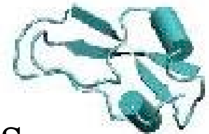
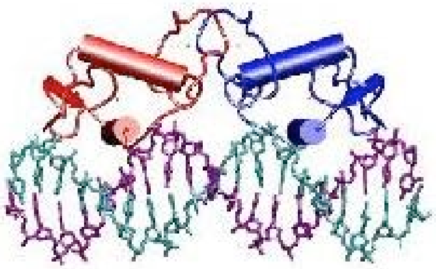
Research Opportunities in the Teraflop Era

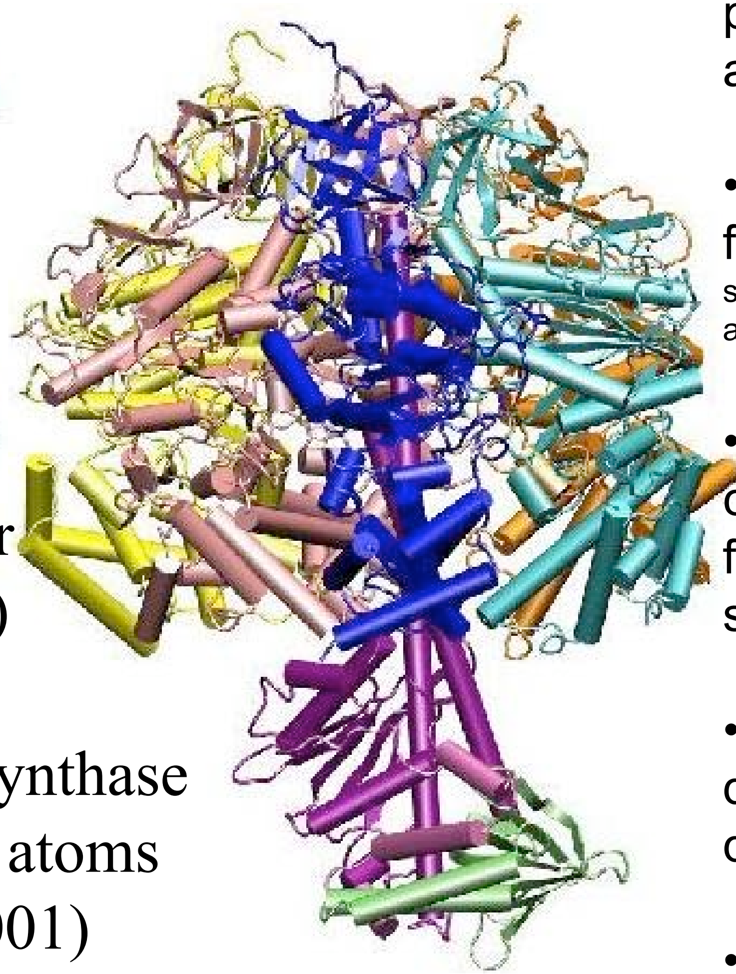
Towards Larger Molecules

BPTI
3K atoms





Estrogen Receptor
36K atoms (1996)



ATP Synthase
327K atoms
(2001)

• Studying protein-protein and protein-nucleic acid recognition and assembly.

• Investigating integral functional units (membrane proteins, signal transduction, motors, bioenergetic apparatus).

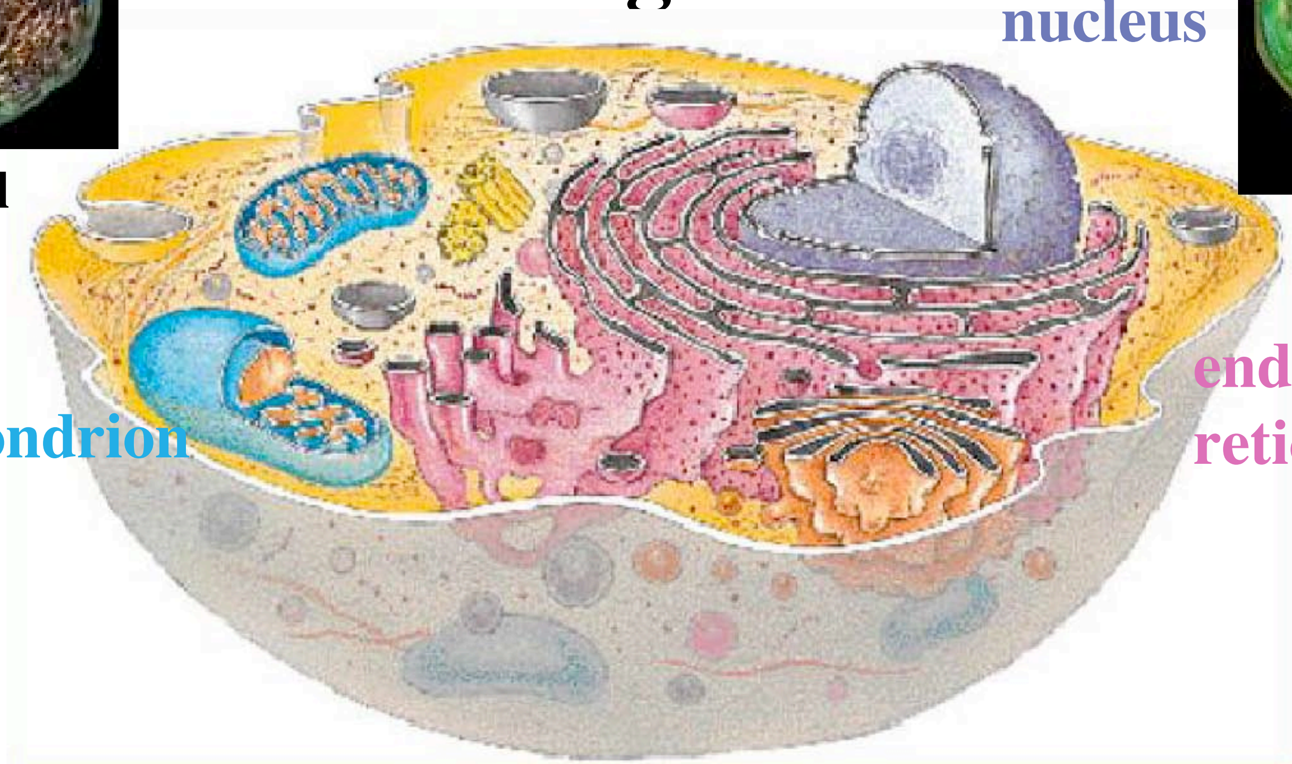
• Bridging the gap between computationally feasible and functionally relevant time scales.

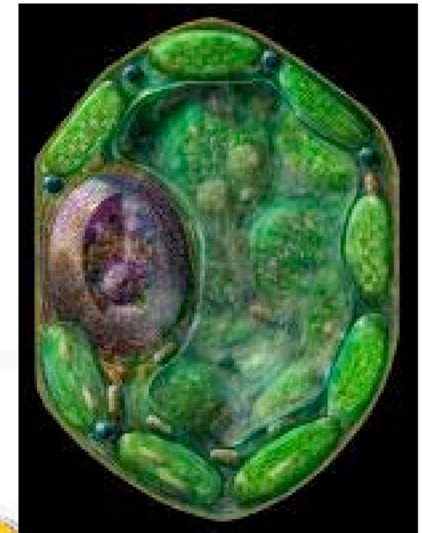
• Combining classical molecular dynamics simulations with quantum chemical forces.

• Describing integral cell functions.

Molecular Machines of the Living Cell

Animal cell



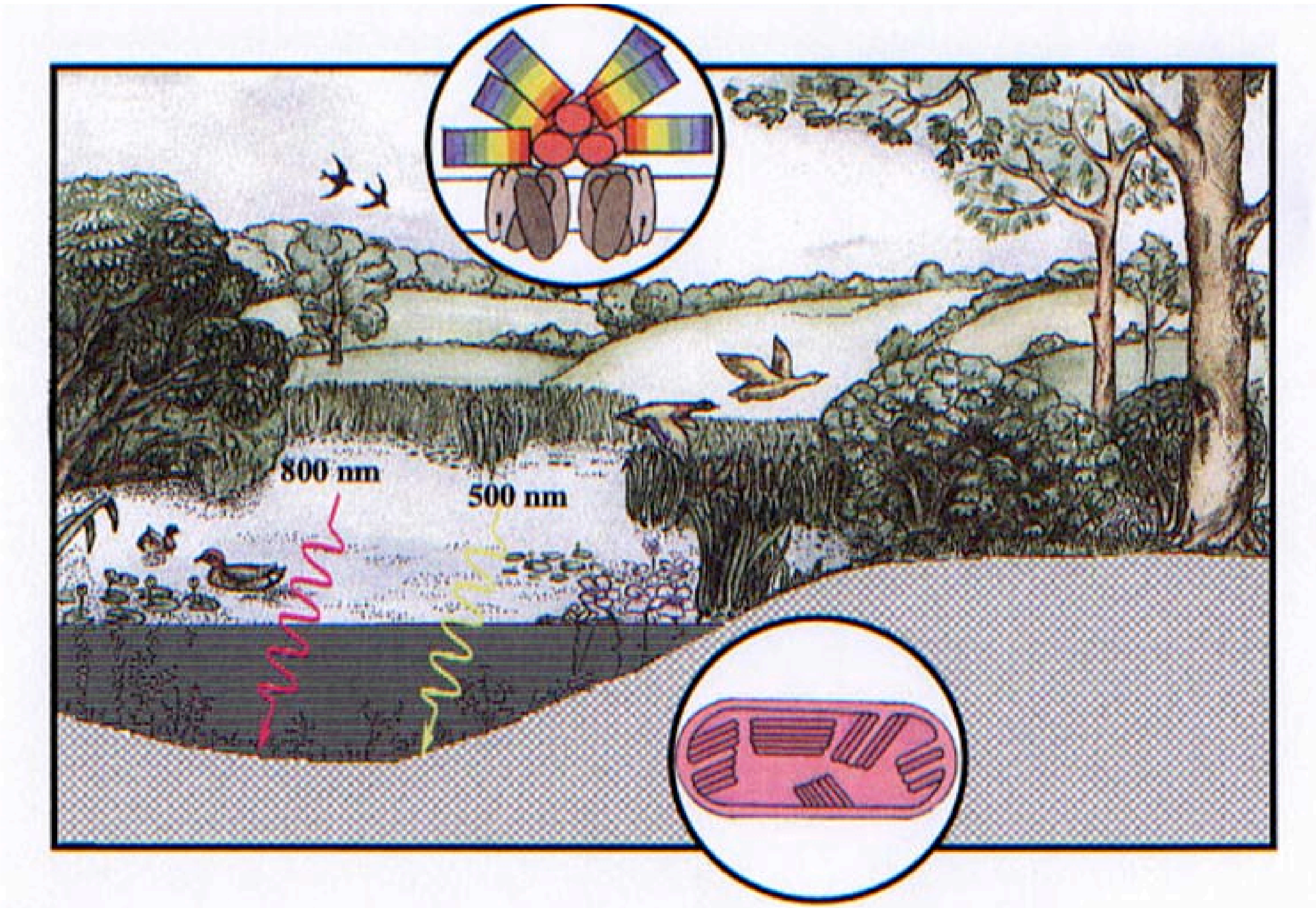


Plant cell

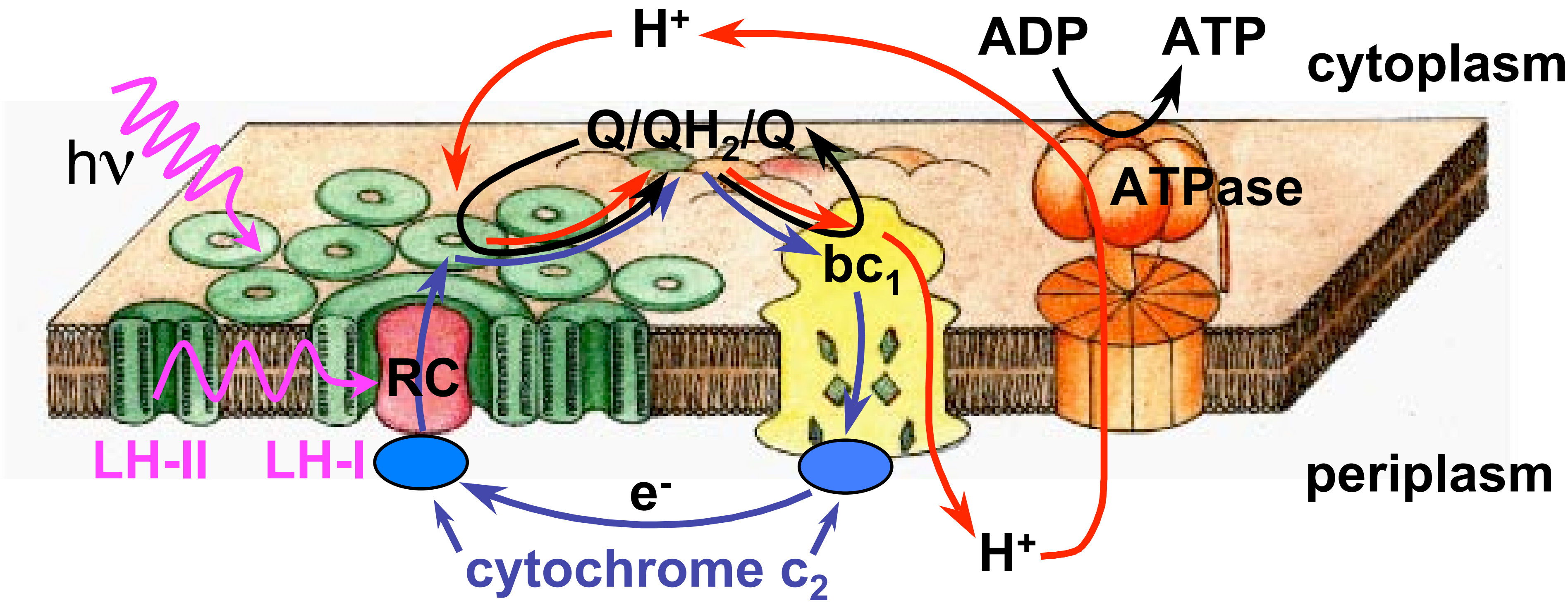
Study of integral cell functions:

gene storage, regulation, and expression; protein synthesis and degradation; energy conversion and storage; cell motion; cell signaling; metabolic pathways; …

Habitats of Photosynthetic Life Forms



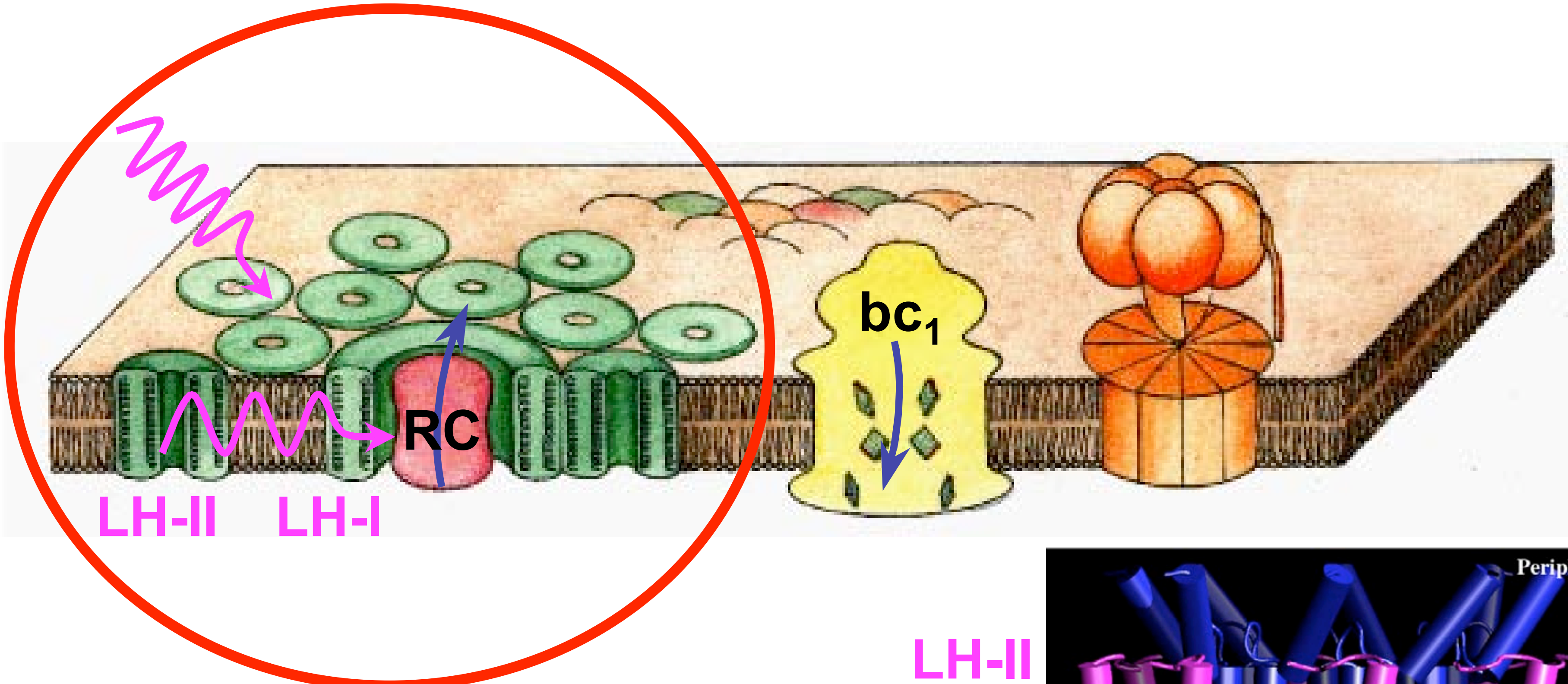
Photosynthetic Apparatus of Purple Bacteria



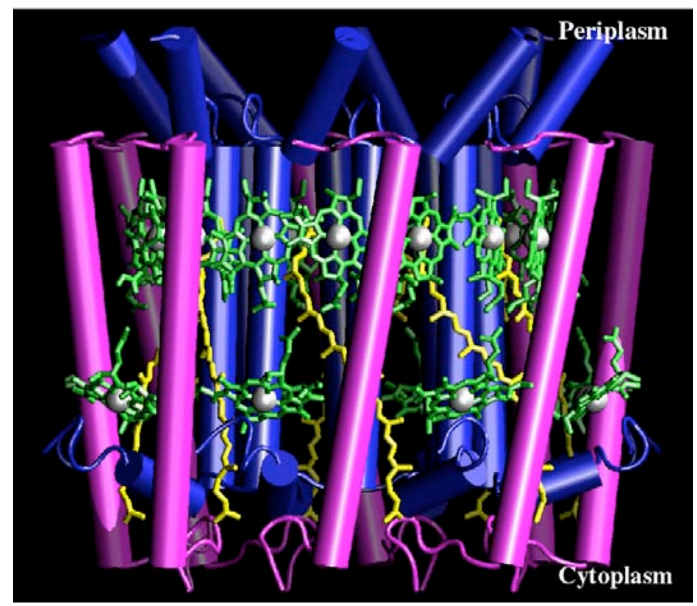
RC - Photosynthetic Reaction Center

LH – Light Harvesting Complex

Light Harvesting in Photosynthesis



LH-II

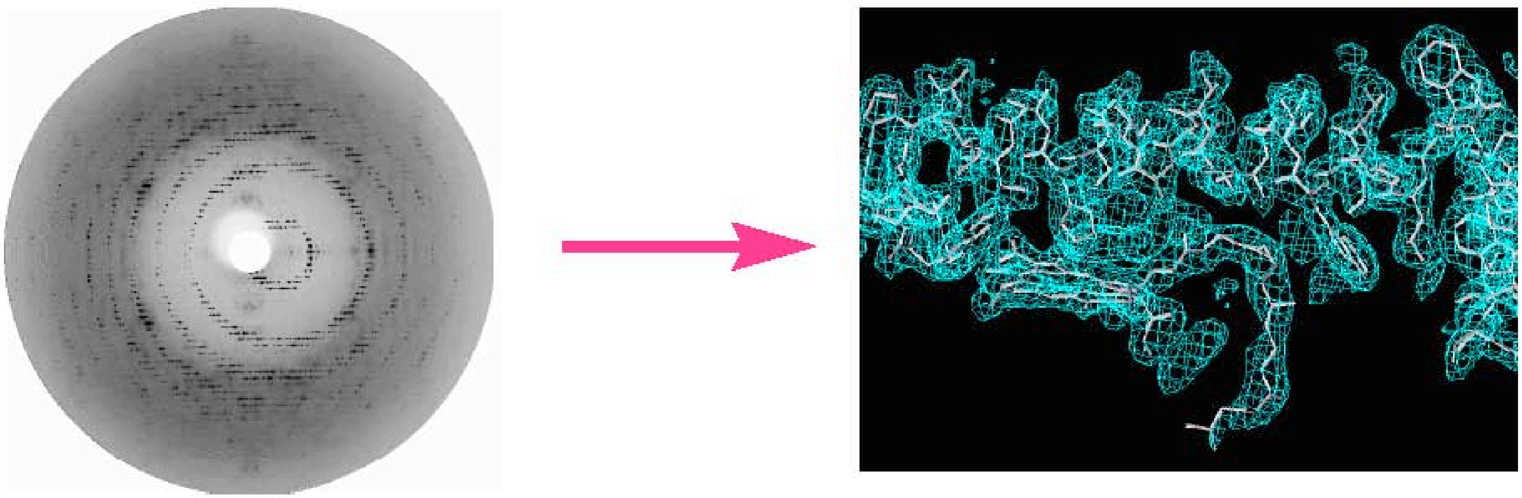


First step: Need to establish the structure of the underlying system.

Phase Problem and Conventional Solutions

Phase Problem

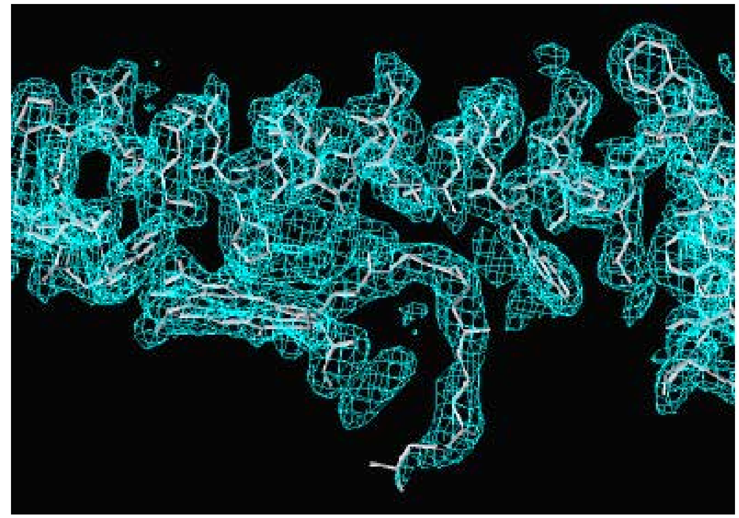
$$\rho(xyz) = \frac{1}{V} \sum_{h=-\infty}^{\infty} \sum_{k=-\infty}^{\infty} \sum_{l=-\infty}^{\infty} F(hkl)\, e^{i\alpha(hkl)}\, e^{-2\pi i\,(hx + ky + lz)}.$$



Method	Requirement
Multiple Isomorphous Replacement	Two or more isomorphous heavy metal derivatives
Molecular Replacement	Known structure of highly homologous protein

Structure of LH-II of *Rs. molischianum* Obtained Through a Computationally Derived Search Model

molecular replacement through modeling



Summary of Crystallographic Data

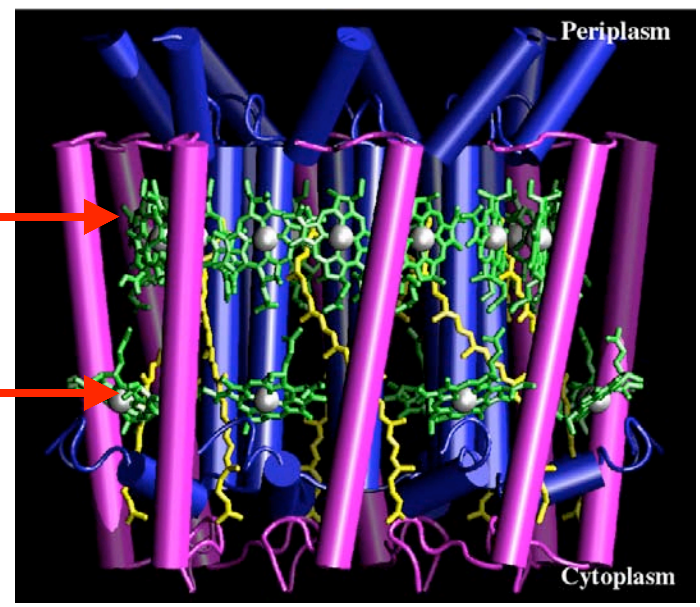
- space group P4212
- resolution range 8-2.4 A
- unique reflection 30309
- completeness 87.2
- R-factor (%) 21.1
- free R-factor (%) 23.2

Koepke et al., Structure, **4**, 581 (1996)

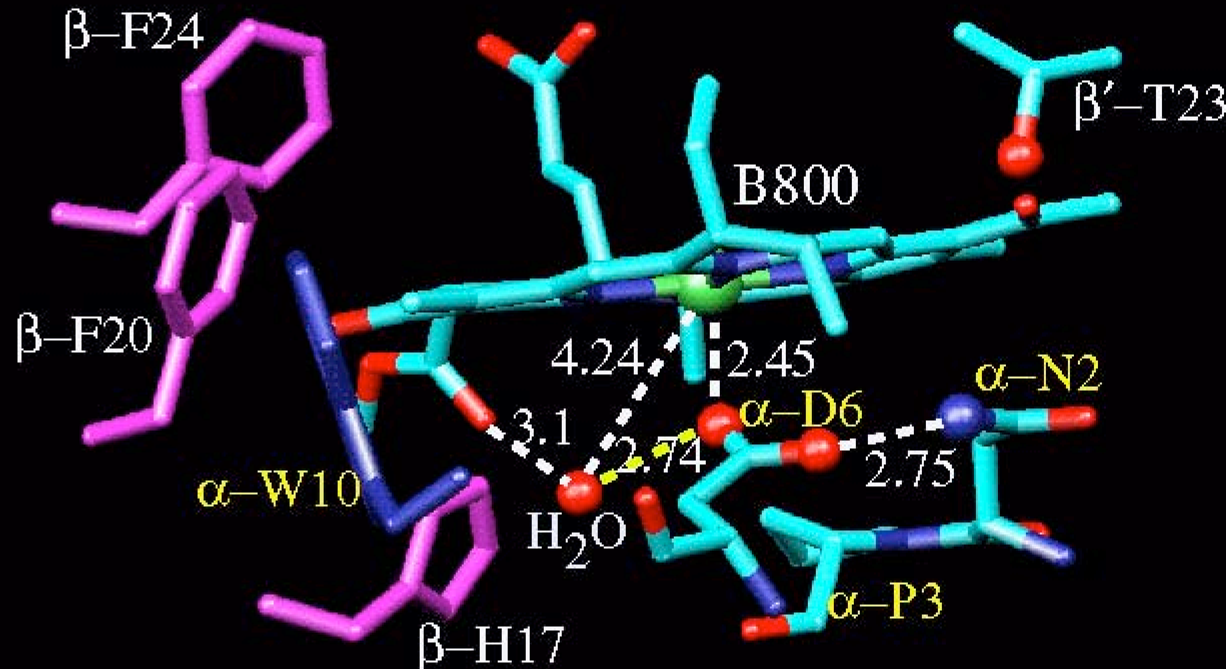
B850 band

B800 band

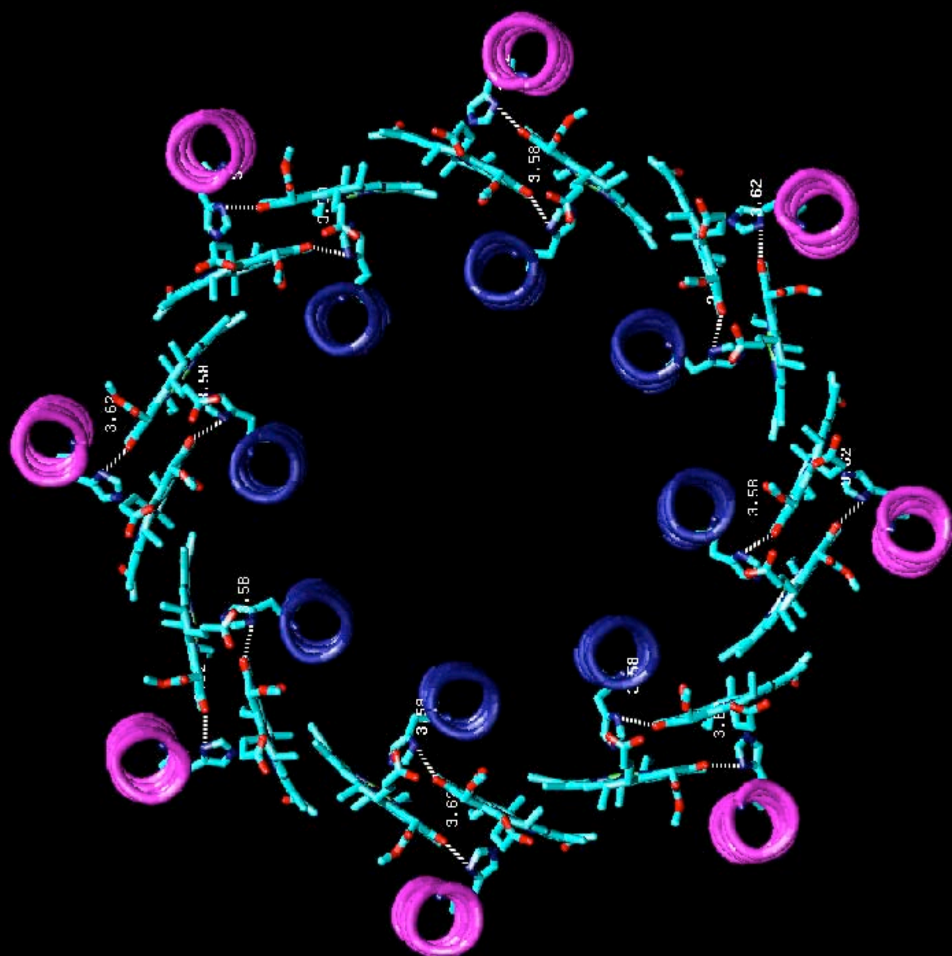
spectrum

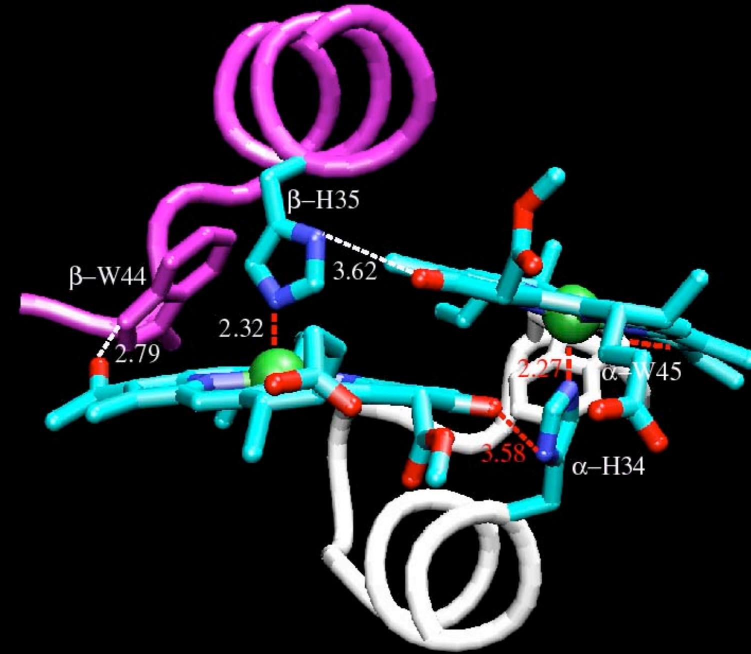


B800 BChl-a Binding Site



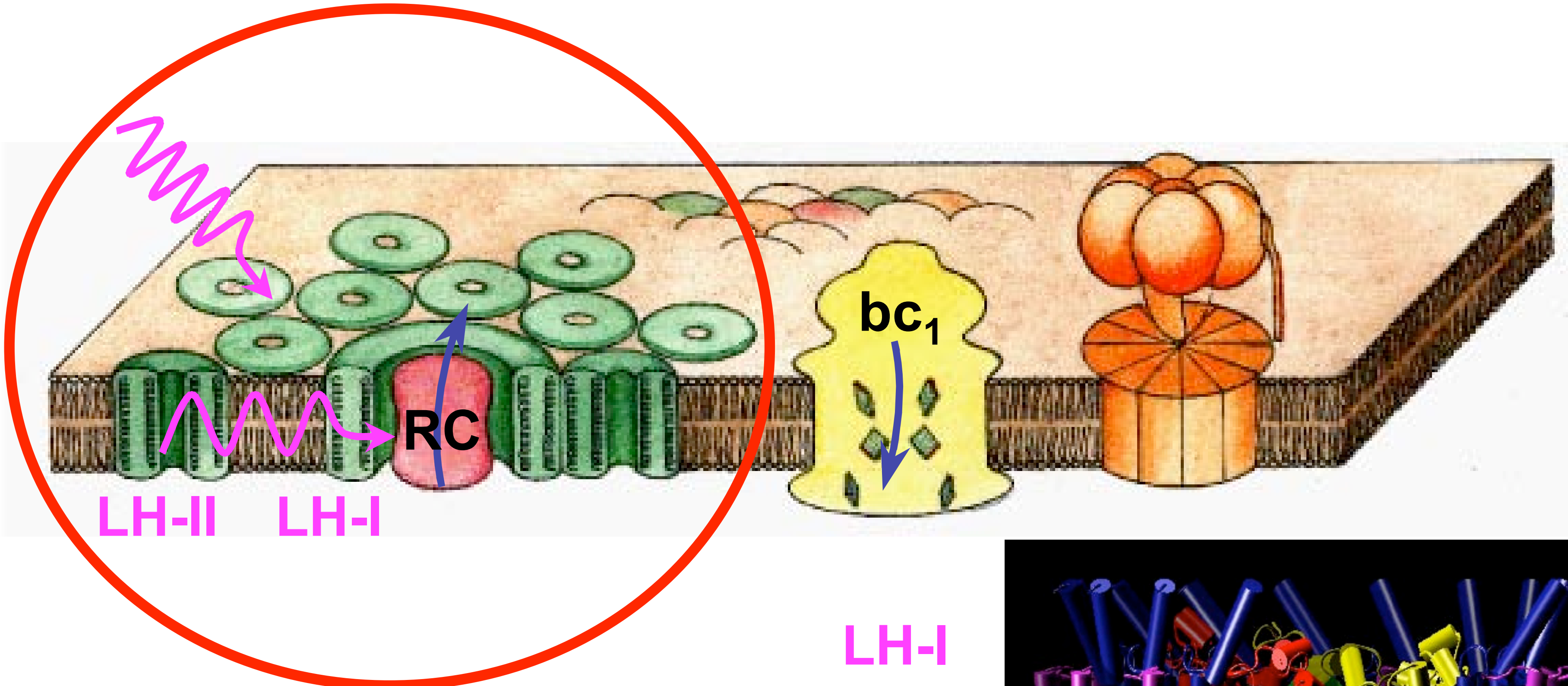
B850 BChls of LH-II of *Rs. molischianum*



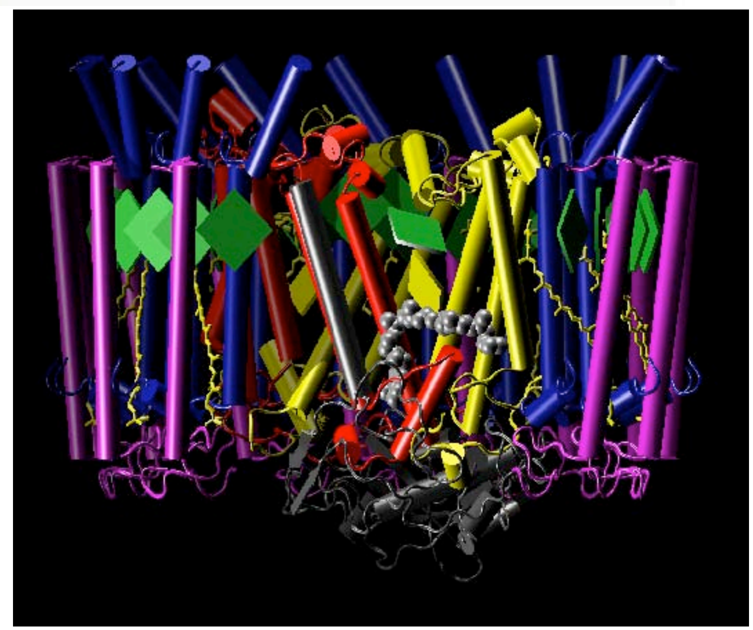


Spectrum tuned through local and excitonic interactions as well as disorder

Light Harvesting in Photosynthesis



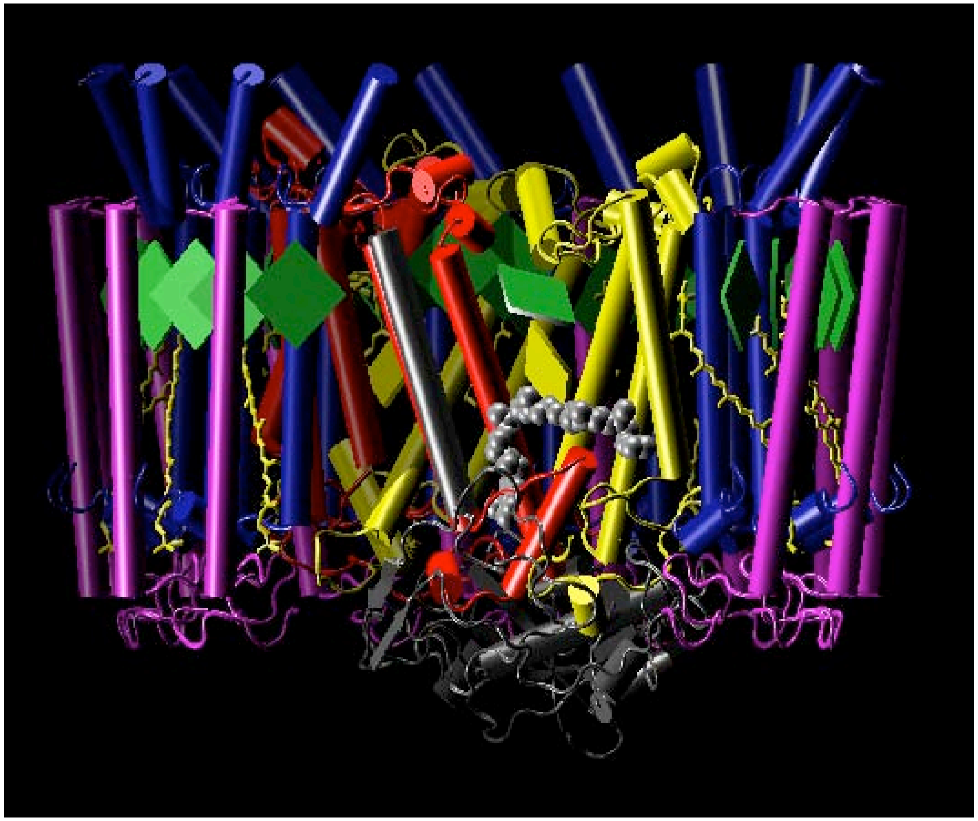
LH-I

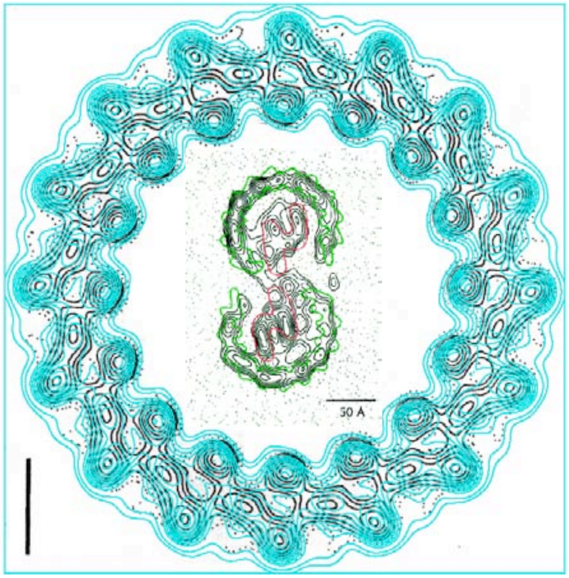


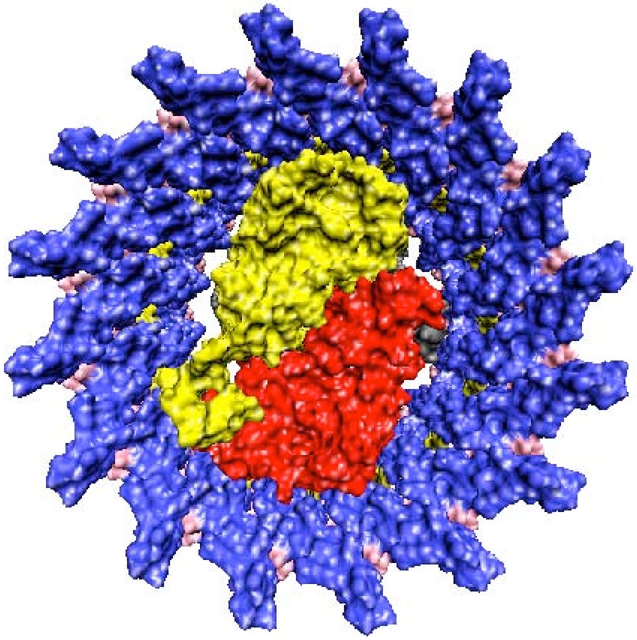
First step: Need to establish the structure of the underlying system

LH-I – RC Complex of *Rb. sphaeroides*

Model agrees well with EM map



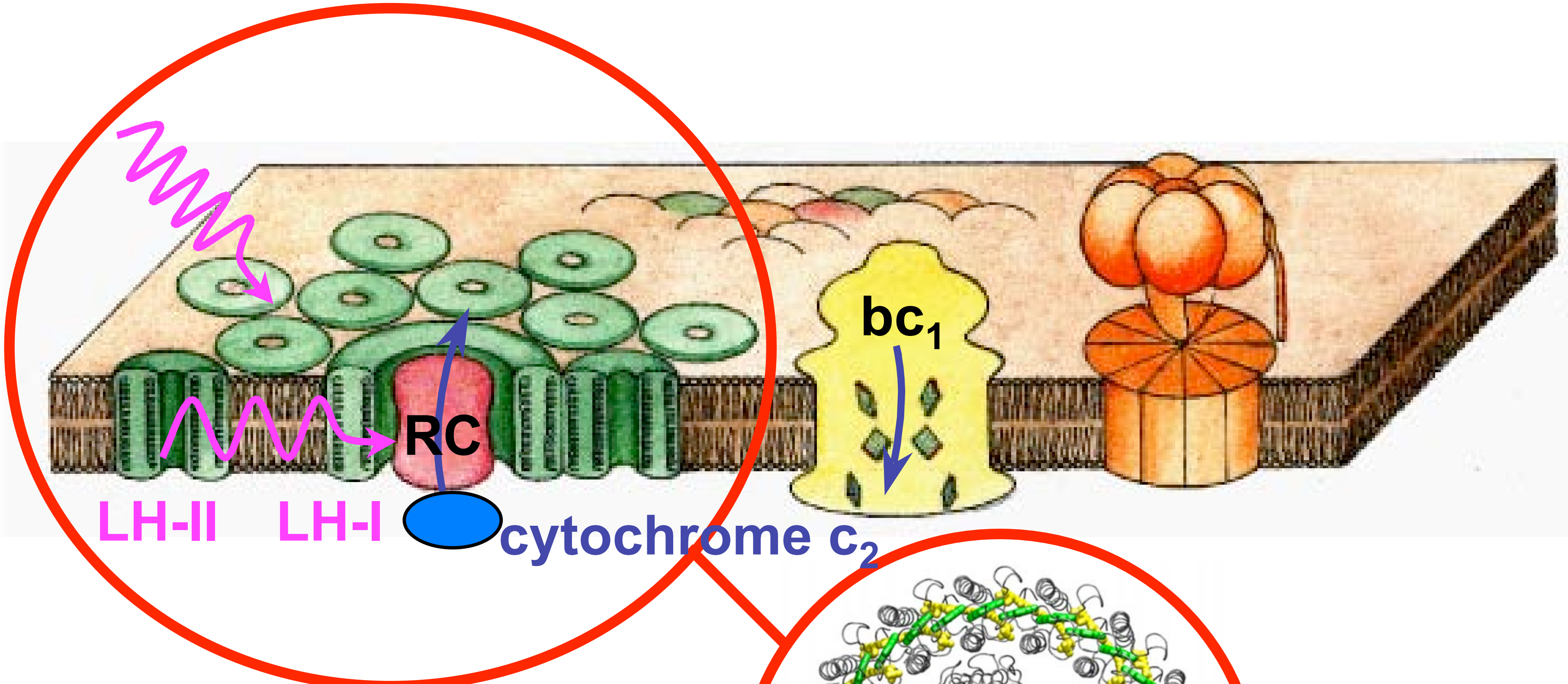


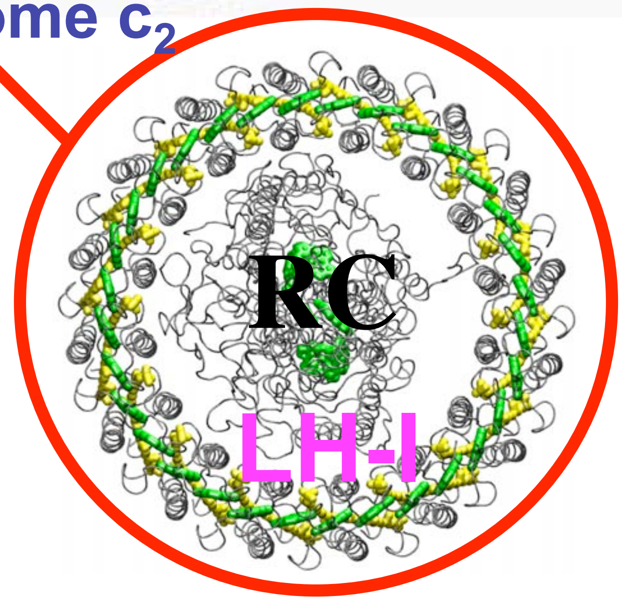


Xiche Hu

View from top

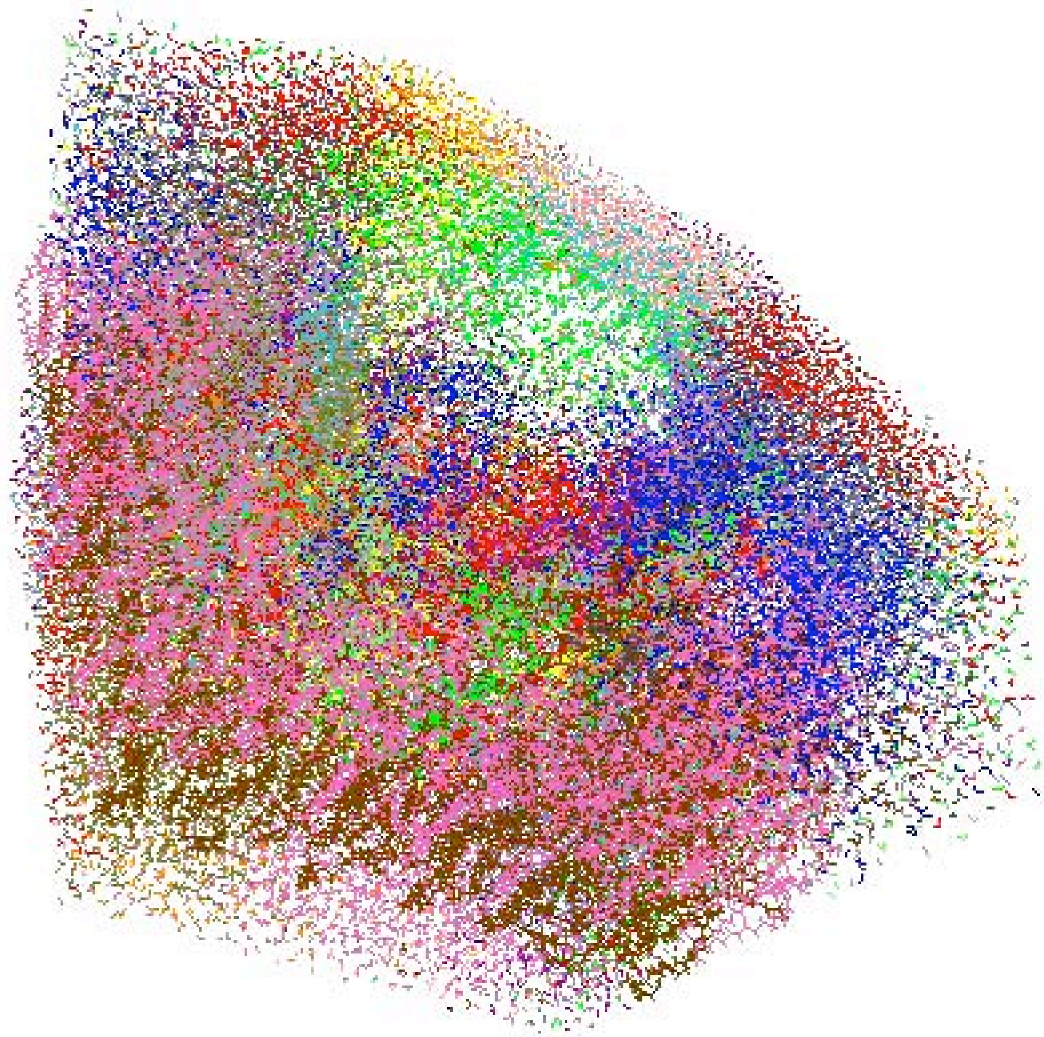
Structure of RC+LH-I+Cyt System





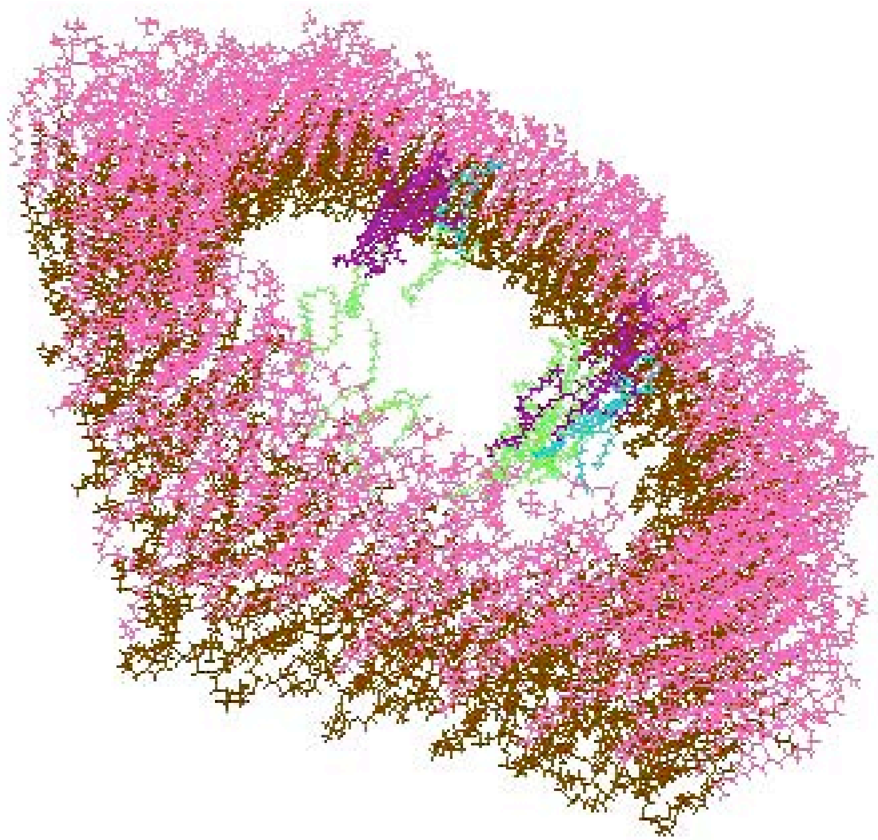
Focussing on the Structure of RC + LH-I

Focussing on the Structure of RC+LH-I+Cyt



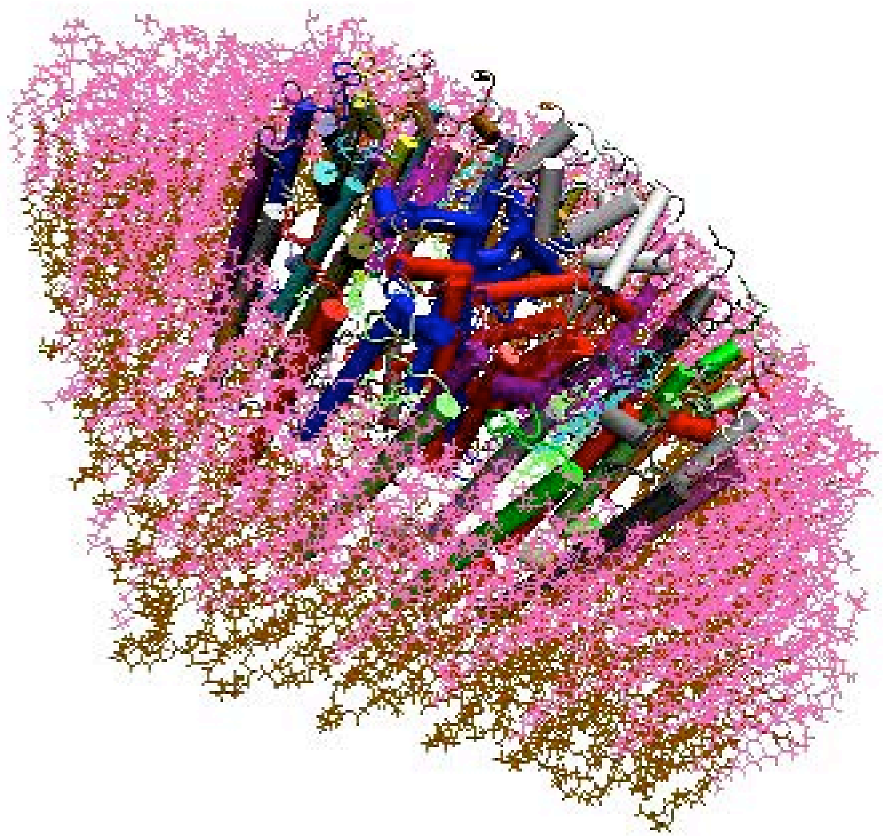
System of Water - Lipids - Protein

Focussing on the Structure of RC+LH-I+Cyt



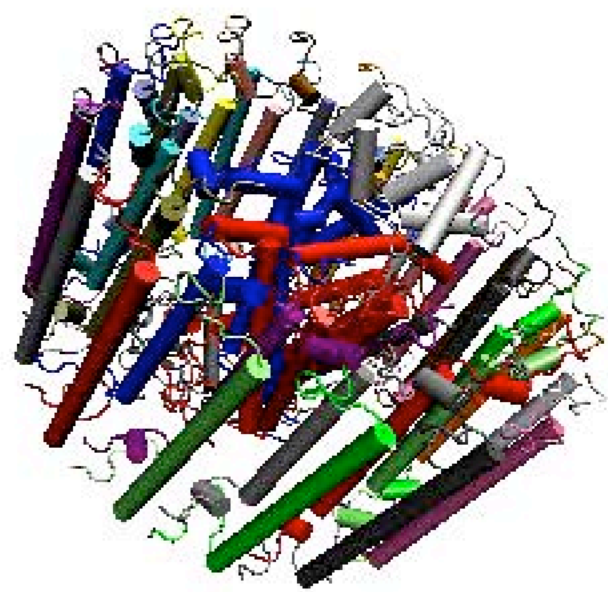
Lipids only

Focussing on the Structure of RC+LH-I+Cyt



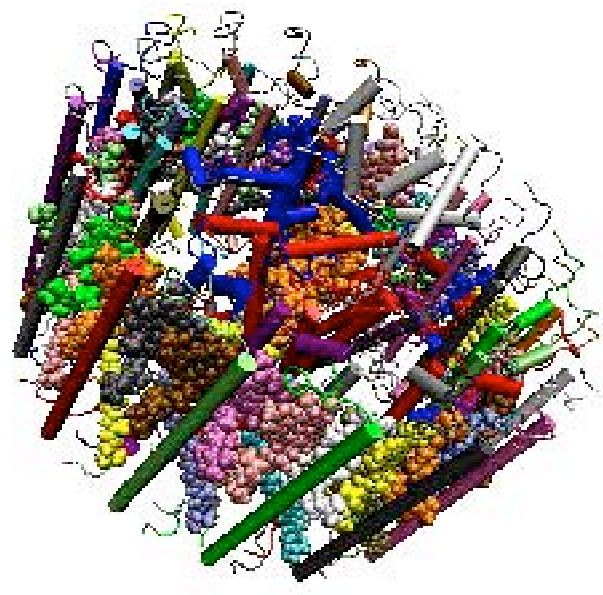
Lipids and Proteins

Focussing on the Structure of RC+LH-I+Cyt



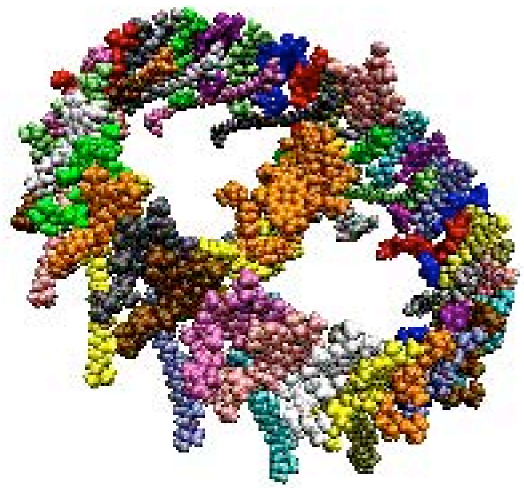
Proteins only

Focussing on the Structure of RC+LH-I+Cyt



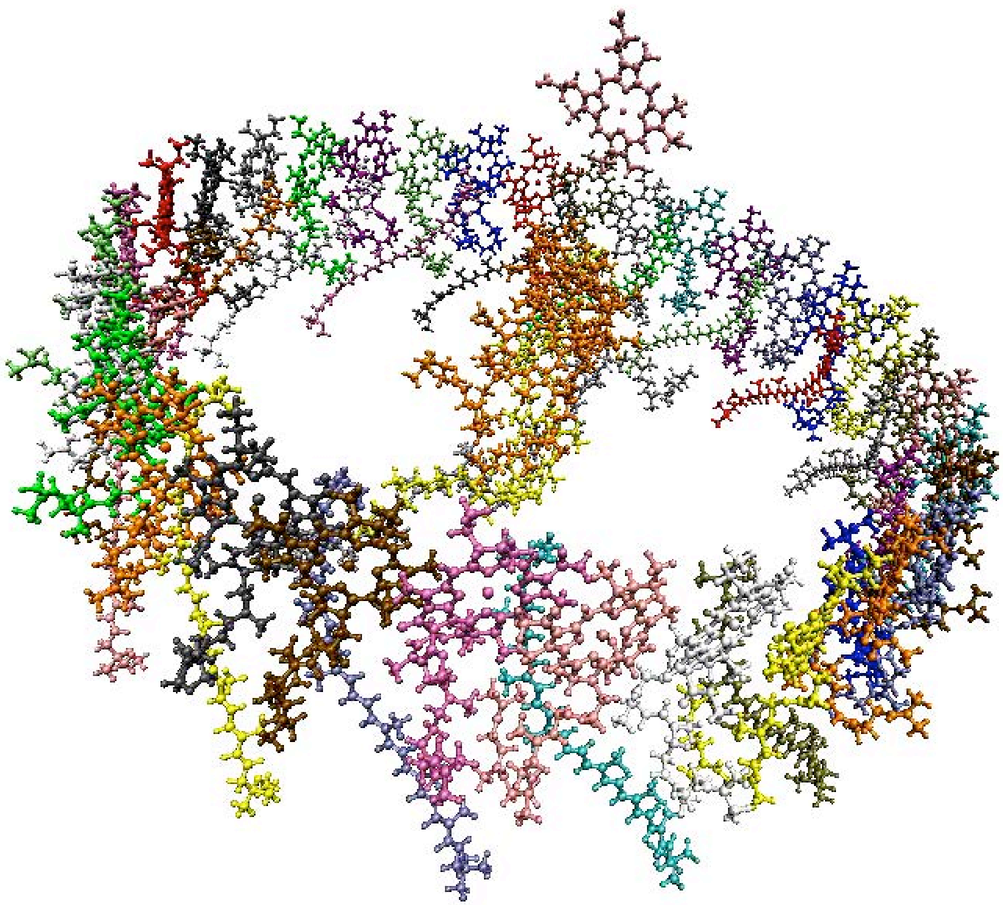
Proteins and Chromophores

Focussing on the Structure of RC+LH-I+Cyt



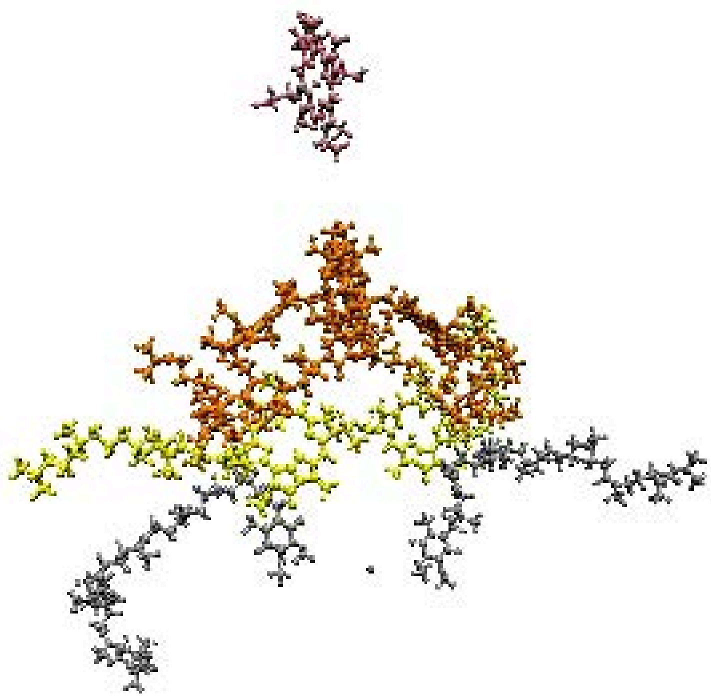
Chromophores only

Focussing on the Structure of RC+LH-I+Cyt

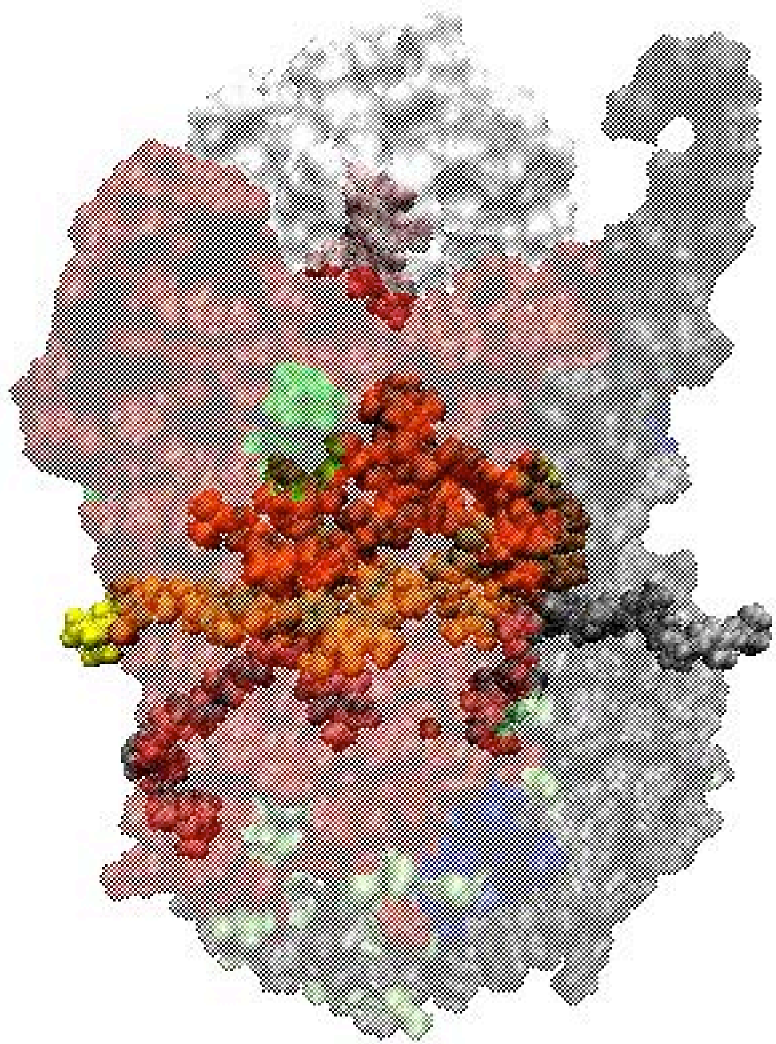


Chromophores only

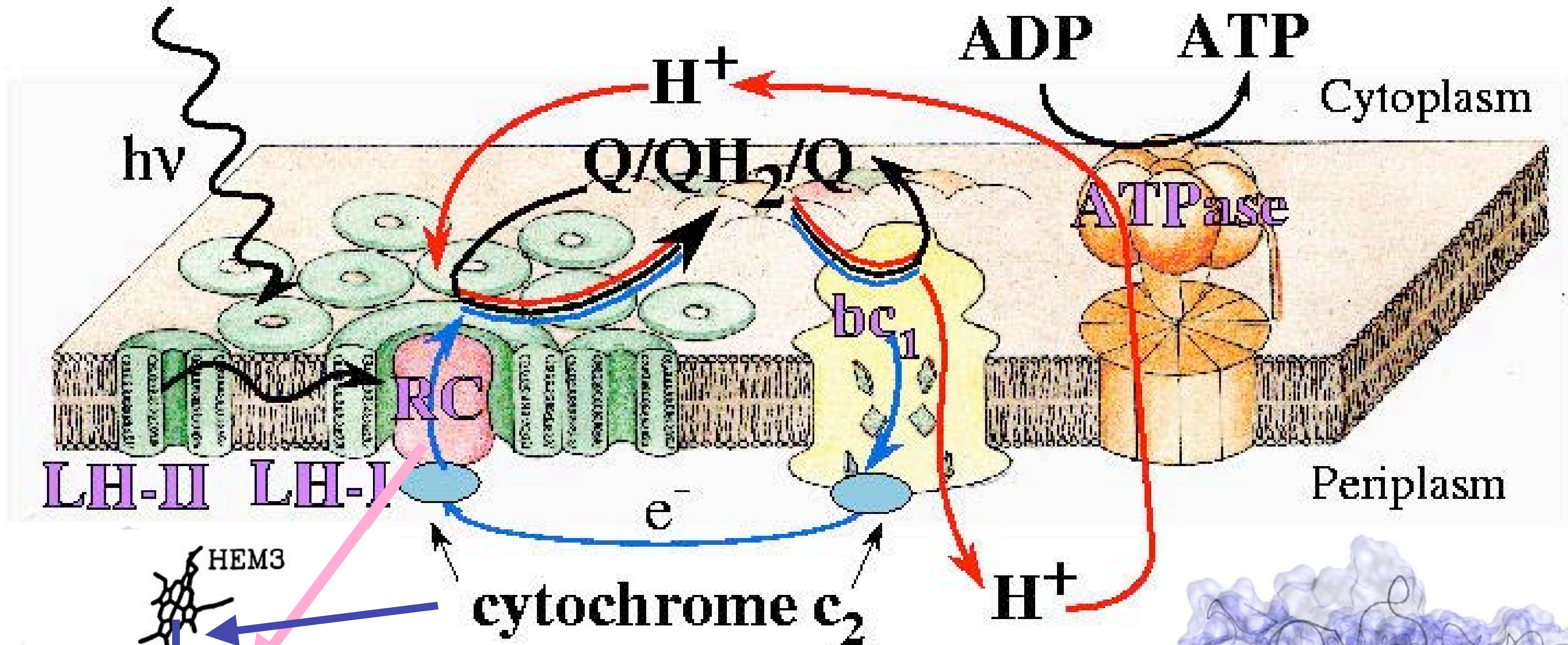
Electron Transfer Chain in RC + Cyt c Complex

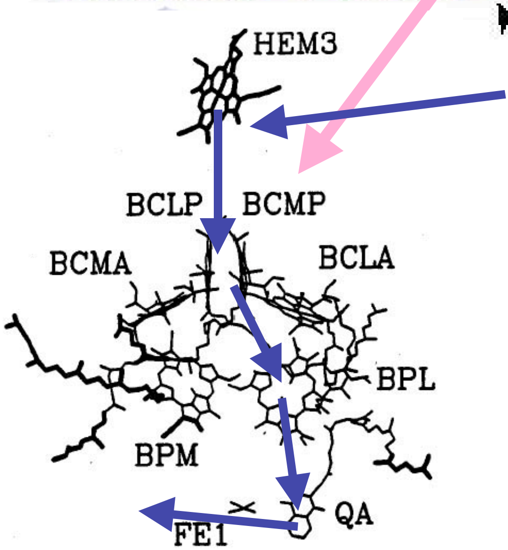


Role of the Protein Matrix on Electron Transfer

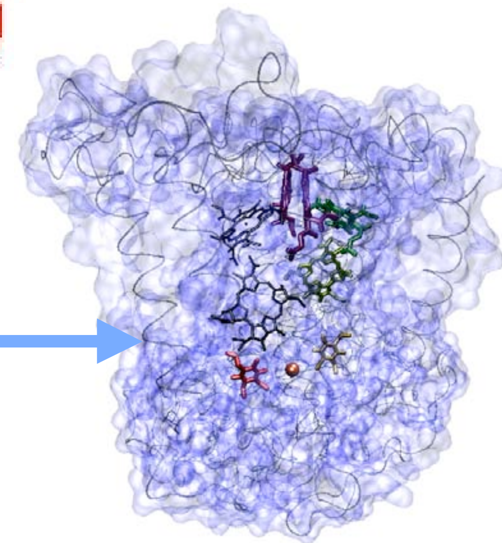


Role of Thermal Disorder on Electron Transfer in the Photosynthetic Reaction Center





We wanted to describe how electron transfer is coupled to the thermal motion of the surrounding protein.

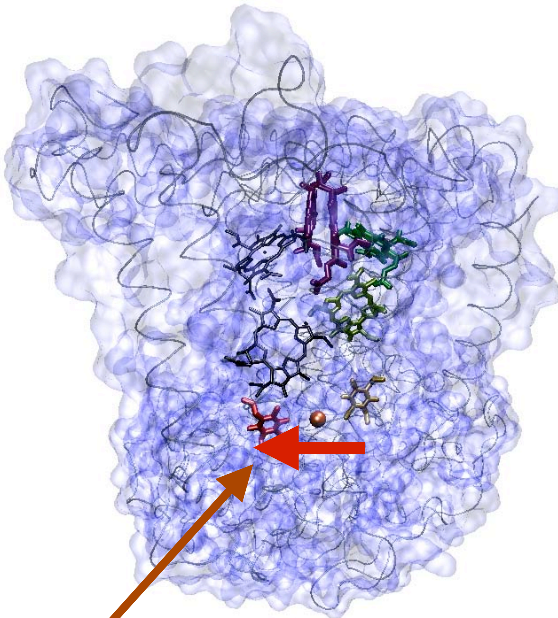


Electron Transfer Process Coupled to the Protein Matrix

We assumed that the electron transfer

$Q_A^- \, Q_B$ -> $Q_A \, Q_B^-$ is coupled to an **ensemble of oscillators representing the protein matrix**

Hamiltonian $$\hat{H}^{(s)}_{\mathrm{qo}} = \begin{pmatrix} \hat{H}^{(s)}_r & v \\ v & \hat{H}^{(s)}_p + E \end{pmatrix}$$



Protein matrix is a bath of oscillators linearly coupled to the electron transfer according to

$$\hat{H}_r = \sum_j \left(\frac{\hat{p}_j^2}{2M_j} + \frac{1}{2} M_j \omega_j^2 q_j^2 \right)$$

$$\hat{H}_p = \sum_j \left(\frac{\hat{p}_j^2}{2M_j} + \frac{1}{2} M_j \omega_j^2 \left(q_j - \frac{c_j}{M_j \omega_j^2} \right)^2 \right)$$

Dong Xu and Klaus Schulten. Chemical Physics, 182: 91--117, 1994.

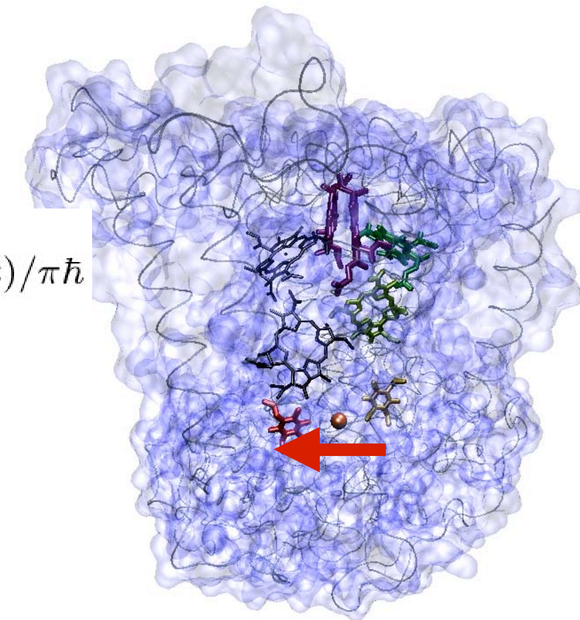
Klaus Schulten. In D. Bicout and M. J. Field, editors, Proc. Ecole de Physique des Les Houches, pp 85--118, Les Editions de Physique, Springer, Paris, 1995.

Klaus Schulten. Science, 290:61--62, 2000.

Electron Transfer Process Coupled to the Protein Matrix

Rate for an ensemble of oscillators (spin boson model, Legett et al)

$$k_{qb}(R \rightarrow P) \;=\; \frac{v^2}{\hbar^2}\int_{-\infty}^{+\infty} dt\; e^{itE/\hbar}\; e^{iQ_1(t)/\pi\hbar}\; e^{-Q_2(t)/\pi\hbar}$$



Relaxation rate

$$k_{\rm rel} \;=\; \frac{2v^2}{\hbar^2}\int_0^{+\infty} dt\,\cos(\quad tE/\hbar)\,\cos(Q_1(t)/\pi\hbar)\; e^{-Q_2(t)/\pi\hbar}$$

$$Q_1(t) \;=\; \frac{\pi}{2}\sum_j \frac{c_j^2}{\hbar\omega_j^3}\,\sin\omega_j t$$

$$Q_2(t) \;=\; \frac{\pi}{2}\sum_j \frac{c_j^2}{\hbar\omega_j^3}\,\coth\frac{\hbar\omega_j}{2kT}\,[1-\cos(\omega_j t)]$$

But we didn't know all the coupling constants c_j ? All we needed to know was J

$$J(\omega) \;=\; \frac{\pi}{2}\sum_j \frac{c_j^2}{\omega_j}\,\delta(\omega \;-\; \omega_j)$$

$$Q_1(t) \;=\; \int_0^{\infty} d\omega\,\omega^{-2} J(\omega)\,\sin\omega t$$

$$Q_2(t) \;=\; \frac{\pi}{2}\int_0^{\infty} d\omega\,\omega^{-2} J(\omega)\,\coth\frac{\hbar\omega}{2kT}\,(1-\cos\omega t)$$

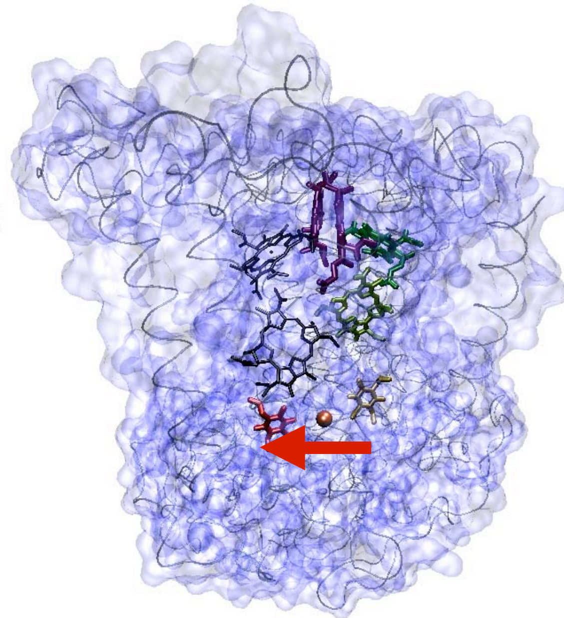
Electron Transfer Process Coupled to the Protein Matrix

Relaxation rate

$$k_{\rm rel} = \frac{2v^2}{\hbar^2} \int_0^{+\infty} dt \, \cos(\quad tE/\hbar) \cos(Q_1(t)/\pi\hbar) \, e^{-Q_2(t)/\pi\hbar}$$

$$Q_1(t) = \int_0^{\infty} d\omega \, \omega^{-2} J(\omega) \sin\omega t$$

$$Q_2(t) = \frac{\pi}{2} \int_0^{\infty} d\omega \, \omega^{-2} J(\omega) \coth\frac{\hbar\omega}{2kT} (1 - \cos\omega t)$$



1994

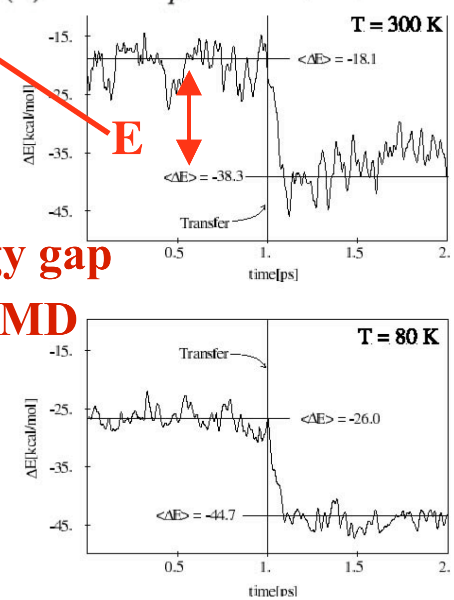
$$\frac{J(\omega)}{\omega} = \frac{\sigma^2}{k_B T} \int_0^{\infty} dt \, C(t) \cos\omega t$$

$$C_{\epsilon\epsilon}(t) = \frac{\langle (\epsilon(t) - \langle\epsilon\rangle) (\langle\epsilon(0) - \langle\epsilon\rangle) \rangle}{\langle\epsilon(0) - \langle\epsilon\rangle \rangle^2}$$

energy gap correlation function

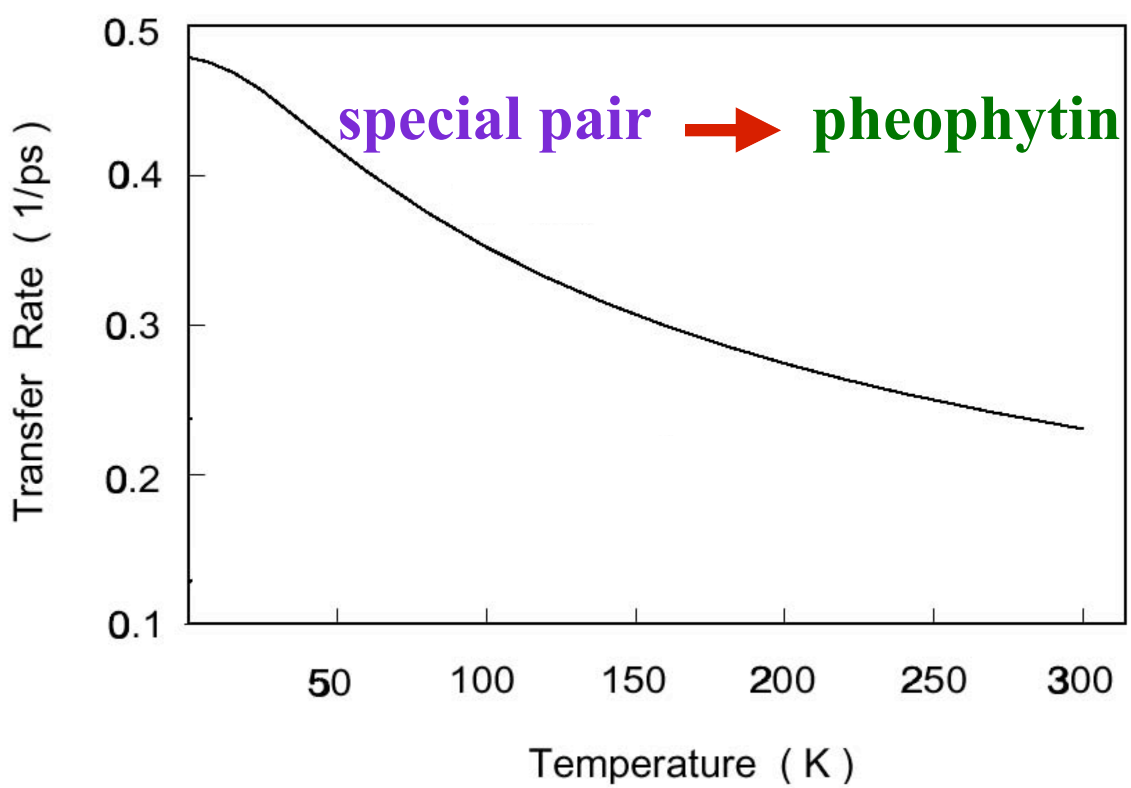
σ **rms deviation of energy gap**

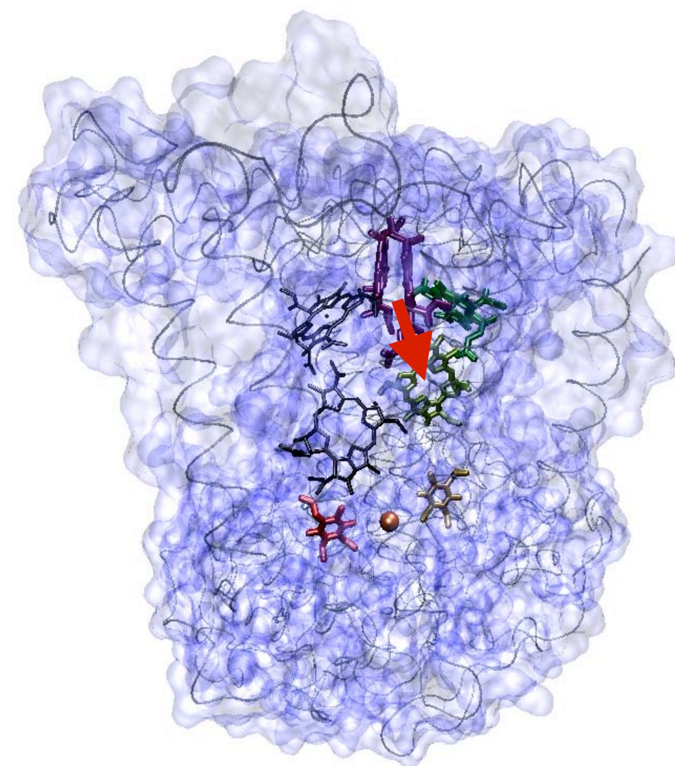
$$\epsilon(t) = \hat{H}_p - \hat{H}_r + E$$



energy gap from MD 1989

Temperature Dependence of Electron Transfer Rate



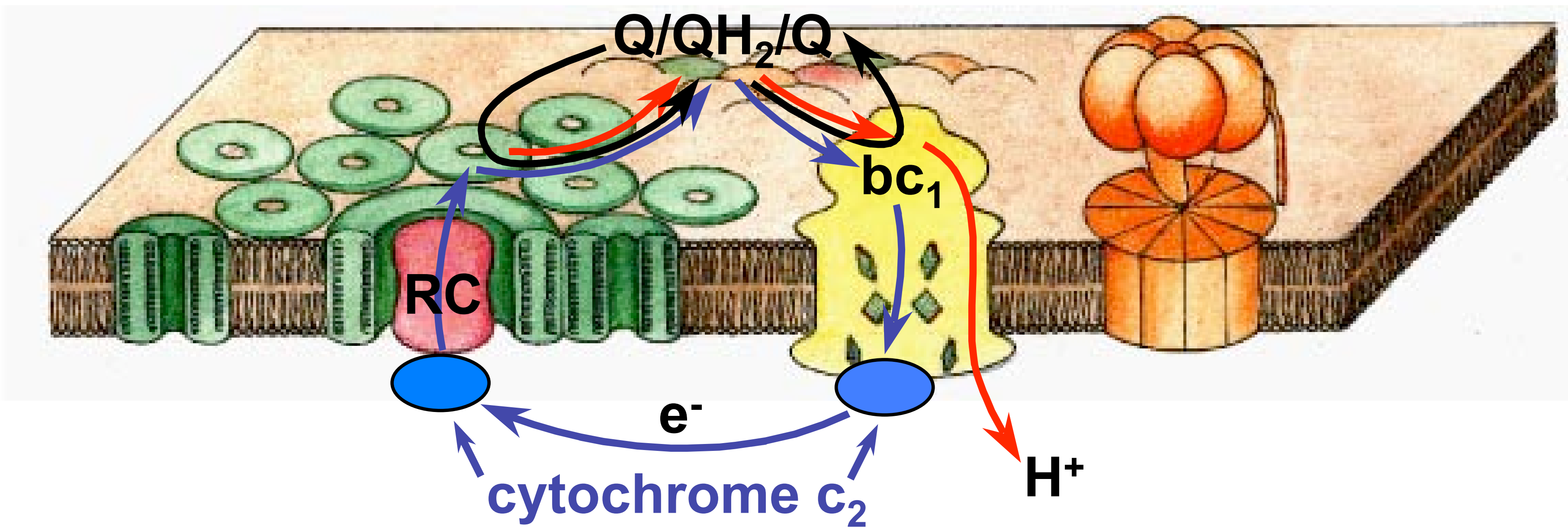


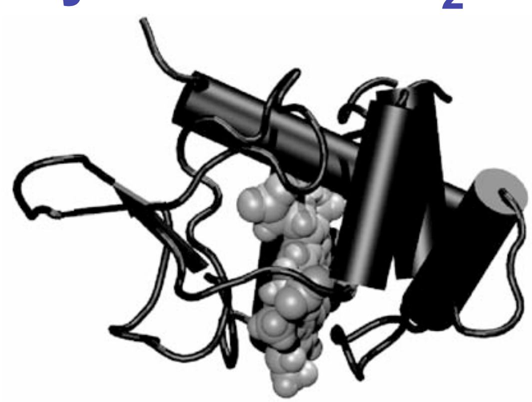
Dong Xu and Klaus Schulten. Chemical Physics, 182: 91--117, 1994.

Klaus Schulten. In D. Bicout and M. J. Field, editors, Proc. Ecole de Physique des Les Houches, pp 85--118, Les Editions de Physique, Springer, Paris, 1995.

Klaus Schulten. Science, 290:61--62, 2000.

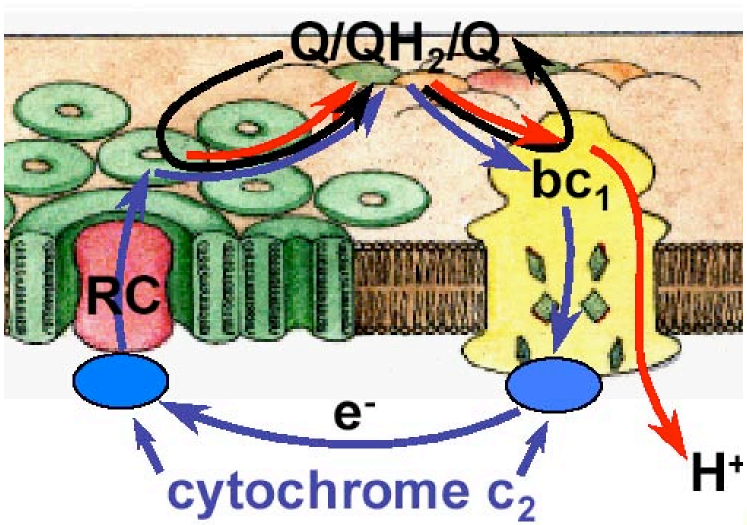
The Role of Cytochrome c_2 in Shuttling Electrons Between the Reaction Center RC and the bc_1 complex

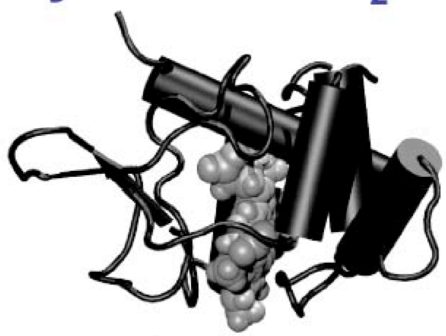


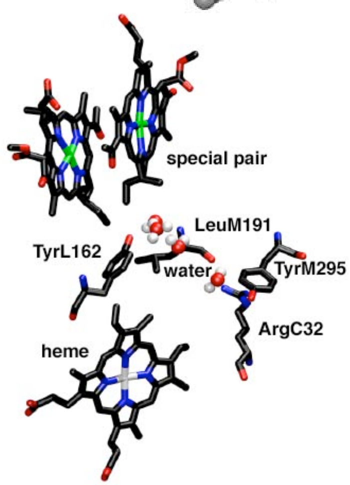


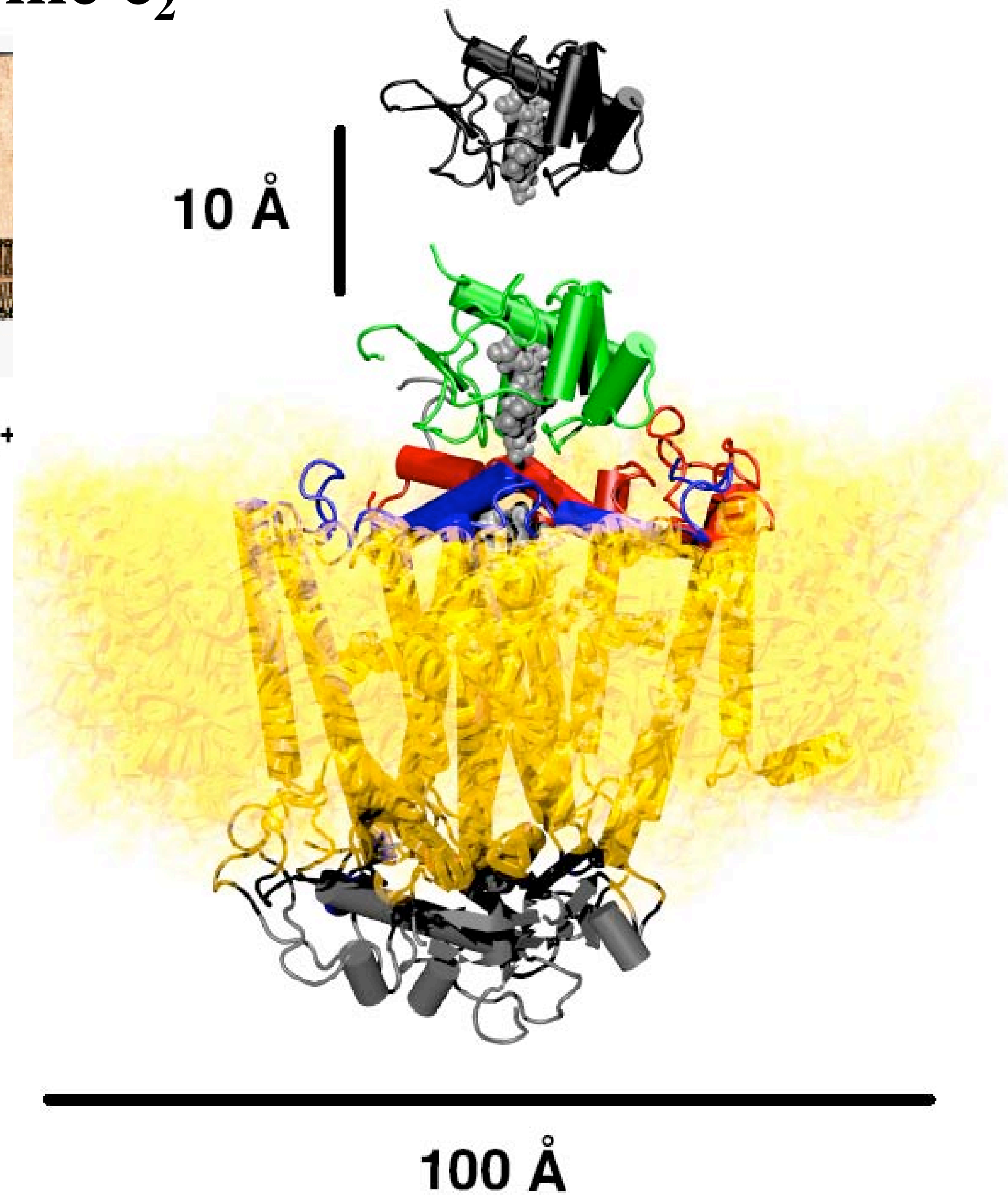
Cytochrome c2

Docking of Cytochrome c_2

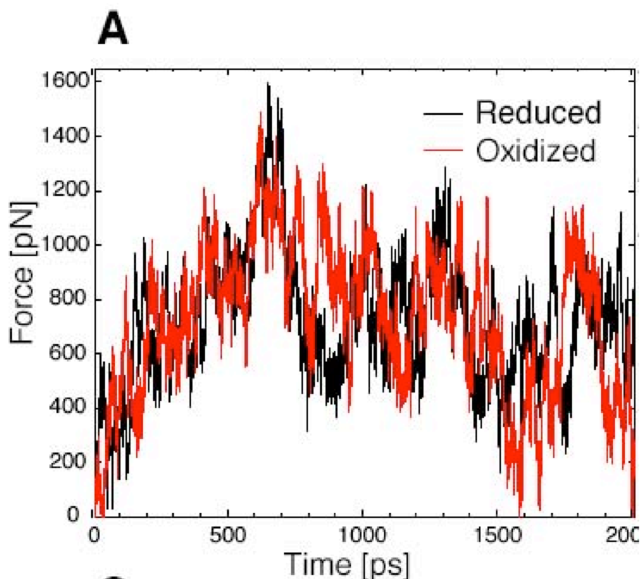


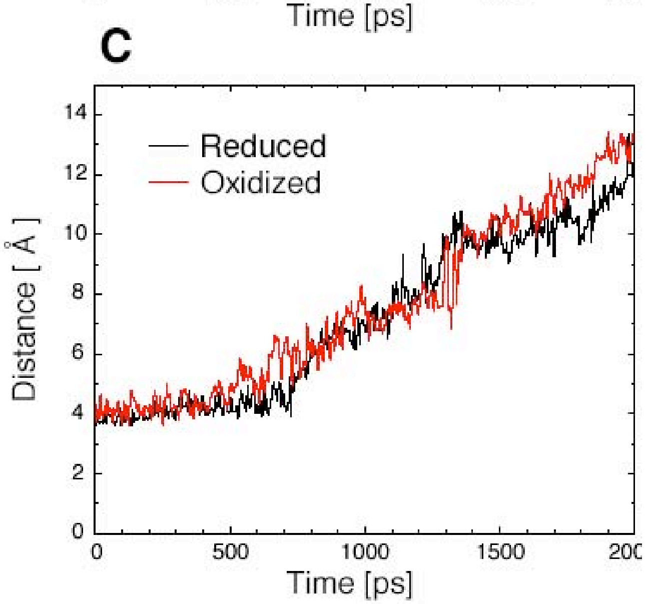


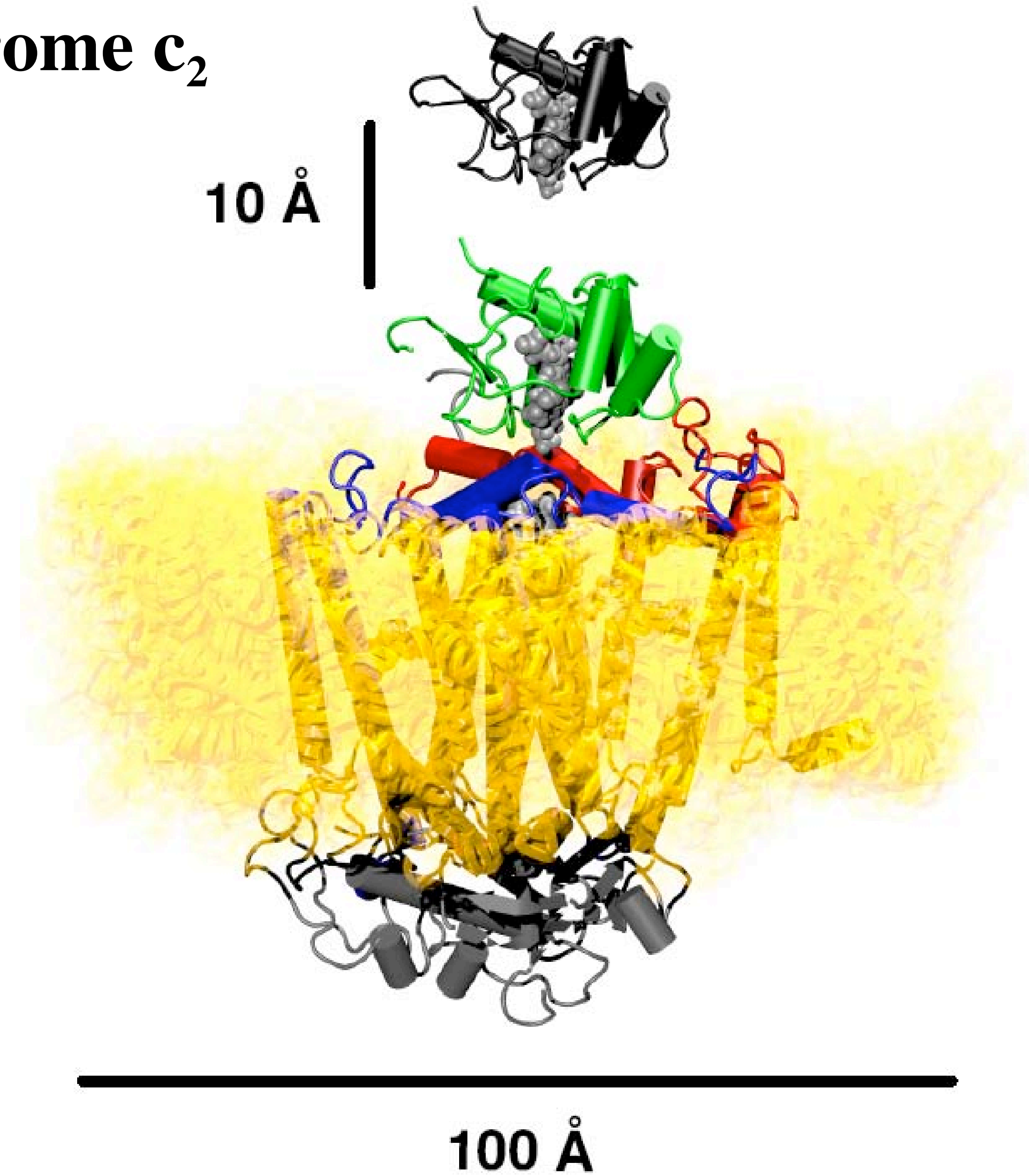




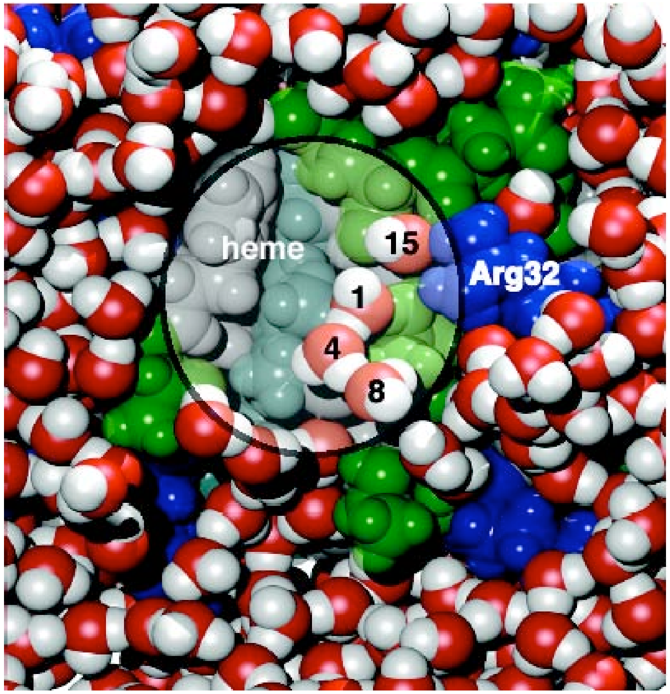
Docking of Cytochrome c_2

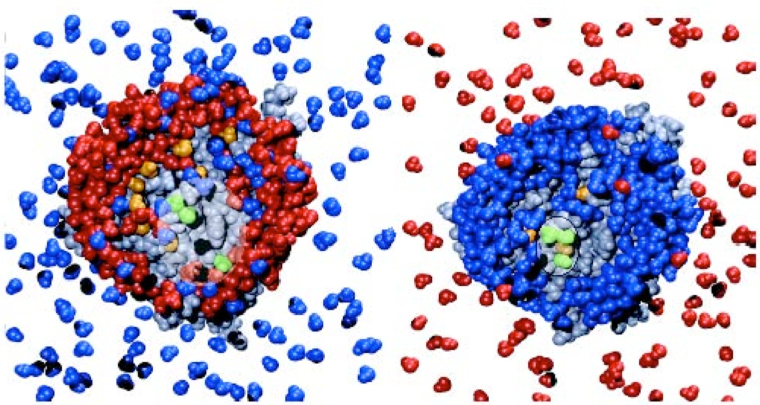


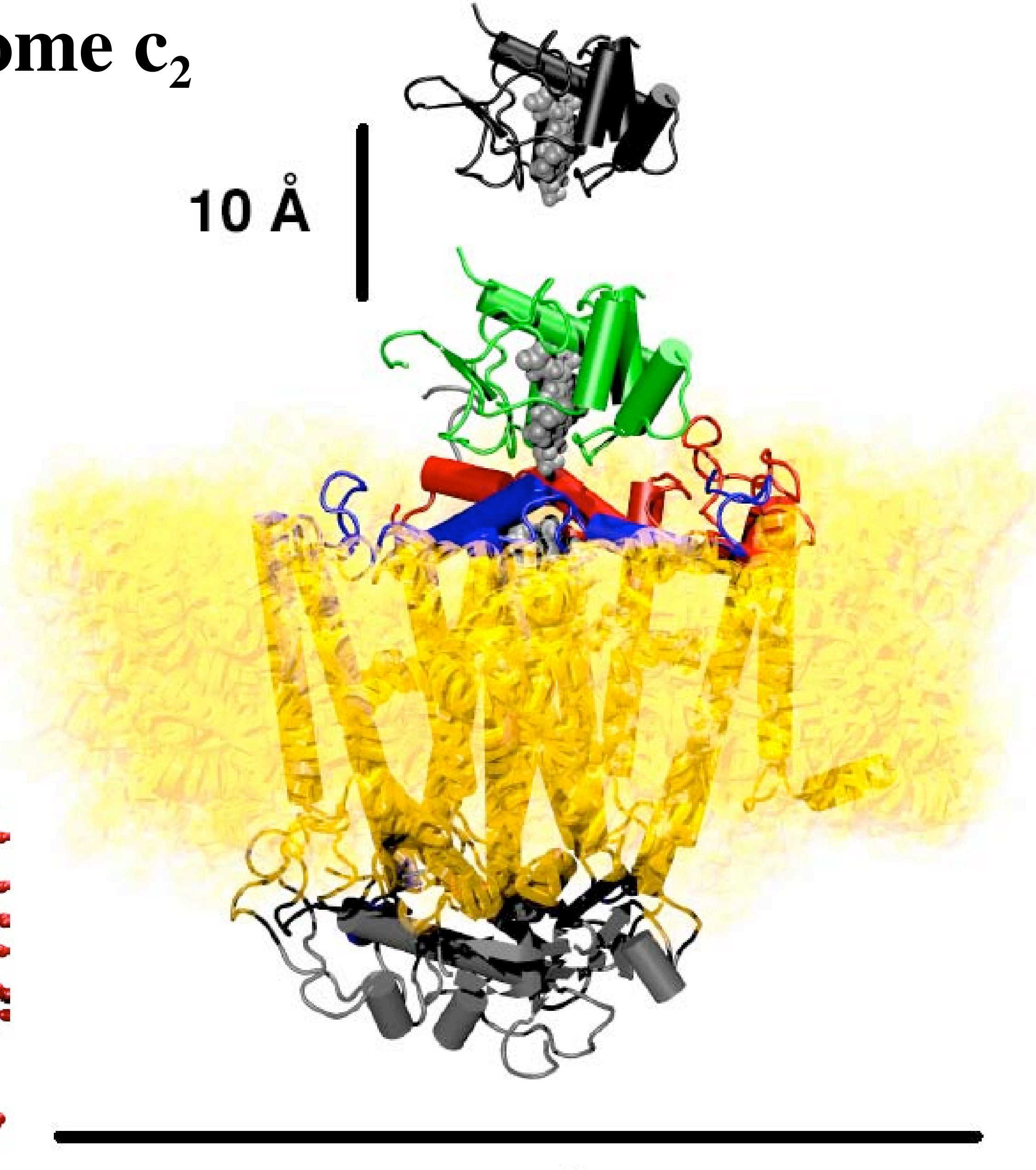




Docking of Cytochrome c_2

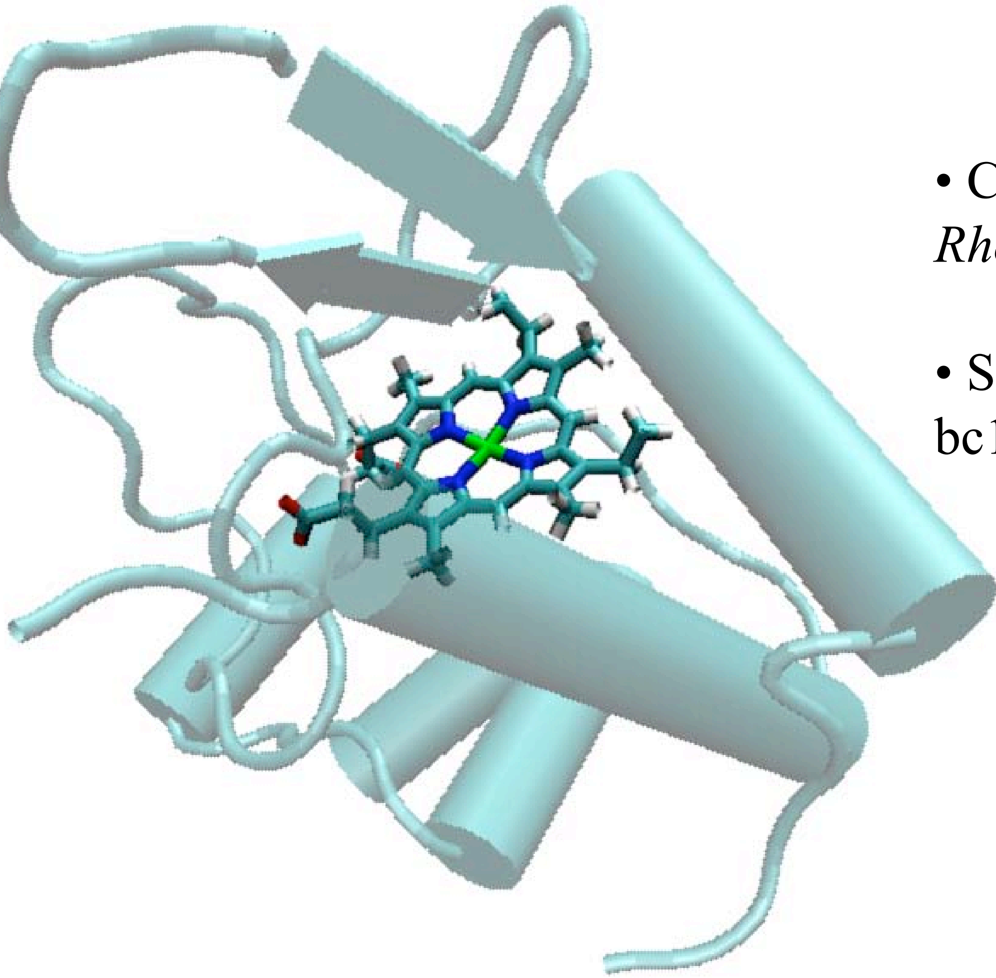






Electron Transfer

Coupling protein motion to electron transfer via MD



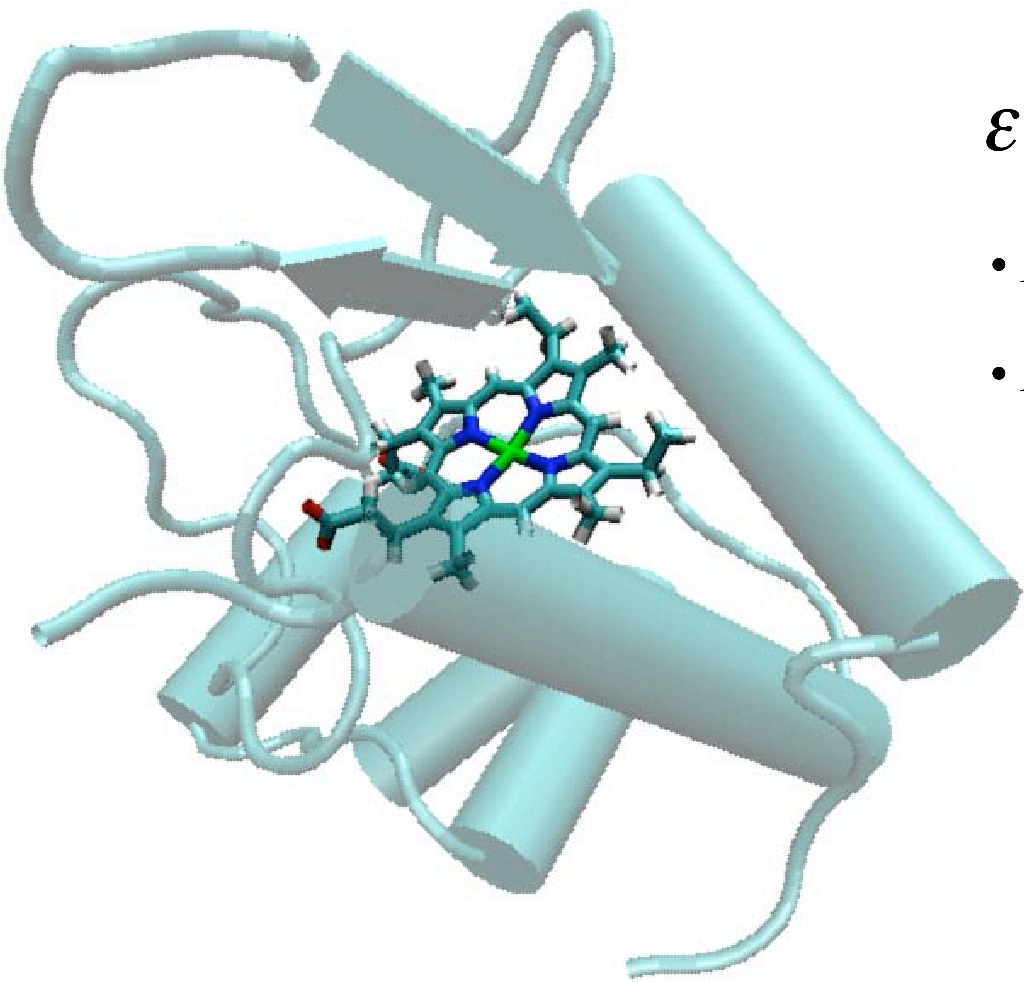
• Cytochrome c_2 from purple bacterium *Rhodobacter sphaeroides*.

• Serves as electron carrier between bc1-complex and reaction center

When the gene encoding cytochrome c_2 is deleted from *Rb. sphaeroides*, the bacterium is unable to grow photosynthetically.

Electron Transfer

The energy gap function



$$\varepsilon(t) = E_P(t) - E_R(t)$$

- *R:* reactant state (reduced)
- *P:* product state (oxidized)

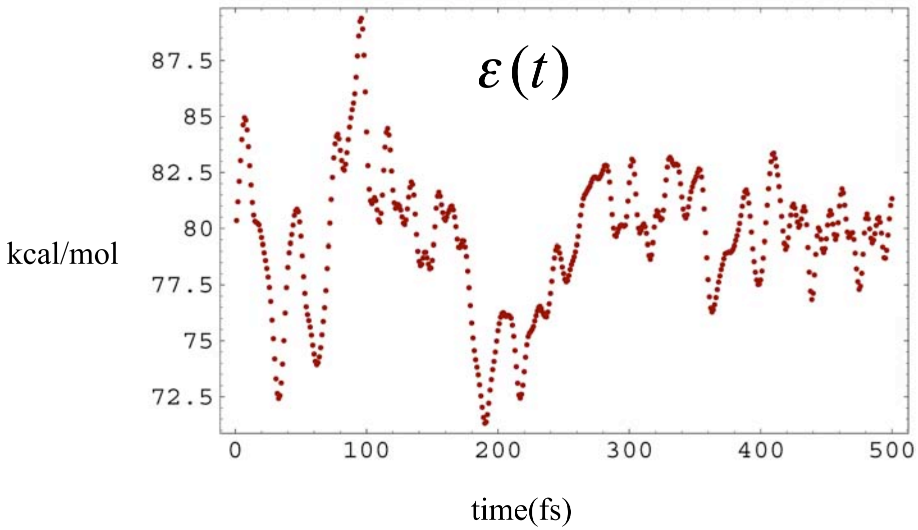
Tutorial:

You will do two consecutive NAMD runs.

- obtain an MD trajectory
- evaluate $\varepsilon(t)$ at each frame of the first trajectory through a second NAMD run

Electron Transfer

MD simulation of the electron transfer process



- ~12000 atoms solvated system

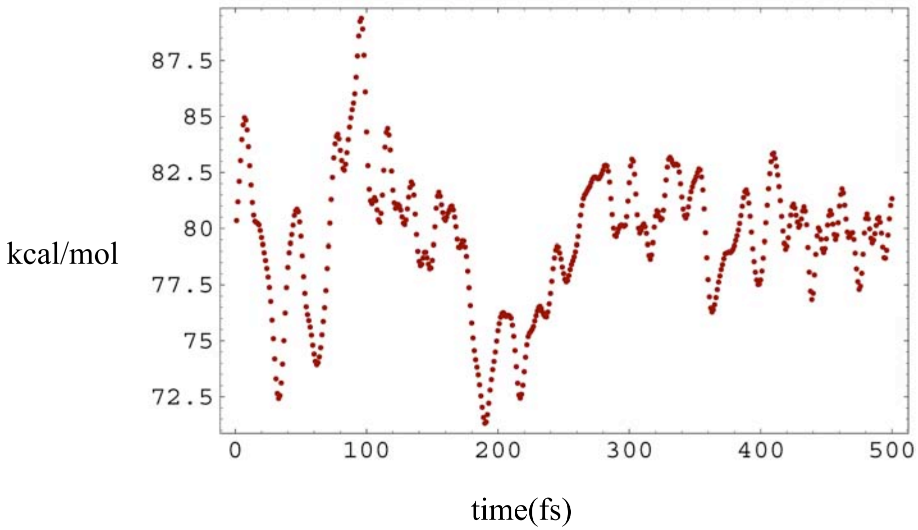
- Already minimized and equilibrated

- You will continue from a restart file

  (so, you do not need to worry about velocity relaxation)

Electron Transfer

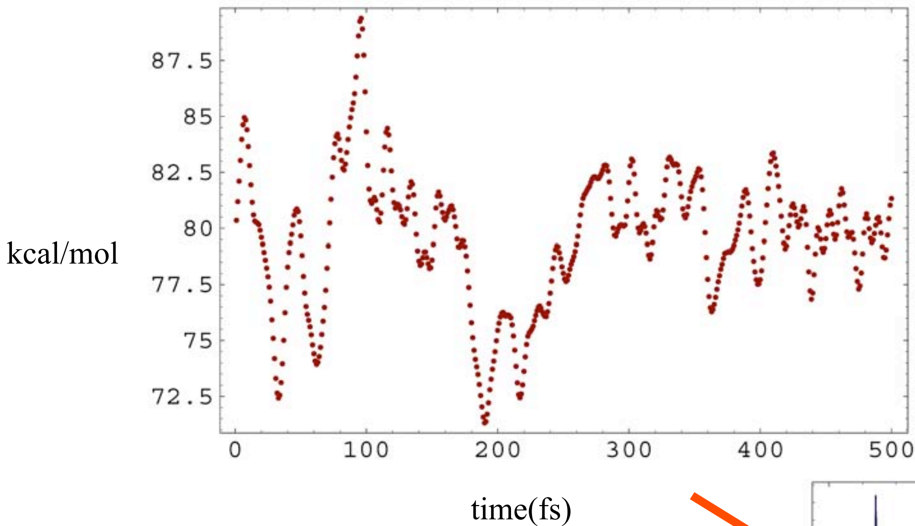
The energy gap function



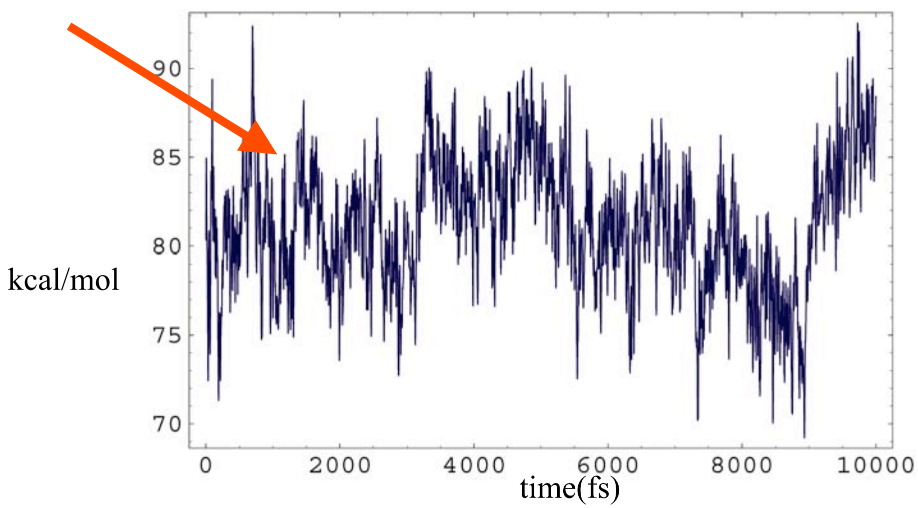
Result from the first 500fs

Electron Transfer

The energy gap function

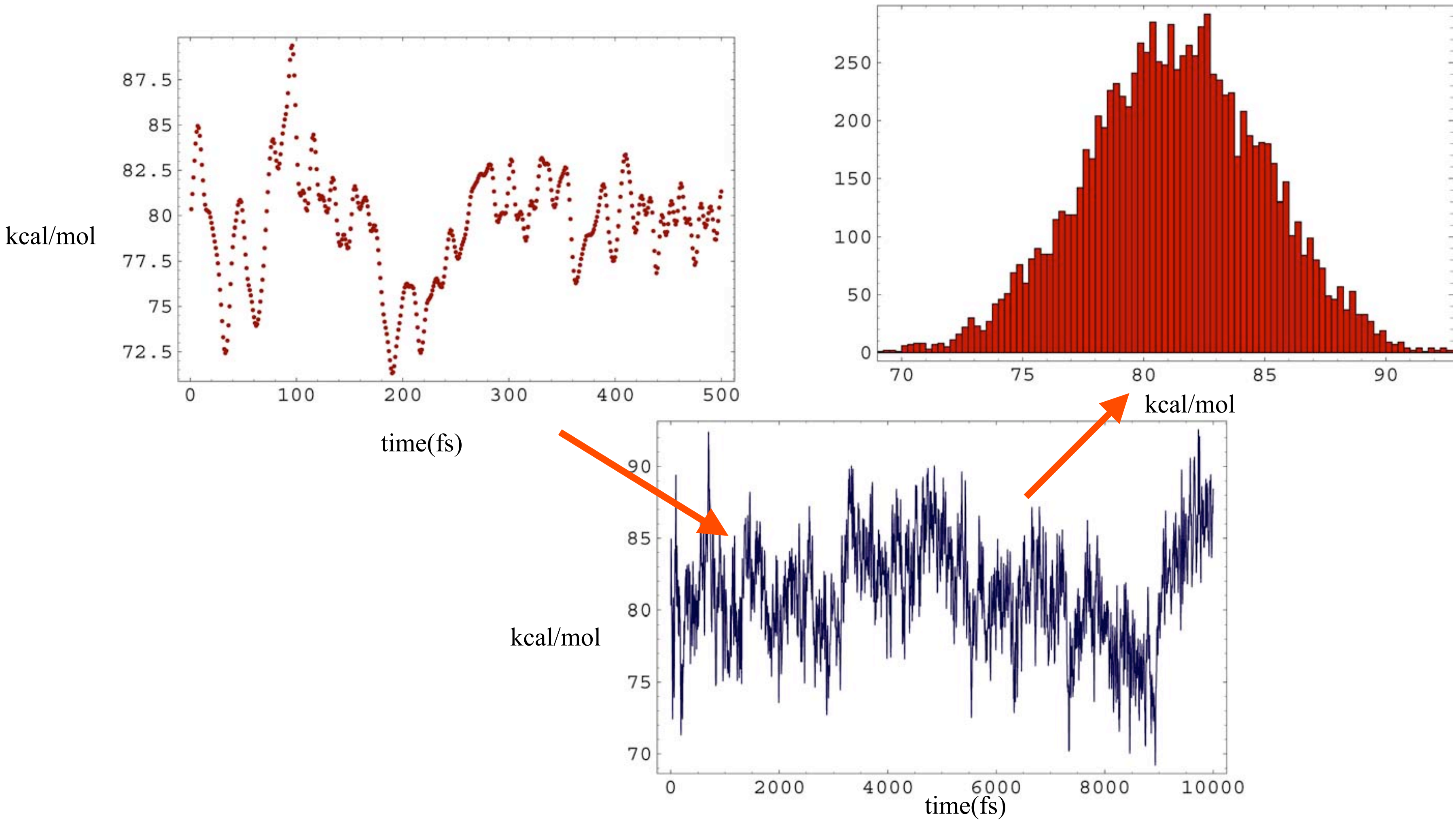


You will be given a longer trajectory…

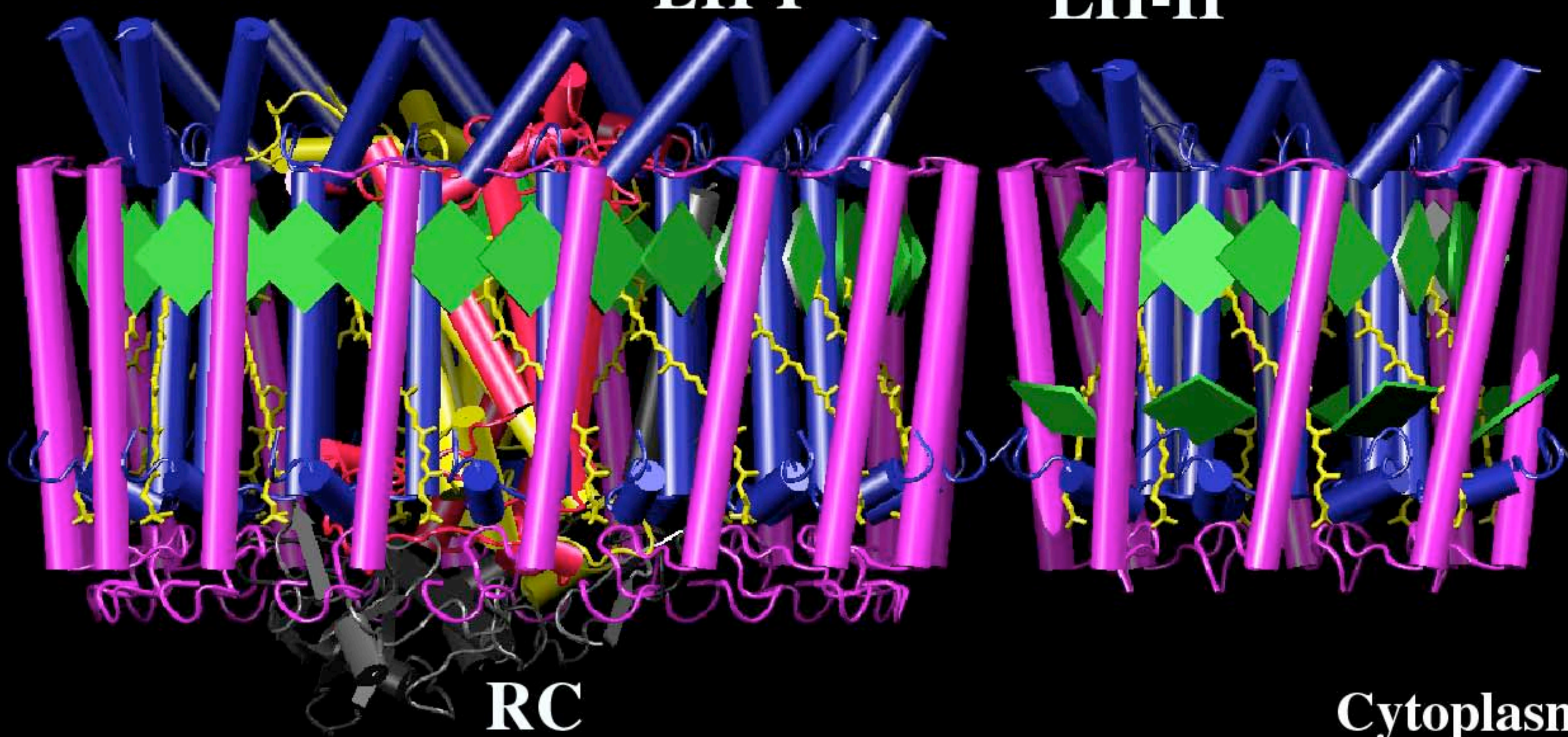


Electron Transfer

The energy gap function

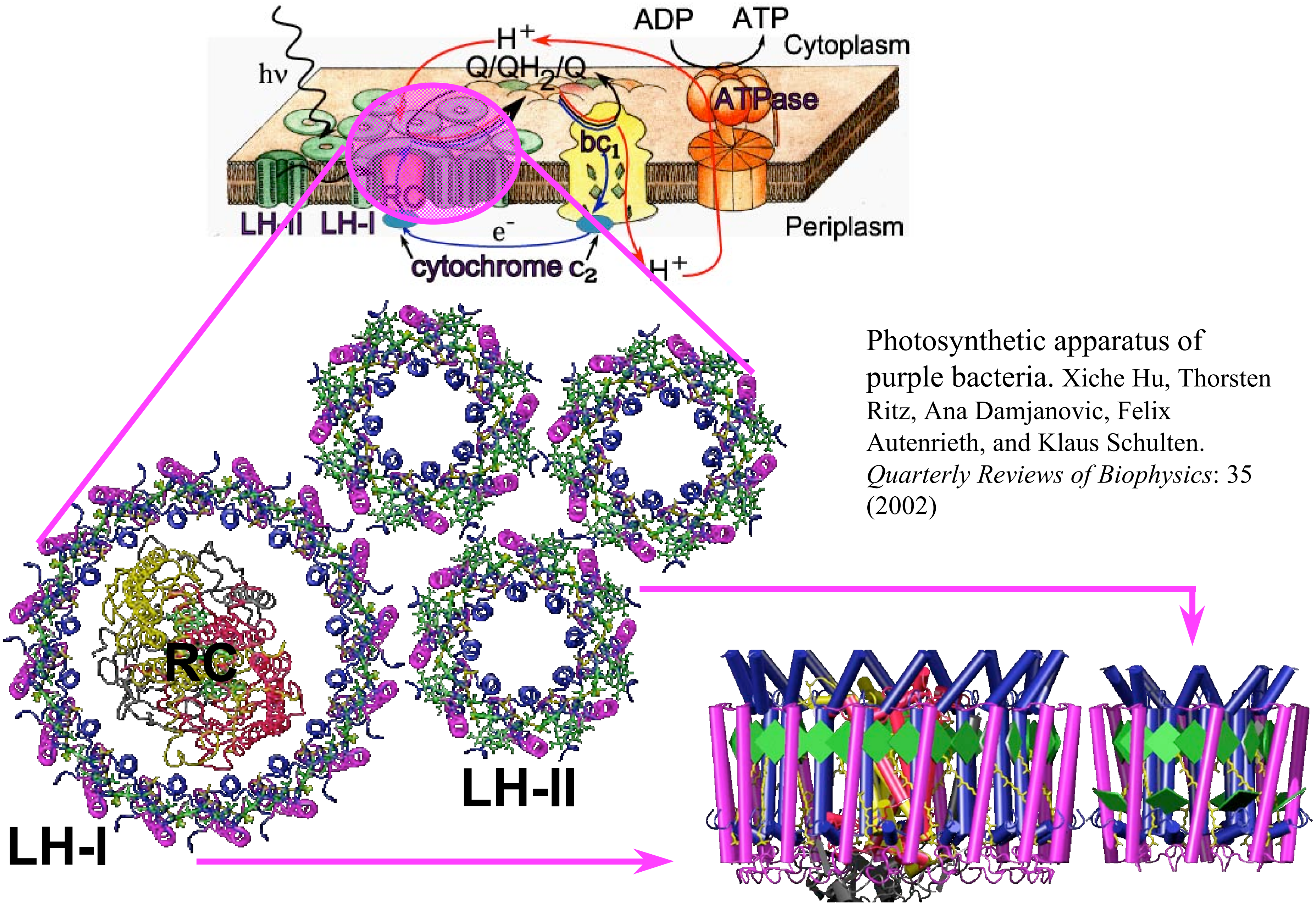


Pigment Organization in the Bacterial Photosynthetic Membrane



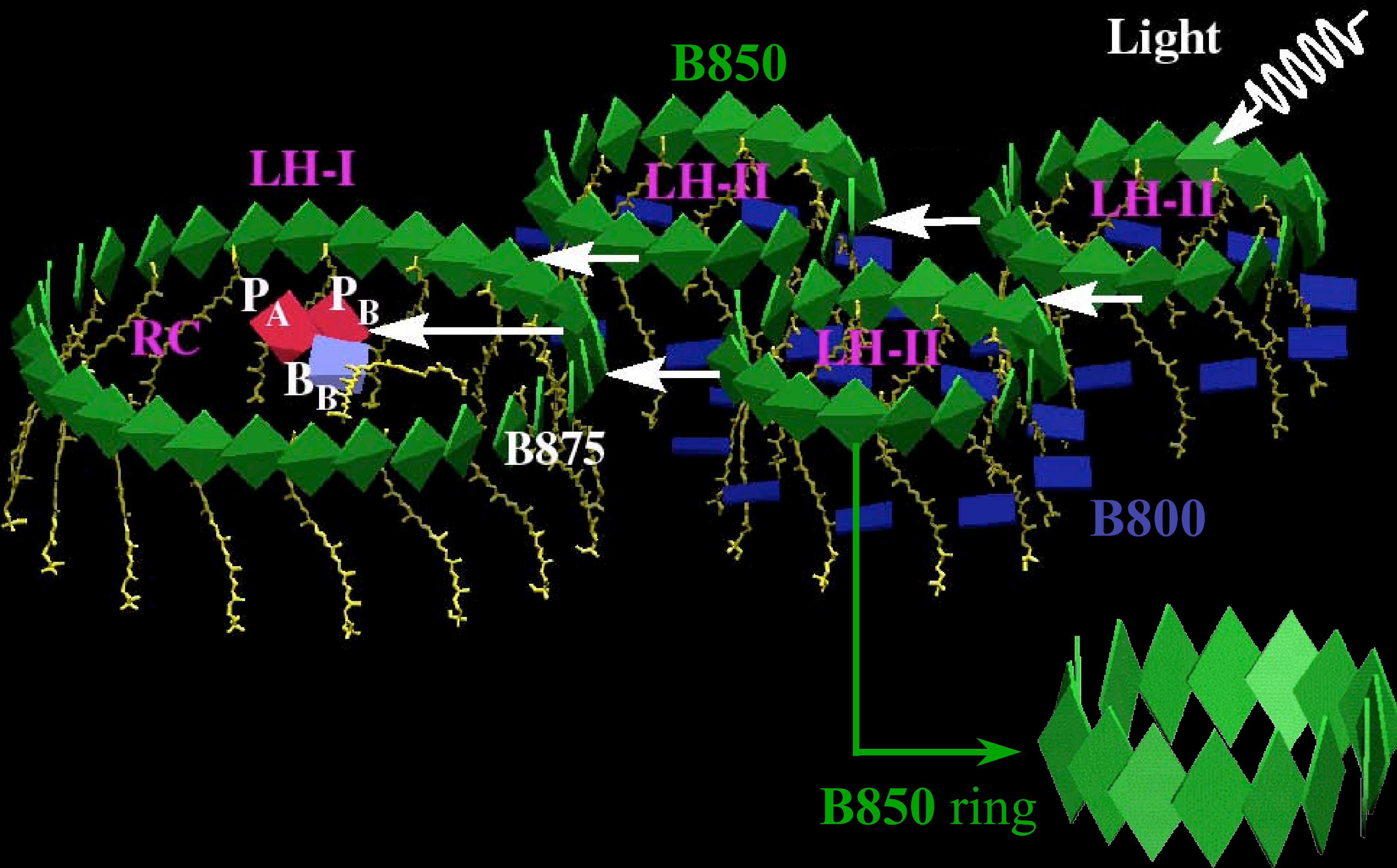
Note the conspicuous arrangement of chlorophyll rings!

Structure of Light Harvesting System

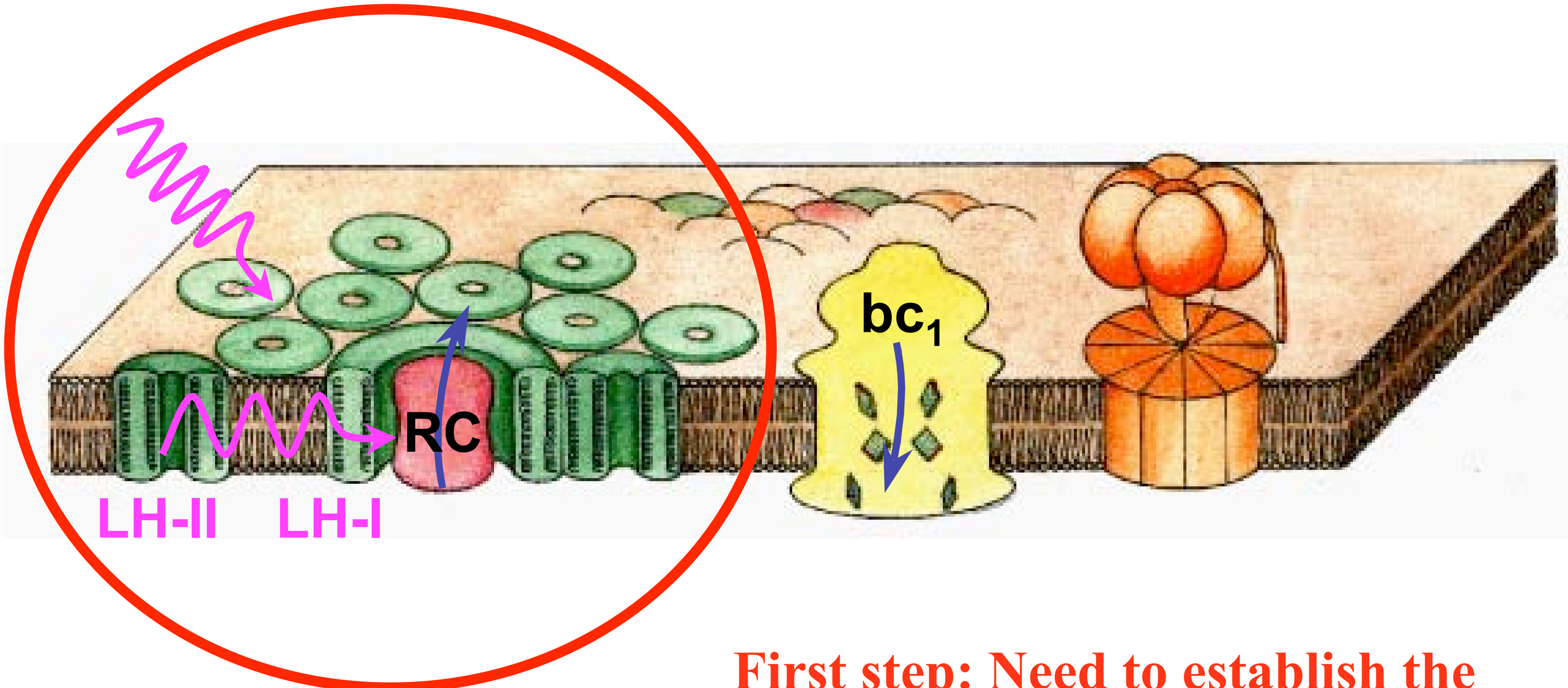


Photosynthetic apparatus of purple bacteria. Xiche Hu, Thorsten Ritz, Ana Damjanovic, Felix Autenrieth, and Klaus Schulten. *Quarterly Reviews of Biophysics*: 35 (2002)

Hierarchical aggregate of *chromophores*

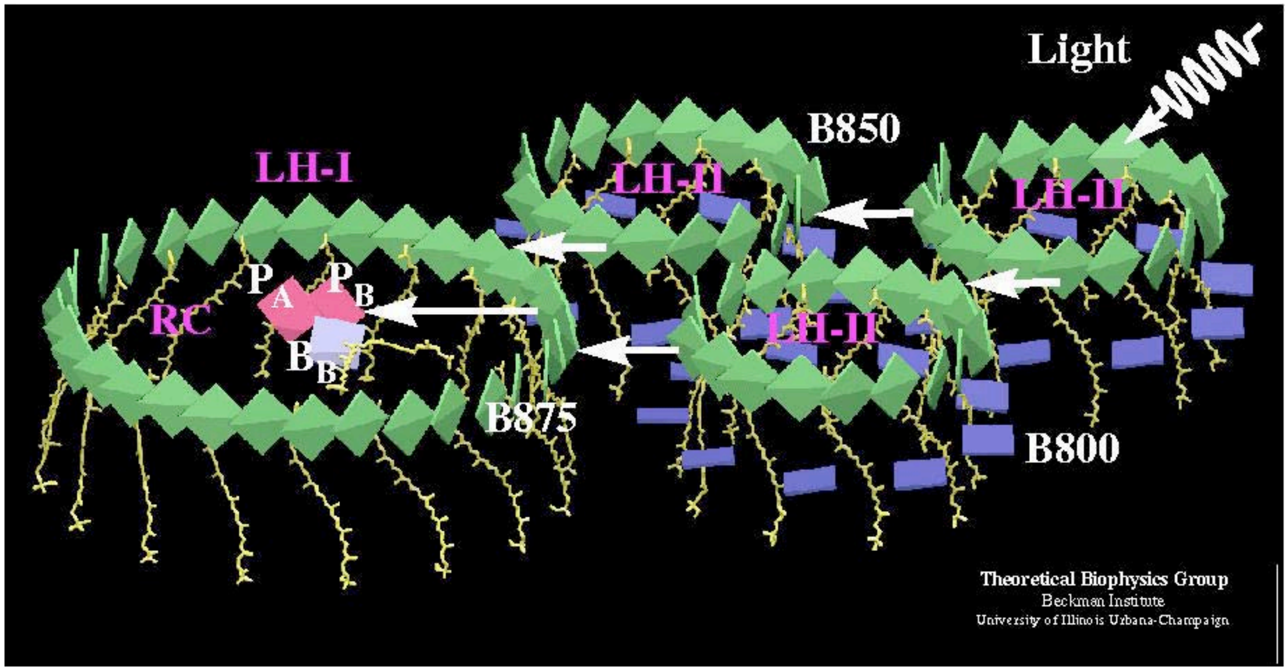


Light Harvesting in Photosynthesis



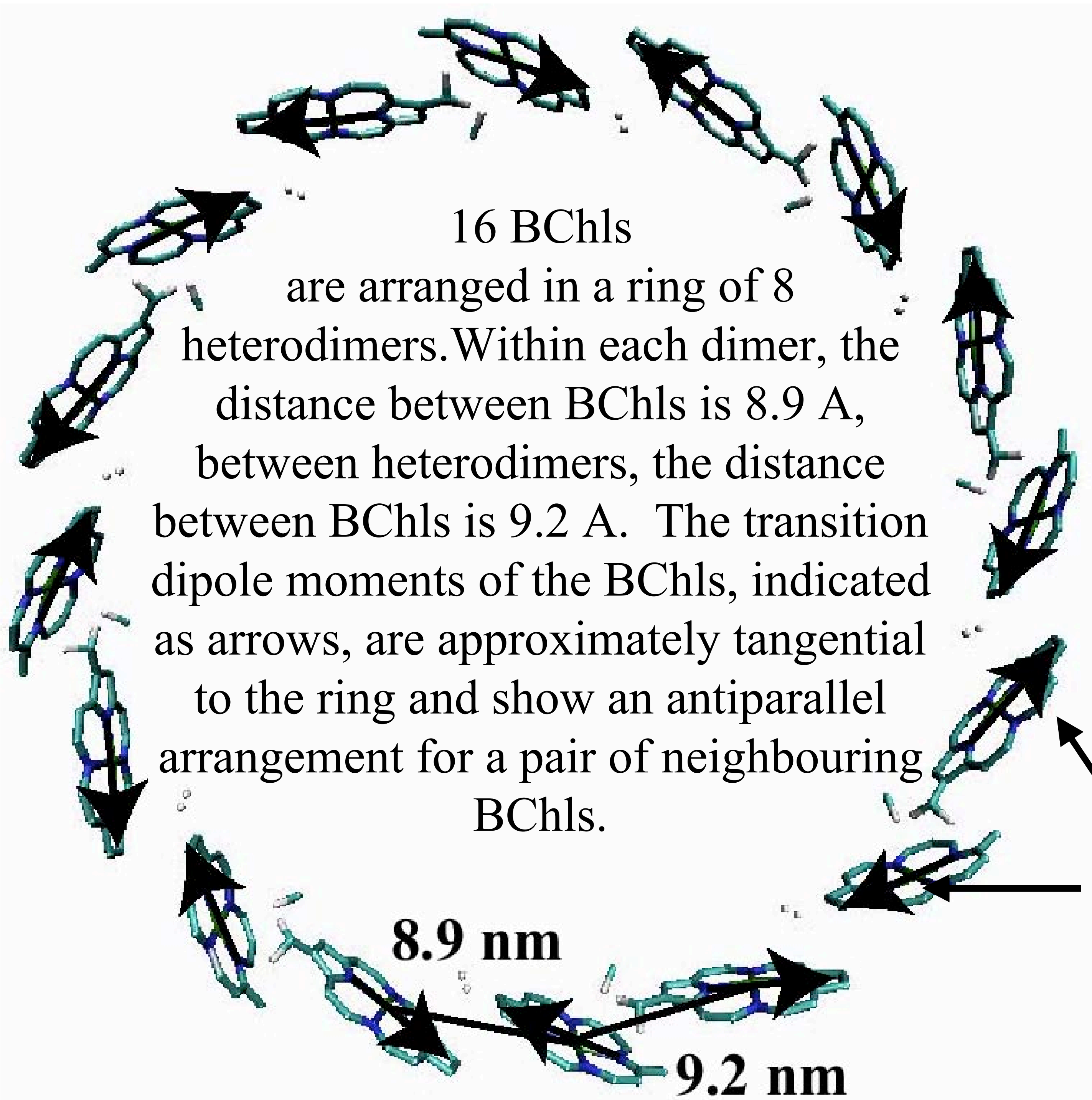
First step: Need to establish the structure of the underlying system

The Hard Earned Model



Here is a lesson to impatient physical scientists to learn: There is no royal road to the model! In the present case and many others, the model is arrived at not through superior inteligence of the physical scientist, but through long (2 years) collaboration with life scientists, in the present case crystallographers (Michel, Cogdell, Glasgow) and electron microscopists (Ghosh, Stuttgart).

B850 BChl aggregate from LH-II of the purple bacterium Rs. molischianum

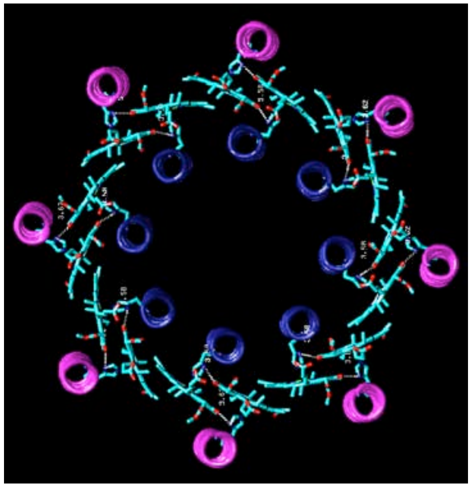


16 BChls are arranged in a ring of 8 heterodimers.Within each dimer, the distance between BChls is 8.9 A, between heterodimers, the distance between BChls is 9.2 A. The transition dipole moments of the BChls, indicated as arrows, are approximately tangential to the ring and show an antiparallel arrangement for a pair of neighbouring BChls.

Eigenvalue Problem for a Circular Dimerized Aggregate

Ring of 2N chlorophylls described by the basis states

$$|n\rangle = |\mathrm{BChl}_1, \mathrm{BChl}_2, \ldots, \mathrm{BChl}_n^*, \ldots, \mathrm{BChl}_{2N}\rangle \ , n = 1, \ldots, 2N$$

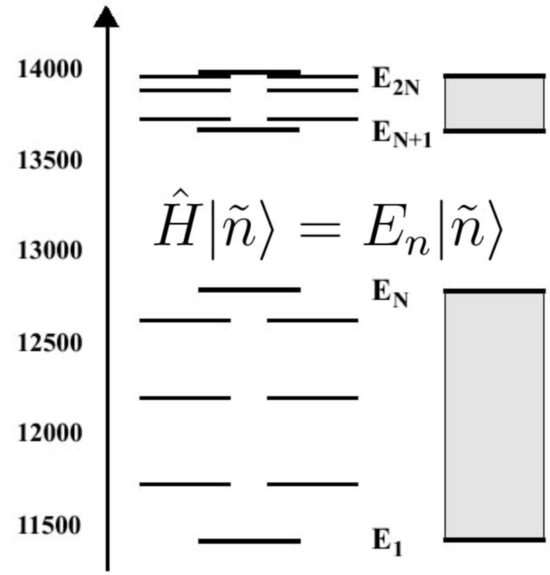


$$H = \begin{pmatrix} \varepsilon_0 & v_1 & W_{1,3} & W_{1,4} & \cdots & . & W_{1,2N-1} & v_2 \\ v_1 & \varepsilon_0 & v_2 & W_{2,4} & \cdots & . & W_{2,2N-1} & W_{2,2N} \\ W_{3,1} & v_2 & \varepsilon_0 & v_1 & \cdots & . & W_{3,2N-1} & W_{3,2N} \\ W_{4,1} & W_{4,2} & v_1 & \varepsilon_0 & \cdots & . & . & . \\ . & & & & & & . & . \\ . & & W_{jk} = C\left(\dfrac{\vec{d}_j \cdot \vec{d}_k}{{r_{jk}}^3} - \dfrac{3(\vec{r}_{jk}\cdot\vec{d}_j)\,(\vec{r}_{jk}\cdot\vec{d}_k)}{{r_{jk}}^5}\right) & & & & . & . \\ . & & & & & & . & . \\ . & . & . & . & \cdots & \varepsilon_0 & v_2 & W_{2N-2,2N} \\ . & . & . & . & \cdots & v_2 & \varepsilon_0 & v_1 \\ v_2 & . & . & . & \cdots & W_{2N,2N-2} & v_1 & \varepsilon_0 \end{pmatrix}$$

N fold axis

$$|\widetilde{n,\beta}\rangle = \frac{1}{\sqrt{N}} \sum_{k=1}^{N} \exp(2ikn\pi/N)\,|k,\beta\rangle$$

Dimerization: 2-D vectors



$$\hat{H}|\tilde{n}\rangle = E_n|\tilde{n}\rangle$$

$$E_1 = \varepsilon_0 + 1.942v_3 - \sqrt{0.576{v_3}^2 + (v_1 + v_2 - 0.638v_3)^2}$$
$$E_8 = \varepsilon_0 - 1.513v_3 - \sqrt{0.089{v_3}^2 + (v_1 - v_2 + 0.038v_3)^2}$$
$$E_9 = \varepsilon_0 - 1.513v_3 + \sqrt{0.089{v_3}^2 + (v_1 - v_2 + 0.038v_3)^2}$$
$$E_{16} = \varepsilon_0 + 1.942v_3 + \sqrt{0.576{v_3}^2 + (v_1 + v_2 - 0.638v_3)^2}$$

Quantum Chemical Determination of Aggregate

$$\hat{H} = \begin{pmatrix} c & v_1 & & & & v_2 \\ v_1 & c & v_2 & & & \\ & v_2 & c & v_1 & W_{i,j} & \\ & & & \ddots & & \\ & W_{i,j} & & & \ddots & \\ v_2 & & & & v_1 & c \end{pmatrix}$$

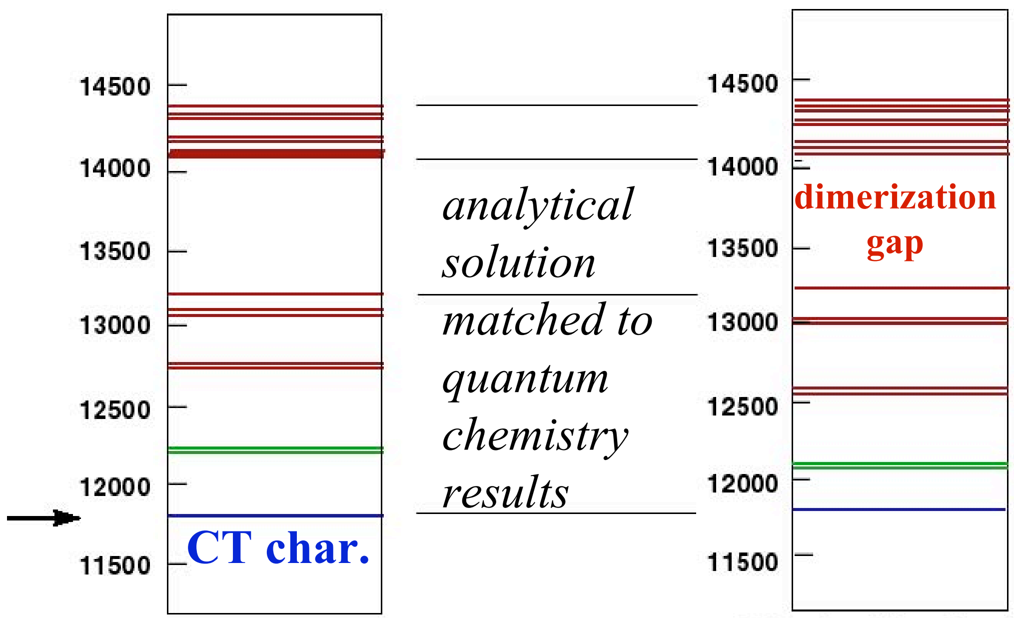
Effective Hamiltonian for Q_y excitations of the B850 ring

Due to circular symmetry and co-planar arrangement of transition dipole moments, degenerate electronic state $E_{2,3}$ carries almost all oscillator strength.

This establishes effective Hamiltonian!

no adjustable parameters

ZINDO/S calculations **effective Hamiltonian calculations**



Zerner et al. **Effective Hamiltonian**

long range coupling narrows band

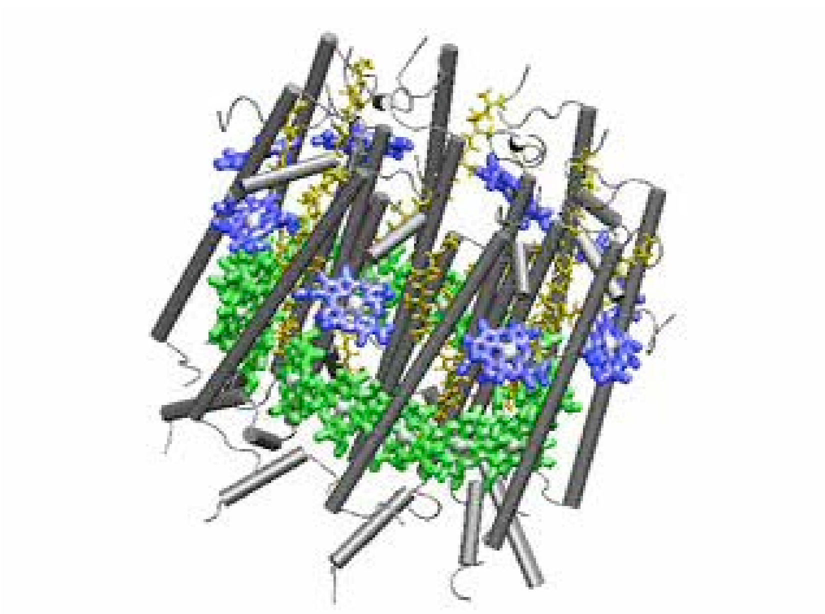
J. Phys. Chem., *B102*, 7640 (1998)
J. Phys. Chem., *B101*, 3854 (1997)
J. Lumin. *76-78*, 310 (1998)

allowed states

$$W_{jk} = C\left(\frac{\vec{d}_j \cdot \vec{d}_k}{r_{jk}{}^3} - \frac{3(\vec{r}_{jk} \cdot \vec{d}_j)\,(\vec{r}_{jk} \cdot \vec{d}_k)}{r_{jk}{}^5}\right)$$

The Effect of Dynamic Disorder

Molecular Dynamics (MD) Simulation



LH2 in membrane: 85,000 atoms; equilibrated for 2ns with NAMD2; NpT ensemble; periodic boundary condition; full electrostatics (PME)

Followed by 0.8ps simulation, trajectory output every 2fs with quantum chemistry calc. of exc. energy, interpolated to "sample" every 0.5 fs

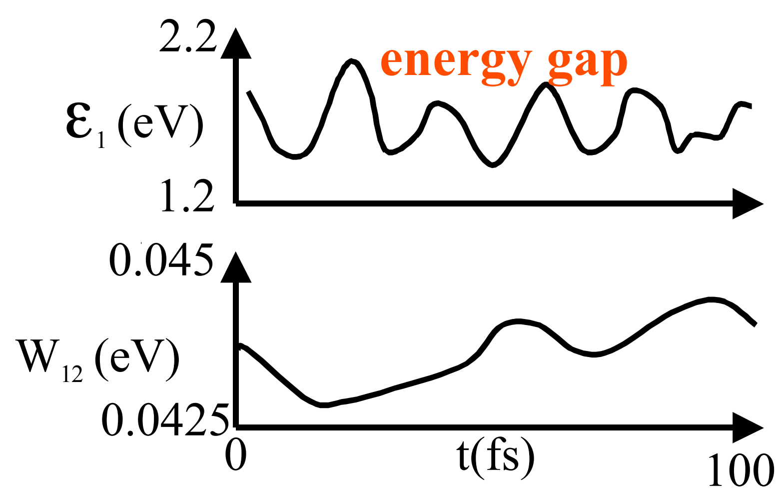
Gaussian 98, HF/CIS, STO-3G basis

from QC → $\epsilon_2(t)$

from MD → $W_{ij}(t)$

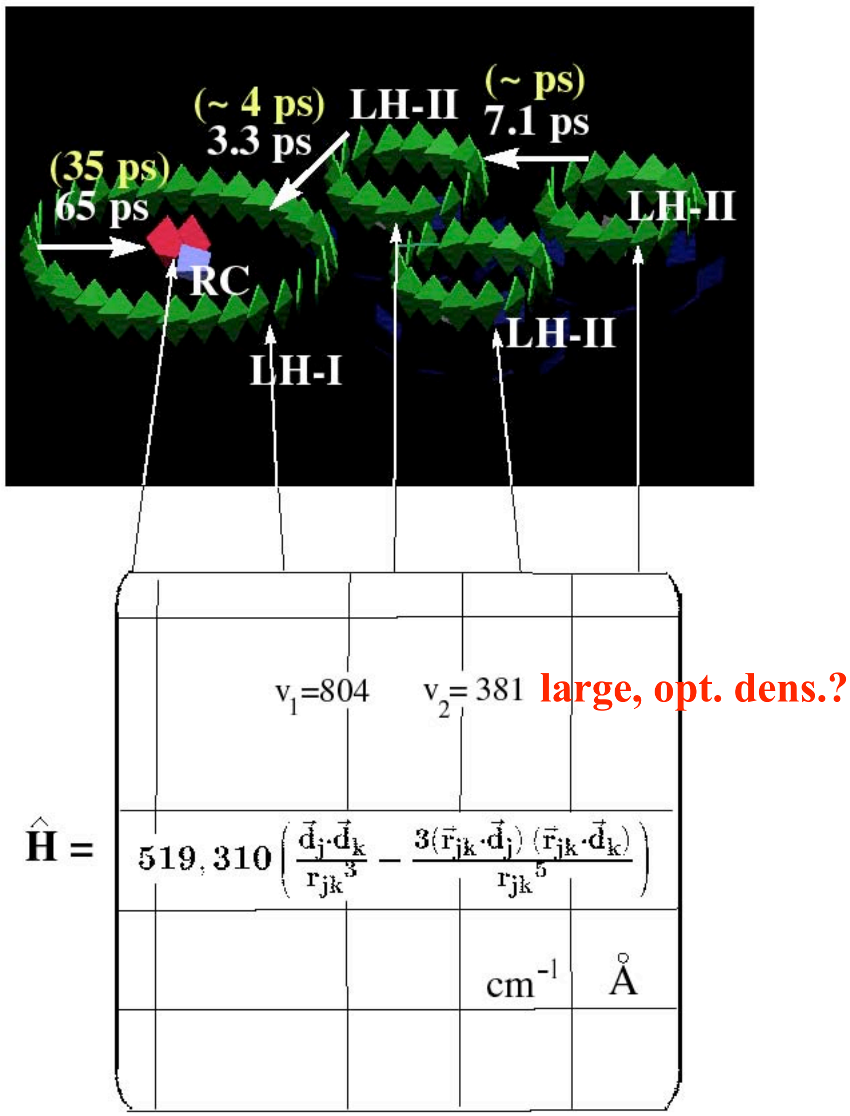
$$\hat{H}(t)^{exc} = \begin{pmatrix} \epsilon_1(t) & & & & W_{ij}(t) \\ & \epsilon_2(t) & & & \\ & & \ddots & & \\ & W_{ij}(t) & & \ddots & \\ & & & & \epsilon_{16}(t) \end{pmatrix}$$

$$W_{jk} = C\left(\frac{\vec{d}_j \cdot \vec{d}_k}{{r_{jk}}^3} - \frac{3(\vec{r}_{jk}\cdot\vec{d}_j)\,(\vec{r}_{jk}\cdot\vec{d}_k)}{{r_{jk}}^5}\right)$$



Ana Damjanovic, Ioan Kosztin, Ulrich Kleinekathoefer, and Klaus Schulten, Phys. Rev.E, 65:031919 (2002)

Effective Hamiltonian for Entire Photosynthetic Unit

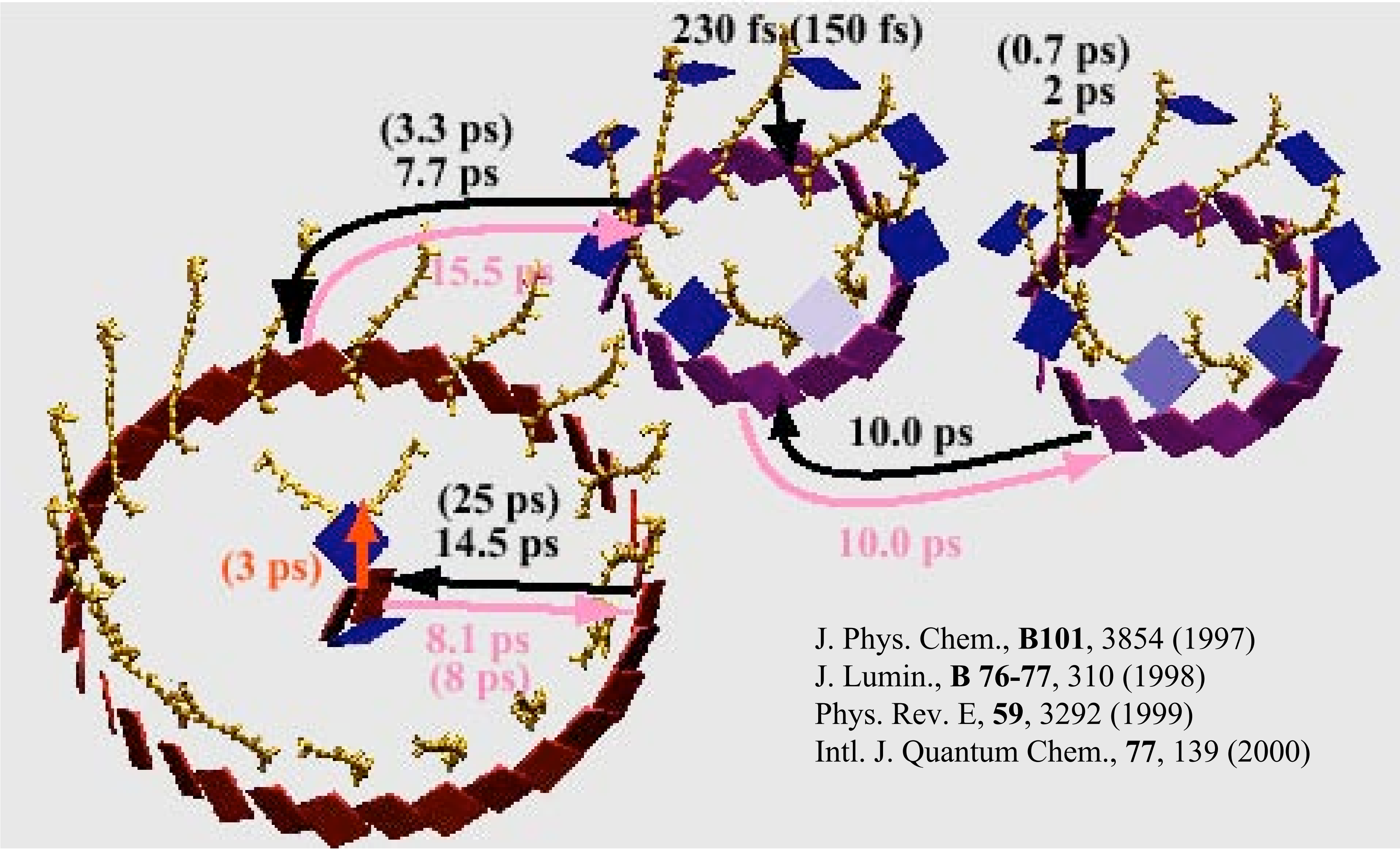


$$k_{DA} = \frac{2\pi}{\hbar} |U_{DA}|^2 J_{DA}$$

$$J_{DA} = \int S_D(E) S_A(E) dE$$ **exp.**

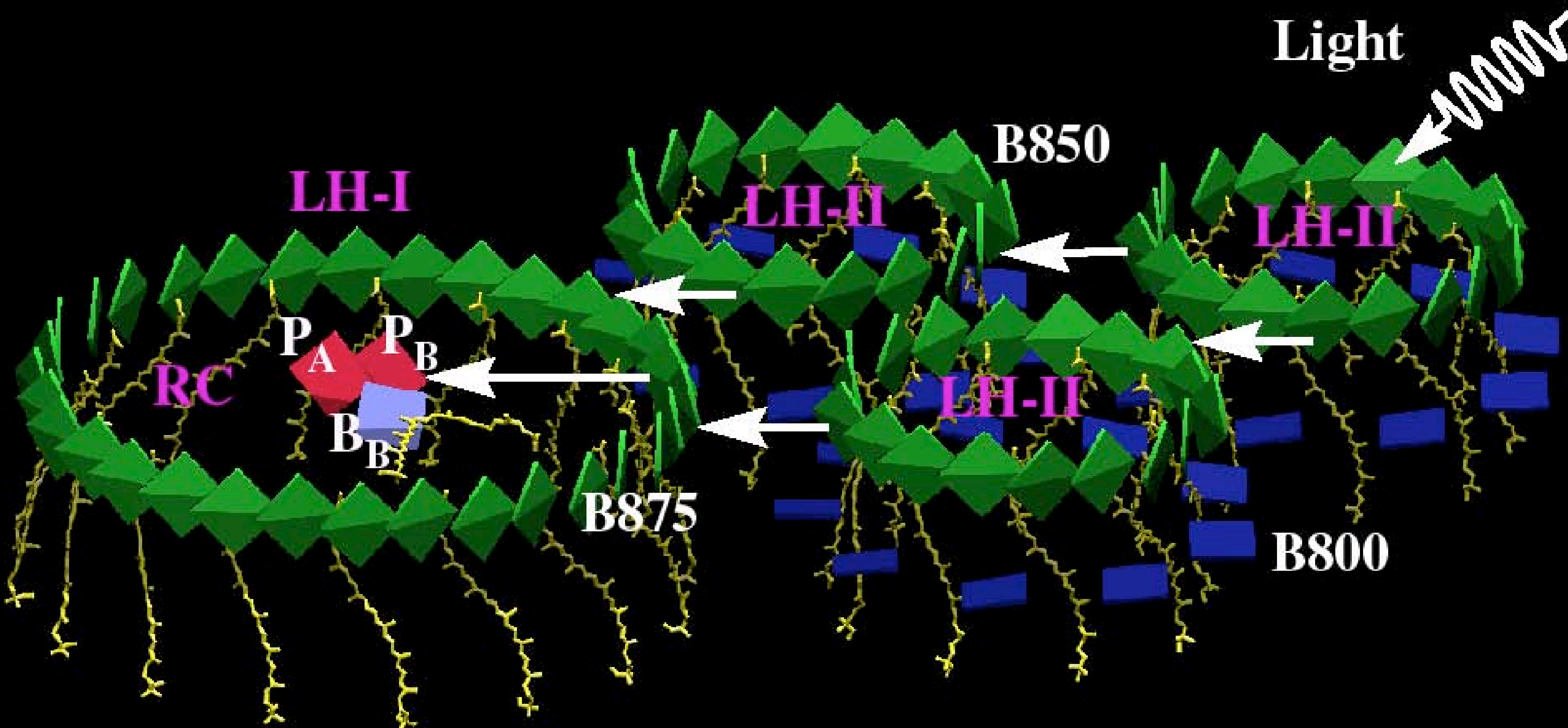
The effective Hamiltonian derived for an LH-II ring is extended to the entire system of light harvesting complexes. i.e., LH-I and LH-IIs, assuming LH-II nearest neighbour couplings and dipolar coupling for non-nearest neighbour interactions, for a geometry of closest packed LH-I and LH-II proteins.

Excitation Transfer in Photosynthetic Unit

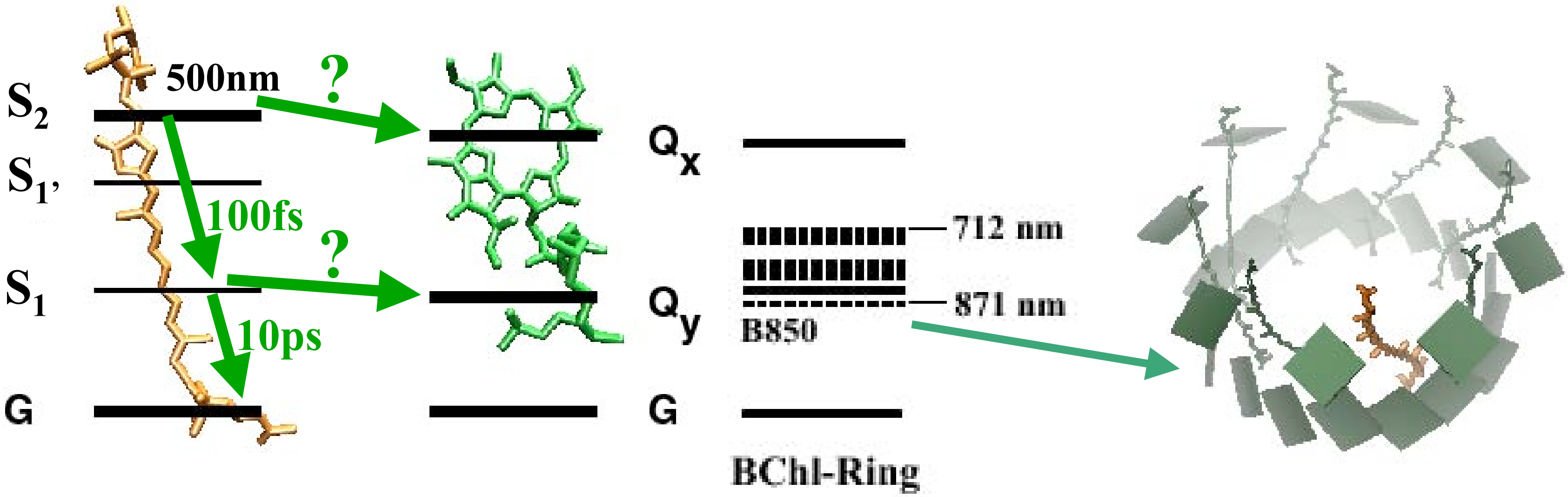


J. Phys. Chem., **B101**, 3854 (1997)
J. Lumin., **B 76-77**, 310 (1998)
Phys. Rev. E, **59**, 3292 (1999)
Intl. J. Quantum Chem., **77**, 139 (2000)

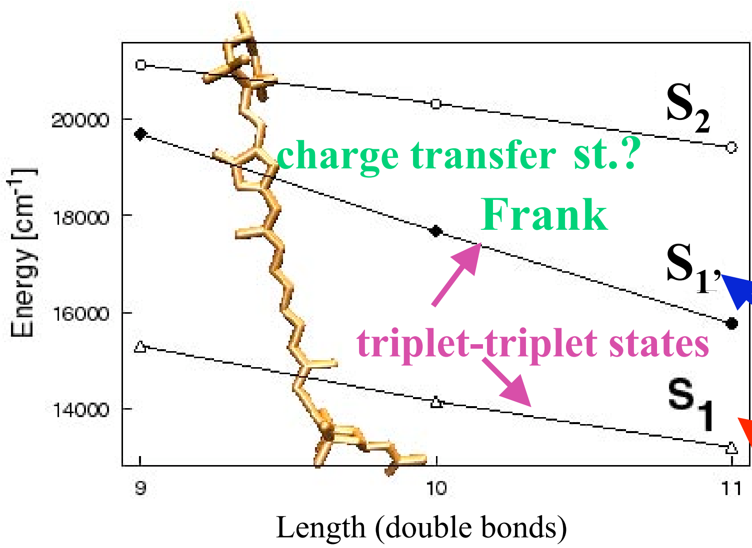
The Role of the Carotenoids in Light Absorption and Excitation Flow



Two Channels for Car-Chl Transfer



Electronic excitations in carotenoids



Correspondence: S_2 => $1B_u^+$ optically allowed

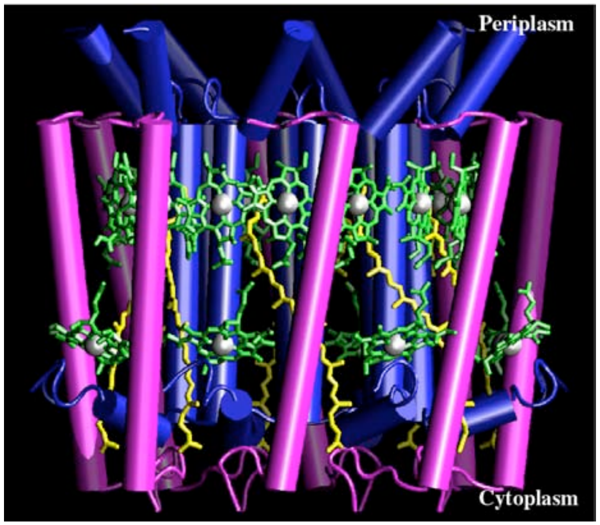
Car ⟷ polyene states

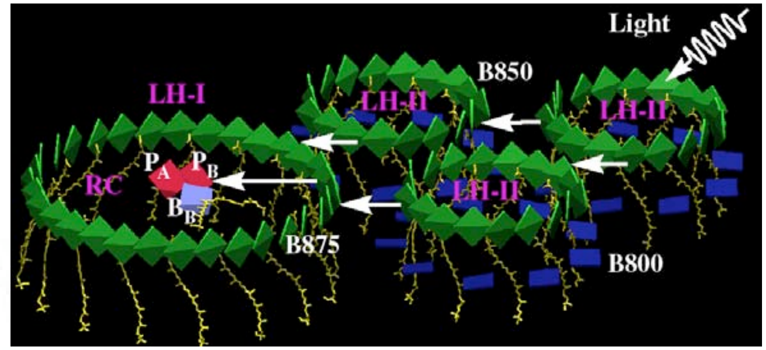
$S_{1'}$ => $1B_u^-$ optically forbidden

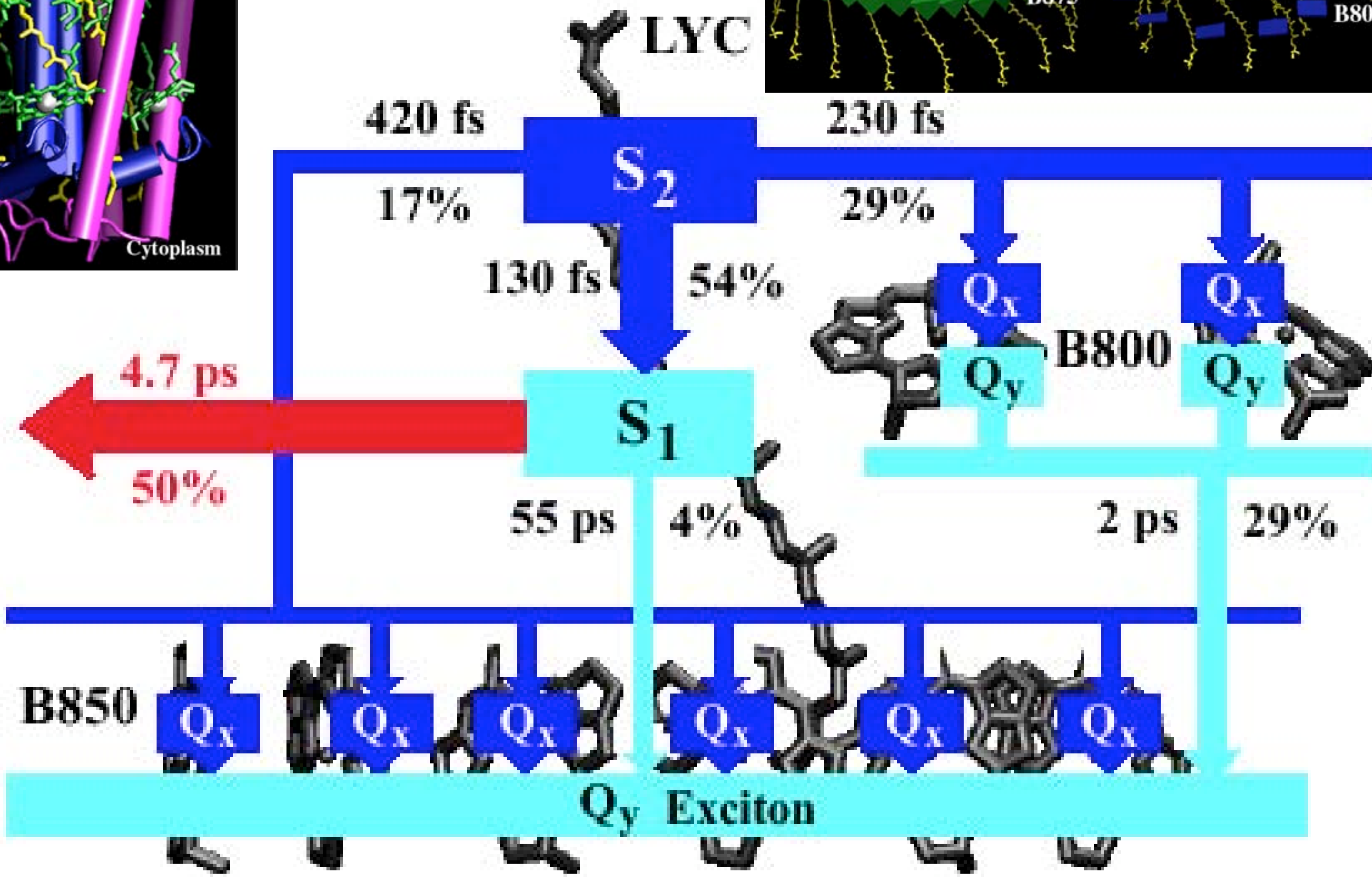
S_1 => $2A_g^-$ optically forbidden

Phys. Rev. B, 36, 4337 (1987) theor.
Chem. Phys. Lett., 299, 187 (1999) exp.
Chem. Phys. Lett., 290, 36 (1998) exp.
Chem. Phys. Lett. 14, 299, 305 (1972) exp., theor.

Conversion times and efficiencies for photons absorbed into the **carotenoid (LYC)** S_2 state in LH2 of *Rs. molischianum*





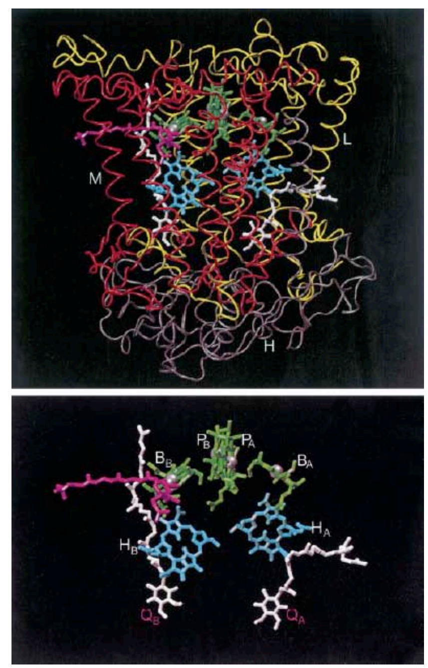


Quarterly Reviews of Biophysics **35**, 1 (2002), pp. 1–62.
DOI: 10.1017/S0033583501003754 Printed in the United Kingdom

Photosynthetic apparatus of purple bacteria

Xiche Hu[1], Thorsten Ritz[2], Ana Damjanović[2], Felix Autenrieth[2]
and Klaus Schulten[2,*]

[1] Department of Chemistry, University of Toledo, Toledo, OH 43606, USA
[2] Beckman Institute and Department of Physics, University of Illinois at Urbana-Champaign, Urbana, IL 61801, USA



The Quantum Physics of Photosynthesis

Thorsten Ritz,[b] Ana Damjanović,[c] and Klaus Schulten*[a]

Biological cells contain nanoscale machineries that exhibit a unique combination of high efficiency, high adaptability to changing environmental conditions, and high reliability. Recent progress in obtaining atomically resolved structures provide an opportunity for an atomic-level explanation of the biological function of cellular machineries and the underlying physical mechanisms. A prime example in this regard is the apparatus with which purple bacteria harvest the light of the sun. Its highly symmetrical architecture and close interplay of biological functionality with quantum physical processes allow an illuminating demonstration of the fact that properties of living beings ultimately rely on and are determined by the laws of physics.

KEYWORDS:

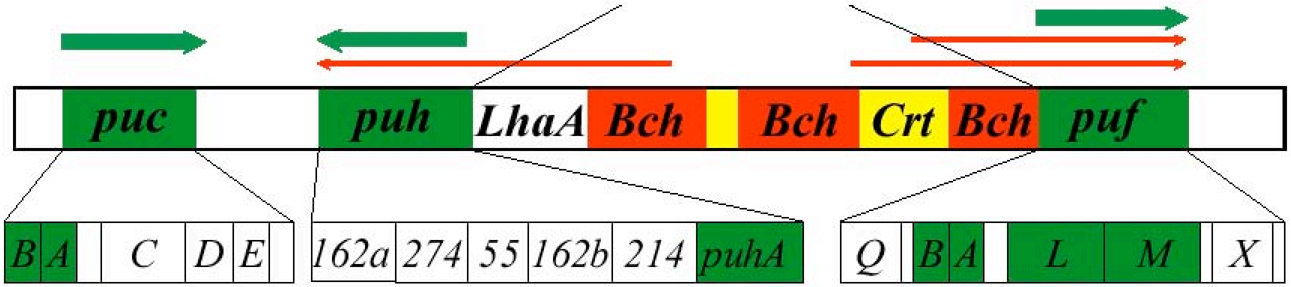
carotenoids · chromophores · electronic excitation transfer · photosynthesis · proteins

  1439-4235/02/03/03 $ 17.50+.50/0

See also: www.ks.uiuc.edu

Genomic Organization of the Light Harvesting Complexes

- BChla metabolism
- carotenoid metabolism

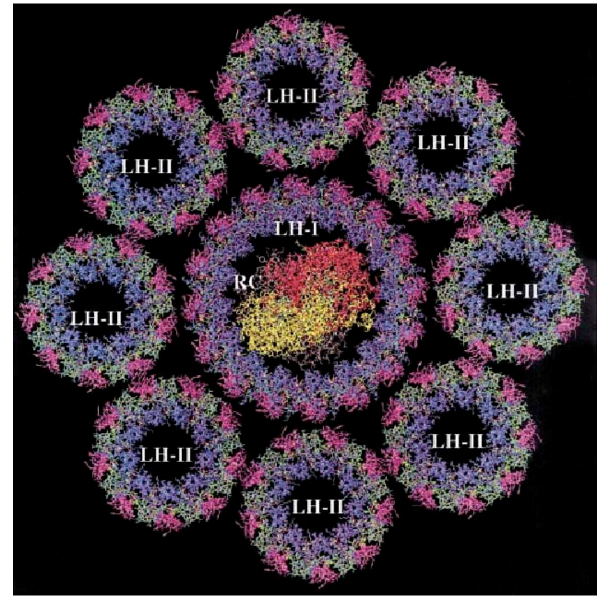


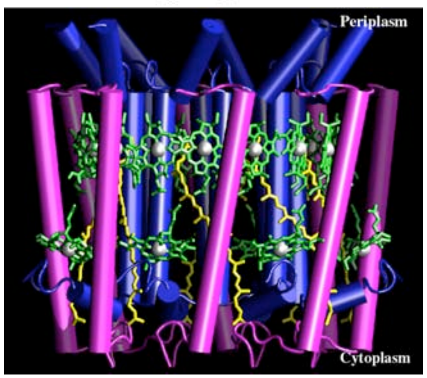
- LH2 apoproteins
- PucC, D, E

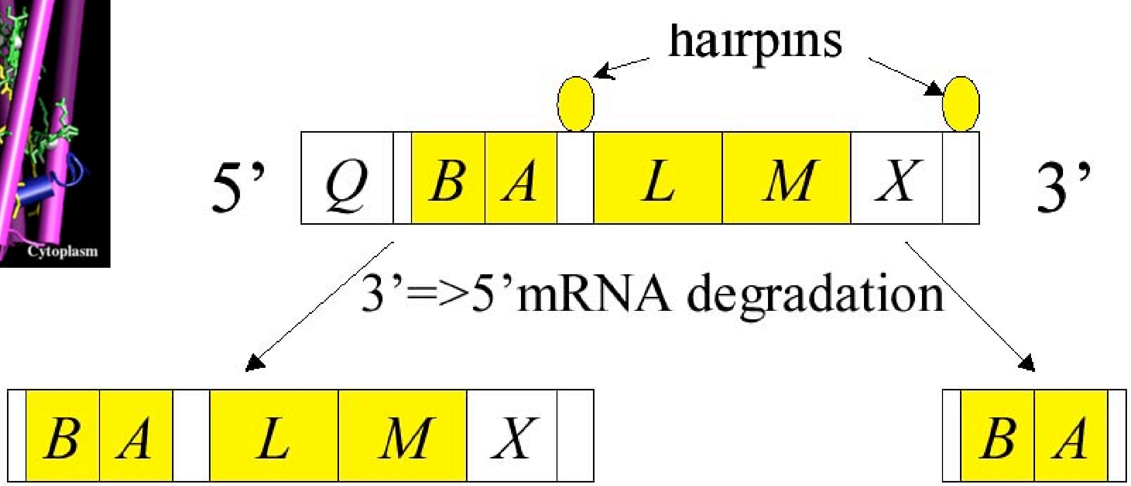
- H-subunit
- 5 ORFs

LhaA = light-harvesting complex assembly

- LH1apoproteins
- L-subunit
- M-subunit
- PufQ, PufX







- half-life 8 min
- half-life > 20 min