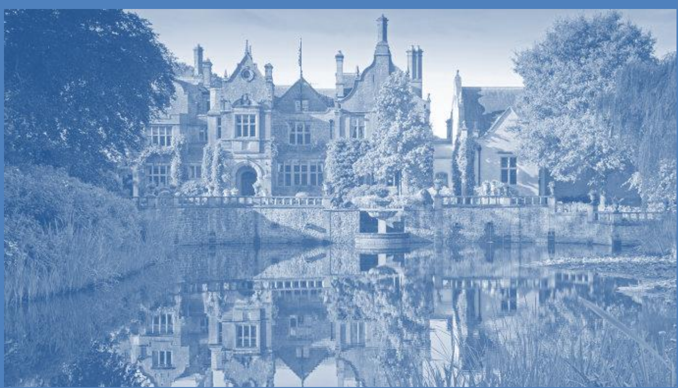
The Guy Foundation

DOES BIOLOGY UTILISE THE ENVIRONMENT TO AMPLIFY QUANTUM EFFECTS?

Abstract proceedings of the 2nd Guy Foundation Symposium on Quantum Biology and Bioenergetics, Autumn 2020

Available January 2021



Alistair Nunn &
Geoffrey Guy
(Eds.)

Driving innovation in medicine through quantum biology

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DOES BIOLOGY UTILISE THE ENVIRONMENT TO AMPLIFY QUANTUM EFFECTS?

– ALISTAIR NUNN

Theoretical and some empirical evidence is building that biology may well have embraced quantum principles, and without them, life would not be possible. This is conceptually believable in that quantum mechanics is the best description of how the Universe works that we have, but practical proof is still proving difficult to show. Acceptance of this concept has been hindered by some well-founded theoretical interpretations of quantum mechanics that would suggest biology is simply too warm and wet for significant quantum effects to occur. In effect, it is possible to suggest that thermally-induced noise results in decoherence and prevents any significant quantum effects other than those expected to happen at the normal sub-nanometer size and time scales of the quantum world. However, this thinking has often been challenged, as it may well be that the noisy environment could have actually been embraced by biology to enhance the very quantum effects thought to be disrupted by it. How come thinking is changing?

When one thinks about the general concept of quantum mechanics, the truth is that it must be describing something fundamental about how our Universe works. The terms used suggest an underlying principle. For example, “resonance”, “coupling”, “waves” and “harmonics” crop up all over the place, which in turn, are incorporated into more complex phrases, such as “quantum dynamics”, “quantum harmonic oscillators”, “many body dispersion”, “plasmonic allostery”, “vibronic coupling” and “coupling across the temporal and spatial dimensions”. Then we move into terms like “coherence/decoherence”, “spin”, “wave function”, “entanglement”, which are the “go to” quantum nomenclature. The term “quantum” describes that the interchange of energy occurs via discrete packets, rather than via a continuum. This is all embraced by the fundamental principle of wave-particle duality, and that energy can move around via wave resonance at the quantum level.

Overall, this all has to integrate with conventional thermodynamics and the classical meso-/macroscopic classical “particle” world; it of course does, or we wouldn’t exist, which given that the field of “quantum thermodynamics” is still only in its infancy, suggests we still have a lot to learn. Indeed, it is clear that life operates at temperatures well above absolute zero, which means at the molecular level, it is constantly vibrating because of energy in the form of heat. For many years, this gave us a Newtonian viewpoint of life, and in terms of modelling, worked well to explain most biochemistry, for instance, catalysis, as well as its importance in say, protein folding.

However, with time, it became clear that to really accurately model chemical reactions, one needed to do it quantum mechanically; this had not been possible until the advent of powerful computers. There has thus been a gradual closing, in biology, between the disciplines of quantum mechanics and classical chemistry, and a realisation that both are telling us something. One of the things it is telling us is that the “environment” in and around proteins does seem to impact the quantum mechanical description of structure and chemical reactions. Previously, it was simply thought that this might destroy any significant quantum effects, but this idea is now rapidly changing, in fact, quite possibly, to the complete opposite position that the environment is essential for life function by controlling quantum effects. This switch in thinking could have profound implications.

One of the simplest ways to understand how life works is to deconstruct it, and this means going back in time to its origins and working out how its core metabolism originated. This is obviously a lot easier said than done. However, there is a growing consensus on at least the prebiotic key ingredients, which are very likely to have existed before life started due to the fundamental nature of planetary and circumstellar chemistry, and the conditions, or "environment", that existed on the Hadean earth. These include metallic minerals, some amino acids, probably some kinds of nucleic acids, and certainly a range aromatic compounds based on carbon, many of which contained phenyl, some lipids and of course, water. Critically, there was also plenty of energy about, either in the form of heat (high temperatures), sunlight, and ion/pH gradients, and of course, these all obeyed fundamental thermodynamic laws, where energy always tries to equilibrate, as well as quantum mechanics. The pre-life mix was set. Somewhere, this mix resulted in the formation of a self-organising negative entropy and replicating structure that dissipated the energy gradient, which because of natural selection, evolved. The big question, of course, is did this structure select and/or rely on amplification of significant quantum effects to function?

It could be argued that at this stage this could have gone two ways: that environmental noise ablated any significant quantum effects, so ruling them out for all life, or it enhanced them, ensuing a selective advantage. Not only is the emerging data, both theoretical, and empirical, suggesting quite strongly it was the latter, but so is the quantum structure of the very molecules that are pivotal to life itself. In short, the emergence of complex protein-based life evolved to enhance, and utilise the environment to drive significant quantum effects that actually make it possible.

Professor Alistair VW Nunn, BSc, PhD

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INTRODUCTION TO THE GUY FOUNDATION – GEOFFREY GUY

The Guy Foundation has been set up to support and promote the investigation of quantum effects in biology, with the aim of improving our understanding of disease and thus medicine. Our belief is that significant quantum effects may well have not only been essential for life to get going, but also enabled it to grow in complexity by amplifying these effects both in space and time. For example, all life is based on iron-sulphur compounds that can display interesting tunnelling properties, which could be enhanced by the addition of proteins and chromophoric molecules. These molecules were all created by well understood geochemical/interstellar chemical processes long before life got going, which coupled with established thermodynamic mathematical principles involving self-organisation of dissipative structures in energy gradients, do provide the basis of a starting point for life. In short, if significant quantum effects are part of life, the failure to maintain this state probably plays a role in disease and thus, the ageing process.

Of course this raises a question, why hasn't anybody thought of using quantum mechanics to explain biology? Well, actually, as indicated in the preface, they had, right from the beginning from the days of the pioneers of quantum physics, and over the years, several leading scientists have discussed the possibilities that biology could be using significant quantum effects. Some, such as Roger Penrose, have even gone as far as suggesting it could explain consciousness itself, which, even today in the 21st century, is still far from being understood. In fact, with time, despite the 20th century optimism that by the 21st century mankind would have found cures for cancer and many other diseases, and possibly even for ageing itself, a deeper understanding of life seems to be still out of reach. It could be even further away as emerging global obesity appears to be *shortening* both a healthy and absolute life expectancy, which is resulting in spiralling health care costs across the planet. Despite mankind's emerging technical mastery of nature, we still have a very long way to go in terms of truly understanding it.

This therefore brings us neatly back to quantum mechanics and biology and the aims of the Foundation. Quantum mechanics is intuitively difficult to understand, and, as has been said, if you think you understand it, then you don't. Only now, after nearly 100 years, is technology reaching the point where one of the most difficult of concepts, quantum entanglement, can be tested. Einstein called it "spooky action at a distance", as he simply didn't believe it because it didn't fit with his general theory of relativity, and despite being one of the founders, he openly said that quantum mechanics had to be incomplete. He often argued with Niels Bohr over this. For many years the concept of "quantum realism" has stood quietly like a large elephant in the room, as many thought that only when a conscious observer observed something did its wave function collapse to give us the Newtonian universe we all understand. The latest experiments to test whether or not quantum entanglement exists continue to suggest that it clearly does, which indicate that two entangled particles, which share the same wave function, can still somehow communicate, instantaneously, even if they are on opposite sides of the galaxy. In fact, it is now finding uses, like other quantum effects, such as tunnelling, in everyday practical devices, such as eaves-dropper safe communication. Thus, it is likely that conventional biology, and quantum mechanics, despite the odd attempt to communicate, have largely passed as ships in the night for nearly a century. The Foundation therefore aims to provide a platform and a forum for upstream pull through and downstream push through of the understanding of the role of quantum effects in biology in health and disease. We recognise these notions to be extremely avant-garde, oftentimes incomprehensible. However, we take a long view and are prepared to fund work which would be very difficult to be funded elsewhere and see ourselves as pioneers in a new wave of medicinal science.

Professor Geoffrey Guy MB BS, LRCP MRCS, LMSSA, DipPharmMed, BSc, DSc

Founder and Chairman of the Board of Trustees, The Guy Foundation

FULL PROCEEDINGS

ABOUT THESE ABSTRACTS – ALISTAIR NUNN

Director of Science, The Guy Foundation

These are abstracts of a series of talks, hosted by the Foundation, that were given on line to an invited audience during the autumn of 2020. They were held virtually due to the COVID-19 pandemic caused by the SARS-COV-2 virus, which resulted in travel being highly restricted.

They have been written by the presenters and have not been formally peer-reviewed. We hope you enjoy them; video recordings of the full lectures can be viewed on the Foundation's website www.theguyfoundation.org.

On the wave of coherence: biology beyond the atomist standpoint – Professor Giuseppe Vitiello

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Biological systems present a great variety of molecular species with a rich biochemical phenomenology. Their study is thus focused on their elementary constituents and a large number of data is accumulated. The problem of combining them into a functional scheme needs then to be considered. Biological systems appear indeed to be complex systems operating at a multitude of interdependent scale levels, from atoms, molecules, cells, to macroscopic structures, whose functional activity requires to be understood on the basis of the knowledge of the elementary components. Among these, water molecules, which in number are the great majority of present molecules and whose absence makes impossible any form of living matter.

At the microscopic level, quantum theories describe charge density distributions, ions and electric dipoles. Even large molecular structures, such as polypeptides, considered building blocks of life, are observed to obey the quantum laws of matter-waves interferences. One further aspect, characterizing living matter, is its *openness* to environment with continuous exchange of energy and matter.

It is also a common observation that separated domains of the system are correlated in quasi-simultaneous way (for example, the neuronal correlations in distant regions in the brain activity), which cannot be explained by classical modeling. In such a respect, one helpful aspect of quantum field theory, which is absent in quantum mechanics, is indeed the possibility of the dynamical generation of coherent long range correlations, triggered by even very weak external stimuli.

Long range correlations are not electromagnetic in nature, but are long range "phase correlations" among the system components, which get thus entangled. They are not "forced" by some interaction. The crucial point is that phase correlations are not mediated by messengers, which allows instantaneous correlations without violation of relativity. Interactions are instead mediated by messengers that cannot travel faster than light. Long range correlations also account for the recurrence of fractals in living matter, which are isomorph to deformed coherent states.

Short range interactions among the system components of course are there accounting for local molecular organization within and consistently with the coherent dynamics ensuring the unitary functional activity of the system. As said, these levels are dynamically interconnected, one of them cannot exist without the other one.

The study of living matter thus requires such an integrated unification of random short range interactions of a crowd of molecular species with the basic dynamical law of coherence.

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QUANTUM CRITICALITY IN BIOLOGICAL MOLECULES – PROFESSOR GÁBOR VATTAY

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Why life persists at the edge of chaos and order is a question at the very heart of evolution. In this talk, we show that molecules taking part in biochemical processes from small molecules to large proteins are critical quantum mechanically. Electronic Hamiltonians of biomolecules are tuned precisely to the metal-insulator transition's critical point separating the localized insulator phase from the conducting disordered metal phase. Using tools from Random Matrix Theory, we confirm that these biomolecules' energy level statistics show the universal transitional distribution of the metal-insulator critical point. The wave functions are multifractals following the theory of Anderson transitions. The findings point to the existence of a universal mechanism of charge transport in living matter. The revealed bio-conductor material is neither a metal nor an insulator but a new quantum critical material that can exist only in highly evolved systems and has unique material properties. Since discovering these peculiar properties of biomolecules, several experimental groups found (independently) that proteins – expected to be insulators - attached firmly to metal electrodes have unexpectedly good conducting properties. The conductance is very close to the conductance of a disordered but ballistic quantum system. It does not decay exponentially with the length of the protein. It has a large and finite value for low temperatures. These findings shed new light on the origins of the electrical properties of biological systems. They can lead to a more detailed understanding of how ligands and receptors work in living cells and can help design drug molecules more consciously than it is today.

WHAT IS COHERENCE AND HOW IS IT HARNESSED IN BIOLOGY? – PROFESSOR GREGORY D. SCHOLES

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Coherence phenomena arise from interference, or the addition, of wave-like amplitudes in phase [1]. While coherence has been shown to yield transformative new ways for improving function, advances have been limited to pristine matter, as quantum coherence is considered fragile. Nevertheless, recent experimental studies of photosynthetic light harvesting complexes have indicated how vibrational and vibronic wavepackets entrain ensembles of molecules—does this teach us anything about coherence in biology?

Solar energy conversion in photosynthesis is triggered by plants harvesting sunlight and distributing that excitation energy to reaction centre proteins through a network of light-harvesting chlorophyll molecules by electronic energy transfer [2,3]. Delocalized exciton acceptor states are found in photosynthetic light harvesting complexes where they can increase rates of energy transfer by an order of magnitude, which has been understood by the development of Generalized Förster Theory [4-6]. While molecular exciton states are robust and represent strong coherence among the phases of molecule-local excitations, weaker kinds of coherence phenomena can modify energy transfer [1, 7-15]. Interest in this field partly stems from the speculations that a contribution of coherence to transport might allow some control of energy migration [16]. One possible outcome of coherence in multi-molecular systems is that non-classical correlations might be present. These quantum correlations are not necessarily relevant to function, but would be interesting to discover and study. The search for coherence in biological light-harvesting systems thus inspired reports predicting the possible involvement of quantum entanglement in the function of photosynthetic light harvesting complexes [17-20]. An historical summary of this recent work and current state of the field is reviewed in ref [21].

Coherence in energy transfer is not necessary to explain the efficient light-harvesting by photosynthetic proteins, but nevertheless, it is interesting to use these systems as model platforms for thinking generally about how different kinds of coherence effects might influence energy transfer [10,15,22]. On this theme, it has been difficult to understand how coherence can prevail sufficiently in disordered systems to enable directed random walks — and this seems to be the “sticking point”. It is important, therefore, to work out how complex molecular systems might overcome disorder to enable coherence effects [10,23,24].

Looking in a different direction, the correlations underpinning coherence might be approached from the concept of synchronization — particularly given how robust synchronization can be in complex systems. Theories for synchronization show how large, complex systems can have unified function, and this paradigm abounds in Nature and engineered systems [25-27]. Examples in the natural world range from the beating of a heart to formations of flashing fireflies. At the molecular scale, synchronization is difficult to achieve and even to work out how to implement, owing to stochastic fluctuations in structure and energy. Even more challenging is to engineer robust synchronization on the quantum scale.

Elucidating how robust synchronization on the macroscale can exhibit or utilize quantum correlations appears to be a key for working out how quantum phenomena might be harnessed by living systems—and thus overturning the paradigm that they are too wet, warm, and noisy to support quantum effects.

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FRÖHLICH COHERENCE AND ITS POSSIBLE ROLE IN CONSCIOUSNESS – PROFESSOR MARCO PETTINI

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Understanding of the physical forces acting between molecules – to explain their assembly into functioning biological structures – is the object of a longstanding debate among physicists. A fundamental issue concerns what drives the dynamics of the impressively complex and efficient network of biochemical reactions hosted by living cells where the biomolecules seem to "know" where to go and when, instead of being essentially randomly driven to their targets by thermal fluctuations.

A longstanding proposal by H. Fröhlich surmised that the activation of collective oscillations of biomolecules, possibly driven by metabolic activity in living matter, by bringing about large oscillating dipole moments could activate resonant (thus selective), intermolecular, attractive, electrodynamic forces acting at a long distance.

At least in some cases, the way the various actors in a given biochemical process, and in the overcrowded cellular space, efficiently find each other could rely on this kind of resonant electrodynamic forces acting at long distances. A Fröhlich-like phonon condensation phenomenon out of thermal equilibrium has been recently given experimental evidence [1] together with the activation of long-range electrodynamic interaction between proteins [2].

In particular, Fröhlich condensation phenomenon is expected to play a twofold action on cell microtubules: i) long-range electrodynamic interactions among tubulin dimers could play a relevant role in microtubule assembly, hence providing a possibility of understanding why the use of electromagnetic fields has been observed to stop the growth of cancer cells [3], opening a new paradigm for medical interventions in diseases such as cancer and neurodegenerative diseases; ii) synchronization of tubulin oscillations, that is, a kind of Fröhlich condensation at intermolecular level, could induce quantum coherence phenomena in π-stacks of aromatic rings along microtubules. Quantum coherent phenomena in microtubules have been invoked by R. Penrose and S. Hameroff [4,5] as the key to the understanding of the emergence of mental phenomena and consciousness due to non-computable quantum processing performed by qubits formed collectively by tubulins. Orchestrated Objective Reduction of the collective wave-function of each microtubule would correspond to the emergence of an "atom of consciousness" and would occur when an objective threshold governing the collapse of quantum-states is attained. The criticism addressed to the Penrose-Hameroff theory that originally focused on quantum superposition of two configuration states of tubulins, can be overcome by looking for quantum information processing through π-stacks of aromatic rings.

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Tunnelling and charge separation in vents – Professor Nick Lane

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Membrane bioenergetics are as universally conserved across life as the genetic code. Ion electrochemical gradients across membranes, notably proton gradients, are responsible for driving ATP synthesis via chemiosmotic coupling, but also CO_2 fixation through proton-motive membrane-integral Fe(Ni)S proteins such as the energy-converting hydrogenase (Ech). Modern membrane bioenergetics couple electron transfer through multiple redox centres to proton extrusion across the membrane, generating a proton-motive force that powers work.

The idea that electrons tunnel between redox centres goes back to Britton Chance in the 1960s, who showed that electron transfer is independent of temperature [1]. More recent work shows that the distance between redox centres is under selection, with shorter distances facilitating tunnelling even against redox potential [2]. How such complex machinery first arose has long been mysterious, but the question is greatly simplified by the hypothesis that life began in alkaline hydrothermal vents, pioneered over 30 years by Mike Russell [3].

The interconnected inorganic micropores in hydrothermal systems frustrate mixing, sustaining steep proton gradients across barriers containing Fe(Ni)S minerals, with a topology and magnitude equivalent to cells [4]. Microfluidic work shows that vectorial electron transfer from H_2 to CO_2 in these systems is pH dependent, with the inorganic barrier maintaining phase separation in a similar way to the cell membrane [5]. Differences in pH modulate the redox potentials of H_2, CO_2 and FeS clusters according to the Nernst equation (~-59 mV per pH unit), whereby H_2 is more reducing in alkaline conditions and CO_2 more easily reduced in acidic conditions, with electron transfer between the two phases requiring electron tunnelling across Fe(Ni)S nanocrystals [6].

Our own work uses Ech as a guide to the origin of membrane bioenergetics in alkaline hydrothermal systems [6]. Ech contains four Fe(Ni)S clusters, two of which are pH sensitive with their redox potential varying by around -50 mV per pH unit [7]. We propose that proton binding increases the redox potential of the Fe(Ni)S 'wire' through the resonance effects of tunnelling, allowing Ech to oxidise H_2. Transient closure of the proton pore allows proton dissociation, lowering the redox potential of Ech by >200 mV, facilitating the apparently endergonic reduction of ferredoxin [6].

Electron tunnelling therefore operates as a redox switch, in which the redox potential of the whole Fe(Ni)S 'wire' is sensitive to local protonation through transient exposure to the extracellular phase via the membrane pore. In broader terms, electron tunnelling enables communication between separate phases with distinct redox potentials, coupling flux to CO_2 reduction and potentially powering growth in geologically structured systems.

We have shown that protocells can form from mixtures of simple amphiphiles under these conditions [8] and will line Fe(Ni)S barriers [9], focusing proton gradients onto the cell membranes themselves. FeS clusters can form spontaneously through chelation by amino acids such as cysteine.

If these clusters associate with the membranes of protocells in a geologically structured system, then electron tunnelling in the presence of steep proton gradients should drive CO_2 reduction, powering protocell growth at the origin of life.

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