

Mixed Quantum-Classical Molecular Dynamics

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Molecular Dynamics

molecular Schrödinger equation

$$H^{\text{tot}}(\mathbf{r}_e, \mathbf{R}_N) \Phi^{\text{tot}}(\mathbf{r}_e, \mathbf{R}_N) = E^{\text{tot}} \Phi^{\text{tot}}(\mathbf{r}_e, \mathbf{R}_N)$$

molecular Hamiltonian

$$H^{\text{tot}}(\mathbf{r}_e, \mathbf{R}_N) = T^{\text{nuc}}(\mathbf{R}_N) + T^{\text{eln}}(\mathbf{r}_e, \mathbf{R}_N) + U(\mathbf{r}_e, \mathbf{R}_N)$$

Molecular Dynamics

Born-Oppenheimer approximation

$$\Phi^{\text{tot}}(\mathbf{r}_e, \mathbf{R}_N) = \Xi^{\text{nuc}}(\mathbf{R}_N) \Psi^{\text{eln}}(\mathbf{r}_e; \mathbf{R}_N)$$

electronic Schrödinger equation

$$H^{\text{eln}}(\mathbf{R}_N, \mathbf{r}_e) \Psi^{\text{eln}}(\mathbf{r}_e; \mathbf{R}_N) = V(\mathbf{R}_N) \Psi^{\text{eln}}(\mathbf{r}_e; \mathbf{R}_N)$$

$$H^{\text{eln}}(\mathbf{R}_N, \mathbf{r}_e) = T^{\text{eln}}(\mathbf{r}_e) + U(\mathbf{r}_e, \mathbf{R}_N)$$

Molecular Dynamics

Born-Oppenheimer approximation

$$\Phi^{\text{tot}}(\mathbf{r}_e, \mathbf{R}_N) = \Xi^{\text{nuc}}(\mathbf{R}_N) \Psi^{\text{eln}}(\mathbf{r}_e; \mathbf{R}_N)$$

nuclear Schrödinger equation

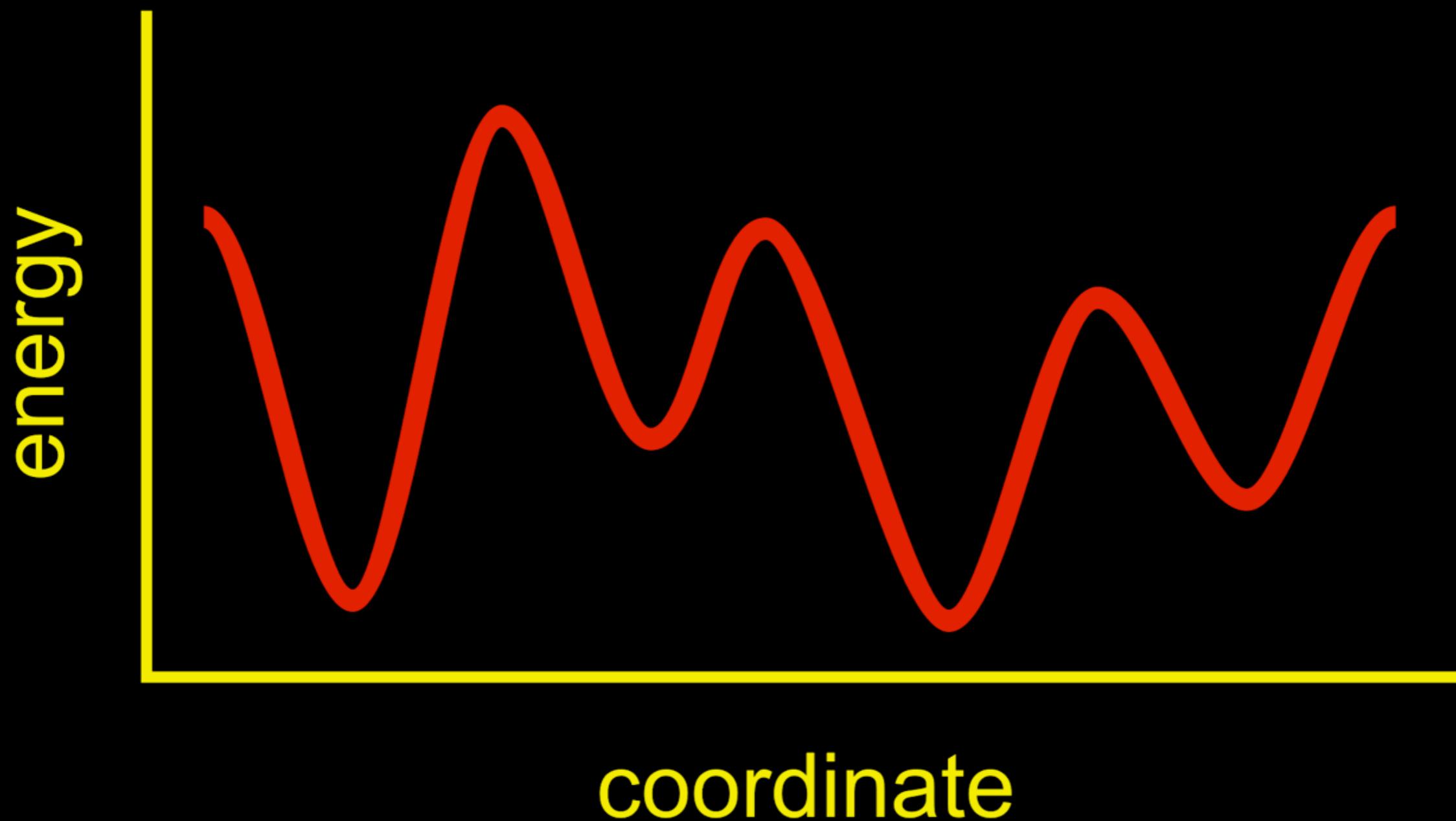
$$H^{\text{nuc}}(\mathbf{R}_N) \Xi^{\text{nuc}}(\mathbf{R}_N) = E^{\text{tot}} \Xi^{\text{nuc}}(\mathbf{R}_N)$$

$$H^{\text{nuc}}(\mathbf{R}_N) = T^{\text{nuc}}(\mathbf{R}_N) + V(\mathbf{R}_N)$$

Molecular Dynamics

potential energy surface for nuclei

$$V(\mathbf{R}) = \langle \Psi^{\text{eln}} | H^{\text{eln}}(\mathbf{R}) | \Psi^{\text{eln}} \rangle$$



Molecular Dynamics

nuclei are classical particles

$$F_n = m_n \ddot{x}_n = -\nabla_{x_n} V(x_1, x_2, \dots, x_N)$$

$$x_n(t) = x_n(t_0) + \dot{x}_n(t_0)(t - t_0) + \frac{1}{2} \ddot{x}_n^2 (t - t_0)^2$$

potential energy and forces

► molecular quantum mechanics

$$V(x_1, x_2, \dots, x_N) = \langle \Psi_e | \hat{H}(x_1, x_2, \dots, x_N) | \Psi_e \rangle$$

► molecular mechanics forcefield

$$V(x_1, x_2, \dots, x_N) = \sum_k v_k(x; p_k)$$

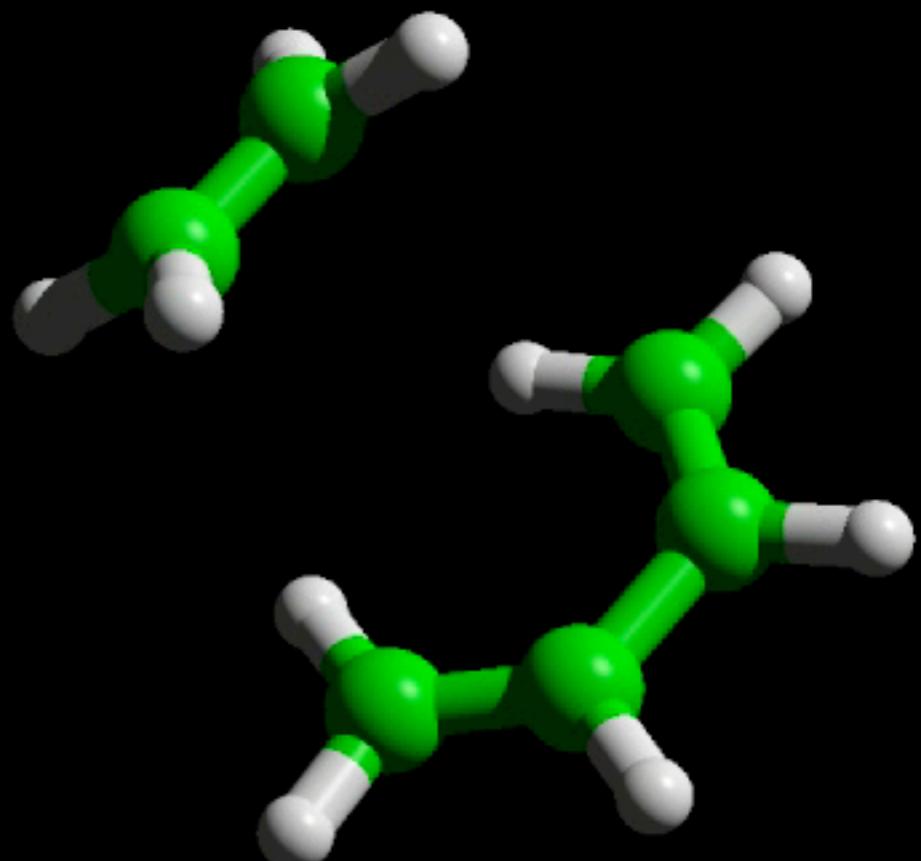
Molecular Dynamics

Hellmann-Feynmann forces

$$F_n = \langle \Psi_e | \nabla H(x_1, x_2, \dots, x_N) | \Psi_e \rangle$$

on-the-fly molecular dynamics

- ▶ reactions
- ▶ photochemistry
- ▶ electron transfer



Molecular Quantum Mechanics

many-electron Schrödinger equation

$$H^{\text{eln}} \Psi^{\text{eln}}(\mathbf{r}) = E \Psi^{\text{eln}}(\mathbf{r})$$

$$H = -\frac{\hbar^2}{2m_e} \sum_i^{n_e} \nabla_i^2 + \sum_i^{n_e} \sum_{j>i}^{n_e} \frac{e^2}{4\pi\epsilon_0 r_{ij}} - \sum_i^{n_e} \sum_A^{N_{\text{QM}}} \frac{e^2 Z_A}{4\pi\epsilon_0 r_{iA}}$$

kinetic energyelectron-electronelectron-nuclei

Molecular Quantum Mechanics

Hartree approximation

- ▶ product of one electron wavefunctions (orbitals)

$$\Psi(r_1, r_2, \dots, r_n) = \phi_1(r_1)\phi_2(r_2)\dots\phi_n(r_n)$$

- ▶ correct if no electron-electron interaction

$$H = -\frac{\hbar^2}{2m_e} \sum_i^{n_e} \nabla_i^2 - \sum_i^{n_e} \sum_A^{N_{QM}} \frac{e^2 Z_A}{4\pi\epsilon_0 r_{iA}}$$

Molecular Quantum Mechanics

Hartree approximation

- ▶ product of one electron wavefunctions (orbitals)

$$\Psi(r_1, r_2, \dots, r_n) \approx \phi_1(r_1)\phi_2(r_2)\dots\phi_n(r_n)$$

- ▶ incorrect due to electron-electron interaction

$$H = -\frac{\hbar^2}{2m_e} \sum_i^{n_e} \nabla_i^2 - \sum_i^{n_e} \sum_A^{N_{QM}} \frac{e^2 Z_A}{4\pi\epsilon_0 r_{iA}} + \sum_i^{n_e} \sum_{j>i}^{n_e} \frac{e^2}{4\pi\epsilon_0 r_{ij}}$$

Molecular Quantum Mechanics

Hartree approximation

- ▶ product of one electron wavefunctions (orbitals)

$$\Psi(r_1, r_2, \dots, r_n) \approx \phi_1(r_1)\phi_2(r_2)\dots\phi_n(r_n)$$

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$$H = -\frac{\hbar^2}{2m_e} \sum_i^{n_e} \nabla_i^2 - \sum_i^{n_e} \sum_A^{N_{QM}} \frac{e^2 Z_A}{4\pi\epsilon_0 r_{iA}} + \sum_i^{n_e} \sum_{j>i}^{n_e} \frac{e^2}{4\pi\epsilon_0 r_{ij}}$$

- ▶ mean field approach

$$\sum_{j \neq i}^{n_e} \frac{e^2}{r_j - r_i} \approx e^2 \int \frac{\rho_{\dots, h, j, k, \dots}(r)}{r - r_i} dr$$

Molecular Quantum Mechanics

Hartree approximation

- ▶ self-consistent-field iteration

Molecular Quantum Mechanics

Hartree approximation

- ▶ self-consistent-field iteration

$$\Psi = \phi_1 \phi_2 \phi_3 \phi_4$$

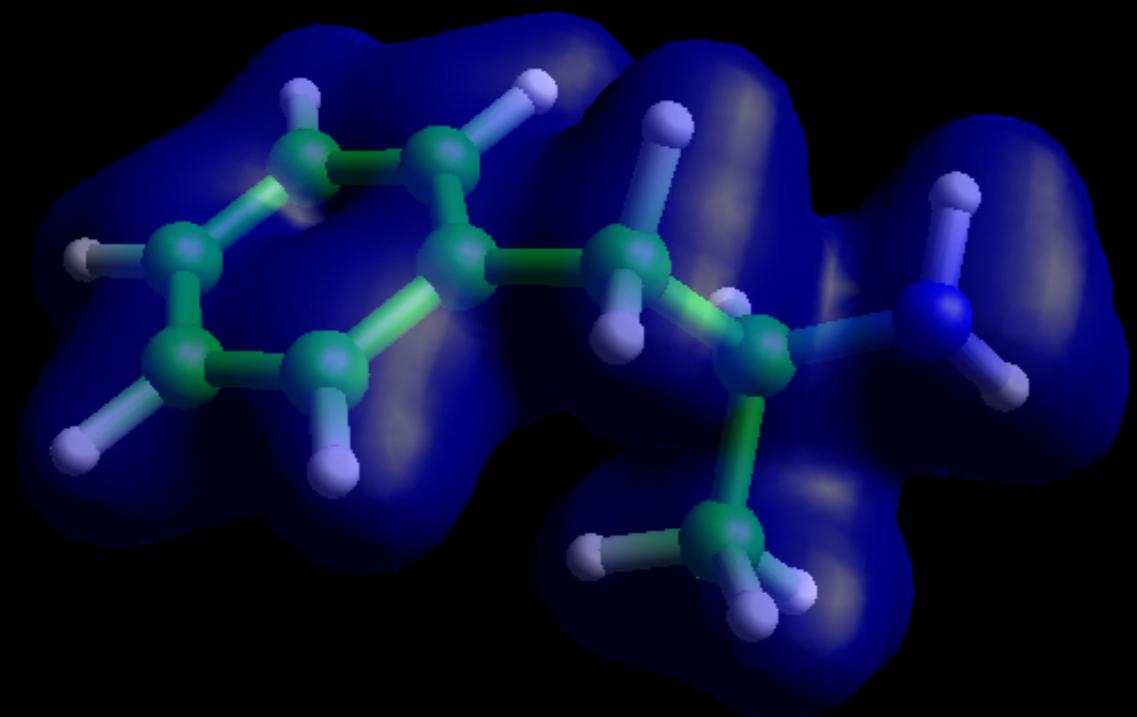
density



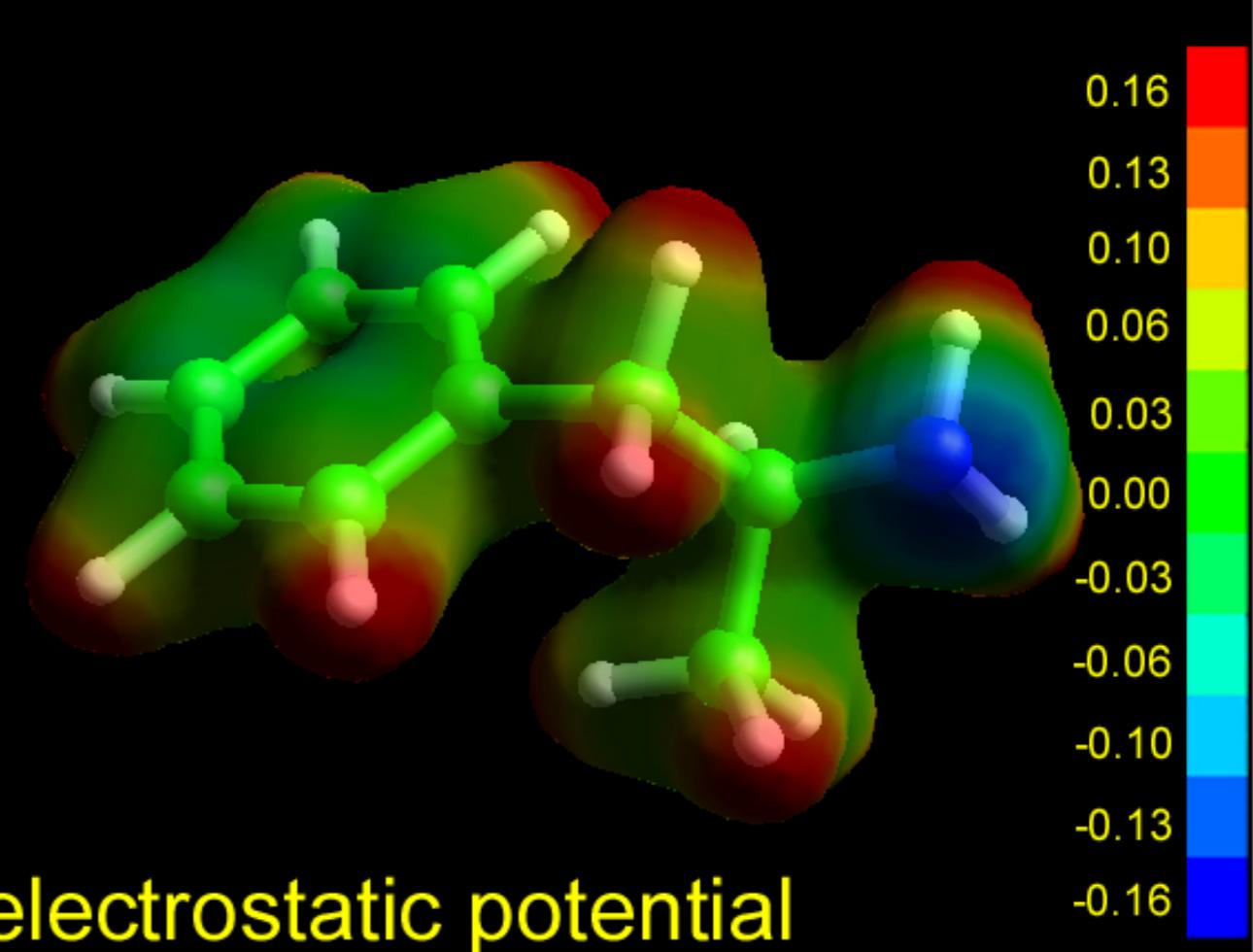
Molecular Quantum Mechanics

electron density

$$\rho(r) = |\Psi(\mathbf{r})|^2$$



electron density



electrostatic potential

Molecular Modeling

Hartree-Fock

mean-field: no electron-electron correlation

post Hartree-Fock methods

configuration interaction

perturbation theory

density functional theory

$$E [\rho(\mathbf{r})] = T [\rho(\mathbf{r})] + V_{\text{coul}} [\rho(\mathbf{r})] + V_{\text{xc}} [\rho(\mathbf{r})]$$

empirical exchange-correlation functionals

Kohn-Sham orbitals

semi-empirical methods

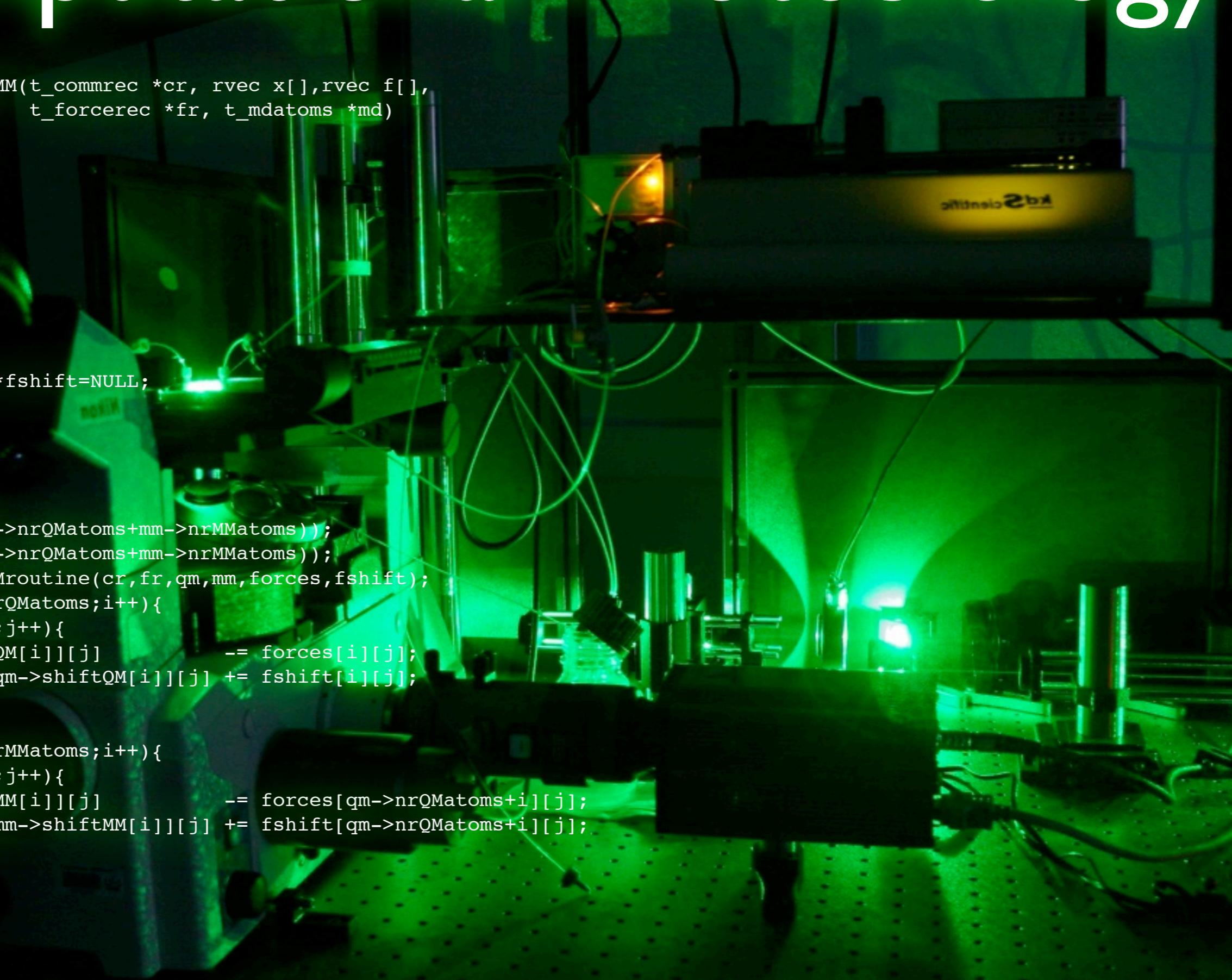
partial neglect of orbital overlap (interactions)

empirical parameters

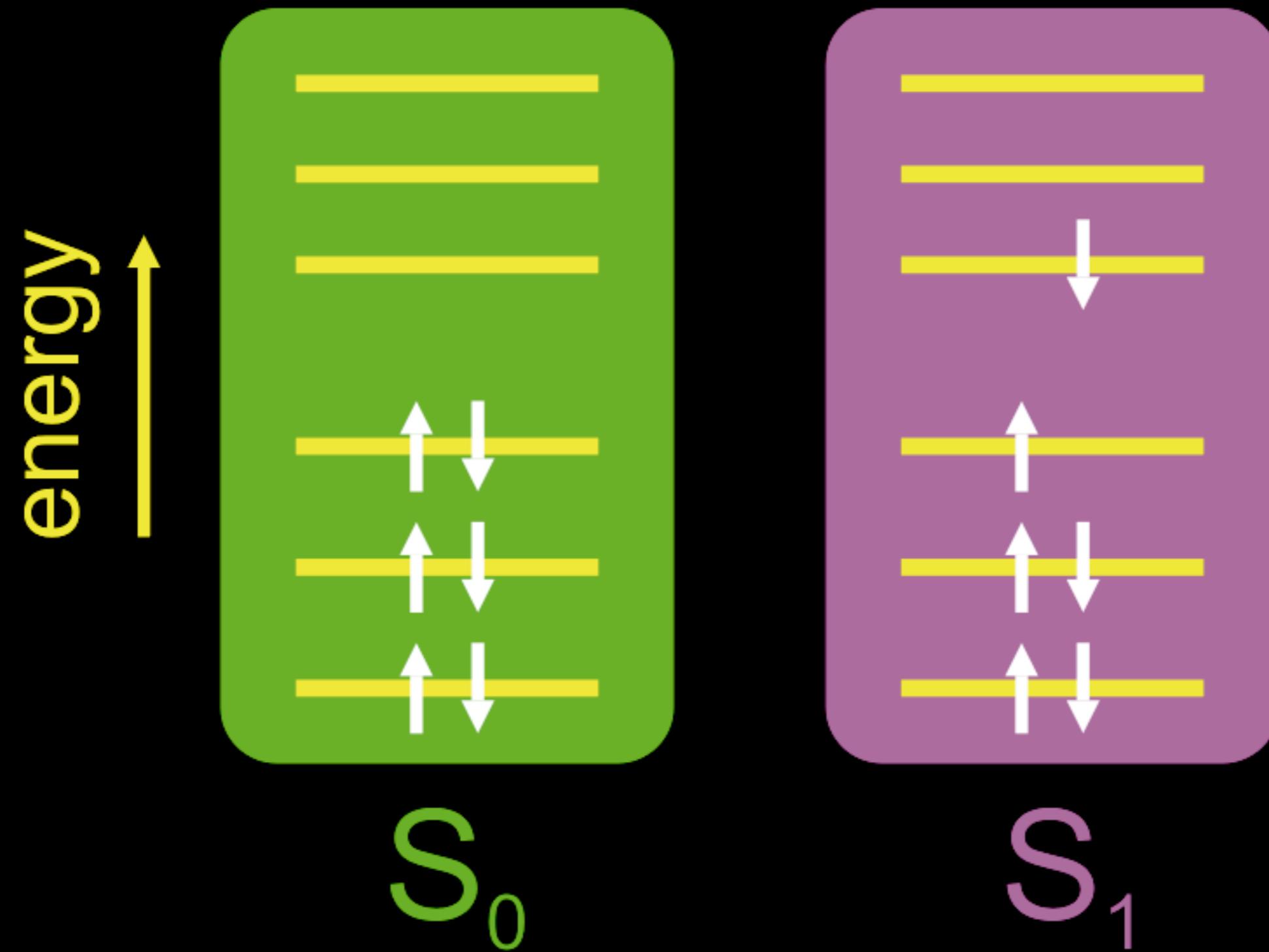
molecular mechanics forcefield

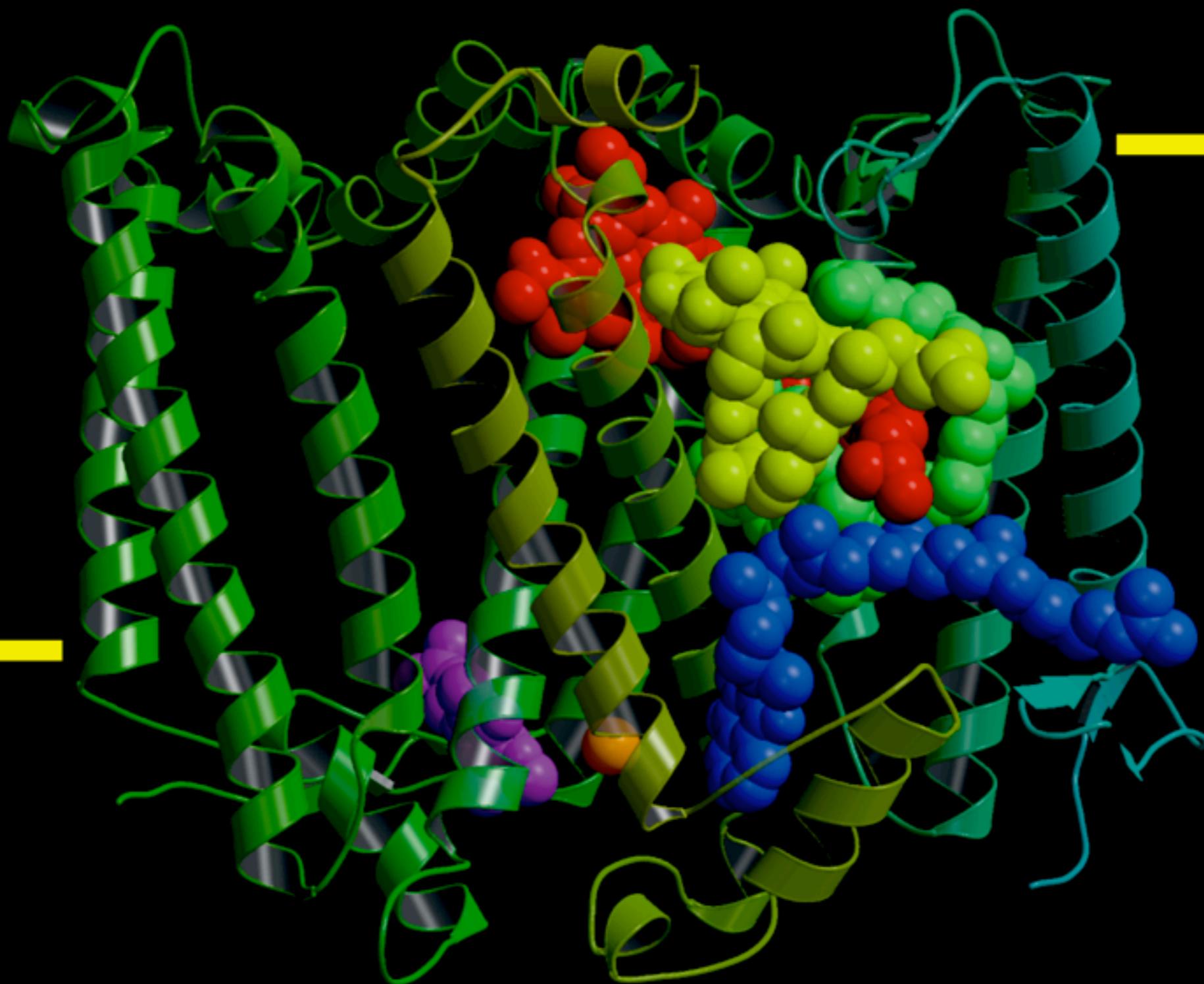
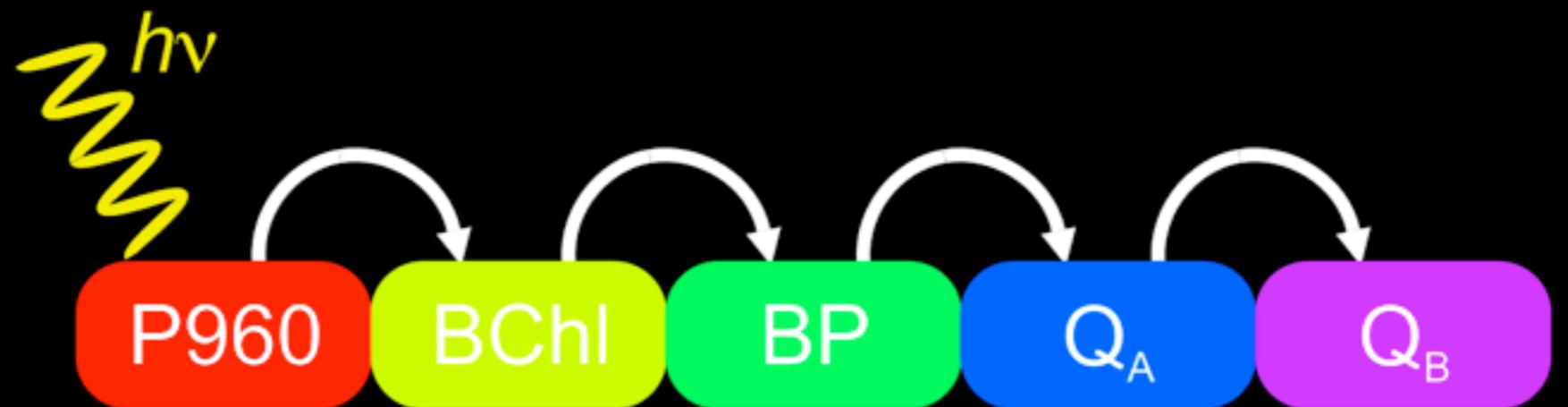
Computational Photobiology

```
real calculate_QMM(t_commrec *cr, rvec x[],rvec f[],
                    t_forcerec *fr, t_mdatoms *md)
{
    real
        QMener=0.0;
    t_QMMrec
        *qr;
    t_QMrec
        *qm;
    t_MMrec
        *mm=NULL;
    rvec
        *forces=NULL,*fshift=NULL;
    int
        i,j,k;
    qr = fr->qr;
    mm = qr->mm;
    qm = qr->qm[0];
    snew(forces,(qm->nrQAtoms+mm->nrMAtoms));
    snew(fshift,(qm->nrQAtoms+mm->nrMAtoms));
    QMener = call_QMroutine(cr,fr,qm,mm,forces,fshift);
    for(i=0;i<qm->nrQAtoms;i++){
        for(j=0;j<DIM;j++){
            f[qm->indexQM[i]][j]      -= forces[i][j];
            fr->fshift[qm->shiftQM[i]][j] += fshift[i][j];
        }
    }
    for(i=0;i<mm->nrMAtoms;i++){
        for(j=0;j<DIM;j++){
            f[mm->indexMM[i]][j]      -= forces[qm->nrQAtoms+i][j];
            fr->fshift[mm->shiftMM[i]][j] += fshift[qm->nrQAtoms+i][j];
        }
    }
    free(forces);
    free(fshift);
}
```



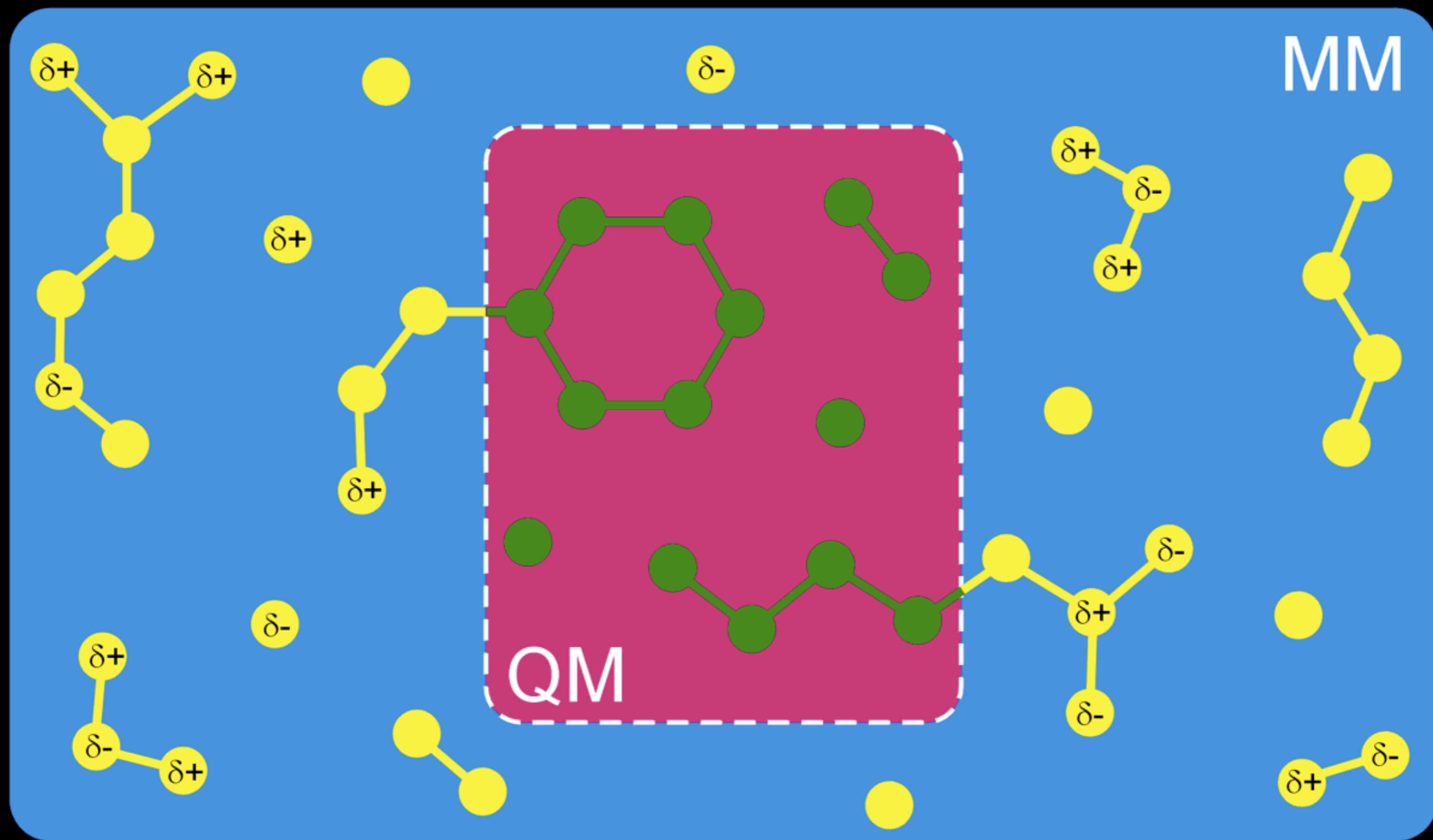
Photochemistry

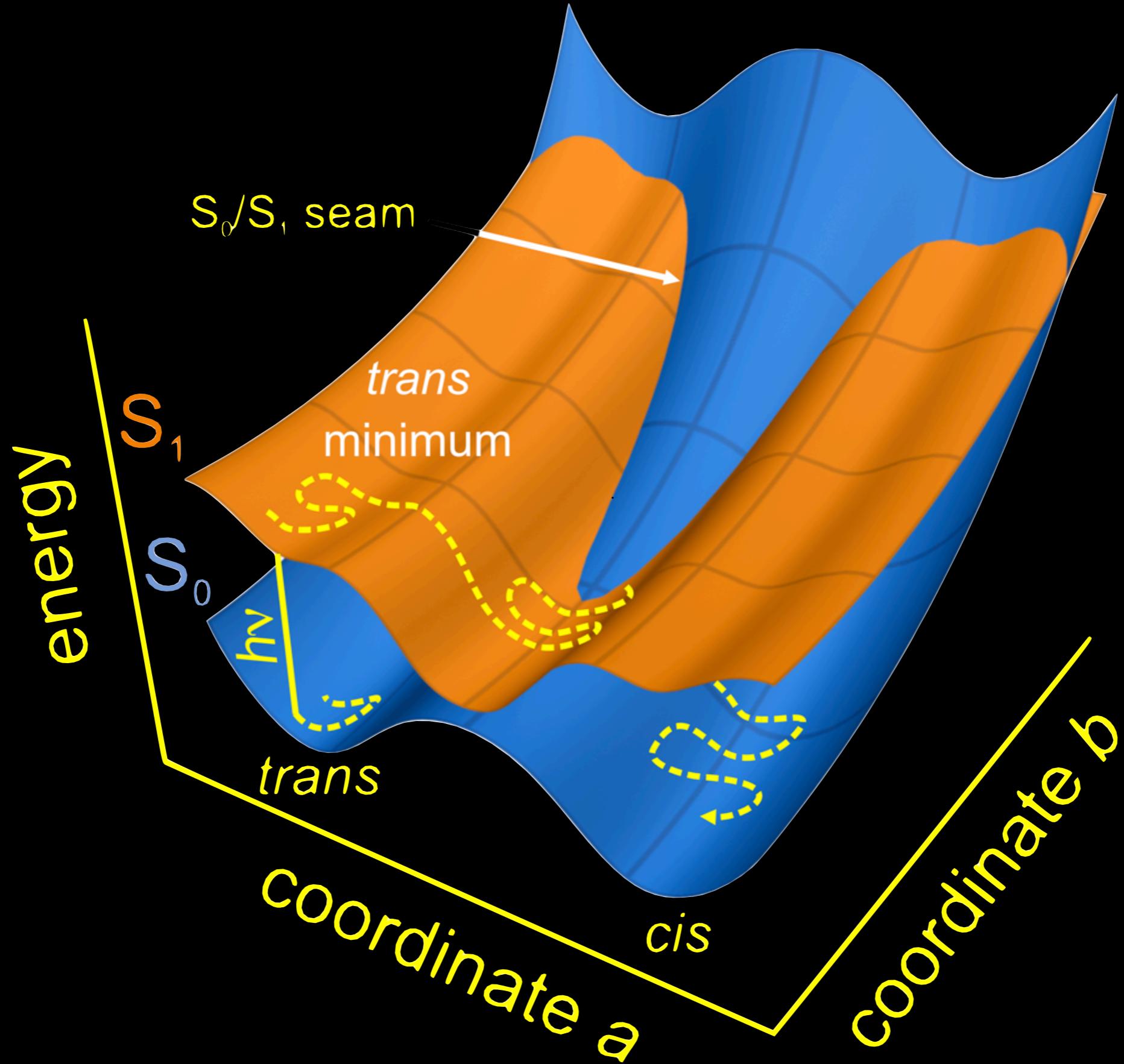




Quantum Mechanics/Molecular Mechanics

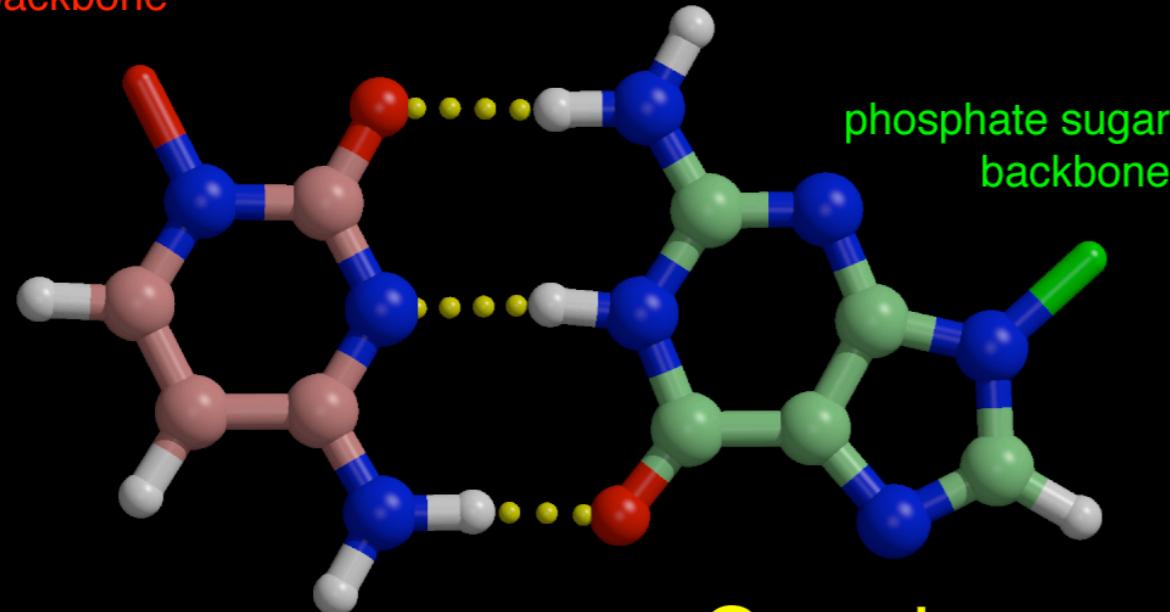
Warshel & Levitt, JMB 103 (1976): 227-249





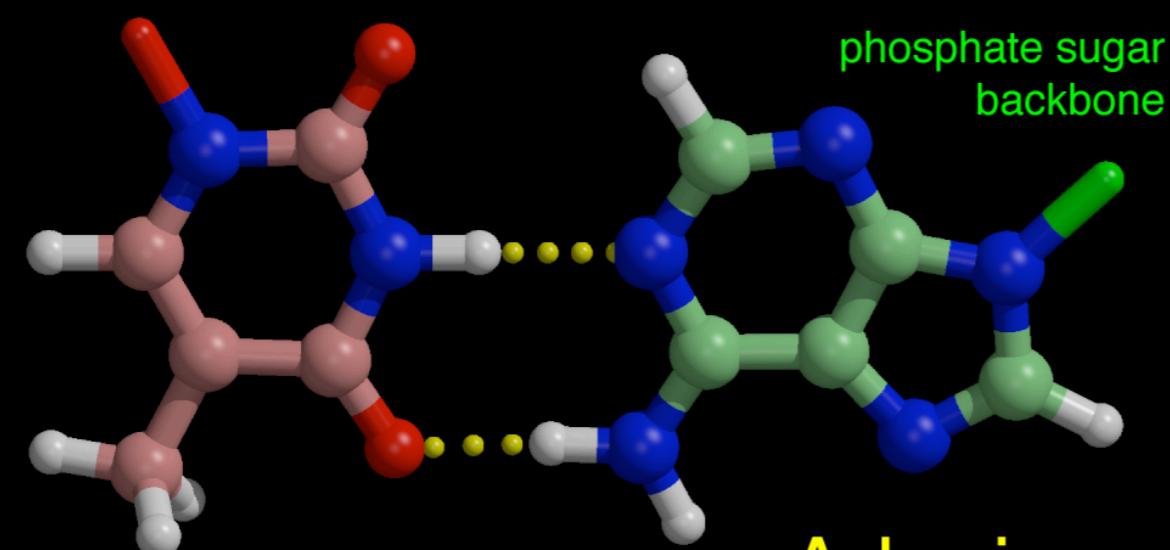
DNA Photochemistry

phosphate sugar
backbone



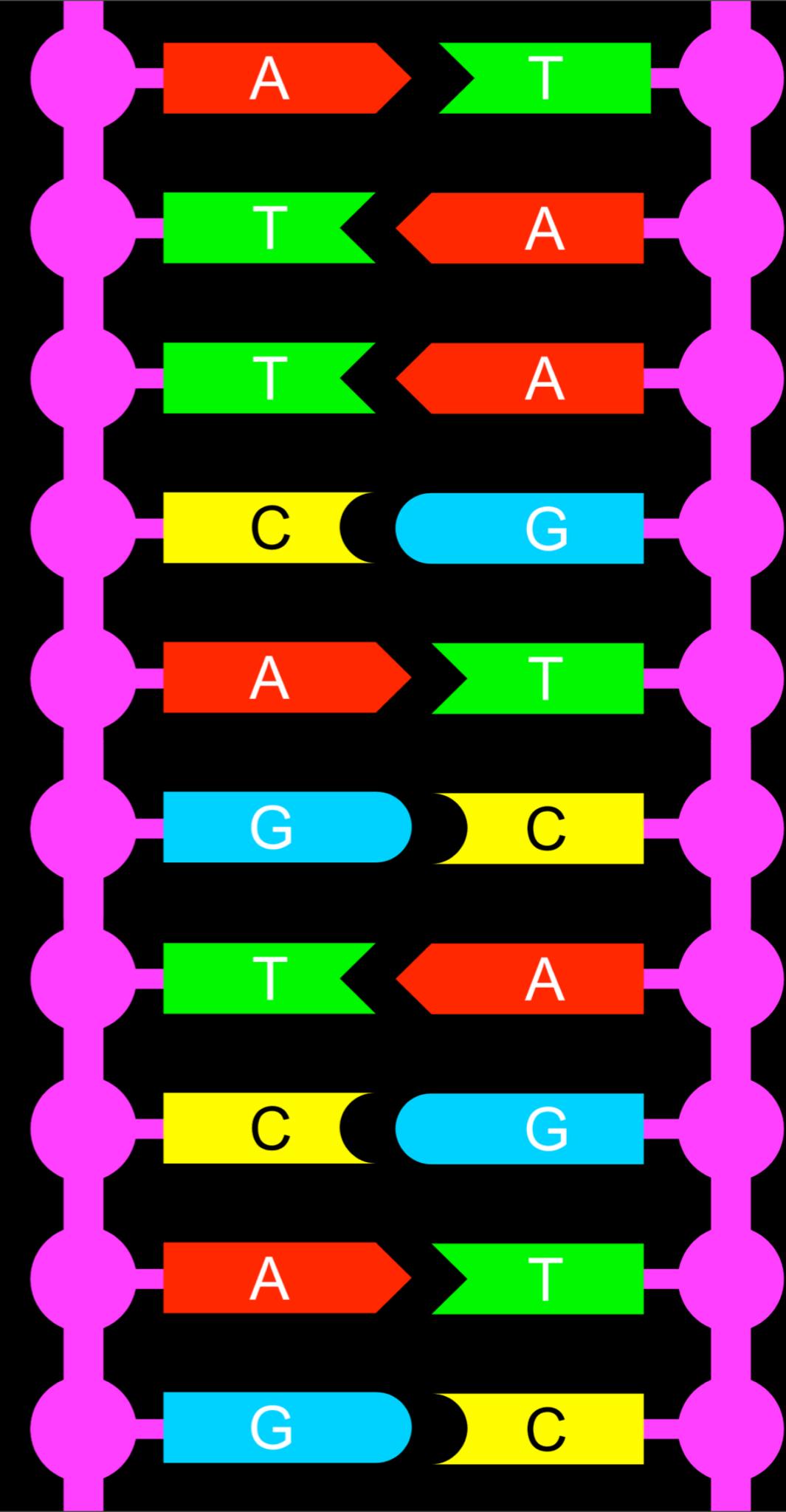
Cytosine

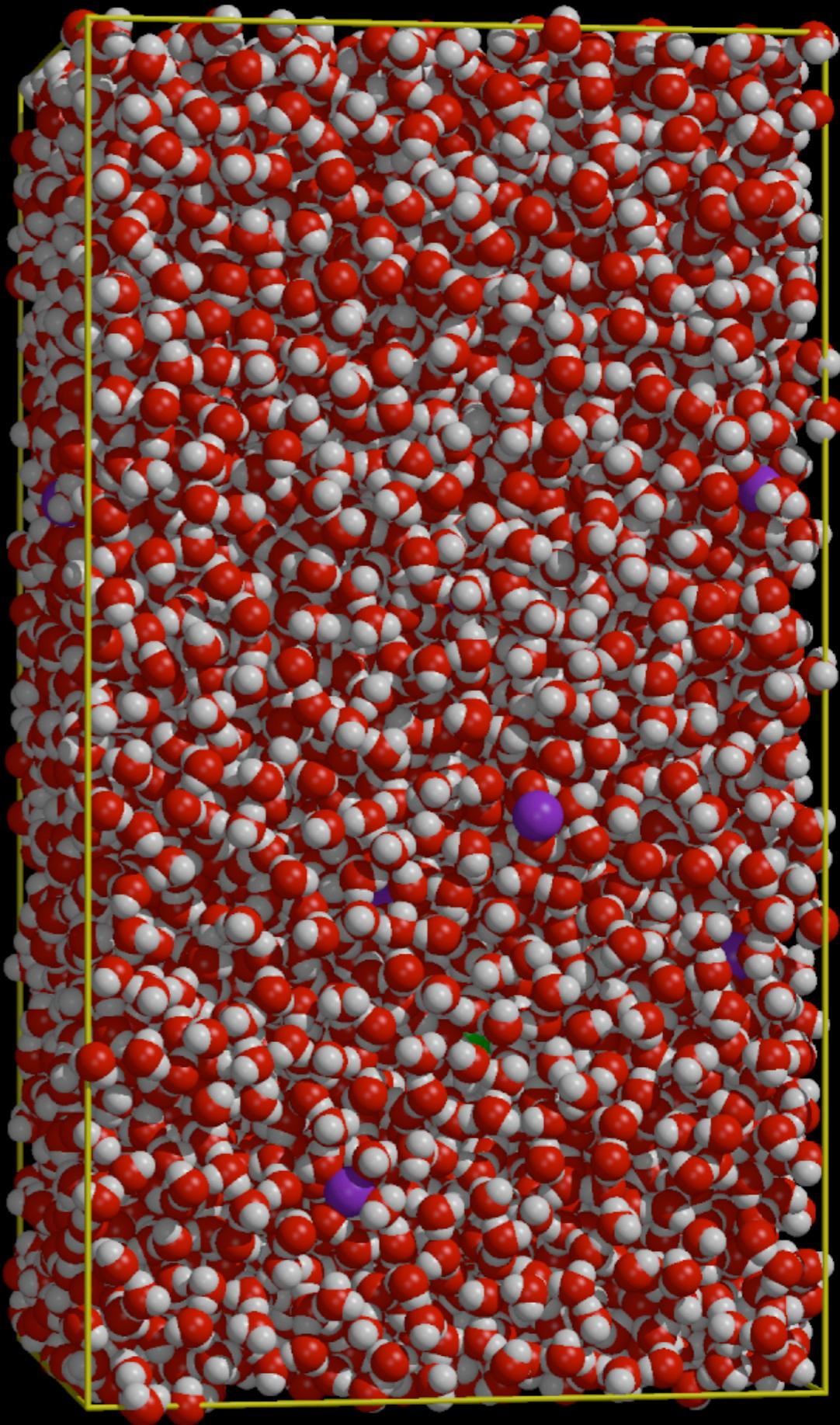
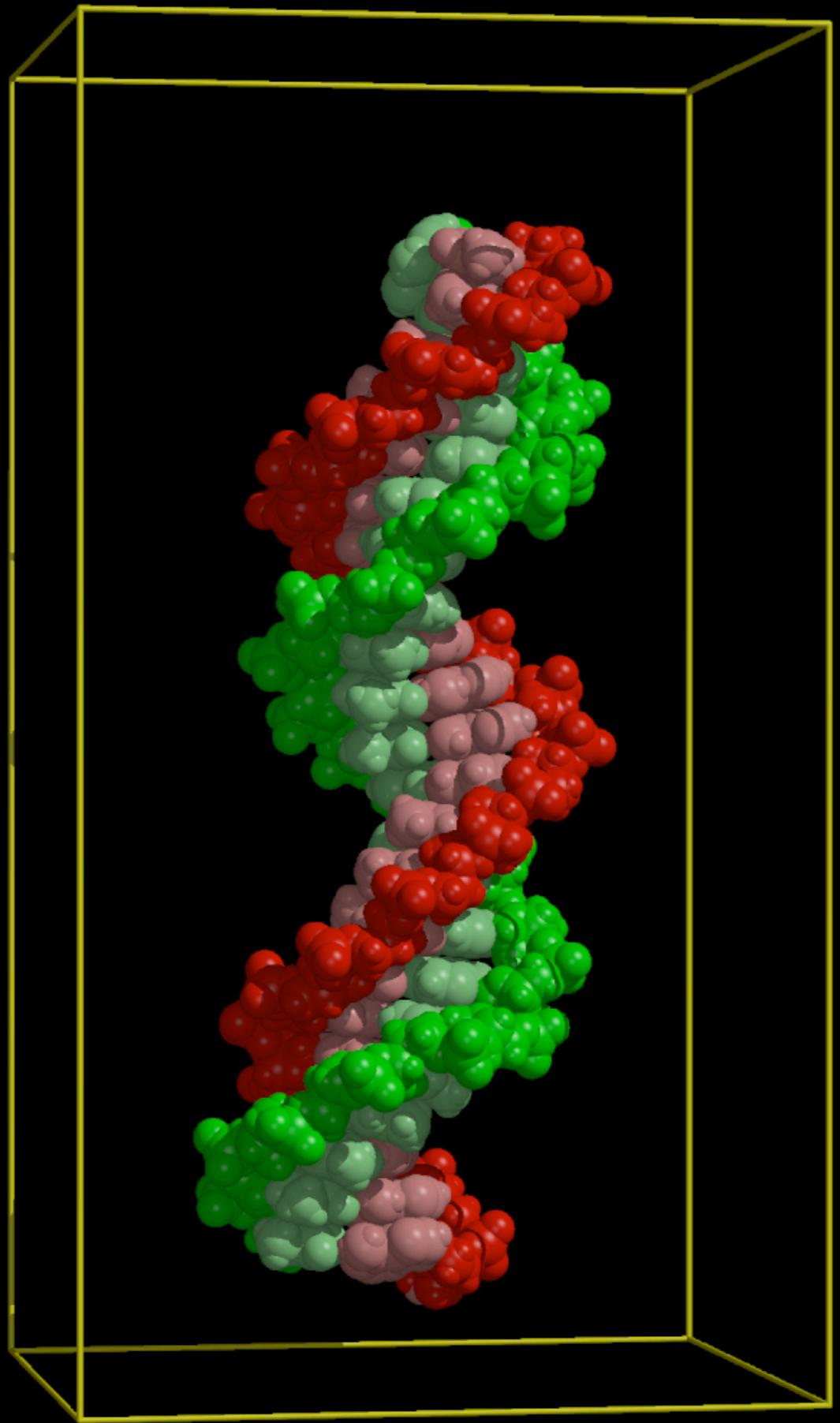
phosphate sugar
backbone

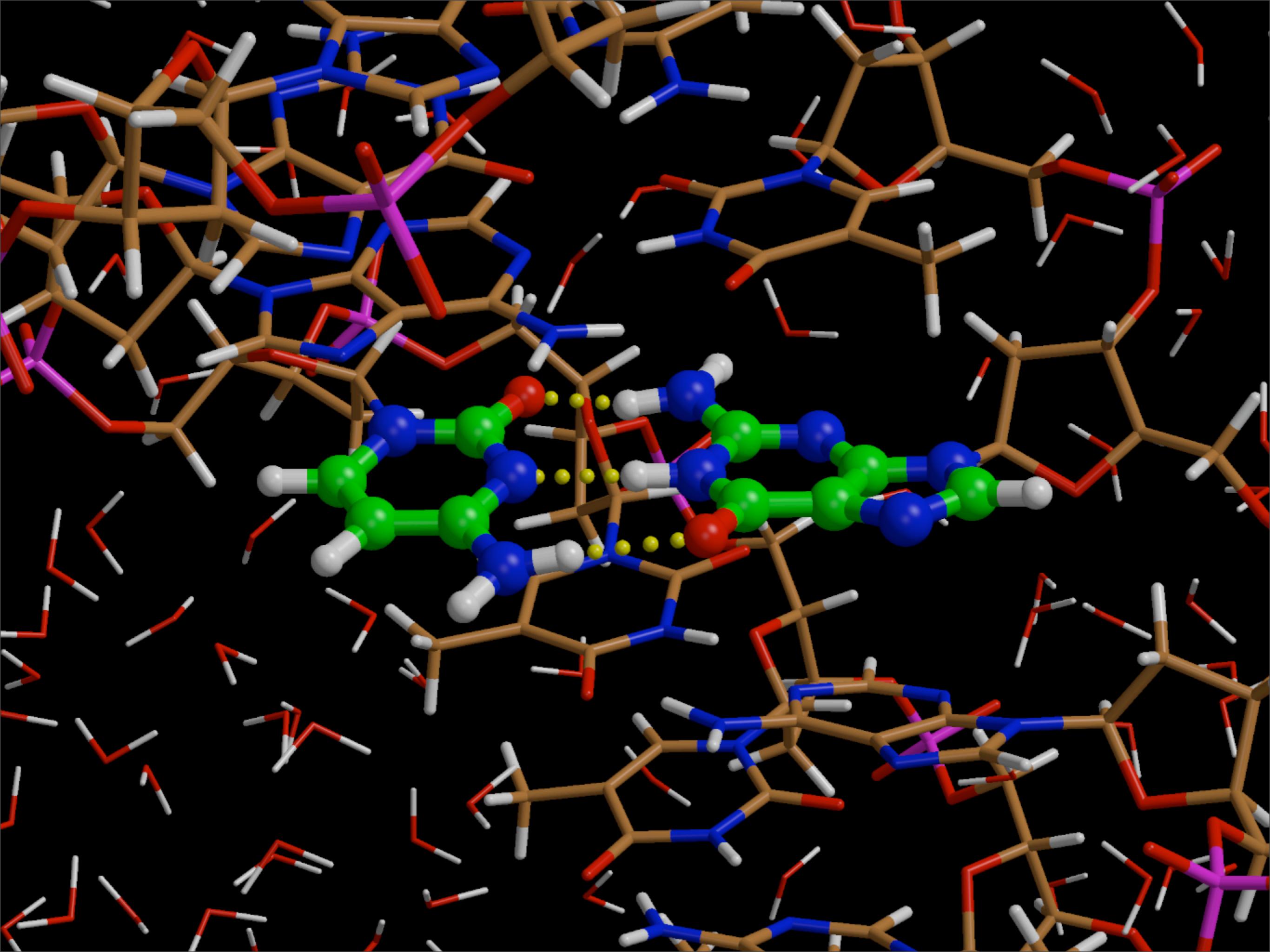


Thymine

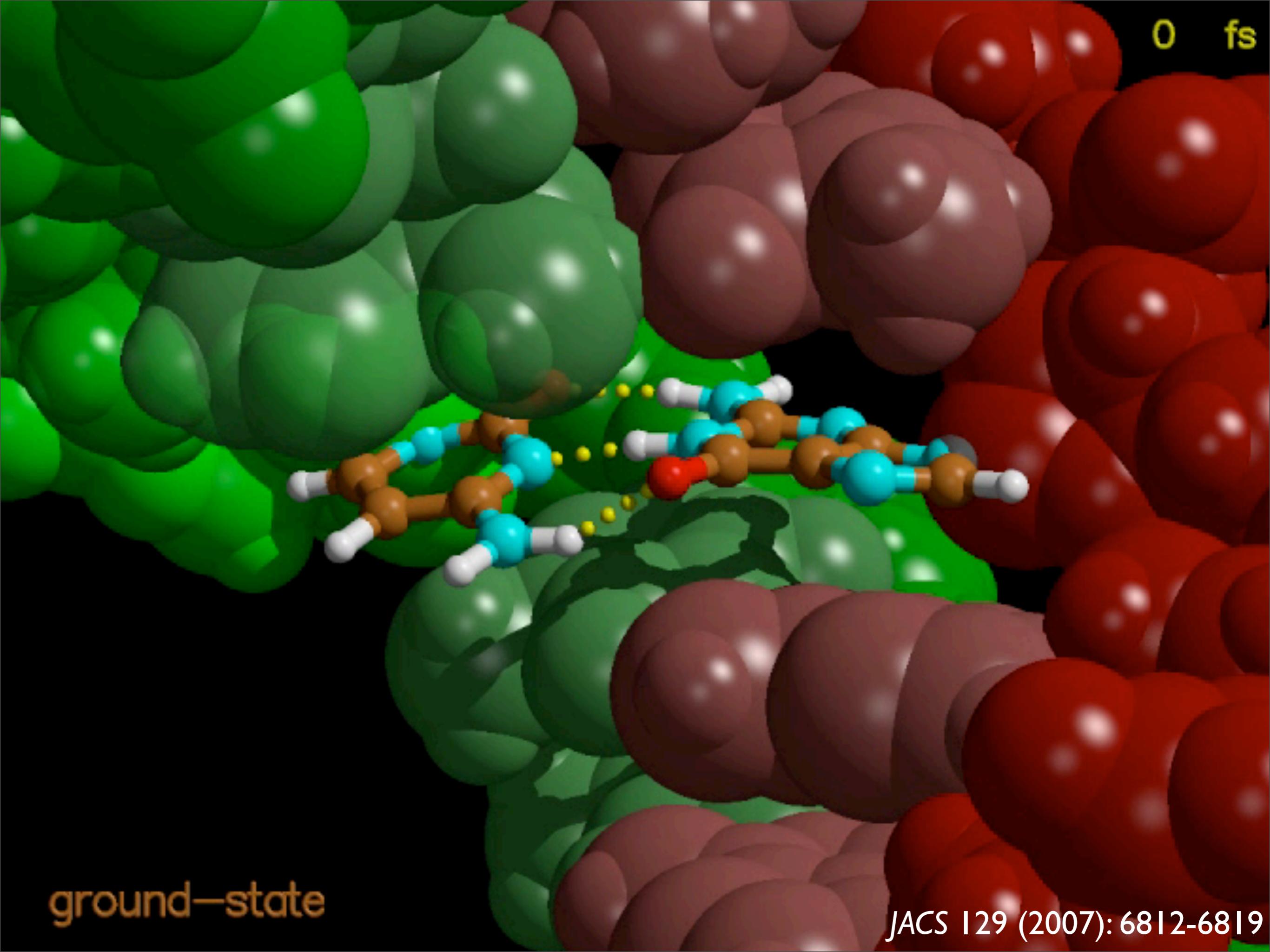
Adenine







0 fs



ground-state

JACS 129 (2007): 6812-6819

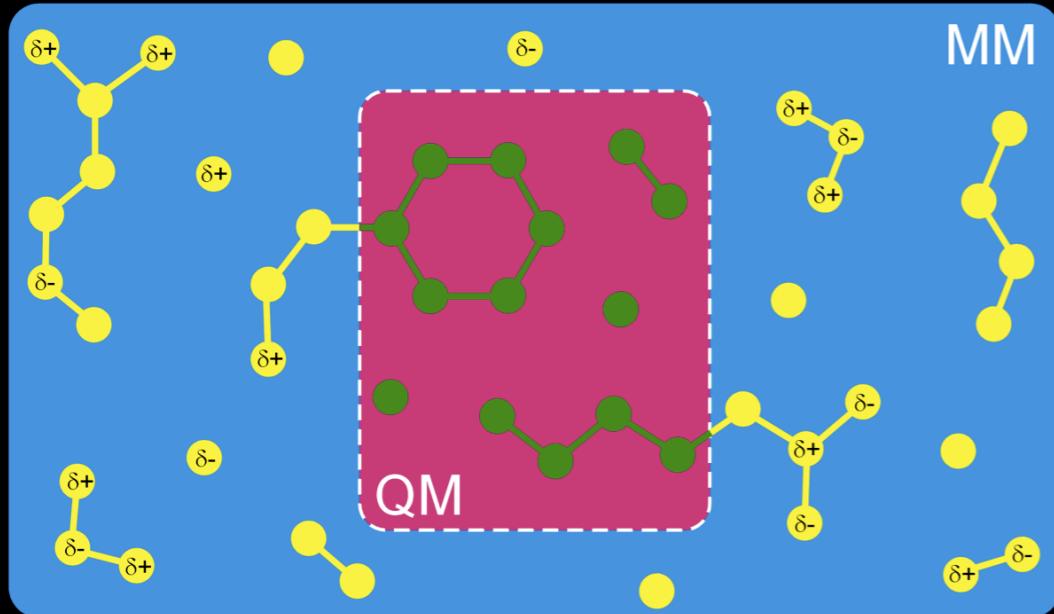
50 fs

ground-state

JACS 129 (2007): 10996-10997

QM/MM Embedding Schemes

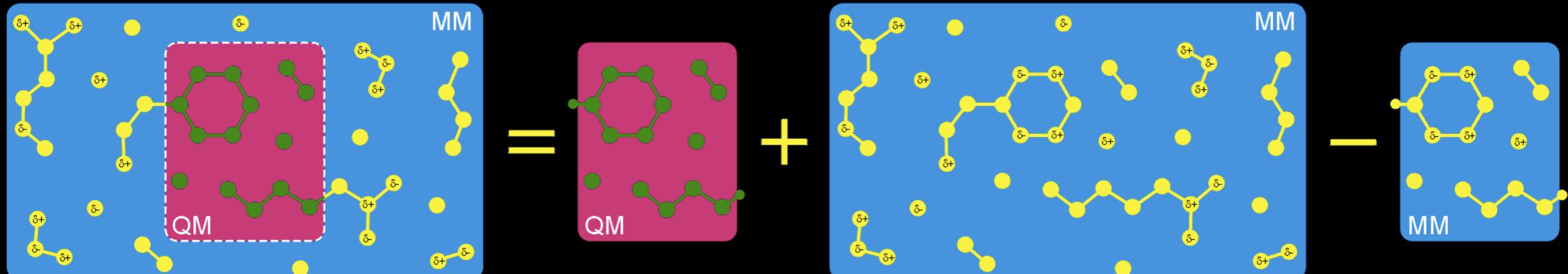
Electrostatic (Field et al. JCC II (1990): 700-733)



QM-MM bonded interactions
QM-MM van der Waals MM

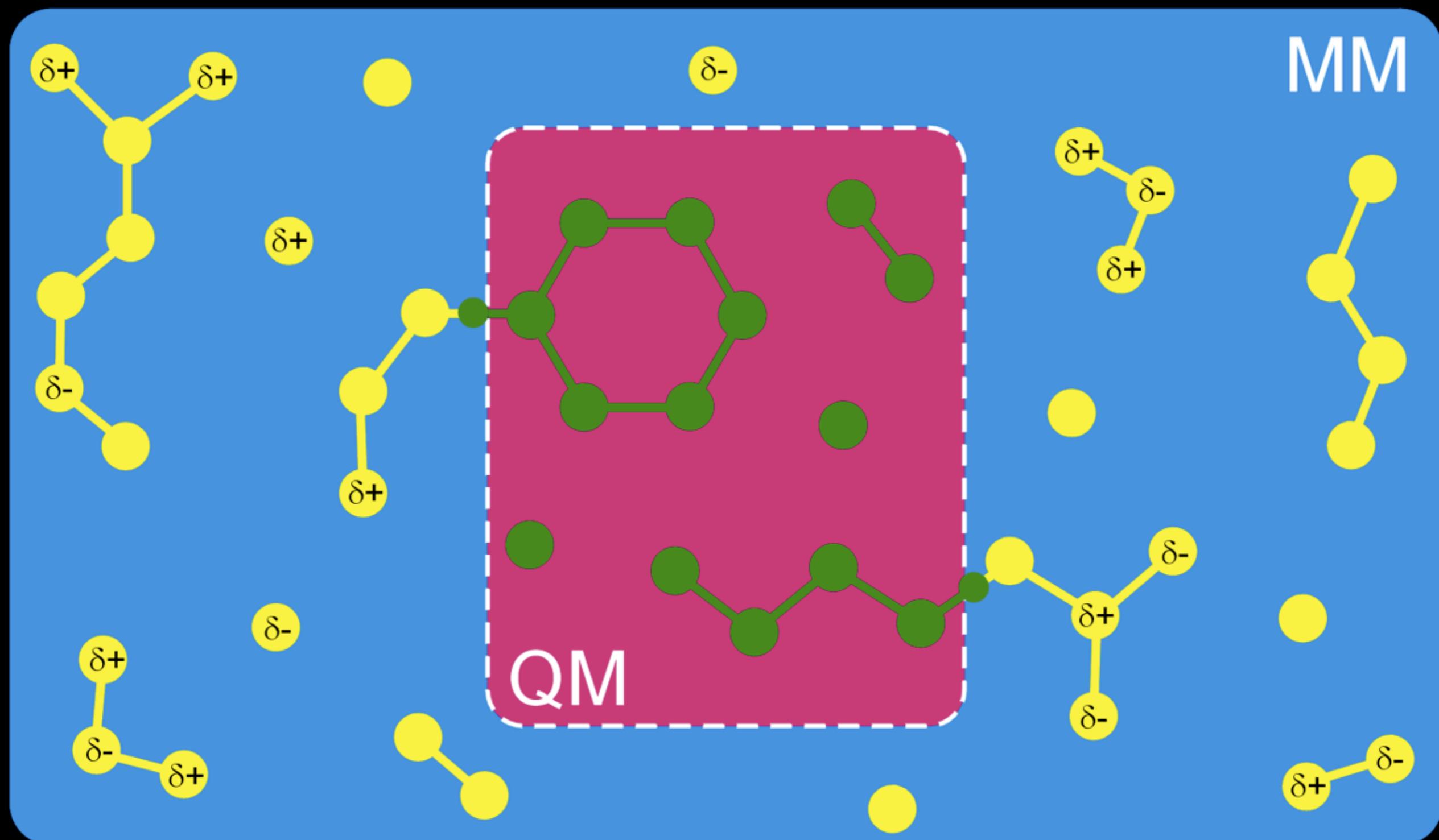
QM-MM coulomb
link atom QM

ONIOM (Svensson et al. JPC 100 (1996): 19357



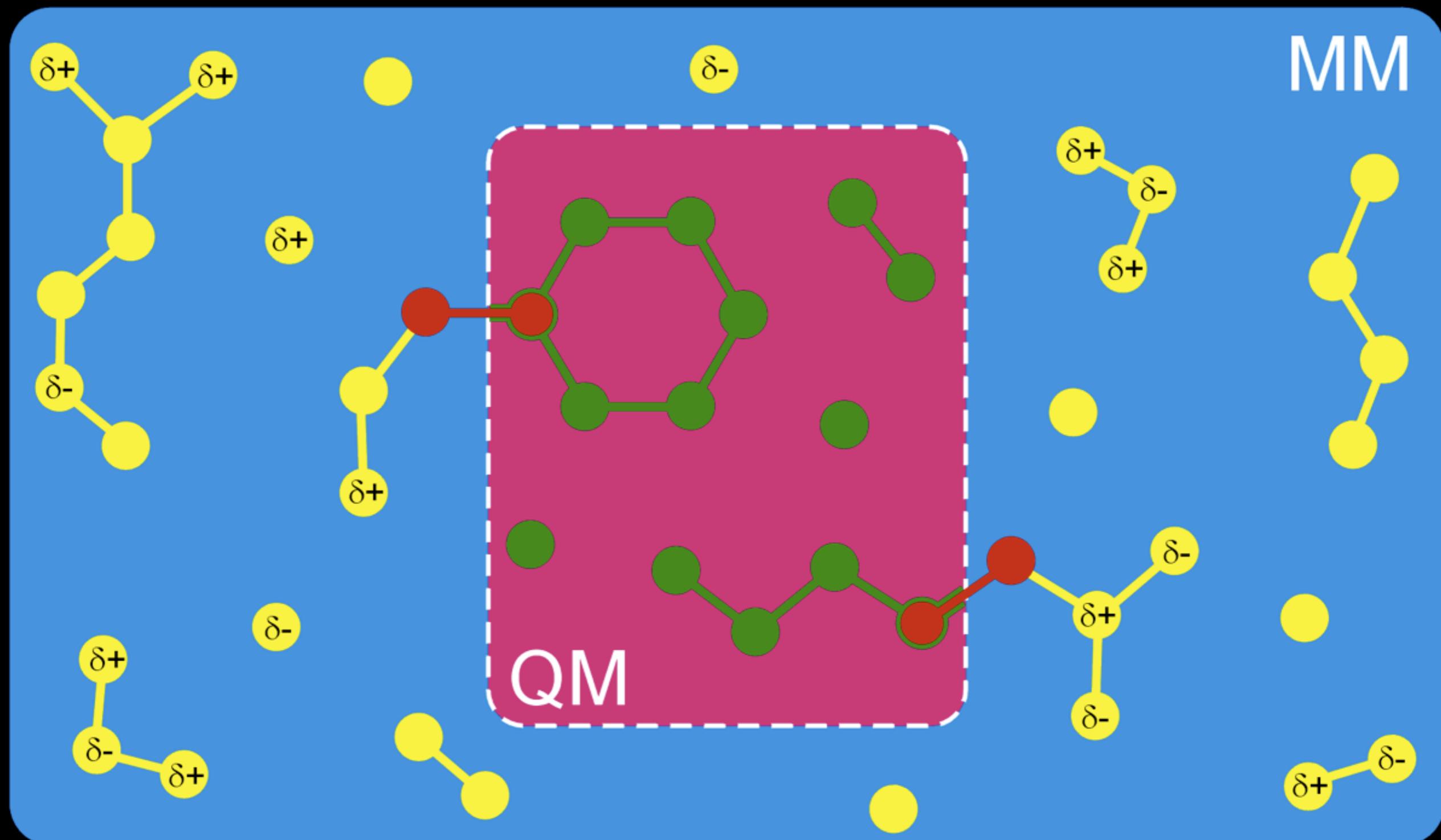
Electrostatic Embedding

Capping the QM subsystem: link atoms



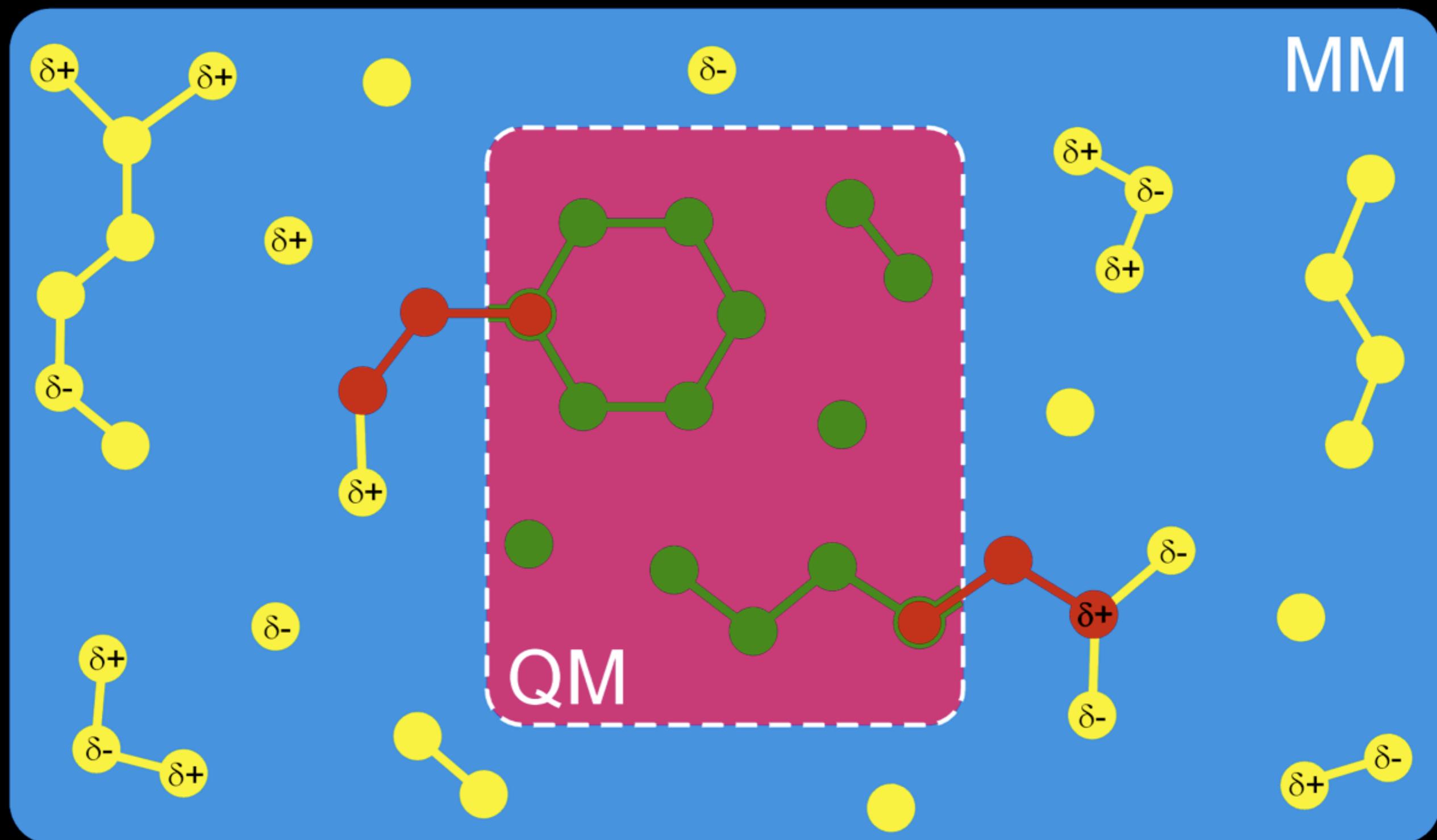
Electrostatic Embedding

MM bonded interactions: bonds



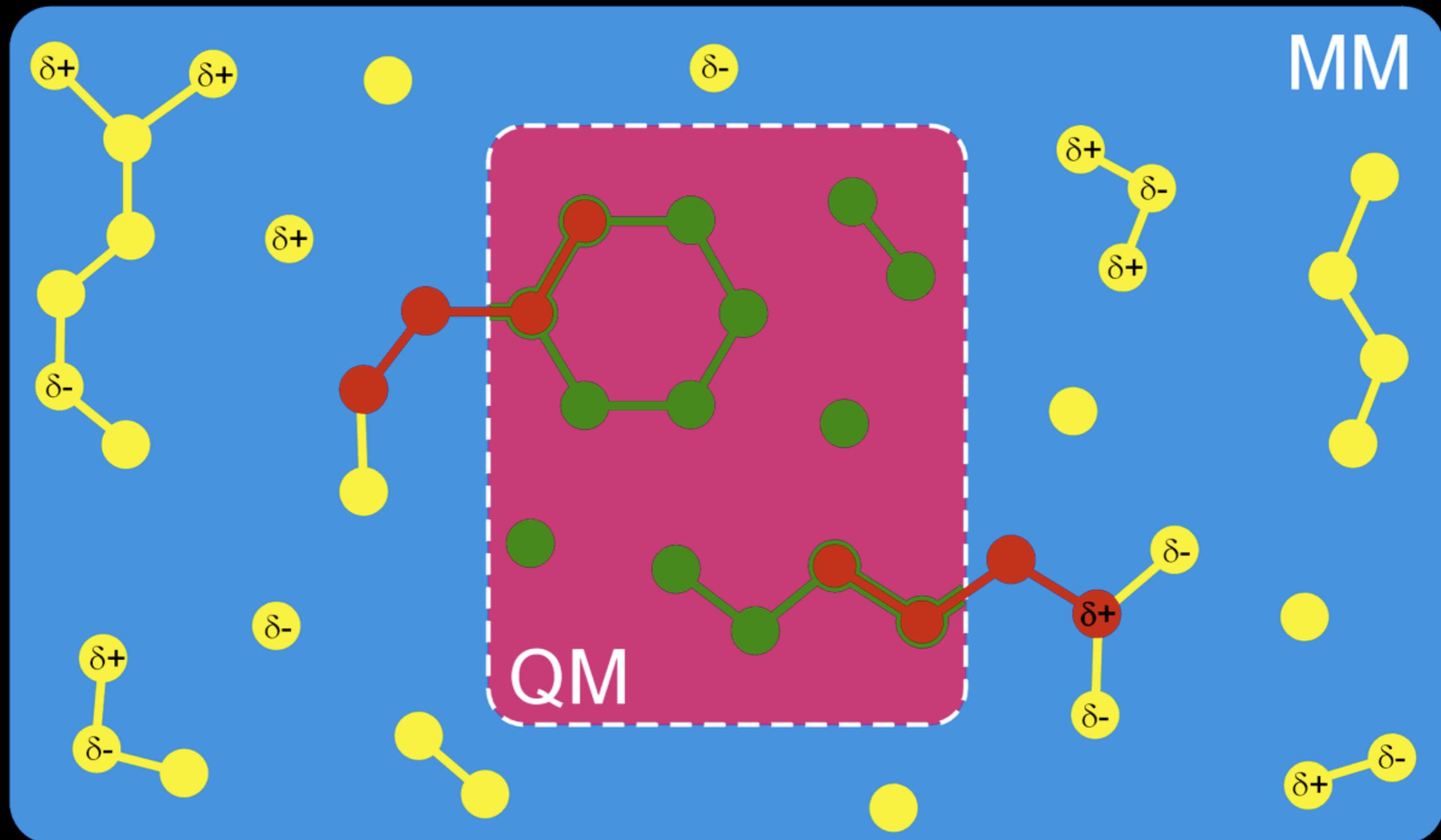
Electrostatic Embedding

MM bonded interactions: angels



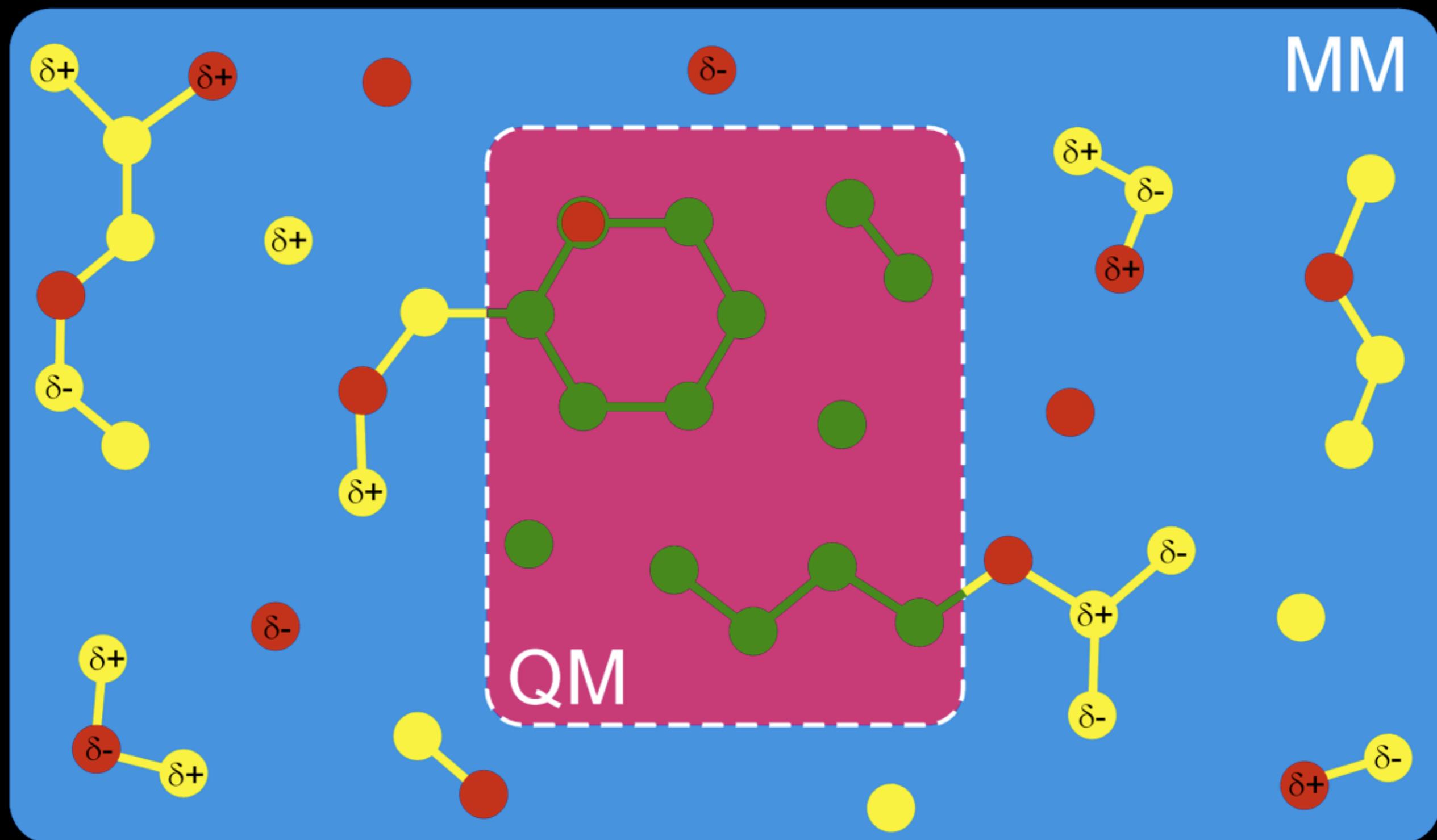
Electrostatic Embedding

MM bonded interactions: torsions



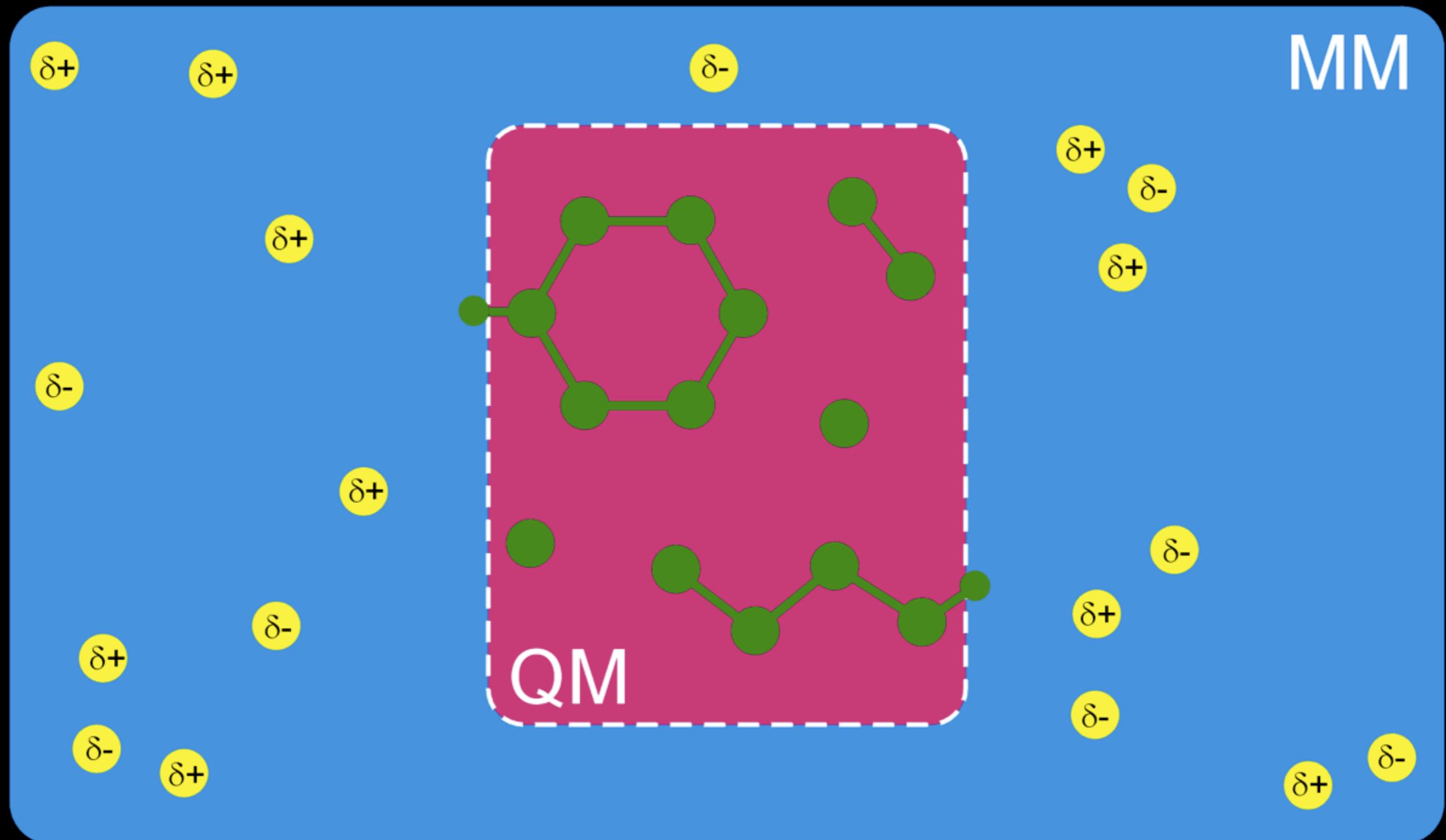
Electrostatic Embedding

MM nonbonded interactions: Lennard-Jones



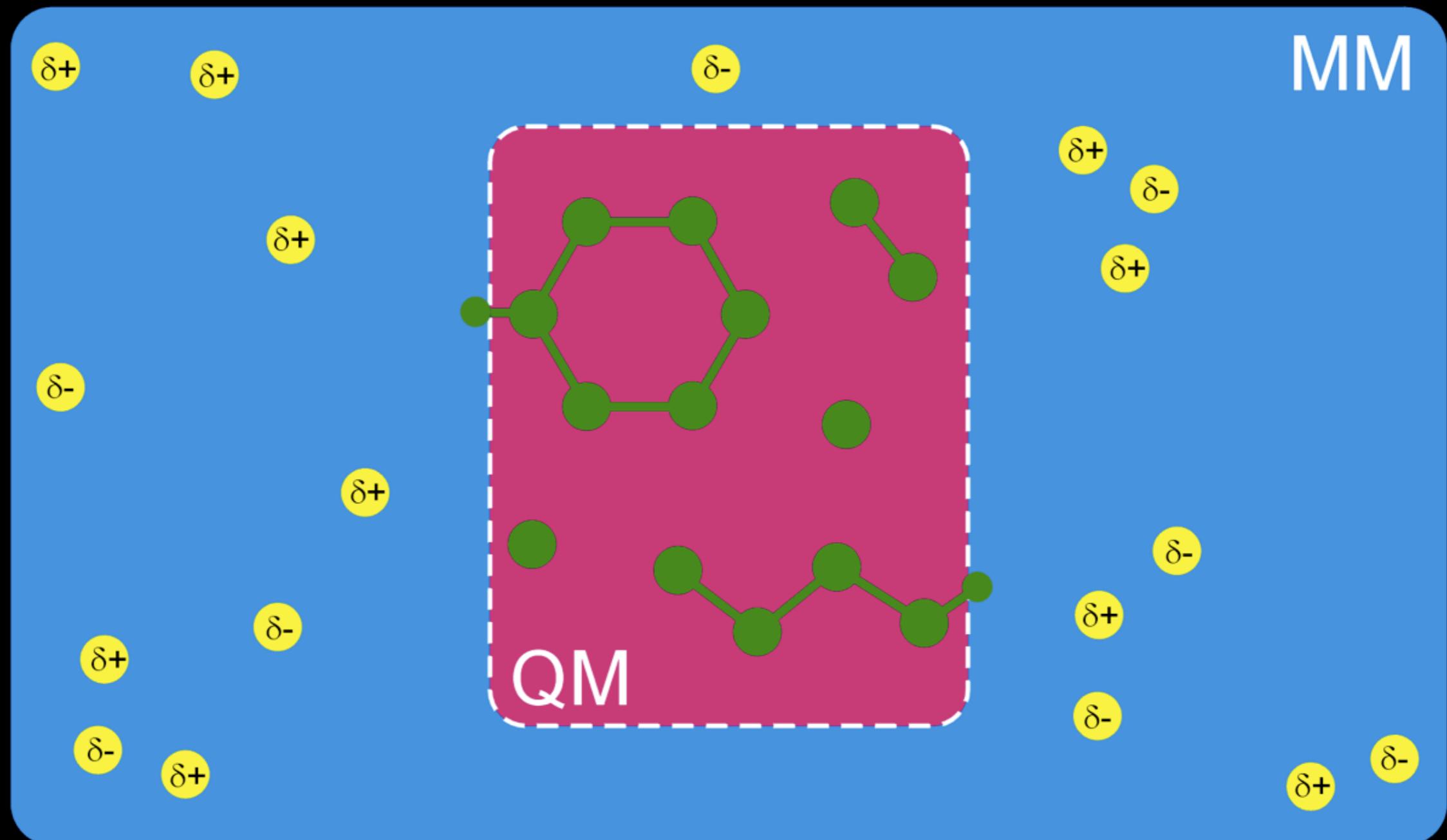
Electrostatic Embedding

QM nonbonded interactions: Coulomb



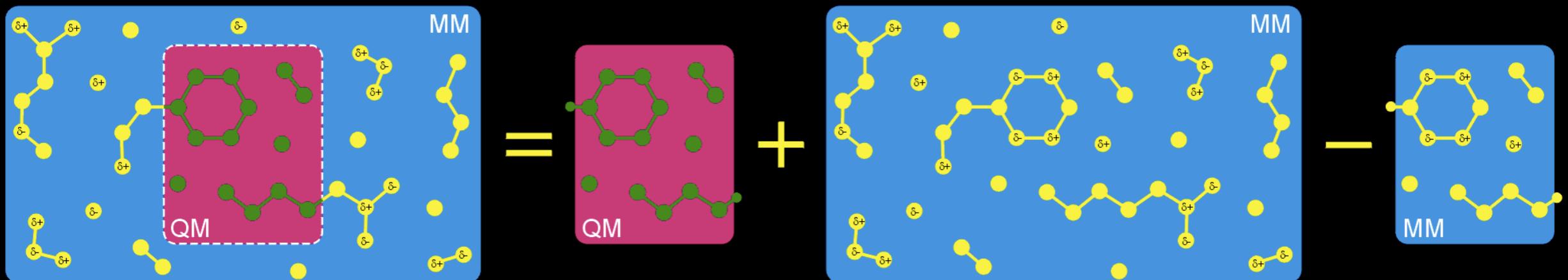
Electrostatic Embedding

$$H = -\frac{\hbar^2}{2m_e} \sum_i^{n_e} \nabla_i^2 + \sum_i^{n_e} \sum_{j>i}^{n_e} \frac{e^2}{4\pi\epsilon_0 r_{ij}} - \sum_i^{n_e} \sum_A^{N_{QM}} \frac{e^2 Z_A}{4\pi\epsilon_0 r_{iA}} + \sum_i^{n_e} \sum_K^{N_{MM}} \frac{e^2 Q_K}{4\pi\epsilon_0 r_{iK}}$$

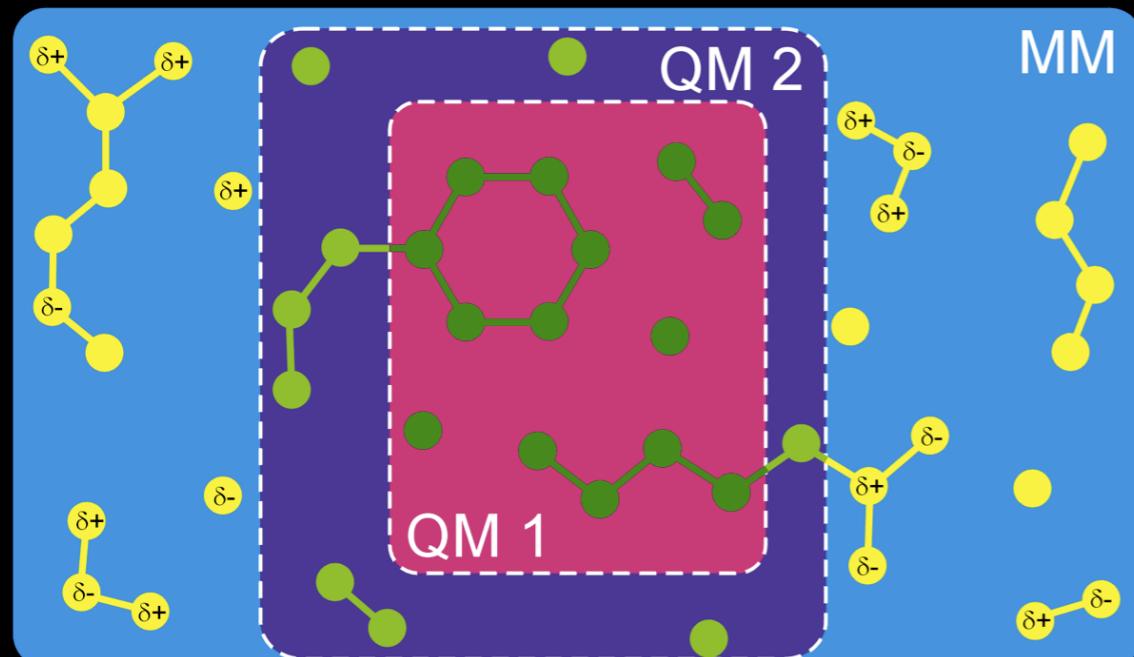


QM/MM Embedding Schemes

ONIOM (Svensson et al. *JPC* 100 (1996): 19357)



multi-layer ONIOM



ab initio

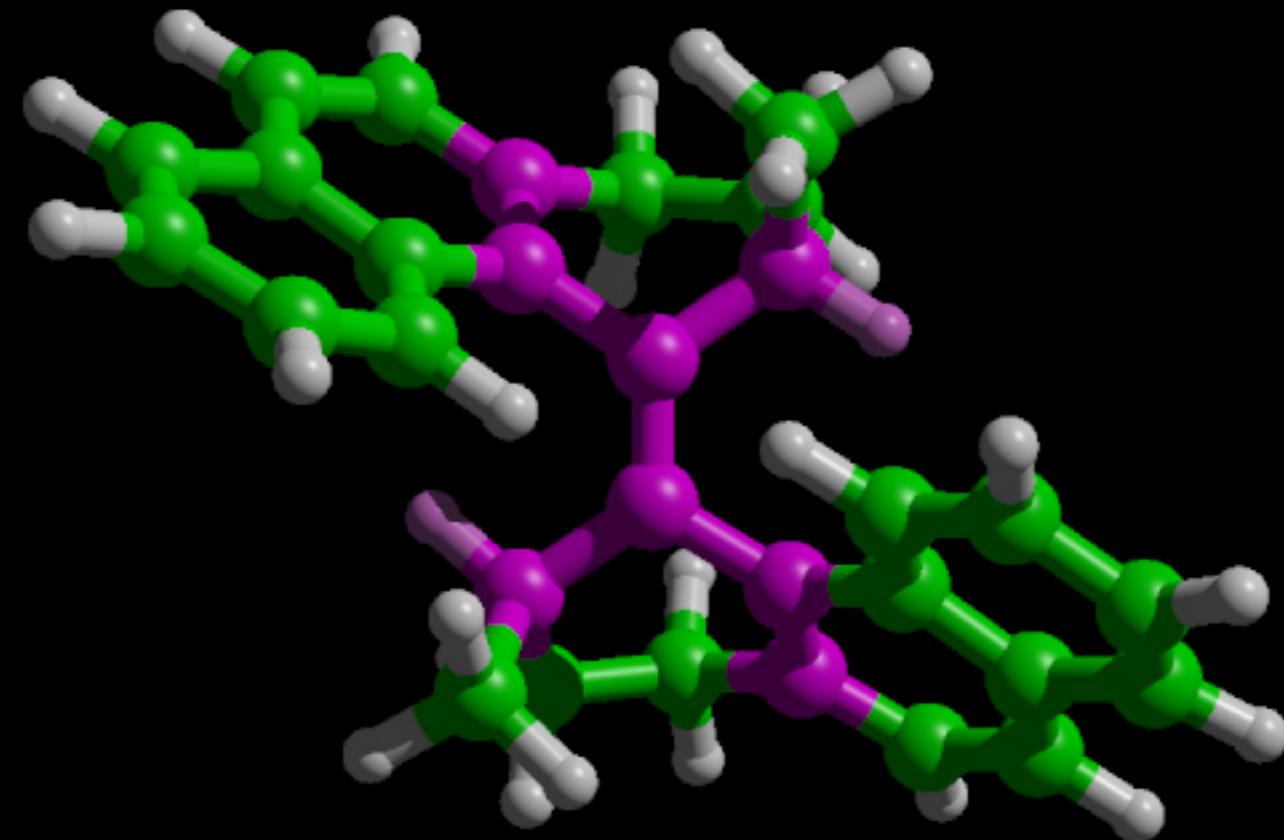
semi empirical

molecular mechanics

Multi-layer ONIOM

uni-directional rotor (B. Feringa, RuG, Groningen)

QM subsystem I (CASSCF)
QM subsystem II (AM1)

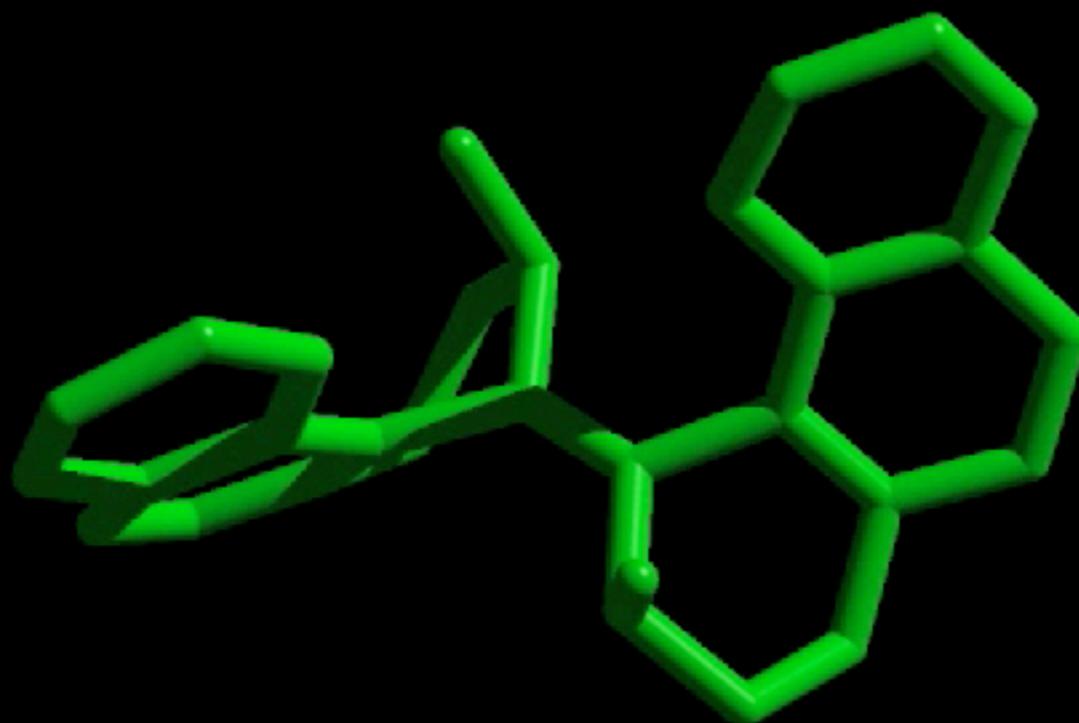


MM subsystem (hexane, Gromos96)

Multi-layer ONIOM

uni-directional rotor (B. Feringa, RuG, Groningen)

ground-state



0 fs

QM/MM Capabilities of Gromacs

Born-Oppenheimer Dynamics

non-adiabatic transitions: surface hopping

rare events: chemical flooding

Geometry Optimization

minima: SD, CG, I-BGFS, ABNR

transition states: nudged elastic band

Supported Quantum Chemistry Packages

file communication: Gaussian, Molcas, Orca

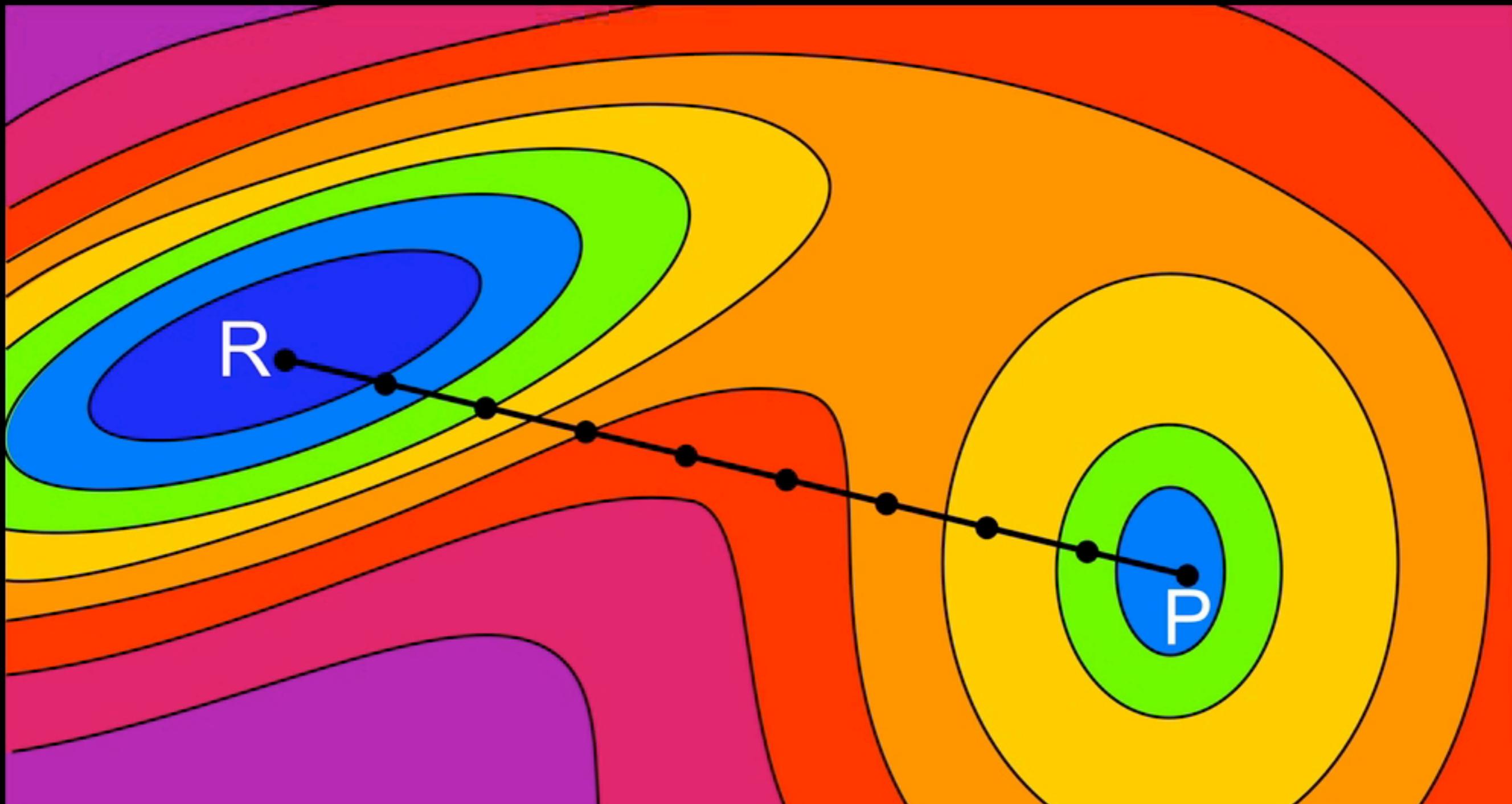
function calls: Gamess-UK, Mopac, DFTB

Nudge Elastic Band Optimization

Rodrigo Martinez-Ruiz, La Rioja, Spain

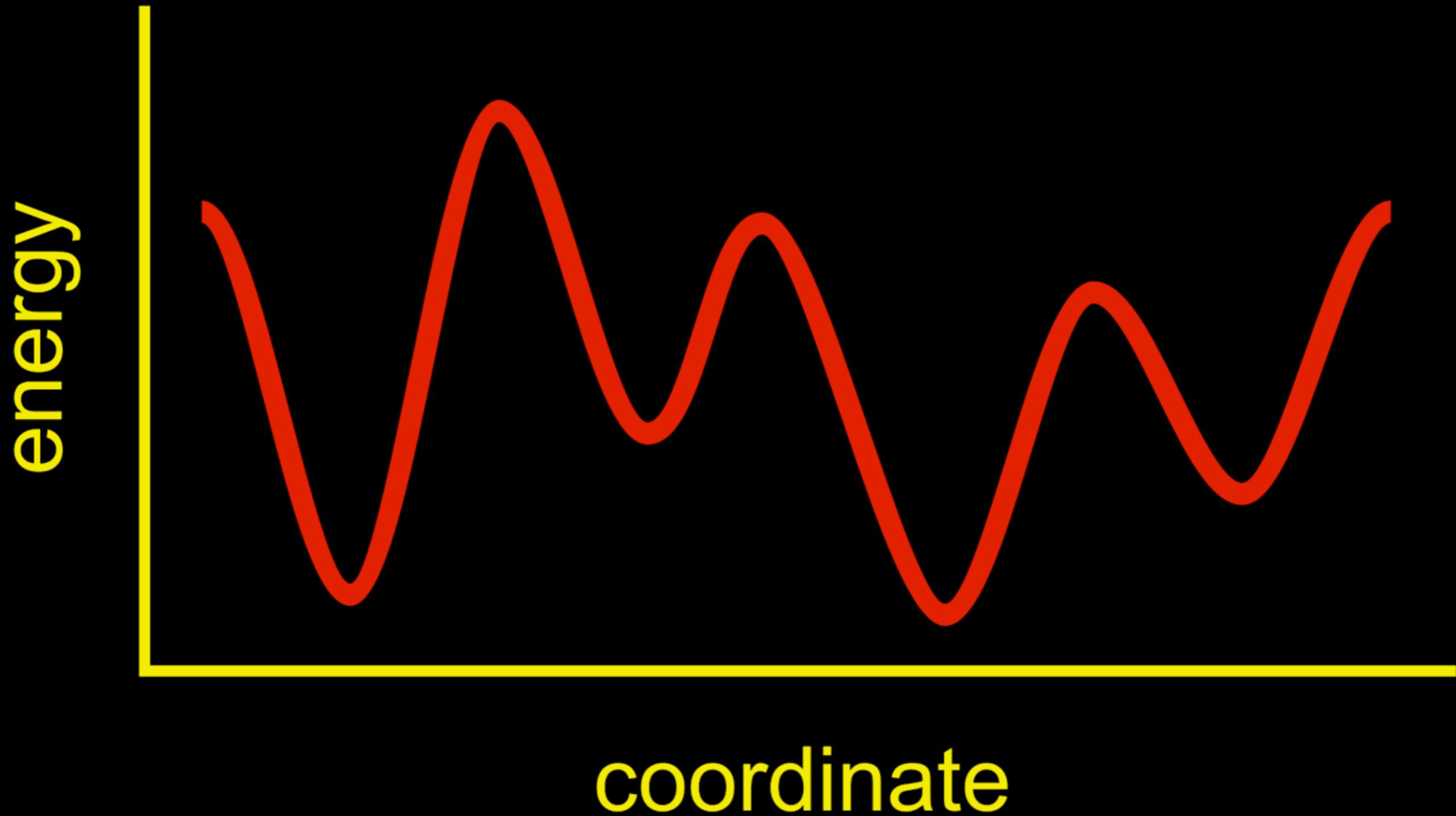
Nudge Elastic Band Optimization

Rodrigo Martinez-Ruiz, La Rioja, Spain



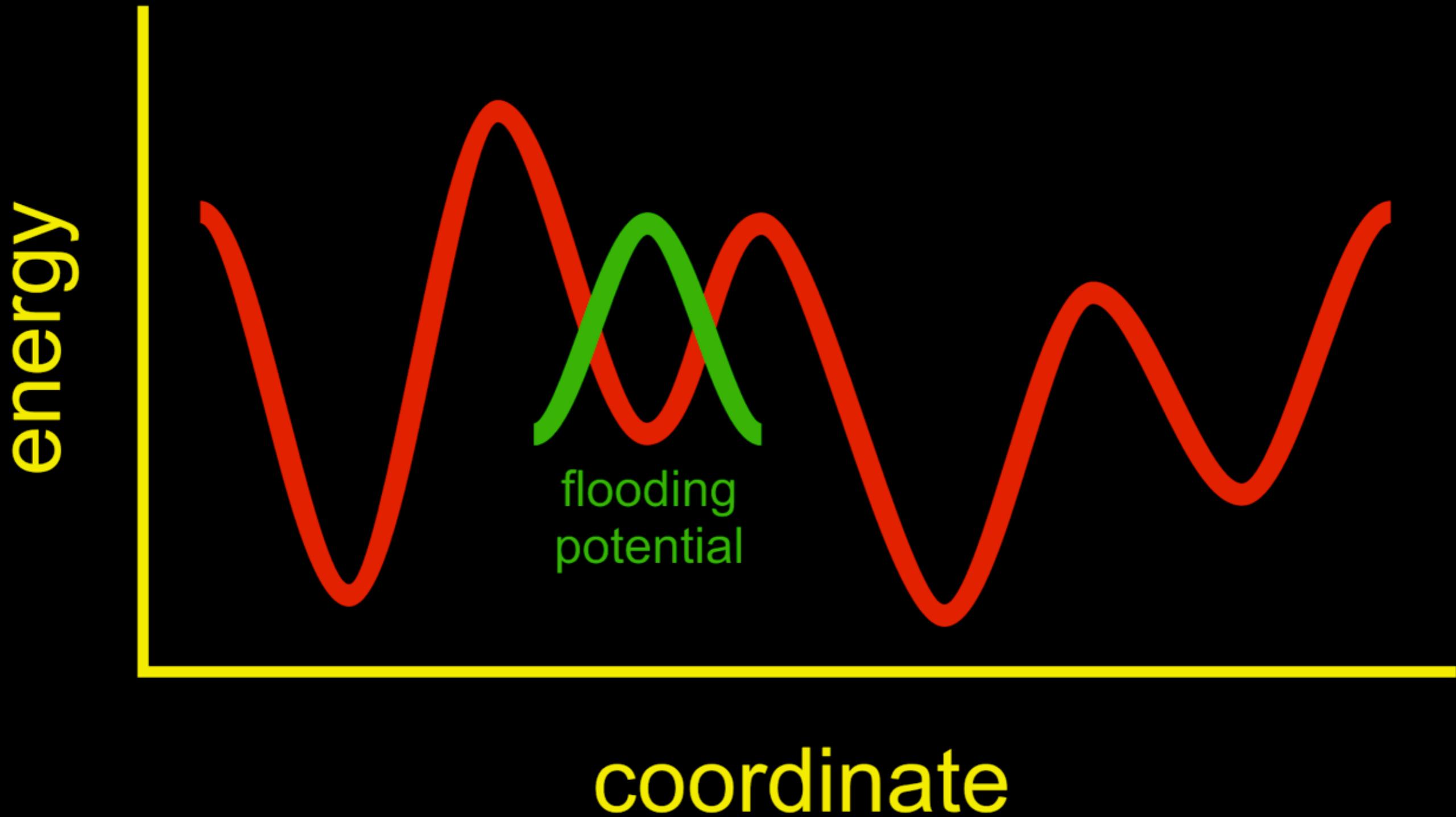
Chemical Flooding

Grubmüller, PRE 52 (1995): 2893-2906



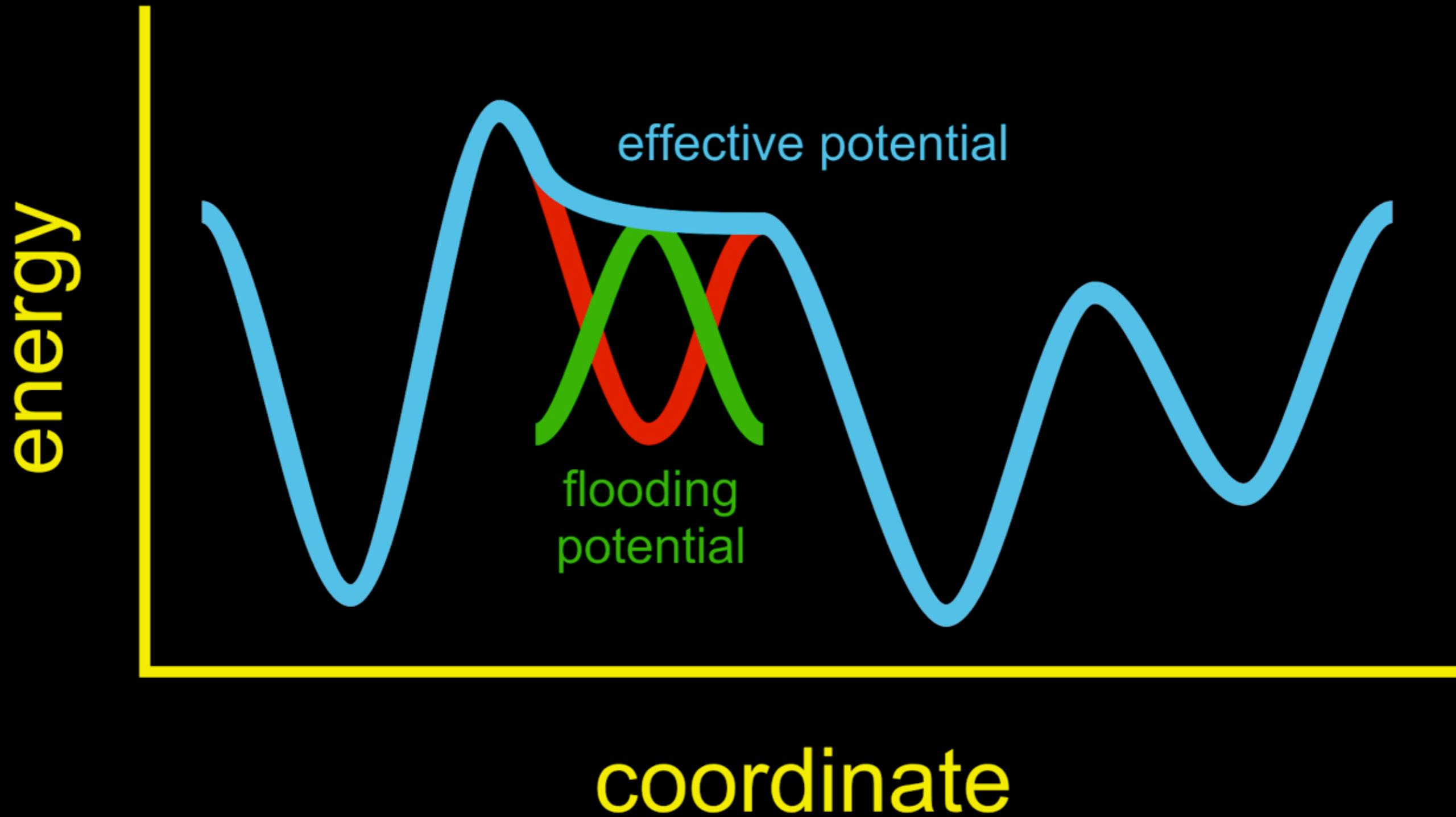
Chemical Flooding

Grubmüller, PRE 52 (1995): 2893-2906

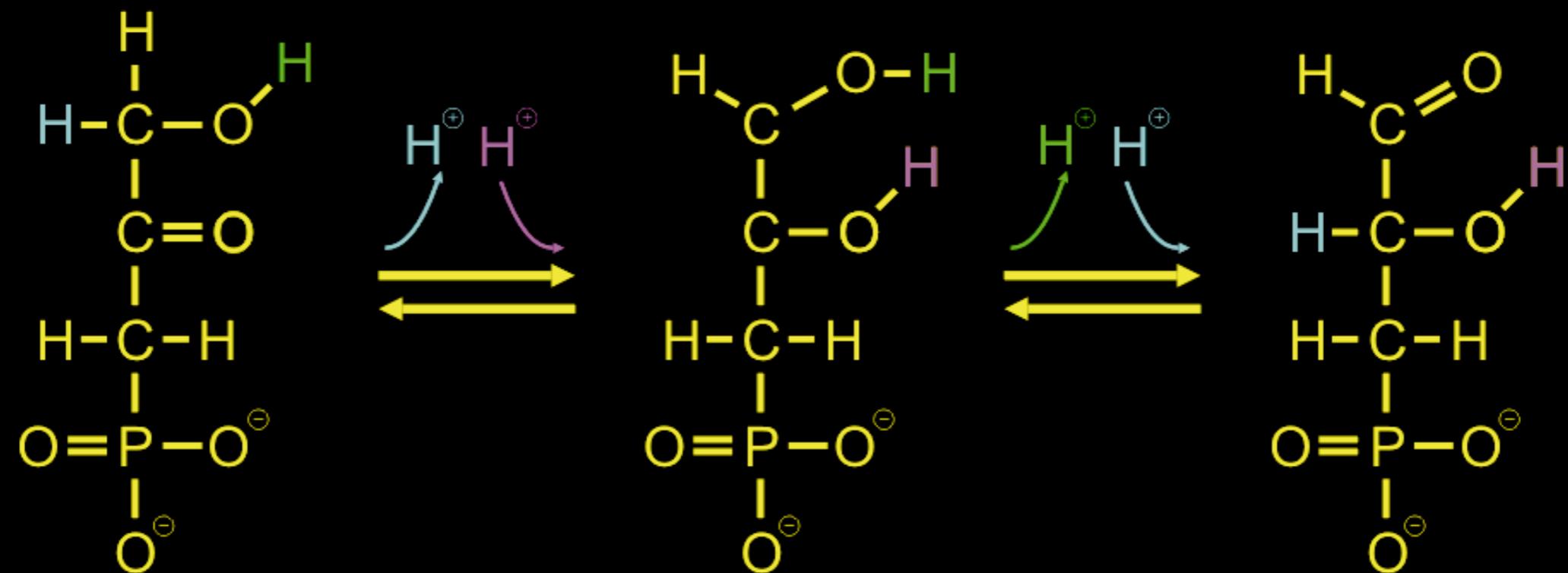


Chemical Flooding

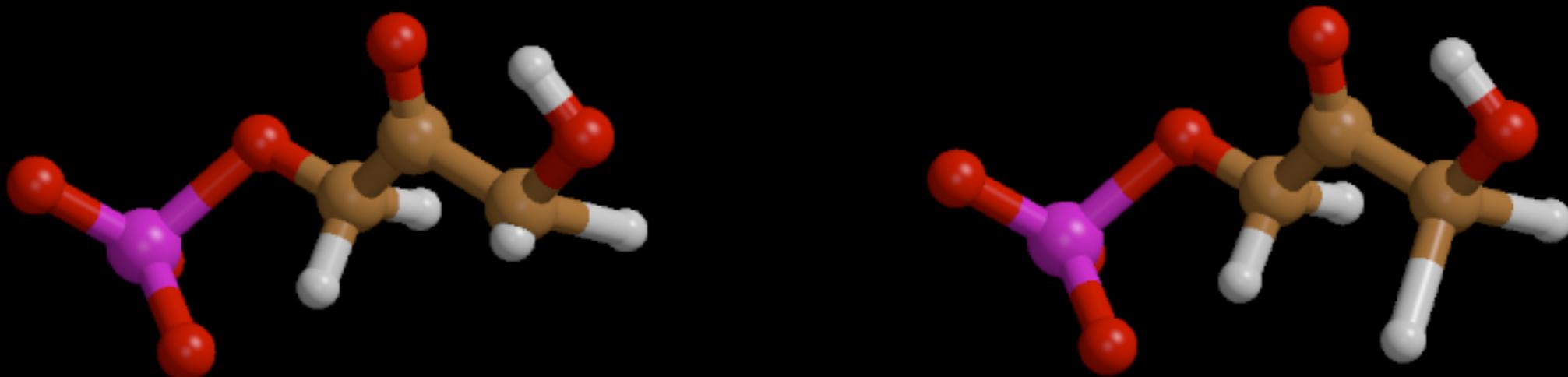
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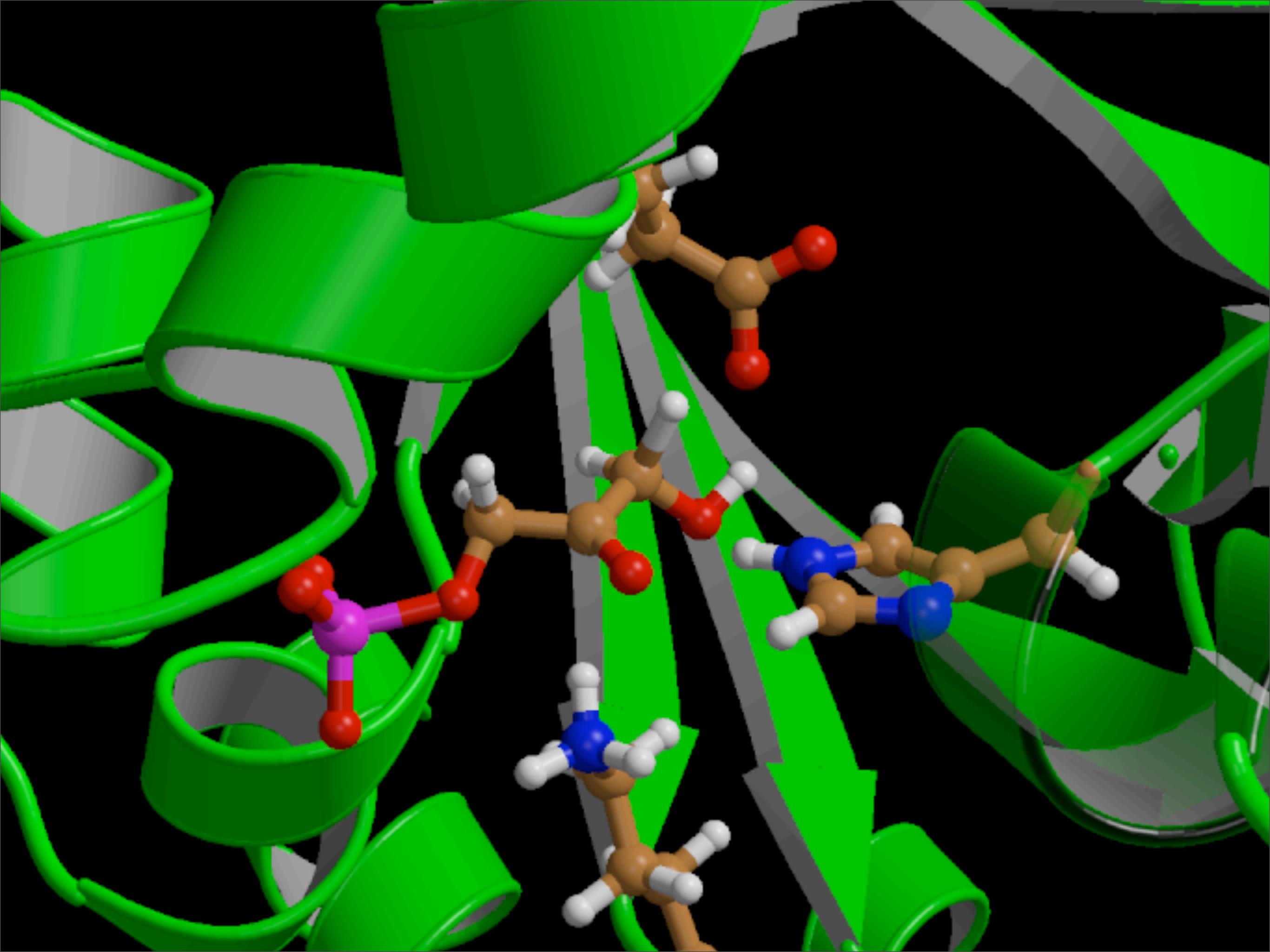


Triosephosphate Isomerase



normal mode analysis





ground state simulations

mdp options

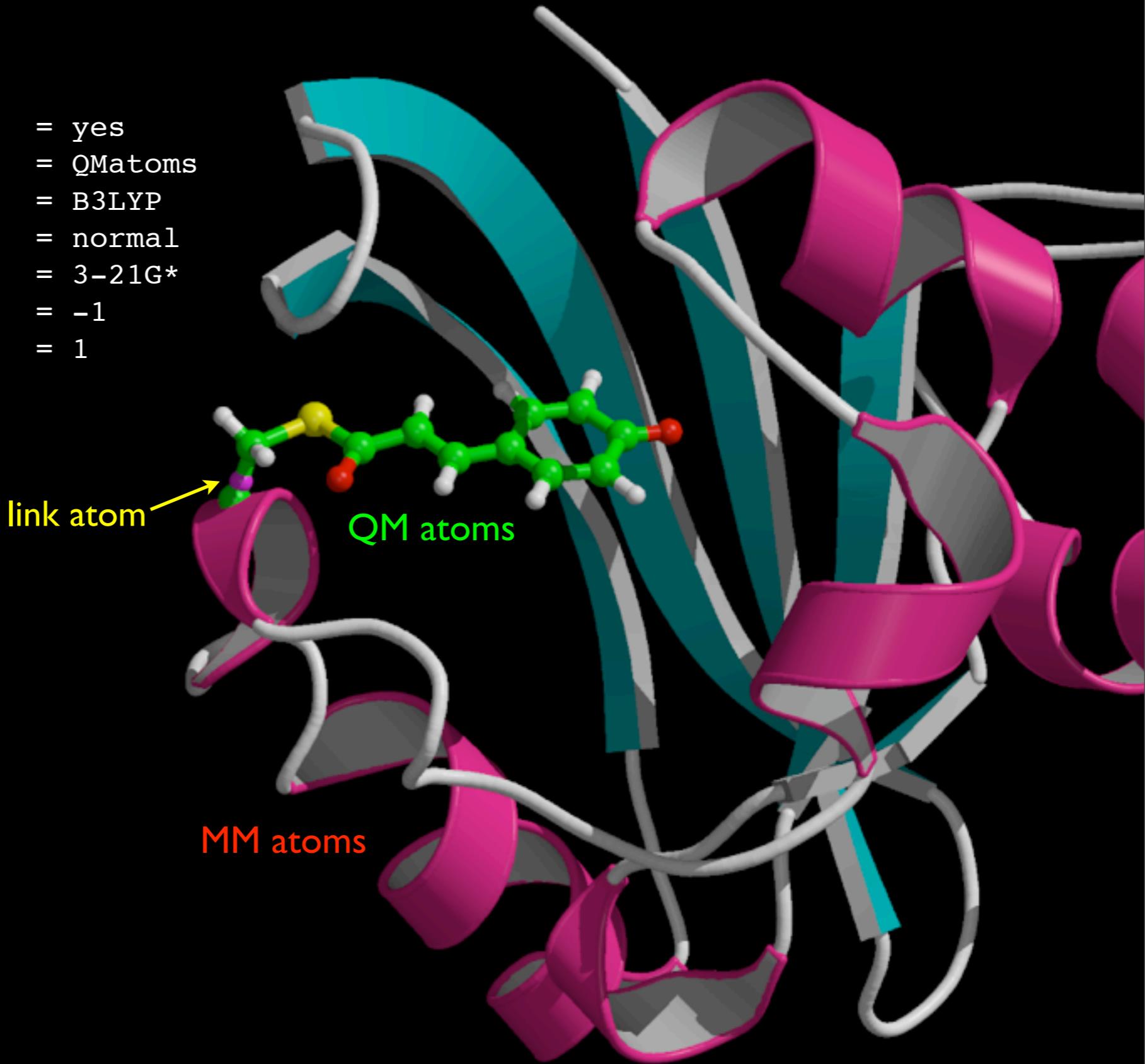
QMMM	= yes
QMMM-grps	= QMatoms
QMmethod	= B3LYP
QMMMscheme	= normal
QMbasis	= 3-21G*
QMcharge	= -1
QMmult	= 1

topology

```
[ bonds ]  
..  
MMatom QMatom 1  
QMatom QMatom 5  
..  
[ dummies2 ]  
LA QMatom MMatom 1 0.65
```

index

```
[ QMAtoms ]  
QMatom1 QMatom2 .. LA
```



acknowledgements

Gromacs team

David van der Spoel

Erik Lindahl

Berk Hess

Carsten Kutzner