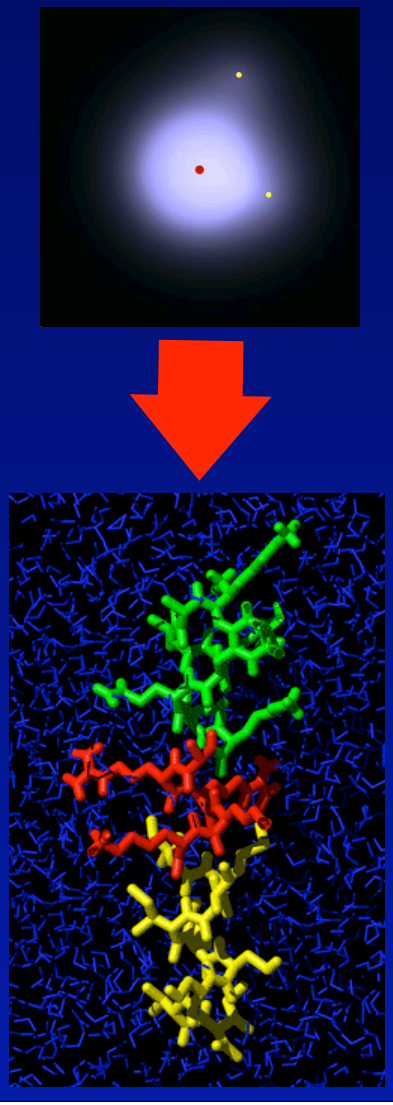
Molecular Dynamics Simulations



Schrödinger equation

$$\hat{H}\phi(\vec{r},\vec{R}) = E\phi(\vec{r},\vec{R})$$

Born-Oppenheimer approximation

$$\hat{H}_e\phi(\vec{r};\vec{R}) = E_e(\vec{R})\phi_e(\vec{r};\vec{R})$$

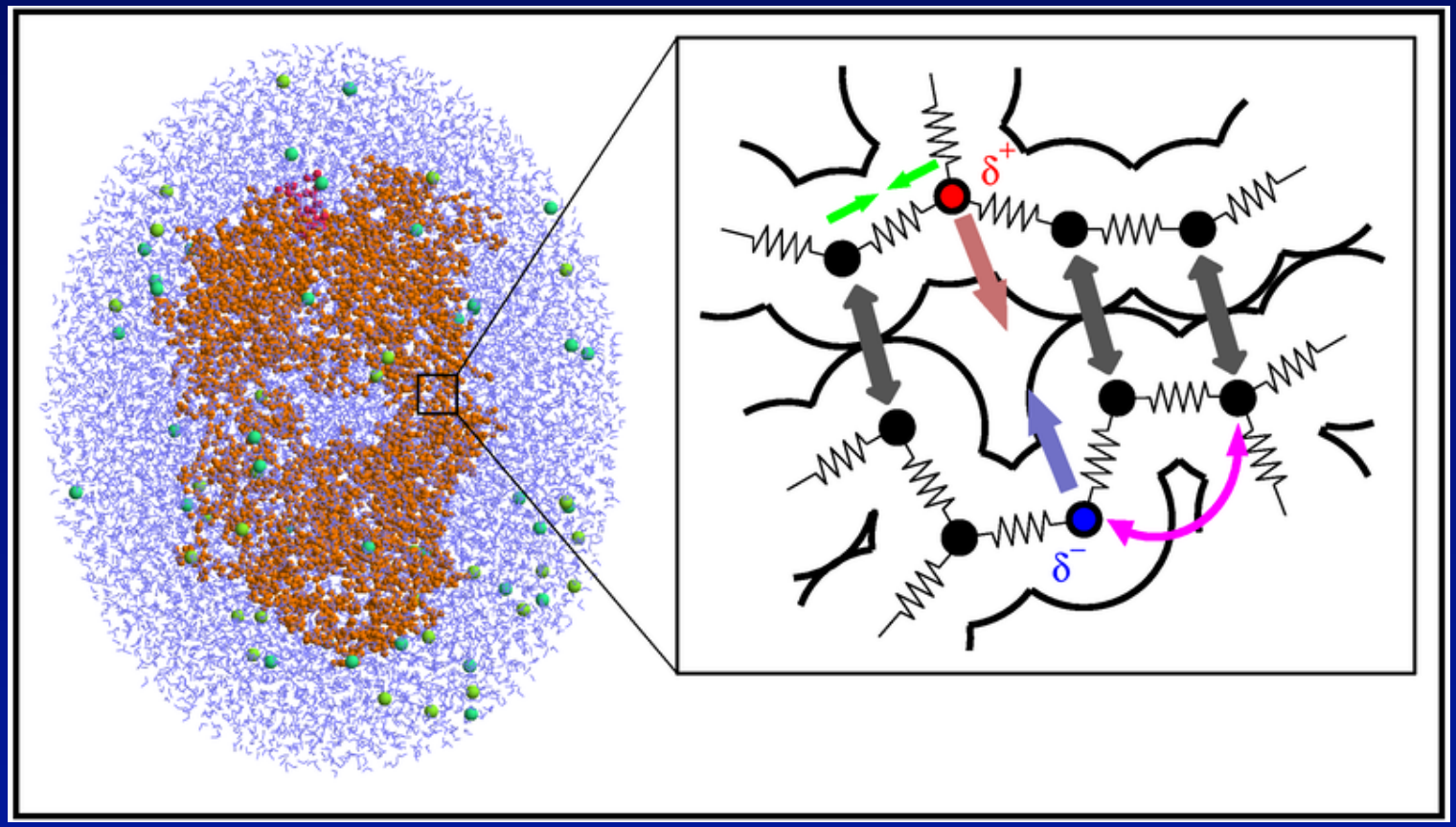
Nucleic motion described classically

$$m_i\frac{d^2}{dt^2}\vec{R}_i = -\vec{\nabla}_i E(\vec{R})$$

Empirical Force field

$$E(\vec{R}) = \sum_{\text{bonded}} E_i(\vec{R}) + \sum_{\text{non-bonded}} E_i(\vec{R})$$

Molecular Dynamics Simulations



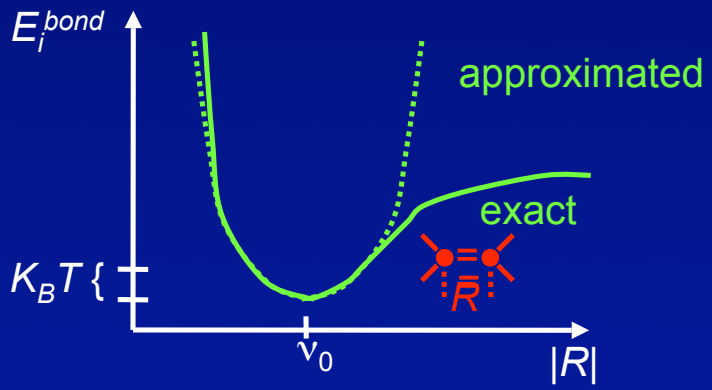
Interatomic interactions

Molecular dynamics-(MD) simulations of Biopolymers

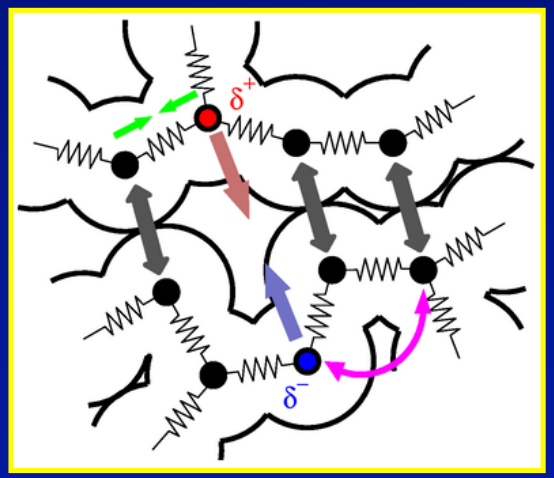
- **Motions of nuclei are described classically,** $(*) \quad m_a \frac{d^2}{dt^2} \boldsymbol{R}_\alpha = -\nabla_\alpha E_{el}(\boldsymbol{R}_1,\ldots,\boldsymbol{R}_N), \quad \alpha = 1,\ldots,N.$
- **Potential function E_{el} describes the electronic influence on motions of the nuclei and is approximated empirically → „classical MD“:**

$$E_{el} \approx \sum_{\substack{\text{Bindungen} \\ i}} E_i^{bond} + \sum_{\substack{\text{Bindungs-} \\ \text{winkel } j}} E_j^{angle} + \sum_{\substack{\text{Dihedral-} \\ \text{winkel } k}} E_k^{dihe} + \sum \left(E_{\alpha,\beta}^{Coul.} + E_{\alpha,\beta}^{rep.} + E_{\alpha,\beta}^{vdW} \right) + \ldots,$$

Covalent bonds

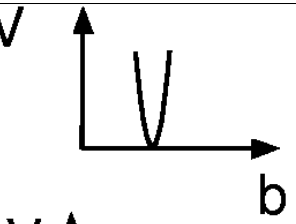


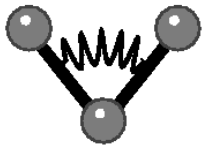
Non-bonded interactions



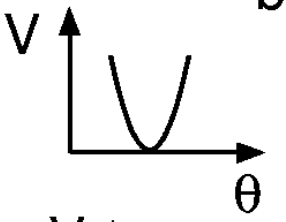
„Force-Field“

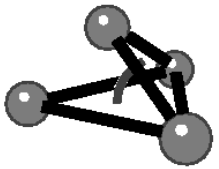
$$V_B = \sum_{\text{Bindungen}} \frac{1}{2} K_b (b - b_0)^2$$



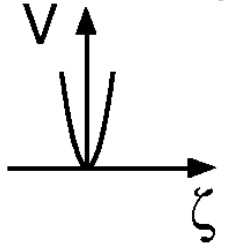


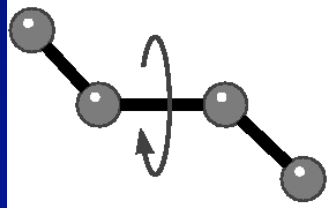
$$V_a = \sum_{\text{Winkel}} \frac{1}{2} K_\theta (\theta - \theta_0)^2$$



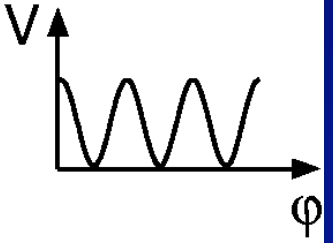


$$V_{imp} = \sum_{\text{Extraplanarwinkel}} \frac{1}{2} K_\zeta (\zeta - \zeta_0)^2$$

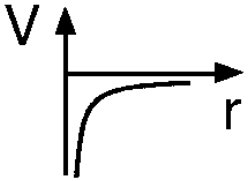




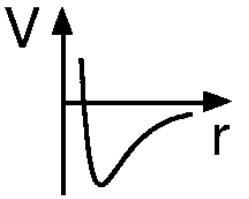
$$V_D = \sum_{\text{Dihedralwinkel}} K_\varphi [1 + \cos(n\varphi - \delta)]$$



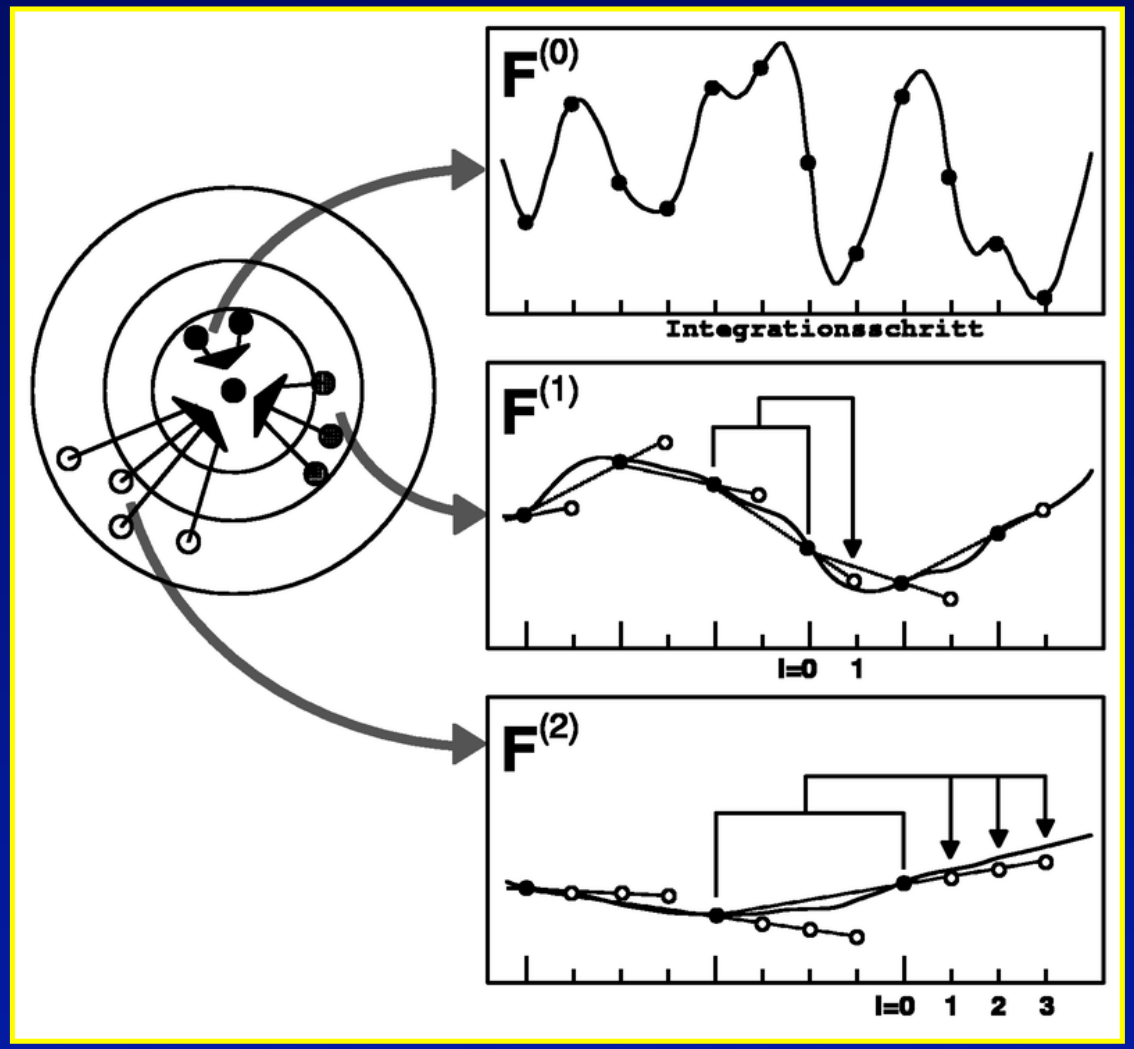
$$V_q = \sum_{\text{Paare(i,j)}} q_i q_j / (4\pi\epsilon_0\epsilon_r r_{ij})$$



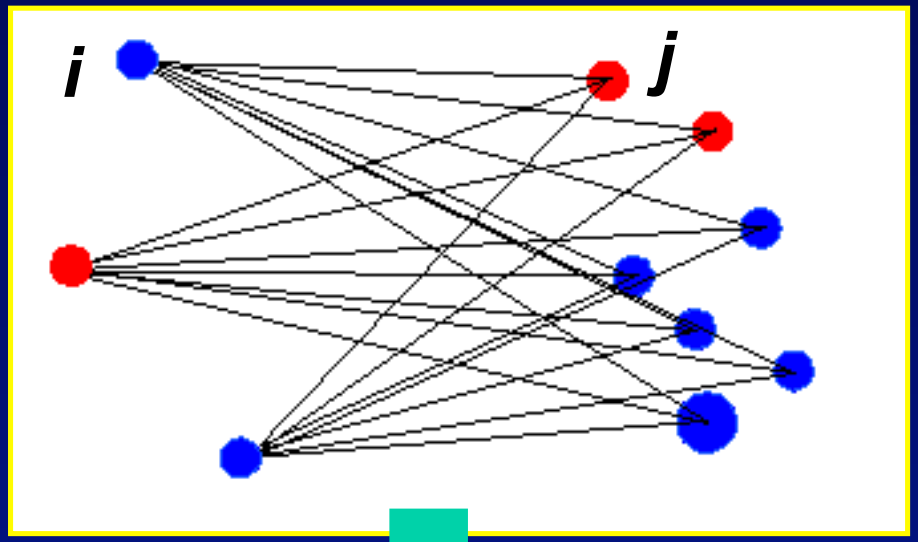
$$V_{vdW} = \sum_{\text{Paare(i,j)}} C_{12}(i,j)/r_{ij}^{12} - C_6(i,j)/r_{ij}^6$$



Multiple Time Stepping



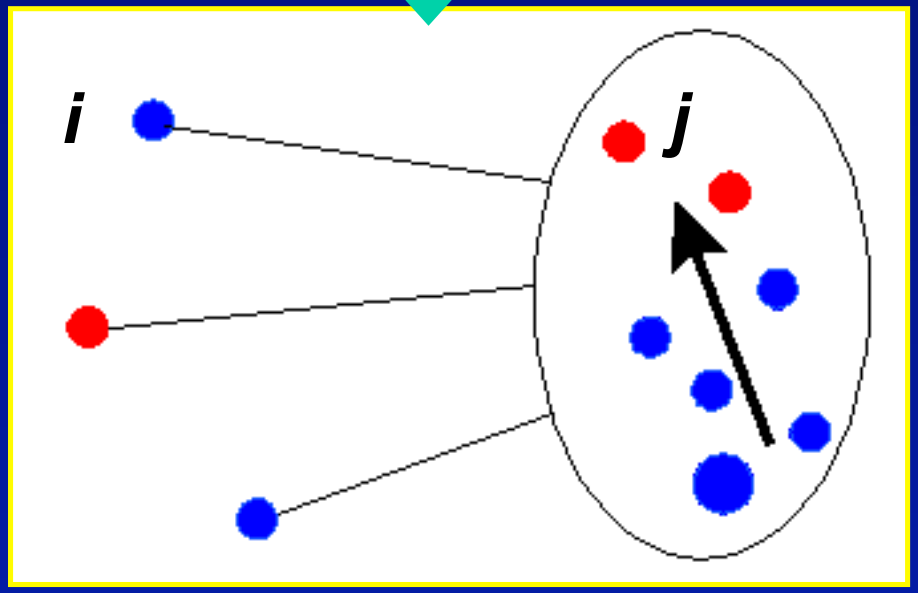
H. Grubmüller, H. Heller, A. Windemuth, K. Schulten; *Mol. Sim.* **6** (1991) 121



Multipole Methods

$O(N^2)$

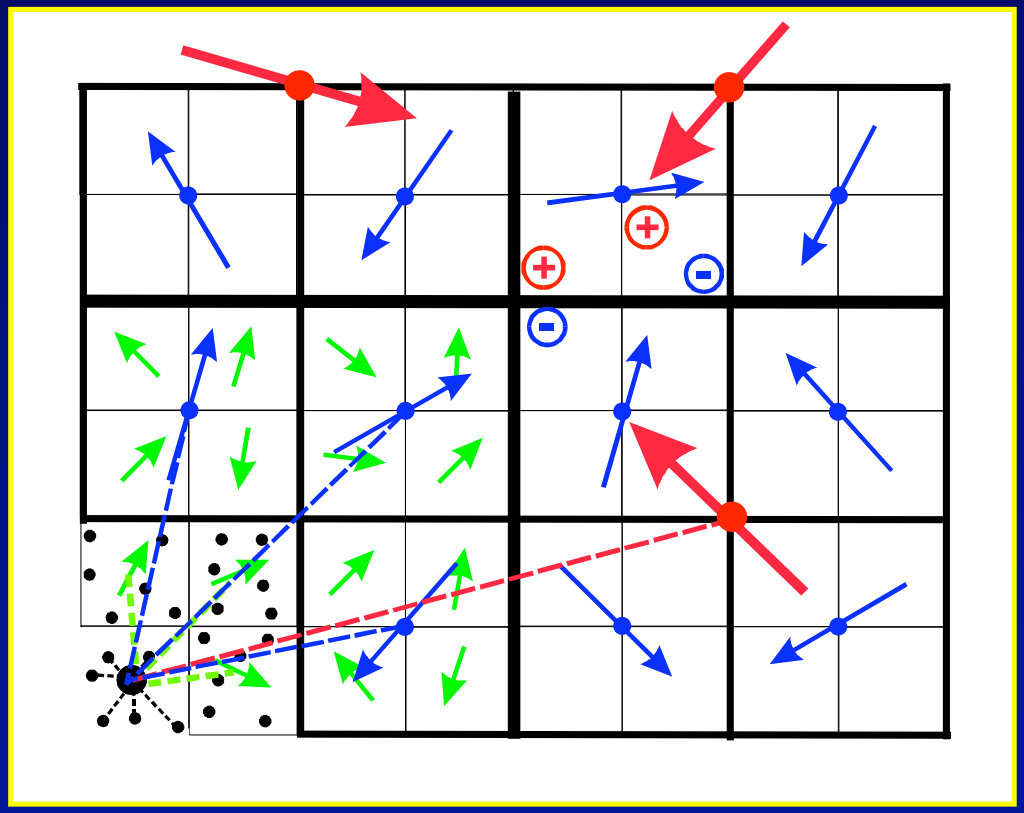
1. Taylor expansion



Exact for infinite multipole series

Fast Multipole Method (FMM)

→ *O(N)*

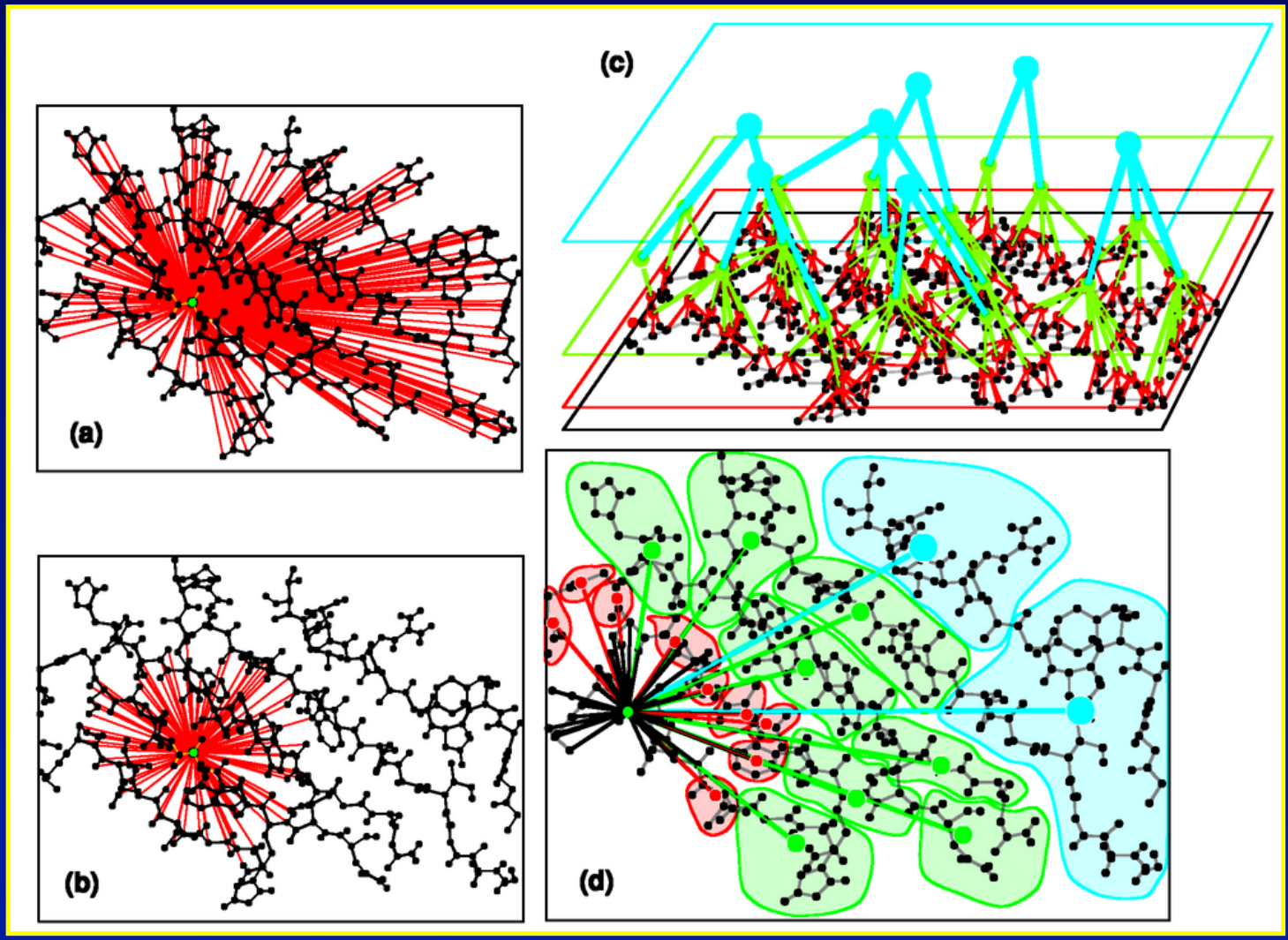


+ arbitrary accuracy

- high order expansions required to achieve moderate accuracy

L. Greengard and V. Rokhlin, *J. Comp. Phys.* **73** (1987) 325

Fast structure-adapted multipole methods: O(N)



M. Eichinger, H. Grubmüller, H. Heller, P. Tavan, *J. Comp. Chem.* **18** (1997) 1729

Molecular Dynamics Simulation

Molecule: (classical) N-particle system

Newtonian equations of motion:

$$m_i \frac{d^2}{dt^2} \vec{r}_i = \vec{F}_i(\bar{r})$$

$$\vec{F}_i(\bar{r}) = -\nabla_i V(\bar{r})$$

with $\bar{r} = (\vec{r}_1, \ldots, \vec{r}_N)$

Integrate numerically via the „leapfrog“ scheme:

$$\boldsymbol{v}(t + \frac{\Delta t}{2}) = \boldsymbol{v}(t - \frac{\Delta t}{2}) + \frac{\boldsymbol{F}(t)}{m}\Delta t$$

$$\boldsymbol{r}(t + \Delta t) = \boldsymbol{r}(t) + \boldsymbol{v}(t + \frac{\Delta t}{2})\Delta t$$

with

$\Delta t \approx 1$fs!

(equivalent to the Verlet algorithm)

Computational task:

Solve the Newtonian equations of motion:

$$m_i \frac{d^2}{dt^2}\vec{x}_i = \vec{F}_i(\vec{x}_1, \ldots, \vec{x}_N) \qquad i = 1 \ldots N$$

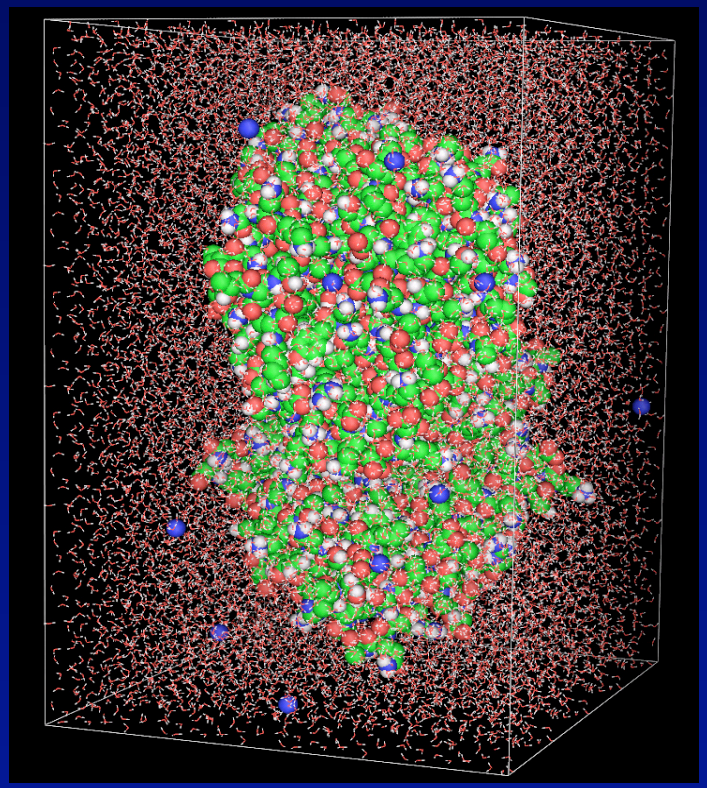
$$\vec{F}_i(\vec{x}_1, \ldots, \vec{x}_N) = -\nabla_i E(\vec{x}_1, \ldots, \vec{x}_N)$$

$$E(\ldots) = E_{\text{bond}}(\ldots) + E_{\text{non-bond}}(\ldots) + E_{\text{ext.}}(\ldots)$$

$$\sum_{\text{bonds } ij} k_{ij}(r_{ij} - r_{ij}^{\text{eq}})^2 \qquad \sum_{\text{pairs } ij} \frac{q_i q_j}{4\pi\varepsilon r_{ij}}$$

$$O(N) \qquad O(N^2)$$

Role of environment - solvent



box

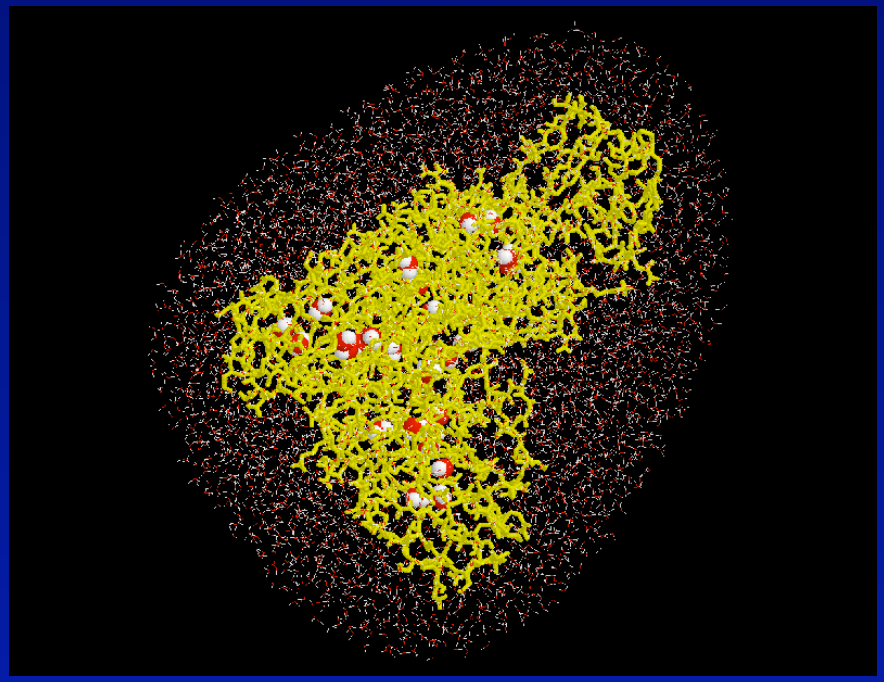
or

droplet?

explicit

or

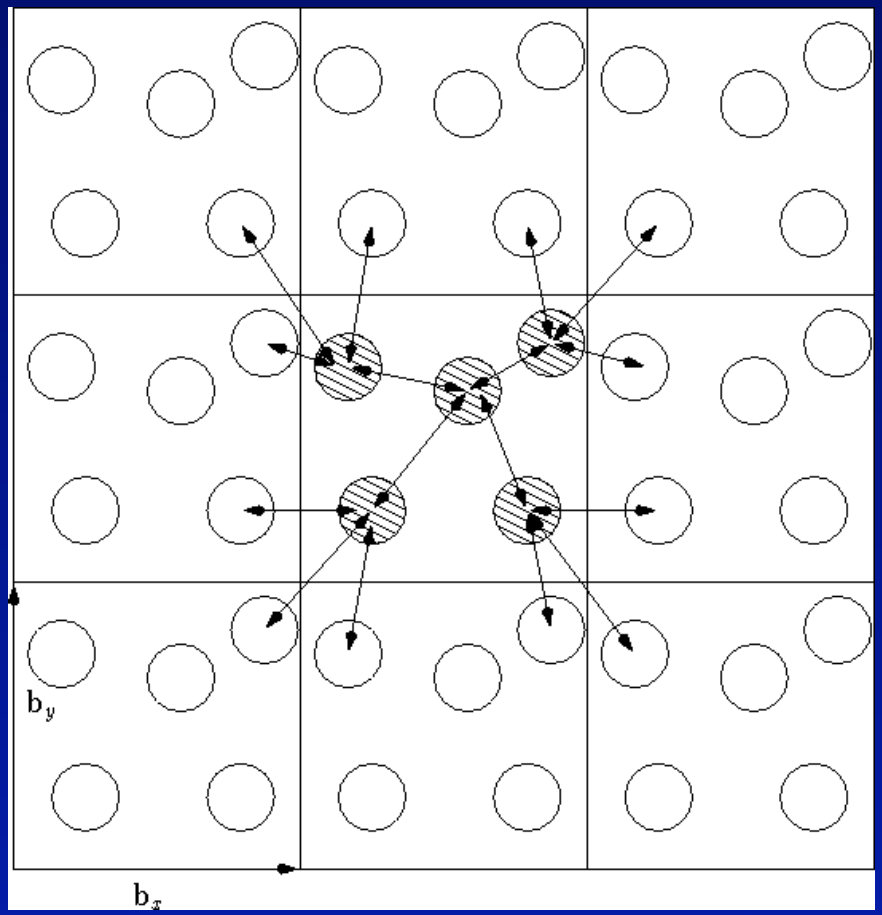
implicit?



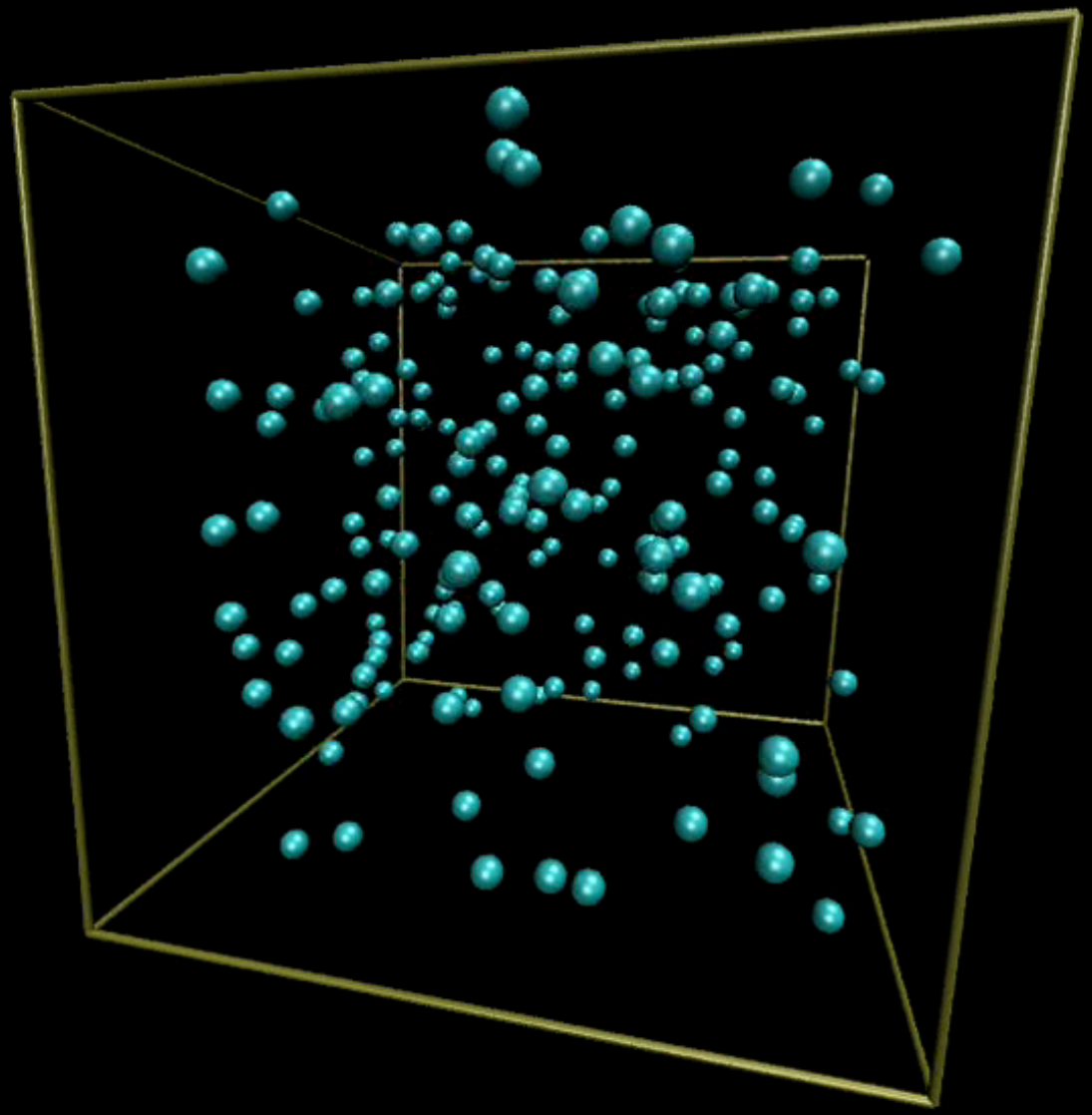
Surface (tension) effects?

periodic boundary conditions

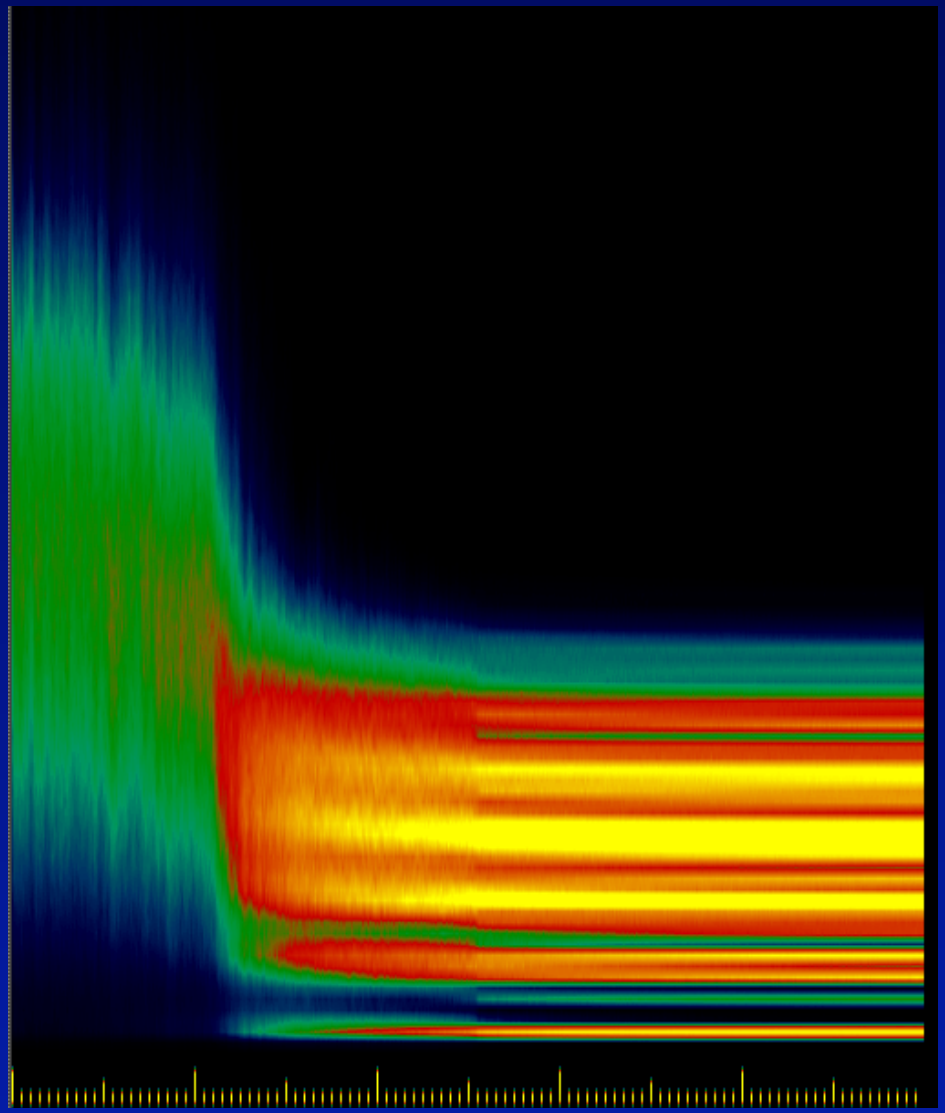
and the minimum image convention



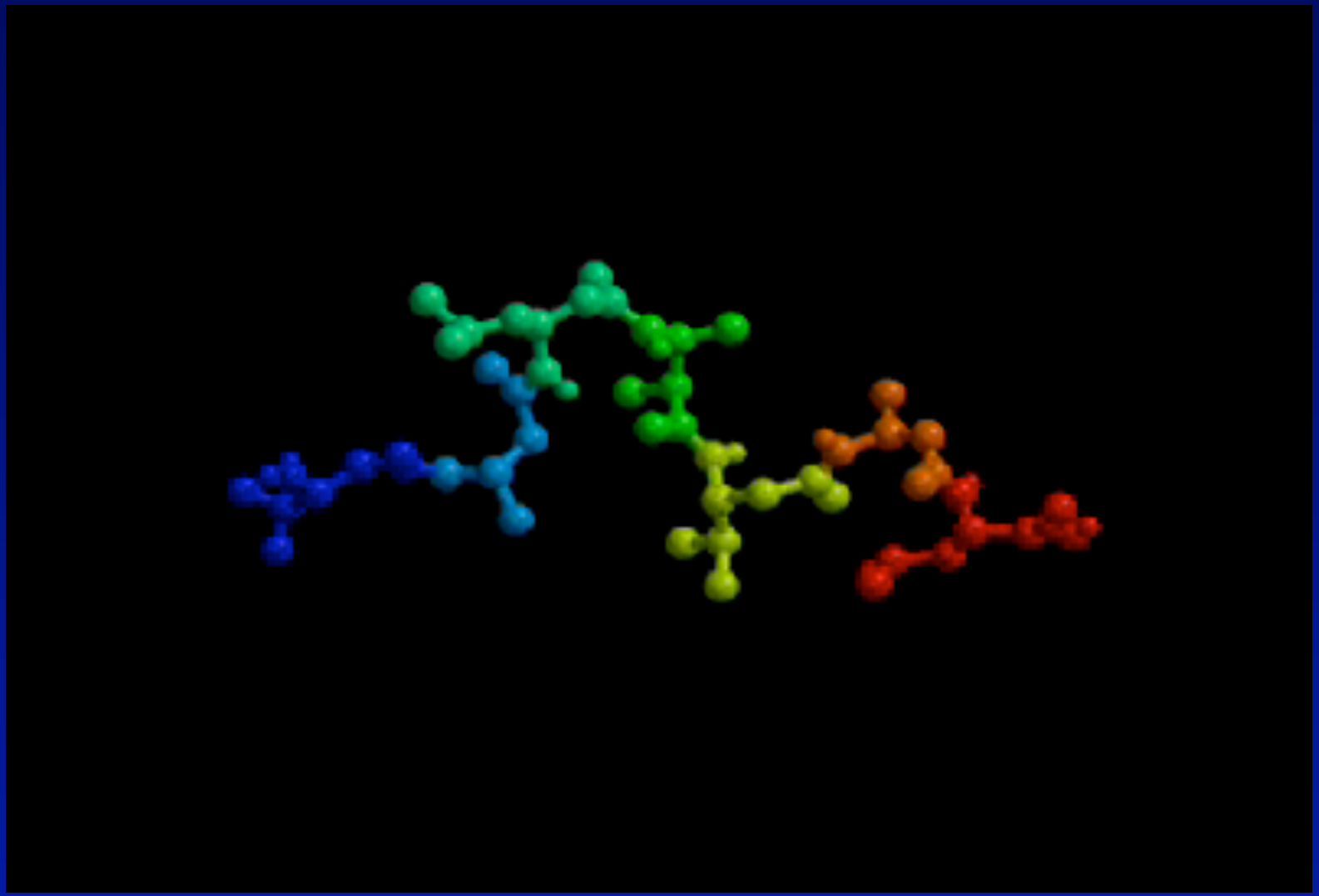
MD-Experiments with Argon Gas



Radial distribution function

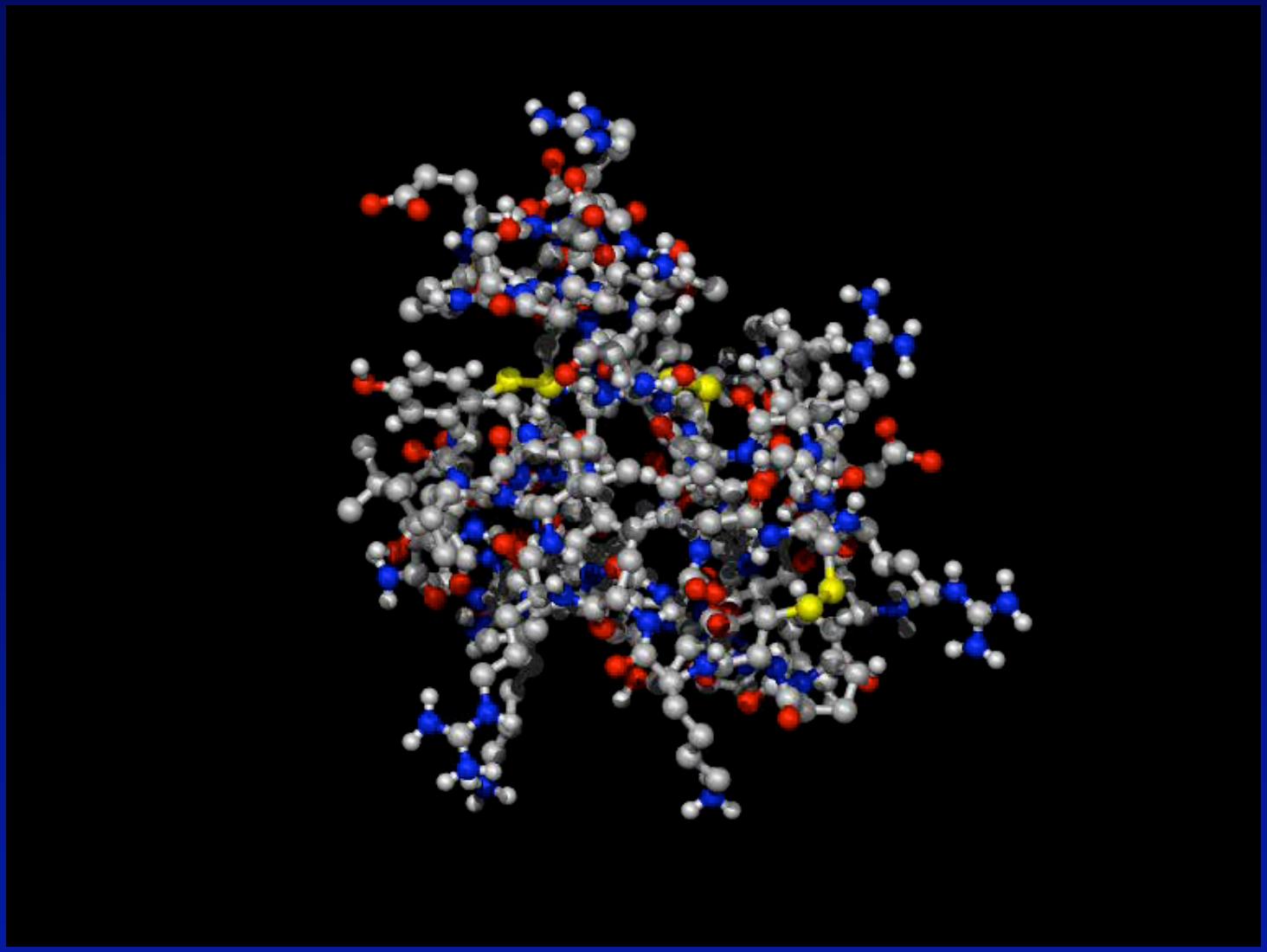


Reversible Folding Dynamics of a β-Peptide

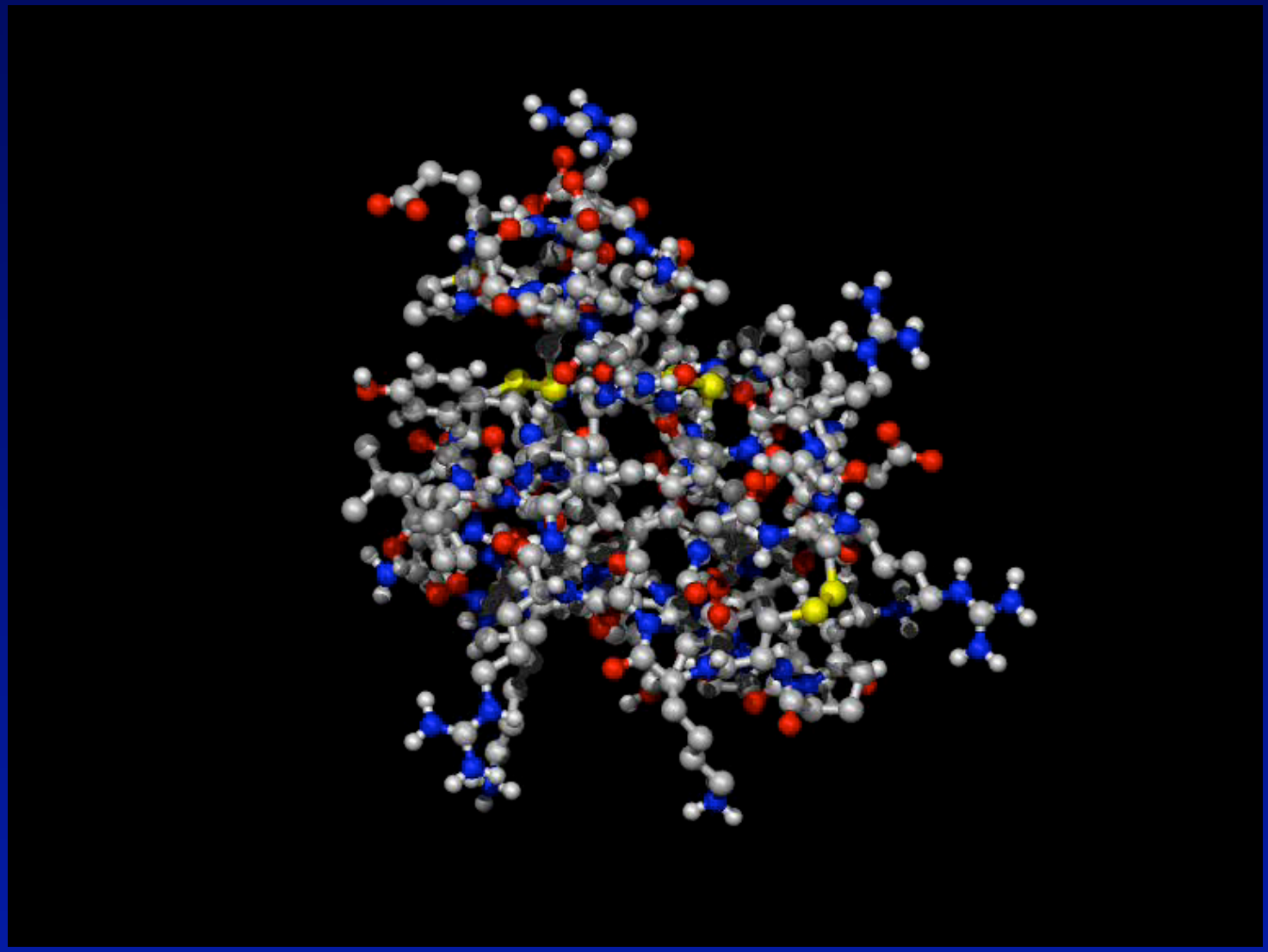


X. Daura, B. Jaun, D. Seebach, W.F. van Gunsteren, A.E. Mark, *J. Mol. Biol.* **280** (1998) 925

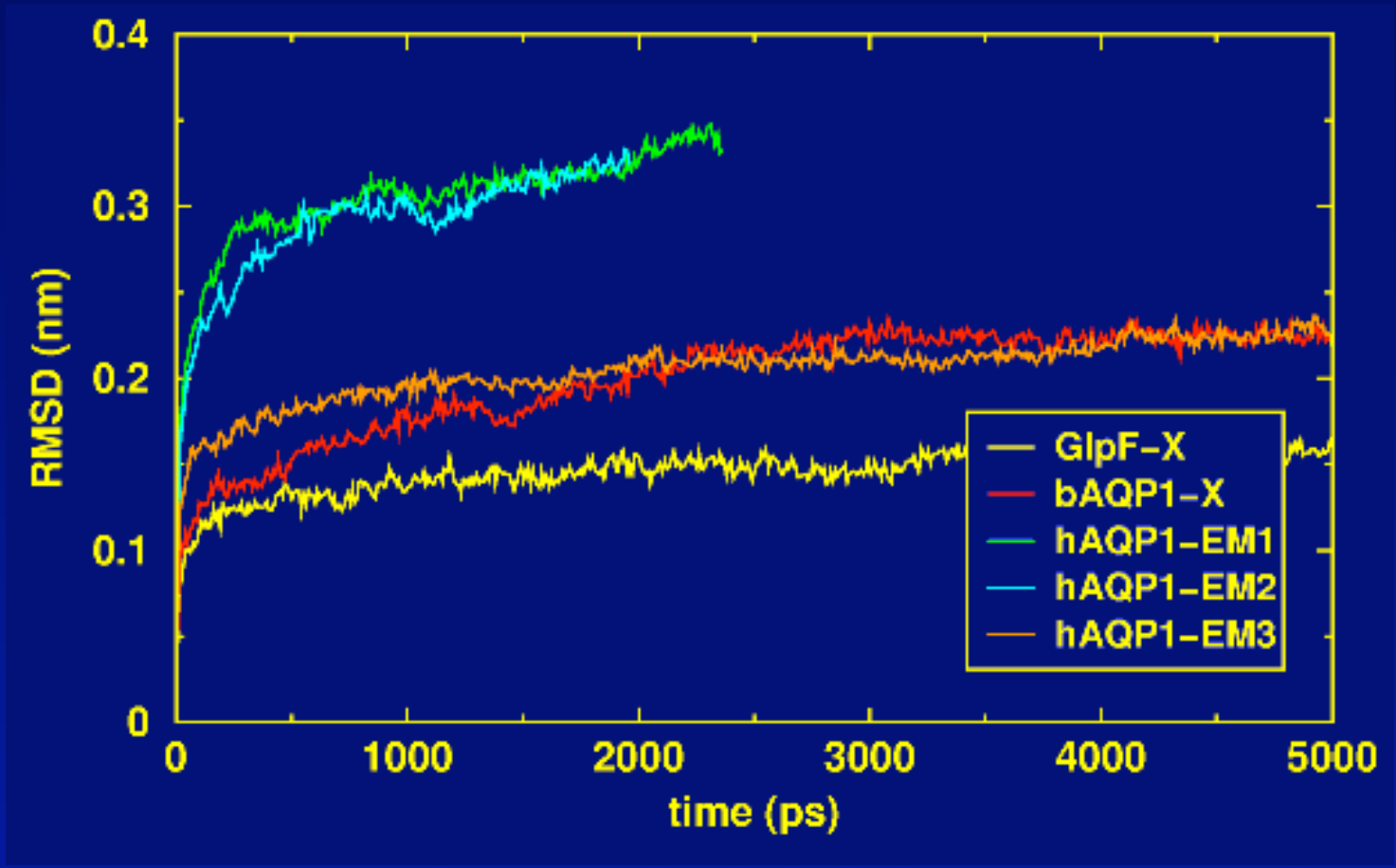
BPTI: Minimization



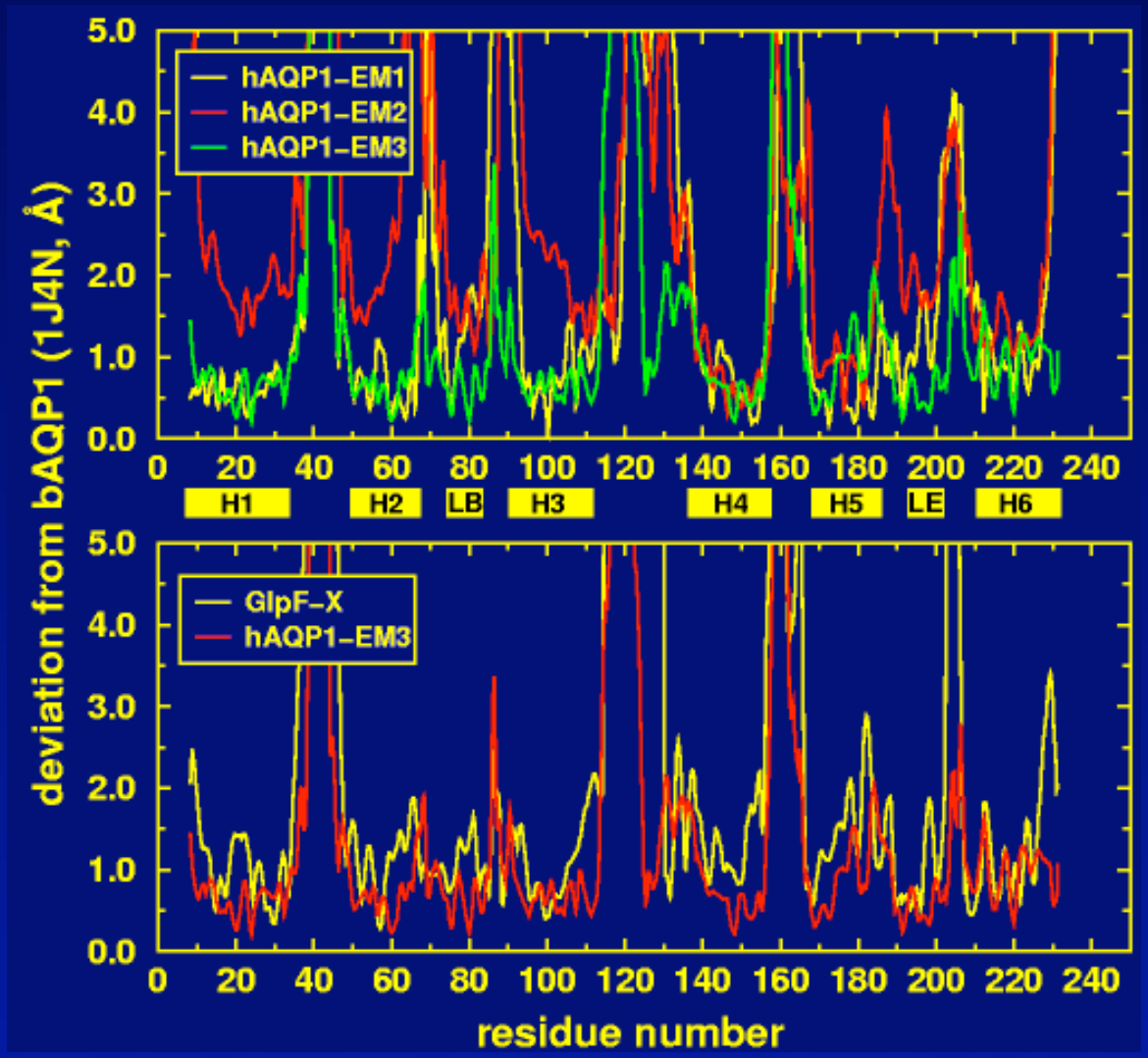
BPTI: Molecular Dynamics (300K)

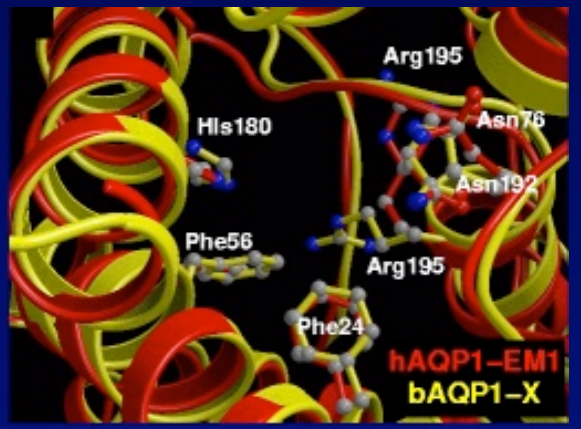


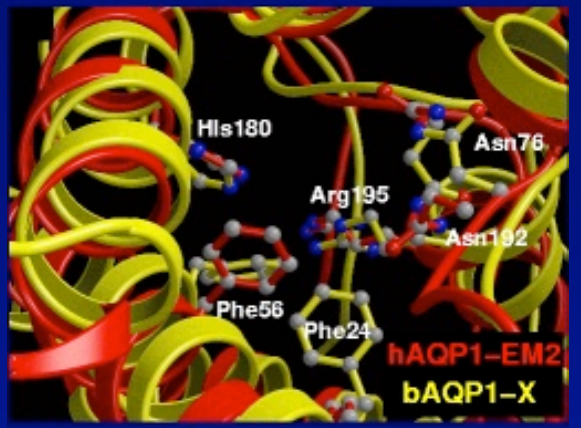
Stability in MD simulations as a structure quality indicator

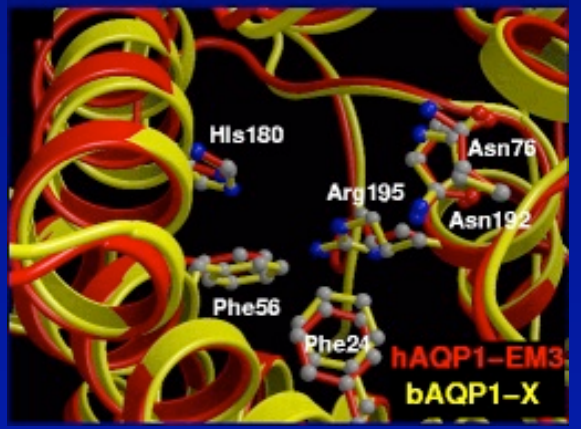


bAQP1 EM per residue deviations from x-ray

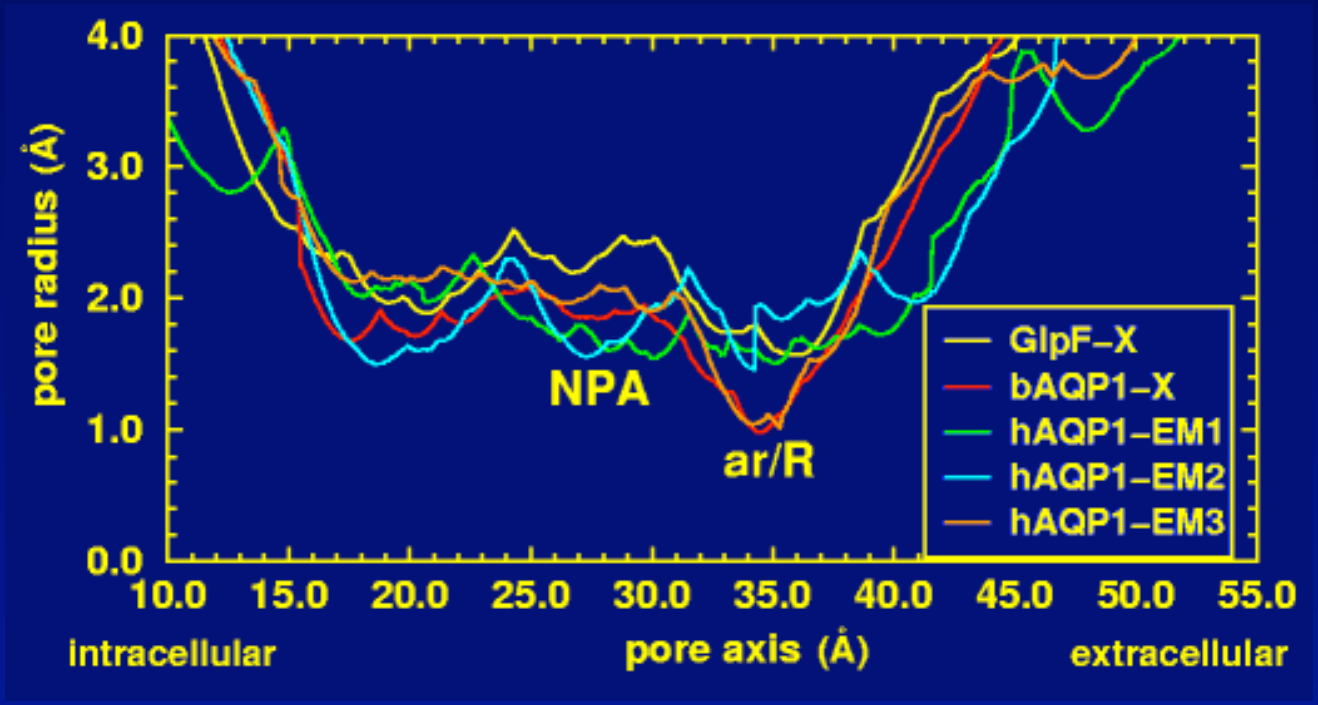




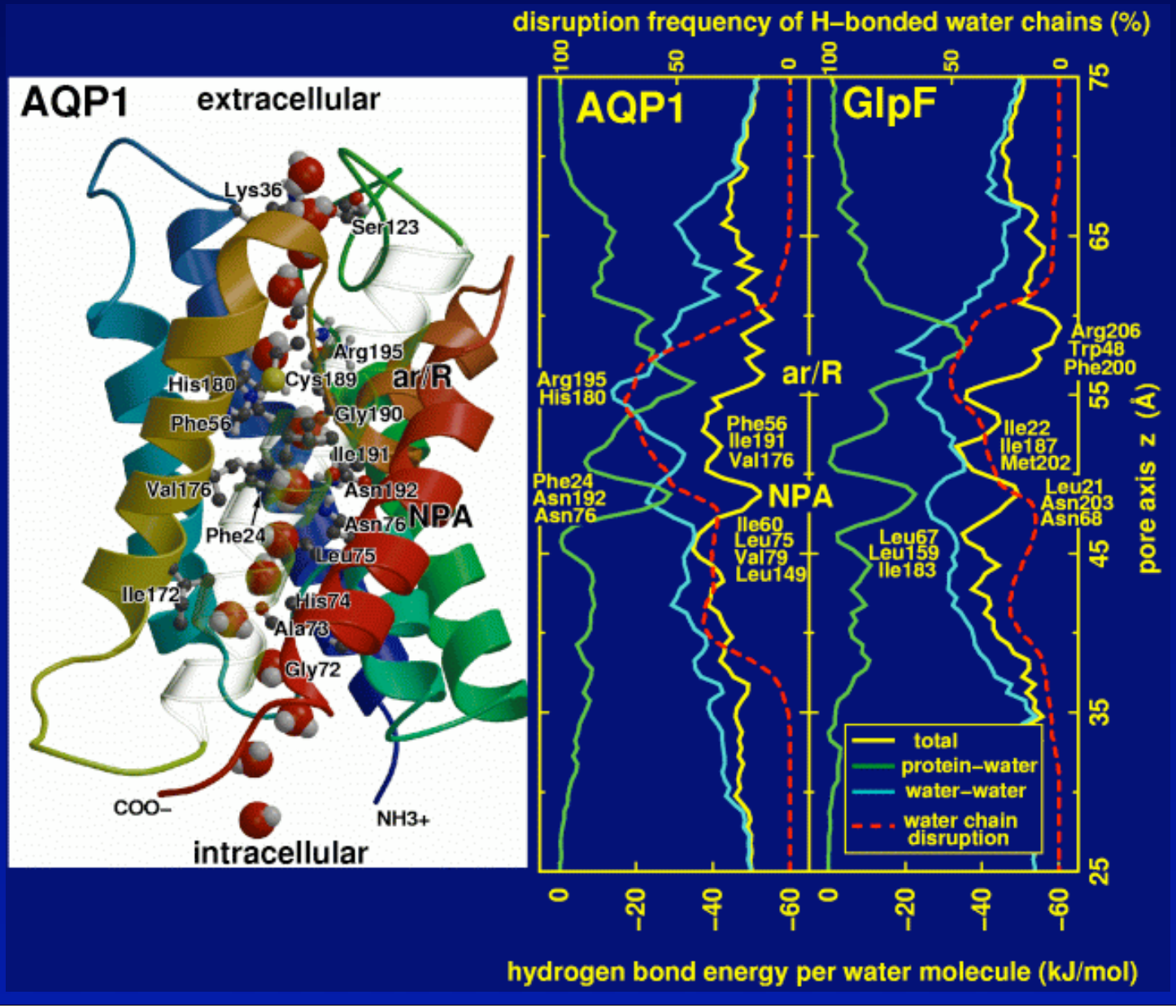




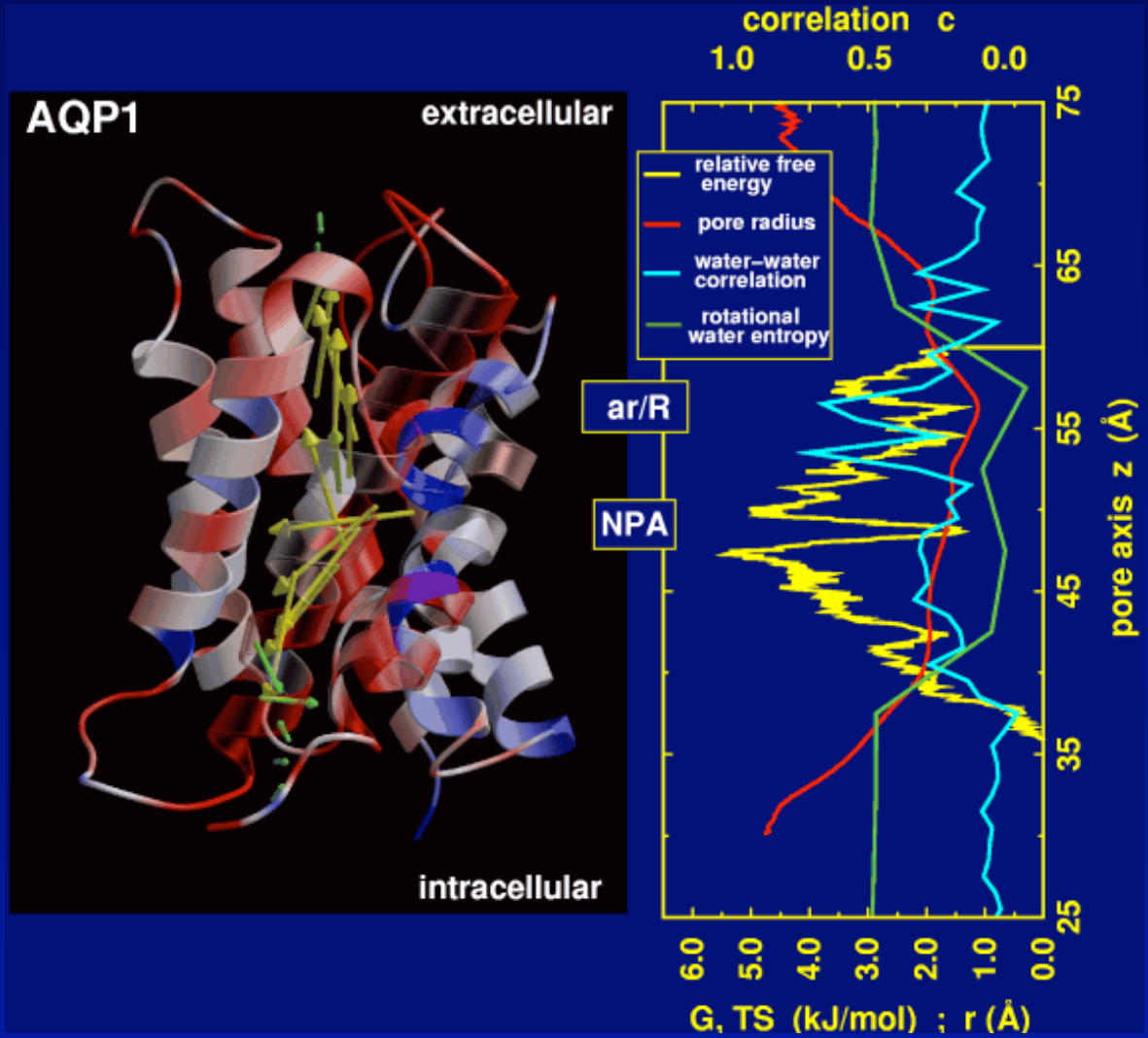
Comparison of pore radius profiles



Water pathway and hydrogen bonding in Aquaporin-1

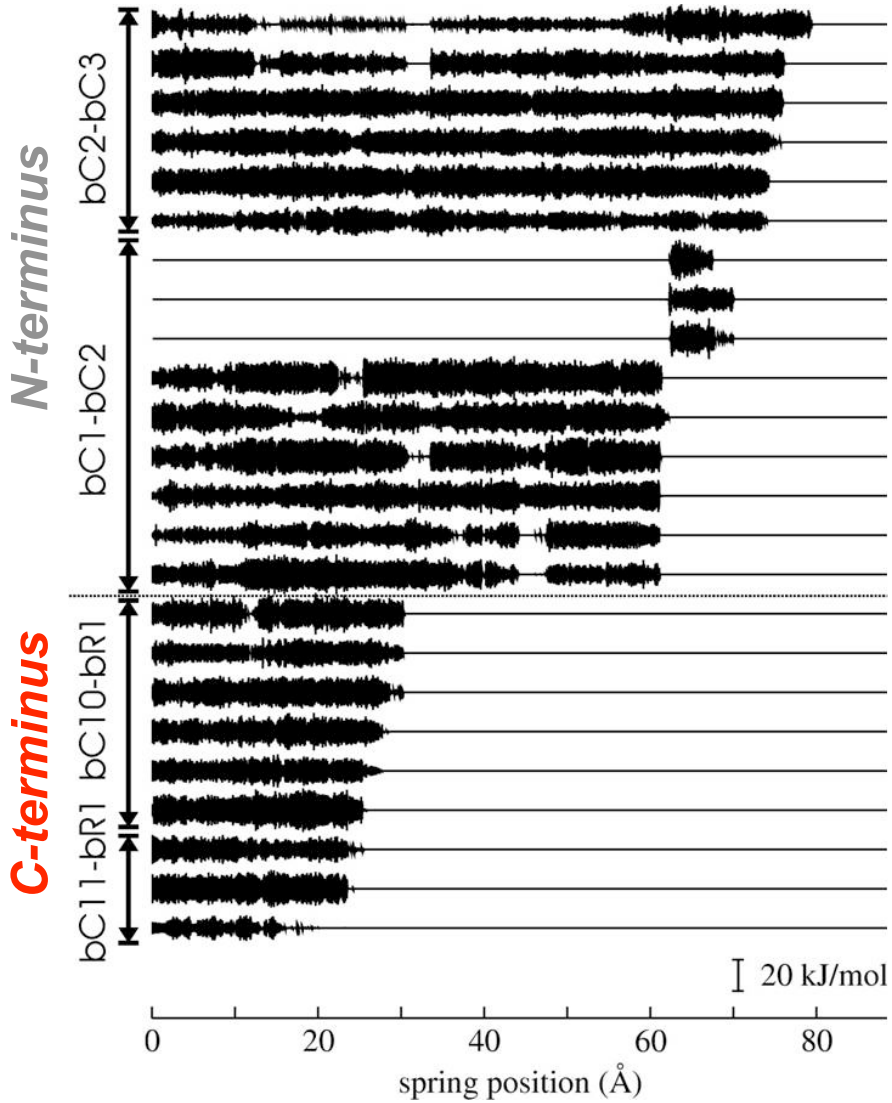


Choreography of water molecules in Aquaporin-1

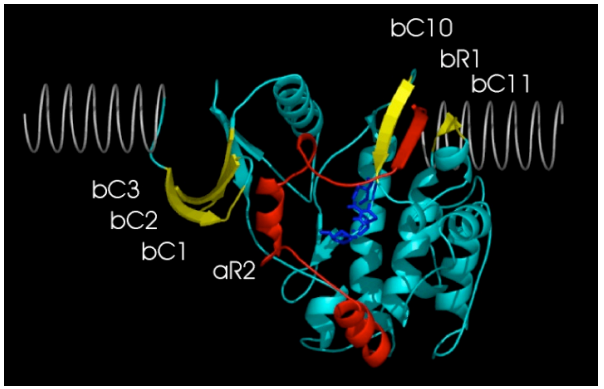


B.L. de Groot, H. Grubmüller, *Science* **294**, 2353 (2001)

Asymmetric rupture of the terminal beta sheets



N



C