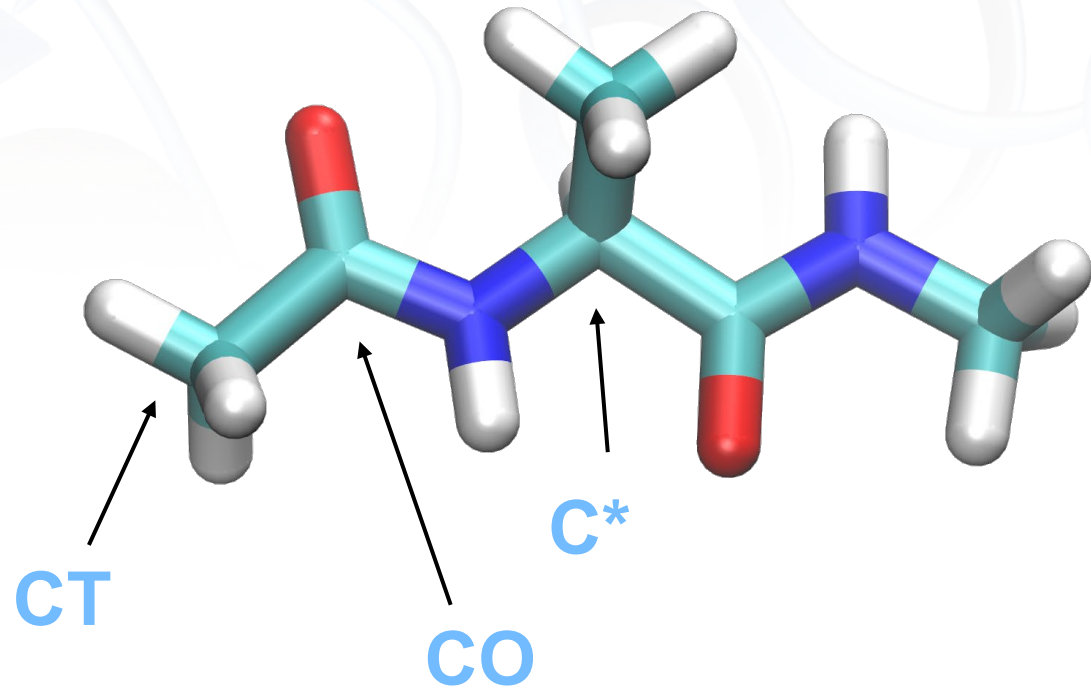
Molecular Mechanics Force Fields (MM FFs)

System Parameters: $r_0, \theta_0, k, V, q_i, \sigma_{ij}$, etc

To define these parameters, **atom-types** are defined based on local information.

Protein and nucleic acid structures are sensitive changes in these **parameters**.

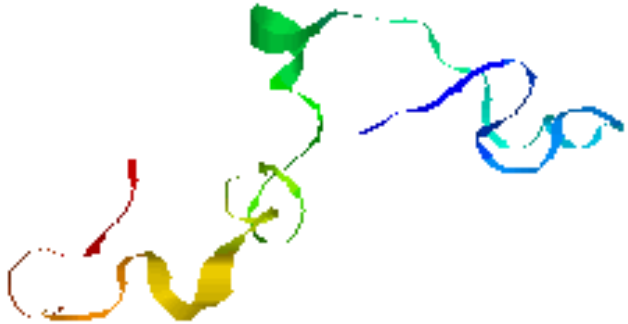
Furthermore, parameterizations depend on the type of system being studied as well as the **solvation model**.



Molecular Dynamics Solvation

$$\Delta G = \Delta H - T\Delta S$$

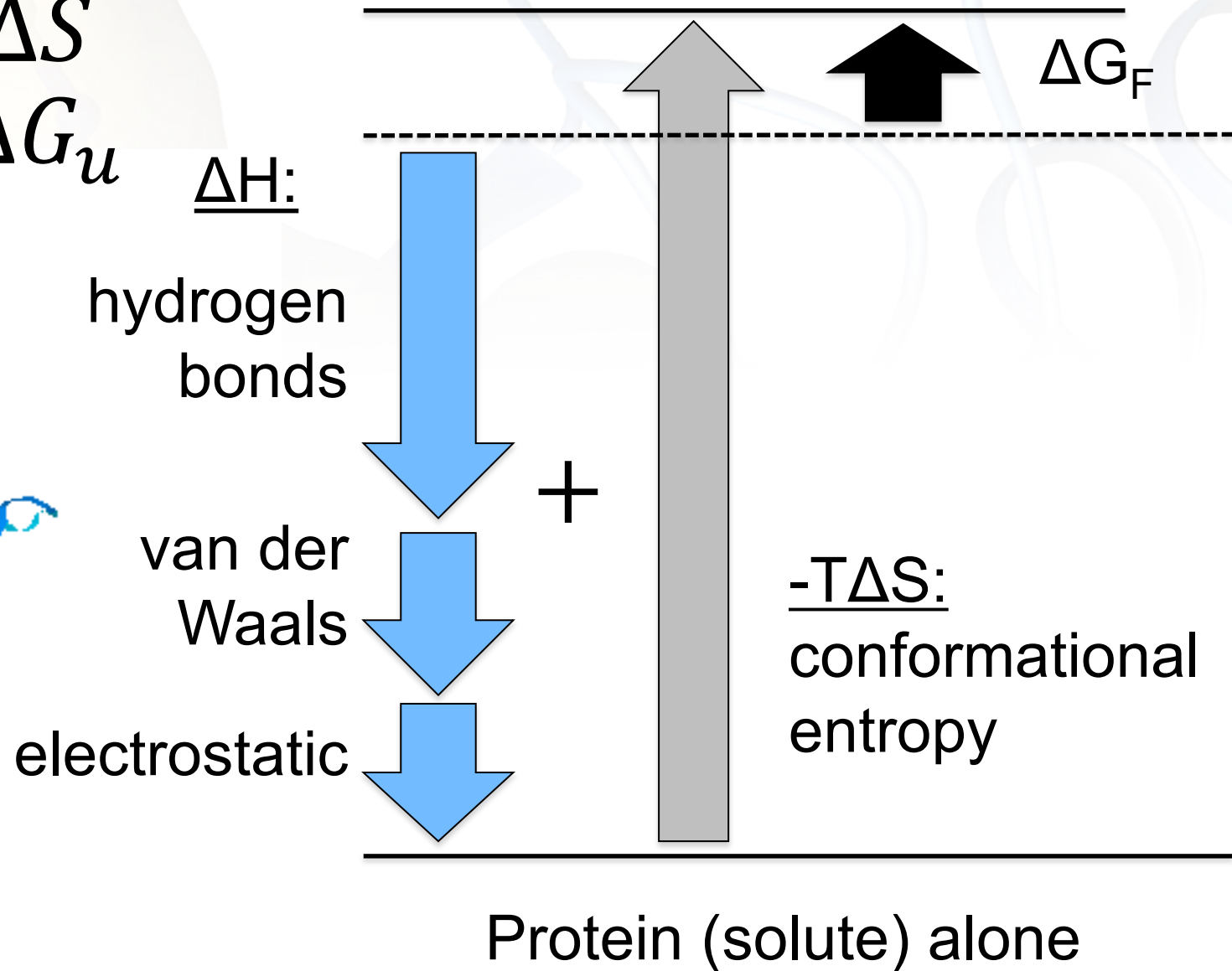
$$\Delta G_F = \Delta G_f - \Delta G_u$$



Molecular Dynamics Solvation

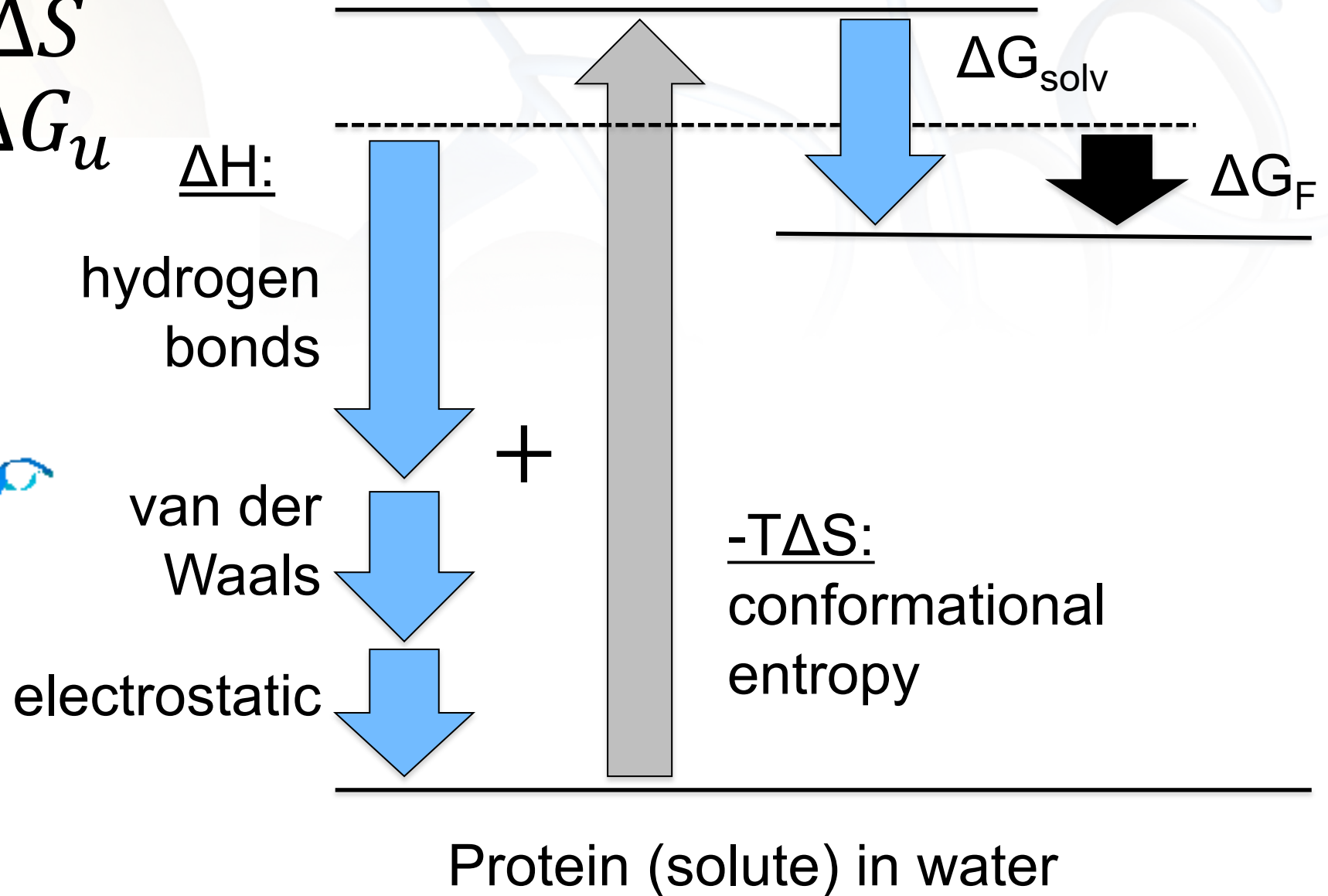
$$\Delta G = \Delta H - T\Delta S$$

$$\Delta G_F = \Delta G_f - \Delta G_u$$

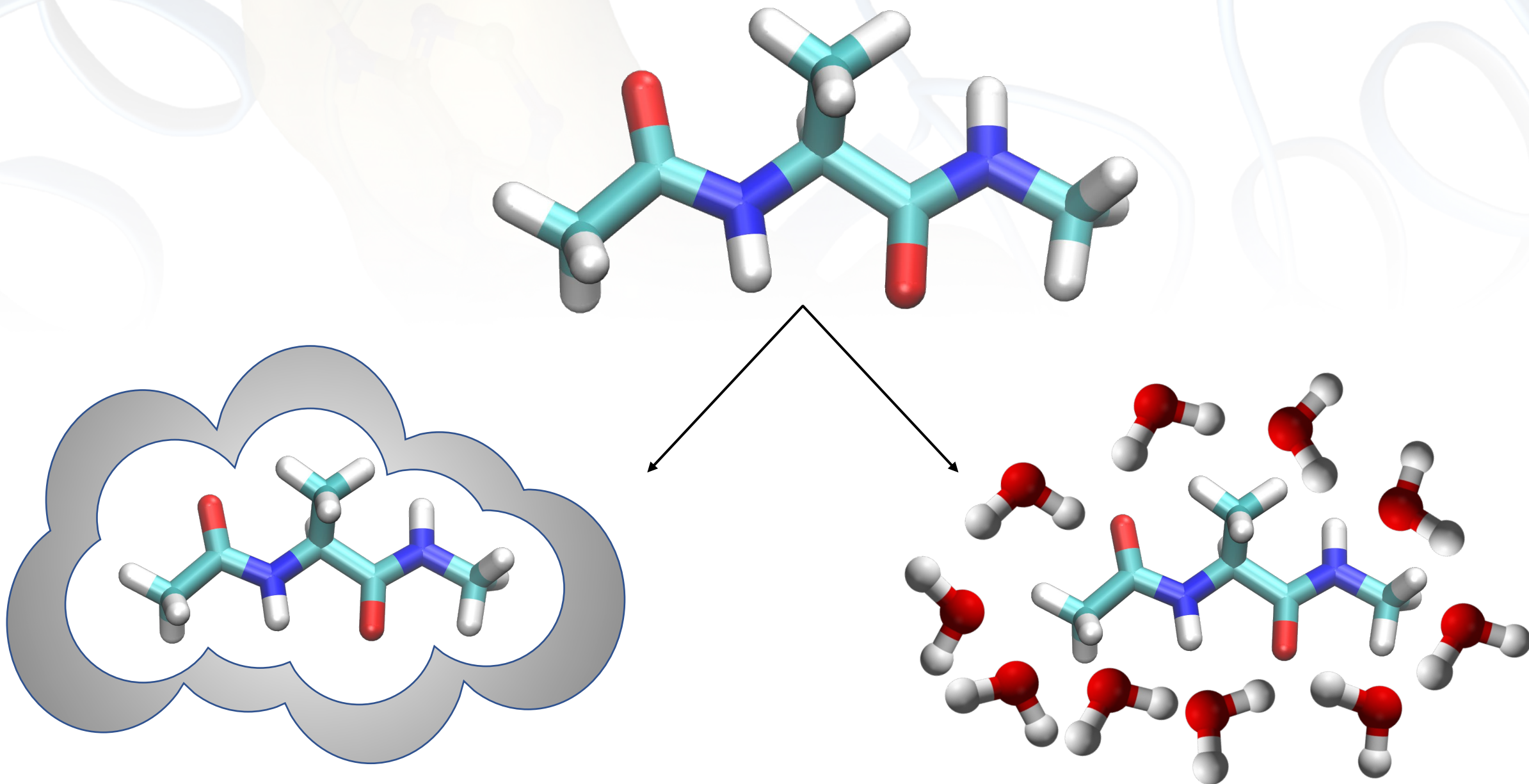


Molecular Dynamics Solvation

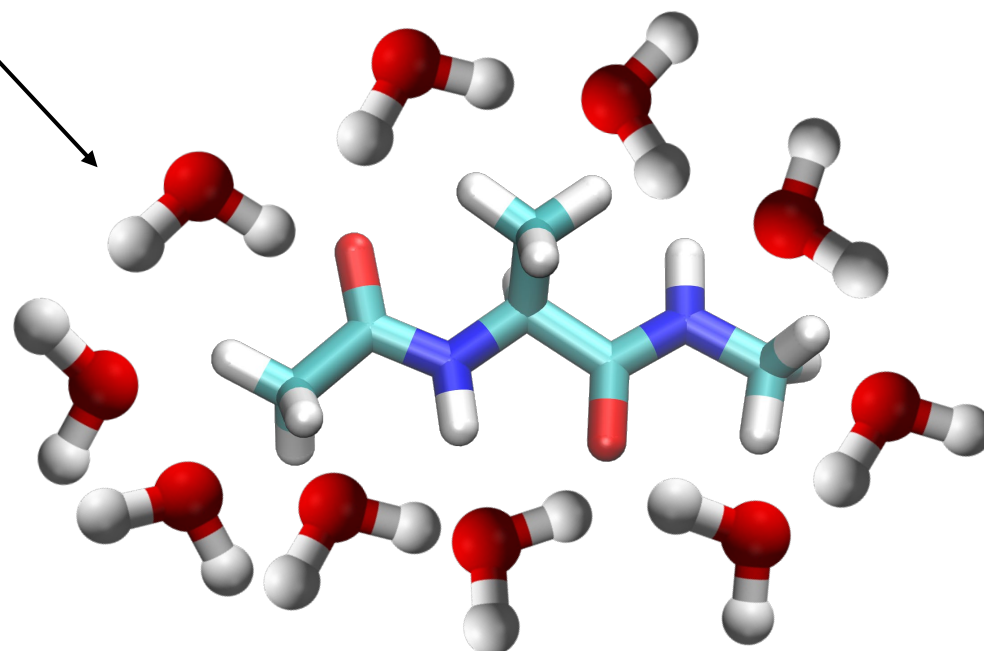
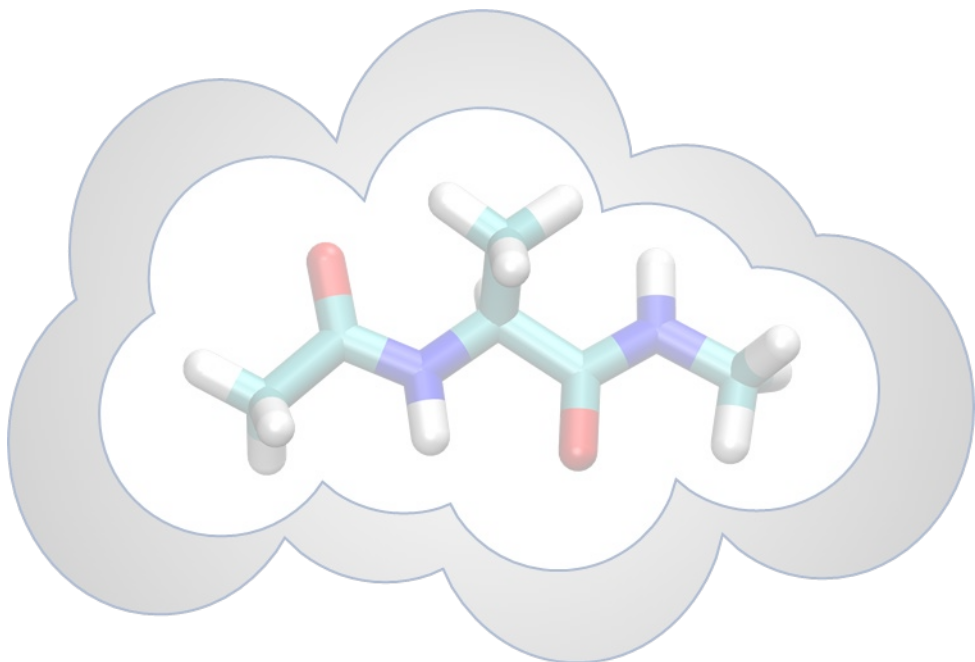
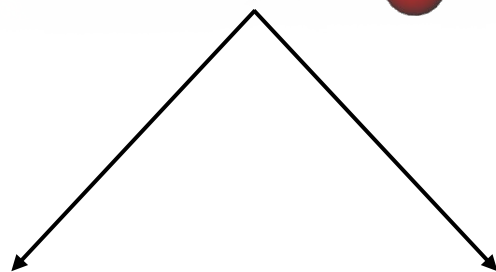
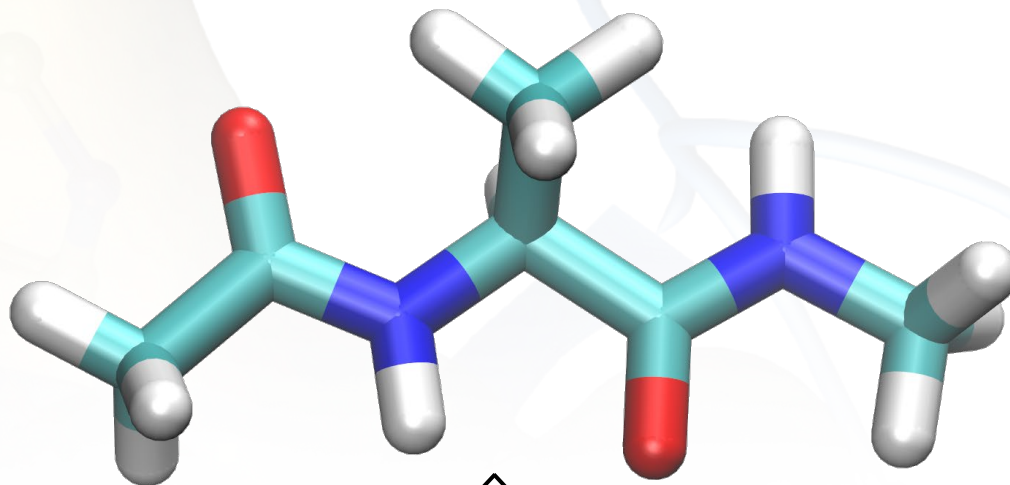
$$\Delta G = \Delta H - T\Delta S$$
$$\Delta G_F = \Delta G_f - \Delta G_u$$



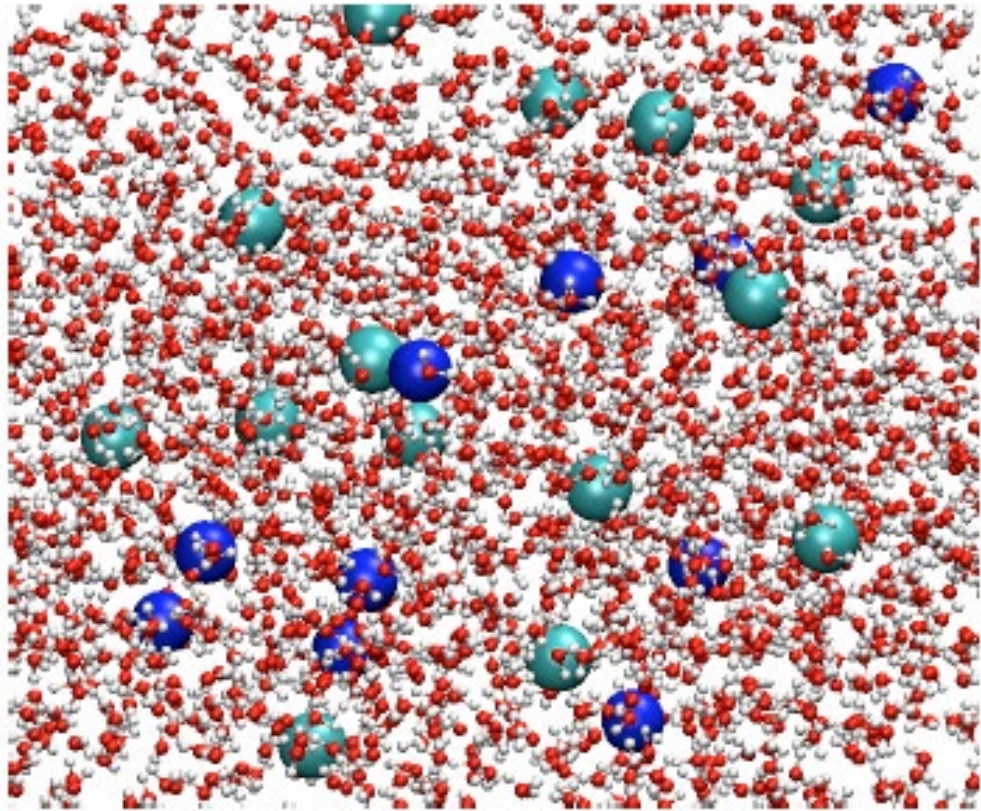
Molecular Dynamics Solvation



Molecular Dynamics Solvation



Molecular Dynamics Explicit Solvation



Explicit solvation uses specific **water models** to simulate bulk properties and electrostatic screening.

Advantages:

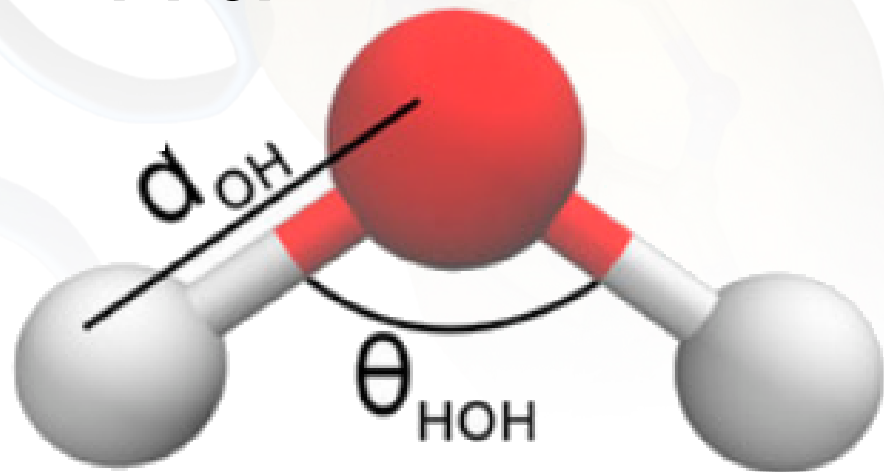
- High level detail (ions, cosolvents, etc)
- Interactions are directly modelled
- No additional terms added to MM FF

Disadvantages:

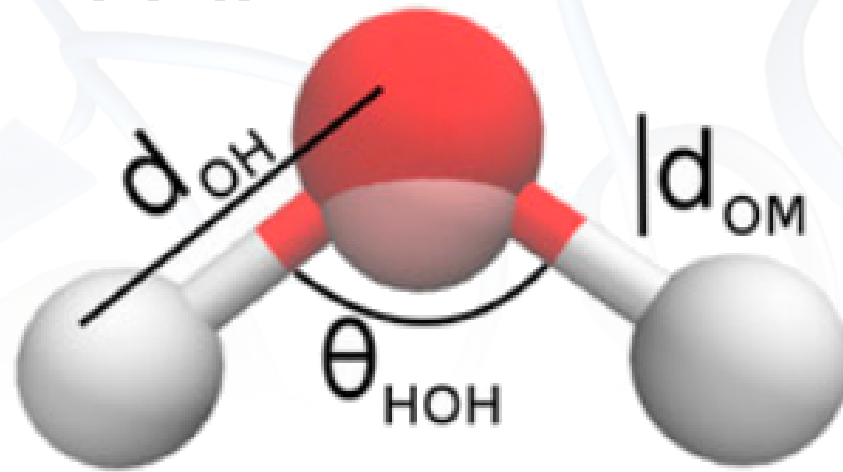
- **High** computational cost
- Slow to converge
- Still a model

Molecular Dynamics Explicit Solvation

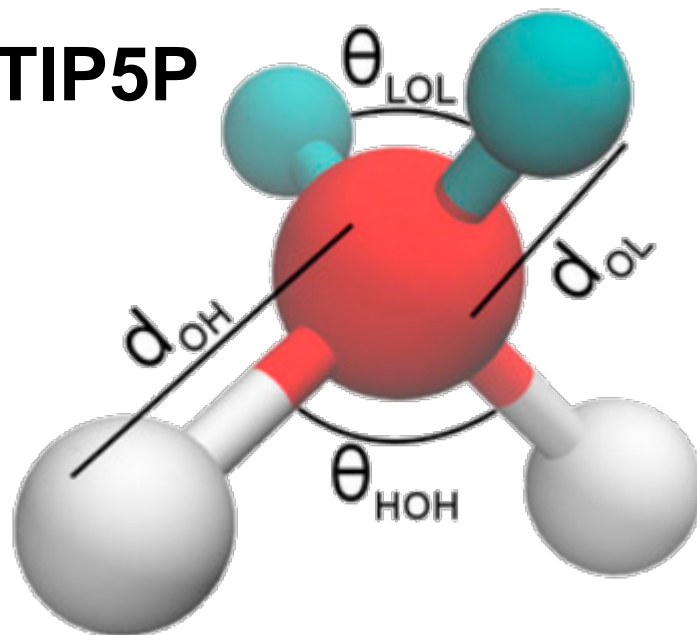
TIP3P



TIP4P

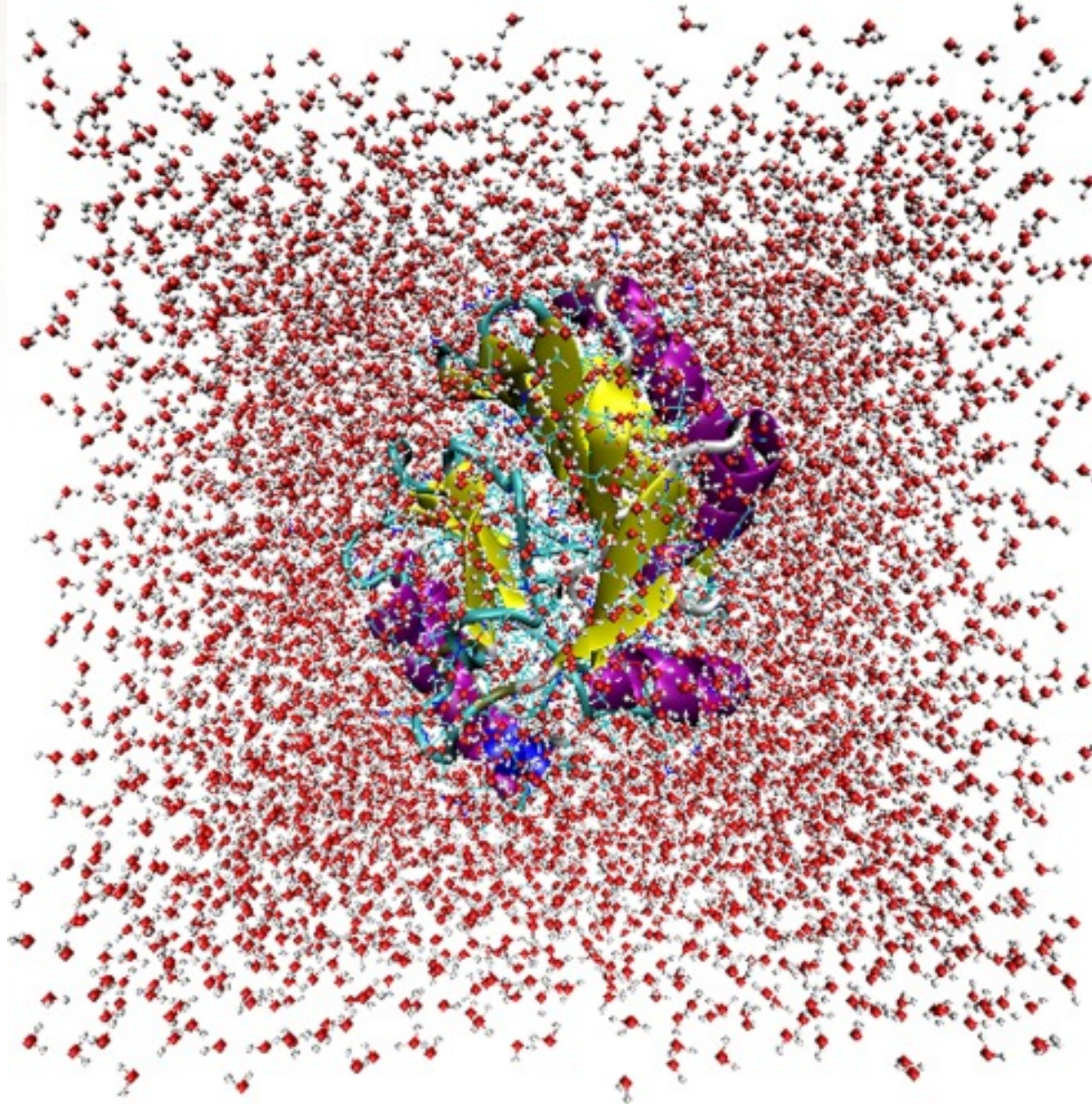


TIP5P

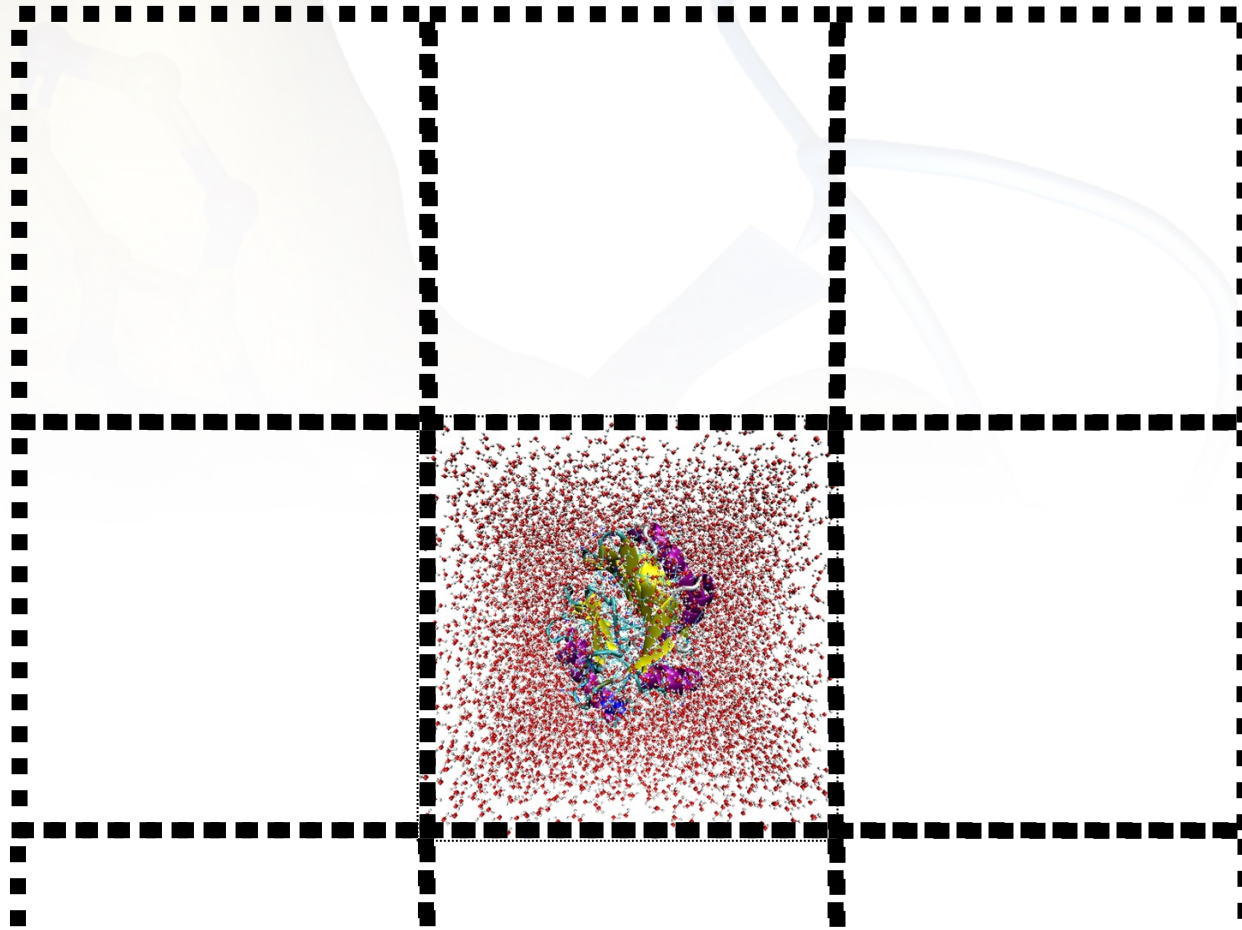


$$\begin{aligned}d_{OL} &= 0.7 \text{ \AA} \\d_{OM} &= 0.15 \text{ \AA} \\d_{OH} &= 0.9572 \text{ \AA} \\\theta_{LOL} &= 109.47^\circ \\\theta_{HOH} &= 104.52^\circ\end{aligned}$$

Molecular Dynamics Explicit Solvation



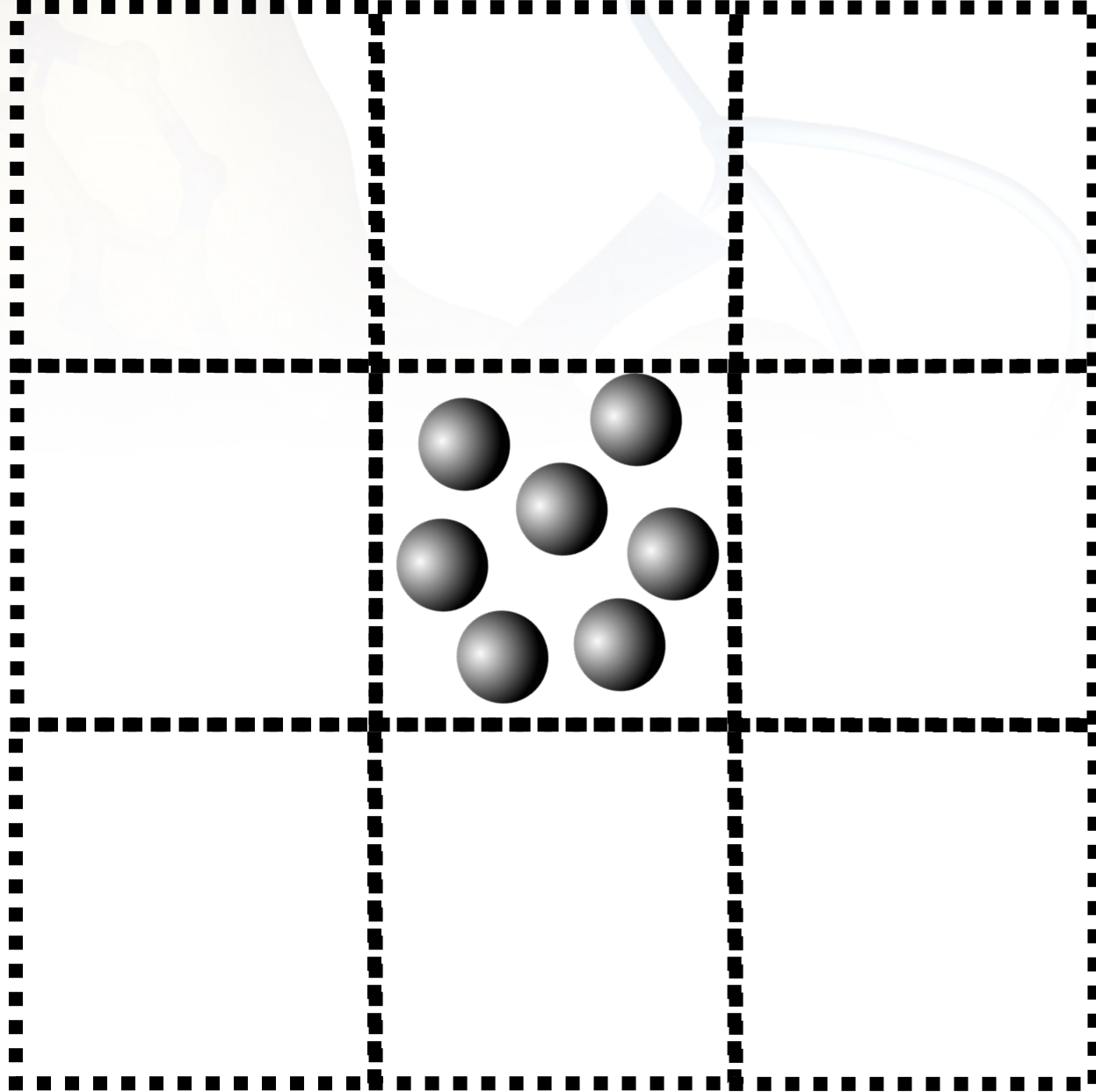
Molecular Dynamics Periodic Boundary Conditions



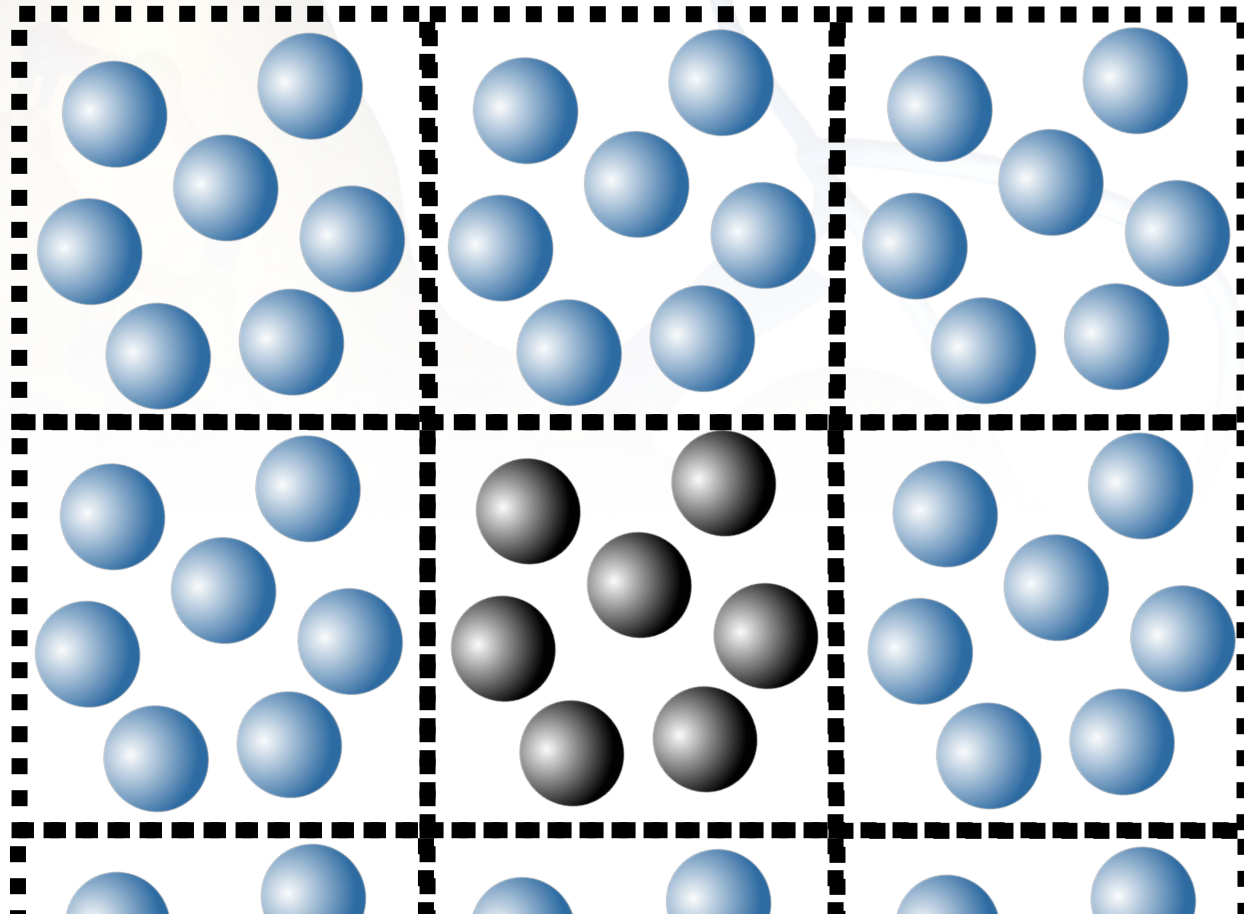
However, when using explicit solvent, **periodic boundary conditions** are *very frequently* used



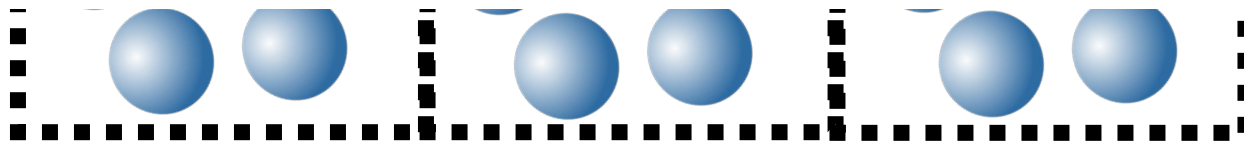
Molecular Dynamics Periodic Boundary Conditions



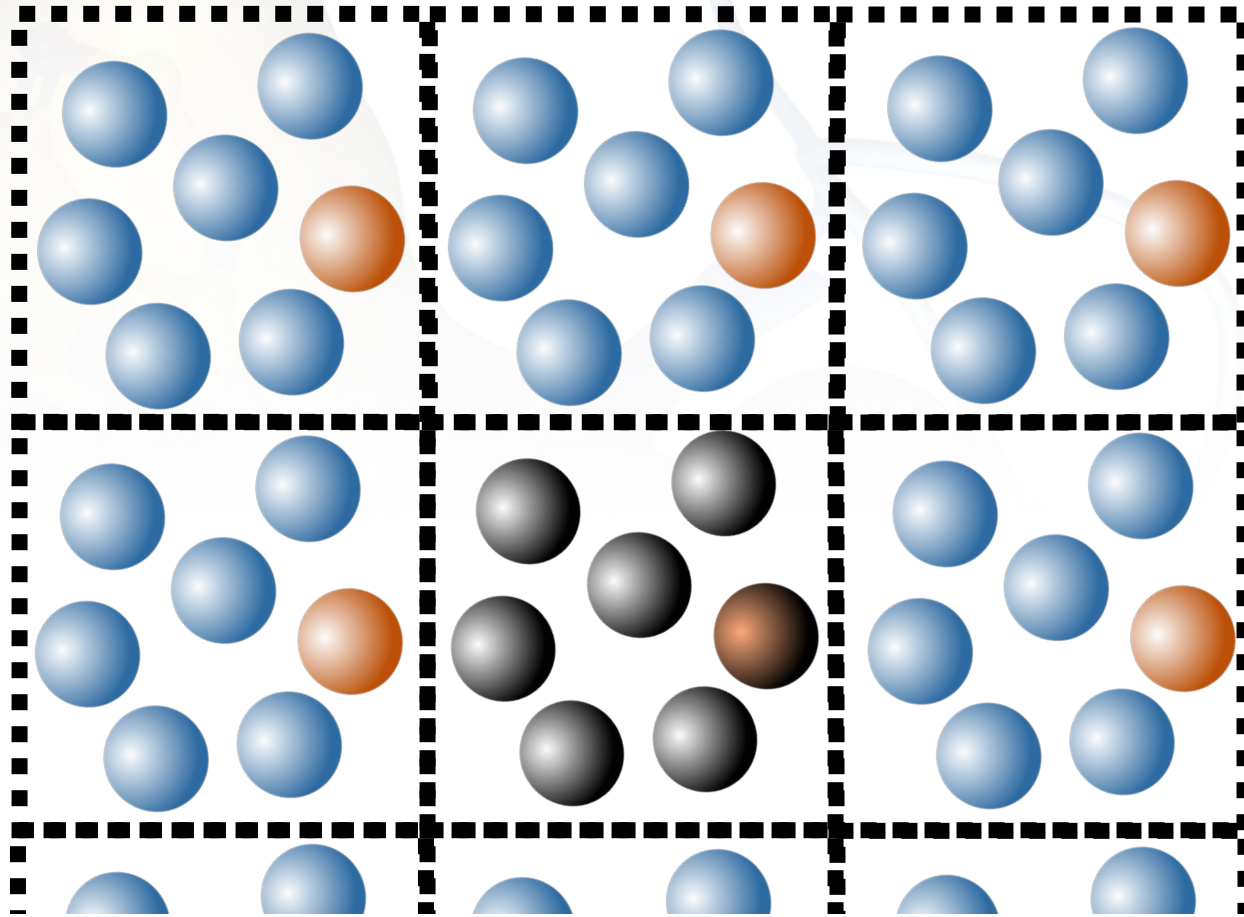
Molecular Dynamics Periodic Boundary Conditions



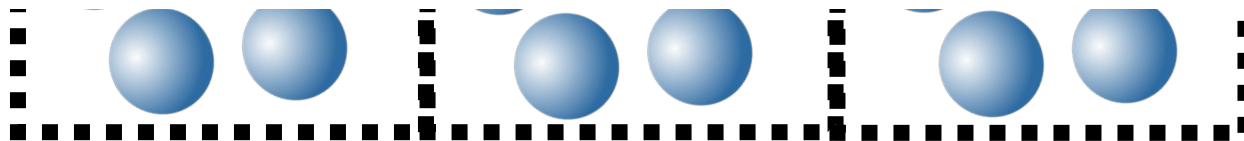
Can be envisioned as virtual images of the primary cell replicated in all directions.



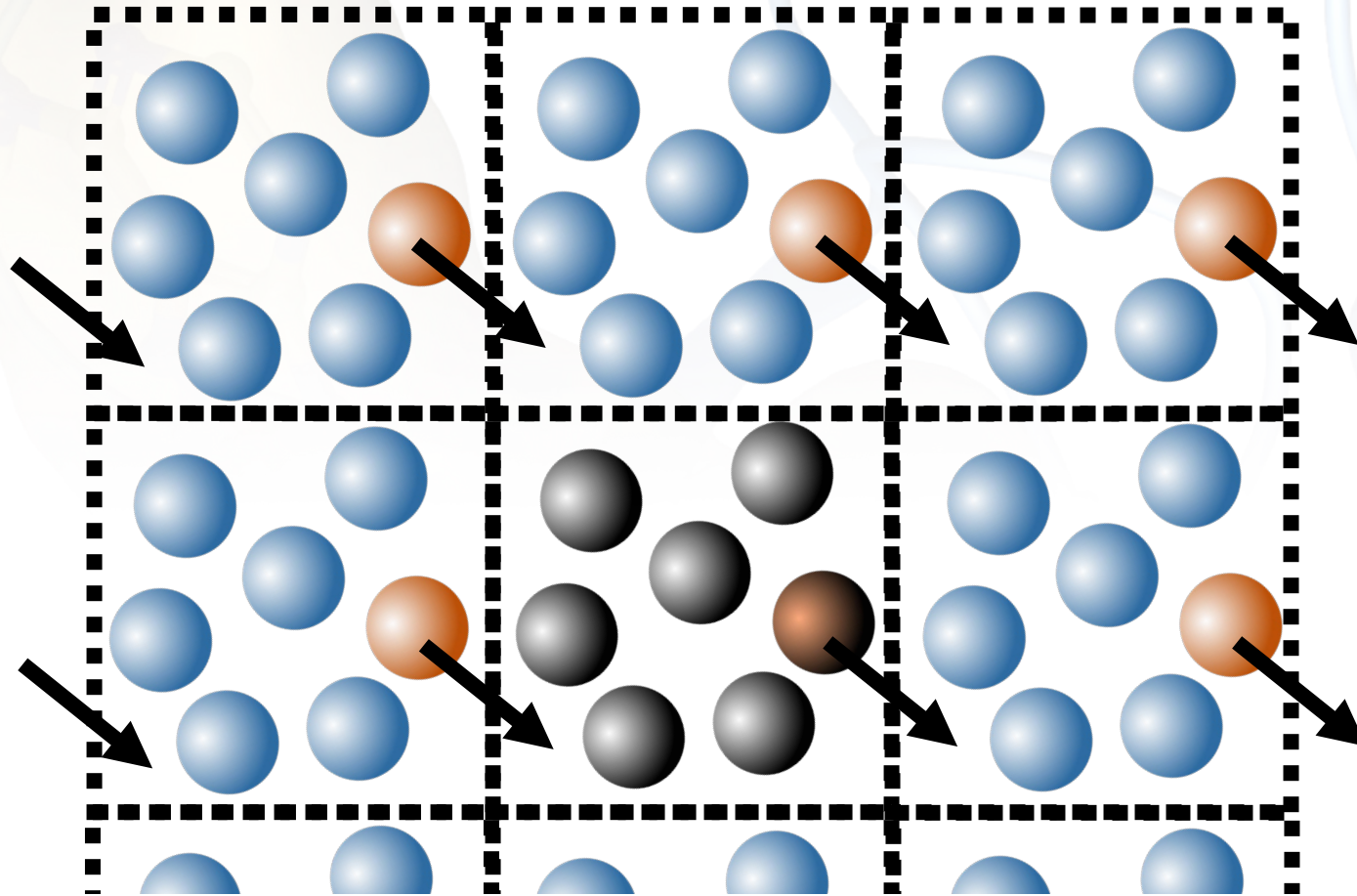
Molecular Dynamics Periodic Boundary Conditions



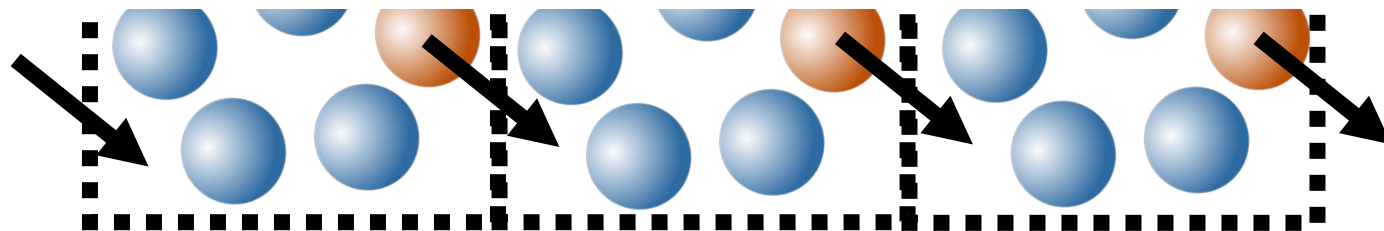
Now we can select one atom in the primary cell, and thus all its images.



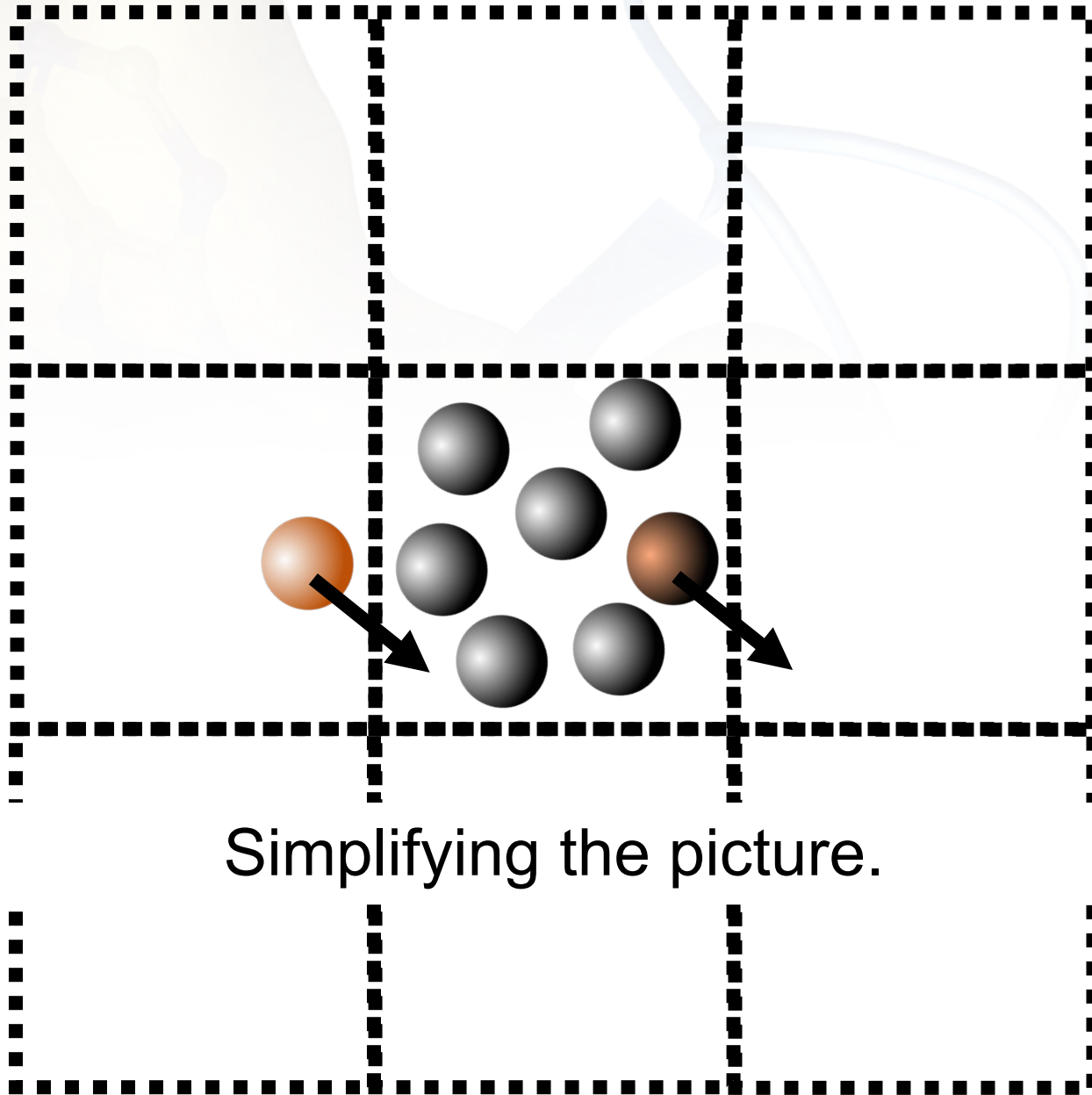
Molecular Dynamics Periodic Boundary Conditions



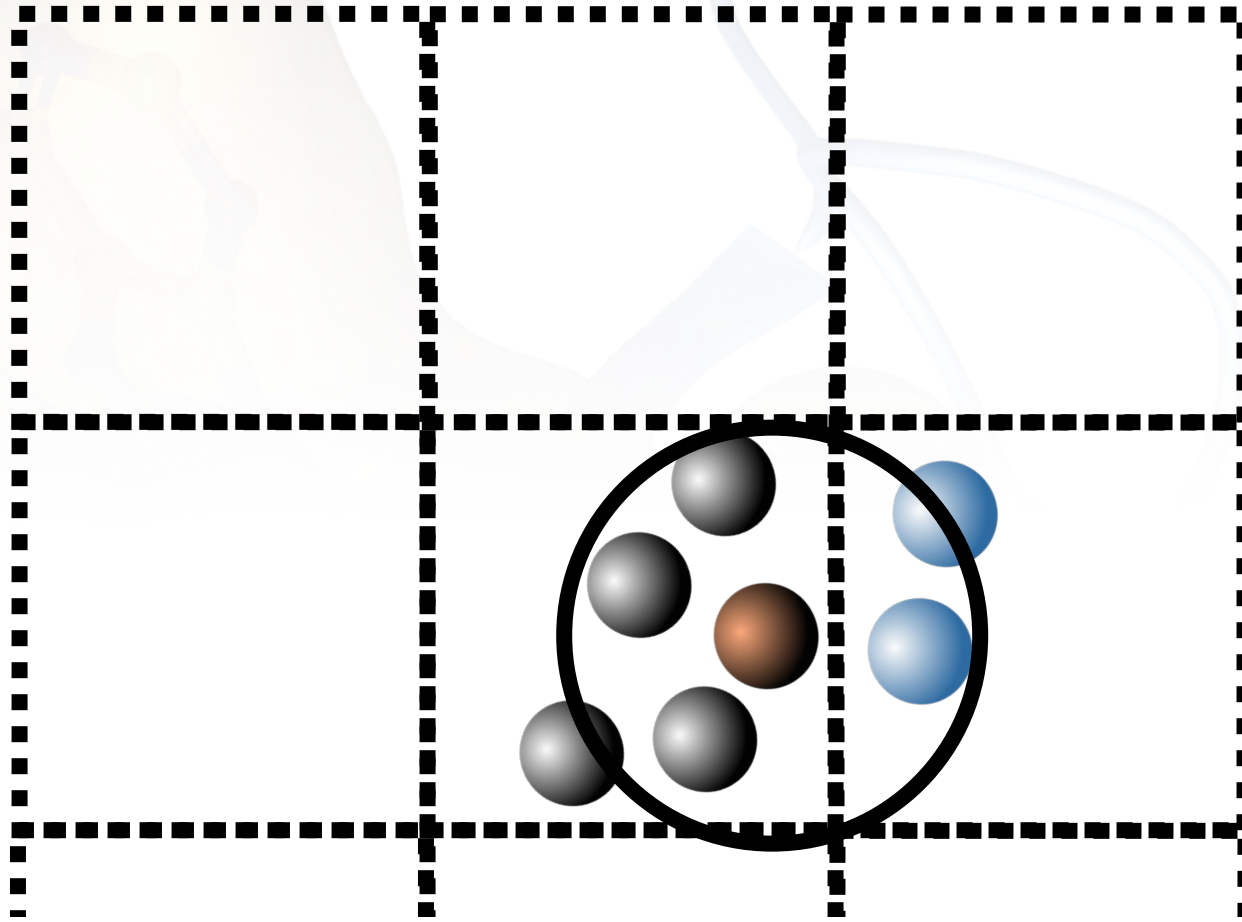
Let's see what happens when it moves.



Molecular Dynamics Periodic Boundary Conditions

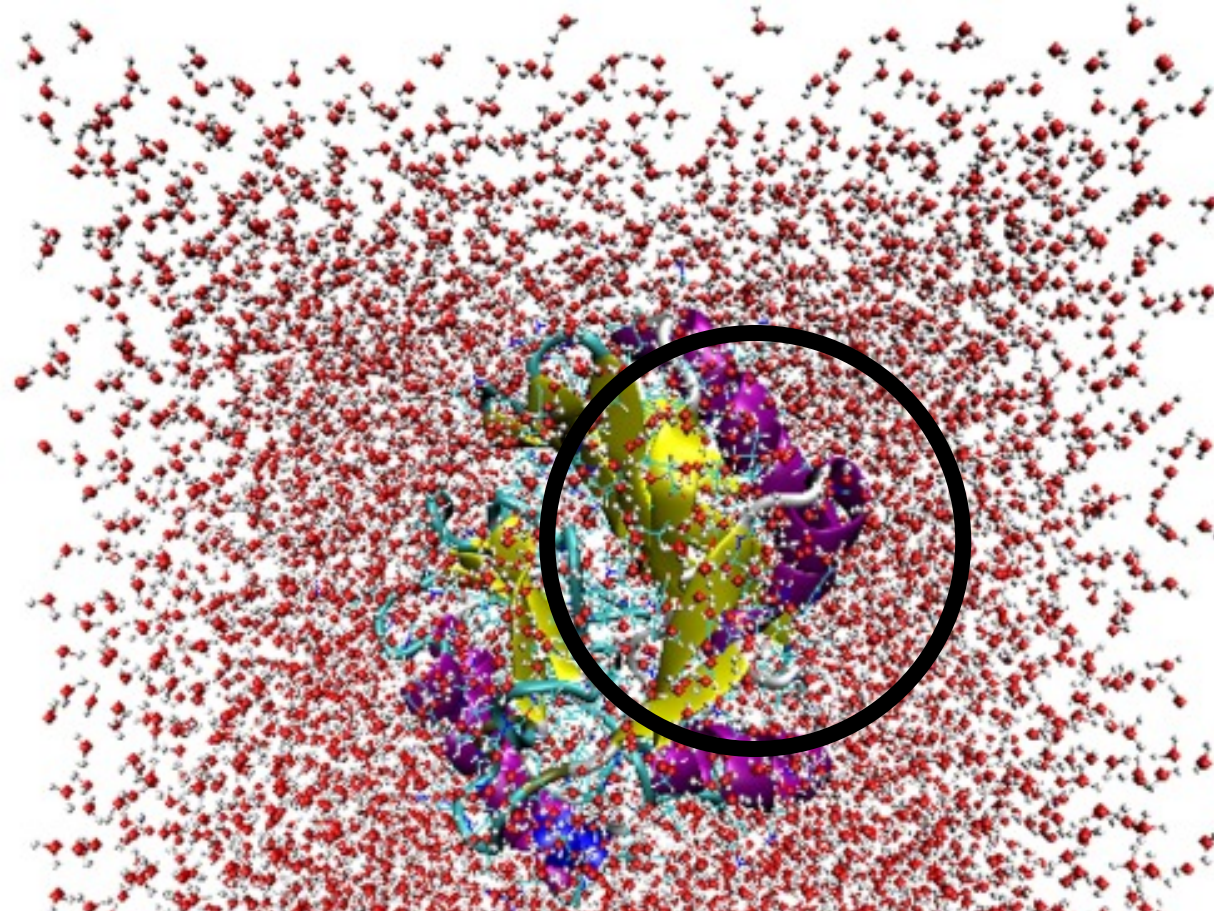


Molecular Dynamics Periodic Boundary Conditions



Apply an interaction (*electrostatic* and *non-bonded*) **cutoff**.
Here, the **minimum image convention** is shown.

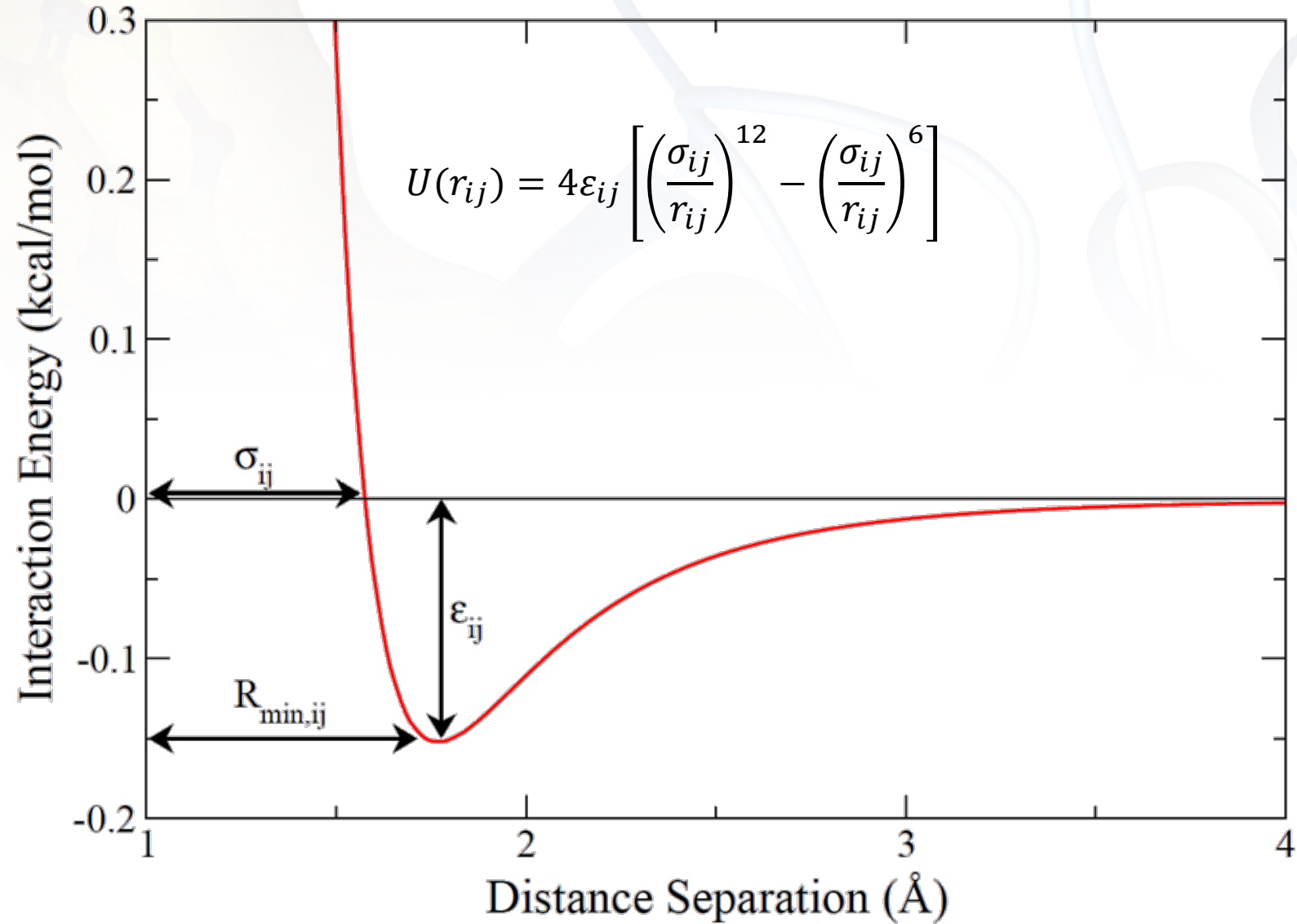
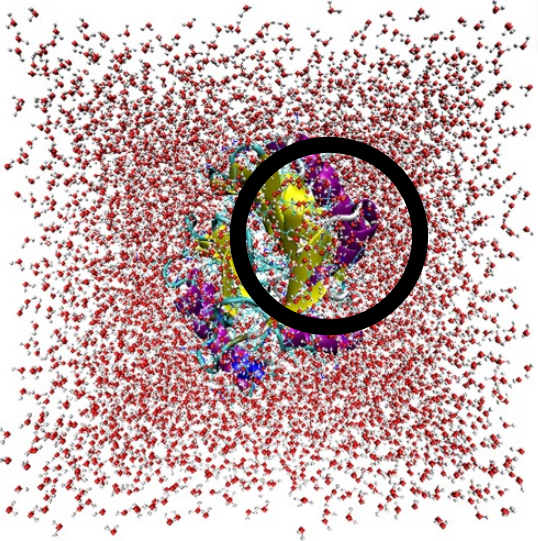
Molecular Dynamics Explicit Solvation



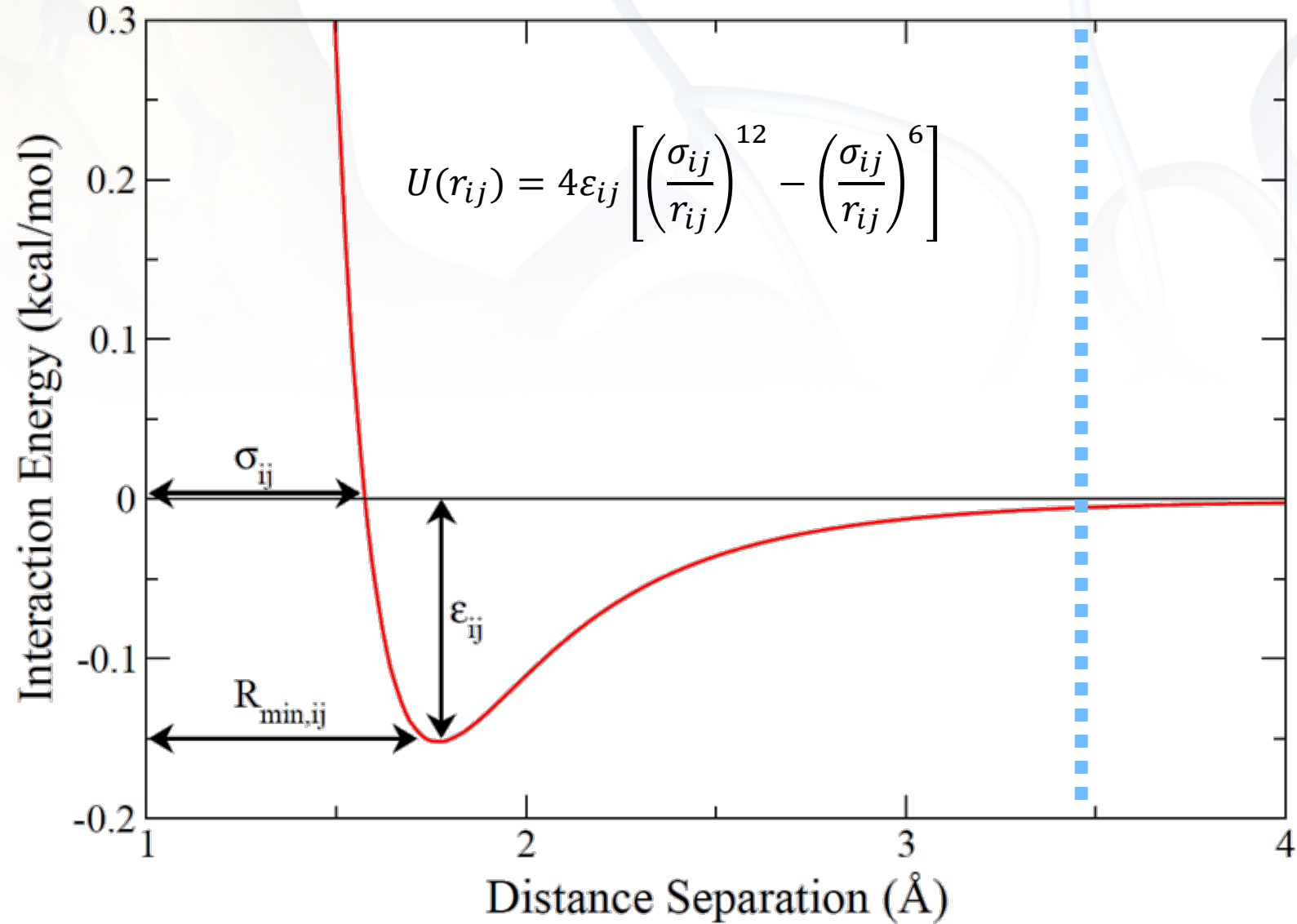
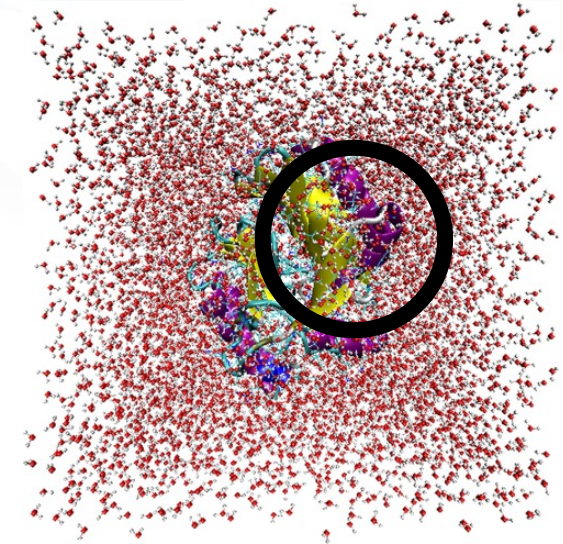
However, even more strict cutoffs *frequently* need to be taken to make a simulation computationally viable.



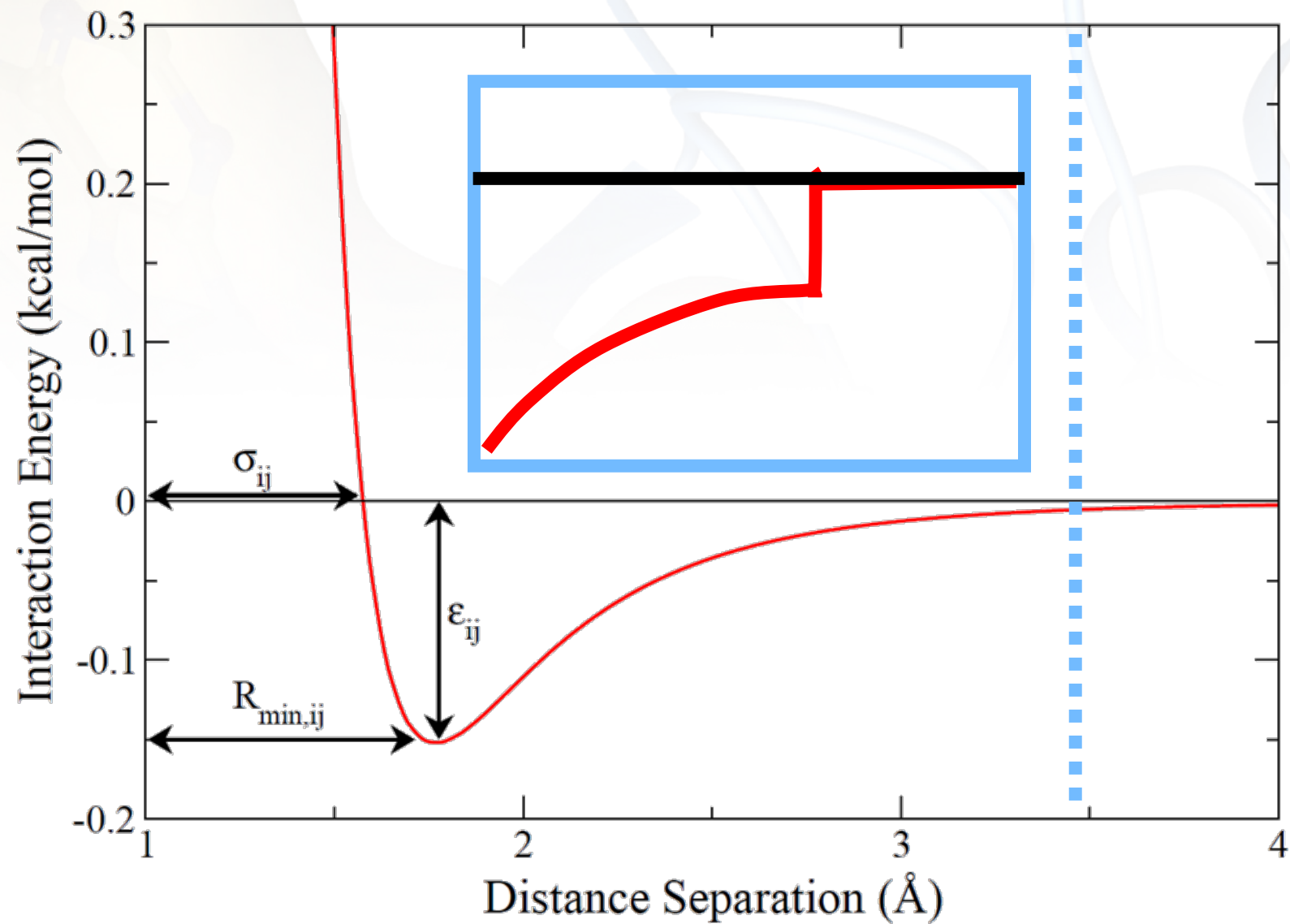
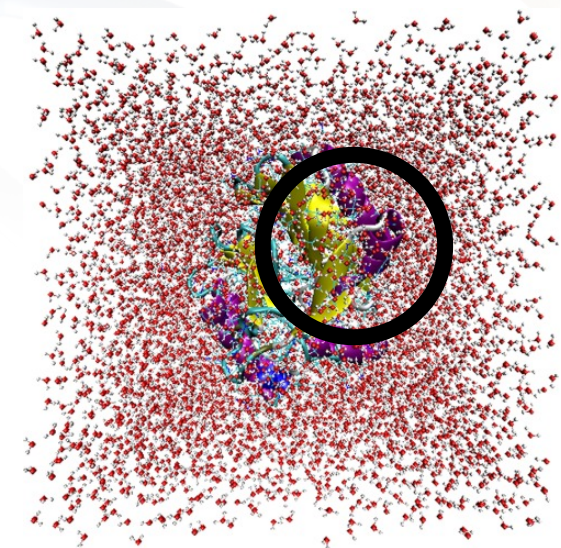
Molecular Dynamics Explicit Solvation



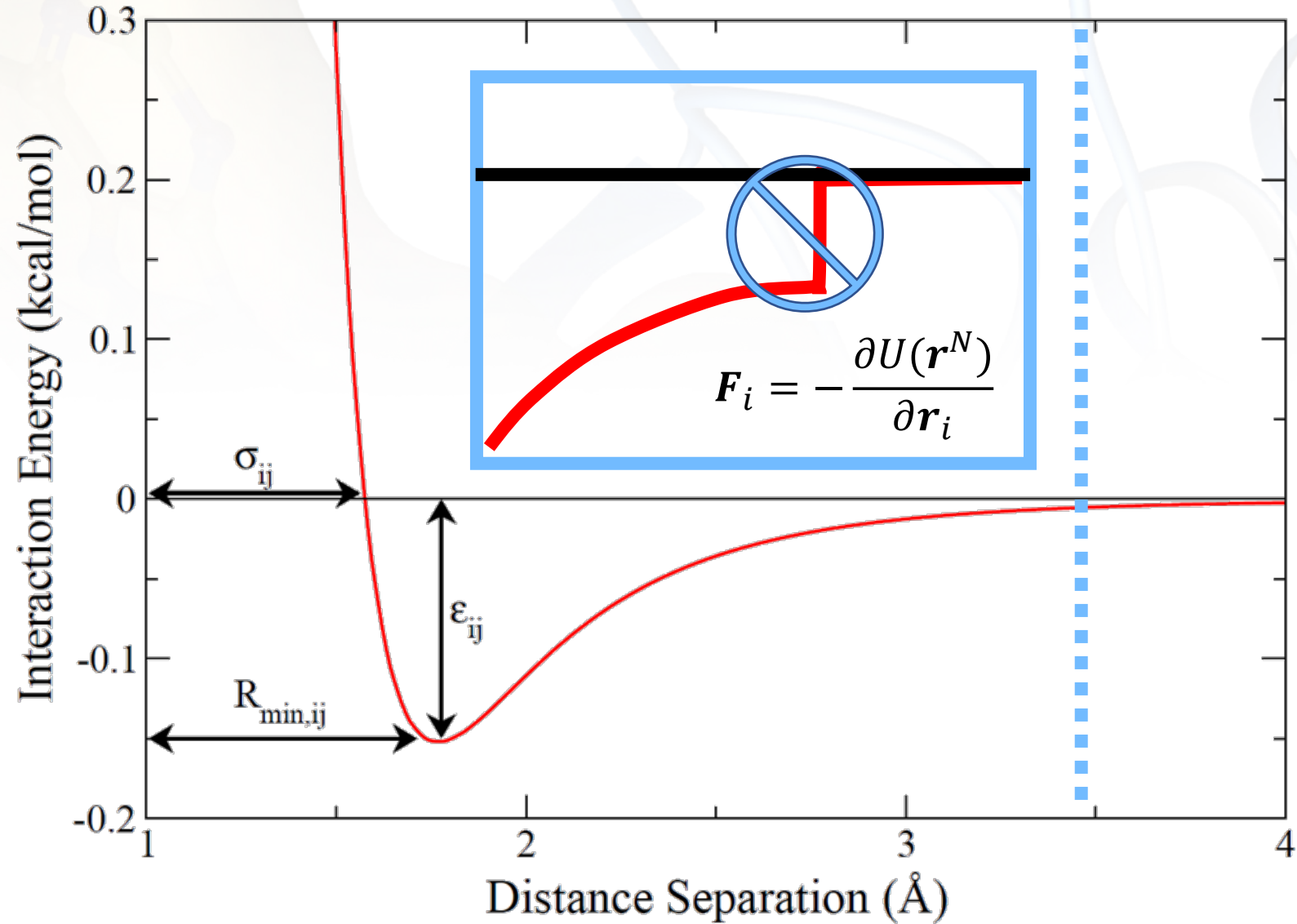
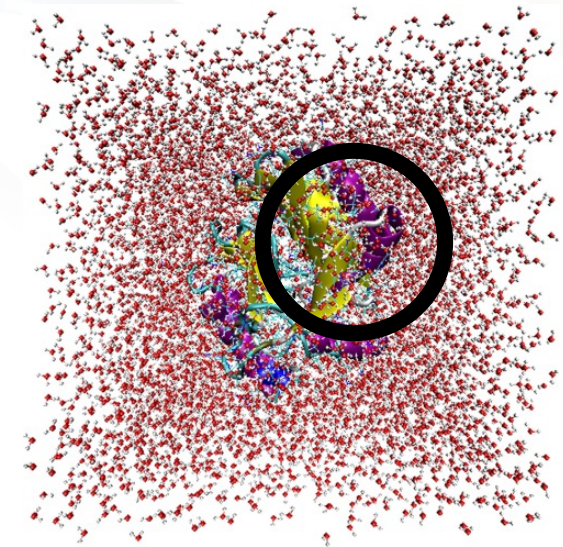
Molecular Dynamics Explicit Solvation



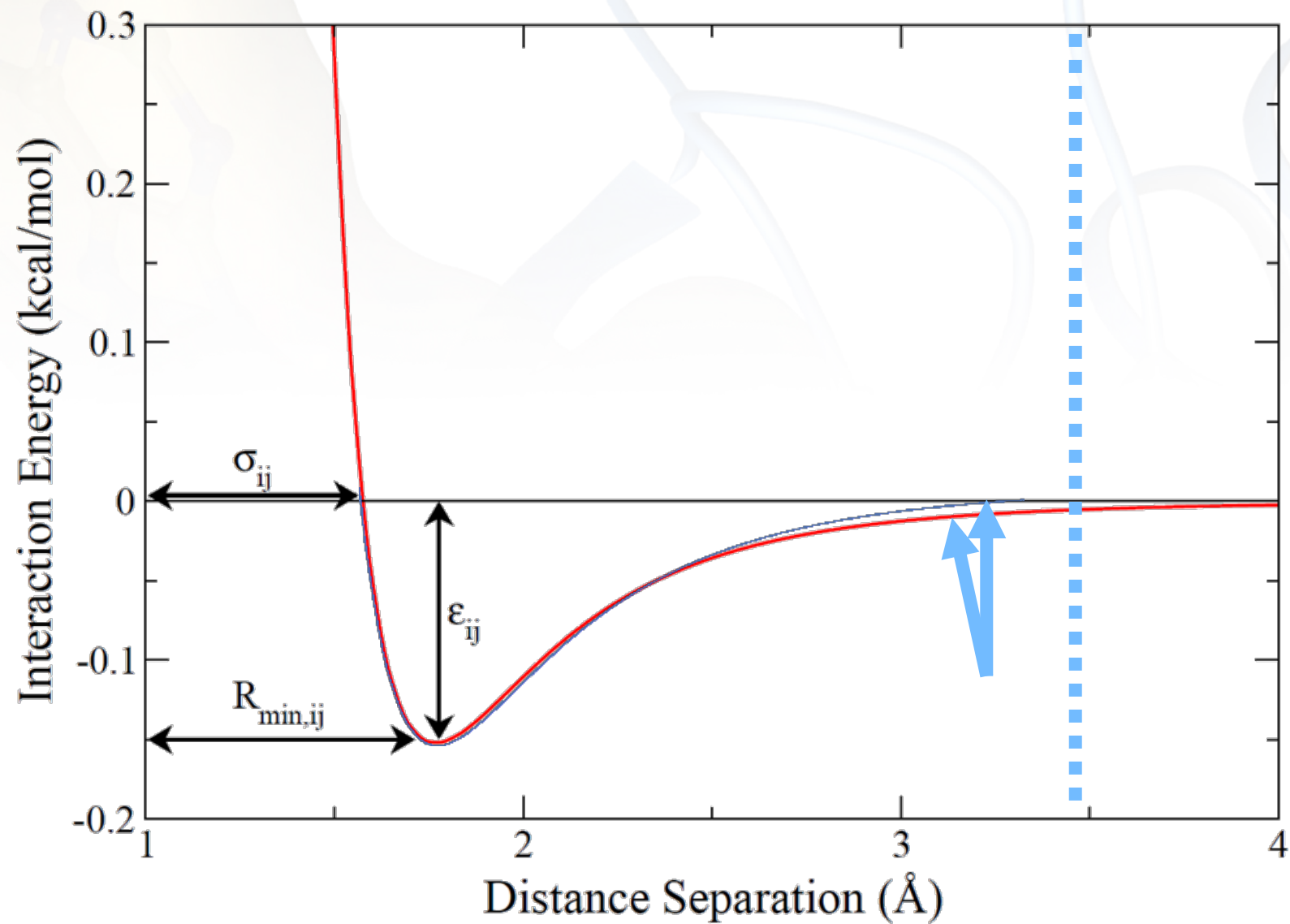
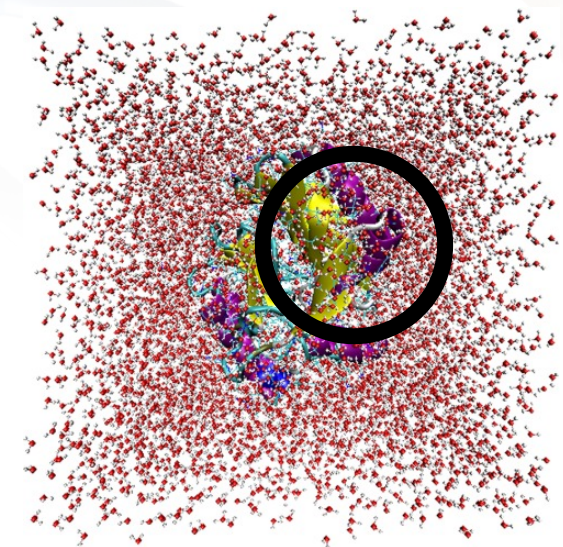
Molecular Dynamics Explicit Solvation



Molecular Dynamics Explicit Solvation

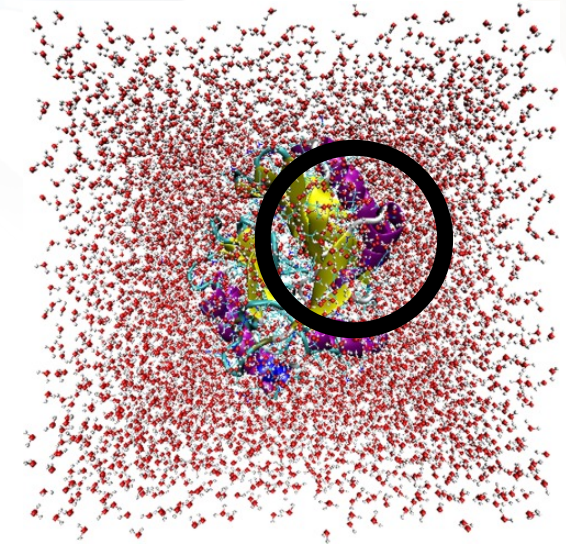


Molecular Dynamics Explicit Solvation



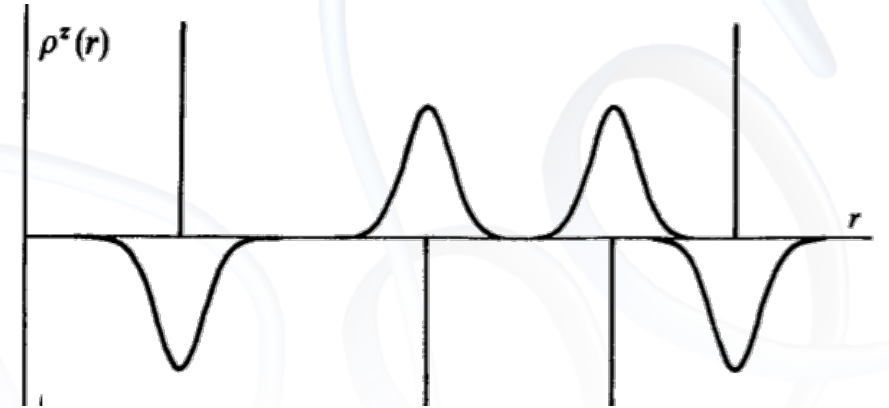
Molecular Dynamics Explicit Solvation

$$U(r_{ij}) = \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}$$

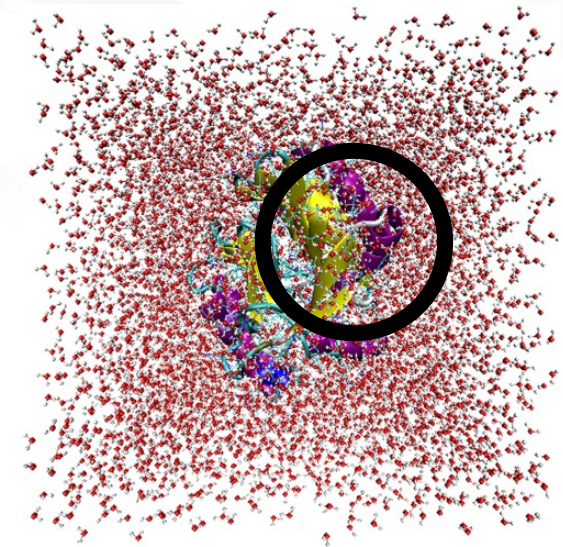


Molecular Dynamics Explicit Solvation

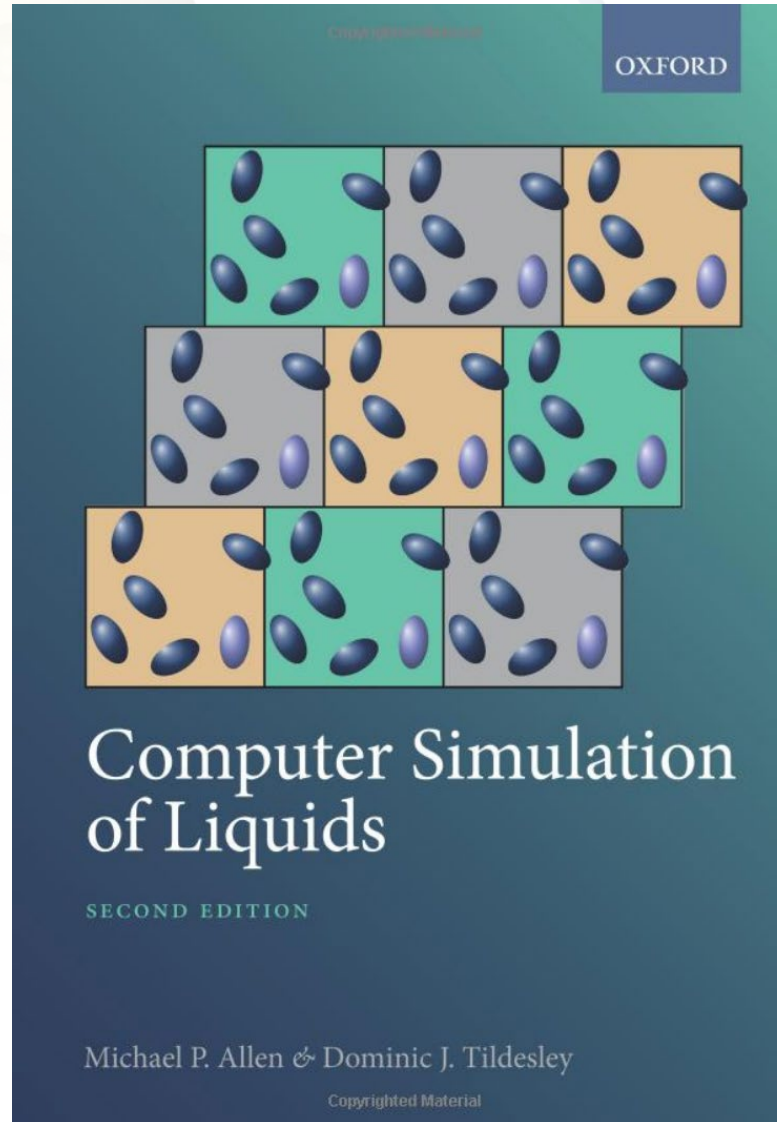
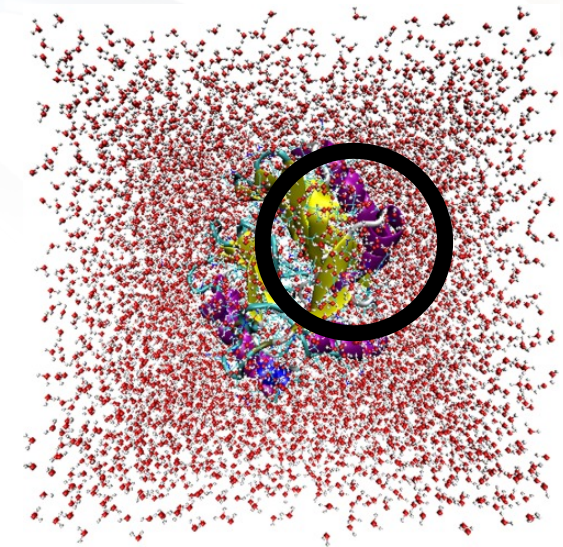
$$U(r_{ij}) = \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}$$



$$\begin{aligned} \psi^{zz}(\epsilon_s = 1) = & \frac{1}{2} \sum_{i=1}^N \sum_{j=1}^N \left(\sum_{|\mathbf{n}|=0}^{\infty} z_i z_j \frac{\text{erfc}(\kappa |\mathbf{r}_{ij} + \mathbf{n}|)}{|\mathbf{r}_{ij} + \mathbf{n}|} \right. \\ & + (1/\pi L^3) \sum_{\mathbf{k} \neq 0} z_i z_j (4\pi^2/k^2) \exp(-k^2/4\kappa^2) \cos(\mathbf{k} \cdot \mathbf{r}_{ij}) \Big) \\ & - (\kappa/\pi^{1/2}) \sum_{i=1}^N z_i^2 + (2\pi/3L^3) \left| \sum_{i=1}^N z_i \mathbf{r}_i \right|^2. \end{aligned}$$

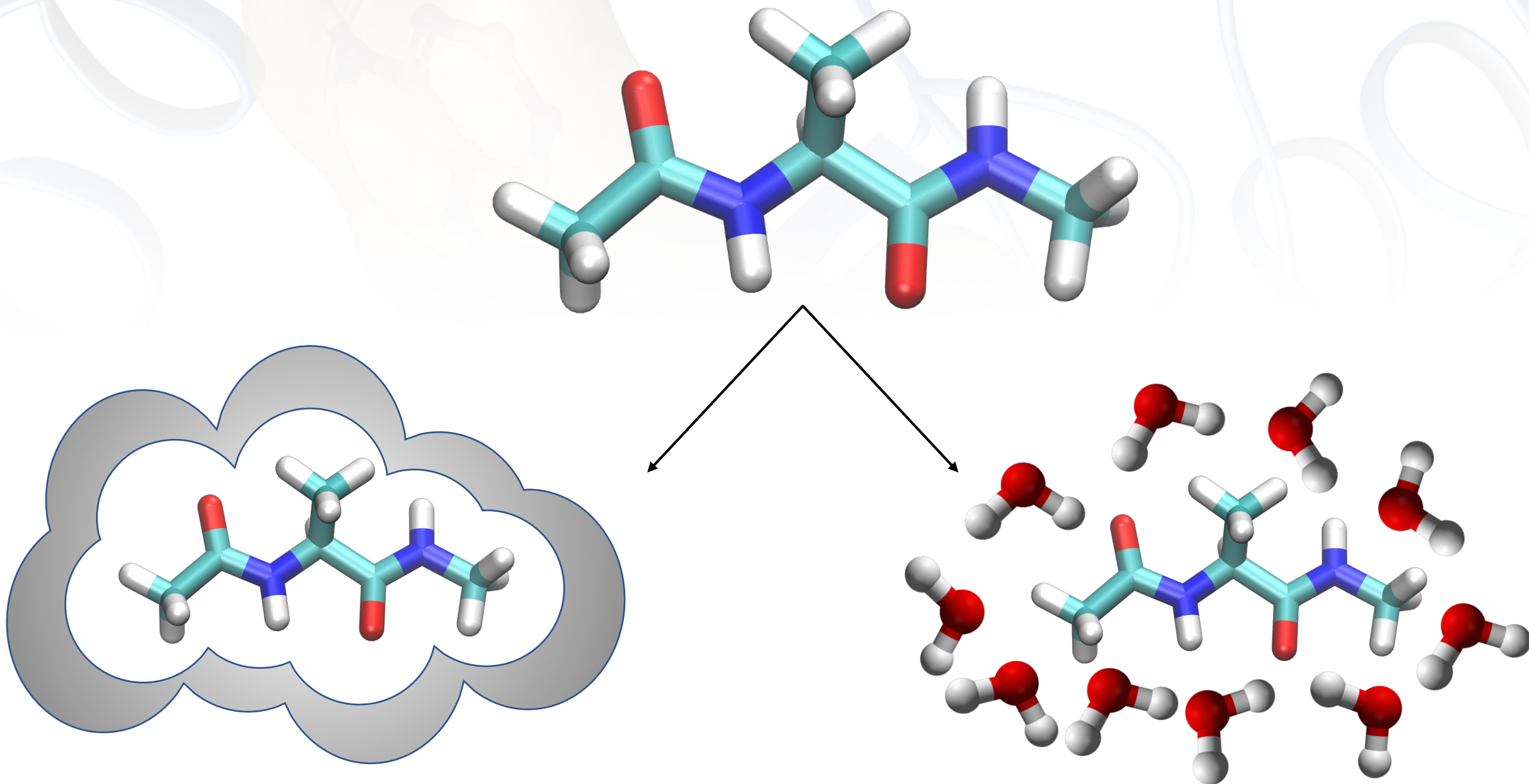


Molecular Dynamics Explicit Solvation

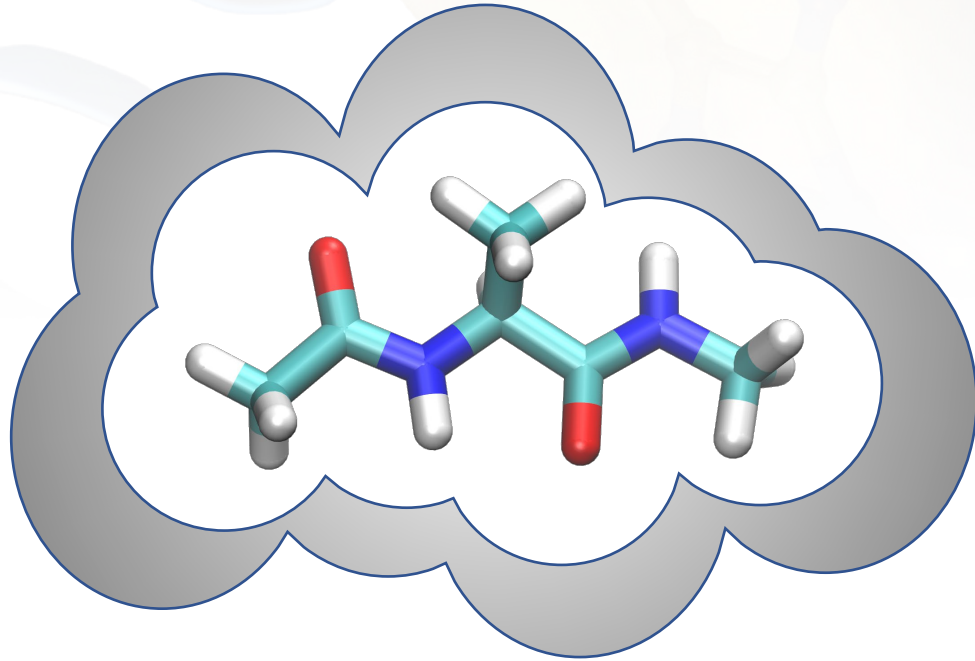


Allen & Tildesley
**Computer Simulations
of Liquids**

Molecular Dynamics Solvation



Molecular Dynamics Solvation



Implicit solvation, or **continuum solvent models**, uses a bulk polarizable medium for electrostatic screening and non-bonded cavitation.

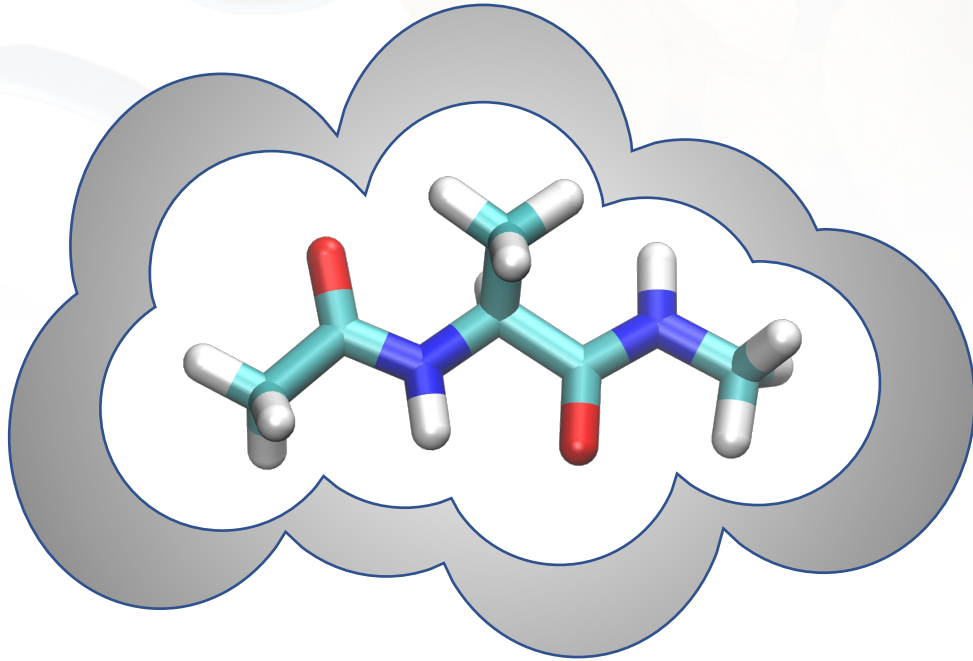
Advantages:

- Lower computational cost
- Fast convergence
- Allows for high-level solutes

Disadvantages:

- Additional terms added to MM FF
- It's a big hunk of metal

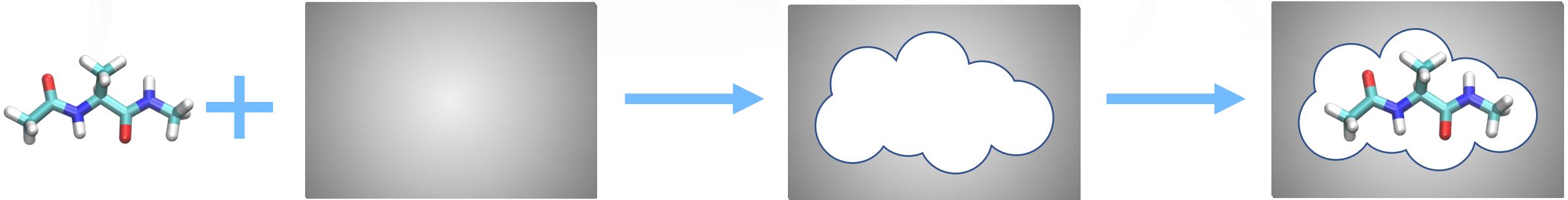
Molecular Dynamics Solvation



$$\begin{aligned} U(\mathbf{r}^N) &= \sum_{bonds} \frac{1}{2} k (r - r_0)^2 + \sum_{angles} \frac{1}{2} k (\theta - \theta_0)^2 \\ &+ \sum_{torsions} \frac{1}{2} V_n [1 + \cos(n\omega - \gamma)] \\ &+ \sum_{i=1}^N \sum_{j>i}^N \left\{ \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} + 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] \right\} \\ &+ U_{solvation} \end{aligned}$$

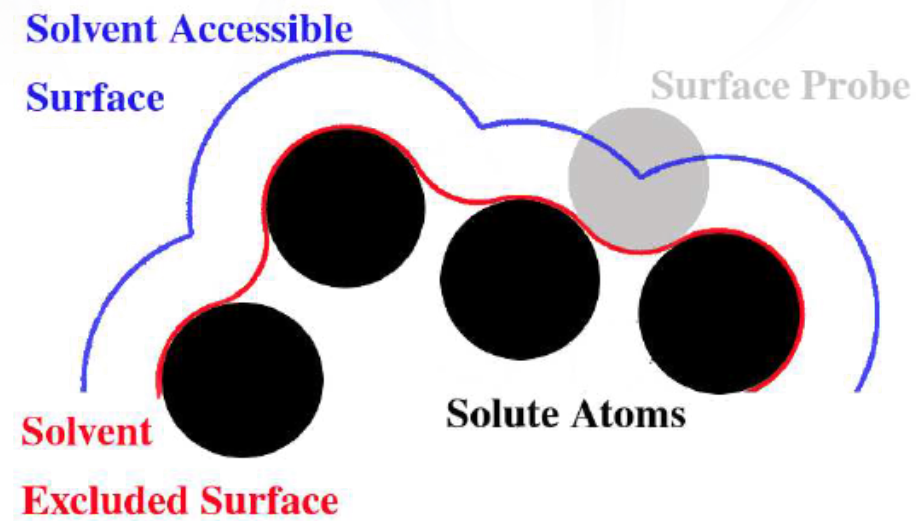
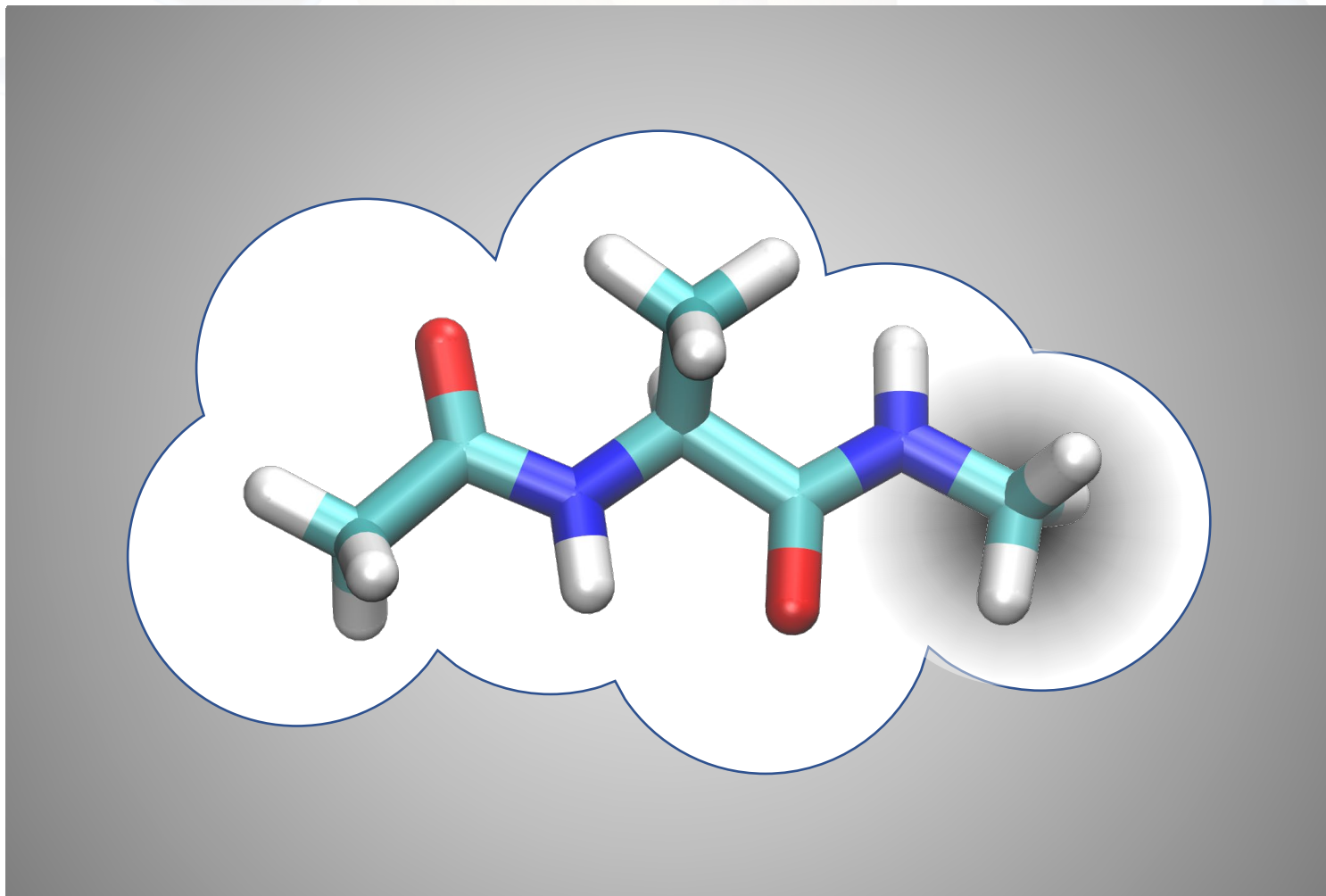
Molecular Dynamics Solvation

$$\Delta G_{\text{solv}} = \Delta G_{\text{cav}} + \Delta G_{\text{vdW}} + \Delta G_{\text{ele}}$$

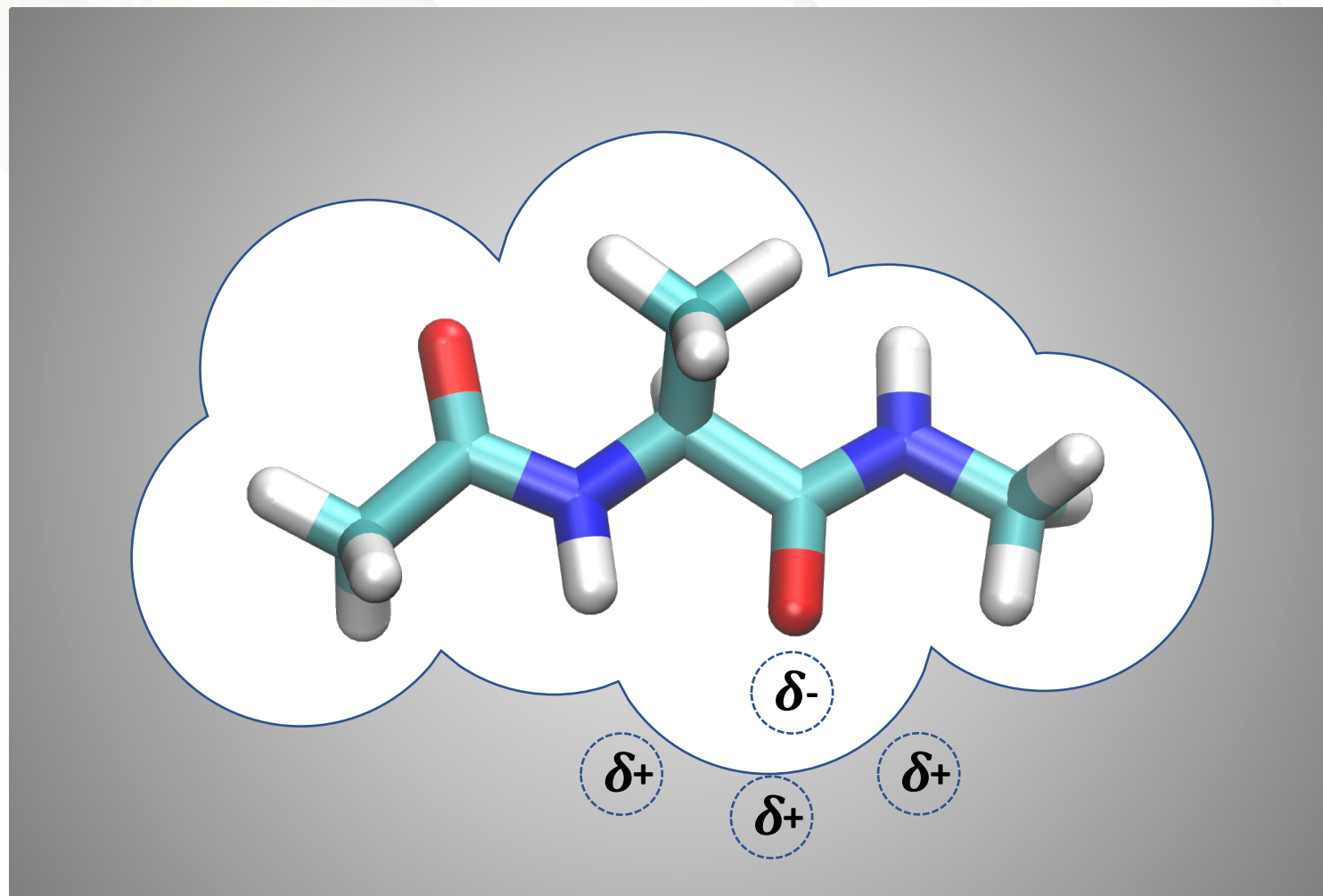


Molecular Dynamics Solvation

$$\Delta G_{\text{cav}} + \Delta G_{\text{vdW}}$$

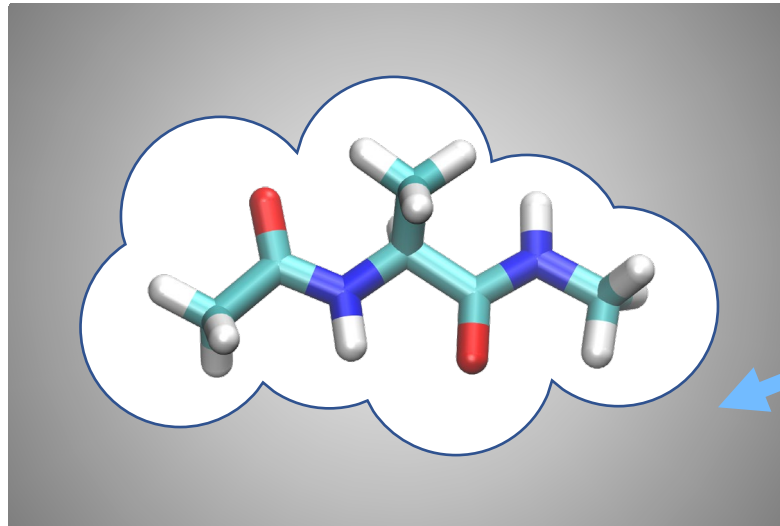


Molecular Dynamics Solvation



Molecular Dynamics Solvation

$$\Delta G_{\text{ele}} = \frac{1}{2} \left(1 - \frac{1}{\epsilon} \right) \sum_{i=1}^N \sum_{j=1}^N \frac{q_i q_j}{f(r_{ij}, a_{ij})}$$

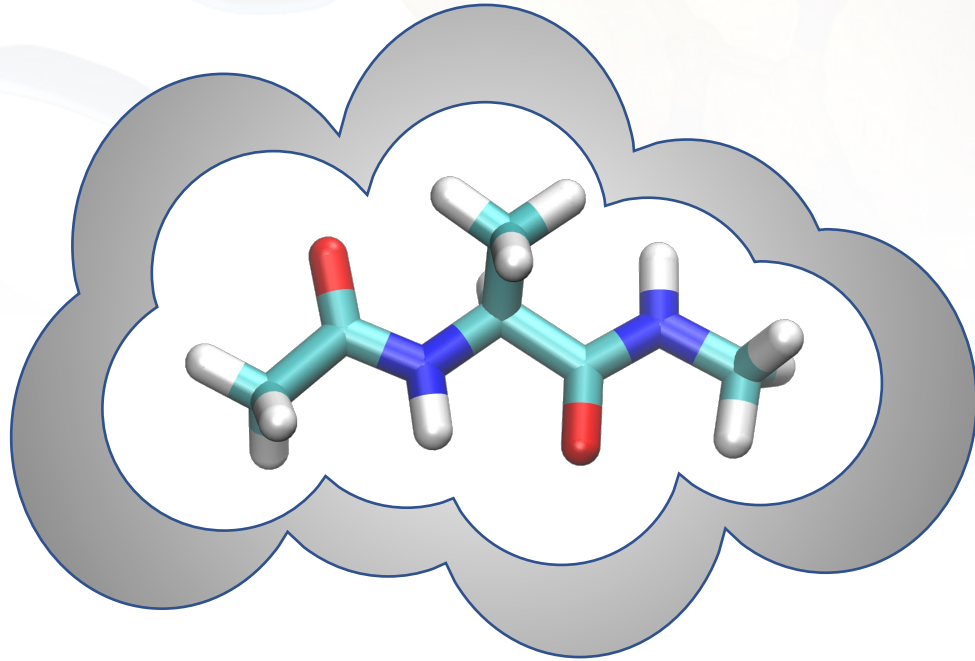


ϵ

Copyright © 2005 Pearson Prentice Hall, Inc.

Material	Dielectric constant ϵ
Vacuum	1.0000
Air (1 atm)	1.0006
Paraffin	2.2
Polystyrene	2.6
Vinyl (plastic)	2–4
Paper	3.7
Quartz	4.3
Oil	4
Glass, Pyrex	5
Rubber, neoprene	6.7
Porcelain	6–8
Mica	7
Water (liquid)	80
Strontium titanate	300

Molecular Dynamics Solvation



Implicit solvation, or **continuum solvent models**, uses a bulk polarizable medium for electrostatic screening and non-bonded cavitation.

Advantages:

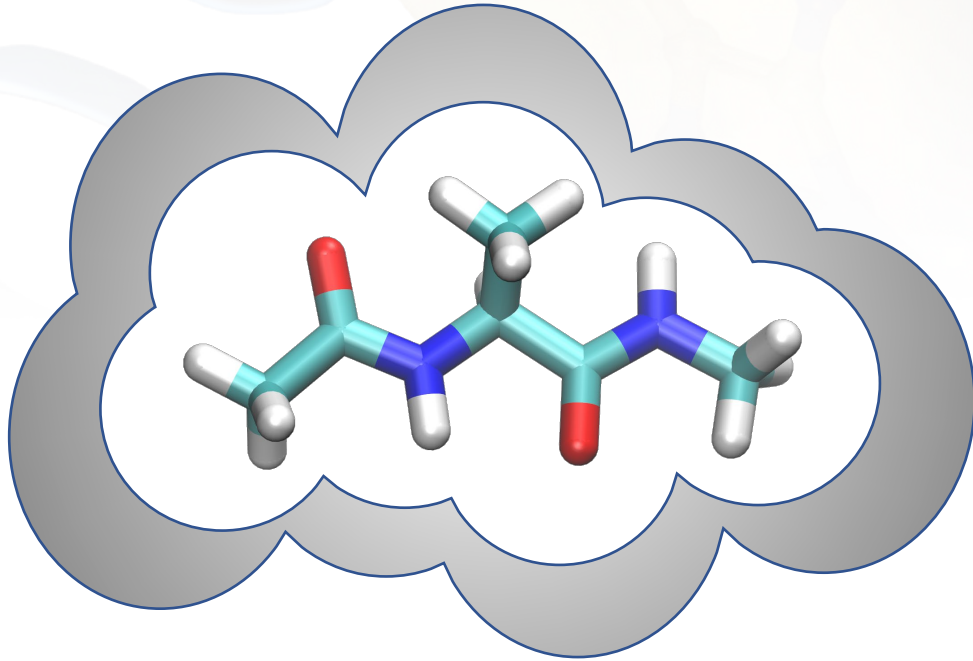
- Lower computational cost
- Fast convergence
- Allows for high-level solutes

Disadvantages:

- Additional terms added to MM FF
- It's a big hunk of metal

Molecular Dynamics Solvation

Implicit solvation



Advantages:

- Very quick
- Allows for more detailed/larger systems

Disadvantages:

- Only accounts for solvent in an average way
 - No direct solvent interactions
 - No hydrogen bonding
 - Problems in cavitation

Introduction to biomolecular simulation

Lecture 2: Force Fields & Solvation Models

