THE GUY FOUNDATION

Genes and metabolism: bioelectricity and the quantum spark of life

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Abstract proceedings of the 2024 Autumn Series

Driving innovation in medicine through quantum biology

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2024 AUTUMN SERIES

GENES AND METABOLISM

BIOELECTRICITY AND THE QUANTUM SPARK OF LIFE

Introduction to the 2024 Autumn Series

The Guy Foundation team

The Guy Foundation 2024 Autumn Series aimed to explore different aspects of bioelectricity, from its fundamental role in sub-cellular and cellular processes, to the electrical networks that constitute the brain. In addition to this the series examined to what extent quantum mechanics might be implicated in – or offer insights into – the electromagnetic effects integral to biological function.

The discovery of DNA forever changed the landscape of biological research. By 2003 the Human Genome Project had, to a large degree, successfully sequenced the genetic blueprint that makes us uniquely human. Despite this landmark scientific achievement, biology remains almost as enigmatic as ever. While genes are undoubtedly integral, they are also subject to epigenetic forces that shape their manifestation in ways that are still not clearly understood. Bioelectricity, for example, plays a pivotal role in shaping living systems and has been a subject of interest for centuries.

The series began with a review of the historical precedent and current evidence for life being electric. Michal Cifra, from the Institute of Photonics and Electronics at the Czech Academy of Sciences, gave a fascinating overview of the original 'animal electricity' experiments conducted on frogs by Luigi Galvani in the 1700s. Michal went on to address the current scientific understanding of electrical effects in biological systems. He outlined the electronic properties of proteins, in particular those with very strong electrical degrees of freedom, such as tubulin proteins and their microtubule aggregates.

In the second session the focus shifted from bioelectricity within cells to the behaviour of cellular collectives such as neural networks. Greg Scholes, from Princeton University, first revisited the subject of microtubules before looking at whether circuits or networks of chromophores or cells are best described by quantum mechanics. Greg introduced some of the core ideas in quantum mechanics, such as superposition and entanglement, before discussing whether these are useful concepts with which to describe 'quantum-like' behaviour in the electrical circuits of the brain.

Johnjoe McFadden, from the University of Surrey, expanded on the importance of electric fields in the brain in the third session of the series, which focused on consciousness. Consciousness is a subject of great fascination and one that remains frustratingly resistant to scientific models. Consciousness research is often framed by dividing it into the easy and the hard questions, where the easy question refers to the hardware, the neural correlates that are the signature of conscious states. The hard question is more intractable, being a question of subjectivity and what is known as qualia, the individual experience of these conscious states. There are many models developed to try to explain consciousness, including quantum biology models such as Orchestrated Objective Reduction. Johnjoe took us through the details of his own theory of consciousness, conscious electromagnetic information (CEMI) field theory, and how situating consciousness in the electromagnetic field generated by the brain allows us to answer some of the outstanding questions regarding what it means to be conscious.

From questions of consciousness, the series moved on to another of the big unanswered questions in biology, the origins of life. Nick Lane, from University College London (UCL), addressed how life itself is arguably our biggest clue as to how life began, particularly if we focus on the three pivotal processes of energy production, metabolism and genetic information. Nick discussed what these processes may have looked like at the origins of life and the integral role of the proton-motive force.

And finally, Michael Levin, from the Allen Discovery Center at Tufts University, concluded the series with his presentation on how bioelectrical information, such as the ion-dependent electric potentials across cell membranes and cellular collectives, is as important as genetic information in determining the shape and development of living organisms.

Introduction to The Guy Foundation

Professor Geoffrey Guy

Founder and Chairman, The Guy Foundation

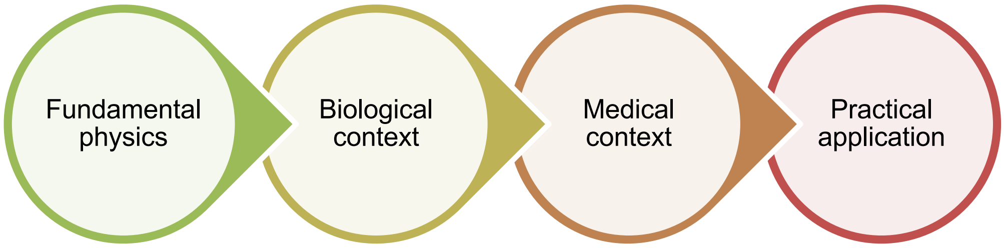
The Guy Foundation supports and promotes the investigation of quantum effects in biology, with the aim of improving our understanding of disease and thus medicine. Our belief is that significant quantum effects may well have been essential for the origins of life as well as the evolution of complex living organisms and thus a better understanding would help unlock new ways of tackling the health and disease issues that we see today.

With the development of technology, the study of quantum effects in biology has been gaining rapid pace in recent years. Classical pharmacology-based explanations for the effects of medicines remain insufficient; we aim to develop research into the effects of electromagnetic fields (both endogenous and exogenous) on biological systems. This will expand the conventional 'ball and stick' or 'lock and key' mechanisms which dominate our understanding of physiological processes, including the action of many pharmaceutical interventions. To this end we focus on the role of intracellular bioenergetics and the role of mitochondria from the point of view of dissipative thermodynamic and quantum theories. In short, if significant quantum effects are part of life, the failure to maintain this state probably plays a role in disease and ageing, and will thus be of importance to medicine.

We have also identified space travel as a key area that will benefit from a greater knowledge of the role that fields play in biology. If life is dependent on significant quantum mechanisms to function, then optimal function will be coupled to the planetary environment in which it evolved: a "Goldilocks zone" of environmental conditions. The Foundation believes that a focus on the ways in which the electromagnetic, gravitational and other effects of the space environment can be potentially mitigated, will optimise the health of astronauts and future passengers. This research would also accelerate progress in quantum biology and the advancement of medicine in general.

It is clear to us that the next generation of significant steps in medicine will need to engage with quantum biology. Our role at the Foundation is to help facilitate this mindset shift to bring quantum biology into the mainstream of medicine for the benefit of healthcare issues including ageing, neurodegeneration, metabolic syndrome, neuropsychiatric disease in the young, cancer and others. The Guy Foundation thus leads, supports and contributes to quantum biological and related research with the ultimate aim of advancing the development of new medical diagnostics and therapeutics.

The Foundation believes this advancement can be achieved in a number of ways, which is reflected by the research we fund as well as the topics we address in our scientific symposia. Our approach is summarised as encompassing research from bench to bedside:



Our priorities encompass the spectrum of theoretical, experimental, and practical advances. Understanding the fundamental physics (e.g., quantum mechanics, electrodynamics, thermodynamics) is important. More specifically we aim to understand this physics within the biological and physiological contexts, with the emphasis on furthering the study of medicine. Overall, we would like to see this knowledge translated and applied in clinical practice.

The Foundation therefore aims to provide a platform and a forum for upstream push through and downstream pull through of the understanding of the role of quantum effects and bioenergetics in biology in health and disease. We have curated and fund a collaborative research group to further investigate these interests, to advance the course of useful knowledge towards the mainstream and bring it to the attention of more conventional funders. We convene a programme of scientific meetings and publications that incorporates the diverse aspects of the field and facilitate engagement from scientists across relevant disciplines.

Abstract Proceedings

These are abstracts of a series of talks, hosted by The Guy Foundation, that were given online to an invited audience during the autumn of 2024.

They have been written by the presenters and have not been formally peer-reviewed. We hope you enjoy them; video recordings of the lectures are available on the Foundation's website **www.theguyfoundation.org**. To receive notifications about new videos, subscribe to our **YouTube channel**.

The Life Electric: The Evidence

Dr Michal Cifra

The Czech Academy of Sciences

View the video recording **here**.

I demonstrated in the lecture that biological systems are fundamentally electrical, as well as chemical, phenomena. This work builds on the historical foundations laid by pioneers such as Luigi Galvani, whose discoveries of "animal electricity" opened a new understanding of life[1]. Bioelectricity is shown to be critical in regulating cellular processes, organismal development, and healing mechanisms, with evidence drawn from both historical and contemporary research[2,3].

The interactions between biomolecules, governed by electro-static and dynamic forces, are shown to underpin essential biological functions such as enzyme activity[4], molecular binding[5], and intracellular communication. Electric fields, generated by cellular structures like proteins and cytoskeletal elements, play a key role in determining cellular architecture and activity. Microtubules, for instance, display distinct charge distributions that contribute to the organization of cells and influence their function. It is highlighted that these fields are crucial for the behavior of molecules and their interactions with the surrounding cellular environment[6].

The importance of membrane potential is established as a defining characteristic of living cells, maintained by ion channels and driving critical cellular functions such as signal transduction and muscular contraction[2]. Disruptions in these bioelectric potentials are associated with pathological conditions, including cancer and neurological diseases, underscoring the significance of bioelectricity in health and disease.

Furthermore, it is shown that bioelectric fields guide collective cellular behavior. The phenomenon of electrotaxis, where cells migrate in response to electric field gradients, is presented as vital in processes like tissue repair and wound healing[7]. This active migration, driven by cytoskeletal reorganization in response to electrical signals, illustrates the broader role of bioelectricity in physiological processes. Practical applications, such as bioelectric dressings that accelerate healing by manipulating electric fields, are also discussed[8].

On a larger scale, it is demonstrated that bioelectricity functions as a blueprint for development. Electric fields provide spatial information necessary for the formation of tissues and organs, guiding morphogenesis and influencing regenerative processes. Studies show that manipulating these fields can lead to the development of abnormal structures, such as two-headed organisms, suggesting potential therapeutic applications in regenerative medicine[9].

Finally, the focus shifts to high-frequency electromagnetic fields in biological systems, an area that remains relatively unexplored[10]. While much is understood about bioelectric phenomena at lower frequencies, recent advancements in technology have allowed the investigation of higher frequencies, such as those in the radiofrequency and terahertz ranges. This presents new opportunities to further understand the electromagnetic dimensions of biological processes.

In conclusion, bioelectricity is presented not merely as an ancillary feature of life but as a fundamental force driving molecular, cellular, and organismal processes. The ability to harness and manipulate these bioelectric fields holds vast potential for medical and biological innovation, suggesting exciting new directions for scientific research and clinical applications.

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Quantum Circuits Compatible with Biological Systems

Professor Gregory Scholes

Princeton University

View the video recording **here**.

We have recently developed[1-3] a means of constructing complex classical networks that mimic the states and correlations—like entanglement—that are signatures of quantum systems. This tangible, physically realizable framework is yielding a new perspective on the quantum world. While the properties of quantum states fade with complexity, eventually transitioning to the classical regime, there is a way of 're-focusing' that transition and producing large, complex classical states that display states akin to those of quantum systems.

This model for quantum-like states anticipates the power of a physical structure in networks (drawn mathematically as *graphs*[4]). The states of these special networks (graphs) mimic the abstract structure underlying the famous superposition of product states endowing quantum systems with special correlations like entanglement. Moreover, contrasting the paradigm that quantum states are fragile, this new principle allows states with 'quantum like' properties to thrive in highly complex systems, regardless of noise and disorder.

The "quantum-like" states and their host graphs provide a platform for conceiving how the machinery of tensor networks can be exploited in neural networks to select circuits needed for a complex task. The tensor product basis of the states articulates all combinations of states of the constituent graphs. Together with the edges linking the graphs, we have converted a collection of 'items' into an ordered arrangement of collections called *posets* (partially ordered sets[5]). The items can be modules of learning, memories, actions, etc. The product graph structure physically encodes a kind of index to these modules. It turns out, for example, that this indexing enables 'model selection'[6,7]; that is, efficient algorithms that decide which items are needed for a particular task or application. No quantum properties are needed nor implied here—the neurons exist in on or off states. Perhaps this structure is a basis for powerful creative thinking?

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The bioelectric field theory of consciousness

Professor Johnjoe McFadden

University of Surrey

View the video recording **here**.

Brains are composed of two distinct but related entities: the visible matter of neurons and the equally physical but invisible electromagnetic (EM) fields generated by neuron firing and synaptic transmission. Until recently, nearly all scientific theories of consciousness (ToCs) have assumed that the seat of consciousness is the visible matter of the brain: its neurons and synapses. However, a key aspect of consciousness is that it represents bound or integrated information. This realization has prompted an increasing conviction that the physical substrate of consciousness must be capable of encoding integrated information in the brain. As Ralph Landauer insisted, 'information is physical' so integrated information must be physically integrated. I will argue here that nearly all matter-based examples of so-called 'integrated information', including neuronal information processing and conventional computing, are only temporally integrated in the sense that outputs are correlated with multiple inputs: the information integration is implemented in time, rather than space. In reality, all classical matter-based information is not integrated but encoded in discrete chunks of matter, such as atoms and molecules. It cannot correspond to physically integrated information at any point in time. Quantum ToCs overcome this problem by proposing that conscious information is integrated into exotic states of matter but these are infeasible in a warm, wet brain. Only energy fields are capable of integrating information in space under normal physiological conditions – that is the fundamental property of physical fields. I will describe electromagnetic (EM) field theories of consciousness (EM-ToCs) including the conscious electromagnetic information (cemi) field theory which proposes that consciousness is physically integrated, and causally active, information encoded in the brain's global electromagnetic (EM) field. I will demonstrate that EM-ToCs perform far better than matter-based ToCs against established criteria for evaluating ToCs. Theories such as the cemi field theory also provide answers to long-standing problems, such as the nature of 'free' will and the evolutionary role of consciousness. I will discuss recent experimental evidence that supports EM-ToCs and describe several untested predictions of the cemi field theory. The cemi field theory predicts that conventional computers will never be conscious but provides a realistic scientific route for designing an artificial consciousness. The cemi field theory proposes a scientific dualism that requires no exotic physics and is rooted in the difference between matter and energy, rather than matter and spirit.

Proton-motive CO_2 fixation, chirality, protometabolism and the emergence of genes

Professor Nick Lane

University College London

View the video recording **here**.

Life is a surprisingly good guide to its own origins, in terms of membrane energetics, metabolism, and the genetic code[1]. Specifically, the use of the proton-motive force to drive work is conserved across all life on earth. The most basal form of work was likely CO_2 fixation, which could in principle drive flux through an autotrophic protometabolism resembling the conserved core of metabolism[2–4]. Patterns in the genetic code suggest genes emerged from this protometabolism via direct physical interactions between amino acids and the bases encoding them[5]. These factors suggest that life arose in structured, continuous flow environments such as alkaline hydrothermal vents[6–8]. I focus here on our own studies, which show that pH differences across freshly precipitated semi-conducting Fe(Ni)S barriers in microfluidic reactors[9] can drive CO_2 fixation to produce formate and acetate. Hydrothermal Fischer-Tropsch-type synthesis can generate mixtures of long-chain fatty acids and fatty alcohols[10], and we show these mixtures will form bilayer membranes under alkaline hydrothermal conditions[11]. Under similar conditions, the amino acid cysteine forms [4Fe-4S] clusters[12], with a midpoint redox potential of -450 mV, in the same range as ferredoxin. Metal ions can catalyse the synthesis of aspartate from oxaloacetate in the presence of the organic cofactor pyridoxamine[13], and we replicate earlier work showing that aspartate is a precursor for a one-pot synthesis of orotate and uracil via the conserved metabolic pathway[14]. Ferric iron can catalyse phosphoryl transfer from acetyl phosphate to ADP to form ATP, generating the universal energy currency[15,16]. I touch on the possible introduction of chirality into gluconeogenesis through chiral-induced spin selectivity on magnetic $[4Fe\text{-}4S]^{2+}$ clusters. Finally, I discuss our work explicating patterns in the genetic code through direct physical interactions[5]. Molecular dynamics simulations and NMR show the predicted physical interactions are real, albeit weak and statistical[17]. We correctly predict codon allocation for 50% of anticodon middle bases[17]. Based on weak physical interactions, we develop an autotrophic protocell model[18] to show that the physical templating of peptides by random RNA sequences enables selection for optimal RNA sequences, promoting the growth of evolvable protocells.

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Bioelectricity and genetics

Professor Michael Levin

Tufts University

View the video recording **here**.

What is the origin of anatomical, physiological, and behavioral patterns in living beings? The current paradigm holds that these patterns are "encoded" by the genome. But what exactly does it mean to say that complex, large-scale traits and competencies (not describable directly by amino acid sequences) are "in" the genes? Moreover, now that we know how bioelectric prepatterns in tissue regulate the size, shape, location, and identity of organ-level structures, what is the relationship of genetics with bioelectric signaling? In this talk, I first discuss what it means for any set of mechanisms to determine shape. Such a claim should enable prediction of features from measurements of the encoding medium, and facilitate control of those features by engineering the content of the medium. I then go over examples of biology of form and function in which outcomes diverge drastically from those predicted by genetic information, and illustrate the numerous cases in which the genetic level is not an efficient level of intervention at which to control complex living systems. I show example of bioelectric information which provides better prediction and control in regenerative medicine settings, and discuss the mechanisms and algorithms by which genetics and bioelectricity are coupled. I end with some speculations about the use of synthetic life forms as vehicles for a systematic exploration of the latent space of forms, which provides crucial input into forms of life and mind beyond the traditional inputs of heredity and environment. I frame evolution as a search through the space of pointers into a rich space of patterns, including the ones studied by Platonist mathematicians but also more complex, agential, biologically-relevant ones. This in turn has many implications for new kinds of regenerative medicine and synthetic biorobotics.

Closing Note

Professor Geoffrey Guy

Founder and Chairman, The Guy Foundation

Professor Alistair Nunn

The Guy Foundation and University of Westminster

View the video recording presenting a recap of the series talks and the questions for roundtable discussion **here**.

The Guy Foundation 2024 Autumn Series ended with a stimulating and wide-ranging discussion, which illustrated how the field of bioelectricity, despite its long history, still elicits as many questions as it answers. The series opened with a historical perspective from Michal Cifra, detailing the original animal electricity experiments conducted by Luigi Galvani in the 1700s and the intersection of these origins with another key figure in the history of electricity: Alessandro Volta. The discussion around electricity was driven by two camps; the biologists and the physicists. In the end the physicists dominated, setting a precedent for the next few centuries as to how we view the creation and utility of electric fields by different types of matter.

While the study of electrical effects in non-living materials went from strength to strength – with the invention of the first electric batteries – the mechanisms behind animal electricity remained elusive. The scale and complexity of the electrical effects that animate living organisms made them difficult to measure accurately and in vivo, and as such the study of bioelectricity suffered from a lack of adequately sensitive technology. In this sense the more recent development of quantum biology mirrors that of bioelectricity, its progress constrained by the ever-decreasing length and time scales at which these effects take place and the concomitant technological expertise this entails.

What the 2024 Autumn Series made clear was just how far the study of electrical effects in living organisms has come since its inception, as well as how much further it needs to go. Electricity is still considered, by many, to be entirely separate from biology, indeed, is often taught this way, despite centuries of thinking otherwise. However, electricity is implicated in the effective functioning of living organisms at every level: from the biochemical to the behavioural. Proteins rely on electrical degrees of freedom, as do cellular collectives. Indeed, as Alistair Nunn made clear in his summary presentation, our understanding of bioelectricity might shed light on the biggest questions in biology: the mysteries at the heart of ageing, the origins of life, and even, as Johnjoe McFadden outlined, consciousness itself.

One way in which this understanding may be fostered is by teasing out the simplest electrical processes common to all living organisms. In the simplest terms, to paraphrase Albert Szent-Györgyi, life is nothing but an electron looking for a place to rest. Furthermore, life, as Nick Lane puts it, is an excellent guide to its own origins. To this end, the 2024 Autumn Series highlighted the commonalities across all forms of life, from the simplest to the most complex. Bioelectricity is both energy source and organising principle, implicated in metabolic processes as well as information processing. What remains to be seen, is to what extent quantum mechanics plays a role in these critical electrical processes, or whether it is enough, as Greg Scholes discussed, to invoke ‘quantum-like’ descriptions as biological systems grow in complexity.

And finally, as Mike Levin so compellingly illustrated, bioelectricity is a profoundly flexible degree of freedom. The predominating paradigm of genetics has conditioned us to think of living organisms as hardwired into their various forms by billions of years of evolution. The manipulation of bioelectrical properties such as membrane potential paints a far less rigid picture. Bioelectricity enables rapid adaptation to changing circumstances by enabling natural selection of the most suited components from information held within these fields. In this way bioelectricity is an epigenetic (above genes) modulating system; any change to the field (e.g., damage to a cell membrane) immediately instigates a best fit homeostatic programme based on natural selection of the best fit response. The genetic and bioelectric properties of living organisms are further intertwined: genes code for proteins, including those ion channel proteins that mediate membrane potential. Perturbation of these interrelated properties can give rise to unpredictable and exciting new forms of life, that challenge and expand our definitions of what it means to be alive.

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