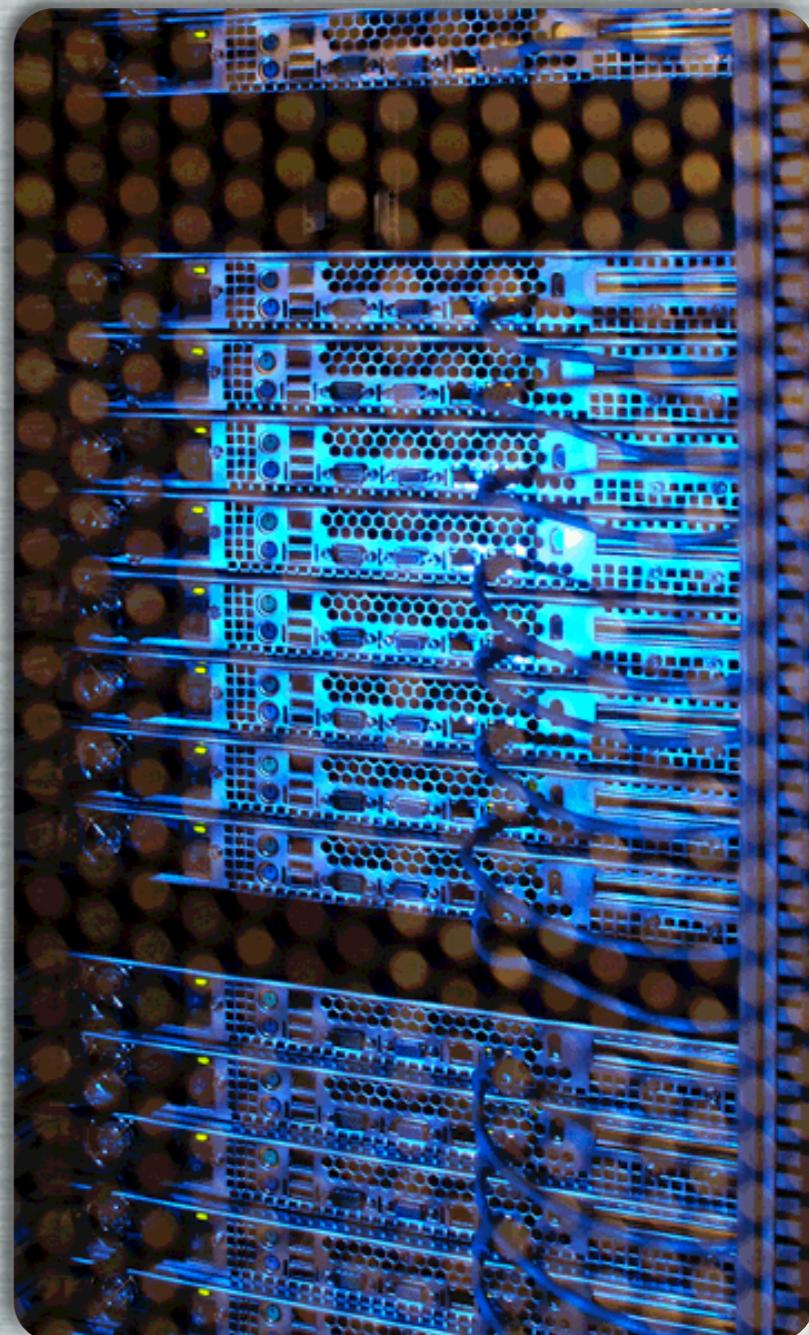
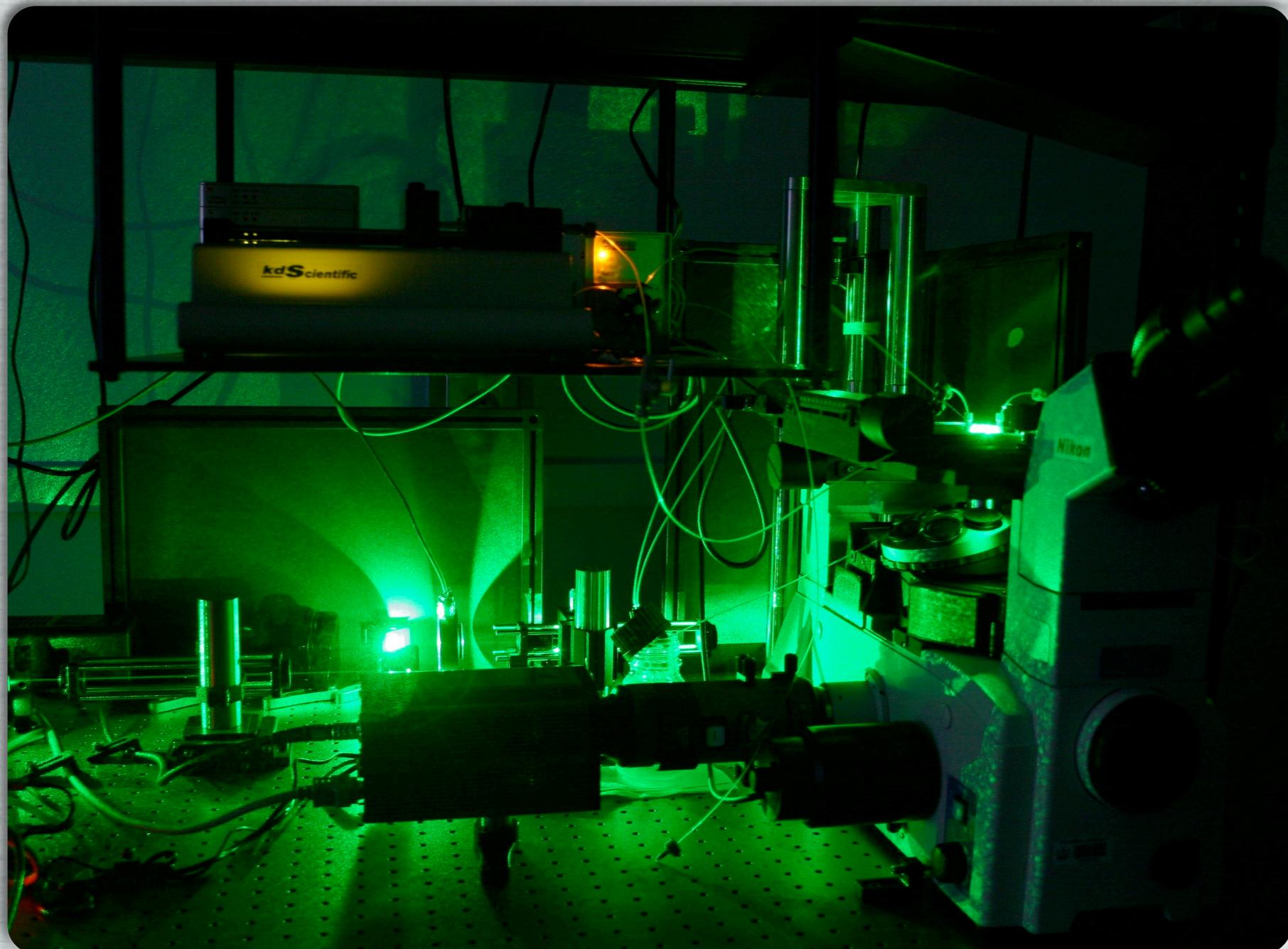


# Computer simulations of chemical processes in complex environments: quantum chemistry



# Chemistry on a computer

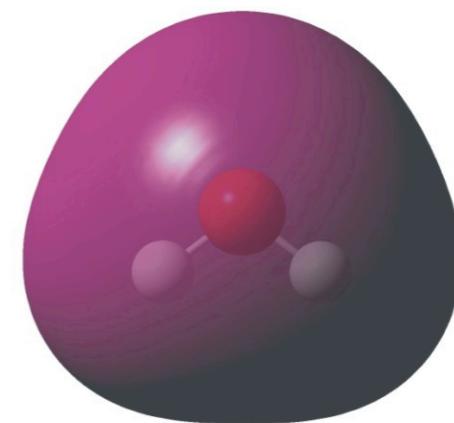
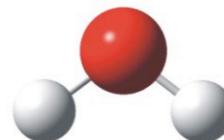
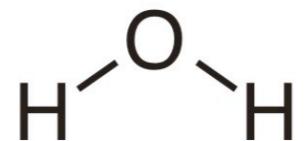
chemistry

electrons (-)

nuclei (+)

molecules

water (2 protons, 1 oxygen, 10 electrons)

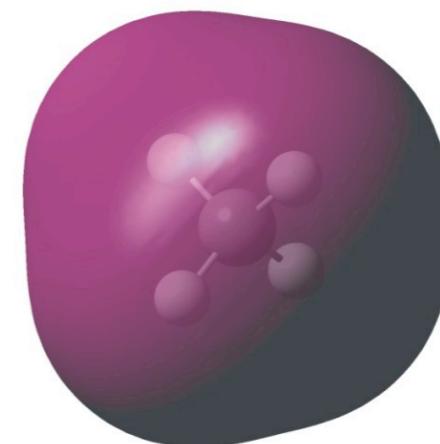
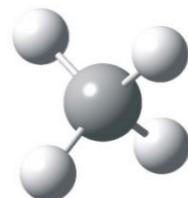
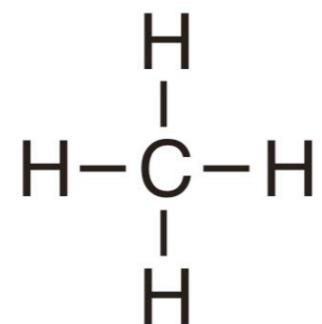


90% of electrons

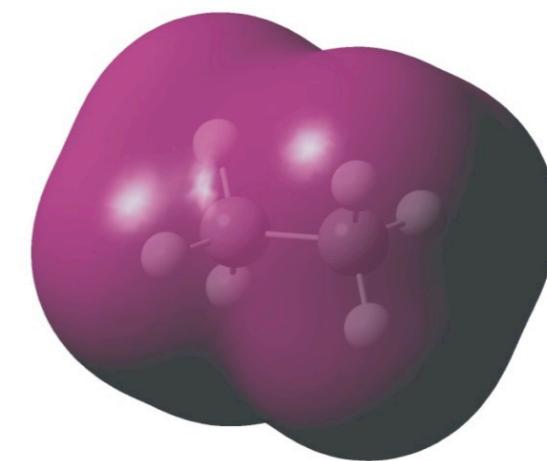
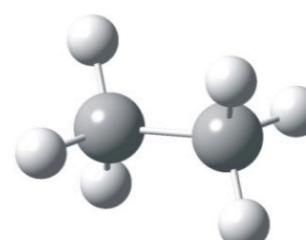
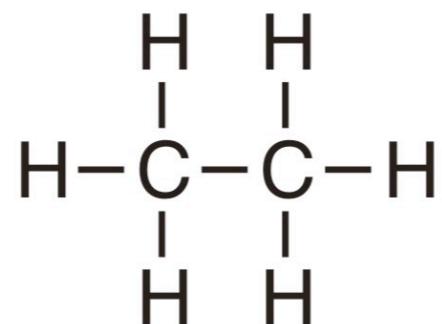
# Chemistry on a computer

## molecules

methane (4 protons, 1 carbon, 10 electrons)



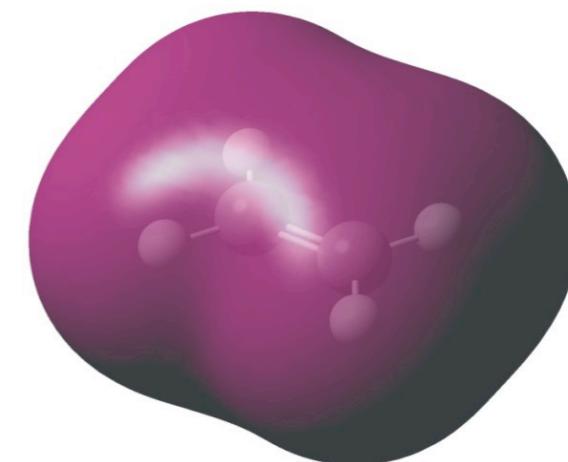
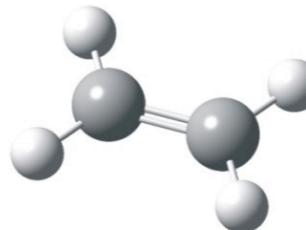
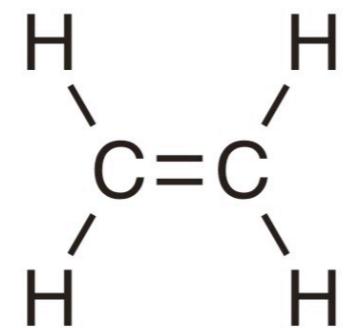
ethane (6 protons, 2 carbons, 18 electrons)



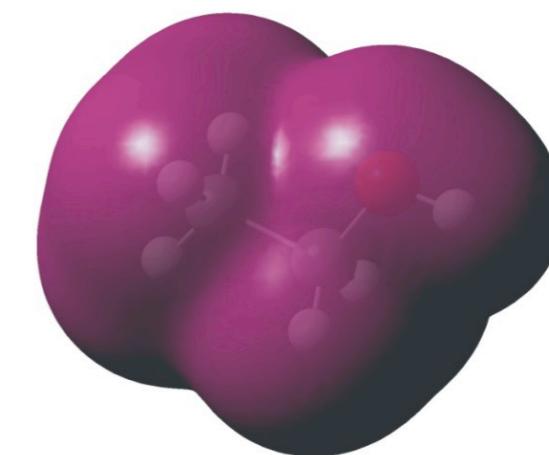
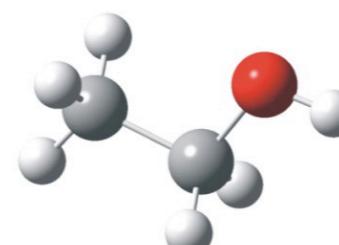
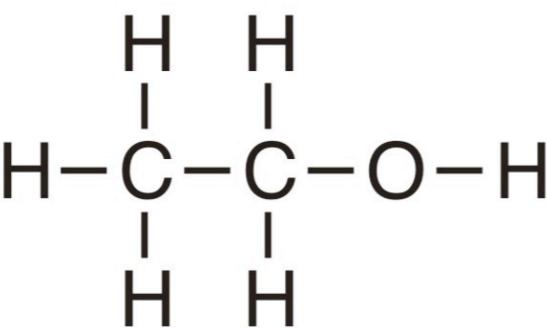
# Chemistry on a computer

## molecules

ethene (4 protons, 2 carbon, 16 electrons)



ethanol (6 protons, 2 carbons, 1 oxygen 26 electrons)



# Chemistry on a computer

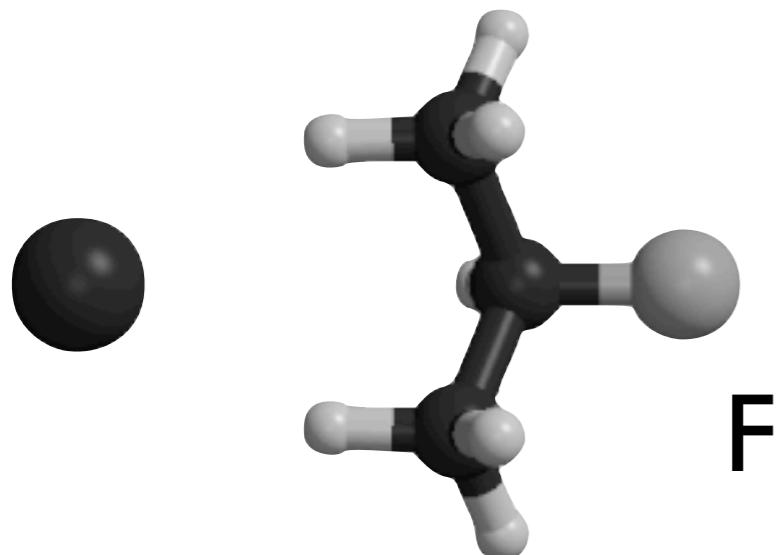
## chemical reactions

### substitution

reactant

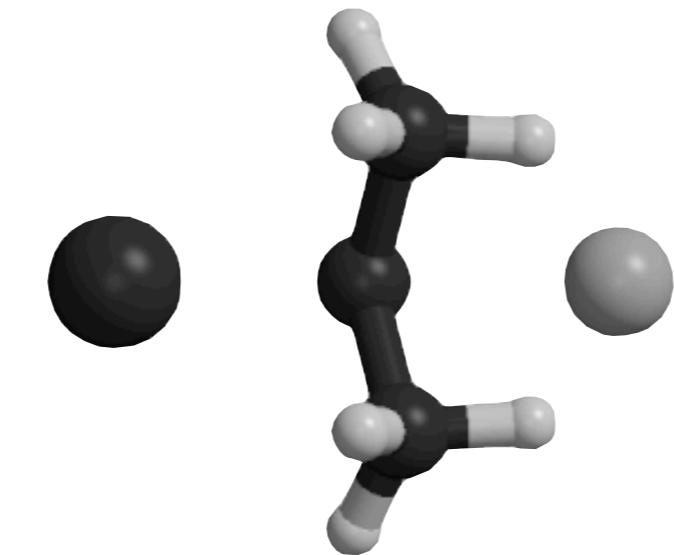
transition state

product

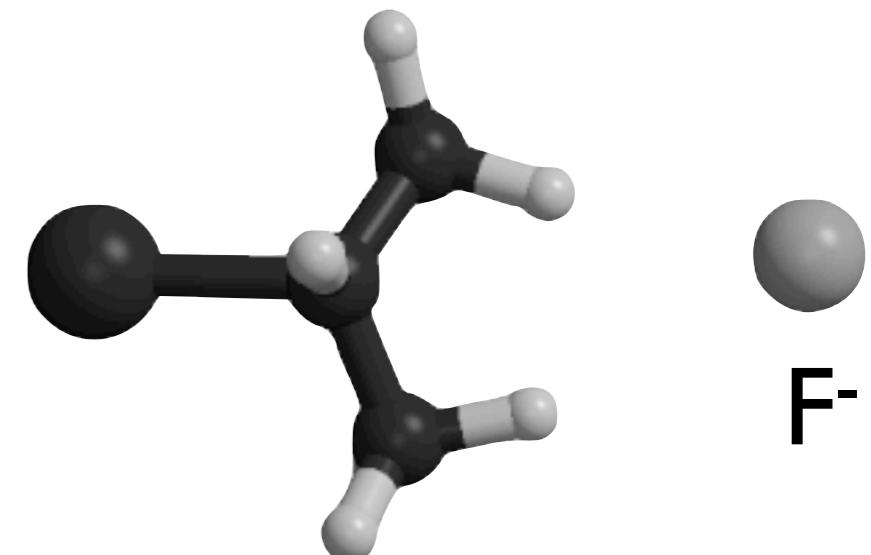


Cl<sup>-</sup>

0 kJ/mol



221 kJ/mol



204 kJ/mol

Br<sup>-</sup>

0 kJ/mol

246 kJ/mol

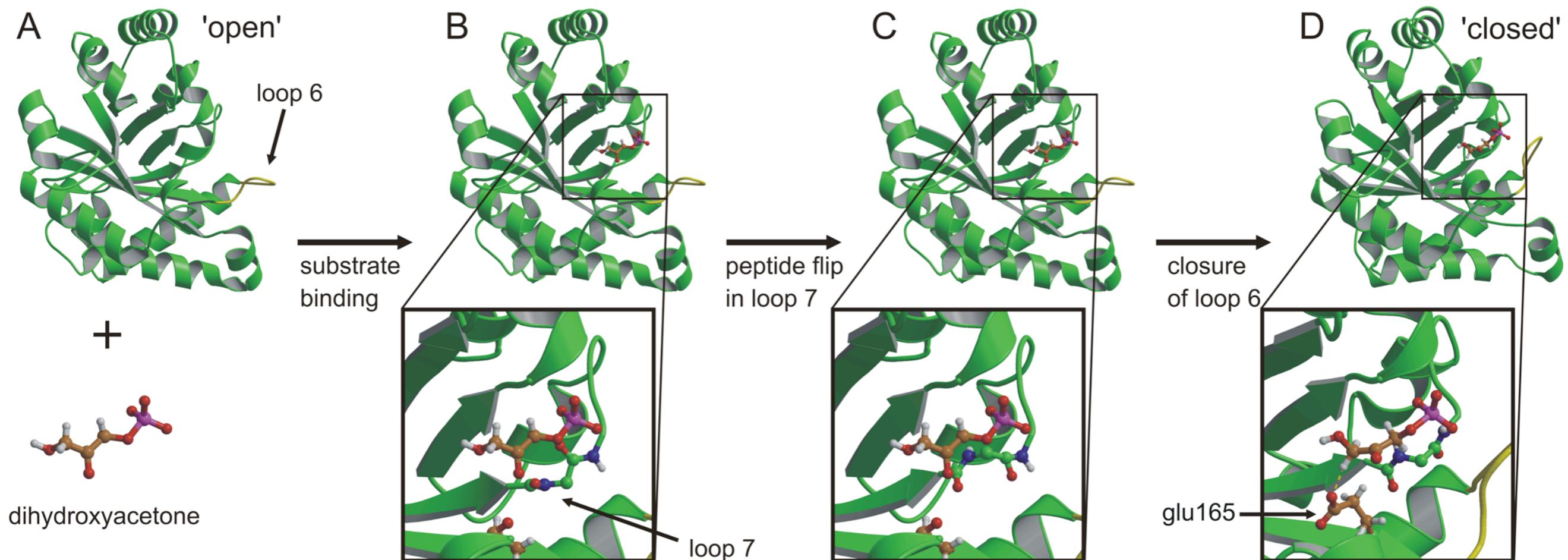
181 kJ/mol

# Chemistry on a computer

## biochemical reactions

### triosephosphate isomerase

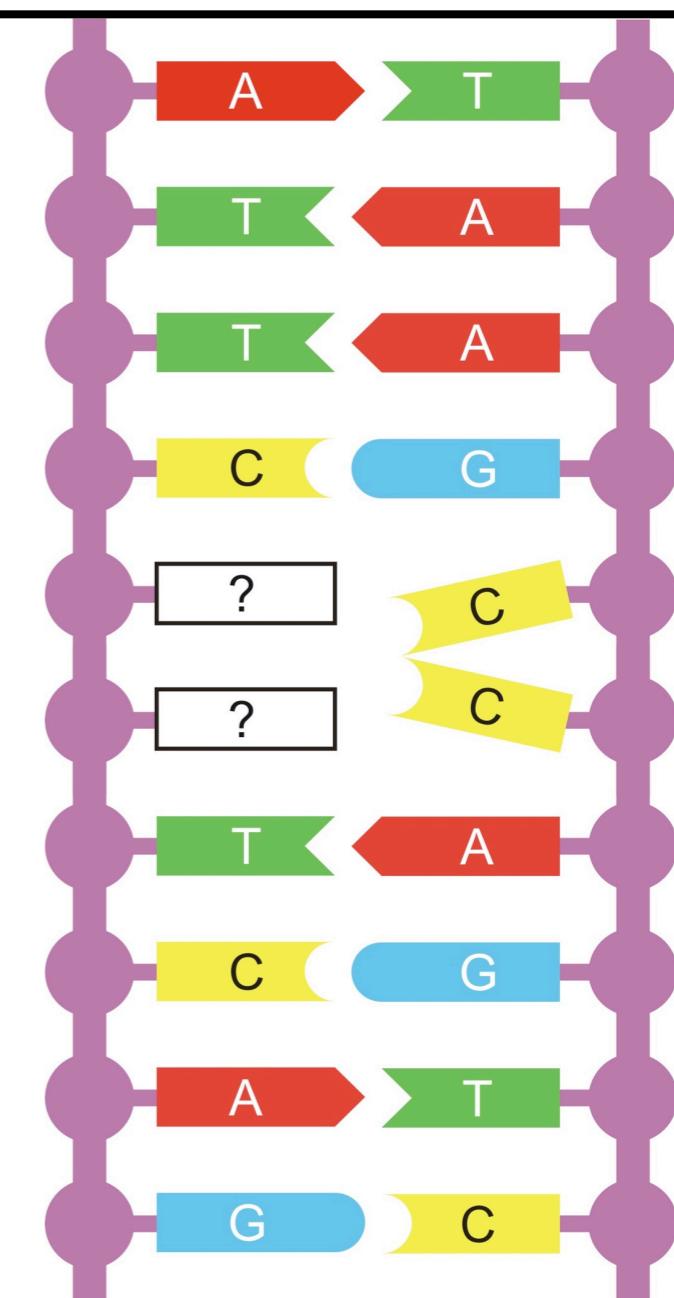
#### different conformations



# Chemistry on a computer

## biochemical reactions

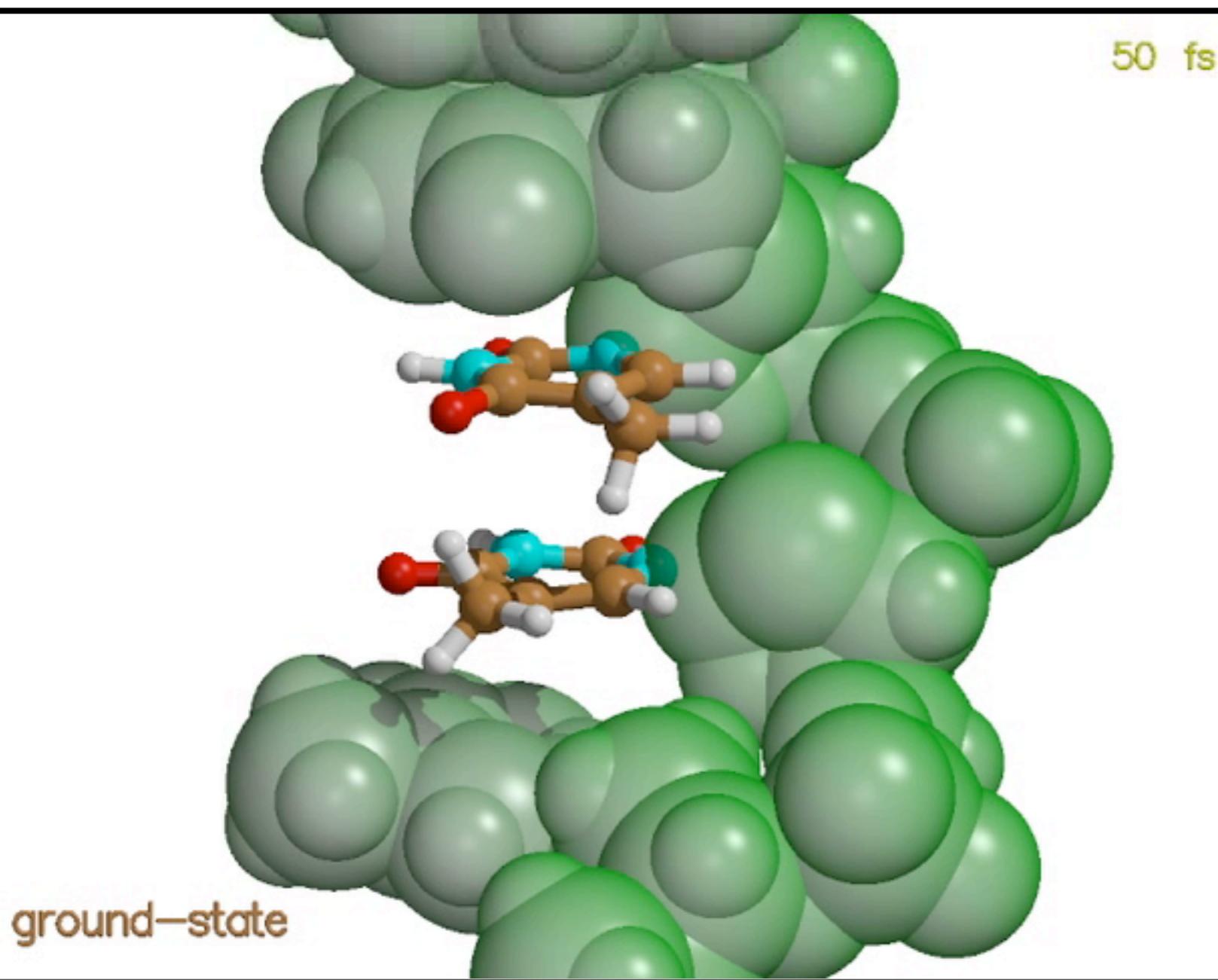
UV radiation damage in DNA:



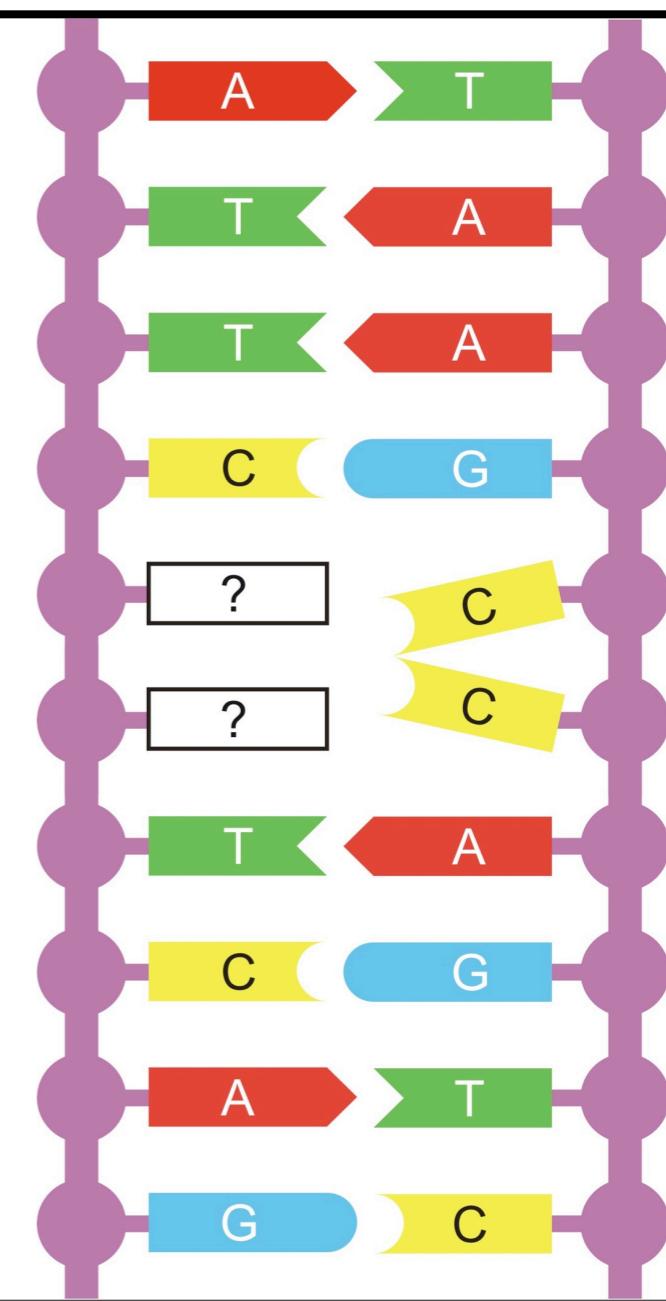
# Chemistry on a computer

## biochemical reactions

UV radiation damage in DNA:



ground-state



# Chemistry on a computer

chemistry

electrons (-)

nuclei (+)

theoretical foundations

electrostatic interactions: Coulomb's law

quantum mechanics: Schrödinger equation

properties to calculate

static: reaction energy, structure, spectra

dynamic: trajectories, thermodynamics

# Quantum mechanics

small particles

wave/particle duality

$$\lambda = \frac{h}{mv}$$

energy quantization

wavefunction concept

Schrödinger equation

$$i\hbar \frac{\partial}{\partial t} \Psi(\mathbf{x}, t) = H\Psi(\mathbf{x}, t)$$

Hamilton operator

$$H = T + V$$

# Quantum mechanics

probability density

$$P(\mathbf{x}, t) = \Psi^*(\mathbf{x}, t)\Psi(\mathbf{x}, t)$$

normalization

$$\int_{-\infty}^{\infty} \Psi^*(\mathbf{x}, t)\Psi(\mathbf{x}, t)d\mathbf{x} = \langle \Psi(\mathbf{x}, t) | \Psi(\mathbf{x}, t) \rangle = 1$$

expectation values

operator corresponding to the observable

$$\langle O(t) \rangle = \int_{-\infty}^{\infty} \Psi^*(\mathbf{x}, t)\mathbf{O}(t)\Psi(\mathbf{x}, t)d\mathbf{x} = \langle \Psi(\mathbf{x}, t) | \mathbf{O}(t) | \Psi(\mathbf{x}, t) \rangle$$

# Quantum mechanics

time-dependent Schrödinger equation

$$i\hbar \frac{\partial}{\partial t} \Psi(\mathbf{x}, t) = H\Psi(\mathbf{x}, t)$$

time-independent Schrödinger equation

$$H\Psi(\mathbf{x}, t) = E\Psi(\mathbf{x}, t)$$

# Quantum chemistry

isolated molecules

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

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

# Quantum chemistry

## Born-Oppenheimer approximation

$$m_e/m_p \approx 1/2000$$

electrons much faster than nuclei

electrons adapt instantly (assumption)

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

## electronic Schrödinger equation

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

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

# Quantum chemistry

## 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

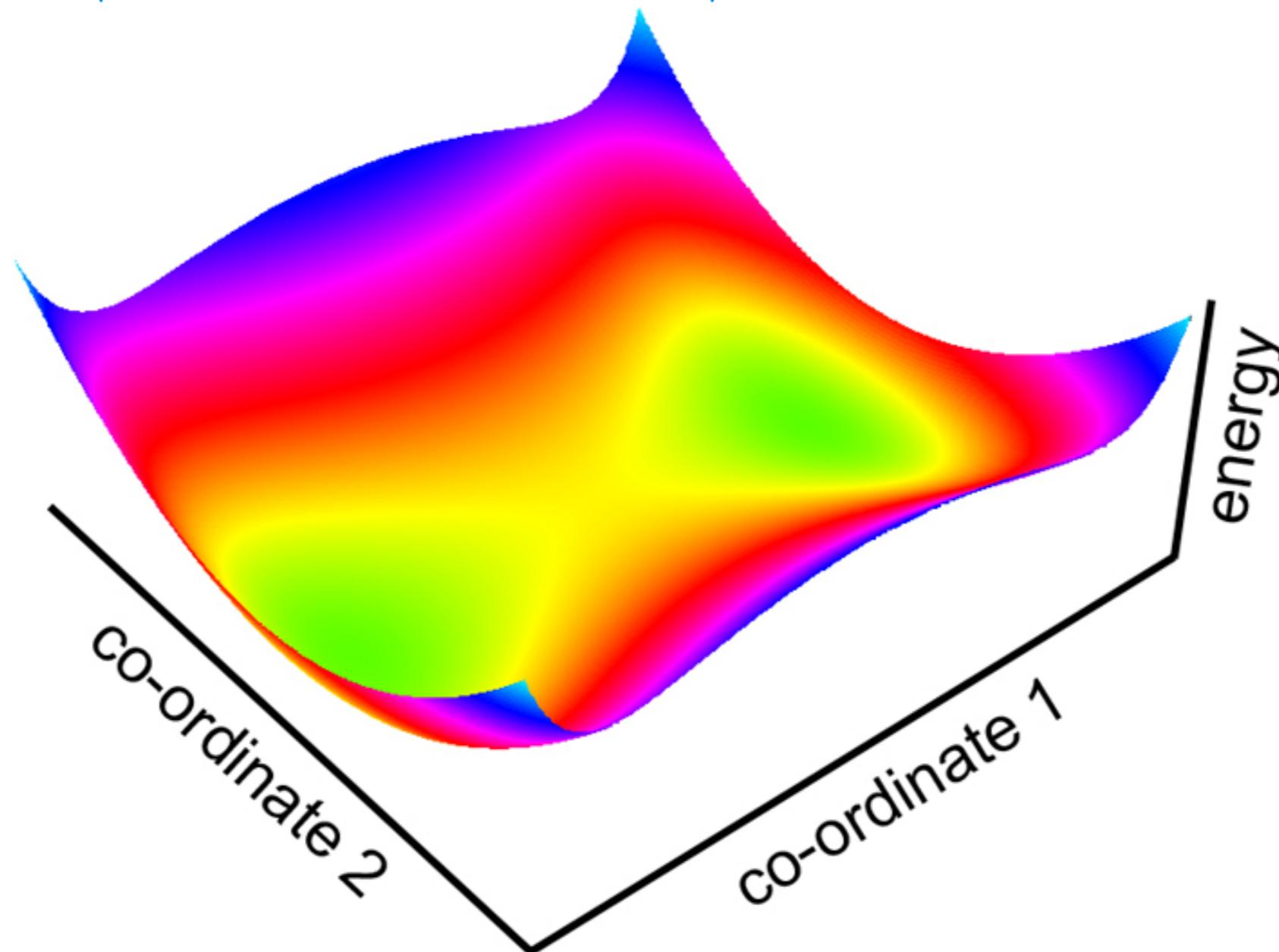
$$H^{\text{nuc}}(\mathbf{R}_N) \Xi^{\text{nuc}}(\mathbf{R}_N) = E^{\text{tot}} \Xi^{\text{nuc}}(\mathbf{R}_N)$$

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

# Quantum chemistry

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 (assumption)

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

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

potential energy and forces

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

limitations

protons (low mass): tunneling through barrier

H/D isotope effect

# Molecular Dynamics

Hellmann-Feynmann forces

$$F_n = -\langle \Psi_e | \nabla H(R_1, R_2, \dots, R_N) | \Psi_e \rangle$$

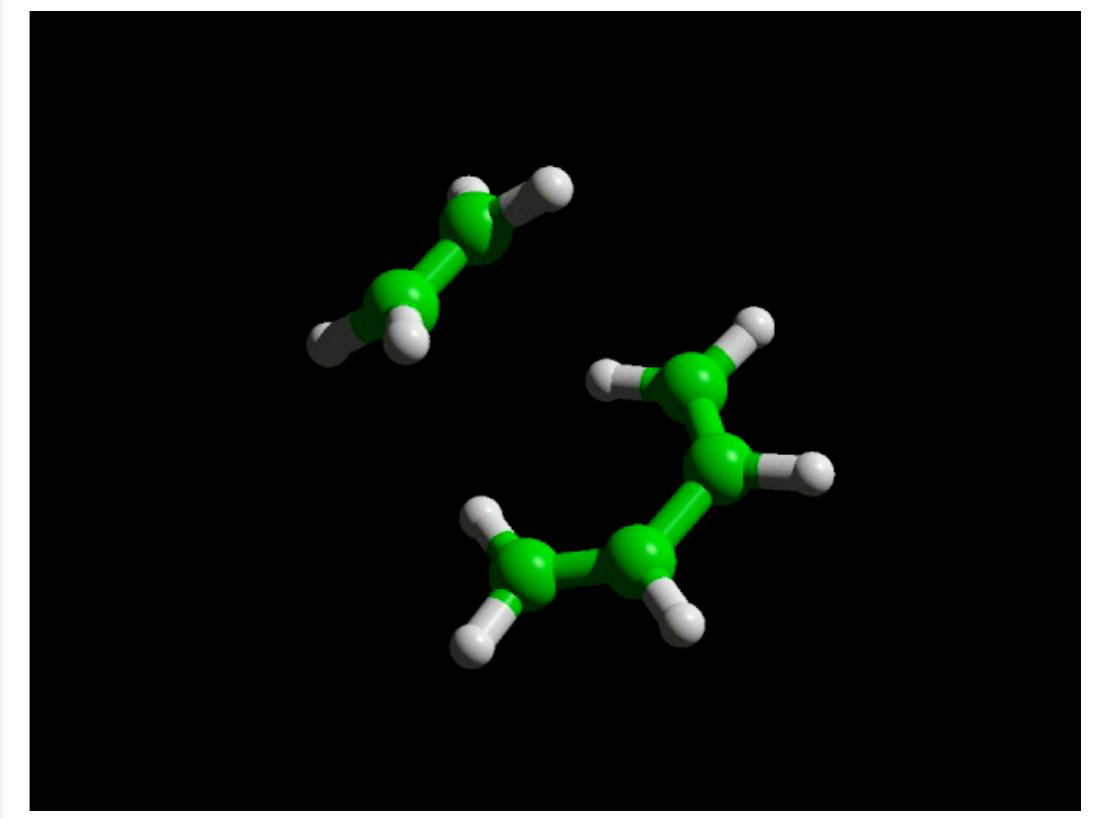
electrons adapt instantly!!

on-the-fly molecular dynamics

reactions

photochemistry

electron transfer



# Molecular Quantum Mechanics

# many-electron Schrödinger equation

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

# 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)

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

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)

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

incorrect due to electron-electron interaction

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

mean field approach

$$v_i^{\text{mf}}(r_i) = \sum_{i \neq j}^{n_e} \frac{e^2}{4\pi\epsilon_0 r_{ij}} \approx e^2 \int \frac{\rho_{\dots, h, j, \dots}(r)}{r - r_i} dr$$

# Molecular Quantum Mechanics

## Hartree approximation

product of one electron wavefunctions (orbitals)

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

mean field Hamiltonian

$$H^{\text{mf}} = \sum_i^{n_e} h_i \quad h_i = -\frac{\hbar^2}{2m_e} \nabla_i - \sum_A^{N_{QM}} \frac{e^2 Z_A}{4\pi\epsilon_0 r_{iA}} + v^{\text{mf}}(r_i)$$

non-linear minimization problem

$$\partial E = \partial \langle \Psi | H^{\text{mf}} | \Psi \rangle = 0$$

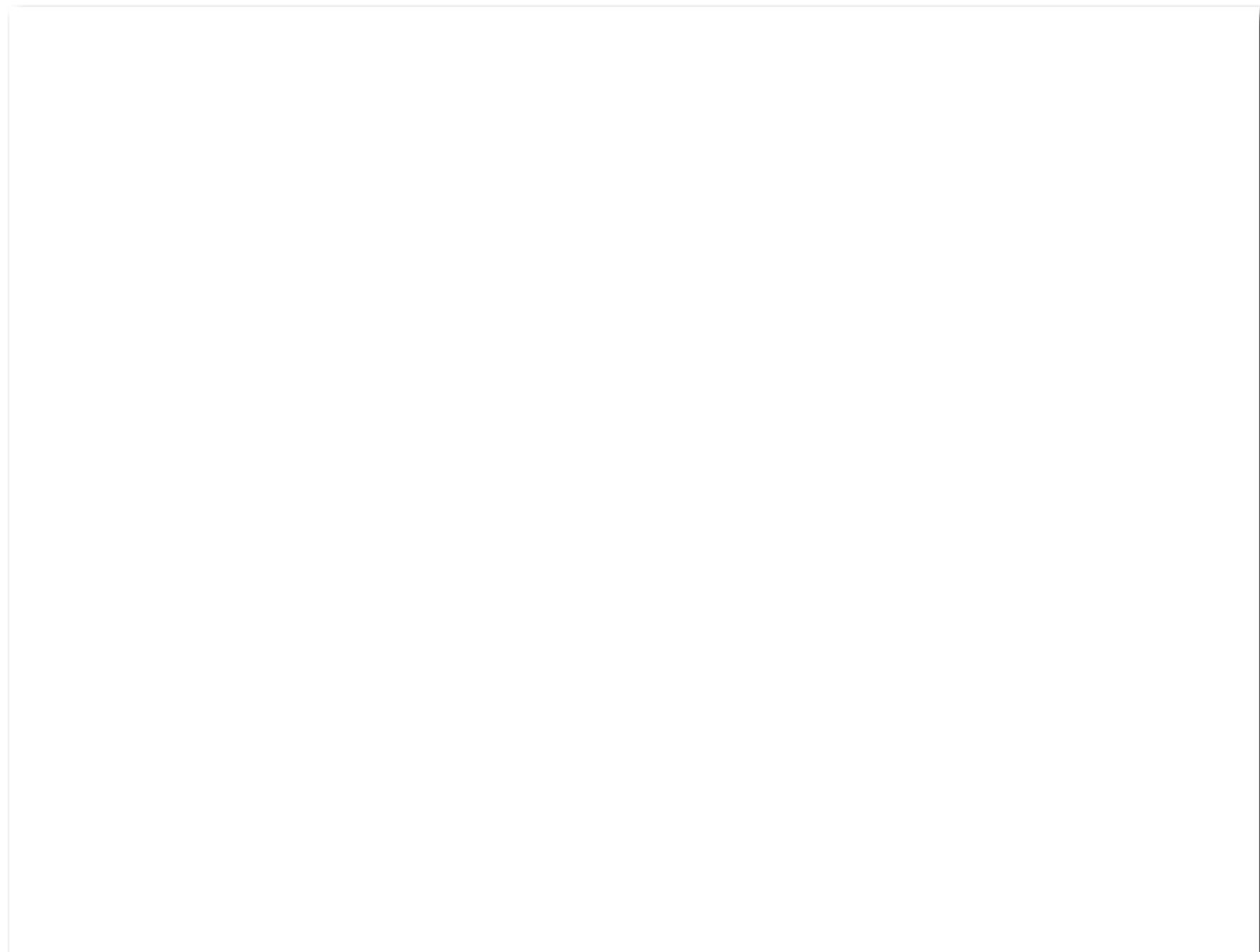
variational principle

$$E_{\text{true}} \leq E_{\text{trial}}$$

# Molecular Quantum Mechanics

## mean field approach

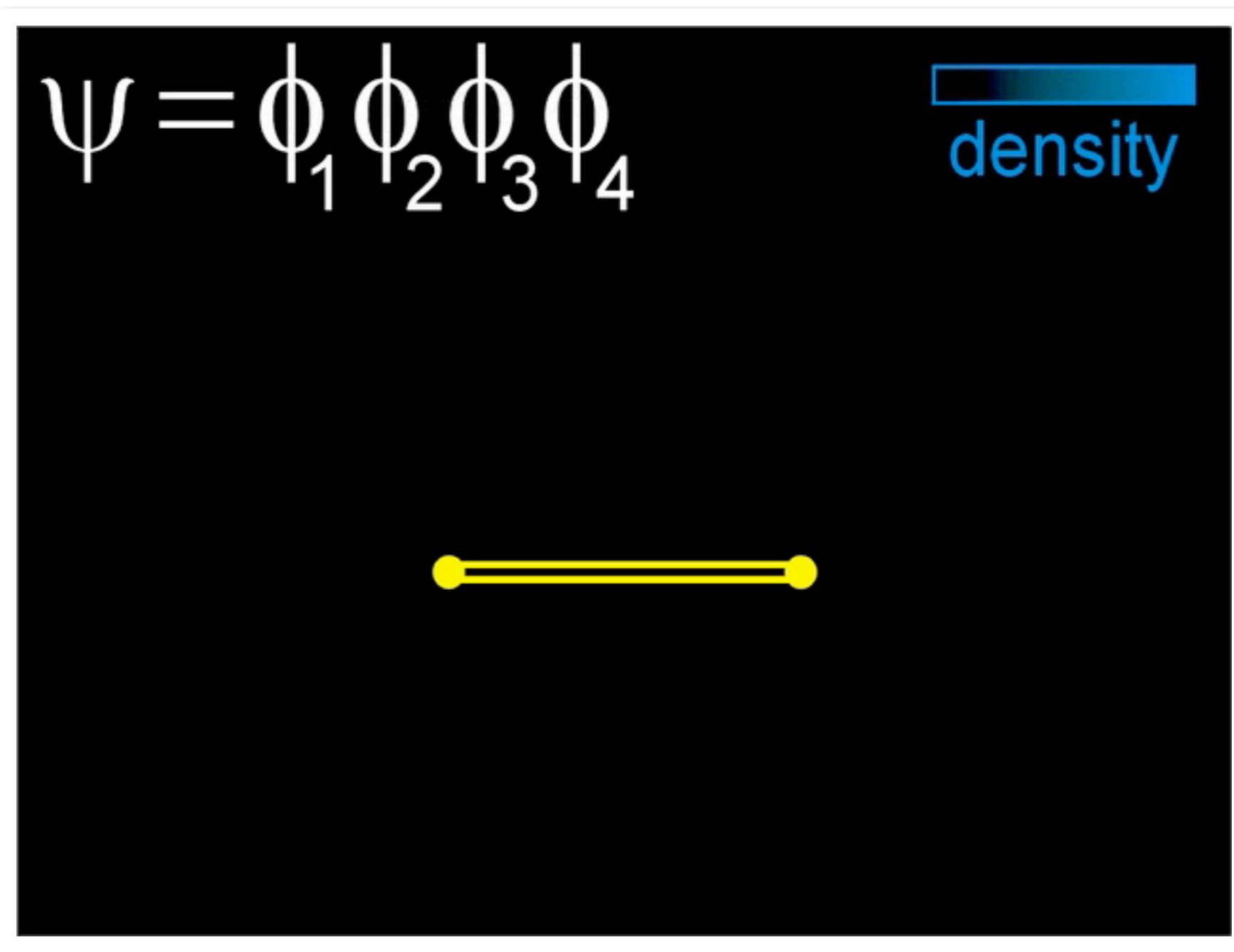
### self-consistent-field iteration



# Molecular Quantum Mechanics

## mean field approach

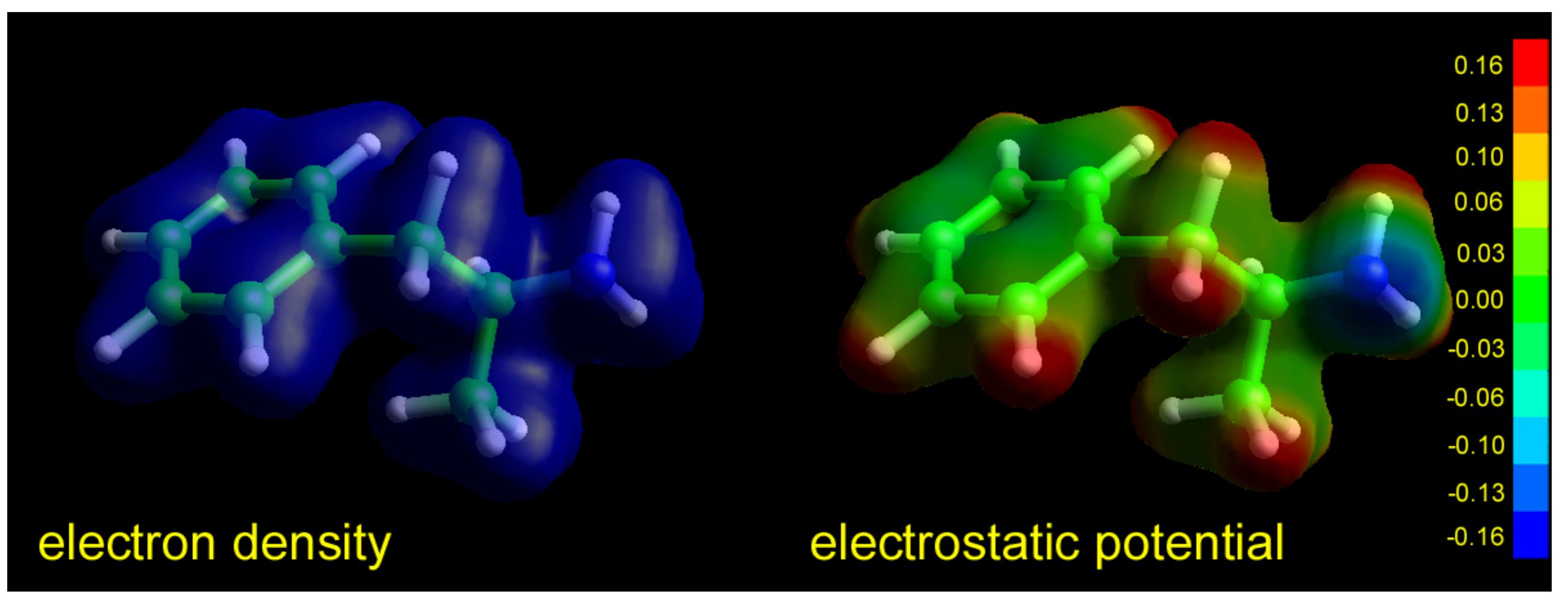
### self-consistent-field iteration



# Molecular Quantum Mechanics

electron density

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



# Molecular Quantum Mechanics

## Pauli principle

electronic wavefunction is anti-symmetric

$$\Psi(..., r_i, r_j, ...) = -\Psi(..., r_j, r_i, ...)$$

same spin electrons cannot occupy same space

## Hartree product wavefunction

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

$$\Psi(..., r_i, r_j, ...) \neq -\Psi(..., r_j, r_i, ...)$$

## Hartree-Fock approximation

anti-symmetric combination of hartree products

# Molecular Quantum Mechanics

## Hartree-Fock approximation

two electron example system

$$\Psi(r_1, r_2) = \frac{1}{\sqrt{2}} (\phi_1(r_1)\phi_2(r_2) - \phi_1(r_2)\phi_2(r_1))$$

anti-symmetric linear combination

$$\begin{aligned}\Psi(r_2, r_1) &= \frac{1}{\sqrt{2}} (\phi_1(r_2)\phi_2(r_1) - \phi_1(r_1)\phi_2(r_2)) \\ &= -\frac{1}{\sqrt{2}} (\phi_1(r_1)\phi_2(r_2) - \phi_2(r_1)\phi_1(r_2)) \\ &= -\Psi(r_1, r_2)\end{aligned}$$

identical weights: no effect on density, energy, etc...

# Molecular Quantum Mechanics

## Slater determinant

general anti-symmetric linear combination

many electron systems

$$\Psi(r_1, r_2, \dots, r_n) = \frac{1}{\sqrt{n}} \begin{vmatrix} \phi_1(r_1) & \phi_2(r_1) & \dots & \phi_n(r_1) \\ \phi_1(r_2) & \phi_2(r_2) & \dots & \phi_n(r_2) \\ \vdots & \vdots & \ddots & \vdots \\ \phi_1(r_n) & \phi_2(r_n) & \dots & \phi_n(r_n) \end{vmatrix}$$

# Molecular Quantum Mechanics

## Slater determinant

general anti-symmetric linear combination

many electron systems

$$\Psi(r_1, r_2, \dots, r_n) = \frac{1}{\sqrt{n}} \begin{vmatrix} \phi_1(r_1) & \phi_2(r_1) & \dots & \phi_n(r_1) \\ \phi_1(r_2) & \phi_2(r_2) & \dots & \phi_n(r_2) \\ \vdots & \vdots & & \vdots \\ \phi_1(r_n) & \phi_2(r_n) & \dots & \phi_n(r_n) \end{vmatrix}$$

# Molecular Quantum Mechanics

one electron wavefunctions

electrons have position and spin

$$\varphi_i(x, y, z, s) = \phi_i(x, y, z)\sigma(s)$$

$$s = -\frac{1}{2}, \frac{1}{2}$$

non-relativistic Hamiltonian

$$H = H(x, y, z)$$

spin label

$$\sigma(+\frac{1}{2}) = \beta \quad \sigma(-\frac{1}{2}) = \alpha$$

# Molecular Quantum Mechanics

restricted Hartree-Fock approximation

molecular orbital, with maximal 2 electrons

$$\varphi_i(x, y, z, -\frac{1}{2}) = \phi_i(x, y, z)\alpha = \phi_i(x, y, z)$$

$$\varphi_i(x, y, z, \frac{1}{2}) = \phi_i(x, y, z)\beta = \bar{\phi}_i(x, y, z)$$

Slater determinant of molecular orbitals

$$\Psi(r_1, r_2, \dots, r_n) = |\phi_1(r_1)\bar{\phi}_1(r_2)\dots\phi_{\frac{n}{2}}(r_{n-1})\bar{\phi}_{\frac{n}{2}}(r_n)|$$

# Molecular Quantum Mechanics

## molecular orbitals

linear combination of atomic orbitals (hydrogen)

$$\phi_i(r) = \sum_j c_{ji} \chi_j(r)$$

example: hydrogen molecule, minimal basis

$$\phi_1(r) = \chi_1(r) + \chi_2(r)$$

$$\phi_2(r) = \chi_1(r) - \chi_2(r)$$



# Molecular Quantum Mechanics

## molecular orbitals

linear combination of atomic orbitals (hydrogen)

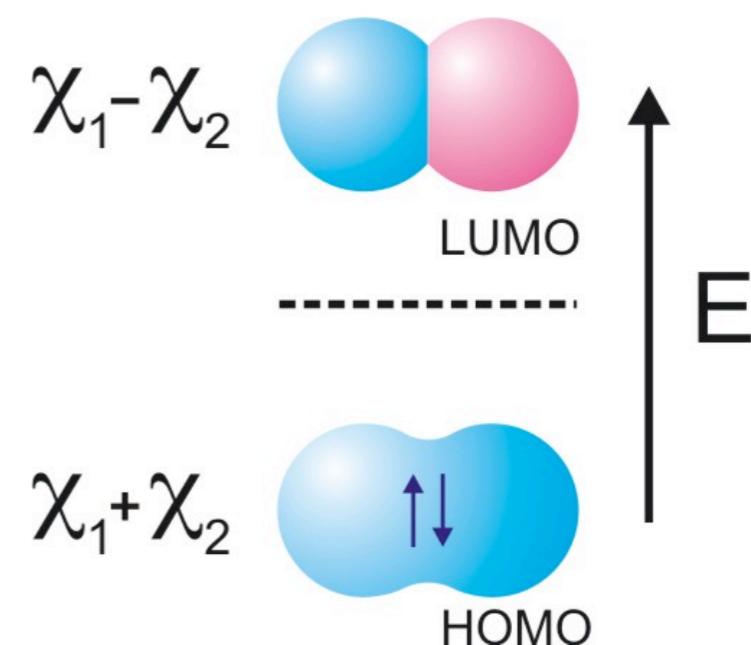
$$\phi_i(r) = \sum_j c_{ji} \chi_j(r)$$

example: hydrogen molecule, minimal basis

$$\phi_1(r) = \chi_1(r) + \chi_2(r)$$

$$\Psi(r_1, r_2) = |\phi_1(r_1)\overline{\phi_1}(r_2)|$$

$$\phi_2(r) = \chi_1(r) - \chi_2(r)$$



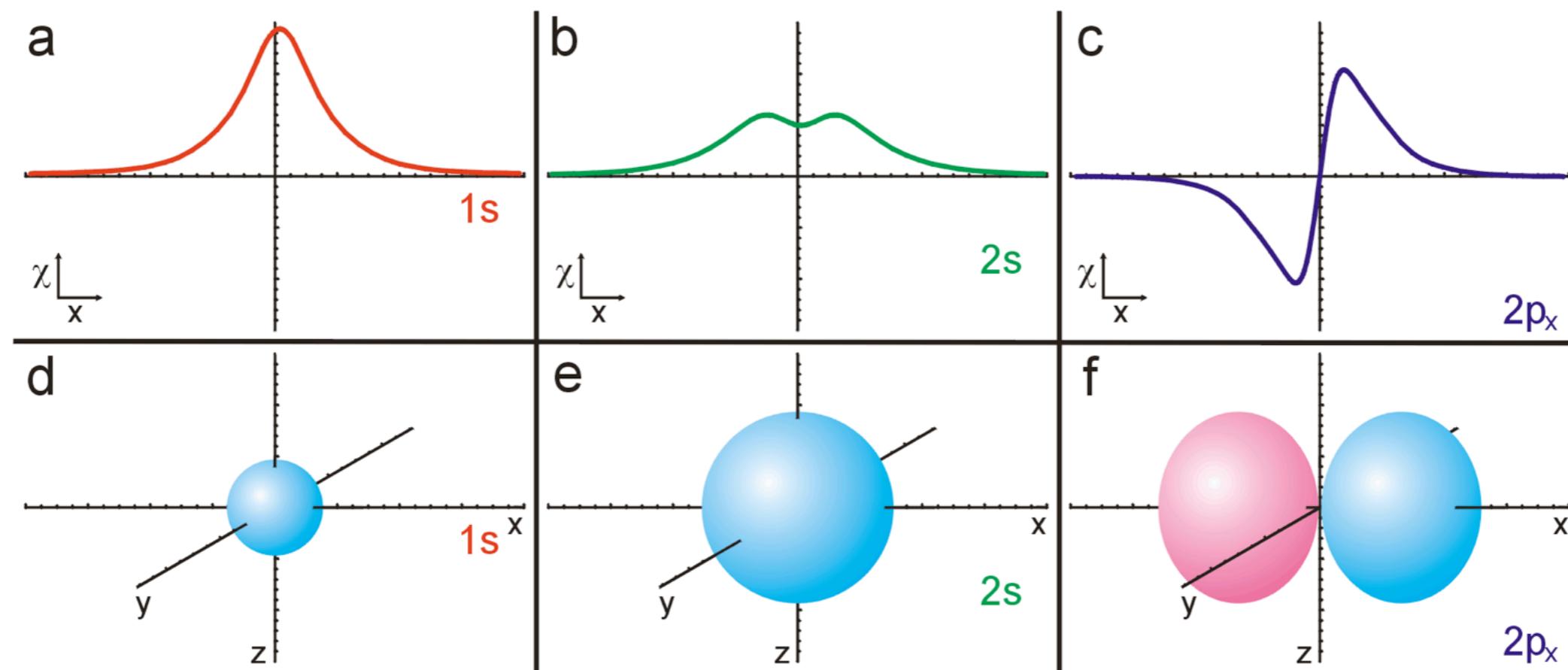
# Molecular Quantum Mechanics

atomic orbitals, basisset

solutions of hydrogen atom

$$\chi_i(r) = \sum_{lm} C_l R_l(r) Y_{lm}(r)$$

gaussian basisst (STO-3G)



# Molecular Quantum Mechanics

## restricted Hartree-Fock

Slater determinant

$$\Psi(r_1, r_2, \dots, r_n) = |\phi_1(r_1)\bar{\phi}_1(r_2)\dots\phi_{\frac{n}{2}}(r_{n-1})\bar{\phi}_{\frac{n}{2}}(r_n)|$$

molecular orbitals

$$\phi_i(r) = \sum_j c_{ji} \chi_j(r)$$

atomic orbitals (basisset)

algorithm

variation principle

find  $c_{ji}$  that minimize the electron energy

# Molecular Quantum Mechanics

minimization of Hartree Fock energy

$$\partial E = \partial \langle \Psi | H | \Psi \rangle = 0$$

with

$$\Psi(r_1, r_2, \dots, r_n) = |\phi_1(r_1)\overline{\phi_1}(r_2)\dots\overline{\phi_{\frac{n}{2}}}(r_{n-1})\overline{\phi_{\frac{n}{2}}}(r_n)|$$

and

$$H = \sum_i h_i + \frac{1}{2} \sum_{ij} \frac{e^2}{4\pi\epsilon_0 r_{ij}}$$

and

$$h_i = \frac{1}{2} \nabla_i^2 - \sum_A^{N_{QM}} \frac{e^2 Z_A}{4\pi\epsilon_0 r_{ij}}$$

# Molecular Quantum Mechanics

## Hartree-Fock energy

energy of a molecular orbital

$$[h_i + \sum_j (2J_j - K_j)]\phi_i(r_i) = \epsilon_i \phi_i(r_i)$$

coulomb integral

$$J_j \phi_i(r_i) = \langle \phi_j(r_j) | \frac{e^2}{4\pi\epsilon_0 r_{ij}} | \phi_j(r_j) \rangle \phi_i(r_i)$$

exchange integral

$$K_j \phi_i(r_i) = \langle \phi_j(r_j) | \frac{e^2}{4\pi\epsilon_0 r_{ij}} | \phi_j(r_i) \rangle \phi_i(r_j)$$

ground-state energy of Slater determinant

$$E = 2 \sum_i^n \epsilon_i - \sum_{ij}^n (2\langle \phi_i(r_i) | J_j | \phi_i(r_i) \rangle - \langle \phi_i(r_i) | K_j | \phi_i(r_i) \rangle)$$

# Molecular Quantum Mechanics

## Roothaan-Hall equations

energy of single molecular orbital

$$[h_i + \sum_j (2J_j - K_j)]\phi_i(r_i) = f_i\phi_i(r_i) = \epsilon_i\phi_i(r_i)$$

substituting atomic orbital expansion

$$f_i \sum_j c_{ji} \chi_j(r_i) = \epsilon_i \sum_j c_{ji} \chi_j(r_i)$$

multiplying from the left by  $\chi_i^*$  and integrating

$$\sum_j c_{ji} \langle \chi_i(r_i) | f_i | \chi_j(r_i) \rangle = \epsilon_i \sum_j c_{ji} \langle \chi_i(r_i) | \chi_j(r_j) \rangle$$

# Molecular Quantum Mechanics

## Roothaan-Hall equations

$$\sum_j c_{ji} \langle \chi_i(r_i) | f_i | \chi_j(r_i) \rangle = \epsilon_i \sum_j c_{ji} \langle \chi_i(r_i) | \chi_j(r_j) \rangle$$

define

$$F_{ij} = \langle \chi_i | f_i | \chi_j \rangle \quad S_{ij} = \langle \chi_i | \chi_j \rangle$$

non-linear eigenvalue problem

$$\mathbf{Fc} = \epsilon_i \mathbf{Sc}$$

solution, if

$$\det(\mathbf{F} - \epsilon_i \mathbf{S}) = 0$$

# Molecular Quantum Mechanics

## Roothaan-Hall equations

non-linear eigenvalue problem

$$Fc = \epsilon_i Sc$$

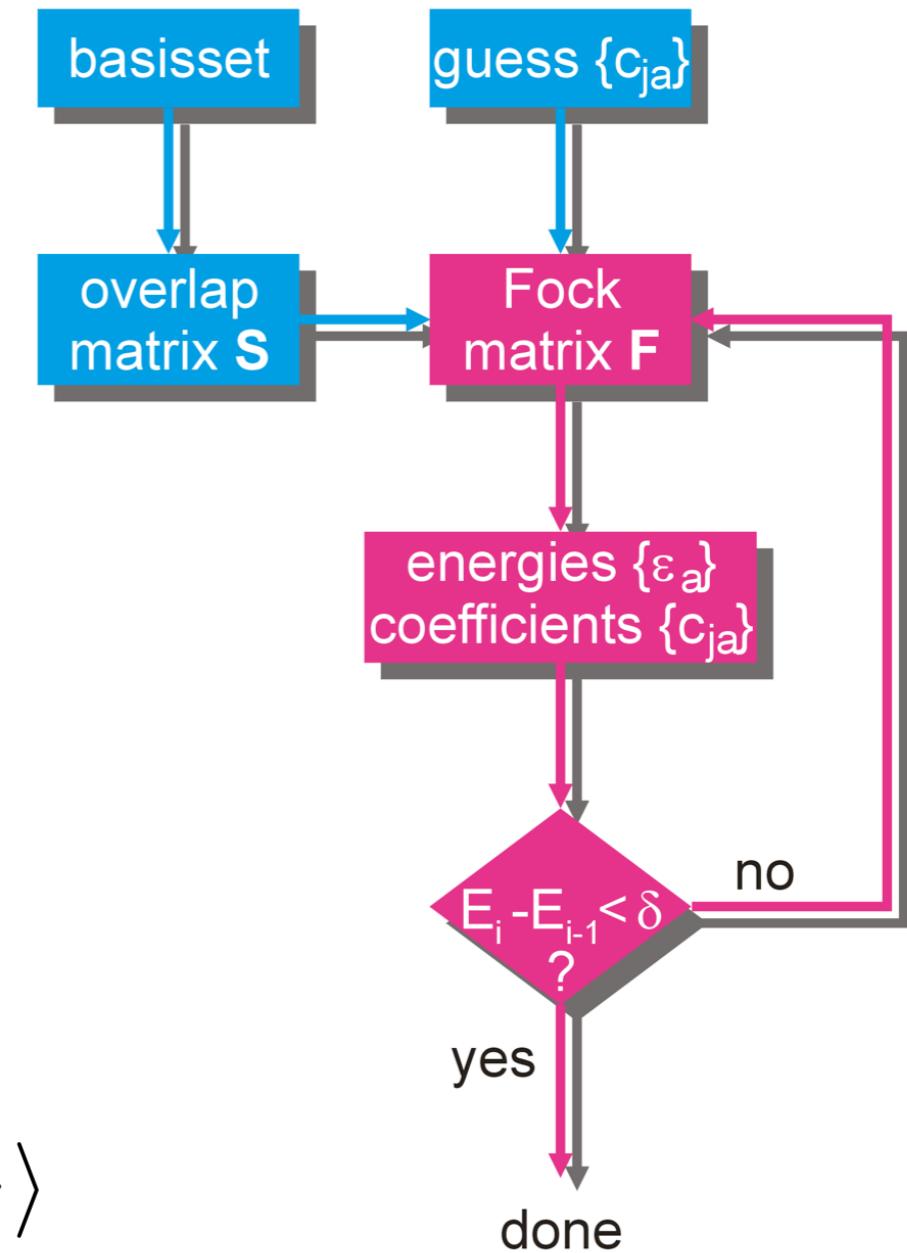
practical algorithm

iterate until self-consistency

pre-compute integrals

$$F_{ij} = \langle \chi_i | f_i | \chi_j \rangle$$

$$S_{ij} = \langle \chi_i | \chi_j \rangle$$



# Molecular Quantum Mechanics

## limitations of Hartree-Fock theory

- ▶ mean-field: no electron correlation

## beyond Hartree-Fock

- ▶ configuration interaction (ci)

$$\begin{aligned}\Psi = & C_0 |\phi_a(r_1)\phi_b(r_2) \dots \phi_k(r_{n-1})\phi_l(r_{n-1})| + \\ & C_1 |\phi_k(r_1)\phi_b(r_2) \dots \phi_k(r_{n-1})\phi_l(r_{n-1})| + \\ & C_2 |\phi_k(r_1)\phi_l(r_2) \dots \phi_k(r_{n-1})\phi_l(r_{n-1})| + \dots\end{aligned}$$

- ▶ multireference self-consistent field (mcscf)

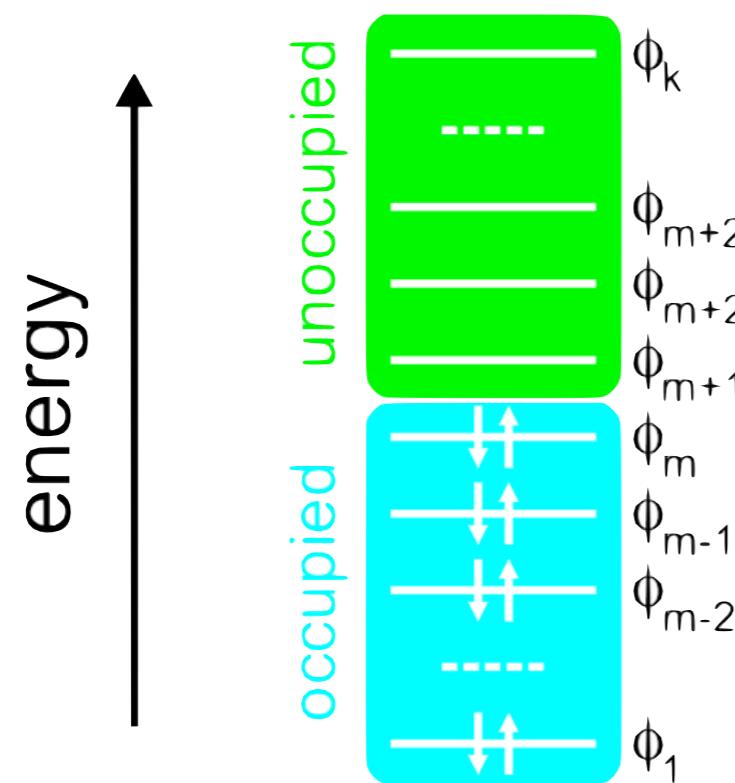
# Molecular Quantum Mechanics

## multi-reference methods

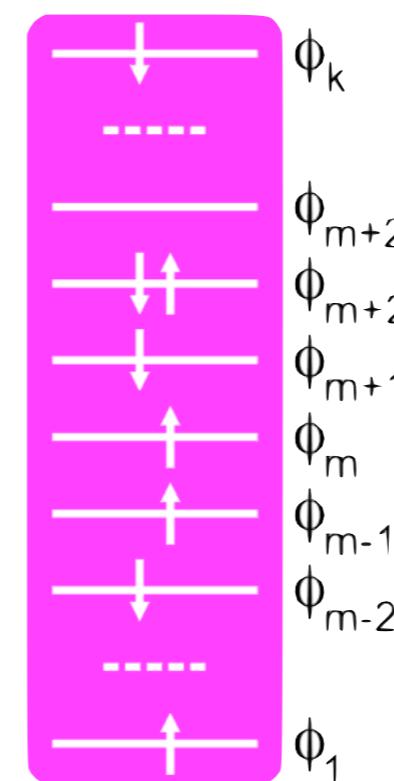
### selection of configurations (Slater determinants)

$$\Psi = \sum_k^M C_k \Psi^{\text{HF}}$$

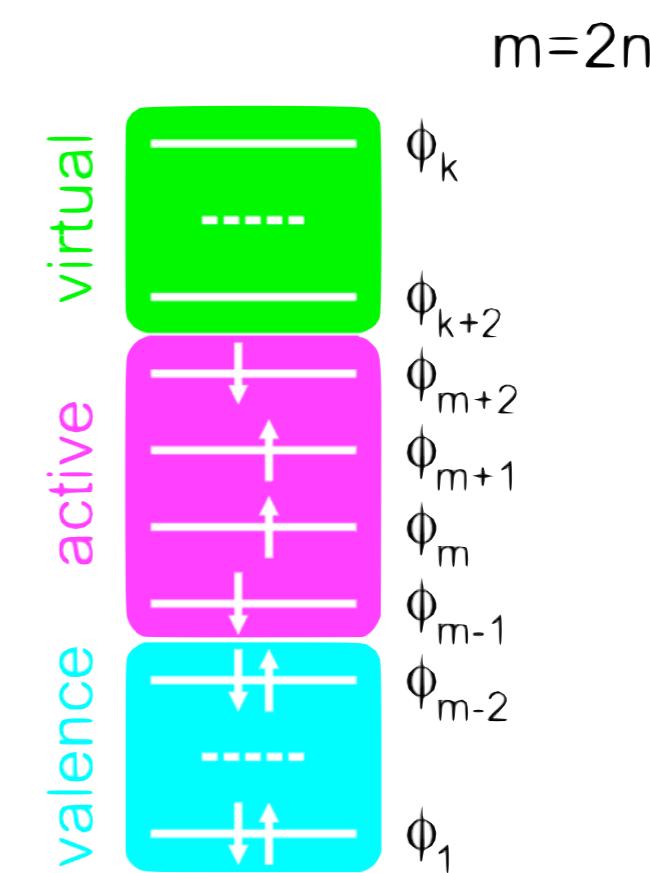
### optimization of configurations



RHF



full CI



CASSCF

# Molecular Quantum Mechanics

limitations of Hartree-Fock theory

no electron correlation

beyond Hartree-Fock

perturbation theory

$$H = H_0 + H^{\text{pert}}$$

$$\Psi = \Psi^{\text{HF}} + \Psi_1^{\text{pert}} + \Psi_2^{\text{pert}} + \dots$$

$$H_0 = \sum_i f_i = \sum_i h_i + v_i^{\text{mf}}$$

$$\Psi_1^{\text{pert}} = \sum_i a_i \Psi_i^{\text{HF}}$$

$$H^{\text{pert}} = \sum_{i < j} \frac{1}{4\pi\epsilon_0 r_{ij}} - \sum_i v_i^{\text{mf}}$$

$$\Psi_2^{\text{pert}} = \sum_i b_i \Psi_i^{\text{HF}}$$

Møller-Plesset: MP2, MP4

# Molecular Quantum Mechanics

## Hartree-Fock theory and beyond

Hartree-Fock wavefunction as starting point

MCSCF (CI, CASSCF, ...)

perturbation theory (MP2, MP4, CASPT2, ...)

high demand on computational resources

## alternative electronic structure methods

density functional theory

semi-empirical methods

molecular mechanics forcefields

# Molecular Quantum Mechanics

density functional theory (Hohenberg, Kohn)

electron density defines all ground-state properties

Kohn-Sham equation

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

Kohn-Sham orbitals, just to get the density,

$$\rho(\mathbf{r}) = \sum_{i=1}^n |\phi(r_i)|^2 \quad \phi_i(r) = \sum_j c_{ji} \chi_j(r)$$

exchange-correlation functional

Roothaan-Hall equations for Kohn-Sham orbitals

# Molecular Quantum Mechanics

## semi-empirical methods

only valence electrons, effective nuclear charge

Roothaan-Hall equations

$$\mathbf{Fc} = \epsilon_i \mathbf{Sc}$$

$$F_{ij} = \langle \chi_i | f_i | \chi_j \rangle \quad S_{ij} = \langle \chi_i | \chi_j \rangle$$

zero differential overlap

$$S_{ij} = \delta_{ij}$$

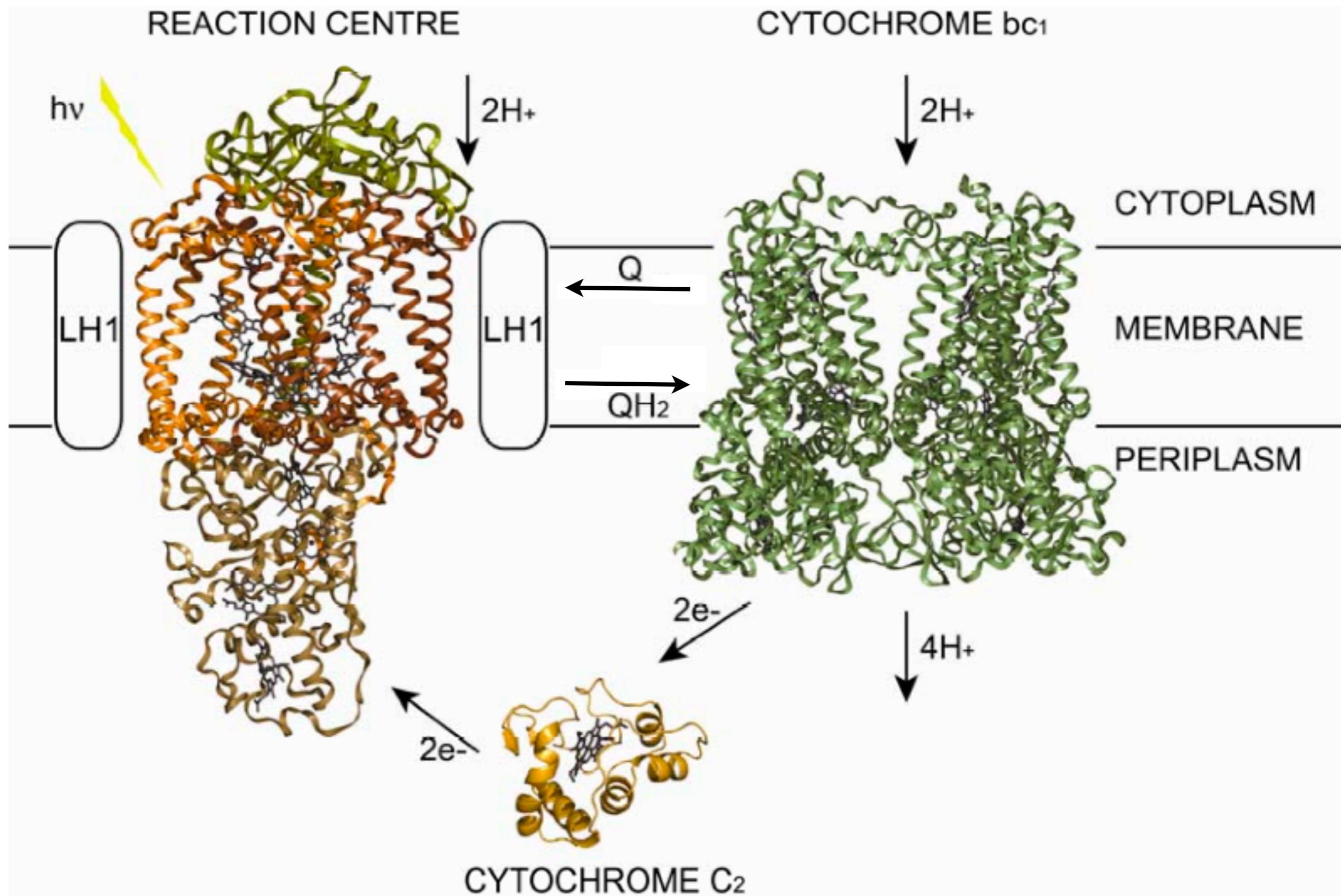
no three center one-electron integrals

no three and four center two-electron integrals

empirical parameters for remaining Fock matrix elem.

CNDO, INDO, MNDO, AMI, PM3, ...

# Bacterial photosynthesis



# Photosynthetic reaction center

*Blastochloris viridis*

photocycle

960 nm light (bChlb)

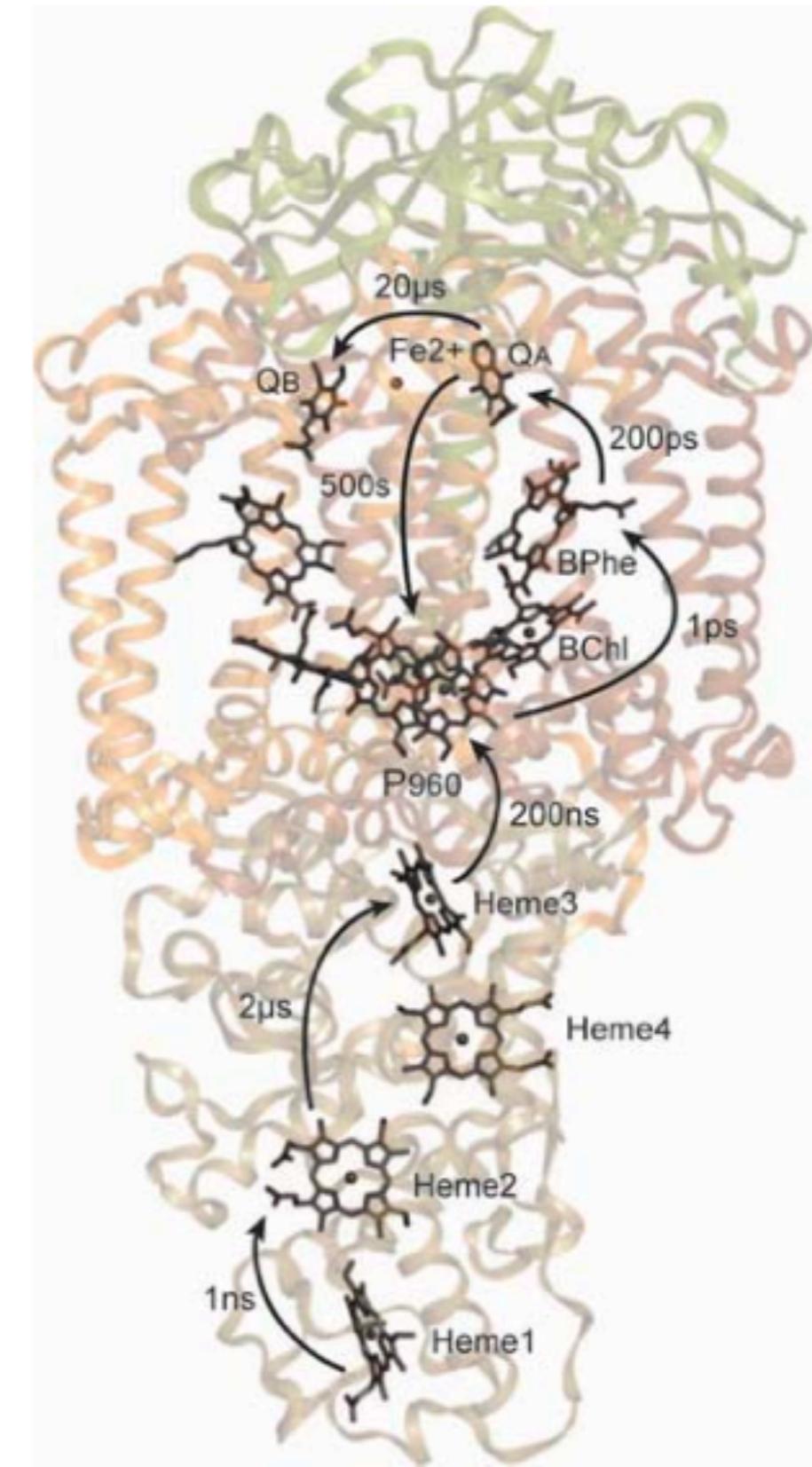
bacteriochlorophyl (bChlb)

photon-induced oxidation

electron transfer

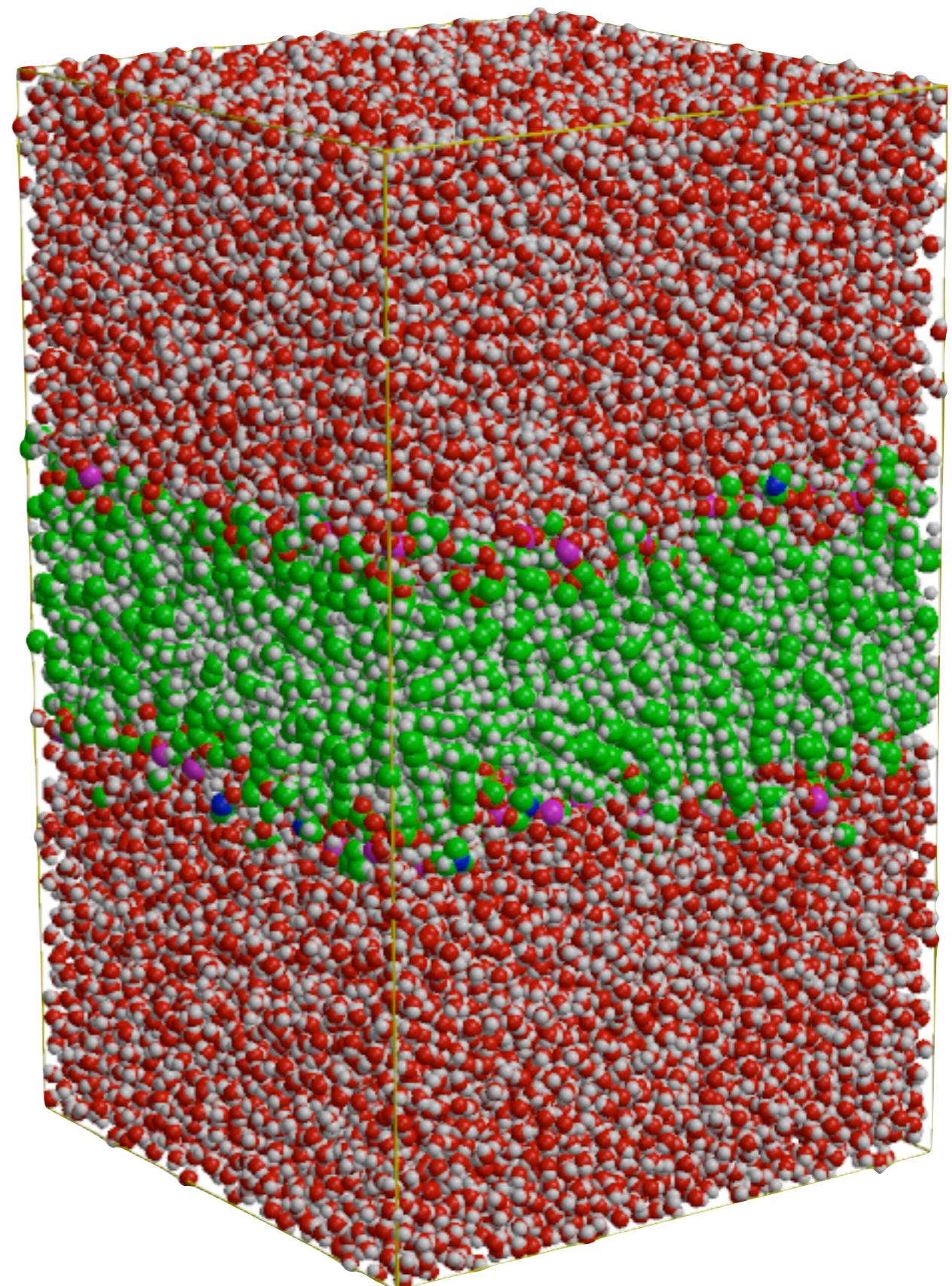
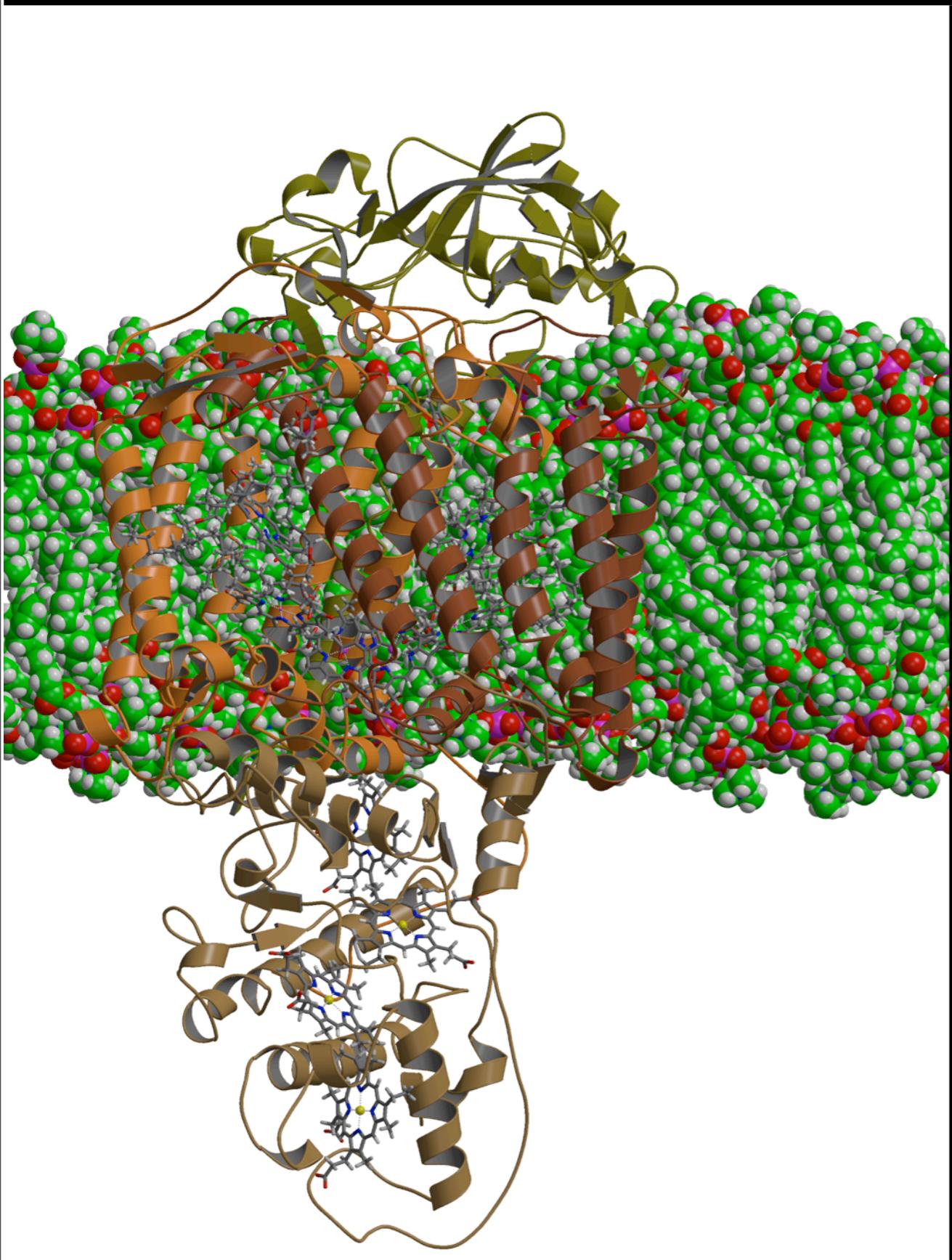
reduction of mobile quinone

reduction of bChlb via hemes



# Photosynthetic reaction center

---



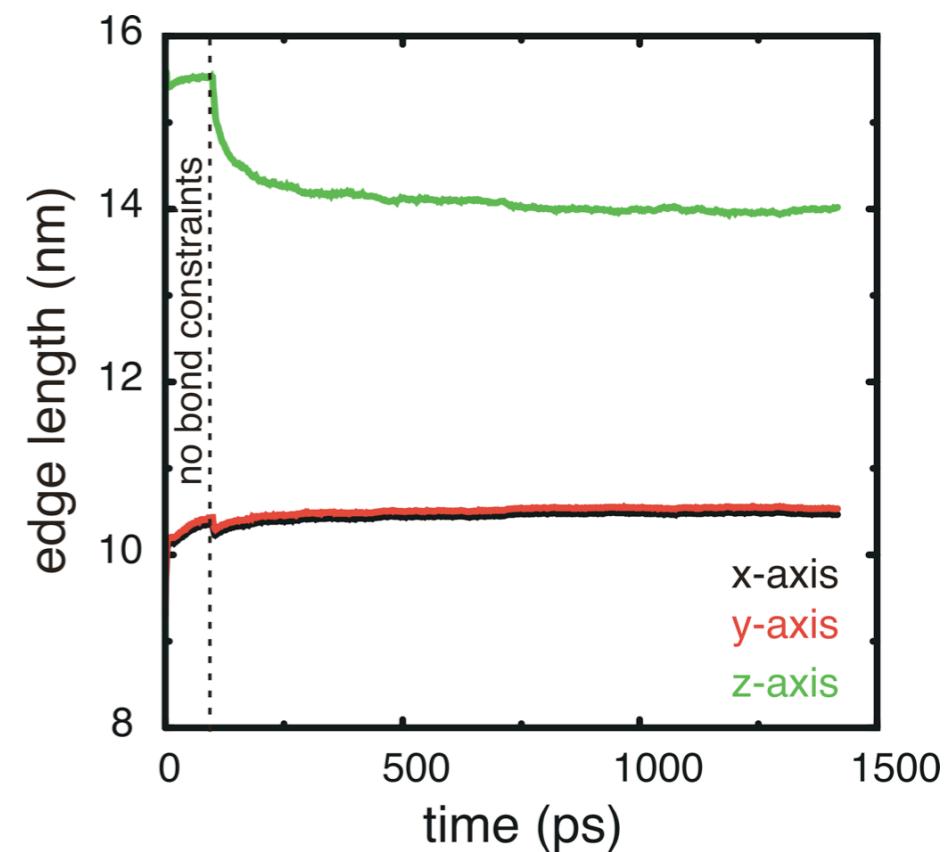
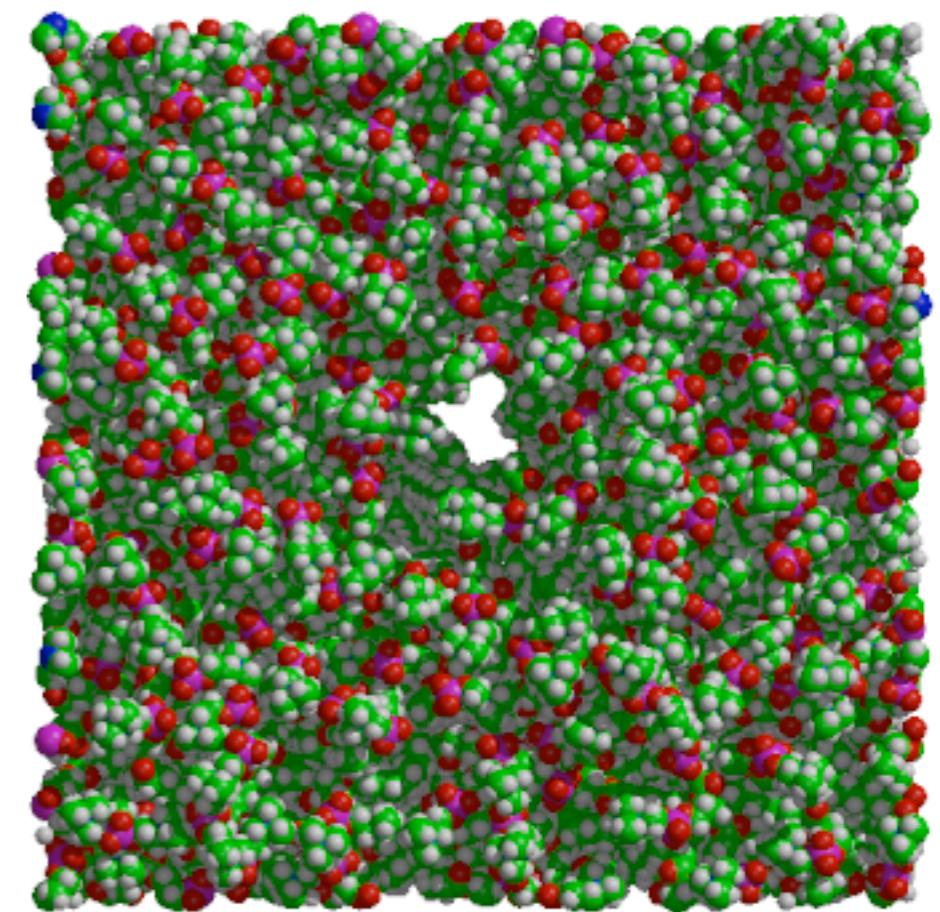
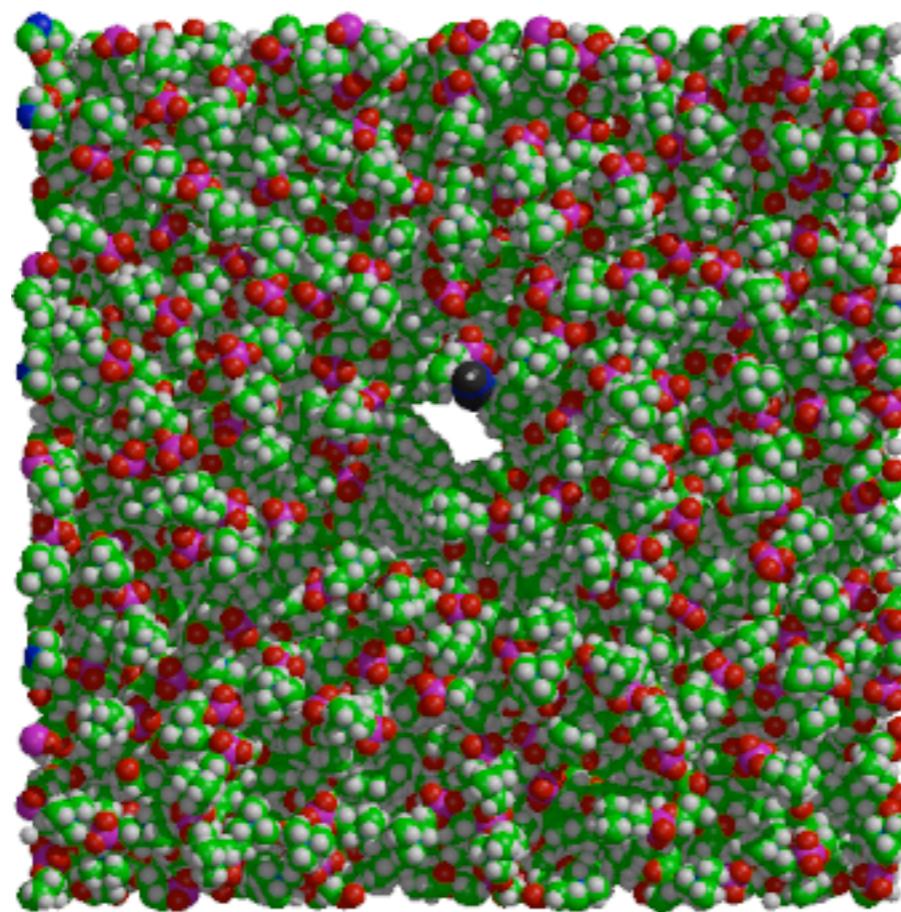
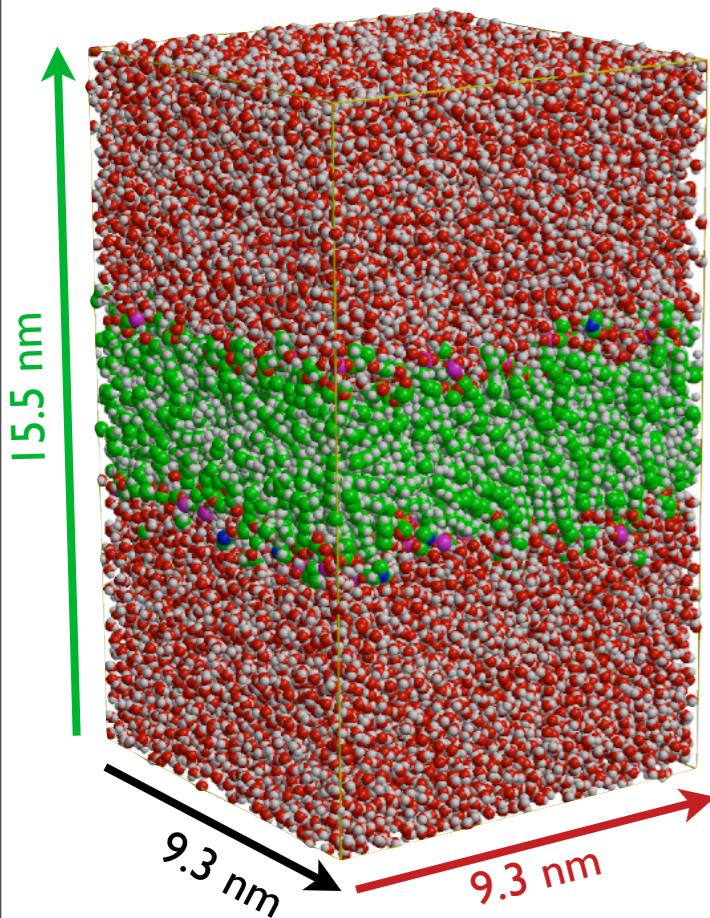
# Insertion into bilayer: g\_membed

protein atoms at  $(\langle x \rangle, \langle y \rangle, z_i)$

'inject needle'

grow atoms to  $(x_i, y_i, z_i)$

equilibrate system



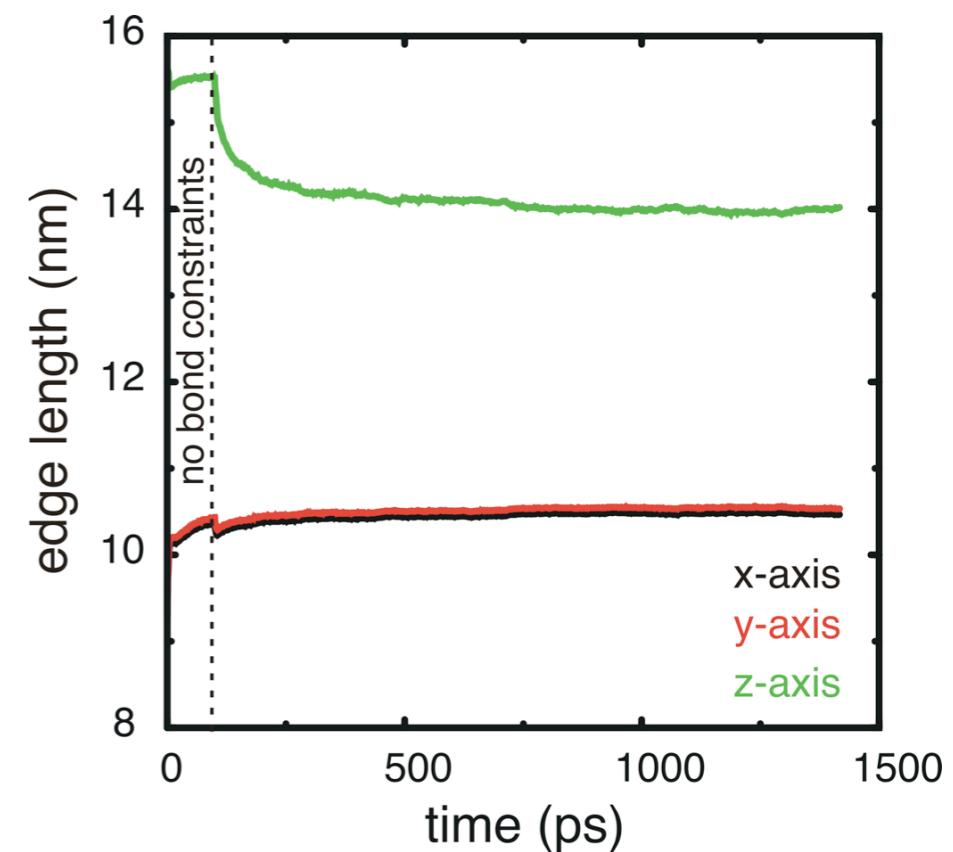
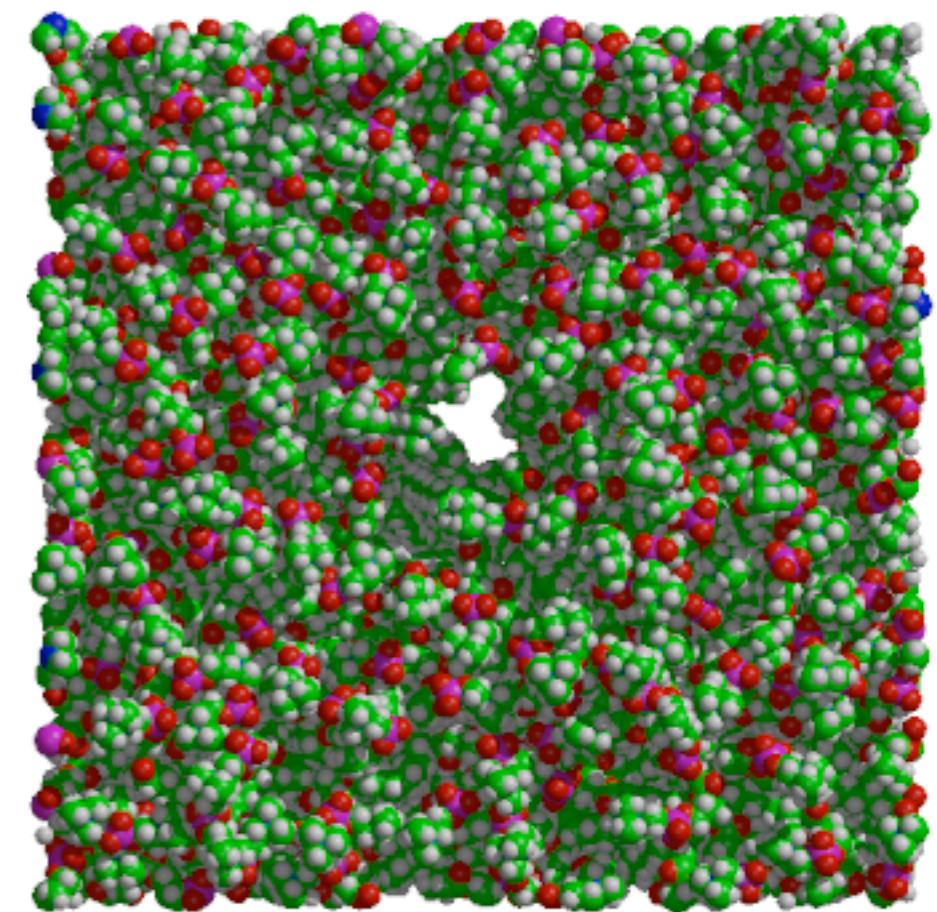
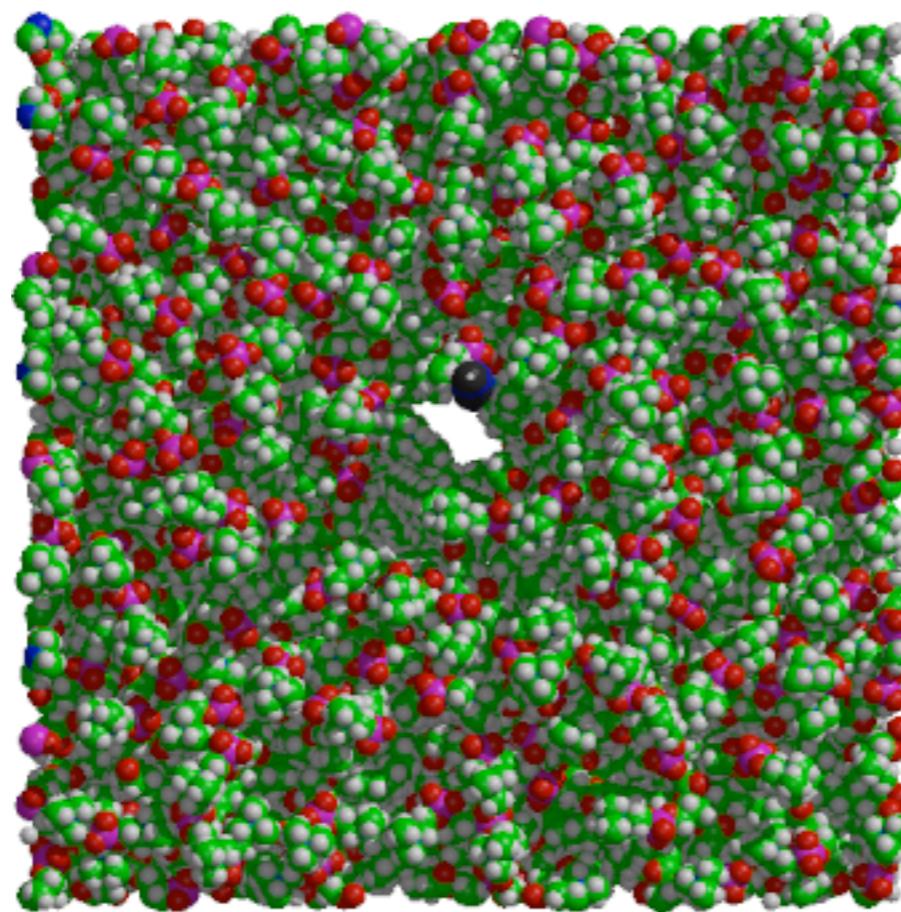
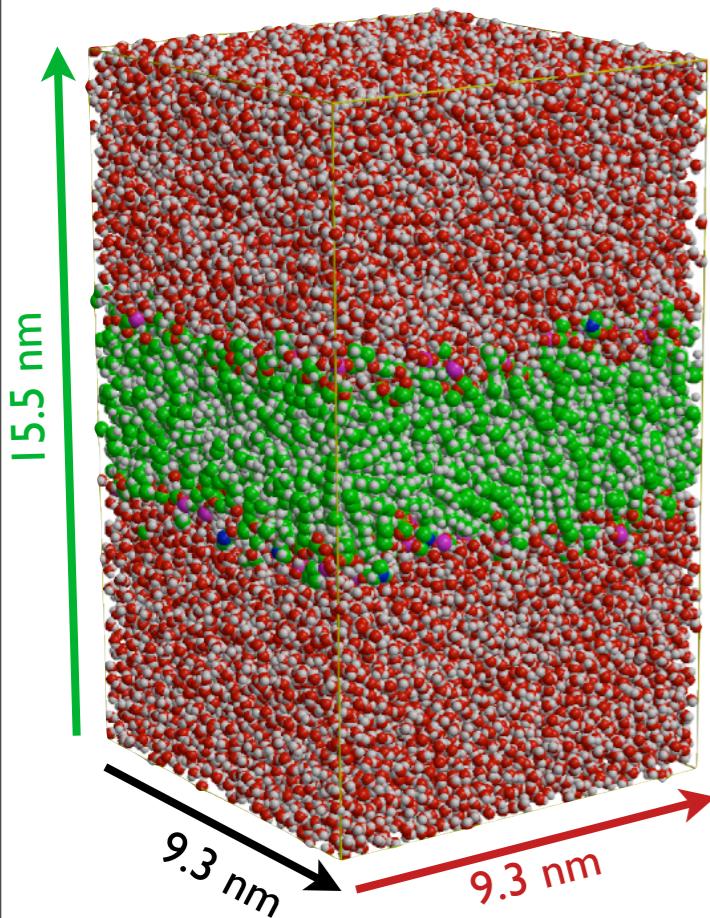
# Insertion into bilayer: g\_membed

protein atoms at  $(\langle x \rangle, \langle y \rangle, z_i)$

'inject needle'

grow atoms to  $(x_i, y_i, z_i)$

equilibrate system



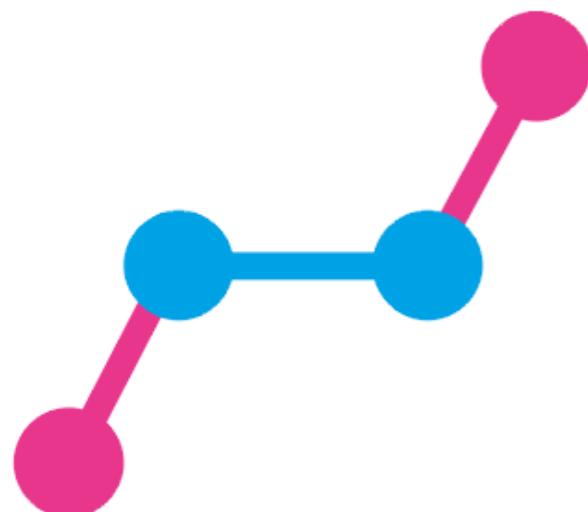
# Molecular Mechanics

throw away the electrons!!!

low-dimensional functions, empirical parameters

$$V^{\text{MM}}(R_1, R_2, \dots, R_N) = \sum_k v_k(R_i, R_j, R_k, R_l; \{p_k\})$$

bonded interaction functions:



$$v_b = \frac{1}{2} k_b (r_{ij} - r_0)^2$$

$$v_a = \frac{1}{2} k_a (\theta_{ijk} - \theta_0)^2$$

$$v_d = \sum_n^5 C_n (\cos(\varphi_{ijkl}))^n$$

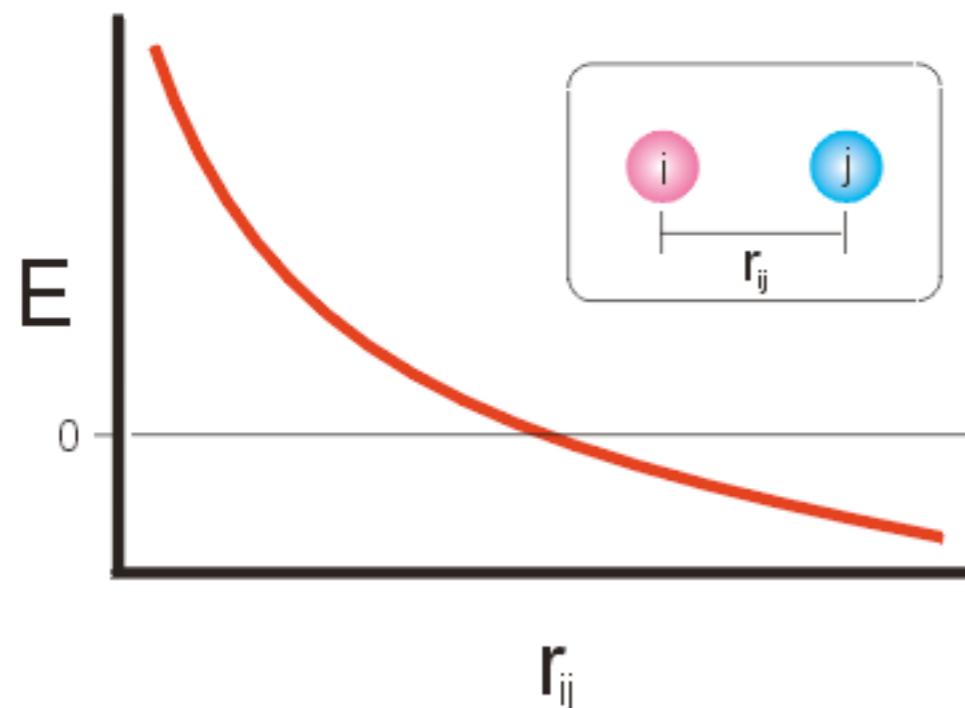
# Molecular Mechanics

throw away the electrons!!!

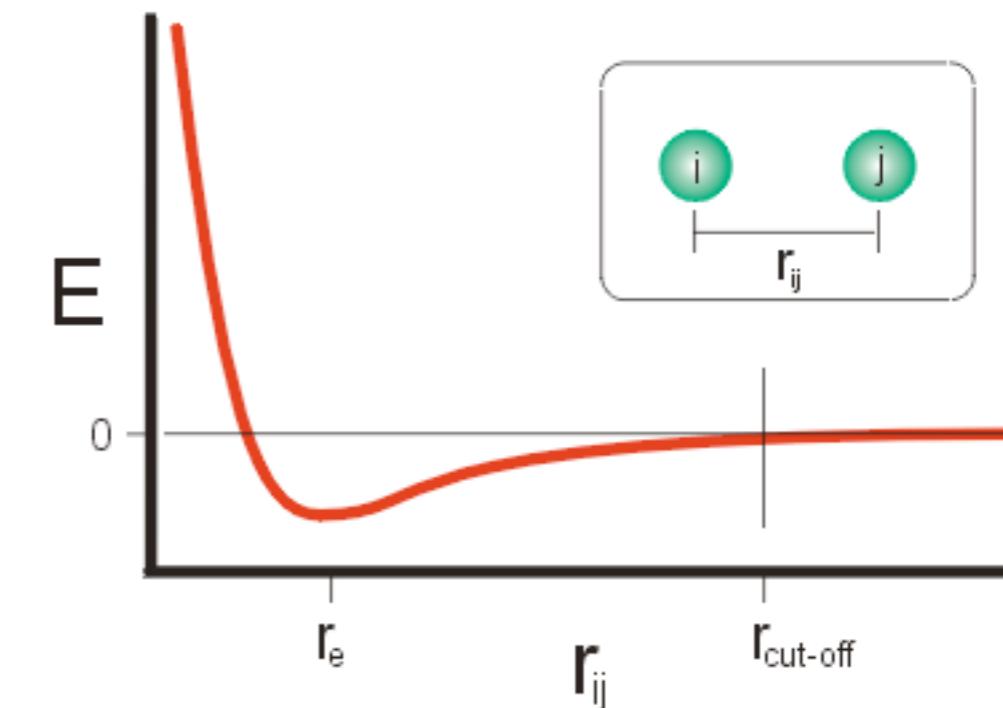
low-dimensional functions, empirical parameters

$$V^{\text{MM}}(R_1, R_2, \dots, R_N) = \sum_k v_k(R_i, R_j, R_k, R_l; \{p_k\})$$

non-bonded interaction functions:



$$v_{\text{Coul}}(r_{ij}) = \frac{e^2 q_i q_j}{4\pi\epsilon_0 r_{ij}}$$



$$v_{\text{LJ}}(r_{ij}) = \frac{C_{ij}^{(12)}}{r_{ij}^{12}} - \frac{C_{ij}^{(6)}}{r_{ij}^6}$$

# 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

# 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

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

# Quantum Mechanics/Molecular Mechanics

electrons treated explicitly in small subsystem  
molecular mechanics forcefield for remainder

