DECOHERENCE AND ELECTRON TRANSFERS WITHIN PROTEINS
ARE QUANTUM EFFECTS RELEVANT FOR BIOLOGY ?

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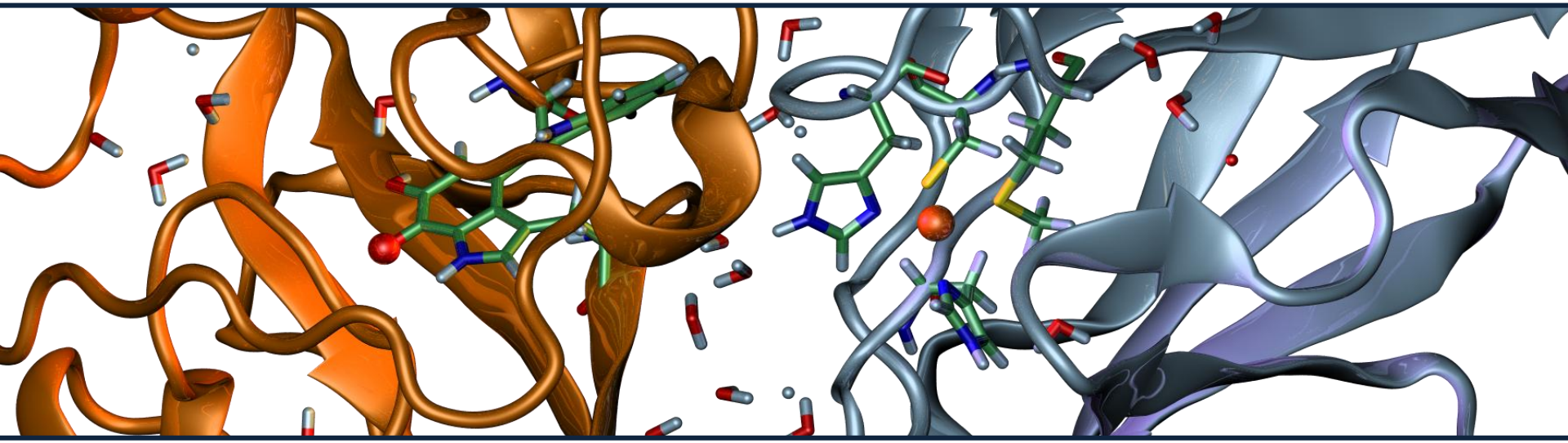


Isabelle Demachy, Bernard Lévy, Fabien Cailliez
Dennis Salahub, Barry Sanders, Jan Rezac

Forum TERATEC
July 1-2 2014

LIFE AT THE MOLECULAR LEVEL

Living cells are composed of small molecules (metabolites), macromolecules (proteins, DNA, RNA, lipids...), ions, water

Biological processes rely on numerous physicochemical processes that take place at the molecular level:

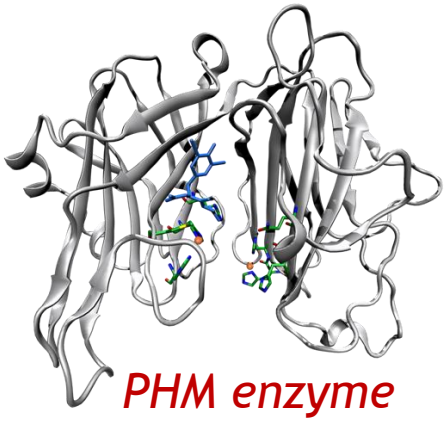
- transport of metabolites, of protons (proton pumps)
- molecular motors (ex ATP synthases)
- synthesis of biomolecules (enzymes)

Our objective is to contribute to the understanding on how physicochemical processes take place in such complex systems

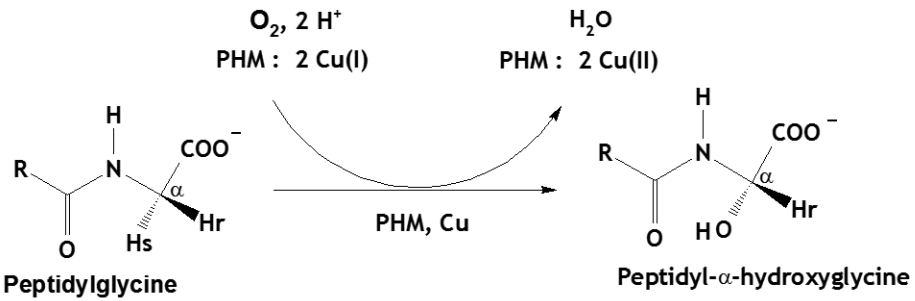
QUANTUM MECHANICS IS MANDATORY FOR UNDERSTANDNG BIOCHEMISTRY

chemical reactions: bond-breakings and bond formations

Enzymatic catalysis, 3D-structures of biomolecule (DNA, proteins...)

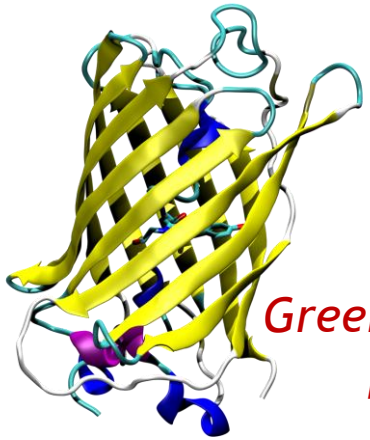


PHM enzyme



Absorption or emission of light by biological chromophores

Fluorescence, bioluminescence …



Green fluorescent proteins

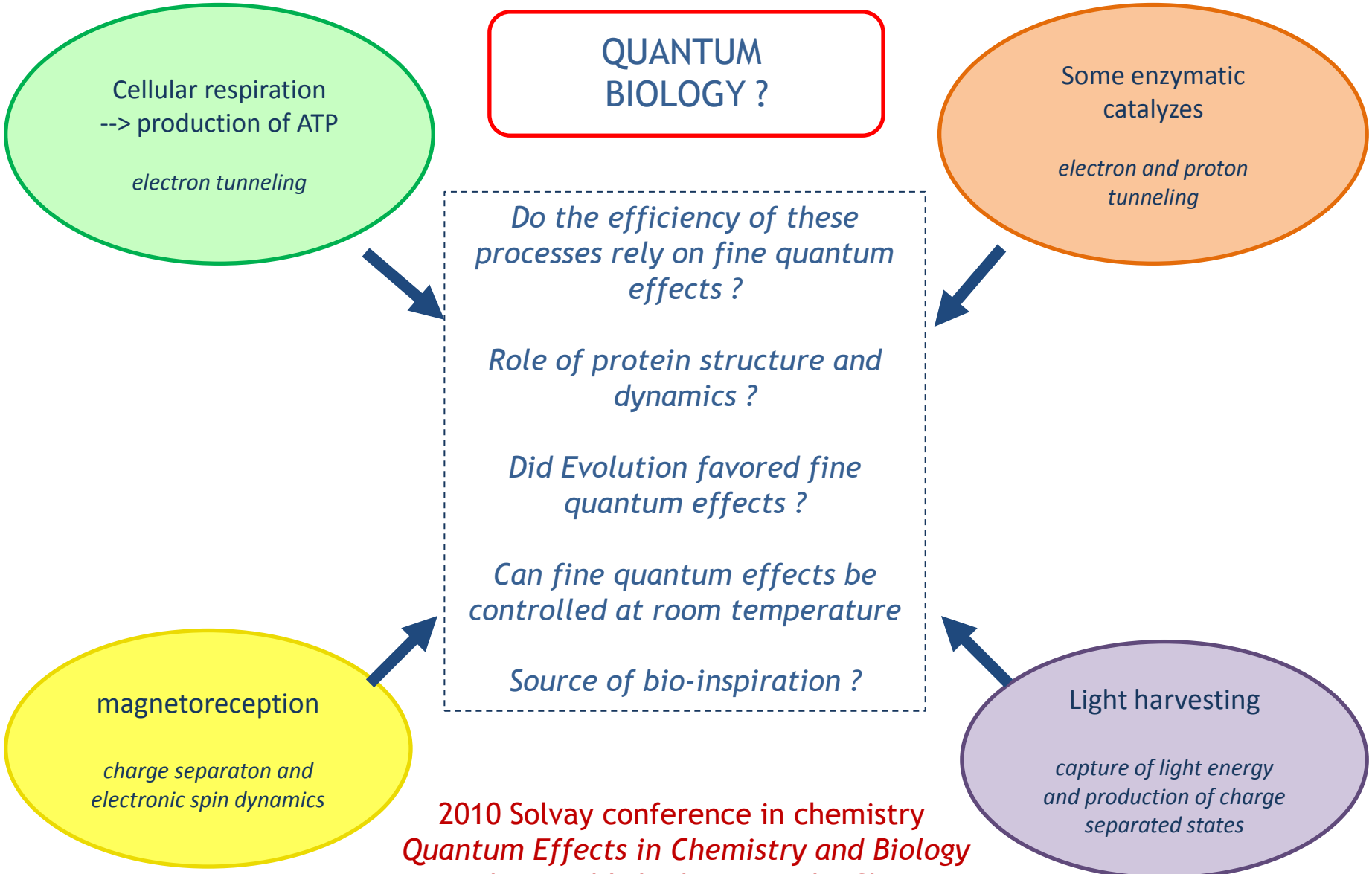
A fine understanding of how enzymes work may inspire strategies for developing efficient artificial catalysts, (biomimetism)

FINE QUANTUM EFFECTS IN BIOLOGY ?

- *Transport of light particles (electrons, protons…) by tunneling*
- *Quantum interferences*
- *Other purely quantum features (e.g. entanglements)*

IS THERE A ROOM FOR "QUANTUM BIOLOGY" ?

THE EMERGING FIELD OF QUANTUM BIOLOGY



2010 Solvay conference in chemistry
Quantum Effects in Chemistry and Biology
proceedings published in Procedia Chemistry

OUTLINE

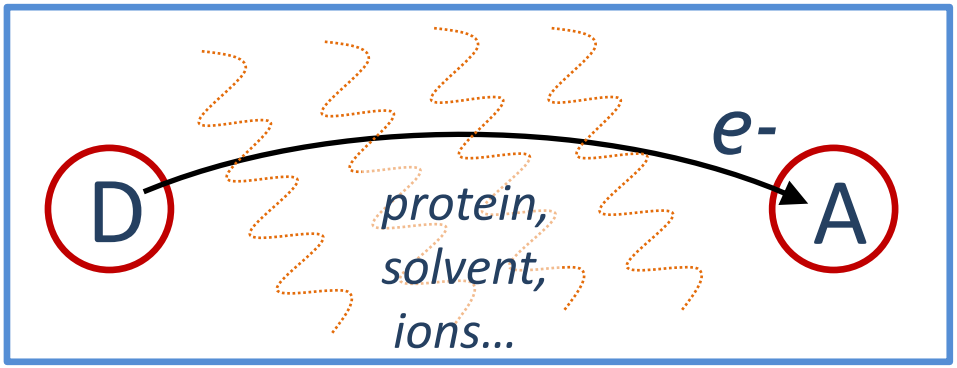
I – Why fine quantum effects are far from obvious in biology

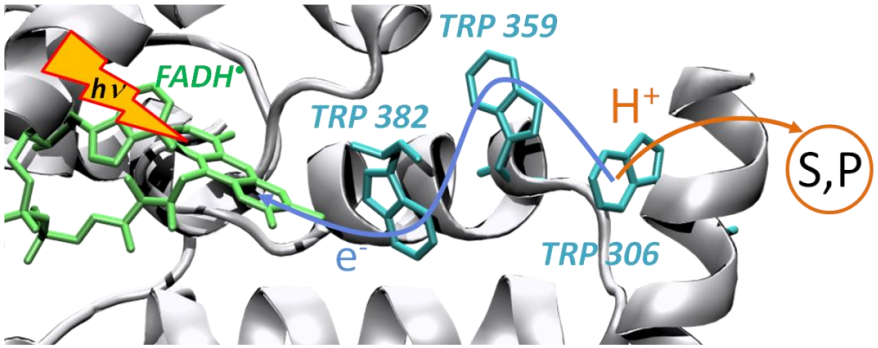
the problem of decoherence in warm environments
how numerical simulations can help ?

III - Understanding the molecular mechanisms of electronic decoherence from molecular dynamics simulations

ELECTRON TUNNELING IN BIOLOGY

- *Within the respiratory chain (transport of electrons)*
- *Enzymatic catalysis (e.g. catalytic steps or activation of the enzyme)*
- *Along DNA strands (e.g. light induced ionization)*
- *In light harvesting processes (e.g. Reaction Center)*





DNA PHOTOLYASES/CRYPTOCHROMES

D

A

organic cofactors:
- *quinones*
- *flavins*
- *NADH…*

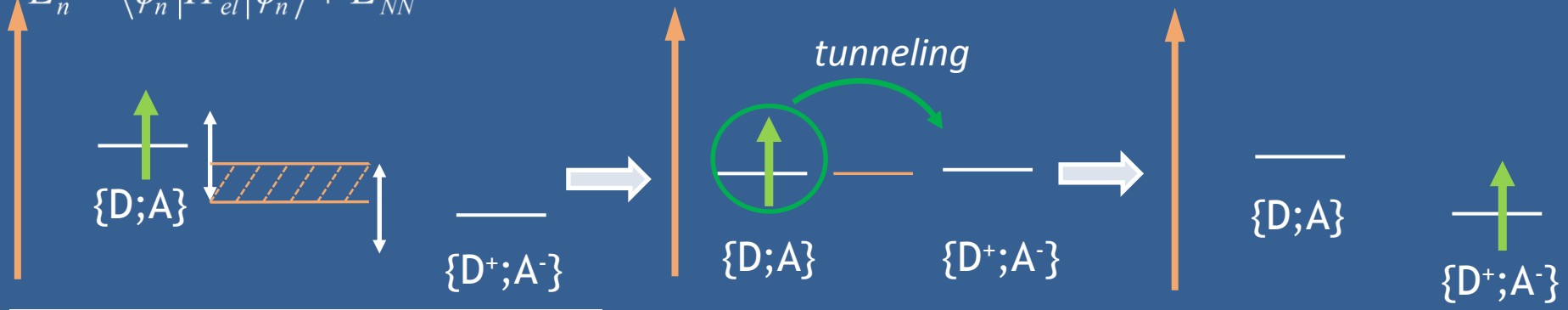
Inorganic cofactors:
- *hemes*
- *chlorophylles*
- *Blue copper centers*
- *iron-sulfur clusters …*

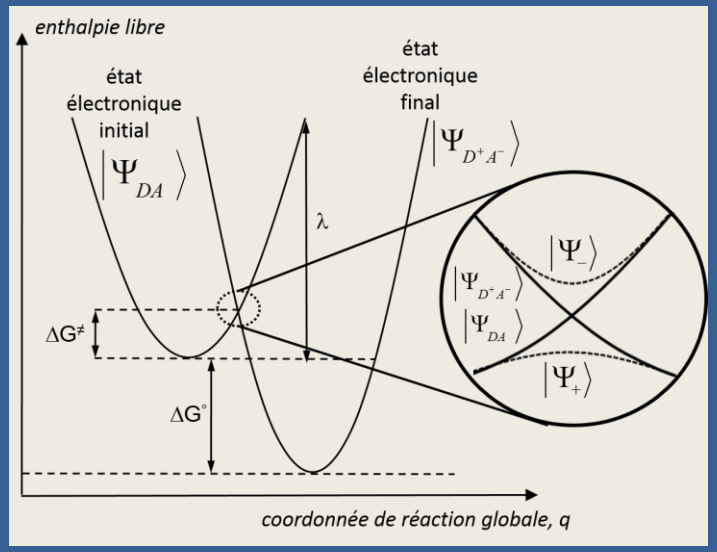
A SIMPLE VIEW OF ELECTRON TRANSFER

ϕ_n : electronic wave function *n*

$$E_n = \langle \phi_n | H_{el} | \phi_n \rangle + E_{NN}$$

Born Oppenheimer approximation
R. A. Marcus and N. Sutin,
Biochim. Biophys. Acta, **1985**, *811*, 265-322





reorganization energy

driving force

$$k_{ET}^{(*)} = 10^{13} \cdot \frac{4\mu^2}{8\hbar^2 + 4\mu^2} \exp\left(\frac{-(\Delta G^\circ + \lambda)^2}{4\lambda RT} \right)$$

$$\mu = H_{12} \times \tau_{decoherence}$$

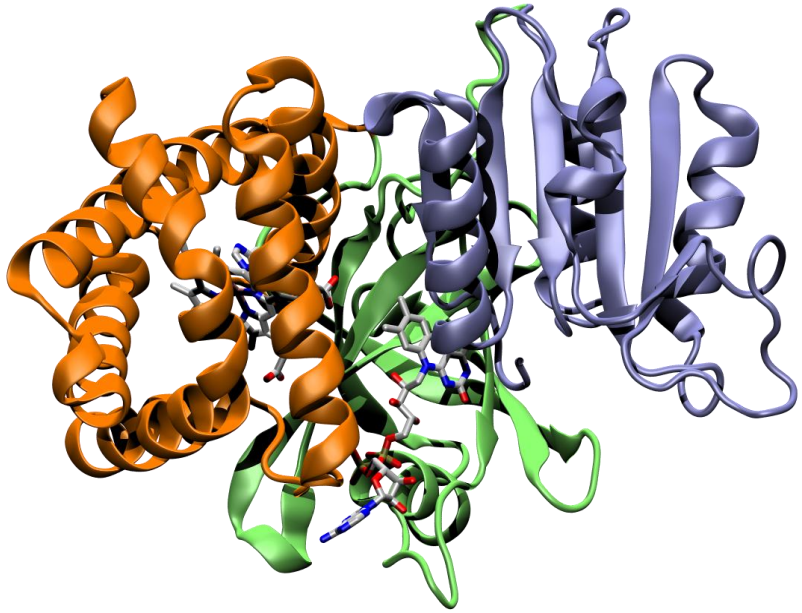
electronic coupling

characteristic decoherence time

*: A. de la Lande, J. Řezáč, B. Lévy, B. C. Sanders, D. R. Salahub, *J. Am. Chem. Soc.* **2011**, 133, 3883

BIOLOGICAL SYSTEMS ARE INTRISICALLY MULTISCALES OBJECTS

allostetic transitions	*0.01 μs - 1 s* 100-500 pm
side chain rotations of burried residues	*0.1 μs - 1 s* 500 pm
relative motions between domains	*0.01 - 100 ns* 100-500 pm
libration motion burried atoms	*0.01 ns - 1ns* 50 pm
side chain rotations of surface residues	*10-100 ps* 500 - 1000 pm
hydrogen bond breaking & formation	*1-10 ps* 1 - 10 pm
nuclear vibrations	*0.01-0.1 ps* 1 - 10 pm
electronic dynamics	*< fs*



→ The energy gaps and the coupling are sensitive to the fluctuations of protein and water atoms

→ Coherences are expected to be destroyed in few femtoseconds

Mc Cammon, *Rep. Prog. Phys.* **1984**, 47, 1-46

DECOHERENCE IN A NUTSHELL

The system is comprised of at least two electronic quantum states embedded in a huge number of nuclear wave packets

$$|\Psi(t)\rangle = \sum_k |\psi_k\rangle \otimes |\phi_k(t)\rangle \qquad |\phi_k(t)\rangle = \sum_l c_{kl}(t)|\varphi_l\rangle$$

electronic wave packets

nuclear wave packets

$$\boldsymbol{\rho}^{e}(t) = \begin{pmatrix} \sum_i c_{1i}^* c_{1i} & \cdots & \sum_i c_{1i}^* c_{ni} \\ \vdots & \ddots & \vdots \\ \sum_i c_{ni}^* c_{1i} & \cdots & \sum_i c_{ni}^* c_{ni} \end{pmatrix}$$

coherences

populations

the coefficients c_{kl} evolve according to the Schrödinger equation

Initial conditions: t=0, c_{11}=1; c_{jj}=0

the coefficients evolve if

⇒ the energy gaps are smaller than the coupling between the electronic states

⇒ the coherences remain larger than 0

DECOHERENCE RATES

H. Hwang, P. Rossky, *J. Phys. Chem. B*, 2004, 108, 6723

$$\rho^e(t) = \begin{pmatrix} \sum_i c_{1i}^* c_{1i} & \cdots & \sum_i c_{1i}^* c_{ni} \\ \vdots & \ddots & \vdots \\ \sum_i c_{ni}^* c_{1i} & \cdots & \sum_i c_{ni}^* c_{ni} \end{pmatrix}$$

Coherences

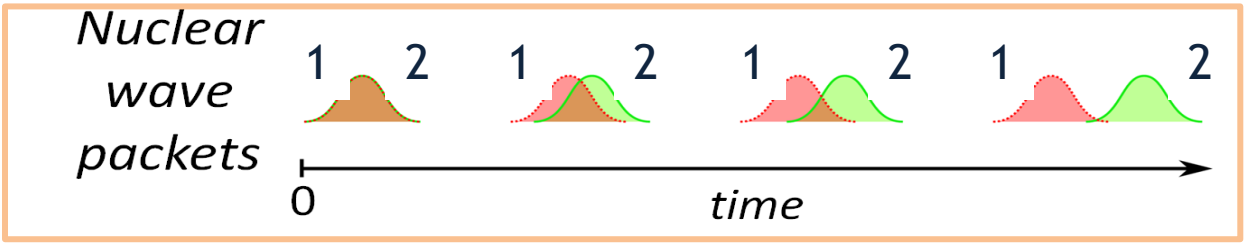
Populations

when coherences tend to zero, the quantum system behaves classical (formal analogy with the Schrödinger's cat)

--> decoherence

For a molecular system, electronic coherences are proportional to nuclear wave packets overlap

population exchanges between electronic states occur as long as the nuclear wave-functions stay in phase.



(!! Reality is more complicated than this simplified real space overlap between Gaussians)

W. H. Zurek, Los Alamos Sci. 2002, N°27, arXiv:quant-ph/0306072vl

O. V. Prezhdo, P. Rossky, *J. Chem. Phys*. **1997**, 107, 5863 (and other illuminating papers by Rossky and coll.)

A. Jasper, D. G. Truhlar *J. Chem. Phys*. **2005**, *123*, 0641030

NUMERICAL SIMULATIONS CAN HELP IN INTERPRETING EXPERIMENTAL DATA

Measuring ET rates in proteins is difficult
--> rates depends on many parameters
--> ET is usually not rate limiting
--> short time scales resolution (< ps) is difficult to achieve

Direct numerical simulations of biological ET

Very rich physical chemistry (large variety of kinetics regimes)
--> computational protocol adapted for each problem

A. de la Lande, N. Babcock, J. Řezáč, B. Lévy, B. Sanders, D. Salahub, Perspective in *Phys. Chem. Chem. Phys.* **2012**, 14, 5902
"Quantum Effect in Biological Electron Transfers"

DECOHERENCE HAS TO DO WITH THE QUANTUM-TO-CLASSICAL TRANSITION

BIOLOGICAL ET : Composite and highly heterogeneous systems with multiscale dynamics (…fs-ms…)

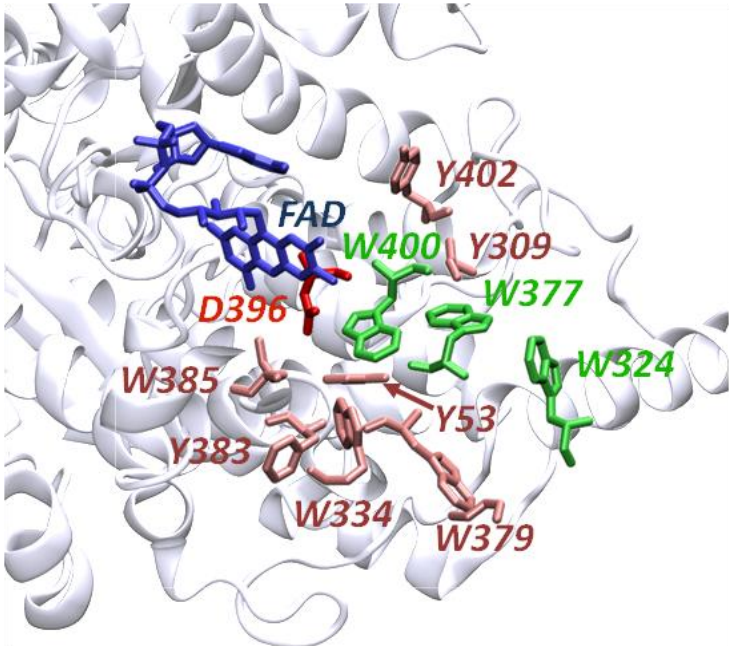
→ ~~Fully quantum~~ dynamics (e.g. "MCTDH" approach)

→ Simulation of the Liouville Von-Neumann with model Hamiltonians

OK, BUT: how to calibrate the Hamiltonian ?
how to include the environment dynamics
lack of (atomic) resolution

→ Semi-classical Molecular Dynamics Simulations
Introduction of the quantum nature of the nuclei *a posteriori*

A FASCINATING EXAMPLE: THE CRYPTOCHROMES



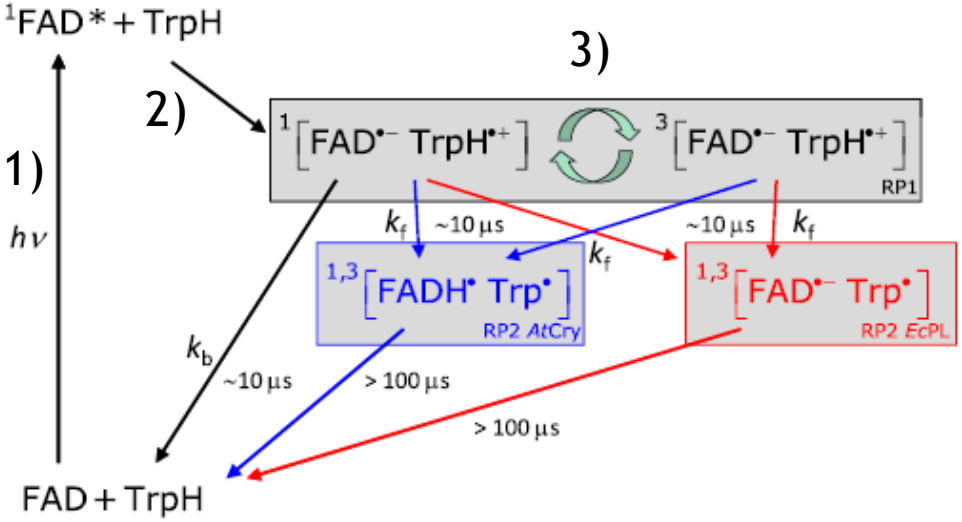
The production of a pair of radicals (single electrons located on two remote molecular fragments) has been proposed has te source of migratory birds to orient in the Earth magnetic field

CT Rodgers Pure Appl Chem, ***2009***, *81, 19*
IA Solov'yov, K Schulten, J. Phys. Chem. B ***2012***, *116, 1089*

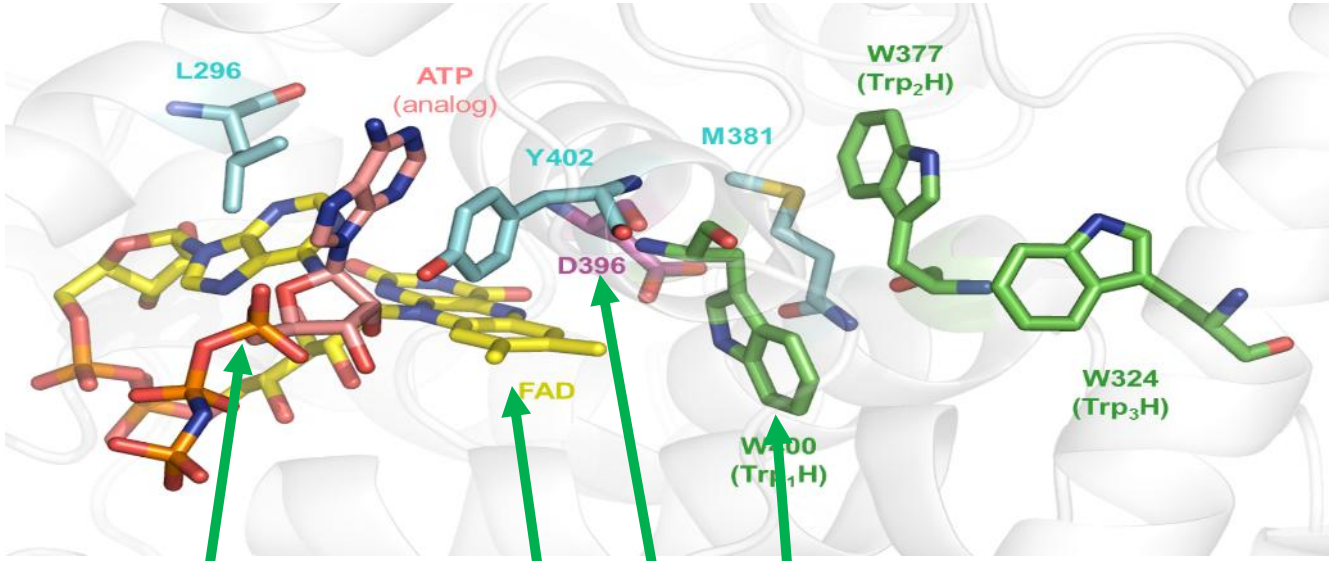
1) Excitation of FAD
2) Ultrafast electron transfer
3) Singlet-triplet electronic dynamics

can depend on weak magnetic fields

Maeda et al. *PNAS* **2012**, 109, 4774



ULTRAFAST ELECTRON TRANSFERS IN CRYPTOCHROMES



Coll. with:
Pavel Müller, Klaus Brettel
(CEA,CNRS, Saclay)
Fabien Cailliez (LCP, Orsay)

Experimental observation[1]:
ATP binding and D396 protonation enhance the primary electron transfer from W400 to FAD*
Computational studies:
ATP inding enhance electron transfer, by creating structural organization of the active site for efficient tunneling[2]

[1]Müller P., Bouly J.P., Hitomi K., Balland V., Getzoff E., Ritz T., Brettel K.
Science reports **2014**
[2] *Cailliez F., Müller P., Gallois M. de la Lande A, submitted for publication*

COMPUTATIONAL STRATEGY

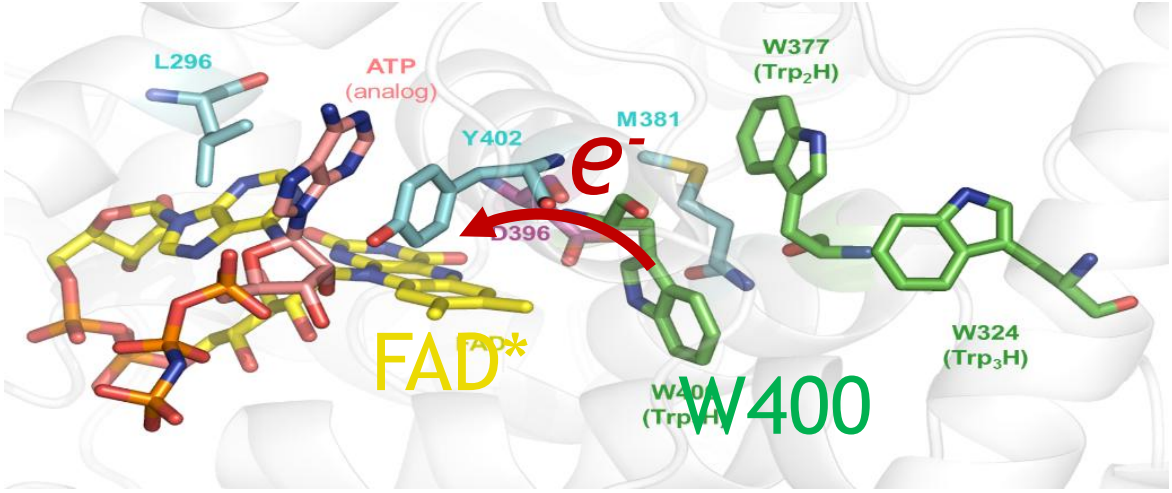
1) molecular dynamics simulations with molecular mechanics force fields (NAMD) (250 nanoseconds for each system)

a) in presence or not of ATP in the binding pocket

b) with D396 protonated or not

2) Time-Dependent Density Functional Theory calculations along the MD simulations (550 structures analyzed for each strutcure)

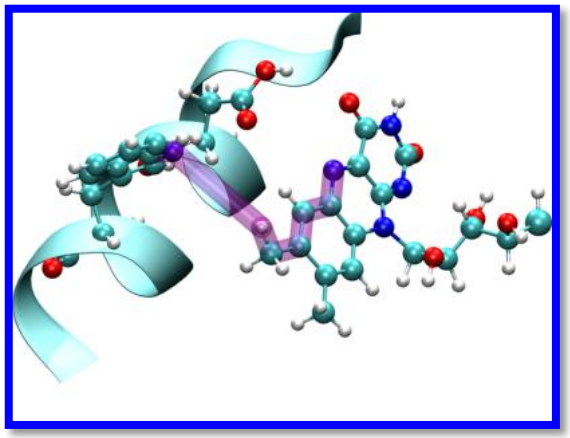
--> Evaluate rate for W400 --> FAD* electron transfer

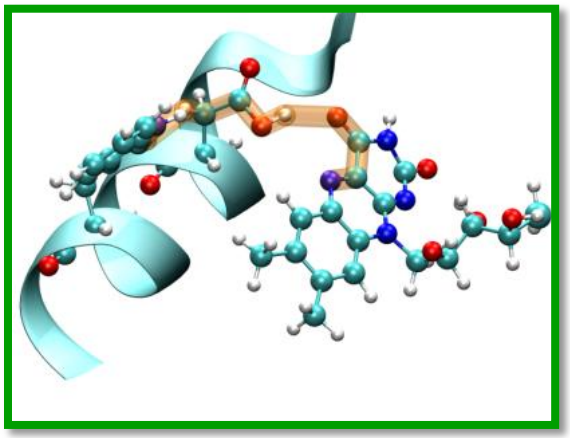


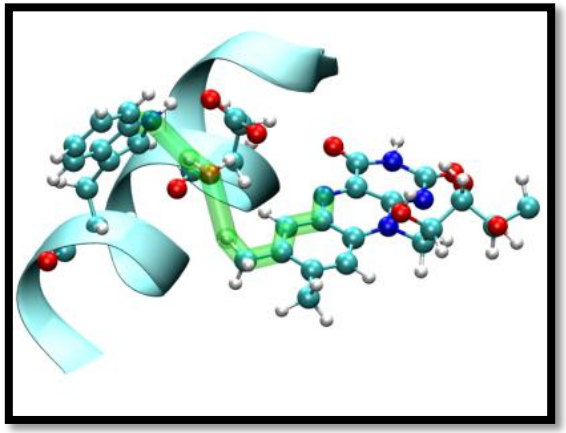
ELECTRON TUNNELING IS ENHANCED WHEN ATP IS PRESENT

Experimental FADH• production	With ATP	Without ATP
pH < 8.0	+++	+
8.0 ≤ pH < 10.0	+++	-

Computational predictions	τ_{ET} (ps) W400 → ISO*
D0	103.2
DA	47.1
P0	11.0
PA	2.1







THE ELECTRON TUNNELING PATHWAYS ARE SHORTER, HENCE MORE EFFICIENT, WHEN ATP IS PRESENT

Cailliez F., Müller P., Gallois M. de la Lande A, submitted for publication

CONCLUSION AND PERSPECTIVES

- Many (bio-)chemical processes operate at the boarder between the quantum and classical worlds
- The semi-classical paradigm ("quantum" electrons and "classical" nuclei) which is prevailing in chemistry is contested in various instances (electron transfers, light harvesting, enzymatic proton tunneling)

- *Does the efficiency of biophysical processes indeed rely on fine quantum effects ?*
- *What is the role of the structure and dynamics of biomolecule in manipulating coherences? What was the role of Evolution (if any) ?*
- *Can fine quantum effect be manipulated at room temperature ? slowing down decoherence?*
- *Source of inspiration for artificial devices ?*

  (artificial photosynthesis, green chemistry ....)

MOST OF THESES QUESTIONS REMAIN TO BE ANSWERED

Progresses in experimental techniques (atto- and femtoseconds lasers, 2D spectroscopies...) start to bring fresh data on these questions

CONCLUSION AND PERSPECTIVES

- Connections between experimental data and theoretical models are not always obvious
- An interdisciplinary approach is necessary (biophysicists , chemists, physical-chemists, physicists…) to unravel the role of coherences in physicochemical processes.
- Numerical approaches certainly have a role to play to interpret exp data

Modelling strategies for addressing the question of "quantum biology" are still in their infancy

- Biological systems are complex and intrinsically multi-scales
- The coupling between electron and nuclear degrees of freedom need to be included
- Simulations algorithms are not well established yet
- Efforts should probably be put on the developments and atomistic simulation tools combining quantum chemistry approaches and molecular dynamics simulations

ACKOWLEDGEMENTS

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Computational resources