Title: Quantum Neurobiology

Speakers: Travis Craddock

Collection/Series: Colloquium

Subject: Other

Date: February 26, 2025 - 2:00 PM

URL: https://pirsa.org/25020026

Abstract:

Quantum biology explores how phenomena like superposition, tunneling, and entanglement influence biological systems, with growing experimental evidence supporting their role in processes such as photosynthesis, enzymatic reactions, DNA mutations, and animal navigation. These discoveries have profound implications for medicine, renewable energy, and our understanding of life. Quantum neurobiology applies this perspective to the brain, exploring how brain cells function beyond traditional models of electrical activity and chemical neurotransmission. Moving beyond classical models of chemical and electrical neuronal signaling, quantum approaches could revolutionize diagnostics and treatments for neurological disorders while offering deeper insights into cognition, behavior, and consciousness. Here will be presented an overview of quantum biology, examining the current state of quantum neurobiology, both theory and experiment, and exploring its potential applications in diagnosing and treating neuroinflammatory conditions such as Alzheimer’s and Parkinson’s disease.

QUANTUM NEUROBIOLOGY

Travis Craddock, Ph.D. (Physics)
Associate Professor, Department of Biology
Tier I Canada Research Chair in Quantum Neurobiology
University of Waterloo, Waterloo, Ontario, Canada

UNIVERSITY OF WATERLOO

Acknowledgements

- Waterloo Quantum Neurobiology Team

Hadi Zadeh-Haghighi, Ph.D.
Research Associate

Lea Gassab, Ph.D.
Postdoctoral Scholar

Caleb Siguenza
MSc Student

Isabella Barichello
Co-op Student

- Collaborators
  - Robert Alfano, City College of New York
  - Stuart Hameroff, University of Arizona
  - Jack Tuszynski, Politechnico di Torino
  - Christoph Simon, University of Calgary
  - Robert Smith, Nova Southeastern University
  - Aarat Kalra, Indian Institute of Technology
  - Nirosha Murugan, Wilfred Laurier
  - Dante Lauretta, University of Arizona

- Funding

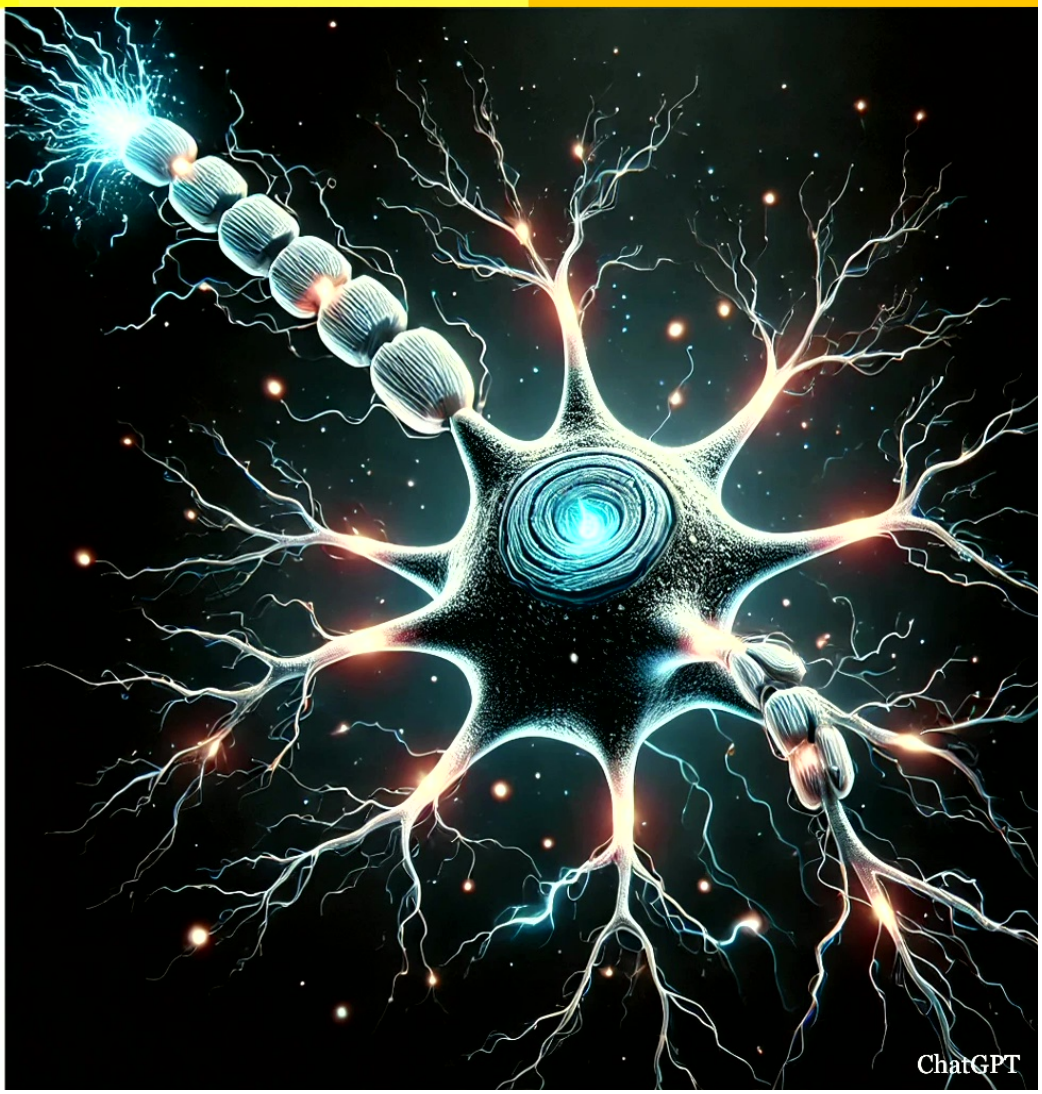
Canada Research Chairs

Canada

UNIVERSITY OF WATERLOO

Overview

1. Introduction
   - What is a Neuroinflammatory Illness?
   - What is Quantum Mechanics?
   - What is Quantum Biology?
2. Magnetic Field Effects
   - Nuclear Spin Effects in Biology
   - Posner Molecules and Quantum Cognition
   - Radical Pair Mechanism
3. Light-Matter Interactions
   - Light Harvesting Antennae
   - Ultraweak Photon Emission
   - Cytoskeleton as a Light Harvesting Device
4. Future Directions
5. Conclusion
6. References
7. Questions

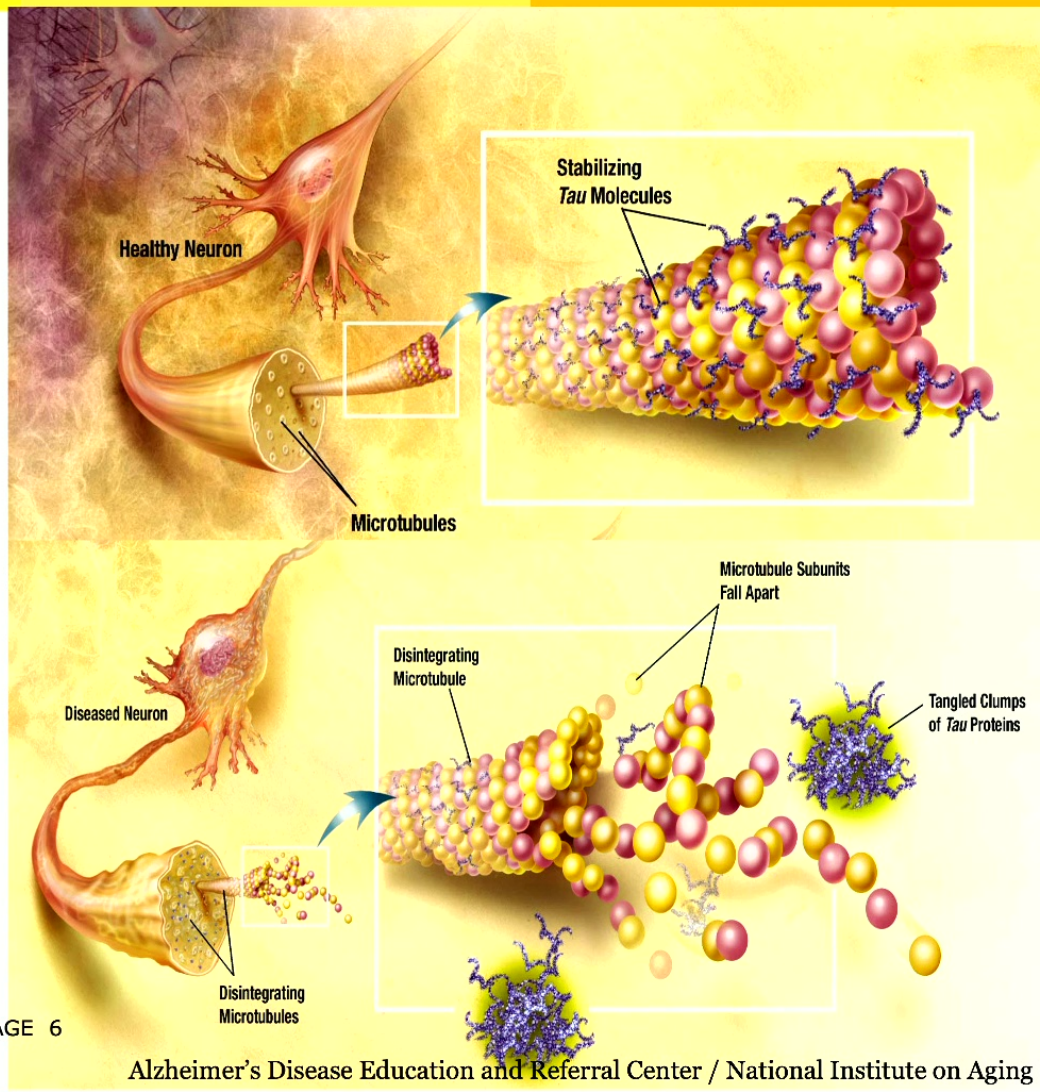


Introduction:
What are Neuroinflammatory Illnesses?

- Neuroinflammation is an inflammatory response in the brain.
  - Oxidative Stress (Reactive Oxygen Species)
  - Imbalance of Metal Ions
- Can be due to physical, chemical or biological insults.
- When short it is protective.
- Long-lasting neuroinflammation leads to neurodegenerative & neurological disorders.

Introduction:
What are Neuroinflammatory Illnesses?

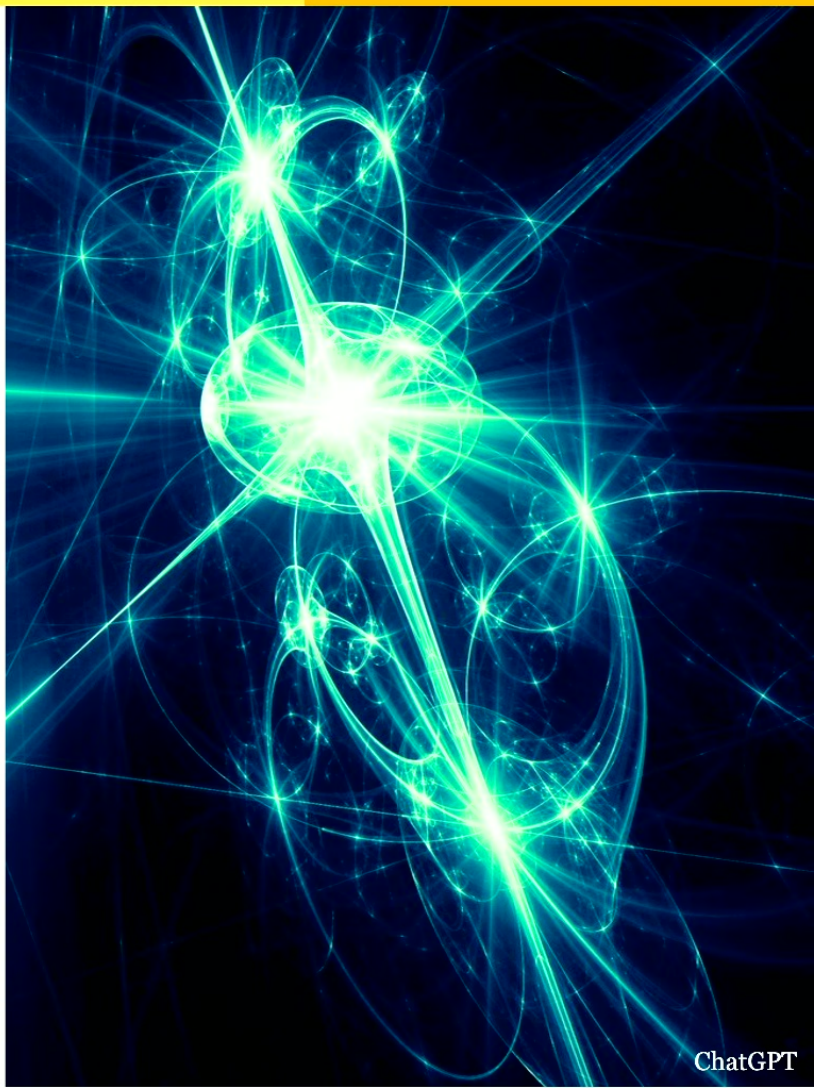
- Neuroinflammation is an inflammatory response in the brain.
  - Oxidative Stress (Reactive Oxygen Species)
  - Imbalance of Metal Ions
- Can be due to physical, chemical or biological insults.
- When short it is protective.
- Long-lasting neuroinflammation leads to neurodegenerative & neurological disorders.
- Neurodegeneration follows from destruction of protein scaffolds (microtubules)
- These events are connected but how is unknown.



Alzheimer's Disease Education and Referral Center / National Institute on Aging

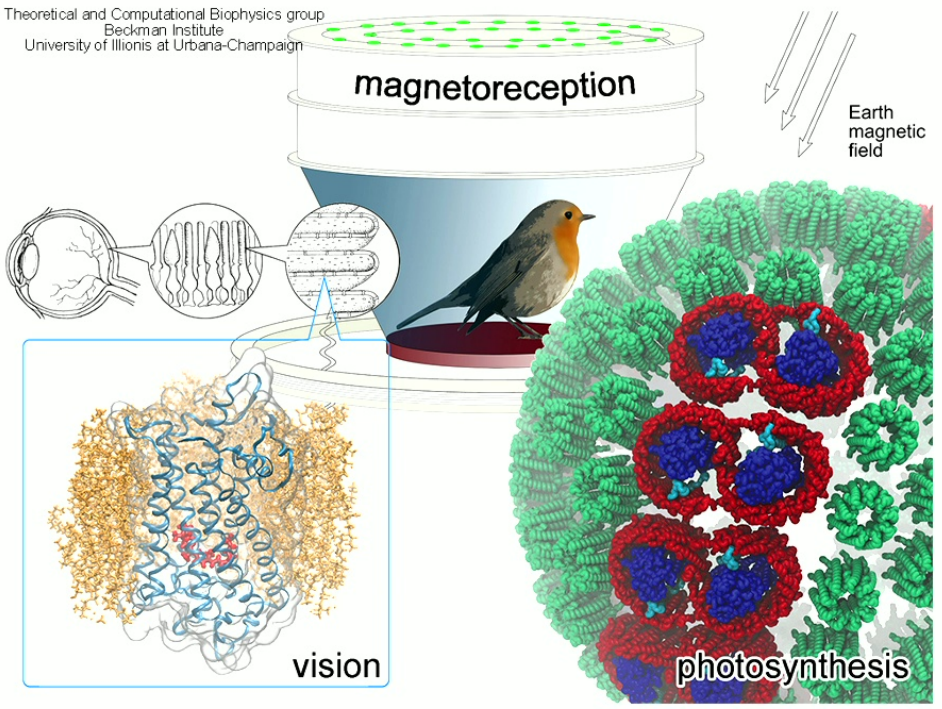
Introduction:
What is Quantum Mechanics?

- Quantization
  - Certain physical properties are quantized and discrete, and some have no classical analogue (i.e. spin).
- Wave–particle duality
  - Probability waves extended throughout space (two places at once).
  - Collapse to single point upon measurement (standard).
- The Uncertainty principle
  - Cannot know both where a particle is and where it is going with complete accuracy.
- Quantum entanglement
  - Entangled particles can send “information” instantaneously, act as one.
- Quantum Tunneling
  - Particles can pass through barriers that classically they could not.



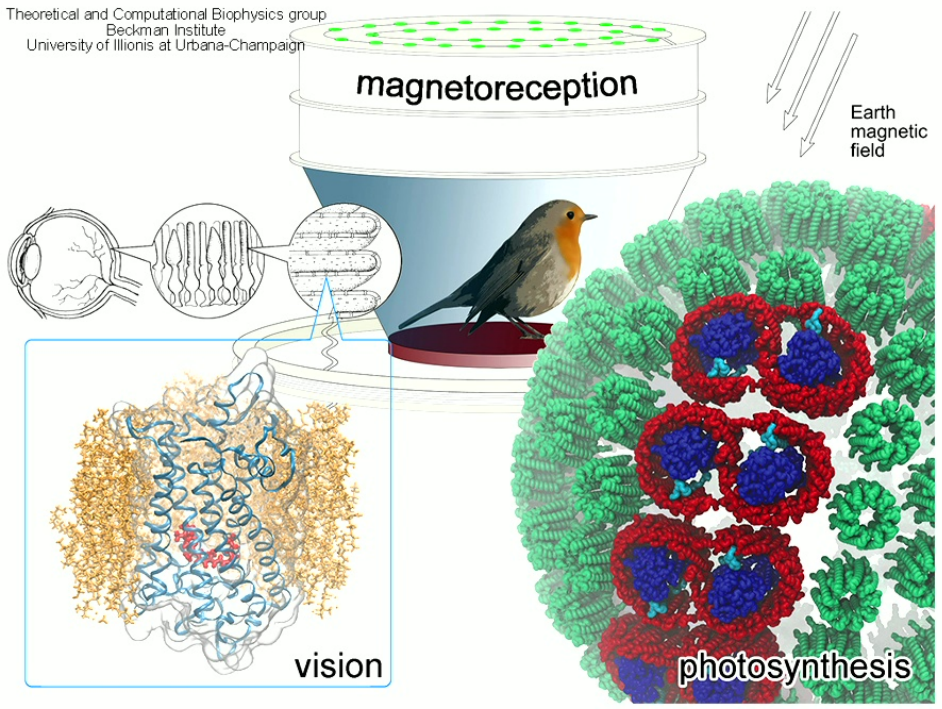
Introduction:
What is Quantum Biology?

- Quantum biology is the application of quantum theory to aspects of biology that cannot be accurately described by the classical laws [2].
- This includes:
  - Light-matter interactions (Photosynthesis, Vision)
  - Electron and proton transport (Ion Channels, Electron Transport Chain)
  - Magnetic field effects (Bird navigation, radical pair chemistry)



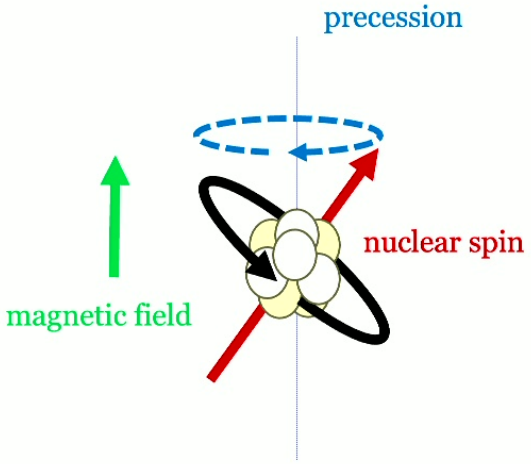
Introduction:
What is Quantum Biology?

- Quantum biology is the application of quantum theory to aspects of biology that cannot be accurately described by the classical laws [2].
- This includes:
  - **Light-matter interactions (Photosynthesis, Vision)**
  - Electron and proton transport (Ion Channels, Electron Transport Chain)
  - **Magnetic field effects (Bird navigation, radical pair chemistry)**



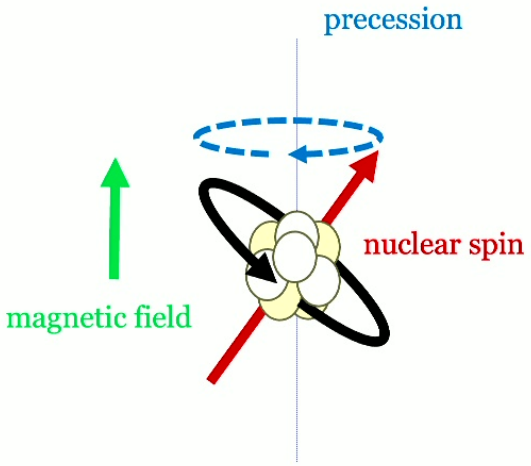
Magnetic Field Effects:
Evidence for Nuclear Spin Effects

- Nuclear spin is a quantum property that represents the angular momentum of the atomic nucleus.
- Determined by number of protons and neutrons
- Isotopes can be the same element with different nuclear spin.
- Classically, isotopes should have no bearing on biochemistry
- However, there is some evidence for isotope effects in biology
  - Lithium-6 and lithium-7 showed different animal behaviors[3].
  - Anesthetic potency of xenon isotopes differs in mice [4].
  - ATP synthesis affected by magnesium isotopes and magnetic fields [5].



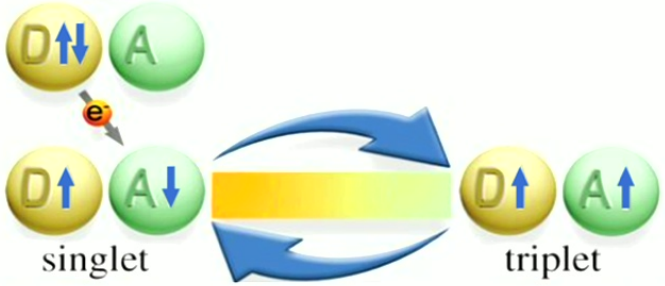
Magnetic Field Effects:
Evidence for Nuclear Spin Effects

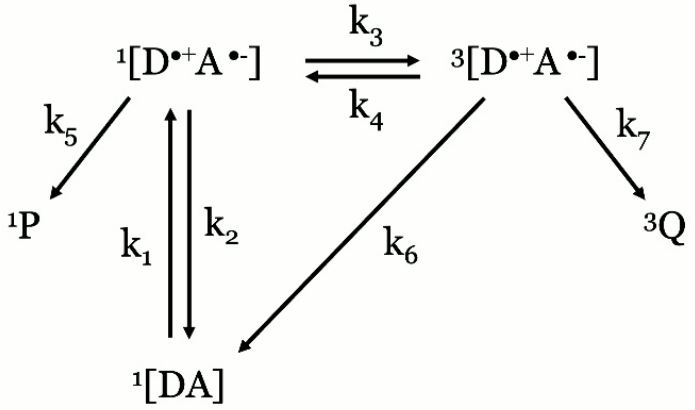
- Nuclear spin is a quantum property that represents the angular momentum of the atomic nucleus.
- Determined by number of protons and neutrons
- Isotopes can be the same element with different nuclear spin.
- Classically, isotopes should have no bearing on biochemistry
- However, there is some evidence for isotope effects in biology
  - Lithium-6 and lithium-7 showed different animal behaviors[3].
  - Anesthetic potency of xenon isotopes differs in mice [4].
  - ATP synthesis affected by magnesium isotopes and magnetic fields [5].
- **But how could this occur?**



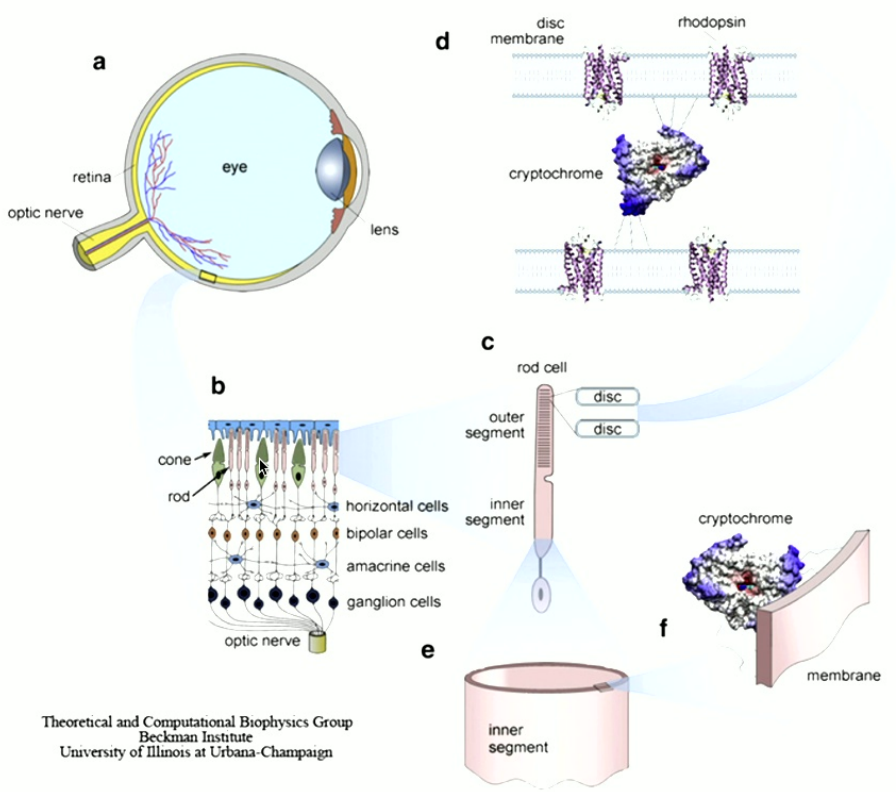
Magnetic Field Effects:
Radical Pair Mechanism[6]

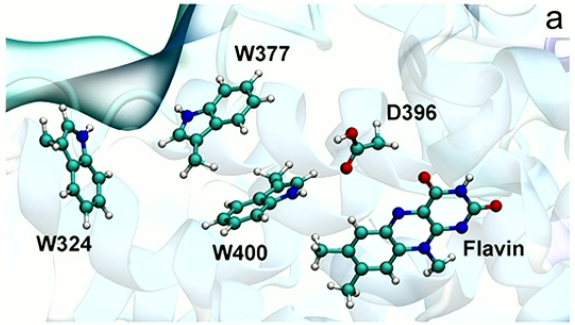
- A radical-pair mechanism explains weak magnetic field and magnetic isotope effects.
- A radical pair is formed when an electron is moved from a donor to an acceptor forming an entangled pair.
- Singlet state and triplet state have different chemical kinetics.
- External magnetic influence (Zeeman) or internal magnetic influence (hyperfine coupling) drives the system towards triplet or singlet state.

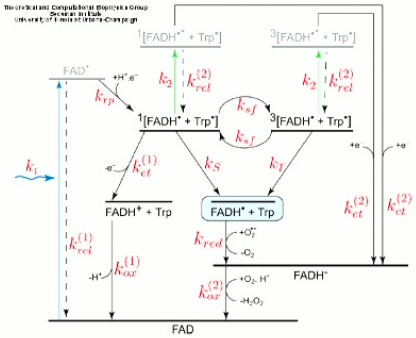




Magnetic Field Effects:
Radical Pair Mechanism - Avian Navigation[7]





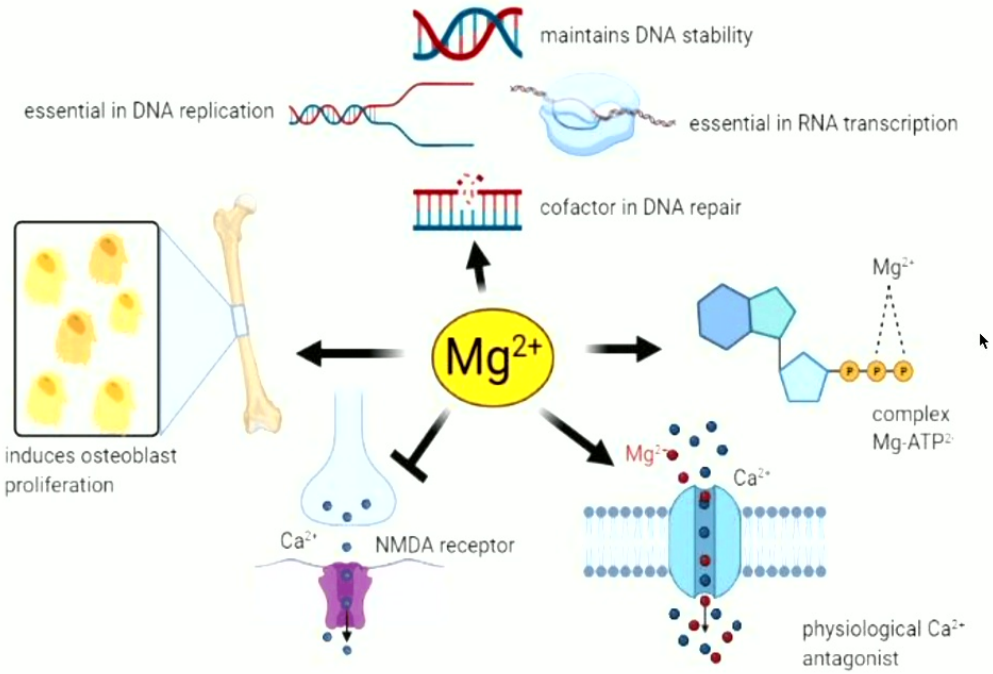


- One of the most well studied examples of quantum biology.
- Cryptochrome molecule in bird eye.
- Light excites Flavin molecules (FAD)
- FAD and Tryptophan form radical pair sensitive to magnetic field
- Affects neuron excitability and allows bird to see magnetic field.

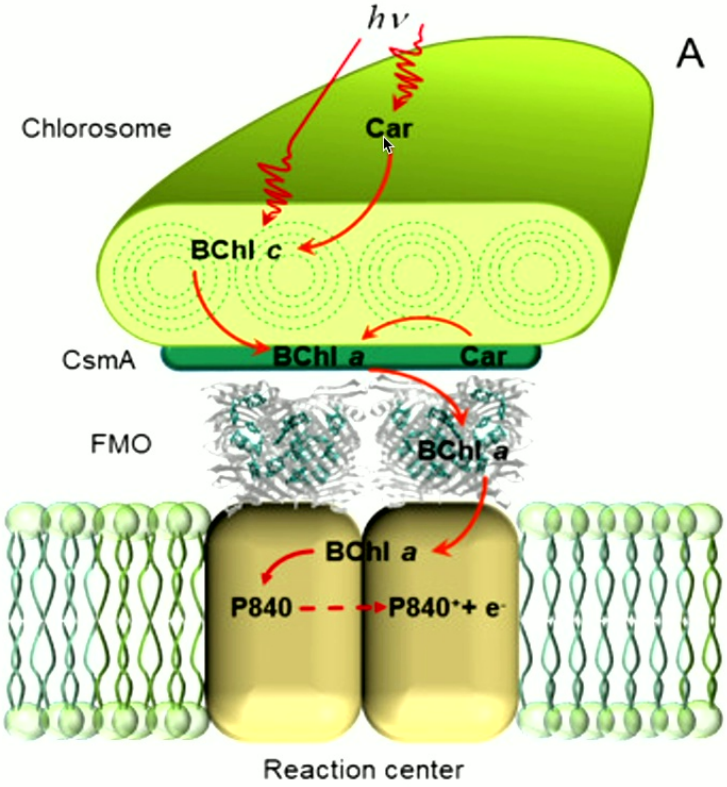
UNIVERSITY OF WATERLOO

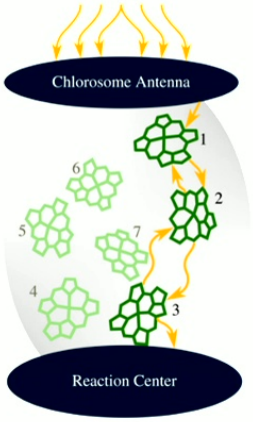
Magnetic Field Effects:
Radical Pair Mechanism - ATP Synthesis[5]

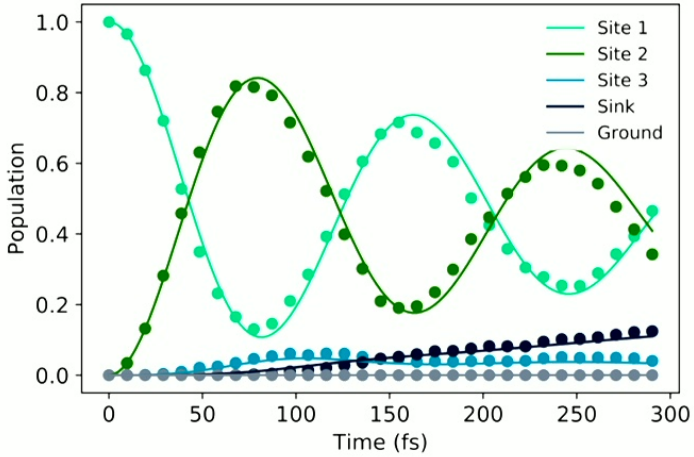
- Magnetic isotope effect observed in the magnesium ion (Mg^{2+}) in the synthesis of adenosine-triphosphate (ATP)
  - $^{25}Mg^{2+}$ is a stable magnetic isotope
  - Natural Mg^{2+} has 10% $^{25}Mg^{2+}$ abundance
- Using magnetic isotope $^{25}Mg^{2+}$ can increase enzymatic ATP yield by 2-3 times. Further increased by application of weak magnetic field.
- Observed in vitro and in bacterial systems.
- Not specific to brain, but electrical activity may affect.



Light-Matter Interactions:
Light Harvesting Antennae[8,9]





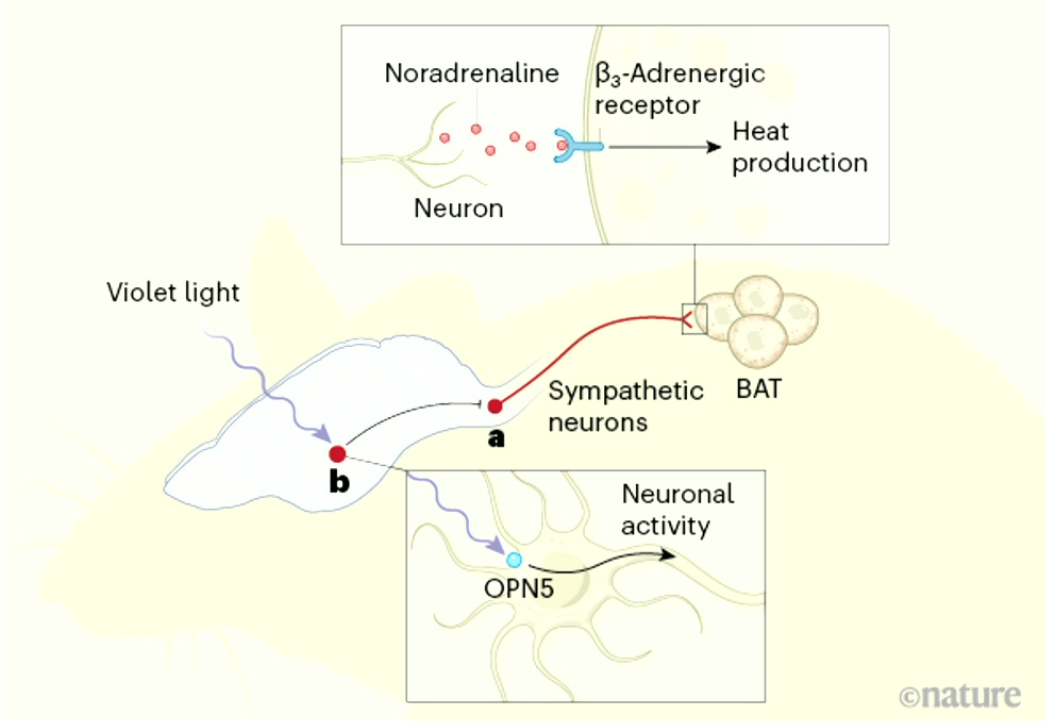


- Another well studied example of quantum biology.
- Light impinges on antenna array.
- Molecules excited coherently (shared) in qbio, individually (hopping) in classical.
- Quantum beats evidence of quantum effects.
- Believed to be "quantum-ish" [9].

Light-Matter Interactions

Light receptors in brain[10]

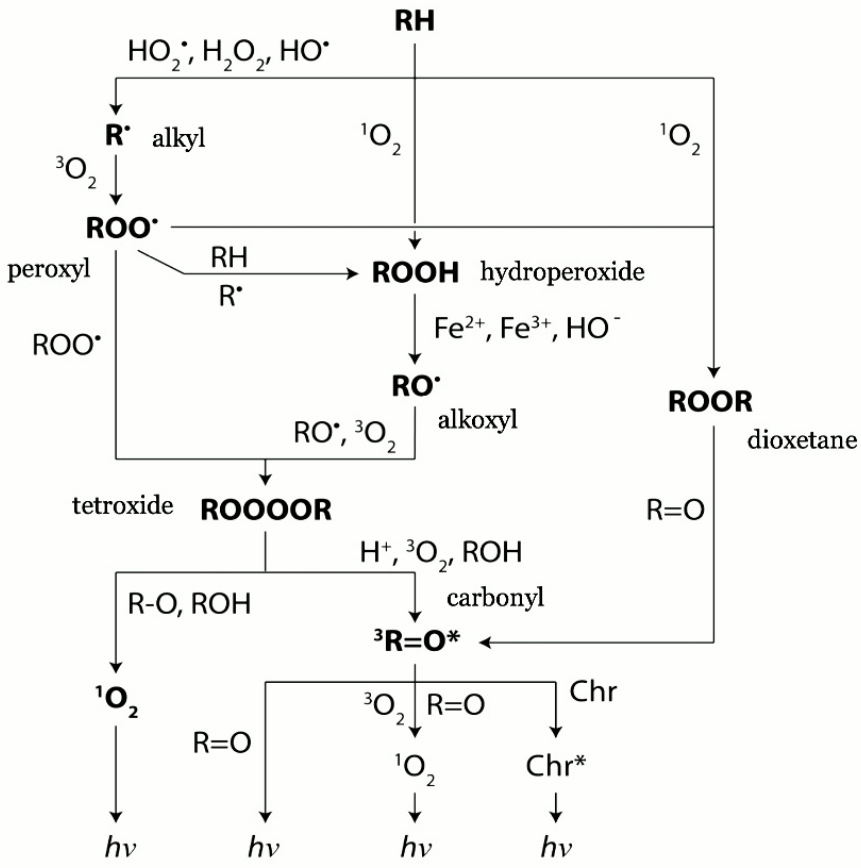
- Like the eye, the brain has light sensitive opsins
  - i.e. OPN5 in hypothalamic preoptic area
- Sensitive to UV and violet light
- Recent work shows OPN5 is light-sensitive deep brain photoreceptor that normally suppresses brown adipose tissue thermogenesis.



Light-Matter Interactions

Ultraweak photon emission (UPE)[11]

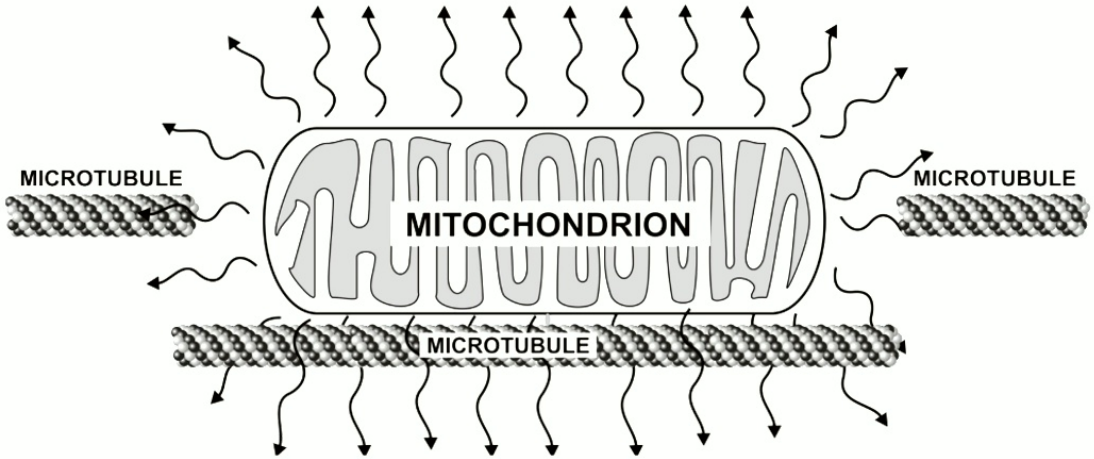
- Oxidative metabolism generates reactive oxygen species (ROS)
- Decomposition of ROS leads to generation of electronically excited chemical groups
- Leads to carbonyls in a triplet excited ^{3}(R=O)* or singlet excited state oxygen
- Excitation energy can be transferred to chromophores molecules or emitted.



UNIVERSITY OF WATERLOO

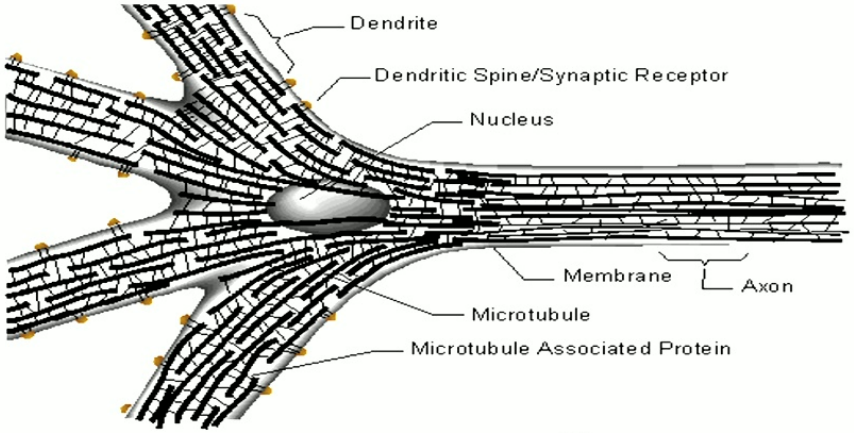
Light-Matter Interactions:

UPE can affect microtubule proteins

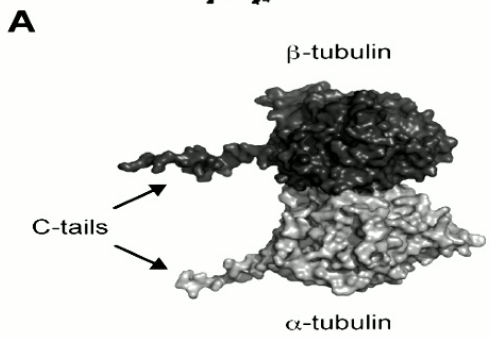


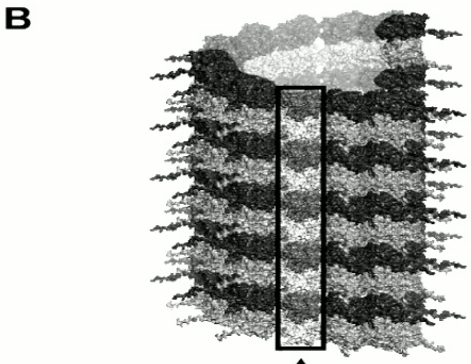
- Microtubules co-localize with mitochondria, especially filamentous mitochondria in neuron [12].
- Microtubule polymerization is sensitive to photostimulation, reorganize/reorient in dose dependent manner [13].
- Potential for ROS generated UPE to damage microtubules.
- Microtubules can act as optical waveguides to funnel UPE energy towards/away from critical sites [14].

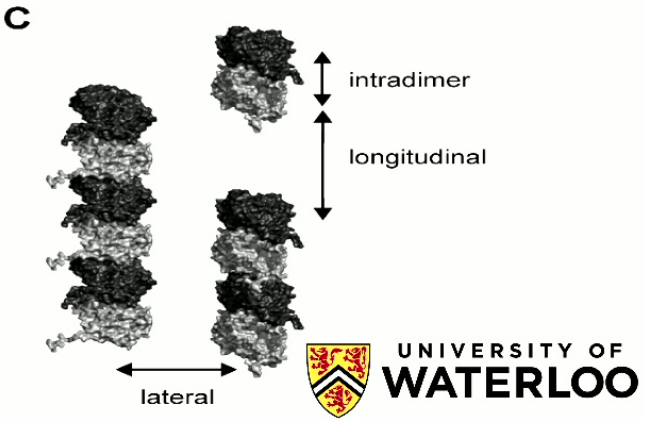
Light-Matter Interactions:
Microtubules as a Light Harvesting Device



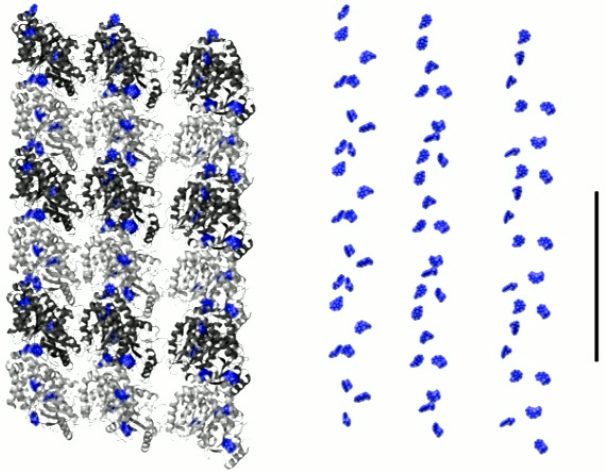
- Most abundant structure of the cytoskeleton.
- MTs are hollow cylindrical polymers of the protein tubulin.
- ~25 nm in diameter and range in length from μm to mm.
- Responsible for maintaining cell morphology, trafficking cell cargo, cell motility, anchoring ion channels, with possible roles in signal transduction.
- All factors may influence synaptic plasticity and as such learning and memory.

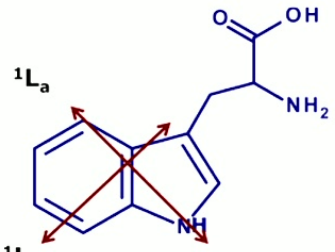


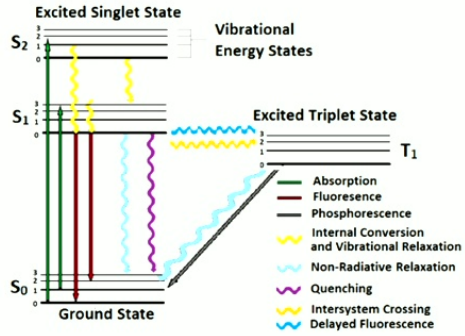




Light-Matter Interactions:
Microtubules as a Light Harvesting Device[16]

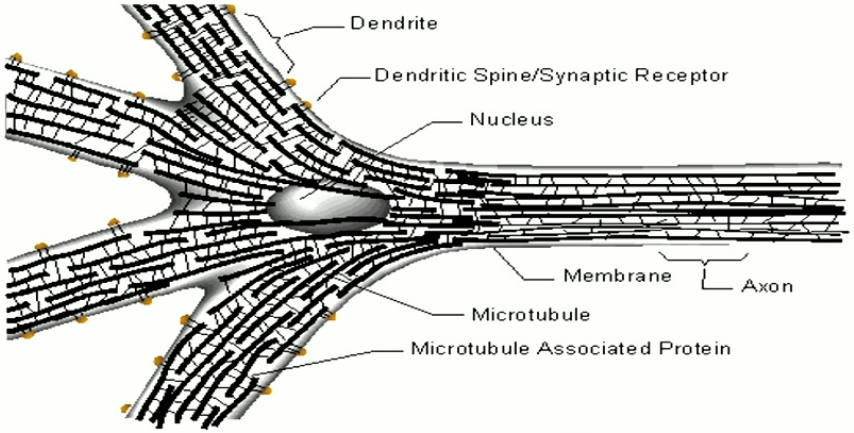




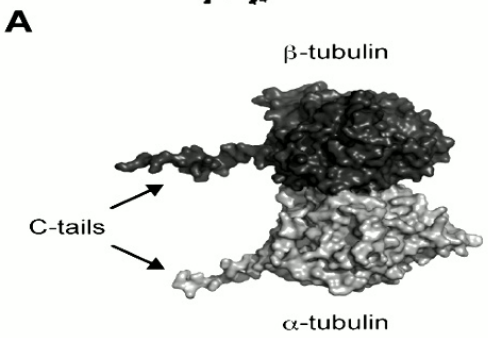


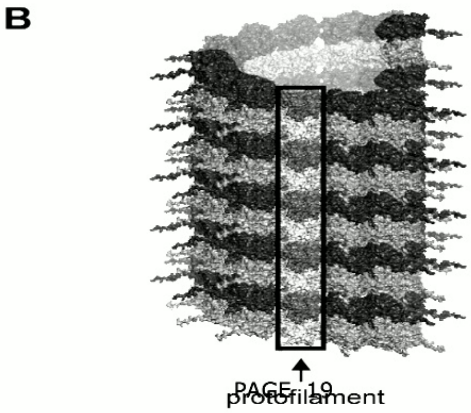
- Symmetry of microtubule makes continuous network of tryptophan analogous to a light harvesting antenna.
- “Aromatic" ring structures provide regions of delocalizable/ polarizable electrons and electronic excited states in proteins
- Tryptophan has an "indole ring" giving it a high electron resonance and fluorescence
- Tryptophan has a comparable transition dipole to chlorophyll of up to ~6 Debye
- Unique pigment having:
  - 2 interchangeable 1st excited states ^1L_a, ^1L_b
  - Can exist in a singlet or triplet excited state

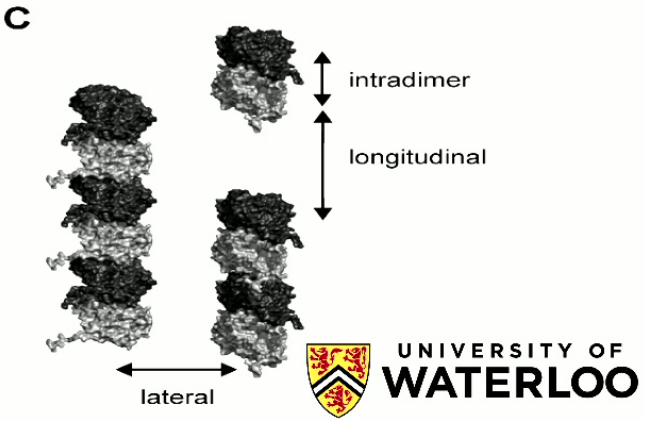
Light-Matter Interactions:
Microtubules as a Light Harvesting Device



- Most abundant structure of the cytoskeleton.
- MTs are hollow cylindrical polymers of the protein tubulin.
- ~25 nm in diameter and range in length from μm to mm.
- Responsible for maintaining cell morphology, trafficking cell cargo, cell motility, anchoring ion channels, with possible roles in signal transduction.
- All factors may influence synaptic plasticity and as such learning and memory.

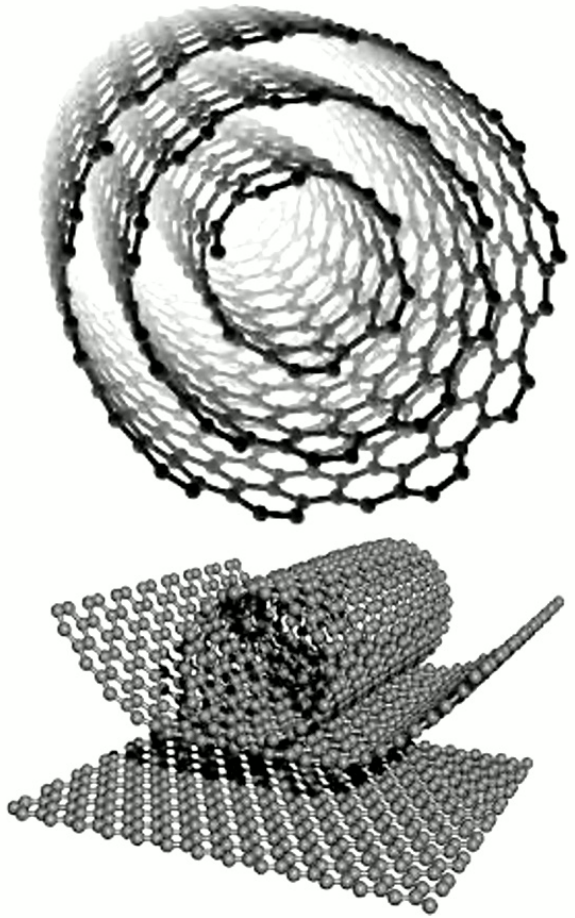




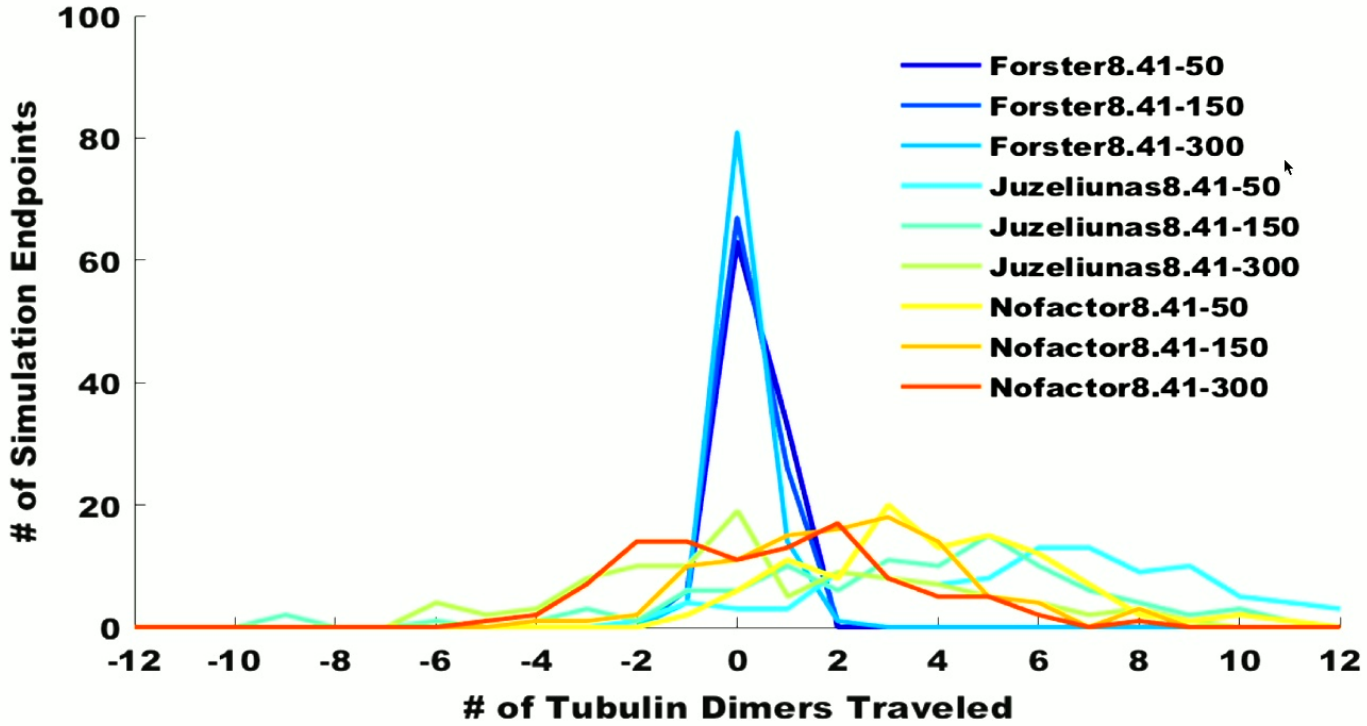


Light-Matter Interactions:
Microtubules as a Light Harvesting Device

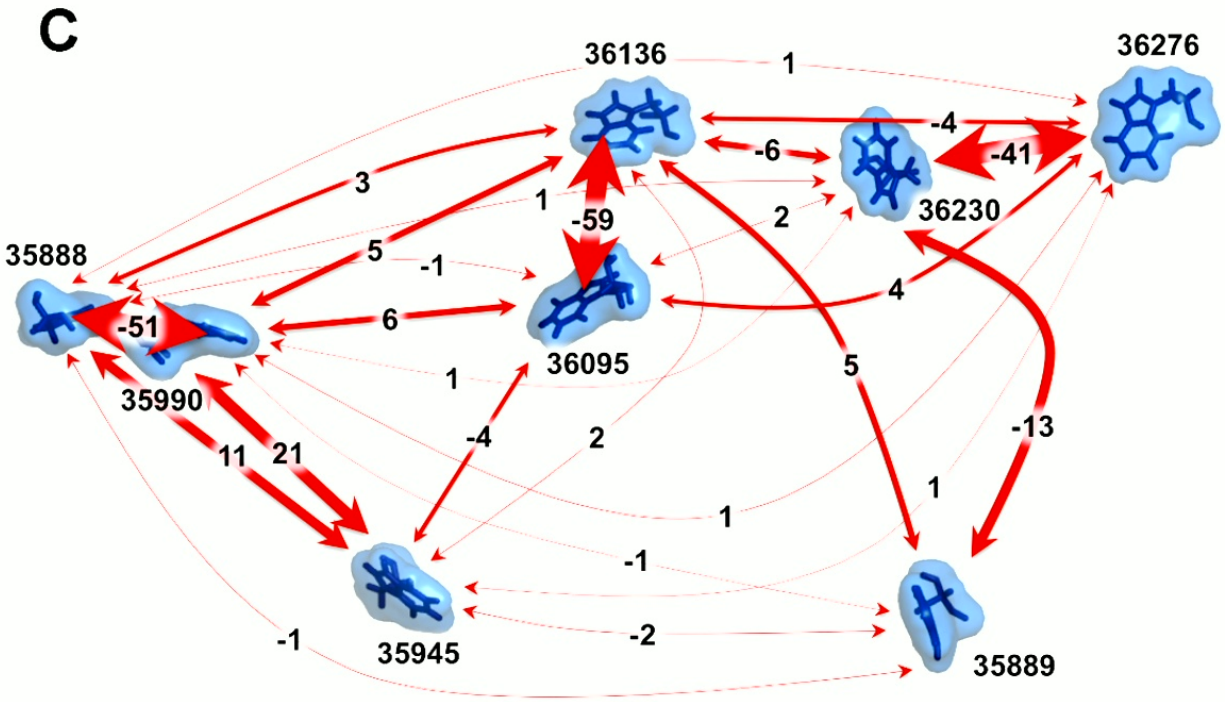
- Multi-walled CNTs (MWCNTs) display a striking similarity in size and morphology to microtubules
  - Inner diameter 1.5-15 nm; Outer diameter 2.5-50 nm
- MWCNTs can possess microtubule biomimetic properties[3]
  - assisting and enhancing microtubule assembly and stabilization
- Goal in bio-nanotechnology to mimic the properties of microtubules.
- Conversely, microtubules could serve as units for as optoelectronic and quantum information devices
- Modeling predicts networks of aromatic amino acids in microtubules have potential for exciton transfer[16,17], superradiance[18], and possess Fano resonant properties[19].



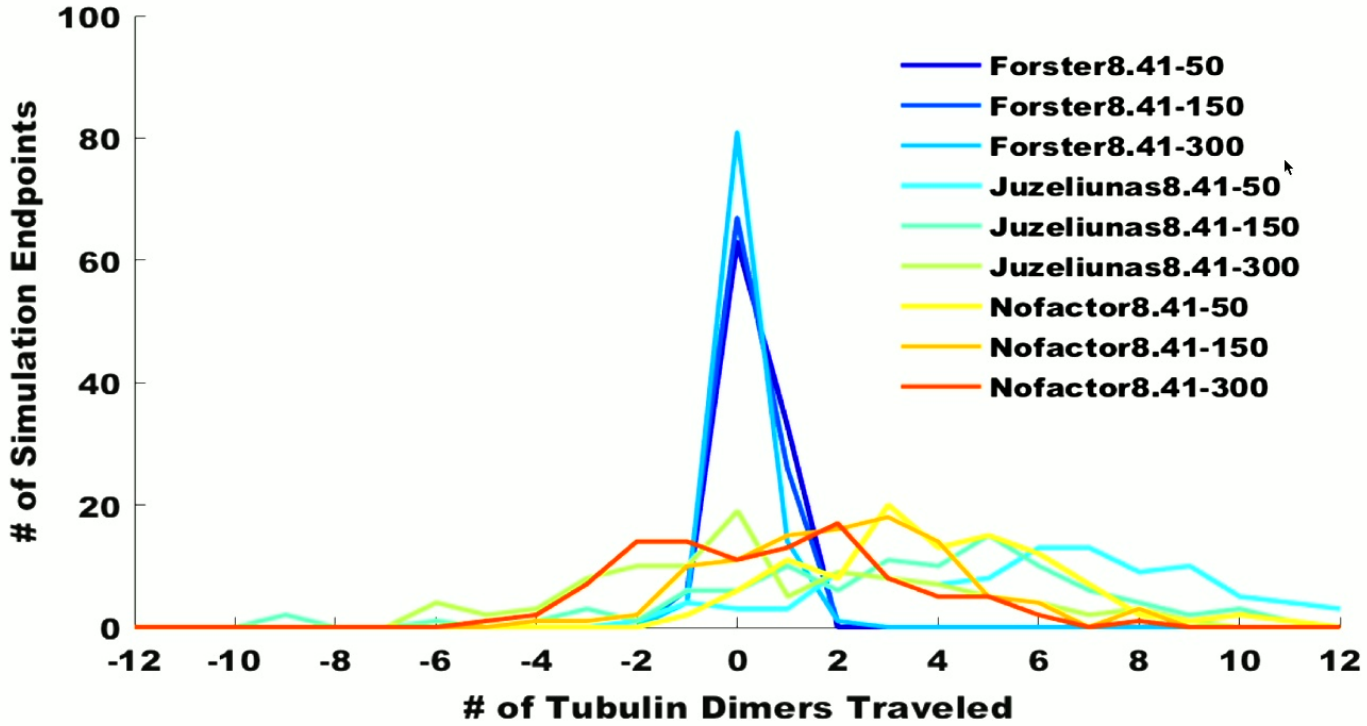
Light-Matter Interactions:
Excitation dynamics[17]



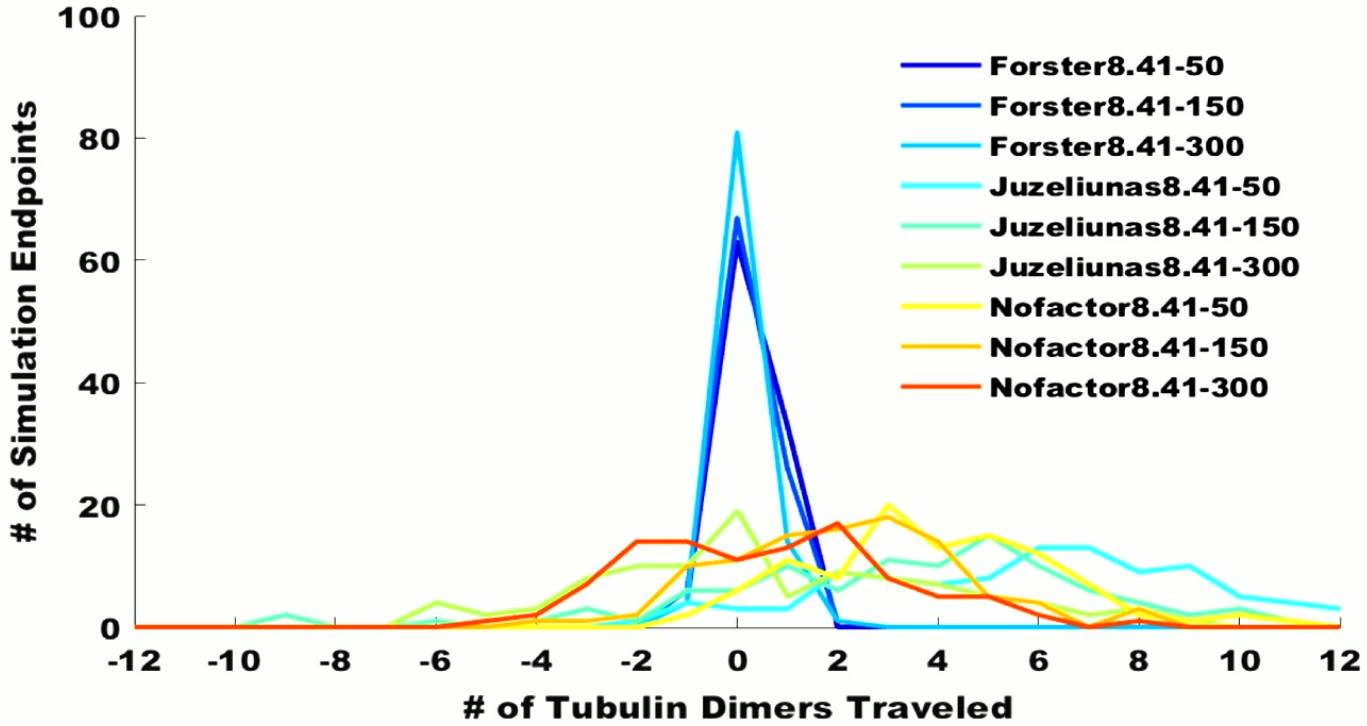
Light-Matter Interactions:
Network of Coupled Dipoles[16]



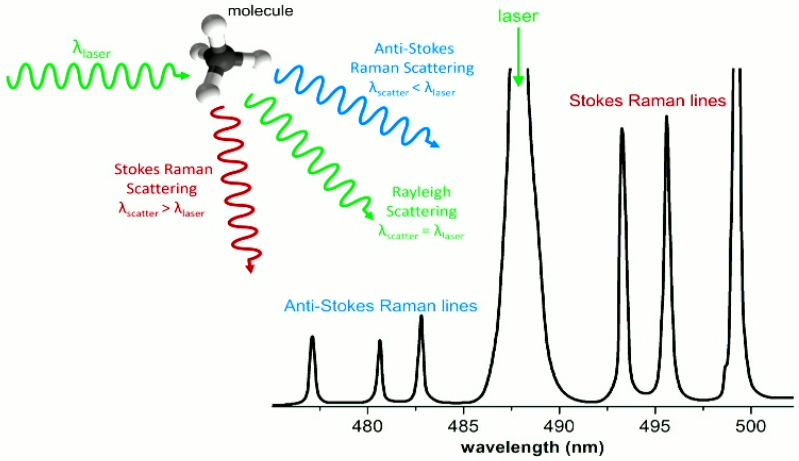
Light-Matter Interactions:
Excitation dynamics[17]



Light-Matter Interactions:
Excitation dynamics[17]

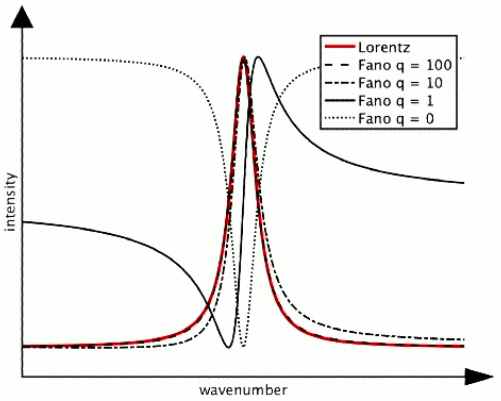


Quantum Optical Effects:
Fano Resonances in Raman Spectra – Experiment [19]



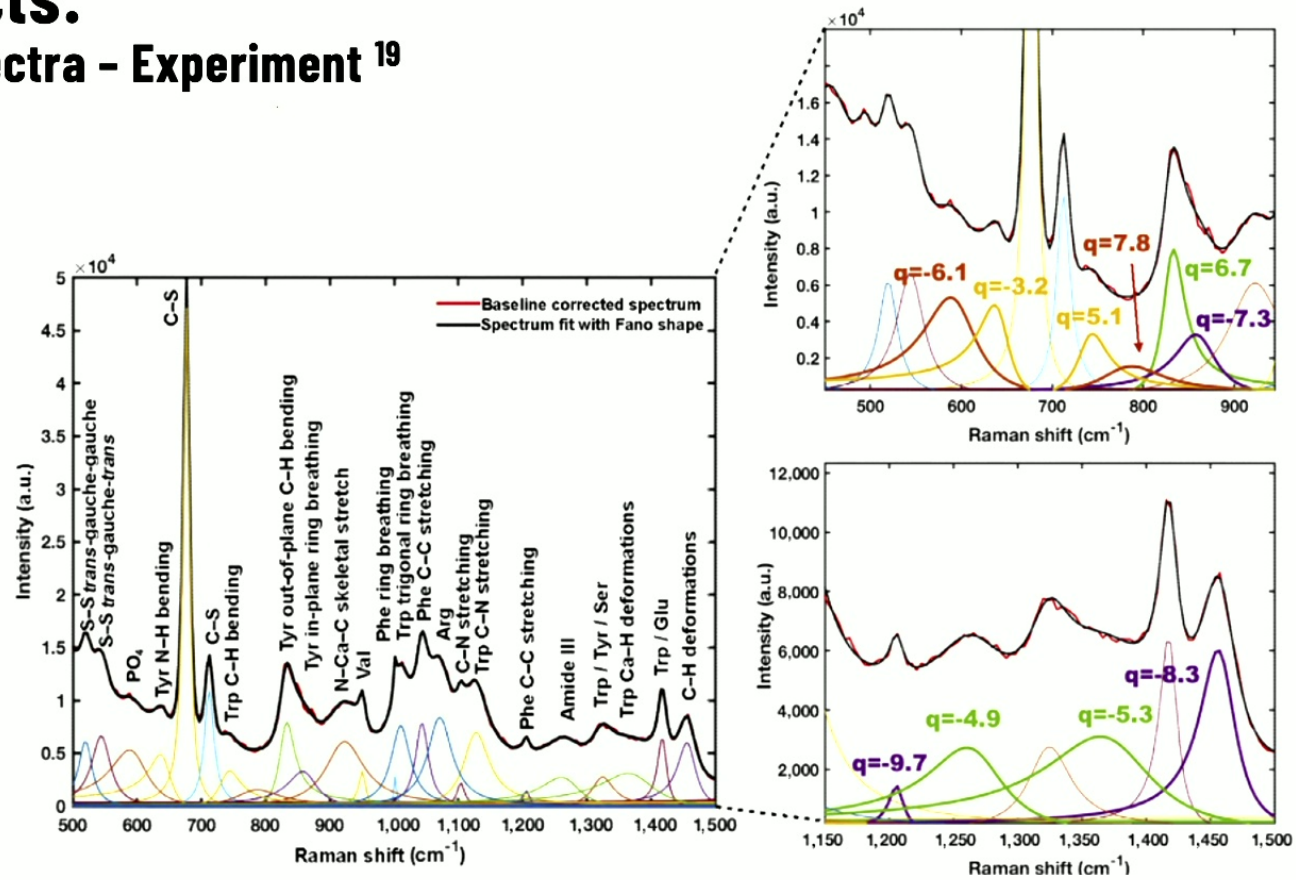
- Various processes affect the line shape in Raman spectra
- Fano resonances can cause the loss of a symmetrical Lorentzian shape
- Fano resonance arises from coupling between a discrete level of vibrational states and a continuum spectrum of electronic excitations
- Purely quantum phenomenon
- The degree of coupling, q, determines the degree of asymmetry

$$I(\omega) = I_{i0}\frac{(1+\frac{w-w_i}{q_i\Gamma_i})^2}{1+(\frac{w-w_i}{\Gamma_i})^2}$$

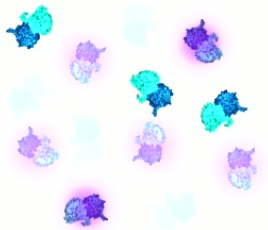


Quantum Optical Effects:
Fano Resonances in Raman Spectra – Experiment [19]

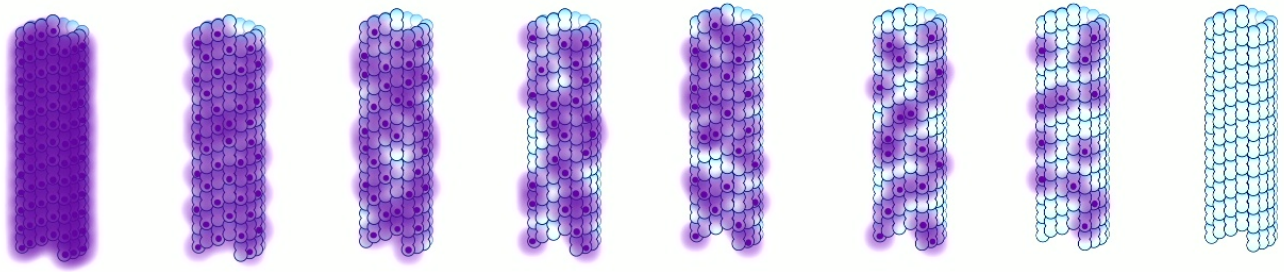
- Fano resonances in microtubules occur for:
  - disulfide bonds
  - tryptophan
  - tyrosine
- Indicates coupling between discrete phonon vibrational states and continuous excitonic many-body spectra.
- Consistent with modelling efforts showing photoinduced excitonic transport in microtubule aromatic amino acid networks.

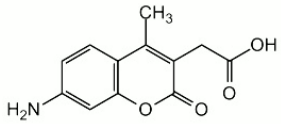


Light-Matter Interactions:
Experimental Measures: Dye Labeling[20]

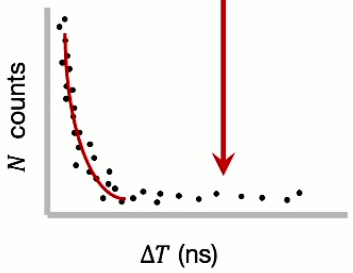


Polymerize @ 37 °C





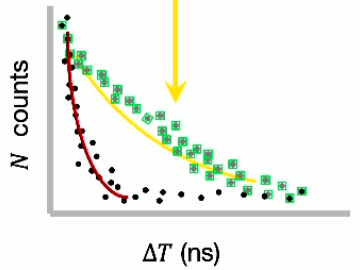
AMCA
Aminomethylcoumarin Acetate



Tryptophan: excite 280-300 nm, emit 320-350nm
AMCA: excite 320-350 nm, emit 420-450 nm

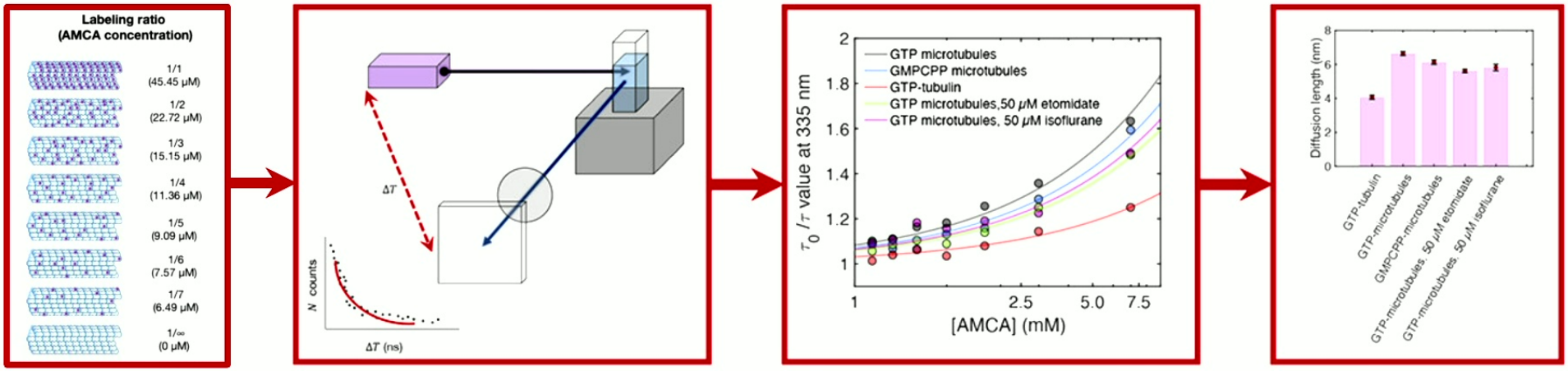
AMCA quenches Tryptophan excitation

Hence, varying the AMCA labelling ratio should lead to changing tryptophan lifetimes

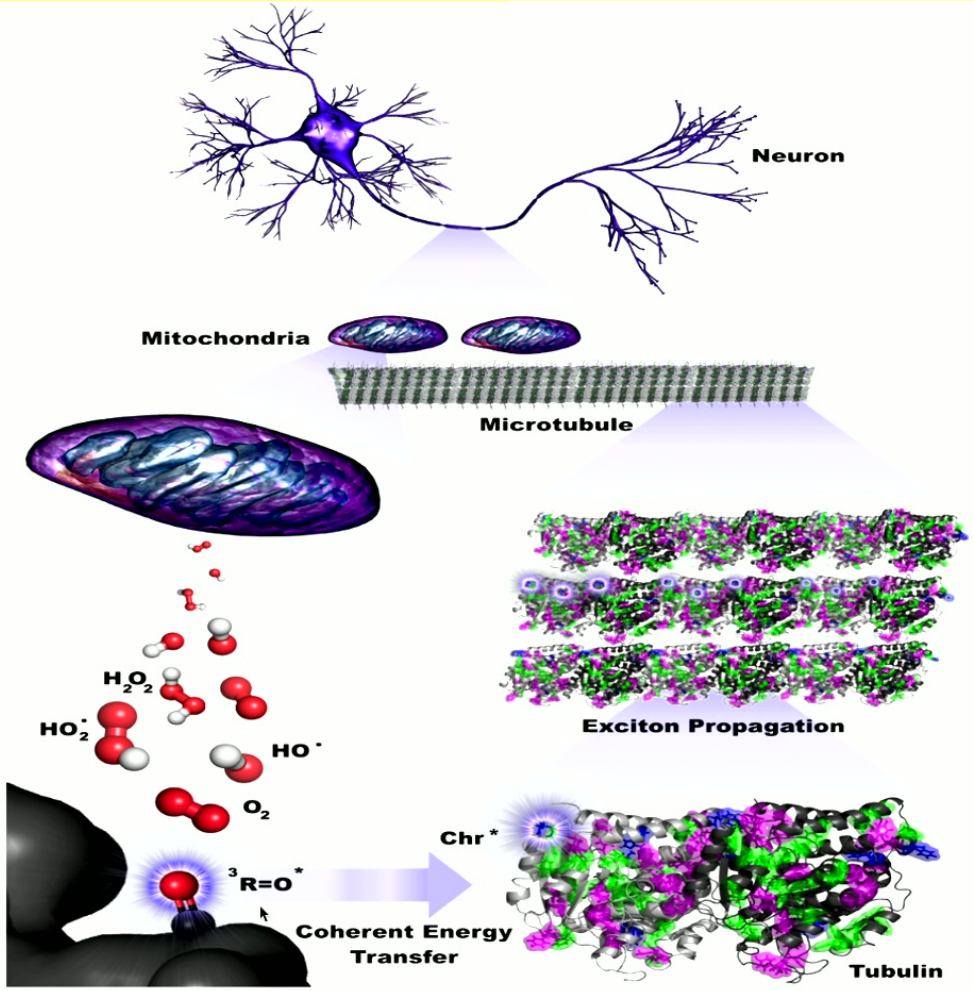


Light-Matter Interactions:

Experimental Measures: Time-correlated Single Photon Counting[20]

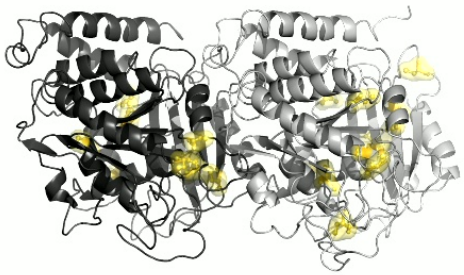


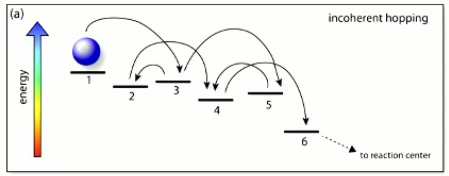
- Measured microtubule excitation diffusion length: 6.64 ± 0.1 nm
- Classically calculated diffusion length: 1.54 nm
- Approximately 4 times difference.
- Reason for difference still under investigation
- Microtubules are effective light harvester.

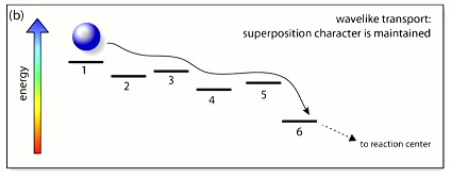

Neuron
Mitochondria
Microtubule
Exciton Propagation
H_2O_2
$HO_2^{\cdot}$
$HO^{\cdot}$
O_2
$^3R{=}O^*$
Chr*
Coherent Energy Transfer
Tubulin

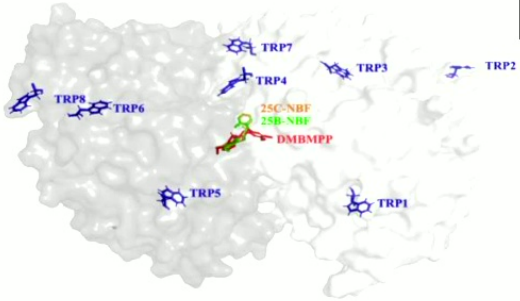
Light-Matter Interactions:
Future Directions

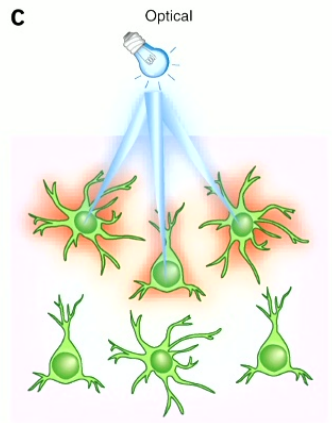
- What happens to the excitation?
  - Lead to microtubule damage (i.e., break disulphide bonds, affect GTP sites)
  - Energy funneled away from sites (protective)
- What mechanism causes increase in energy migration?
  - Coherent mechanism, unaccounted for co-factors
- Can migration be modified?
  - Addition of chemical cofactors[21]
- Does these mechanisms have a biological effect?
  - Affecting microtubule growth and hence axonal growth, synaptic plasticity











UNIVERSITY OF WATERLOO

Conclusions

- Studying quantum biological effects in the brain is an extension of computational and theoretical neuroscience.
- Quantum effects in the brain may affect enzymatic processes, ion channel function, nerve impulse (avian compass), and may allow manipulation of neurons by light and magnetic fields.
- All living tissue emits photons at ultraweak intensity.
- This UPE is tied to oxidative metabolism and ROS.
- Can be used as a measure of oxidative stress.
- Understanding the role of UPE in neuroscience can lead to deeper understanding of neuron function.
- Microtubules are key structures capable of modulating receptor and ion channel activity and can influence synaptic plasticity.
- Theoretically aromatic amino acid networks in microtubules can support UPE generated energy transfer
- This is supported by experiments using Raman spectroscopy and Time Correlated Single Photon Counting.
- Future work is on-going.

Thank you! Any questions?

Contact: travis.craddock@uwaterloo.ca