The **quantum side** of nature

Dr Carlos Martino, Assistant Professor from the Florida Institute of Technology, and **Dr Robert Usselman**, Researcher at Montana State University, introduce the emerging research field of quantum biology that is set to bridge the knowledge gap between physics and cellular function

Why have you chosen to focus your research efforts on the emerging field of quantum biology and, more specifically, quantum phenomena?

The notion of quantum effects in biology was suggested by Erwin Schrödinger, Pascual Jordan and others during the early development of quantum mechanics. Because everything in nature follows the rules of quantum physics at the atomic level, it is intriguing to consider how biological molecules and systems might utilise quantum properties in their normal functions.

Novel research tools and experimental designs have emerged in the field known as quantum biology, to identify quantum phenomena in biology. Recent studies have demonstrated possible quantum processes in key mechanisms for bird navigation, olfactory sensing and photosynthesis.

While in our research programmes we did not seek to join the field of quantum biology, we quickly realised that our research direction certainly fell under the rubric of this exciting and evolving field. Our fundamental interests now entail capturing signatures of quantum phenomena at the molecular level and connecting them with effects persisting at the cellular level.

What are the main objectives of your current projects?

Our work focuses on exploring possible quantum effects in cellular metabolism; in particular, the biological production of reactive oxygen species (ROS). ROS were primarily thought of as deleterious side products of oxidative metabolism, but are now also considered as important cellular signalling molecules in key biochemical pathways. The overarching objective in our current projects is to understand how certain flavoenzyme reactions involving the activation of molecular oxygen control the branching between superoxide and hydrogen peroxide product channels.

By what means will you investigate the possible impact of quantum phenomena in metabolic processes of ROS?

We aim to discover, at the biomolecular level, if the action of certain flavoenzymes involves a radical pair mechanism. We hypothesise that internal control of singlet-triplet mixing might provide a means to 'switch' function and ROS products, in a manner analogous to redox switching proteins. Realisation of this goal would provide new insights into structure-function relationships in flavoenzyme activity, and identify a new control mechanism for ROS signalling pathways.

Several research groups are exploring the ROS chemical pathways that can influence proliferation, transcription and differentiation. Our aim is to elucidate quantum effects at the point of ROS origin. The intriguing feature of quantum coherence effects is that the chemical reaction is poised to take both paths, then projects into its products. As Yogi Berra might say, when you arrive at a branch point in a reaction pathway: take it.

How will your work advance prior studies?

The challenge in quantum biology, and the source of some criticism, is the difficulty of undertaking direct, rigorously controlled measurements of quantum processes in biological environments. Our work not only explores a completely new area of quantum biology, but also introduces advanced methodologies for probing quantum evolution in certain biochemical reactions.

Why are you determining mechanisms and quantum effects by radio frequency magnetic fields (RF) in biological systems?

Applying weak RF magnetic fields allows us to perform a type of reaction yield-detected magnetic resonance (RYDMR) spectroscopy – an experimental method that is well-established in the study of radical pair chemical reactions. RF magnetic fields influence singlet-triplet mixing in the radical pairs.

In the reaction of flavoenzyme semiquinones and superoxide spin-correlated radical pairs, the magnetic fields affect the distribution of ROS products of the chemical reaction. The key idea is to measure specific ROS relative product yields with and without RF exposure. Ultimately, we hope it is possible to control the relative concentrations of various ROS species and thus modulate pathways associated with ROS signalling.

Scales of **knowledge**

Funded by the **Air Force Office of Scientific Research** and the **Florida Institute of Technology Start-up**, an international research group is exploring quantum phenomena in metabolic processes

MAGNETORECEPTION IS A growing field of study and represents a way by which biological systems can respond to magnetic fields. It is thought to be responsible for birds' ability to navigate with great accuracy over long distances and growth responses of plants such as *Arabidopsis thaliana*. A proposed magnetosensing, light-dependent mechanism, which could potentially cause physiological responses to changes in magnetic field, is through the production of spin-correlated radical pairs via flavoenzymes.

Certain classes of flavoenzymes can produce reactive oxygen species (ROS), including hydrogen peroxide and superoxide, during photoexcitation or regular function. ROS were traditionally thought to wreak havoc in cells, but now are being ascribed additional roles as signalling molecules, whereby ROS production patterns result in specific signal transduction cascades and cell-cell communication.

MAGNETIC EFFECTS IN METABOLISM

ROS formation begins with a reduced flavoenzyme reacting with molecular oxygen to produce a superoxide and a semiquinone radical pair. These may form a 'spin-correlated radical pair', a quantum process. In this situation, the two radicals are related and can exhibit a phenomenon called quantum coherence, potentially conferring sensitivity to magnetic fields. Magnetosensitivity may arise by the magnetic field influencing the quantum state of the paired electrons, such as by singlet-triplet mixing of the spin-correlated radical pair.

The reaction can continue to form two distinct products: either superoxide is released or superoxide is converted to hydrogen peroxide before being released by the flavoenzyme. Different ROS distributions can create unique signalling patterns in the cell – possibly creating distinct physiological results. The reaction outcomes are determined by the spin correlation of the radical pair, which may be influenced by the local protein environment.

FROM CELLS TO ORGANISMS

Drs Carlos Martino of the Florida Institute of Technology and Robert Usselman at Montana State University aim to understand the role of quantum processes in ROS formation in cell biology and flavoenzymology.

Currently, Martino and Usselman are investigating radio frequency magnetic fields in rat and human neural cell cultures to identify spin biochemistry effects of radical pairs and ROS products. In collaboration with Dr Margaret Ahmad from the University of Paris VI, France, they are exploring magnetic sensitivity in a form of light-dependent radical formation in whole organisms: the plant *Arabidopsis thaliana* and the fly *Drosophila*.

In these organisms, the group uses point mutations in the photoreceptor protein, cryptochrome, that affect the formation of spin-correlated radical pairs. The goal is to understand quantum mechanisms behind physiological effects observed from applying weak magnetic fields. To link cellular observations to biomolecular functions, isolated flavoenzymes are studied. This approach helps to connect molecular, cellular and organism levels for understanding the quantum processes in cell biology.

INCREASING THE COHERENCE OF QUANTUM BIOLOGY

The truly interdisciplinary work conducted by Martino and Usselman on understanding the quantum effects of the mechanisms of ROS formation could potentially lead to novel therapeutics for ROS-related diseases: "Overproduction of ROS is implicated in many diseases including atherosclerosis, cancer and neurodegeneration," add the researchers. "Our work should lead to a fundamental understanding of ROS regulation that will advance knowledge of the causes, and potential therapeutics, of diseases involving ROS."

Additionally, bioinspired sensors using quantum biology principles could be created. More generally, further understanding of how quantum effects influence biology has the potential to inspire technological advances at the interface of medicine and research: "Our efforts to elucidate the effects of quantum phenomena in biology will open entirely new areas for technological development in medical and electronic interfacing with biological systems," Martino and Usselman conclude.

INTELLIGENCE

QUANTUM PHENOMENA

OBJECTIVE

To explore possible quantum effects, resulting from the biological production of reactive oxygen species (ROS), in cellular metabolism. More specifically, to understand how certain flavoenzyme reactions involving the activation of molecular oxygen control the branching between superoxide and hydrogen peroxide product channels.

PARTNER

Dr Margaret Ahmad, University of Paris VI, France

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DR CARLOS MARTINO received a PhD in Mechanical Engineering from the University of Colorado Boulder, USA, in 2008 for dissertation work on low-level static magnetic field effects in cellular systems. He spent two years at the Institute of Medical Engineering at the Technical University of Munich, Germany, as part of his graduate work. Martino's current research interests include establishing the frequency and magnetic field dependence of the spin-correlated radical pairs in oxidative metabolism.

DR ROBERT USSELMAN has multidisciplinary skills in molecular biology, clinical biochemistry, biophysics and magnetic resonance. Following his PhD at Montana State University, USA, he has had a postdoctoral joint appointment at the University of Denver and the University of Colorado Health Science Center. He recently was a National Research Council postdoctoral fellow at the National Institute of Standards and Technology (NIST-Boulder). His research interests are in developing novel methodologies for exploring quantum effects in biological systems.

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