When life gets physical

Quantum effects in selected biological systems have been confirmed experimentally, but how widespread is their role remains unclear

Andrea Rinaldi

The subatomic world is nothing like the world that biologists study. Physicists have struggled for almost a century to understand the wave-particle duality of matter and energy, but many questions remain unanswered. That biological systems ultimately obey the rules of quantum mechanics might be self-evident, but the idea that those rules are the very basis of certain biological functions has needed 80 years of thought, research and development for evidence to begin to emerge (Sidebar A).

Until very recently, it was not even possible to investigate whether quantum phenomena such as coherence and entanglement could play a significant role in the function of living organisms. As such, researchers were largely limited to computer simulations and theoretical experiments to explain their observations (see *A quantum leap in biology*, www.emboreports.org). Recently, however, quantum biologists have been making inroads into developing methodology to measure the degree of quantum entanglement in light-harvesting systems. Their breakthrough has turned once ephemeral theories into solid evidence, and has sparked the beginning of an entirely new discipline.

How widespread is the direct relevance of quantum effects in nature is hard to say and many scientists suspect that there

are only a few cases in which quantum mechanics have a crucial role. However, interest in the field is growing and researchers are looking for more examples of quantum-dependent biological systems. In a way, quantum biology can be viewed as a natural evolution of biophysics, moving from the classical to the quantum, from the atomic to the subatomic. Yet the discipline might prove to be an even more intimate and further-reaching marriage that could provide a deeper understanding of things such as protein energetics and dynamics, and all biological processes where electrons flow.

Among the biological systems in which quantum effects are believed to have a crucial role is magnetoreception, although the nature of the receptors and the underlying biophysical mechanisms remain unknown. The possibility that organisms use a ferromagnetic material (magnetite) in some cases has received some confirmation, but support is growing for the explanation lying in a chemical detection mechanism with quantum mechanical properties. This explanation posits a chemical compass based on the light-triggered production of a radical pair—a pair of molecules each with an unpaired electron—the spins of which are entangled. If the products of the radical pair system are spin-dependent, then a magnetic field—like the geomagnetic one—that affects the direction of spin will alter the reaction products. The idea is that these reaction products affect the sensitivity of light sensors in the eye, thus allowing organisms to ‘see’ magnetic fields.

The research comes from a team led by Thorsten Ritz at the University of California Irvine, USA, and other groups, who have suggested that the radical pair reaction

takes place in the molecule cryptochrome. Cryptochromes are flavoprotein photoreceptors first identified in the model plant *Arabidopsis thaliana*, in which they play key roles in growth and development. More recently, cryptochromes have been found to have a role in the circadian clock of fruit flies (Ritz *et al*, 2010) and are known to be present in migratory birds. Intriguingly, magnetic fields have been shown to have an effect on both *Arabidopsis* seedlings, which respond as though they have been exposed to higher levels of blue light, and *Drosophila*, in which the period length of the clock is lengthened, mimicking the effect of increased blue light signal intensity on cryptochromes (Ahmad *et al*, 2007; Yoshii *et al*, 2009).

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Direct evidence that cryptochrome is the avian magnetic compass is currently lacking, but the molecule does have some features that make its candidacy possible. In a recent review (Ritz *et al*, 2010), Ritz and colleagues discussed the mechanism by which cryptochrome might form radical pairs. They argued that “Cryptochromes are bound to a light-absorbing flavin cofactor (FAD) which can exist in three interconvertible [sic] redox forms: (FAD, FADH[•], FADH⁻),” and that the redox state of FAD is light-dependent. As such, both the oxidation and reduction of the flavin have radical

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Sidebar A | Putting things in their place

Pascual Jordan [pictured above] and the dawn of quantum biology. From 1932, Jordan started to outline the new field's background in a series of essays that were published in journals such as *Naturwissenschaften*. An exposition of quantum biology is also encountered in his book *Die Physik und das Geheimnis des organischen Lebens*, published in 1941. Photo courtesy of Luca Turin.

Although Erwin Schrödinger (1887–1961) is often credited as the ‘father’ of quantum biology, owing to the publication of his famous 1944 book, *What is Life?*, the full picture is more complex. While other researchers were already moving towards these concepts in the 1920s, the German theoretical physicist Pascual Jordan (1902–1980) was actually one of the first to attempt to reconcile biological phenomena with the quantum revolution that Jordan himself, working with Max Born and Werner Heisenberg, largely ignited. “Pascual Jordan was one of many scientists at the time who were exploring biophysics in innovative ways. In some cases, his ideas have proven to be speculative or even fantastical. In others, however, his ideas have proven to be really ahead of their time,” explained Richard Beyler, a science historian at Portland State University, USA, who analysed Jordan’s contribution to the rise of quantum biology (Beyler, 1996). “I think this applies to Jordan’s work in quantum biology as well.”

Beyler also remarked that some of the well-known figures of molecular biology’s past—Max Delbrück is a notable example—entered into their studies at least in part as a response or rejoinder to Jordan’s work. “Schrödinger’s book can also be read, on some level, as an indirect response to Jordan,” Beyler said. Jordan was certainly a complex personality and his case is rendered more complicated by the fact that he explicitly hitched his already speculative scientific theories to various right-wing political philosophies. “During the Nazi regime, for example, he promoted the notion that quantum biology served as evidence for the naturalness of dictatorship and the prospective death of liberal democracy,” Beyler commented. “After 1945, Jordan became a staunch Cold Warrior and saw in quantum biology a challenge to philosophical and political materialism. Needless to say, not all of his scientific colleagues appreciated these propagandistic endeavors.”

species as intermediates. “Therefore both forward and reverse reactions may involve the formation of radical pairs” (Ritz *et al*, 2010). Although speculative, the idea is that a magnetic field could alter the spin of the free electrons in the radical pairs resulting in altered photoreceptor responses that could be perceived by the organism. “Given the relatively short time from the first suggestion of cryptochrome as a magnetoreceptor in 2000, the amount of studies from different fields supporting the photo-magnetoreceptor and cryptochrome hypotheses [...] is promising,” the authors concluded. “It suggests that we may be only one step away from a true smoking gun revealing the long-sought after molecular nature of receptors underlying the 6th sense and thus the solution of a great outstanding riddle of sensory biology.”

Research into quantum effects in biology took off in 2007 with groundbreaking experiments from Graham Fleming’s group at the University of California, Berkeley, USA. Fleming’s team were able to develop tools that allowed them to excite the photosynthetic apparatus of the green sulphur bacterium *Chlorobium tepidum* with short laser pulses to demonstrate that wave-like energy transfer takes place through quantum coherence (Engel

et al, 2007). Shortly after, Martin Plenio’s group at Ulm University in Germany and Alán Aspuru-Guzik’s team at Harvard University in the USA simultaneously provided evidence that it is a subtle interplay between quantum coherence and environmental noise that optimizes the performance of biological systems such as the photosynthetic machinery, adding further interest to the field (Plenio & Huelga, 2008; Rebentrost *et al*, 2009). “The recent Quantum Effects in Biological Systems (QuEBS) 2011 meeting in Ulm saw an increasing number of biological systems added to the group of biological processes in which quantum effects are suspected to play a crucial role,” commented Plenio, one of the workshop organizers; he mentioned the examples of avian magnetoreception and the role of phonon-assisted tunnelling to explain the function of the sense of smell (see below). “The study of quantum effects in biological systems is a rapidly broadening field of research in which intriguing phenomena are yet to be uncovered and understood,” he concluded.

“The area of quantum effects in biology is very exciting because it is pushing the limits of quantum physics to a new scale,” Yasser Omar from the Technical University of Lisbon, Portugal commented. “[W]e are finding that quantum coherence plays a

significant role in the function of systems that we previously thought would be too large, too hot—working at physiological temperatures—and too complex to depend on quantum effects.”

Another growing focus of quantum biologists is the sense of smell and odorant recognition. Mainstream researchers have always favoured a ‘lock-and-key’ mechanism to explain how organisms detect and distinguish different smells. In this case, the identification of odorant molecules relies on their specific shape to activate receptors on the surface of sensory neurons in the nasal epithelium. However, a small group of ‘heretics’ think that the smell of a molecule is actually determined by intramolecular vibrations, rather than by its shape. This, they say, explains why the shape theory has so far failed to explain why different molecules can have similar odours, while similar molecules can have dissimilar odours. It also goes some

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Fig 1 | Diagram of a vibration-sensing receptor using an inelastic electron tunnelling mechanism. An odorant—here benzaldehyde—is depicted bound to a protein receptor that includes an electron donor site at the top left to which an electron—blue sphere—is bound. The electron can tunnel to an acceptor site at the bottom right while losing energy (vertical arrow) by exciting one or more vibrational modes of the benzaldehyde. When the electron reaches the acceptor, the signal is transduced via a G-protein mechanism, and the olfactory stimulus is triggered. Credit: Luca Turin.

way to explaining how humans can manage with fewer than 400 smell receptors.

A recent study in *Proceedings of the National Academy of Sciences USA* has now provided new grist for the mill for ‘vibrationists’. Researchers from the Biomedical Sciences Research Center “Alexander Fleming”, Vari, Greece—where the experiments were performed—and the Massachusetts Institute of Technology (MIT), USA, collaborated to replace hydrogen with deuterium in odorants such as acetophenone and 1-octanol, and asked whether *Drosophila* flies could distinguish the two isotopes, which are identically shaped but vibrate differently (Franco *et al*, 2011). Not only were the flies able to discriminate between the isotopic odorants, but when trained to discriminate against the normal or deuterated isotopes of a compound, they could also selectively avoid the corresponding isotope of a different odorant. The findings are inconsistent with a shape-only model for smell, the authors concluded, and suggest that flies can ‘smell molecular vibrations’.

“The ability to detect heavy isotopes in a molecule by smell is a good test of shape

and vibration theories: shape says it should be impossible, vibration says it should be doable,” explained Luca Turin from MIT, one of the study’s authors. Turin is a major proponent of the vibration theory and suggests that the transduction of molecular vibrations into receptor activation could be mediated by inelastic electron tunnelling (Fig 1; see also *The scent of life*, www.emboreports.org). “The results so far had been inconclusive and complicated by possible contamination of the test odorants with impurities,” Turin said. “Our work deals with impurities in a novel way, by asking flies whether the presence of deuterium isotope confers a common smell character to odorants, much in the way that the presence of -SH in a molecule makes it smell ‘sulphuraceous’, regardless of impurities. The flies’ answer seems to be ‘yes’.”

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One of the study’s Greek co-authors, Efthimios Skoulakis, suggested that flies are better suited than humans at doing this experiment for a couple of reasons. “[The flies] seem to have better acuity than humans and they cannot anticipate the task they will be required to complete (as humans would), thus reducing bias in the outcome,” he said. “*Drosophila* does not need to detect deuterium *per se* to survive and be reproductively successful, so it is likely that detection of the vibrational difference between such a compound and its normal counterpart reflects a general property of olfactory systems.”

Jennifer Brookes, a physicist at University College London, UK, explained that recent advances in determining whether quantum effects have a role in odorant recognition has involved assessing the physical violations of such a mechanism in the first instance, and finding that, given certain biological parameters, there are none. “The point being that if nature uses something like the quantized vibrations of molecules to ‘measure’ a smell then the idea is not—mathematically, physically and biologically—as eccentric as it at first seems,” she said. Moreover, there is the possibility that quantum mechanics could play a much broader role in biology than simply underpinning the sense of smell. “Odorants are not the only small molecules that interact unpredictably with large proteins; steroid hormones, anaesthetics and neurotransmitters, to name a few, are examples of ligands that interact specifically with special receptors to produce important biological processes,” Brookes wrote in a recent essay (Brookes, 2010).

The question of whether quantum mechanics really plays a non-trivial role in biology is still hotly debated by physicists and biologists alike. “[A] non-trivial quantum effect in biology is one that would convince a biologist that they needed to take an advanced quantum mechanics course and learn about Hilbert space and operators etc., so that they could understand the effect,” argued theoretical quantum physicists Howard Wiseman and Jens Eisert in their contribution to the book *Quantum Aspects of Life* (Wiseman & Eisert, 2008). In their rational challenge to the general enthusiasm for a quantum revolution in biology, Wiseman and Eisert point out that a number of “exotic” and “implausible” quantum effects—including a quantum life principle,

quantum computing in the brain, quantum computing in genetics, and quantum consciousness—have been suggested and warn researchers to be cautious of “ideas that are more appealing at first sight than they are realistic” (Wiseman & Eisert, 2008).

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Keeping this warning in mind, the view of life from a quantum perspective can still provide a deeper insight into the mechanisms that allow living organisms to thrive without succumbing to the increasing entropy of their environment. But does quantum biology have practical applications? “The investigation of the role of quantum physics in biology is fascinating because it could help explain why evolution has favoured some biological designs, as well as inspire us to develop more efficient artificial devices,” Omar said. The most often quoted examples of such devices are solar collectors that would use efficient energy transport mechanisms inspired by the quantum proficiency of natural light-harvesting systems, and quantum computing. But there is much more ahead. In 2010, the Pentagon’s cutting-edge research branch, DARPA (Defense Advanced Research Projects Agency, USA), launched a solicitation for innovative proposals in the area of quantum effects in a biological environment. “Proposed research should establish beyond any doubt that manifestly quantum effects occur in biology, and demonstrate through simulation proof-of-concept experiments that devices that exploit these effects could be developed

into biomimetic sensors,” states the synopsis (DARPA, 2010). This programme will thus look explicitly at photosynthesis, magnetic field sensing and odour detection to lay the foundations for novel sensor technologies for military applications.

Clearly a number of civil needs could also be fulfilled by quantum-based biosensors. Take, for example, the much sought-after ‘electronic nose’ that could replace the use of dogs to find drugs or explosives, or could assess food quality and safety. Such a device could even be used to detect cancer, as suggested by a recent publication from a Swedish team of researchers who reported that ovarian carcinomas emit a different array of volatile signals to normal tissue (Horvath *et al*, 2010). “Our goal is to be able to screen blood samples from apparently healthy women and so detect ovarian cancer at an early stage when it can still be cured,” said the study’s leading author György Horvath in a press release (University of Gothenburg, 2010).

Despite its already long incubation time, quantum biology is still in its infancy but with an intriguing adolescence ahead. “A new wave of scientists are finding that quantum physics has the appropriate language and methods to solve many problems in biology, observing phenomena from a different point of view and developing new concepts. The next important steps are experimental verification/falsification,” Brookes said. “One could easily expect many more new exciting ideas and discoveries to emerge from the intersection of two major areas such as quantum physics and biology,” Omar concluded.

CONFLICT OF INTEREST

The author declares that he has no conflict of interest.

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