The Guy Foundation

FROM QUANTUM BENCH TO BEDSIDE: HOW TO REALISE THE POTENTIAL OF QUANTUM BIOLOGY IN MEDICINE

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(Eds.)

Driving innovation in medicine through quantum biology

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FROM QUANTUM BENCH TO BEDSIDE: REALISING THE POTENTIAL OF QUANTUM BIOLOGY IN MEDICINE

– BETONY ADAMS AND ALISTAIR NUNN

The 16th century physician, Paracelsus, is often quoted as saying:

> Medicine is not only a science; it is also an art. It does not consist of compounding pills and plasters; it deals with the very processes of life, which must be understood before they may be guided.

Over the last two years The Guy Foundation lectures have explored a range of quantum biology and bioenergetics research areas. Many of these lectures have focused on the fundamental science – both physics and biology – that underpins living systems, towards the aim of better understanding the processes of life and thus guiding these processes from disease back to health. As one of this season's speakers put it: understanding life's secrets could lead to fixing life's mistakes. But, while medicine can undoubtedly benefit from the production of new knowledge, it also involves the more quotidian task of making this knowledge common, with all the rules, regulations and trials that this entails. The development of a new medicine requires the standardisation of that medicine, but it also involves making that medicine the standard. If the medicine in question is outside of the given paradigm this process is that much more difficult. To this end, the 2022 Spring Series considered how quantum biology research might be translated into advancing medicine and what hurdles this translation might present. Each session involved presentations that outlined fundamental research as well as how this research might result in worthwhile medicines.

On the bench side of things, the fundamental research that was presented touched on many of the themes of previous lectures. This included the role that electromagnetic fields play in biological systems and disease, particularly in the context of cancer. But also, how electromagnetic fields might be turned – or tuned – towards health. Mitochondria, a recurrent topic of interest to The Guy Foundation, were again a central feature in a number of presentations. Redox processes and reactive oxygen species were back up for debate; on the one hand deeply implicated in the emergence and evolution of the very processes of life, on the other hand targeted by the therapeutic repurposing of luminol. The question of repurposing old chemicals into new medicines was complemented in a later session by the consideration of new quantum explanations for the action of old medicines, such as lithium.

At the other end of things, the presentations detailed the approaches taken towards the application of this new knowledge. Established approaches, such as the one developed by Cancer Research UK (CRUK), prioritised collaboration as key in the development of new medicines to treat cancer. This lesson might be adopted in translating quantum biology research into new therapeutics, with the scientific collaboration weighted towards physicists rather than medicinal chemists. Cancer offers an additional lesson as well. As a collection of diseases, rather than one single disease, the treatment of cancer requires a number of therapeutic approaches. Therapeutics derived from quantum biological research might

augment more established treatments, rather than replacing them altogether. They might also benefit from a systems biology rather than single target approach.

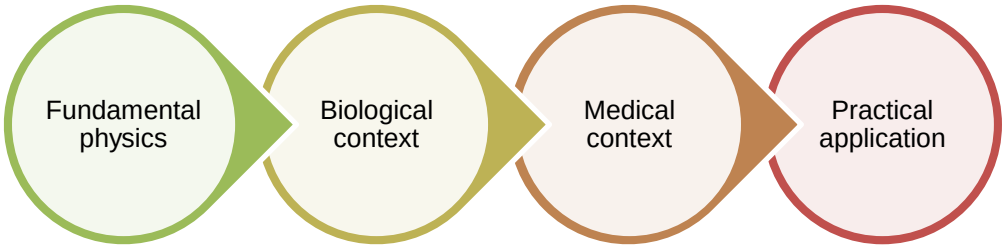
Fundamental research into quantum biology may indeed reveal an entirely new layer to the body: the physics that underlies the chemistry of life. But what will this mean in therapeutic terms. Paracelsus is perhaps most famous for his ideas on toxicology, the Janus face of medicine: the cure that is also a curse. “Solely the dose”, he wrote, “determines that a thing is not a poison”. What remains to be determined, in the translation of quantum biological research into new therapeutics is precisely this fine-tuning: the dosages, the durations, the deliveries that maximise the therapeutic effect. This is the province of regulation and clinical trial, of the incremental progression of an idea towards an accepted medicine. How this process might differ when the originary idea is rooted in quantum biology was the topic of discussion in the final session of the Series.

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 began, 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, and, of course, medicine.

The pioneers of thermodynamics and quantum physics, and – over the years – several leading scientists, embracing many different disciplines, have discussed the possibility 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.

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 cross-section of scientists invited to give presentations. 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 new diagnostics and therapeutics.

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 in biology in health and disease. We recognise these notions to be extremely avant-garde, oftentimes incomprehensible. However, we take a long view and see ourselves as pioneers in a new wave of medicinal science. With an emphasis on building a research community to further investigate these interests, The Guy Foundation operates in a spirit of collaboration rather than straightforward grant funding, to advance the course of useful knowledge towards the mainstream and bring it to the attention of more conventional funders. We aim to do this in various ways. For instance, by curating a programme of scientific meetings and publications that incorporates the diverse aspects of the field and facilitates engagement from scientists across relevant disciplines; as well as by identifying what we see as research priorities and building a network of interested scientists through the funding of collaborative projects to accelerate relevant high-quality scientific research.

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

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

ABSTRACT PROCEEDINGS

These are abstracts of a series of talks, hosted by the Foundation, that were given online to an invited audience during the spring of 2022.

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 are available on the Foundation's website www.theguyfoundation.org.

ELECTROMAGNETIC FIELDS AND CANCER AND THE THERAPEUTIC PERSPECTIVE: PART I

– DR JAN POKORNÝ

Institute of Physics, Academy of Sciences of the Czech Republic

An interdisciplinary framework of phenomena related to cancer development is presented, with special attention to the causes and consequences of disturbed cellular electromagnetic activity. The main focus is on mitochondrial dysfunction (the Warburg effect) which is supposed to be a result of oncogenic mutation. However, it is also a common phenomenon connected with a viral activity in a cell. Our extensive immunological study on 12,000 patients suggests chronic viral infections to be a crucial risk factor for cancer development. Lowered respiration connected with the Warburg effect leads to a reduced proton transfer through mitochondrial membrane and reversed polarity of ordered water layers around mitochondria. The water layers then emit electrons, resulting in damped electromagnetic activity of the affected cell. Frequency and power changes of the generated electromagnetic field result in broken communication between cells and hypothetically in reduced control over chemical reactions, with an increased probability of random genome mutations. Morphological changes then follow due to disturbed ordering forces. According to the underlying mechanism, there are three fundamental cancer phenotypes: (1) Warburg effect (differentiated) cancers with mitochondrial dysfunction in a cancer cell, (2) reverse Warburg effect (undifferentiated) cancers with a pathological cooperation between a cancer cell and associated fibroblasts, (3) cancers initiated by conductive nanofibres such as asbestos; short-circuiting by the fibres leads to similar effects as damping due to mitochondrial dysfunction. Except short-circuiting, the central process is mitochondrial dysfunction in a cancer cell (the Warburg effect) or in fibroblasts associated with a cancer cell (the reverse Warburg effect). Understanding fundamental mechanisms of cancer initiation and development is a prerequisite to defining effective therapy targets as well as developing quantitative diagnostic methods.

ELECTROMAGNETIC FIELDS AND CANCER AND THE THERAPEUTIC PERSPECTIVE: PART II

– PROFESSOR STEVE WEDGE

Professor of Stratified Cancer Medicine Discovery at Newcastle University and Head of the Cancer Research UK (CRUK) Newcastle Drug Discovery Unit

Cancer Research UK (CRUK) is the largest fundraising medical research charity in the world, contributing to the development of new knowledge as well as helping to bring 11 new drugs to market. In 2020/21 it spent £421 million on projects ranging from fundamental biological research through to late phase clinical trials. As such the charity offers valuable insight into how new therapeutics are developed from first to final stages. CRUK has a unique network of researchers and infrastructure which includes core research institutes, laboratories equipped to exploit biological insights, medical centres for translational and clinical application, drug development and clinical trial capability.

Small molecule drug discovery is a multidisciplinary effort, involving biologists, structural biologists and medicinal chemists, who work together as an integrated team. The process begins with identifying and validating targets, finding chemical leads against the target, and optimising the leads through a process involving iterative chemical design and testing. Potency and selectivity also need to be balanced against multiple other factors that affect a compound's suitability for clinical development, including its metabolic liabilities, and suitability for oral or parenteral administration. This process is not one that can be undertaken in isolation. Strategic partnerships with both academia and commercial enterprises allow CRUK to open up new areas of biology, identify novel treatments, and progress these treatments into clinical evaluation.

Since cancer is a large collection of diseases, involving diverse molecular drivers and an ability to bypass tumour control mechanisms and detection by the immune system, its treatment demands varied therapeutic approaches which may be used in combination. For tumour cell intrinsic targets, the use of large cancer cell panels with genetic or pharmacological perturbation, can help to tailor treatments towards specific patient subgroups.

CRUK has brought all of its drug discovery and commercialisation activity together in a new innovation engine called Cancer Research Horizons. This supports a collaborative approach to cancer research and treatment in order to facilitate the convening of discovery science and its translation into novel therapeutic strategies, with the ultimate aim of delivering breakthrough therapies for cancer patients.

NATURAL PRODUCTS AS REDOX MODULATORS AND THE THERAPEUTIC PERSPECTIVE: PART I

– PROFESSOR ALISTAIR NUNN

Visiting Professor, Research Centre for Optimal Health, University of Westminster and Director of Science, The Guy Foundation

"Inflammaging" is the concept that ageing and inflammation are entwined, whereby inflammatory tone rises with age due to a gradual decrease in the ability of an organism to adapt to stress. It is associated with a decreasing ability to channel electrons correctly and rising oxidative stress. Equally, as hormesis describes the ability to adapt to stress, it is intimately related to inflammation; hormetic inflexibility thus indicates decreasing robustness and frailty, which can lead to a failure of homeostasis and death. As the field of adaptive thermodynamics of far from equilibrium self-organising structures, driven by entropy and thus dissipation of energy potentials describes life, then both hormesis and inflammation can be described from this perspective. A key observation about this theory is that as malfunctioning dissipative systems can damage others, and that these structures effectively retain information, then natural selection can lead to their removal. Equally, with a lot of energy, thermodynamics also describes that once these structures reach a certain size, due to loss of internal order, they will replicate to maintain dissipation. Hence, both reproduction and death fall naturally out of physical laws. For life, this suggests that inflammation is largely scale invariant, operating from the molecular to the whole species level. Additionally, with time, it also suggests life will always become more complex. Optimal health, and thus lifespan, will be dependent on the ability to dissipate. Dissipation due to charge movement will create electric fields, which could hold valuable information about homeostasis and shape, supporting the morphogenetic theory and why cooperation evolved due to synergism to survive stress. As dissipation is reliant on the movement of electrons and other ions, maintenance of structures that can support significant quantum effects could be important in life, whereas its loss signals damage. One example of a key structure is the mitochondrion, which is central in inflammation and ageing. As many biological compounds evolved as sunscreens, there has been a billion-year evolution of resonant electronic quantum structures that can both dissipate photon and electron energy. In effect, structures that can deal with energetic stress; with time, complex metabolic systems have evolved around them enabling adaptation to multiple different stressors. They have thus become core components of modern life, especially plants, which, because of the similar biochemistry, means they can also manipulate the stress systems of animals. If disease is related to a failure of a system to maintain dissipation, then many natural products may have the ability to restore this to some degree, hence they will appear to be redox modulators, and will thus have anti-inflammatory, anti-cancer, anti-ageing and likely, anti-pathogen activity. They will thus have many targets, but a key one will be the mitochondrion; they will also display biphasic effects as dose has evolved to have multiple effects across several systems as defined by the concept of hormesis.

NATURAL PRODUCTS AS REDOX MODULATORS AND THE THERAPEUTIC PERSPECTIVE: PART II

– DR WOLFGANG BRYSCH

Chief Scientific Officer and Chief Medical Officer, MetrioPharm AG

Cellular redox imbalance and oxidative stress are major upstream triggers of pro-inflammatory signaling in cells of the innate immune system, namely macrophages. Oxidative stress has been identified as a central driver and/or major confounding factor in a wide spectrum of chronic inflammatory and degenerative diseases, like COPD, Parkinson's Disease, chronic kidney failure, NASH and Alzheimer's Disease to name just a few prominent examples. However, despite the undisputed importance of oxidative stress and elevated levels of cellular reactive oxygen species (ROS) in these pathologies, antioxidant-based therapies have largely failed in the clinic.

New research findings in recent years have revealed that ROS are not just toxic waste products of cellular energy metabolism and/or external factors like toxins or radiation. Rather low levels of ROS fulfil a crucial and physiologic role in cell signaling. Thus, interventions which indiscriminately scavenge all cellular ROS will also interfere with physiologic cell signaling. The challenge of therapeutic interventions lies therefore in neutralising excessive ROS (oxidative stress) while sparing the low levels of ROS necessary for vital cellular functions.

MP1032 is a stable and biologically active (i.e. druggable) form of the amino-phtalhydrazide Luminol. This compound acts as a self-regulated ROS scavenger. At low, physiologic cellular ROS levels, this compound is biologically inactive. However, elevated ROS levels as encountered with oxidative stress activate the antioxidant capacity of MP1032, which then in turn reduces ROS levels by donating electrons to ROS. This creates a self-regulating feedback loop which stops its antioxidant activity once physiologic ROS levels have been re-established.

MP1032 has shown consistent anti-inflammatory and anti-infective efficacy in a number of pre-clinical disease models and in human clinical trials. This type of auto-regulated redox modulation promises to overcome the obstacles that antioxidative therapies have struggled with in the past and represent a key to unlock the vast therapeutic potential that lies in targeting the cellular redox system.

ENTANGLED POSNER MOLECULES AND THE THERAPEUTIC PERSPECTIVE: PART I

– PROFESSOR MATTHEW FISHER

Professor of Physics, University of California Santa Barbara

Building a laboratory quantum computer is now a billion-dollar enterprise. But might we, ourselves, be quantum computers [1]? While maintaining quantum coherence on macroscopic time scales is exceedingly unlikely in the warm wet brain, there is one exception: Nuclear spins [2]. I have been seeking the biochemical substrate and mechanisms that could host such putative nuclear spin quantum processing, and have identified a specific neural qubit and a unique collection of ions, molecules and organelles. In this exploration, lithium isotopes have played a central role, since experiments have found a differential isotope dependence across a myriad of bio-chemical scales, ranging from calcium-phosphate precipitation in vitro, to mitochondrial calcium regulation and to modulating rat behavior [3]. Such an isotope dependence is highly suggestive of an underlying quantum mechanism, especially since lithium-6 and lithium-7 have very different nuclear spin dynamics. Moreover, these experiments point to the possibility that the rare lithium isotope could serve as a new psychiatric pharmaceutical. Additionally, if we can identify the proteins that are responsible for regulating the dynamics of calcium-phosphate in mitochondria, targeting said proteins could affect mitochondrial function with possible therapeutic implications. In this talk I will summarize our efforts in these directions.

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ENTANGLED POSNER MOLECULES AND THE THERAPEUTIC PERSPECTIVE: PART II

– DR DAVE ECKER

Co-Founder and Vice-President of Strategic Innovation, Ionis Pharmaceuticals.

Ionis Pharmaceuticals is a biopharma company founded and run by scientists for the past 32 years. Ionis pioneered the development of oligonucleotides as medicines. Conventional pharmaceuticals generally target proteins. When Ionis first suggested that a pharmaceutical intervention might alter protein synthesis at the source, by binding to RNA, the idea met with considerable scepticism. Unmodified oligonucleotides are quickly degraded by the body. Despite this, Ionis, through a concerted investment in medicinal chemistry, developed stable precision genetic medicines to treat a number of diseases. This strategy has proved itself especially potent in the treatment of spinal muscular atrophy, a devastating autosomal recessive disease. Spinraza was the first licensed drug to treat spinal muscular atrophy and is now approved in 50 countries worldwide. And now precision genetic medicine is entering the mainstream. This experience of developing a successful medicine from impossible idea to life-saving intervention has led Ionis to question what the next wave of medical innovation might look like.

Ionis is interested in research in quantum biology because of the possibility that it will reveal underlying biological and physiological mechanisms that might be leveraged towards new therapeutics. An understanding of germ theory led to the development of antibiotics and vaccines in much the same way as an understanding of the genome has informed gene therapies. In this way, understanding life's secrets could lead to fixing life's mistakes, which is disease. What remains to be seen, however, is how this new knowledge will play out. For now, we envisage three main approaches. First, can diseases with unknown aetiologies be explained through an understanding of quantum processes that are foundational to a biological process of life, and furthermore, how do genetic causes interfere with these quantum processes? Second, can we use quantum processes as tools to intervene in diseases that are not necessarily quantum in origin? This could involve the use of magnetic and electric fields and would address the question of life's preferred frequencies. And finally, could quantum mechanics be used to develop precision genetic mechanisms? For instance, the use of a 'quantum trigger' could narrow the target of CRISPR technology to a specific diseased tissue.

LIGHT-MATTER INTERACTIONS AND THE THERAPEUTIC PERSPECTIVE: PART I – DR LISE HÉBERT

Senior Vice-President, Research and Clinical Affairs, Klox Technologies

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Fluorescent Light Energy (FLE) is a new form of photobiomodulation, and whereas fluorescence has been used in diagnostic tools, Klox Technologies is the only company as yet utilising FLE as a therapeutic. Klox has completed multiple clinical studies and proof-of-concept work demonstrating the effects of FLE on various conditions and diseases. Their lead programmes include Kleresca for moderate to severe acne vulgaris and LumiHeal for acute and chronic wounds, including post-operative scar management applications. The FLE is generated using a specially formulated topical gel or matrix that is LED light activated; the photoactivation and subsequent emission of fluorescence by the activated molecules is absorbed by photoacceptors within the skin, which in turn modulates various cellular activities including mitochondrial activity. FLE has been shown to favorably impact every phase of healing (Inflammatory, Proliferative, and Remodeling). It alters inflammation by reducing pro-inflammatory cytokines. It has also been demonstrated to modulate mitochondrial morphology, activate fission/fusion mechanisms as well as increase adenosine triphosphate (ATP) production. Furthermore, FLE increases important growth factors necessary in wound healing and induces angiogenesis. It also increases and improves the production and deposition of collagen. Klox has attained approvals for FLE in a number of countries. These include approvals with CE Mark in the EU and ARTG in Australia, which were early commercial adopters of the technology. Recent clearance and approvals include FDA De Novo in the US and NMPA in China, as recently as December 2021. Future prospects for Klox include a pipeline into further applications in dermatology, wound care, oral health, select rare diseases, and aesthetic injectables.

LIGHT-MATTER INTERACTIONS AND THE THERAPEUTIC PERSPECTIVE: PART II – PROFESSOR GREG SCHOLES

William S. Tod Professor of Chemistry, Princeton University.

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? 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 [2,3,4]. 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 [5-7]. 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.

Understanding this synchronization might in turn offer some insight into how new therapeutic interventions exert their effects. Conventional pharmaceuticals target individual components of living systems, such as single proteins. Synchronisation, on the other hand, offers a systemic understanding of living systems, in which a potential disruption or disease upsets the proper timing of essential processes. Light therapies, in which electromagnetic radiation is shown to lower inflammatory markers and promote healing, might potentially be understood as resetting the synchronisation of a system.

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LIGHT-MATTER INTERACTIONS AND THE THERAPEUTIC PERSPECTIVE: PART III

– BRENT VAUGHAN

CEO, Cognito Therapeutics

Cognito Therapeutics applies knowledge gained from optogenetics to the treatment of neurodegeneration, particularly Alzheimer's disease. This works by driving specific frequencies of electrical activity in the brain for downstream therapeutic outcomes. Electricity is the fundamental currency of the brain. The brain has evolved to generate, store and transmit electricity. Rhythmic neural activity in the gamma range (30-80 Hz) has been demonstrated to be disrupted in several neurological conditions. Sensory stimuli can be used to induce oscillations at specific frequencies in the brain. Cognito Therapeutics uses light and sound stimulation at 40 Hz to stimulate neural oscillations in the gamma range in a process called Gamma Entrainment Using Sensory Stimuli (GENUS). This opens a new space for therapeutic techniques that exploit electrical rather than chemical principles. Traditional drugs have major treatment limiting side-effects and the development of new drugs do not account for patient heterogeneity. Modulating the chemistry of the brain can also undermine the inherent systems biology of the brain, particularly given the fact that it is difficult to attenuate dosages based on brain response. Results from research done by Cognito show that stimulating electrical activity in the brain, particularly gamma synchrony, activates microglia to clear protein pathologies and promotes blood flow for glymphatic clearance. This in turn leads to reductions in A-beta and tau and improved neuron morphology, cognitive function and circadian rhythms. Gamma synchrony also prevents brain atrophy and improves memory. Invasive brain treatments increase costs, while at the same time lowering adoption and compliance. Cognito's non-invasive device-based treatment, on the other hand, is easily implementable and safe enough for home-based care. While preliminary clinical trials show promising results, Cognito is currently launching two pivotal studies in Alzheimer's disease and Mild Cognitive Impairment (MCI) and a Ph2 is starting in Parkinson's disease.

CLOSING NOTE: REINVENTING THE DEAL

– PROFESSOR GEOFFREY GUY

If a thread could be said to have emerged from this series, it concerned the practical translation of new science into worthwhile therapeutic or diagnostic interventions. Drawing on previous experience in developing both synthetic and natural medicines, we closed the series by outlining some of the ways in which conventional approaches might fall short in the context of quantum biology derived – or related – therapeutics.

The origin of new medical interventions might be said to fall into two camps, those derived from empirical discovery and those arrived at through theoretical hypotheses. The Spring Series lectures showcased both: the serendipitous finding of Klox's Fluorescent Light Energy treatment and Cognito's use of gamma synchrony to treat Alzheimer's disease. Somewhere between the two of these was the familiar medicine with a novel mechanism of action, as in the case of lithium. Regardless of the origin of the idea, however, all prospective medicines must pass through a rigorous system of regulation.

One of the principal points that emerged during the series was the complication that arises when the notion of a single drug, single target has to be dispensed with. Many of the proposed pharmaceuticals outlined in the presentations dealt with systemic effects and relative rather than absolute targets. Metriopharm, for example, emphasised that reactive oxygen species, far from being purely destructive, are also integral to a balanced signalling system. Their target, therefore, was the relative concentration of reactive oxygen species, redox rebalancing rather than redox scavenging. In response to Klox's experimental results, Professor Greg Scholes suggested that light therapy alters a process, such as synchronisation, rather than a discrete entity.

The history of pharmaceutical development is almost exclusively imagined in terms of a single (usually soluble) drug targeting a single appropriate receptor. While the regulatory side of this development has been slightly more open to expanding this to include systemic effects, especially for rare diseases, the reality remains that the tools developed to evaluate the quality, safety and efficacy of new therapeutics have primarily been developed with the idea of single targets in mind. For multimodal therapeutics these tools will need to be rethought and refined.

Many of the presentations in this and previous Series addressed how fundamental entities such as electrons, protons, photons and phonons underpin macroscopic outcomes in biological systems. This means expanding the common view that chemicals are at the heart of biological systems, by considering the effects that fields have. The therapeutic application of fields differs from the ingestion of a chemical in its method of application: device versus medicine. Each of these has its own regulatory route, burden of proof, cost structure and business model. While the distinction between certain proposed therapeutics is very clear – luminol is clearly a medicine, whereas gamma synchrony is device based – in other instances this distinction is more ambiguous. Klox's light therapy involved the use of a topical gel in conjunction with the application of light. The gel, conventionally considered a medicine is more

accurately an extension of the device, as it does not require contact with the skin in order to exert its effect.

The translation of fundamental science into worthwhile therapeutics involves a number of other processes that may require such adaptation in the context of quantum-based therapeutics. The patenting and protecting of an idea, for instance, might be invalidated by unauthorised disclosures or inconsistencies between the patented invention and the resultant therapeutic. This is no doubt complicated by the fact that quantum mechanisms of action remain difficult to grasp or explain. But this will be felt outside of the patenting context as well. Clinical evaluation of new medicines has established pre-clinical laboratory models and tests. But these are developed for certain classes of drugs only. Novel interventions require novel models. This will pose a real challenge if the proposed intervention harnesses quantum effects. What, in this case, is the therapeutic agent and how will it be tested? What does a dose mean and how will this be justified to the regulators? What would a stress test look like? Will an entirely new trials methodology need to be developed? It is worth noting that fifty percent of all phase three clinical trials fail, not always because of any problem with the proposed medicine.

In summary, these regulatory steps are what determine the final labelling of the new therapeutic. Given the uncertainty and novelty of regulating quantum therapeutics, will the promise of this label be enough to attract the necessary funding? While there are some other avenues of fundraising many of the small start-ups looking to develop new therapeutics will need to take the conventional route. However, with an idea derived from a theoretical hypothesis that is difficult to understand, aimed at modulating a system rather than targeting a single receptor, with ambiguity as to whether the therapeutic is device or medicine, and how to patent this, no well established or accepted evaluations and an unclear methodology of late-stage clinical trials, the attraction of conventional funding might prove challenging.

These questions and considerations are in no way meant to deter those looking to translate quantum biology research into worthwhile therapeutics. Rather they are meant to begin the conversation around developing new regulatory processes appropriate to these therapeutics and attracting the funding to do so. Once this is in place, the next stage of the conversation will be how to get life scientists and clinicians on board to take these notions into the mainstream.

May 2022