Quantum Biology

Johnjoe McFadden

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What is Life?

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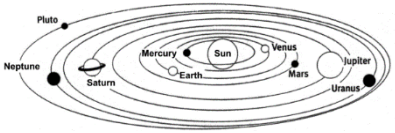
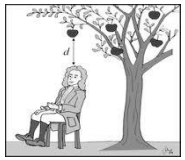
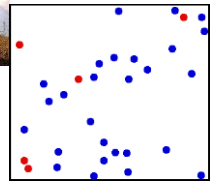
Life on the Edge

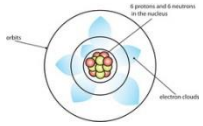
Classical World

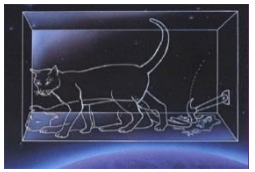






Quantum World





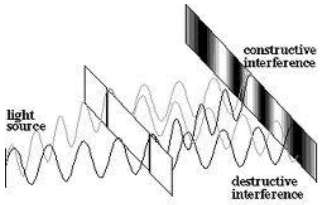


Fig 1: Interference of Light Waves

Wave-particle duality

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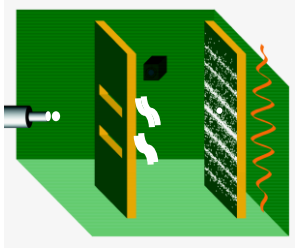
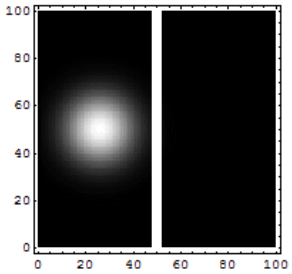
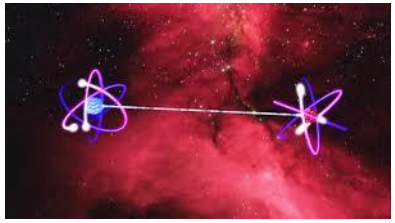
Quantum weirdness



- Coherence – particles can be in two places at once or in two states at once.



- Tunnelling – particles can ‘walk through walls



- Entanglement – particles can have ‘spooky’ connections

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But quantum weirdness is, usually, very delicate!

- Requires ‘coherence’ – all particle waves need to wave in-step.
- Easily lost in complex, hot molecularly noisy environments

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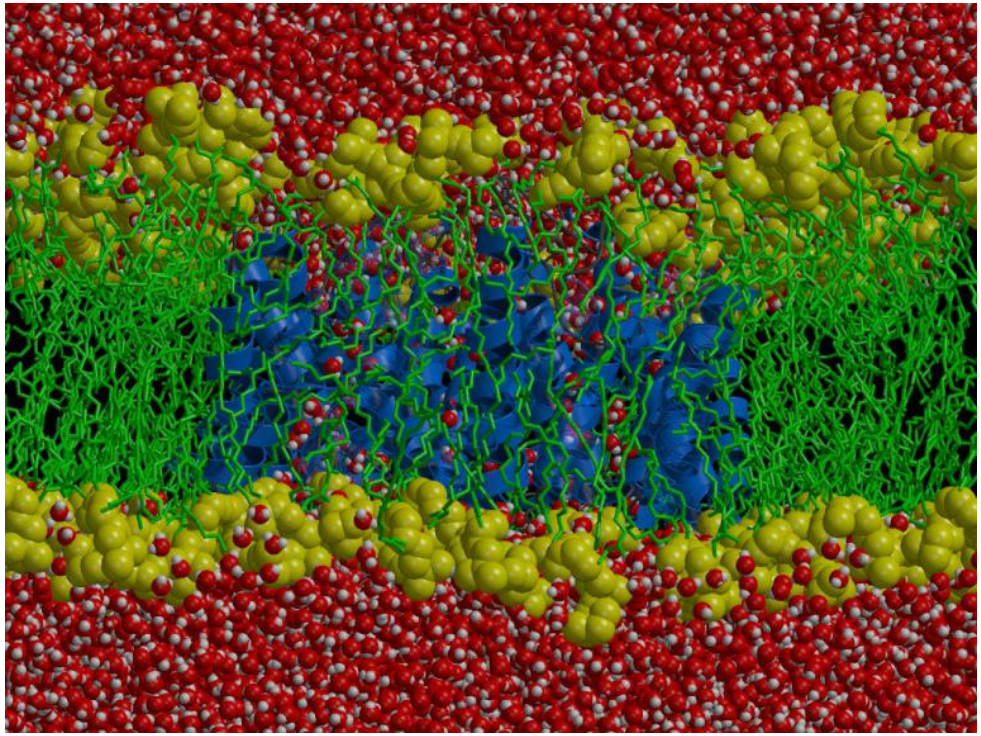
Quantum coherence needs stillness



The hot, wet and molecularly noisy living cell

Bert de Groot – B.L. de Groot and H. Grubmüller: Science 294, 2353-2357 (2001)

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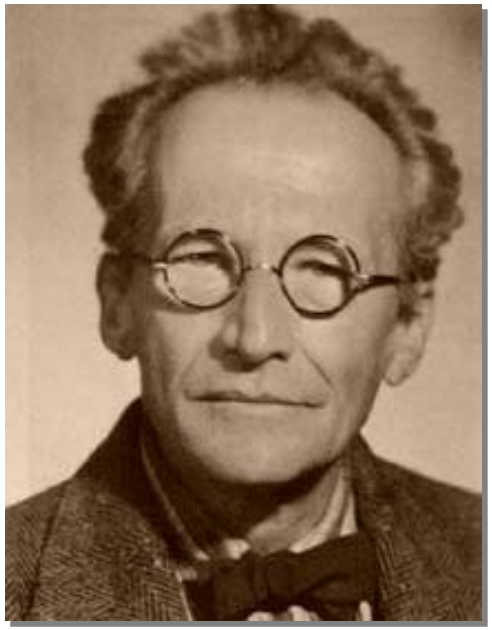
Erwin Schrödinger

‘The living organism seems to be a macroscopic system which in part of its behaviour approaches purely mechanical (as contrasted to thermodynamical) behaviour to which all systems tend, as the temperature approaches the absolute zero and the molecular disorder is removed.”

“*What is Life*”, 1944



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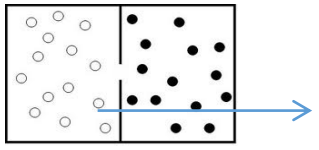
Schrödinger's argument

Order from disorder



Statistical Mechanics

$S = k \,.\, log\, W$

- Schrödinger noted that the standard *exact* laws that govern the behaviour of most macroscopic objects (gas laws, thermodynamics, diffusion) are statistical in nature and are obeyed only because of the statistical averaging of the (random behaviour) of very large numbers of particles in big objects: *order from disorder*.
  - Errors (noise) in these laws $\propto 1/\sqrt{N}$, where *N* is number of particles.
  - As the number of particles in an object is reduced, its behaviour becomes more and more random and unpredictable.

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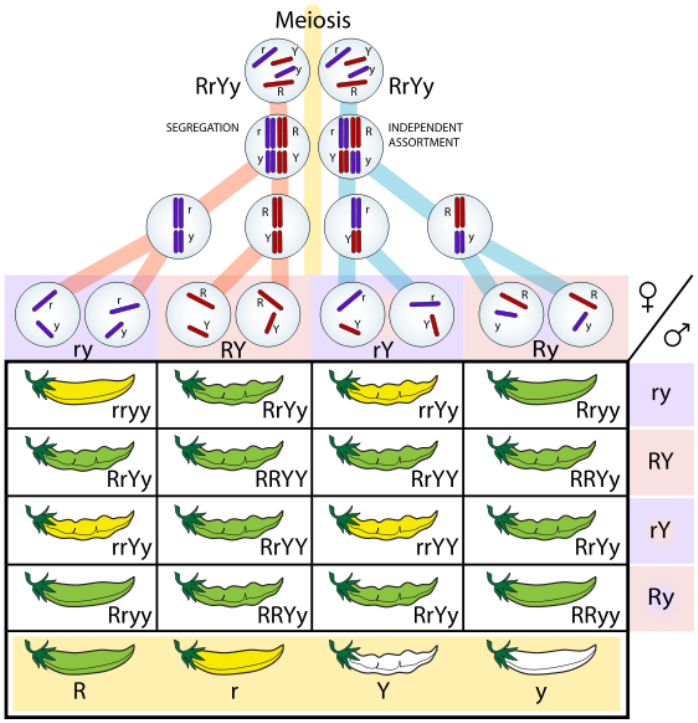
Schrödinger's argument



- So how does heredity work?
  - Schrödinger was impressed by the stability of heredity ("*genes … breed true, that is, they are perfectly inherited*"): characters can be passed down with (more-or-less) absolute fidelity for hundreds of generations.
  - This fidelity implies that heredity is subject to some kind of exact law
    - Order from disorder?

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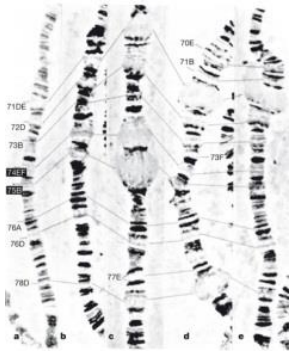
Schrödinger's argument



400 million years

- Schrödinger estimated the size of a gene from cytogenetic and mutagenesis studies to be a unit composed of approximately 1000 atoms.
- This number is far too small to provide regularity in the face of the $1/\sqrt{N}$ rule

  "How can we, from the point of view of statistical physics, reconcile the facts that the gene structure seems to involve only a comparatively small number of atoms (of the order of 1,000 and possibly much less), and that value nevertheless it displays a most regular and lawful activity -with a durability or permanence that borders upon the miraculous?"

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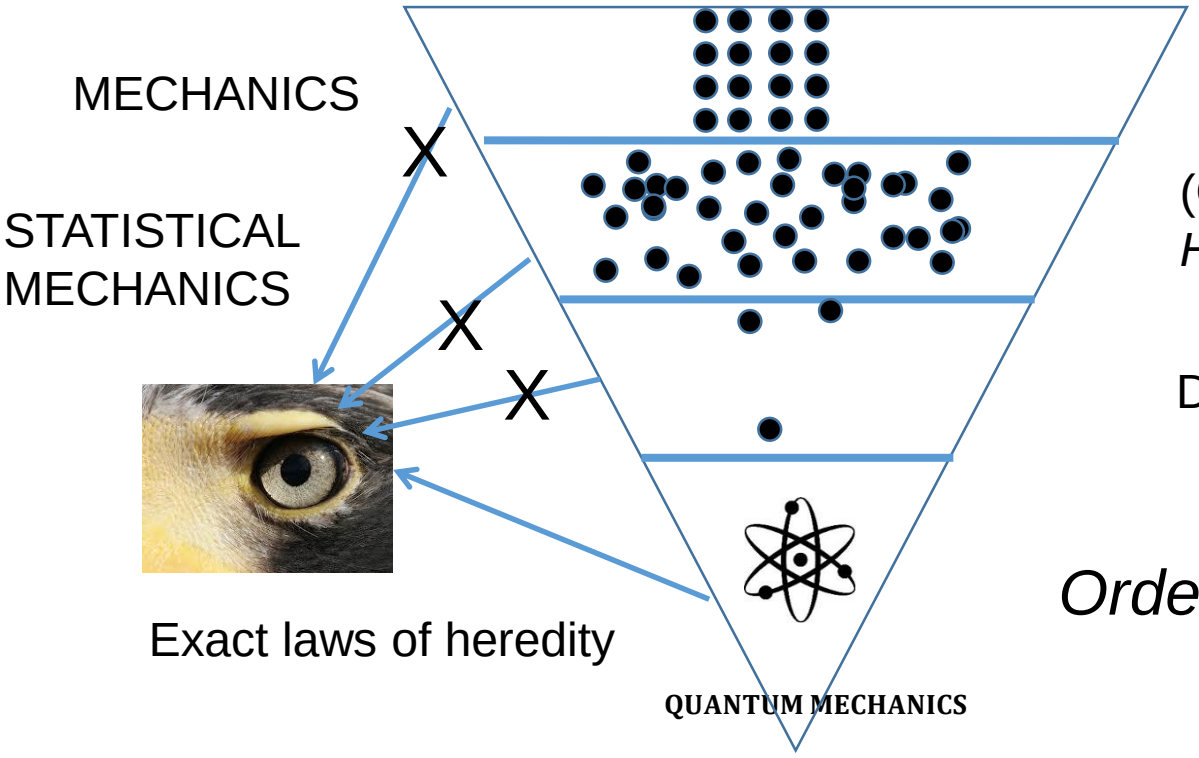
Order from quantum mechanics?



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Schrödinger's proposal

'*The living organism seems to be a macroscopic system which in part of its behaviour approaches purely mechanical (as contrasted to thermodynamical) behaviour to which all systems tend, as the temperature approaches the absolute zero and the molecular disorder is removed*.

- Genes behaved like highly structured solids – some kind of crystal.
  - But they had to encode lots of information:
- Gene were single molecules with the structure of '*aperiodic crystals*'.

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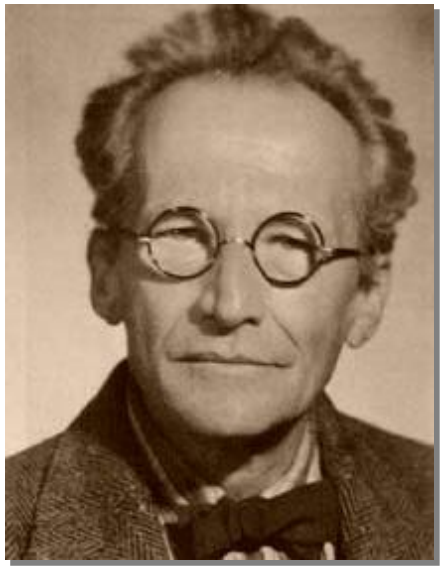
Has Life found another way?



- *"a gene – or perhaps the whole chromosome fibre chromosomes … [is] an aperiodic crystal [in which] every atom, and every group of atoms, plays an individual role … which has to be a masterpiece of highly differentiated order, safeguarded by the conjuring rod of quantum theory."*

  What is Life, Erwin Schrödinger, 1944

  - Before structure of DNA was known

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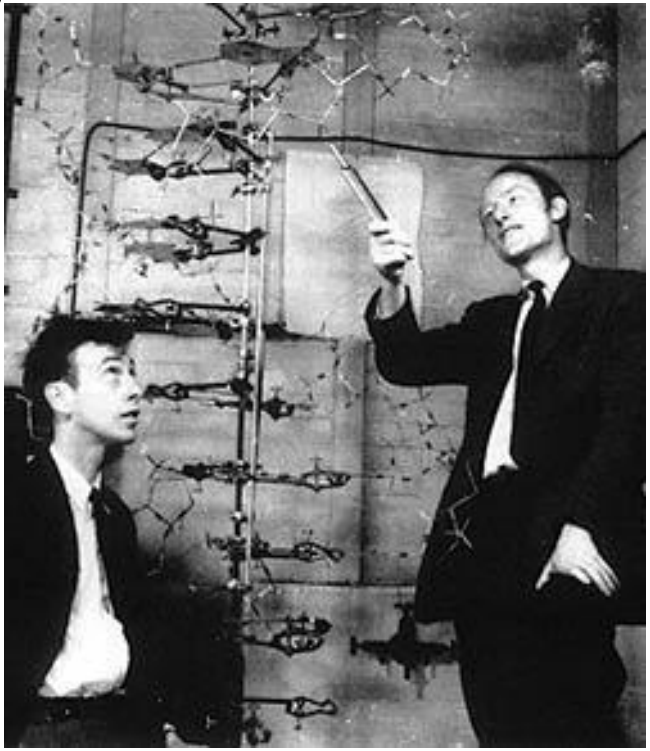
1953
The triumph of molecular biology



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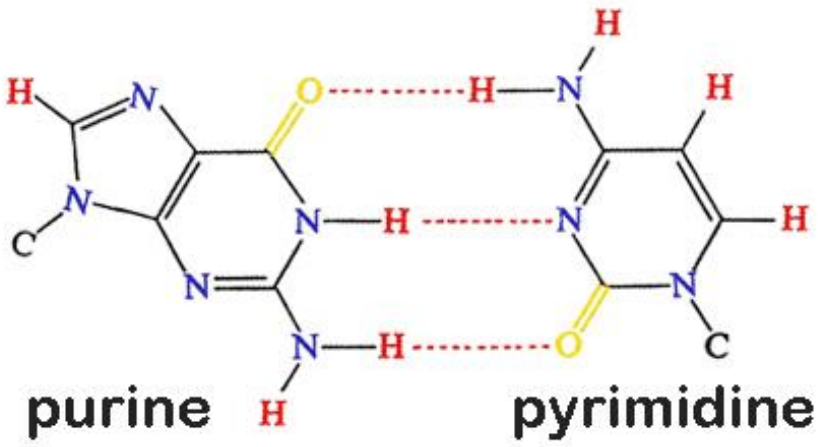
DNA base-pair
one letter of the genetic code



- *[in which] <u>every atom, and every group of atoms, plays an individual role</u>*
  - What is Life, Erwin Schrödinger, 1944

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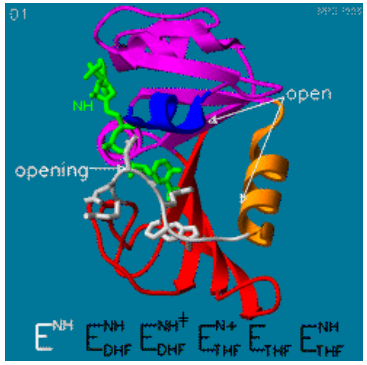
Life is Molecular Engineering

DNA replication



Enzyme action
dihydrofolate reducase

- At a molecular level, life involves the manipulation of fundamental particles (electrons, protons) atoms, and molecules.
- Life is quantum-level molecular engineering.

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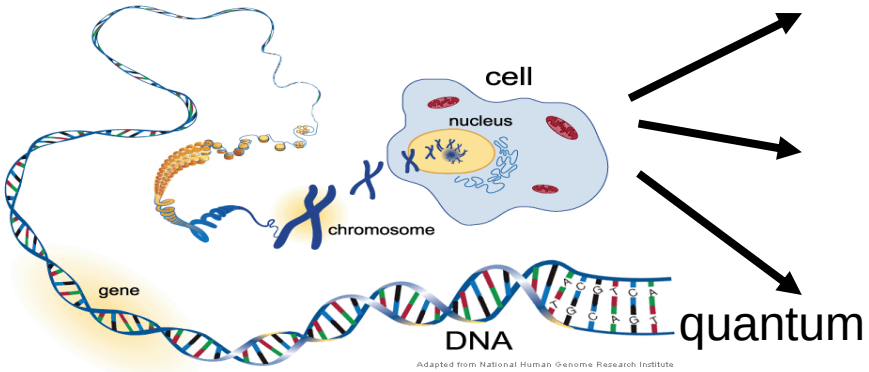
Life, uniquely, amplifies quantum-level events to the macroscopic level



macroscopic

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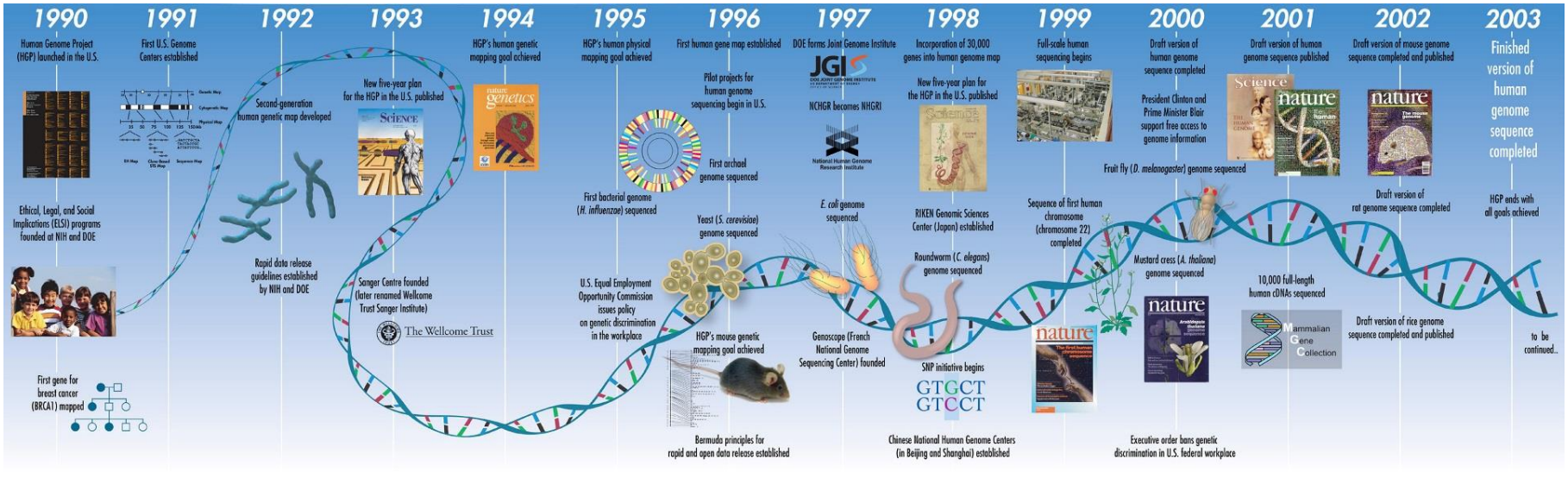
The triumph of molecular biology



Without considering the quantum nature of the genetic code

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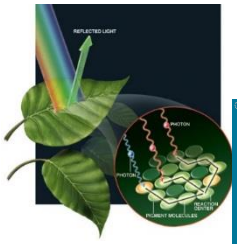
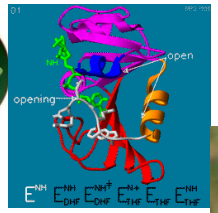
Candidates for quantum biology

- Photosynthesis
- Enzymes
- Magnetoreception
- Smell
- DNA mutations
- Origin of life
- Consciousness





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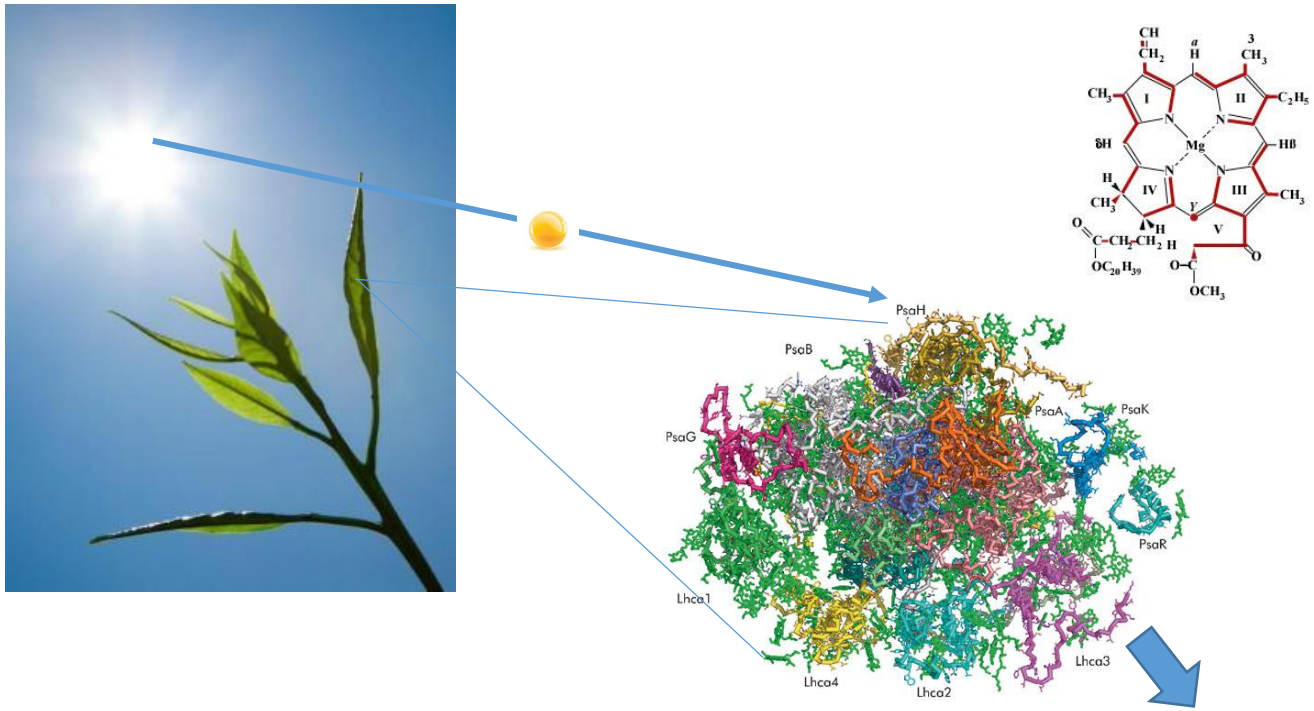
Photosynthesis



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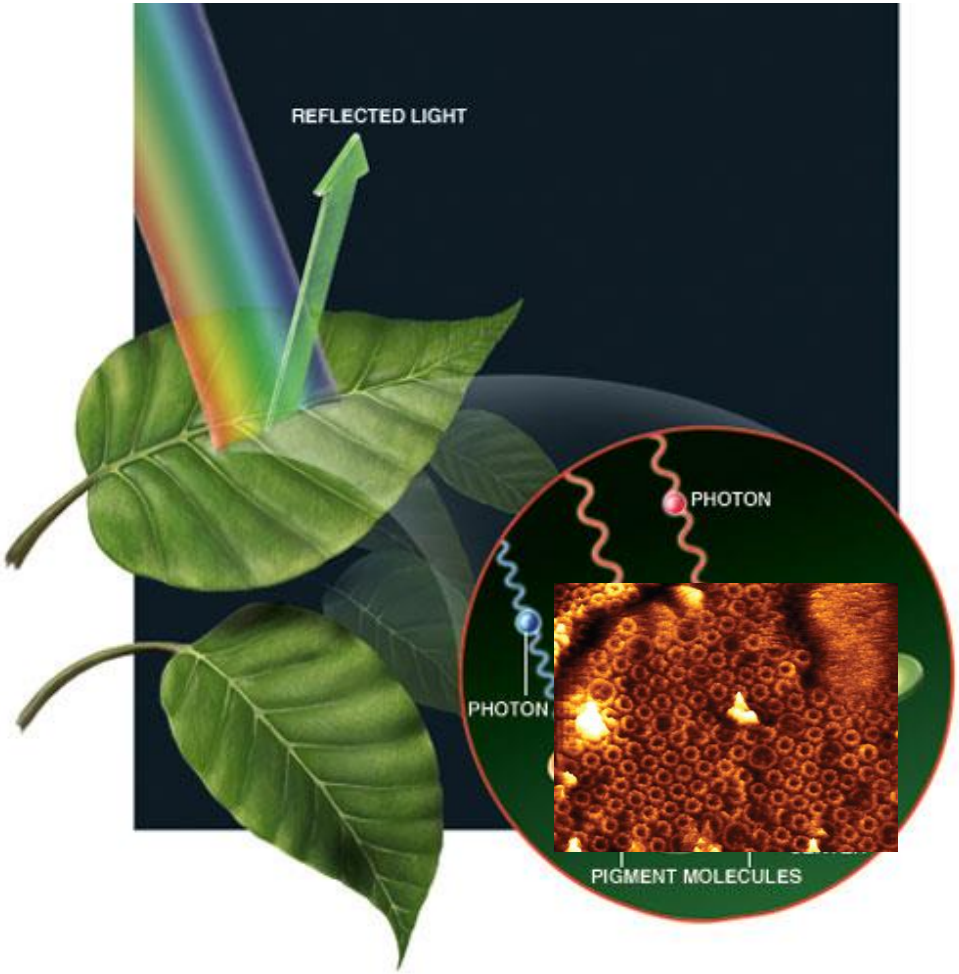

- The first step in photosynthesis involves the capture of a photon of light by the antennae pigment and its conversion to an oscillating exciton that travels to the reaction centre where its unstable electrical energy is converted to stable chemical energy.
- This reaction has the highest efficiency of any energy transport process – close to 100% under optimal conditions
- Classically, it shouldn't
  - Travelling salesman problem

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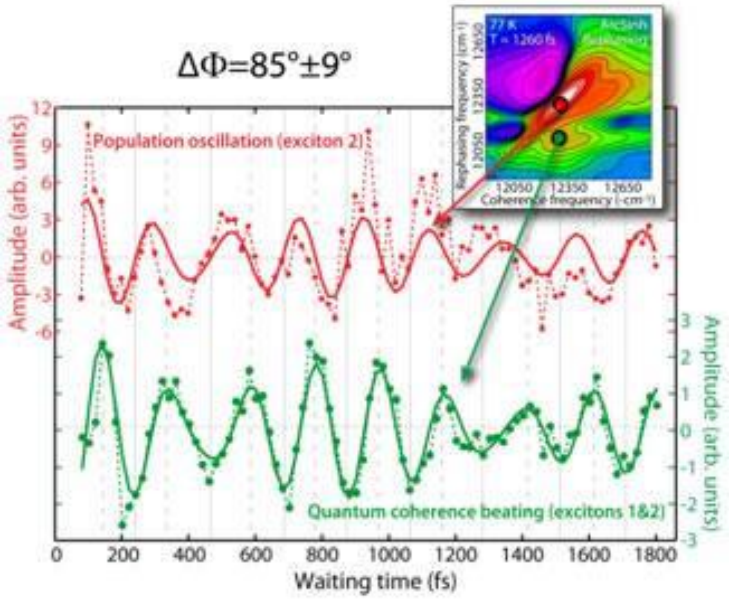
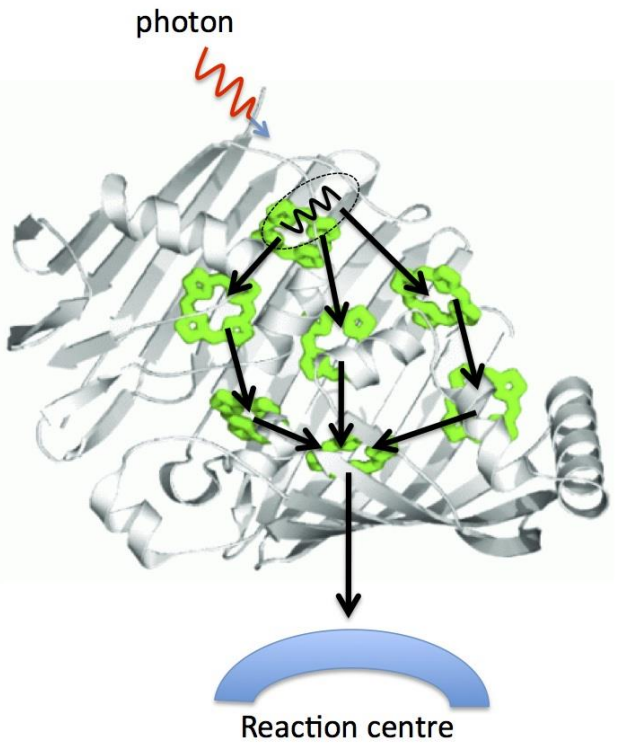
Quantum beats in photosynthesis



Greg Engel
University of Chicago



- Femtosecond spectroscopy: exciton travels to the reaction centre as a coherent quantum wave that samples all routes simultaneously to find the fastest route to the reaction centre via a quantum computation – quantum walk

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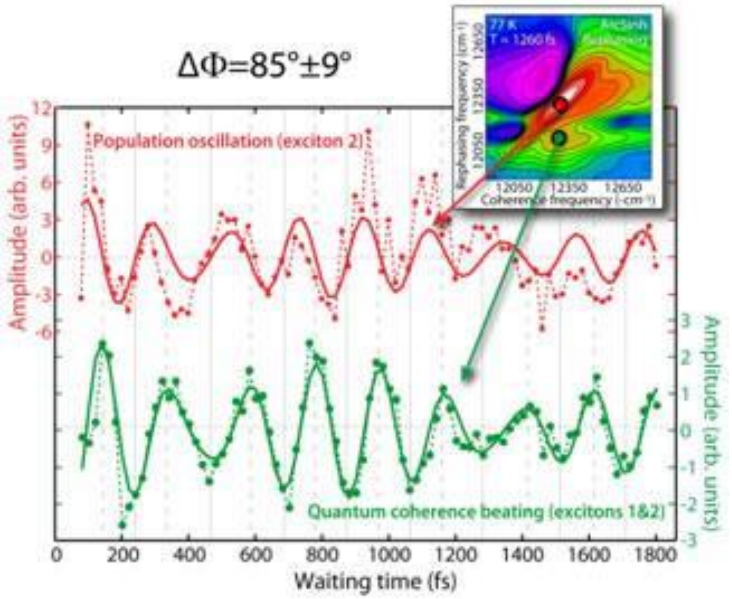
Quantum beats in photosynthesis



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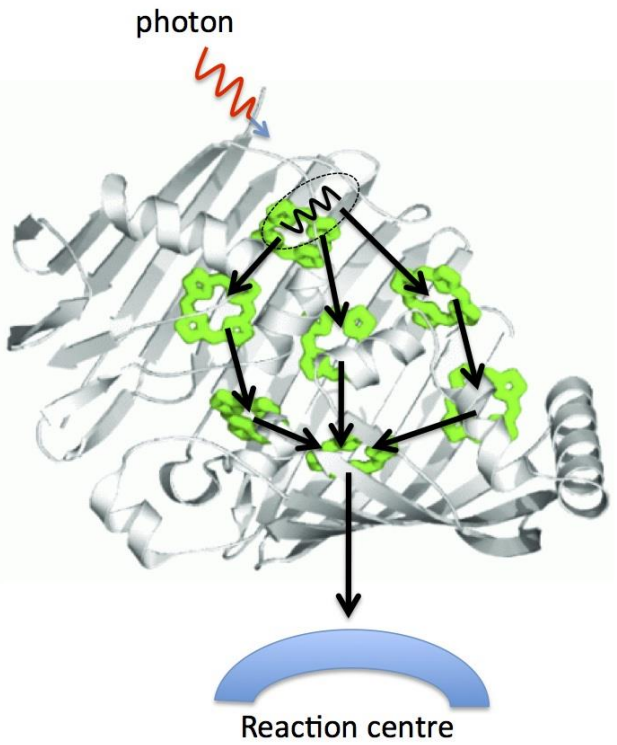

- Decoherence is tuned within the system so that it performs a measurement that localises the exciton preferentially at the reaction centre via the fastest route (Seth Lloyd)

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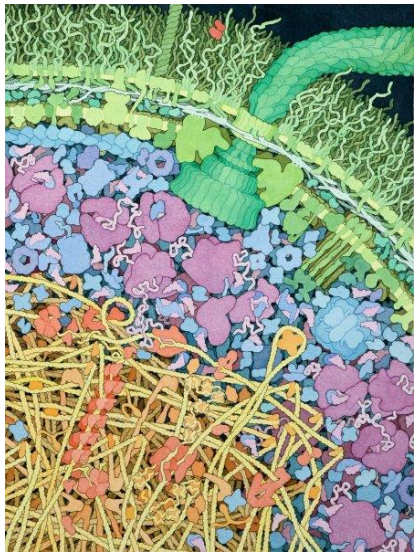
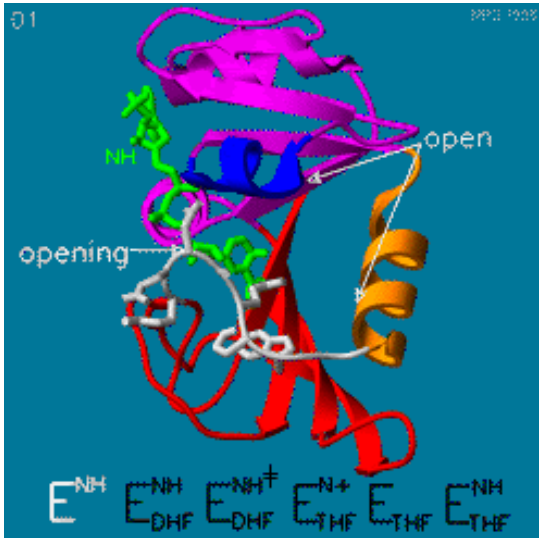
Enzymes



- The engines of life
- All biomolecules are made by enzymes
- All life is made by enzymes



- Enzymes speed up chemical reactions by factors as high as 10^{20}.
  - Very difficult to account for by known mechanisms.
- Enzymes manipulate fundamental particles
- Nature's quantum engineers

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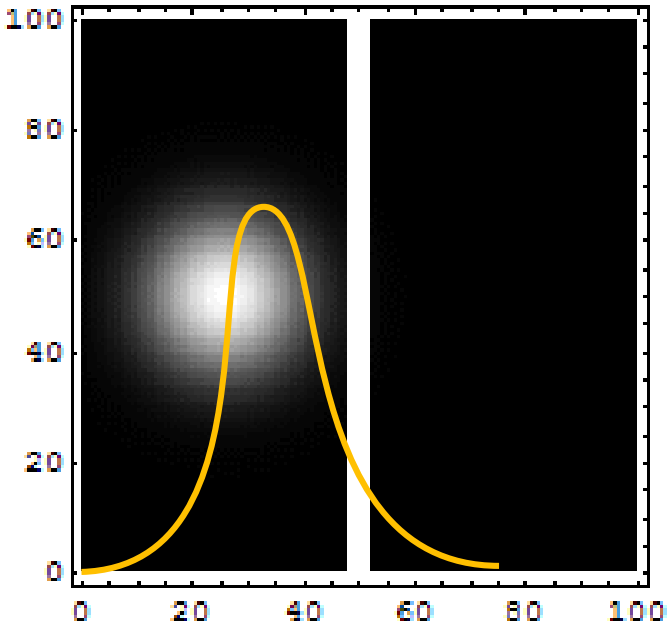
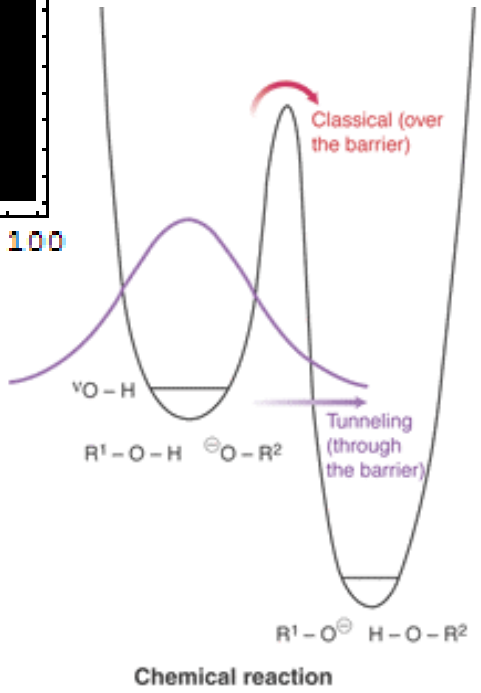
Quantum Tunnelling





- Quantum particles can flow through classically-impenetrable barriers as waves.

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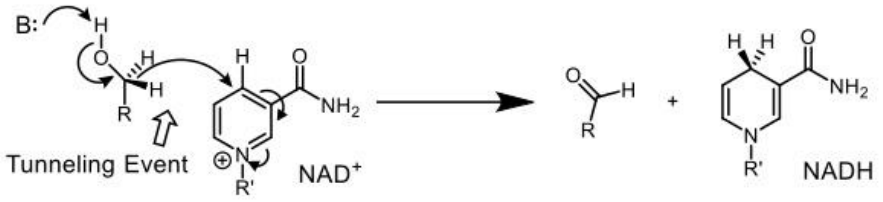
Tunnelling in Enzymes
Nature's subway

Examples in Organic and Biochemistry

Biochemistry: Enzymes

It has been shown that the reaction mechanism of many enzymes involve tunneling, often hydrogen tunneling. For instance, the oxidation of an alcohol via the enzyme alcohol dehydrogenase has been shown to involve hydride tunneling (mechanism shown below).



Other examples on enzymes and proteins known the utilize tunneling include the following:

- Amine Oxidases
- Lipoxygenase
- Electron Transport Chain in respiration and photosynthesis (electron tunneling)

REFERENCES: *Acc. Chem. Res.*, **1998**, *31* (7), pp 397–404, *Biochemistry*, **2014**, *53* (14), pp 2212–2214, *Elsevier*, **2006**, *1757*(9–10), pp 1096–1109, *Nature*, ***1999***, **399**, 496-499

- Tunnelling may fill the activity gap
  - Electron tunnelling demonstrated in respiratory enzymes by DeVault and Chance in 1970's - across several tens of Angstroms.
  - More recently, proton tunnelling demonstrated by Judith Klinman (California) and Nigel Scruton (Manchester) showing how enzyme reactions are slowed when hydrogen is replaced by deuterium
  - Quantum tunnelling enhances enzyme reactions by promoting quantum tunnelling of protons and electrons

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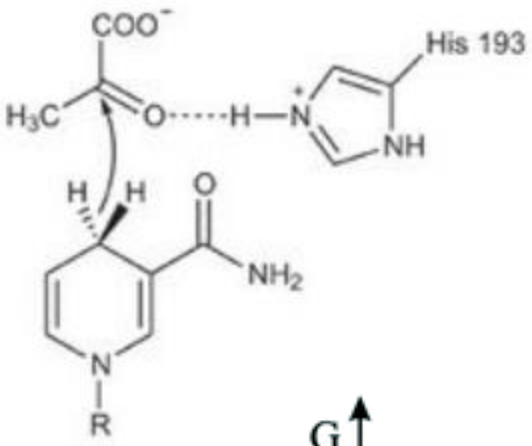
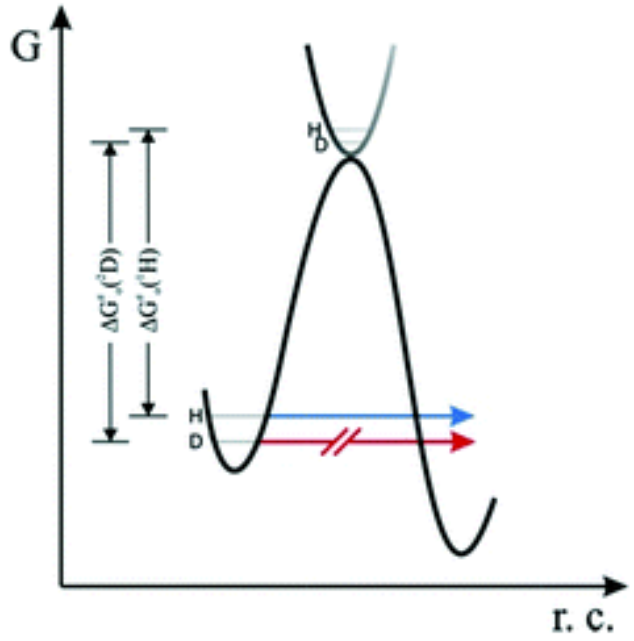
Hydride transfer in dehydrogenase reactions – Kinetic isotope Effect (KIE) in Aromatic Amine Dehydrogenase (AADH)





- Since Hydrogen is lighter than Deuterium, it has a larger de Broglie wavelength and so is able to tunnel at lower energies.
- In AADH the KIE ratio between Hydrogen and Deuterium is about 55, which is much larger than expected if the reaction only involved over the barrier transitions.
  - Good vibrations in enzyme-catalysed reactions. Sam Hay & Nigel S. Scrutton. Nature Chemistry 4, 161–168

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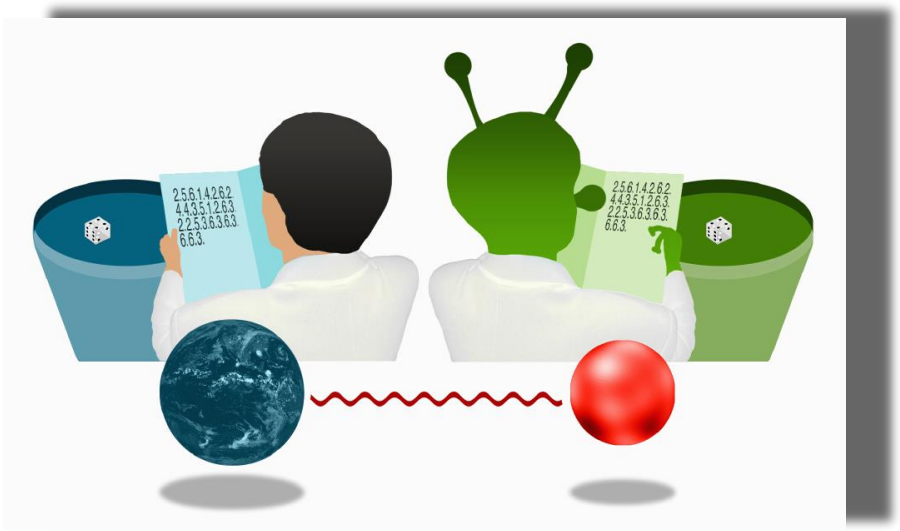
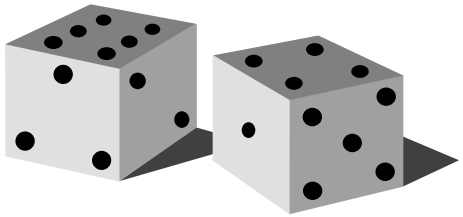
Entanglement

This is due to instantaneous connections between two or more quantum particles which can be very far apart.





Magnetoreception in birds' navigation

European robin

British robin

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- Magnetic compass of European robin, Wolfgang Wiltschko and Roswintha Wiltschko, Science 176 (1972) 62-64
  - Robin compass required light
  - It was an inclination compass
    - Finds nearest pole but cannot distinguish between poles.

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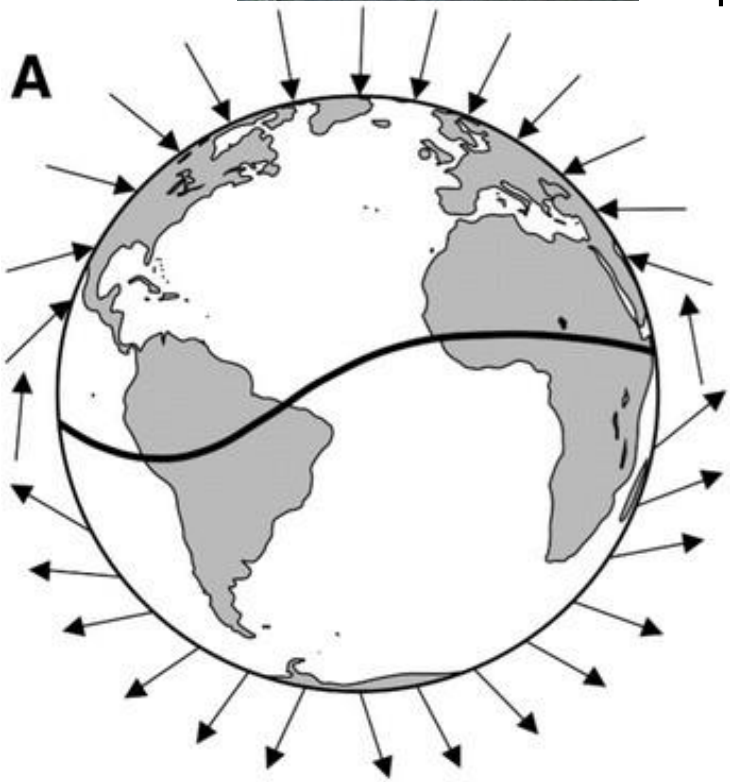
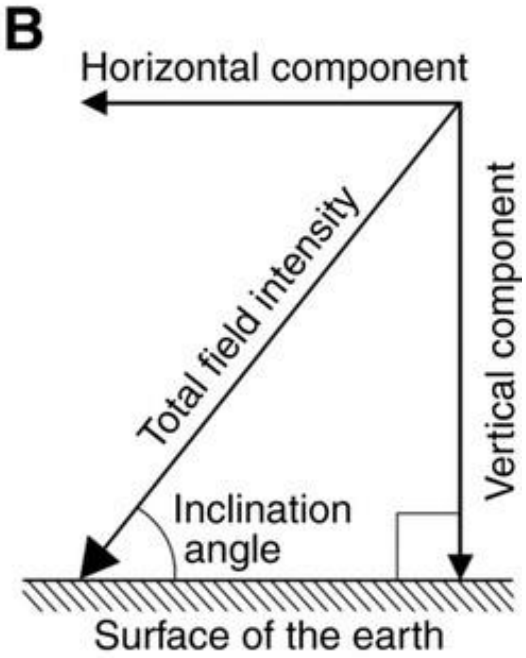
Angle of inclination NOT direction of field





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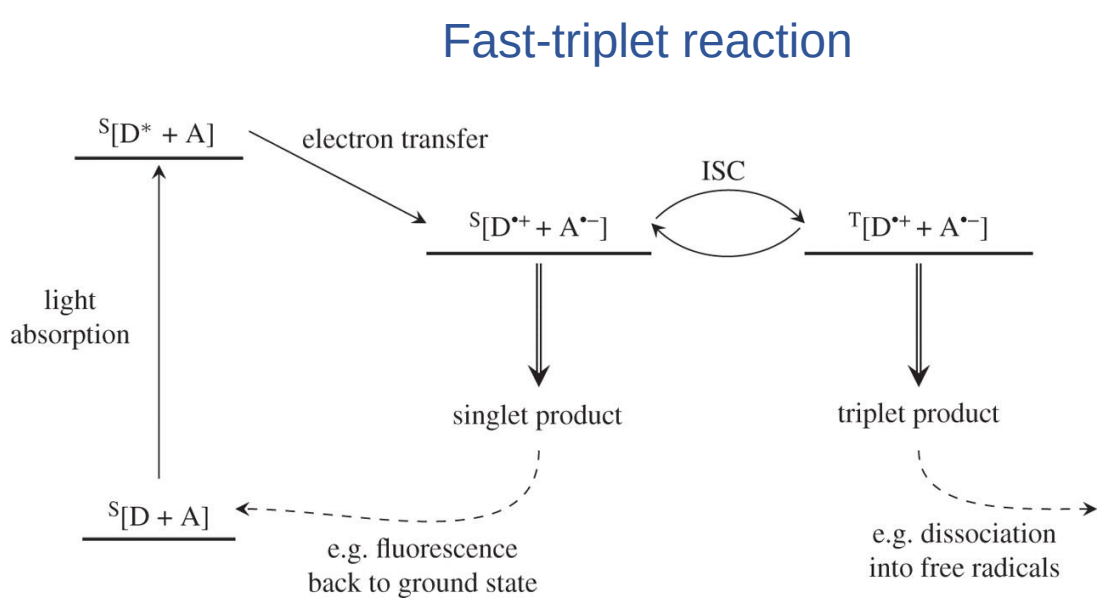
Chemical Compass



- In 1976 Klaus Schulten demonstrated that certain chemical reactions involving the formation of free radicals are sensitive to magnetic fields and the effect was likely caused by quantum entanglement between unpaired electrons.
- Schulten went on to propose that this kind of chemical compass was the mechanism behind the enigmatic avian compass.
  - But which biomolecules are involved and how?

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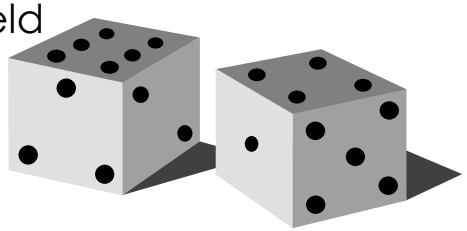
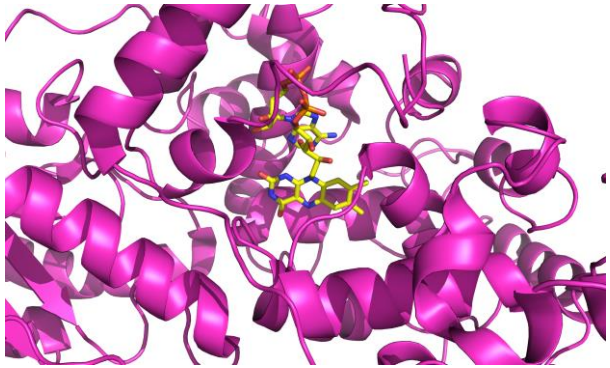
Thorsten Ritz, UCIrvine

The Quantum Radical Pair mechanism

A Model for Photoreceptor-Based Magnetoreception in Birds, Ritz, Adem and Schulten, *Biophysical Journal* **78** (2000) 707

Cryptochrome protein in photoreceptor neurons in back of retina
Proposed that a pair of entangled electrons detect earth's magnetic field





In 2004 experiments demonstrated that the robin's compass was disrupted by high frequency radio waves – as predicted by the theory

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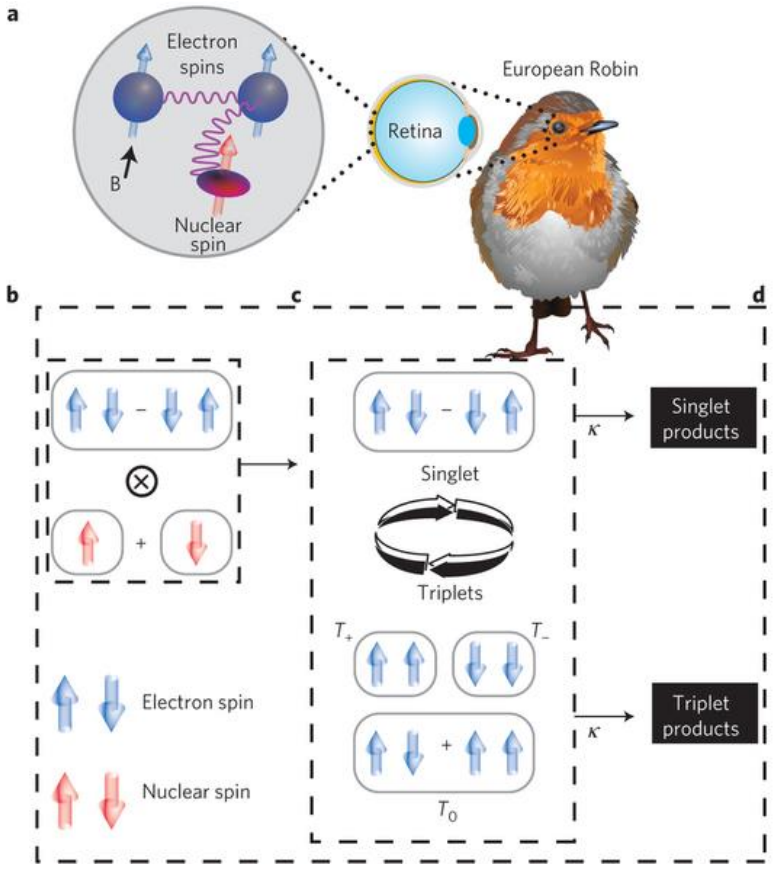
The Entanglement Model



- Ritz and the Wiltschko's demonstrated that the robin's compass was disrupted by weak external magnetic fields oscillating at radio frequencies (7 MHz) – as predicted by the model.
- T. Ritz, P. Thalau, J. B. Phillips, R. Wiltschko, and W. Wiltschko. Resonance effects indicate a radical-pair mechanism for avian magnetic compass. Nature 429 (6988):177-180, 2004.

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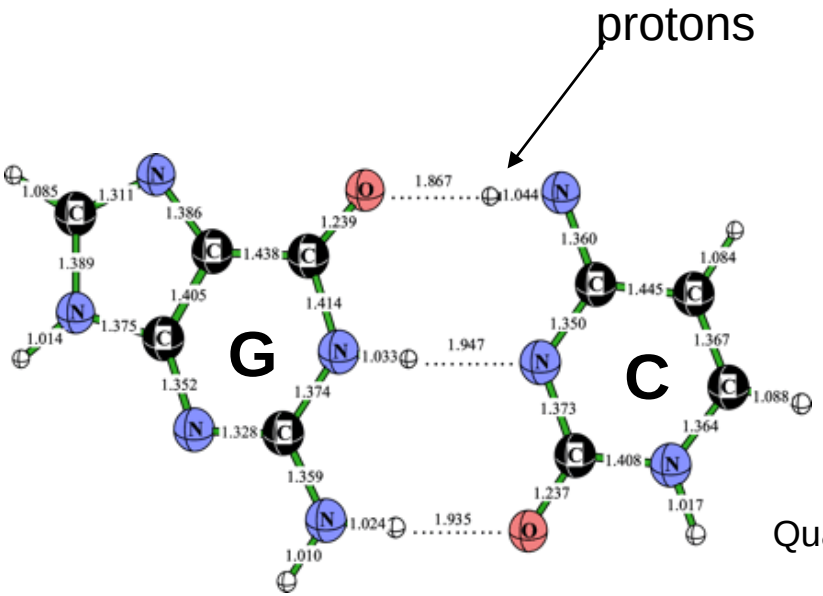
Schrödinger's other proposal: mutations represent quantum jumps



- *"Thus we account, by the very principles of quantum mechanics, for the most amazing fact about mutations, … that they are 'jumping' variations"*

Quantum-level coding

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PER-OLOV LÖWDIN (1916 – 2000)

- Lowdin pointed out that the DNA code is essentially a quantum code written in proton position
- He proposed that mutations may be caused by protons tunnelling into the ‘wrong’ position.

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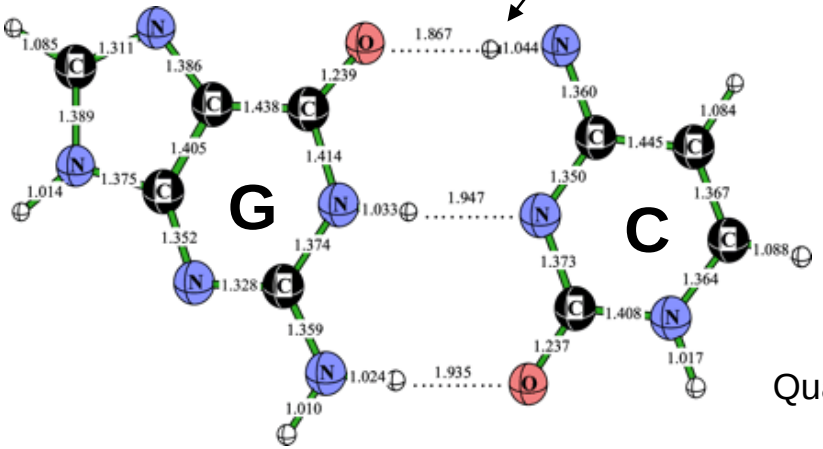
Genetic information is written into proton positions

protons



Quantum-level coding

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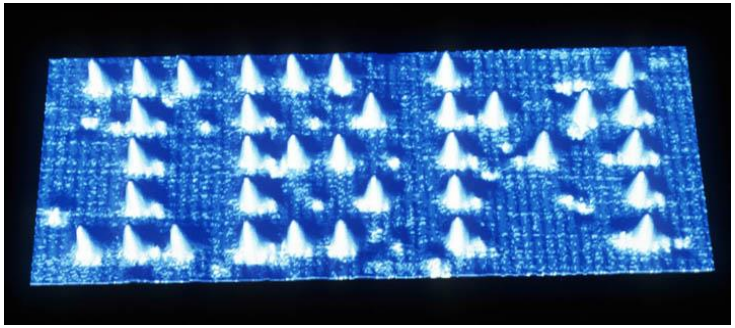
Biological quantum coding invented 3.8 billion BC



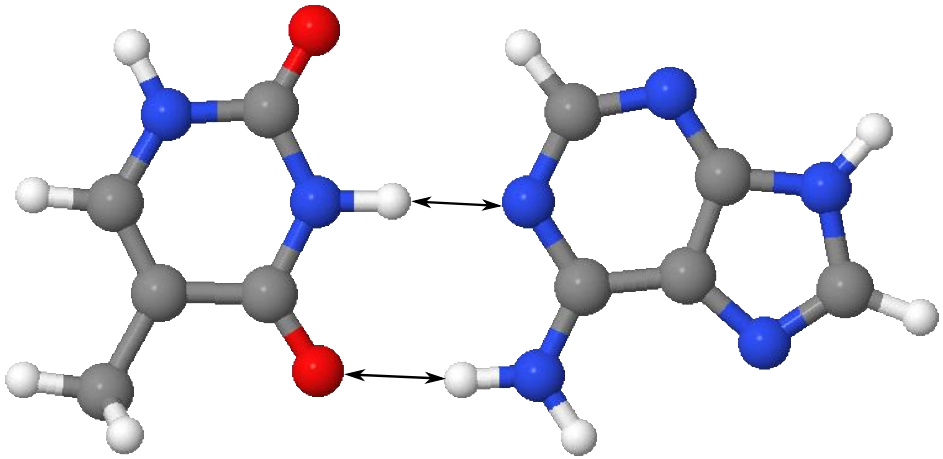
protons

Artificial quantum coding 1989

G **C**

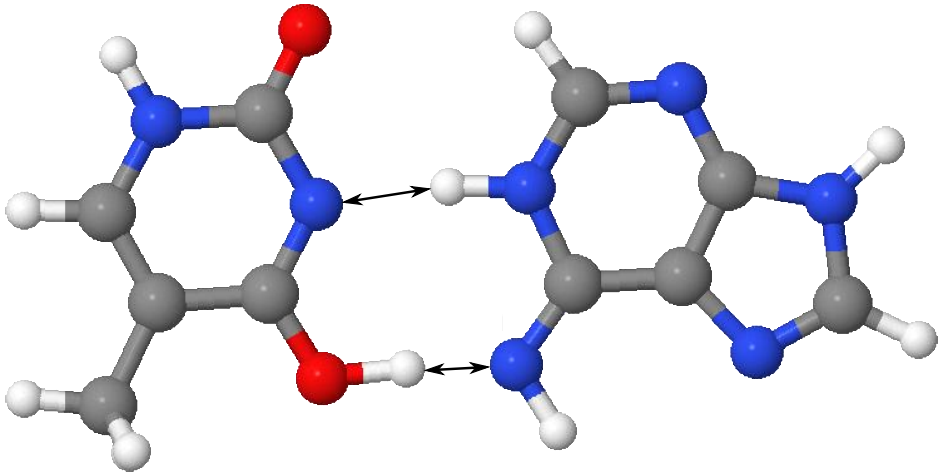
Quantum tunnelling and mutation

A : T base pair



Quantum tunnelling and mutation

A : T base pair



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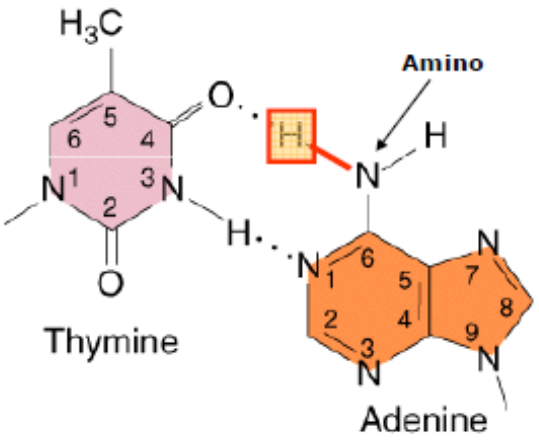
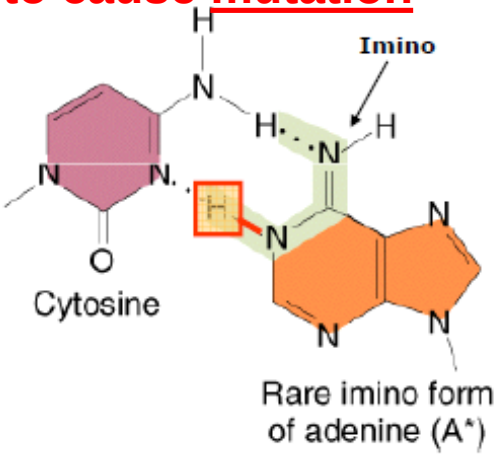
A:C mispairs

NORMAL:
amino tautomer A pairs with T



Correct base-pairing

RARE:
imino tautomer of A pairs with C
to cause mutation



Incorrect base-pairing -> mutation

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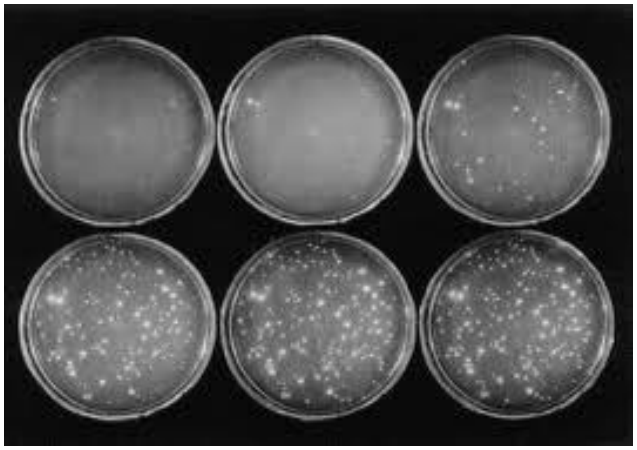
- 1999 McFadden and Al-Khalili proposed a quantum mechanical model to account for ‘adaptive mutations’ (John Cairns, 1988) that appear to be more frequent when they provide a growth advantage to bacterial cells.



ELSEVIER

BioSystems 50 (1999) 203–211

BioSystems

A quantum mechanical model of adaptive mutation

Johnjoe McFadden [a,*], Jim Al-Khalili [b]

[a] *Molecular Microbiology Group, School of Biological Sciences, University of Surrey, Guildford, Surrey GU2 5XH, UK*
[b] *Department of Physics, University of Surrey, Guildford, Surrey GU2 5XH UK*

Received 10 August 1998; accepted 15 January 1999

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Density Function theory to calculate tunnelling probability in A:T base-pair

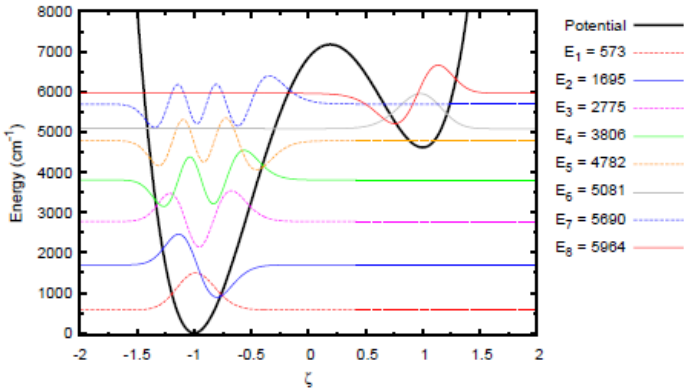
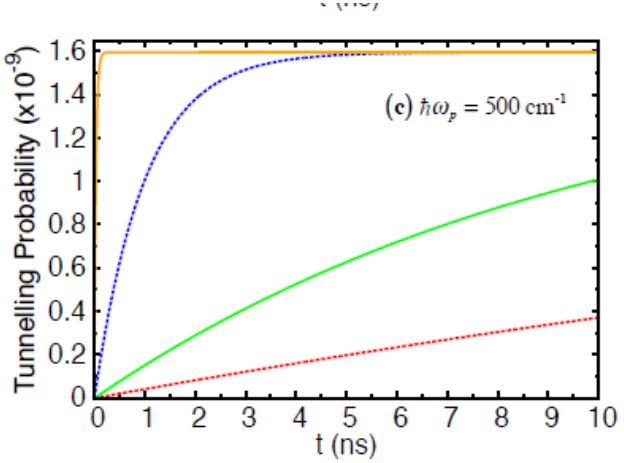


Fig. 5 Energy eigenstates of adenine-thymine base pair 1-D model.



- The influence of quantum tunnelling on proton transfer within a base pair H-bond (modelled as the DFT deduced double-well potential) investigated by solving the time-dependent master equation for the density matrix.
- The effect on a quantum system by its surrounding water molecules wasexplored via the inclusion of a dissipative Lindblad term in the master equation, in which the environmentis modelled as a heat bath of harmonic oscillators.
- Low tunnelling probability (10^{-9}) but boosted by thermally-assisted coupling with the water bath.

Godbeer, A. D., Al-Khalili, J. S., & Stevenson, P. D. (2015). Modelling proton tunnelling in the adenine-thymine base pair. Phys Chem Chem Phys, 17(19), 13034-13044. doi:10.1039/c5cp00472a

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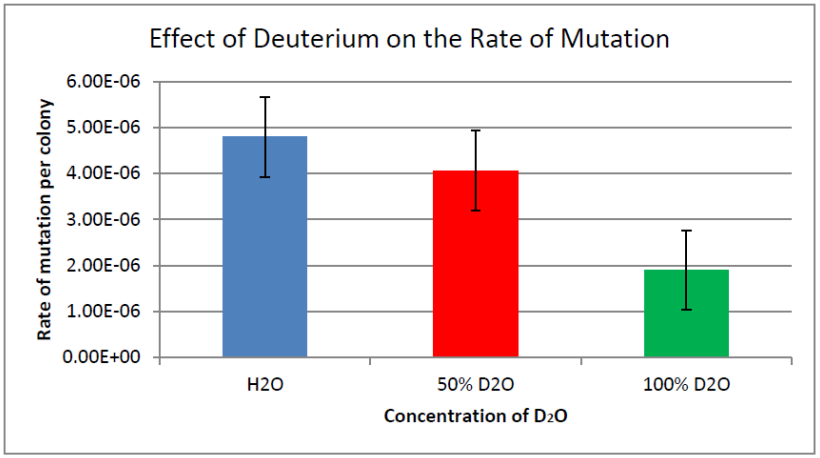
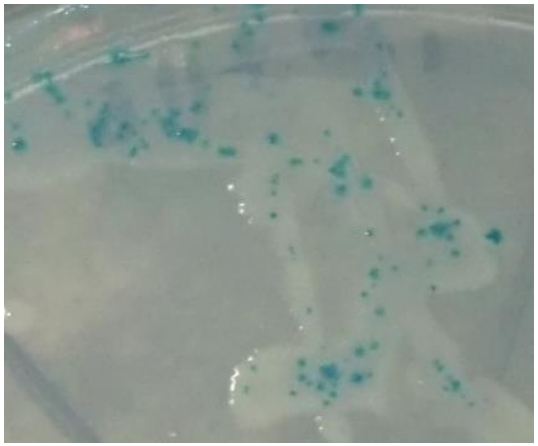
But does tunnelling influence mutation? Heavy isotope effect





- Tunnelling should be severely depressed if hydrogen nuclei (protons) in DNA are replaced with deuterium nuclei.
- We grew *E. coli* in media made up in normal water and deuterated water and measured lac^- (white) to lac^+ (blue) mutation.
- Mutation rates reduced in deuterated media …

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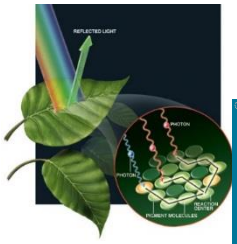
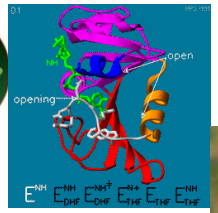
Candidates for quantum biology

- Photosynthesis
- Enzymes
- Magnetoreception
- Smell
- DNA mutations
- Origin of life
- Consciousness?





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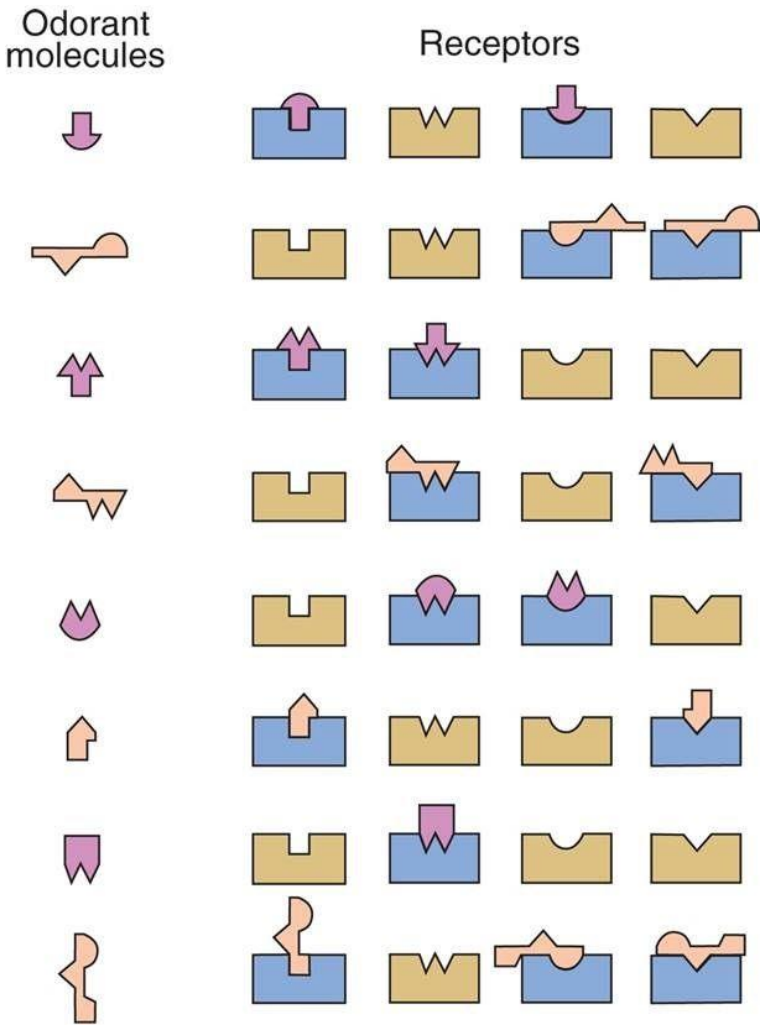
The puzzle of smell



- The standard theory of olfaction is a lock-and-key mechanism – shape determined smell
  - But …
  - Very differently-shaped molecules smell the same
  - Very similarly-shaped molecules smell very different
- Odour often seems to correlate with functional groups rather than shape
- Vibrational theory of olfaction - was first proposed by Malcolm Dyson in 1928

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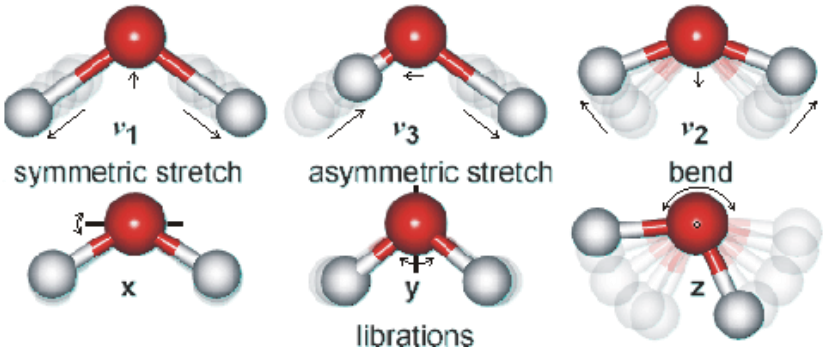
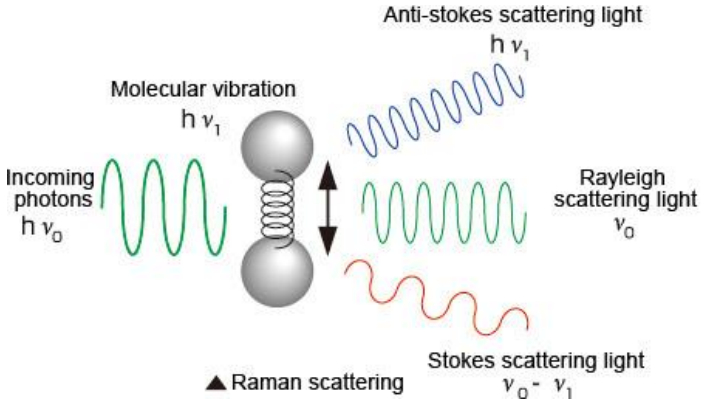
Vibrational spectroscopy





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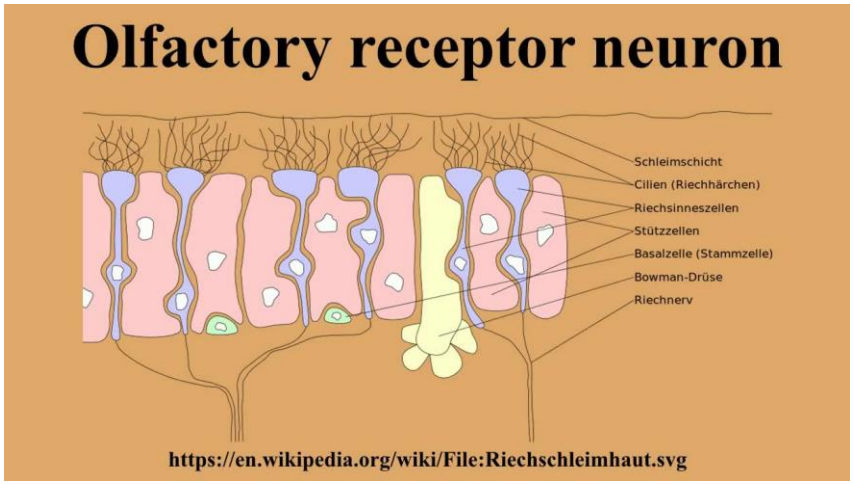
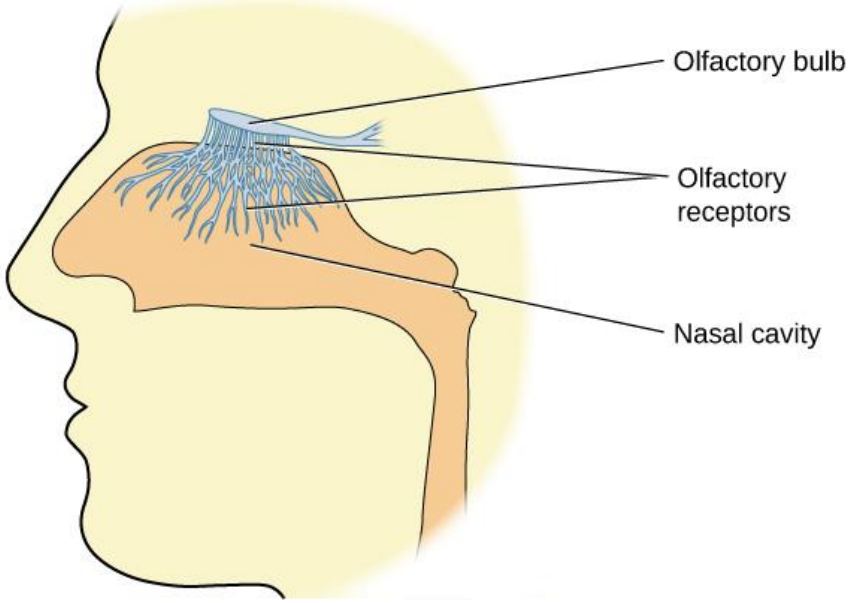
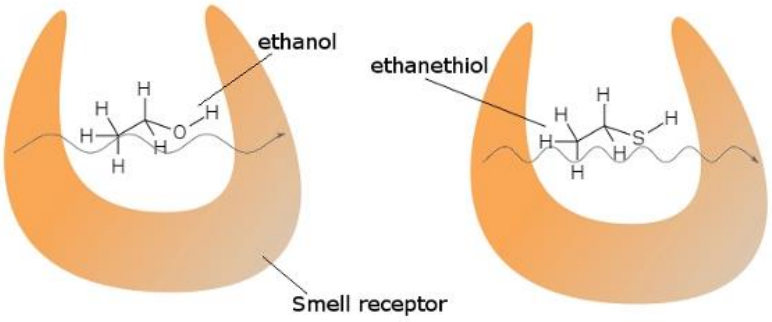
But how to detect a vibration in the nose?







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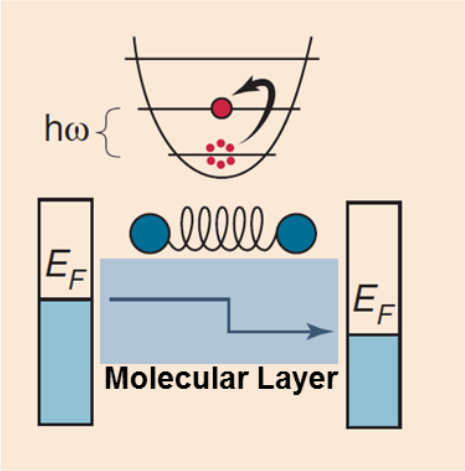
Inelastic electron tunnelling spectroscopy (IETS)

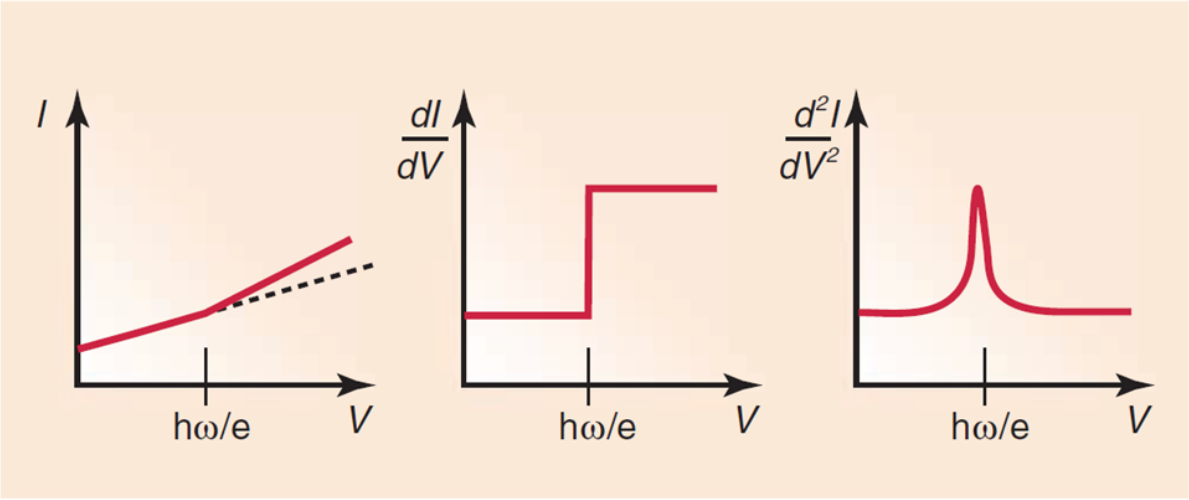


Electron transport through molecular layer by tunneling effect

Inelastic tunneling channel open when

$eV = \hbar\omega_{vib}$

V: bias of the junction
ω: frequency of the vibrational mode



Current change by inelastic process is presented by its second derivative measured by lock-in technique

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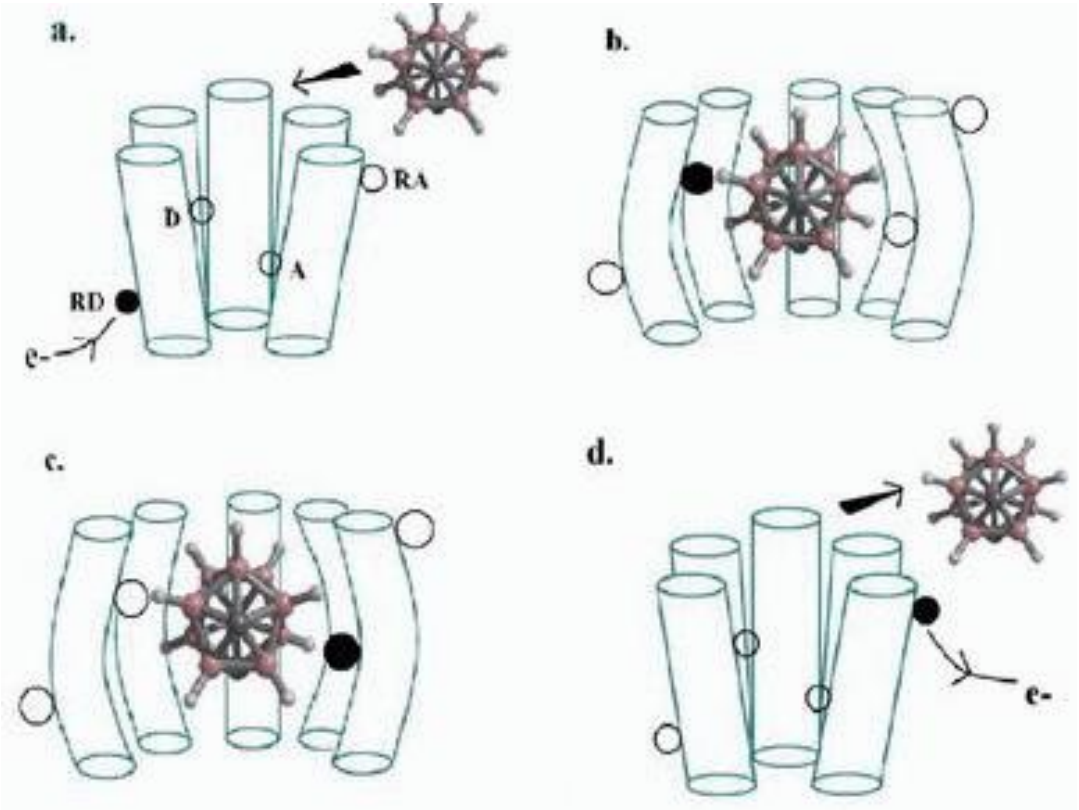
The Luca Turin model of smell via resonance-mediated electron tunnelling:



a) an electron in the nasal receptor finds its way to the donor component of the receptor
b) and (c), a scent molecule's vibrational frequency enables the electron to tunnel to a different energy state
d) electron travels to the acceptor unit and molecule leaves

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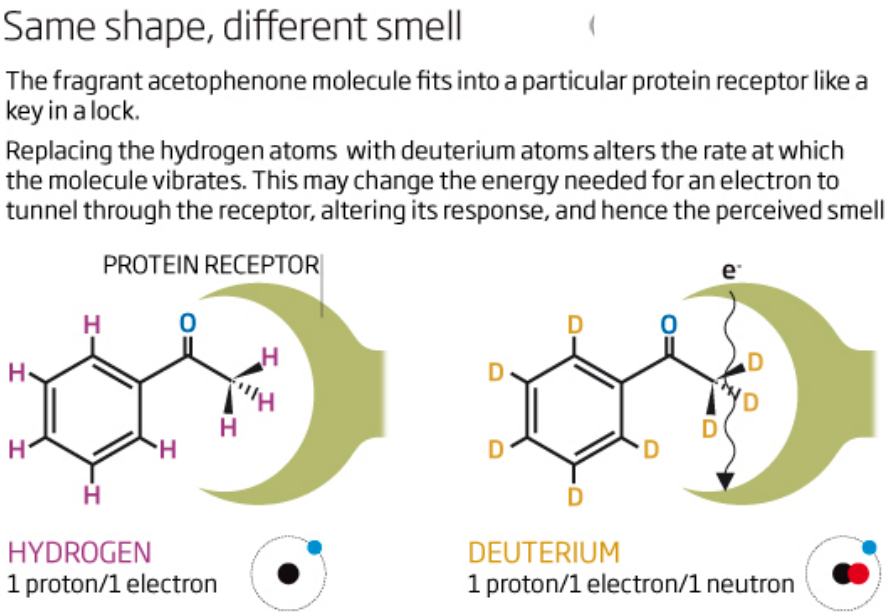

- Turin and Skoulakis replaced hydrogen with deuterium in odorants and tested whether Drosophila melanogaster can distinguish these identically shaped isotopes.
- Friut flies not only differentiate between isotopic odorants, but can be conditioned to selectively avoid the common or the deuterated isotope.
- These findings are inconsistent with a shape-only model for smell, and instead support the existence of a molecular vibration-sensing component to olfactory reception.

Franco, M. I., et al. (2011). "Molecular vibration-sensing component in Drosophila melanogaster olfaction." Proc. Natl. Acad. Sci. U. S. A 108(9): 3797-3802.

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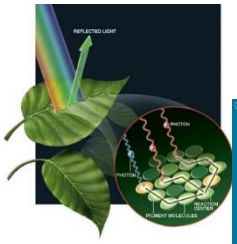

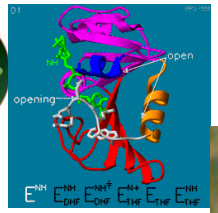

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PhD Studentship Opportunities in Quantum Biology

University of Surrey

Qualification type:	PhD	**Placed on:**	22nd March 2018
Location:	Guildford	**Closes:**	9th April 2018
Funding for:	UK Students, EU Students	★ View Employer Profile	
Funding amount:	£14,553 per annum		
Hours:	Full Time		

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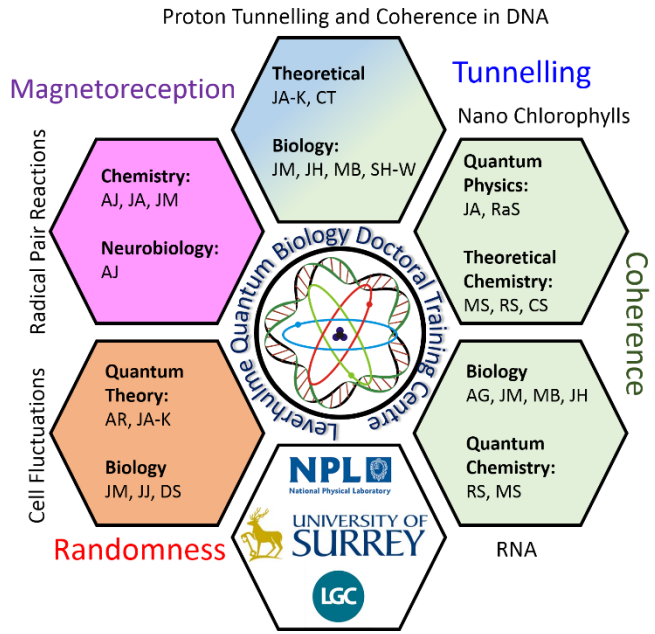
Leverhulme Doctoral Training Centre in Quantum Biology at the University of Surrey



- 21 PhD students over 5 years
- Looking to establish collabrations
  - Collaborative projects
  - Collaborative PhD's
  - Paired PhD's

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Quantum Biology

Johnjoe McFadden

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