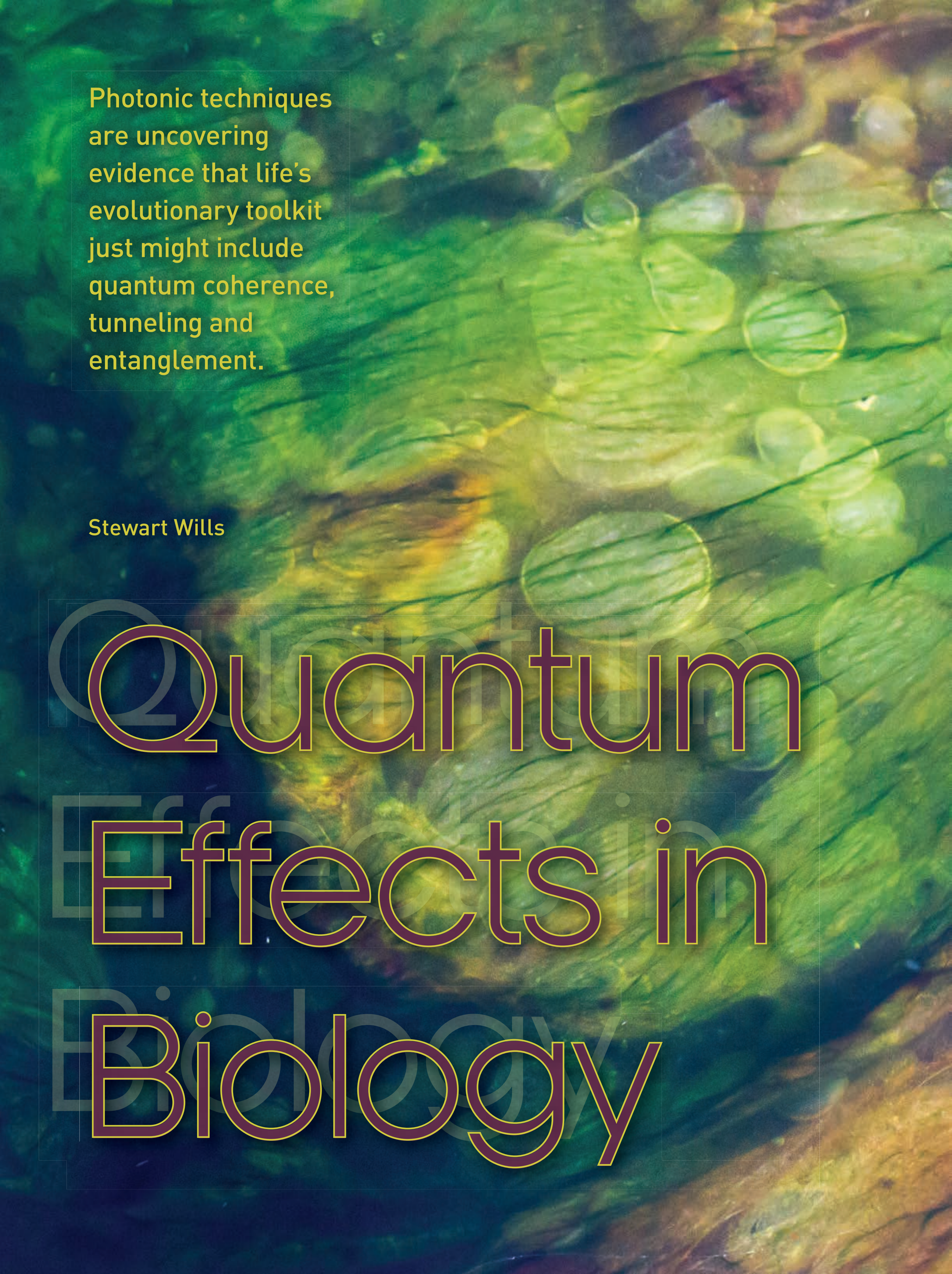


Quantum Effects in Biology

Photonic techniques are uncovering evidence that life's evolutionary toolkit just might include quantum coherence, tunneling and entanglement.

Stewart Wills

Quantum Effects in Biology

Photosynthetic bacterium isolated from hot springs.

Getty Images

Mention the word quantum today, and the mind jumps to visions of next-generation technology. Ultra-low-noise quantum sensors. Exotic computers that corral delicate quantum bits in optical lattices or frigid superconducting circuits. A future "quantum internet" of hyper-encrypted communications riding on laser beams.

Yet an emerging community of physicists, chemists and biologists is teasing out the roles that quantum effects might play in a decidedly low-tech setting: the hot, messy world of life itself. Tools such as ultrafast lasers and 2-D spectroscopy are letting scientists peer into biological systems at ever finer length and time scales. And they're uncovering tantalizing hints that quantum phenomena—coherence, tunneling and entanglement—could operate in processes ranging from photosynthesis to enzyme catalysis to the annual navigation of birds.

It's a speculative undertaking—but one with a significant potential payback. "We have to tread carefully," says Jim Al-Khalili, a theoretical physicist at the University of Surrey, U.K., who's investigating the potential contribution of quantum tunneling to DNA mutation. But, he adds, "if life has evolved the ability to utilize the quantum world in a way that we haven't really appreciated, that's very exciting, and it gives us something new."

That new something could shed light not only on the workings of life, but on how they might be reverse-engineered to improve human-made quantum devices, or inspire entirely new ones. Those prospects will be highlighted in an OSA Incubator Meeting on quantum biophotonics later this month in Washington, D.C.

The quest for the nontrivial

In a sense, finding the quantum in biology isn't difficult, because ultimately *everything* is quantum mechanical. "If you go down far enough in [length or time] scale, you have to encounter the quantum world," says OSA Fellow Jennifer Ogilvie of the University of Michigan, USA, who has studied evidence for quantum coherence in photosynthetic bacteria. The question, she continues, is "at what length scale do you need to include quantum effects, and where?"

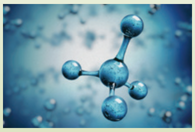
That quandary boils down to the search for so-called nontrivial quantum effects—those that go beyond quantum's role in explaining basic molecular structure, and that classical physics won't capture. Sometimes, "you use all the quantum theory to describe the transitions, but it turns out that you can envision a classical system—say, a spring oscillator—that can describe it," explains Alexandra Olaya-Castro of University College London (UCL). "When you cannot find that kind of classical analog, that's a process that we would call nontrivially quantum."

BIOLOGY'S QUANTUM SIDE

Experiments and modeling have given hints that quantum phenomena may lurk in biological processes—though in many cases, whether the quantum effect helps drive the process remains unproven. Here are some areas where investigators are exploring biology's quantum side:

Photosynthesis

Long-lived vibronic coherence could help solar energy captured in light-harvesting antenna complexes find its way to reaction centers to drive chemical processing.

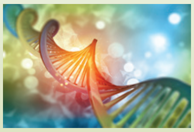


Enzyme catalysis

Chemical experiments suggest that proton tunneling plays a key role in the molecules that speed up biochemical reactions.

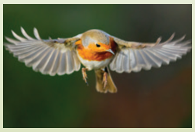
Olfaction

Electron tunneling, tuned to the different vibrational frequencies of odorant molecules, could help the nose distinguish among thousands of different smells.



Mutation

Some researchers are investigating whether quantum tunneling in the hydrogen bonds in DNA provides the mechanism for genetic mutation.



Magneto-navigation

Some birds and other organisms could navigate by sensing Earth's magnetic field, through a mechanism involving electron-spin entanglement.

A quantum brain?

In a particularly speculative and controversial area, a few scientists have argued that quantum effects could underlie consciousness and cognition.

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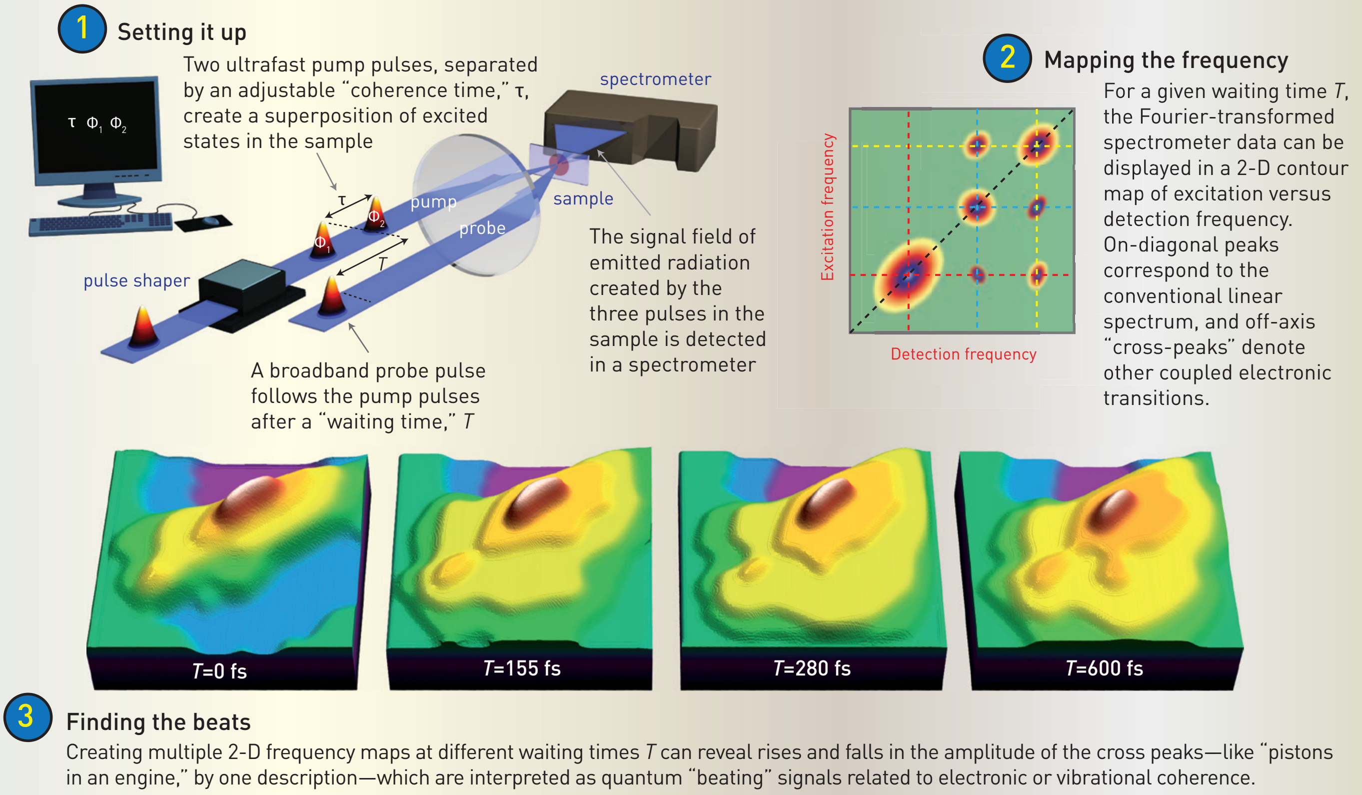
2-D electronic spectroscopy

Experiments using 2-D electronic spectroscopy have supported a possible role for electronic-vibrational coherences in photosynthesis



Setting it up

Two ultrafast pump pulses, separated by an adjustable "coherence time," τ, create a superposition of excited states in the sample

The signal field of emitted radiation created by the three pulses in the sample is detected in a spectrometer

A broadband probe pulse follows the pump pulses after a "waiting time," *T*

Mapping the frequency

For a given waiting time *T*, the Fourier-transformed spectrometer data can be displayed in a 2-D contour map of excitation versus detection frequency. On-diagonal peaks correspond to the conventional linear spectrum, and off-axis "cross-peaks" denote other coupled electronic transitions.

Finding the beats

Creating multiple 2-D frequency maps at different waiting times *T* can reveal rises and falls in the amplitude of the cross peaks—like "pistons in an engine," by one description—which are interpreted as quantum "beating" signals related to electronic or vibrational coherence.

Illustration by Phil Saunders

Such nontrivial effects generally involve phenomena sometimes labeled "quantum weirdness" in the popular press. They include properties like *coherence*, the ability of a single quantum particle, because of its wavelike nature, to exist in a correlated superposition of states; *tunneling*, the nonzero probability that a quantum particle will bore through a potential-energy barrier that would be insurmountable in classical mechanics; and *entanglement*, the correlated behavior of spatially separated particles that, in classical mechanics, should know nothing about each other.

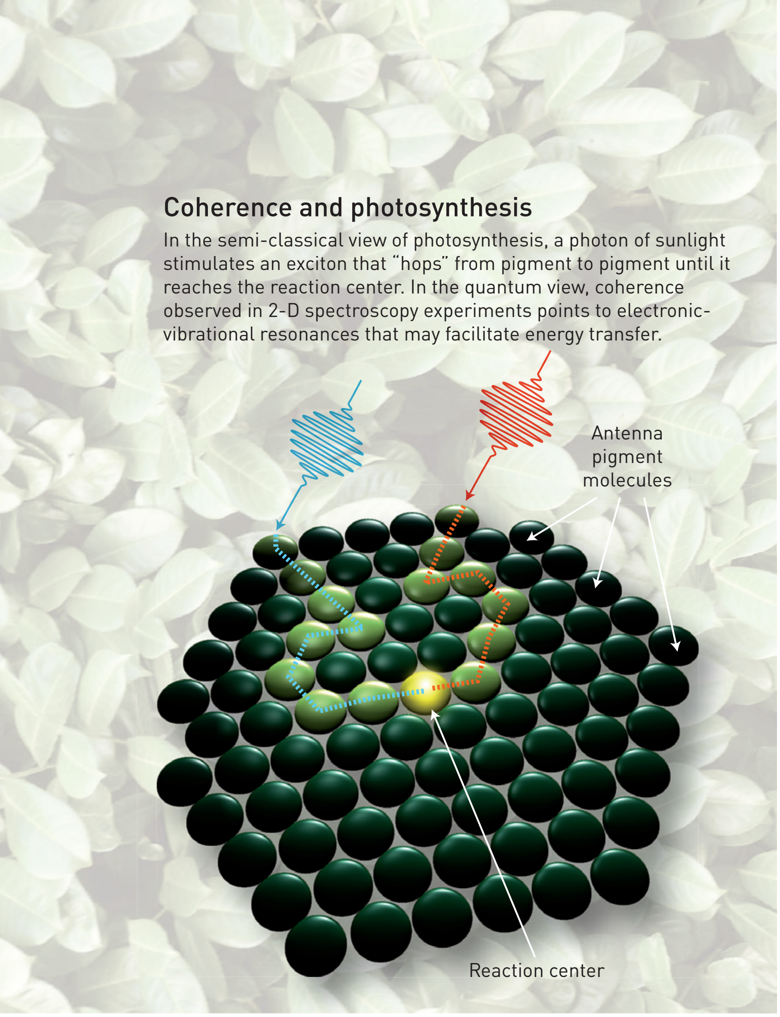
Searching for these effects in biology has a needle-in-a-haystack flavor. That's because biological systems are "warm, wet and noisy," with processes occurring on timescales orders of magnitude longer than the femtosecond room-temperature coherence times familiar in the quantum physics lab. In that thermally noisy, non-equilibrium environment, how could delicate quantum states survive long enough to make any difference?

One possible response is that in fashioning the many complex steps that make up something like photosynthesis, natural selection may still use fundamental quantum laws as building blocks. Under this thinking, by tuning parameters such as intramolecular distances and vibrational modes to gain the maximum advantage from those laws, evolution might optimize the chemistry and physics undergirding life. One 2011 conference paper even proposed a "quantum Goldilocks effect"—in which natural selection drives systems "to a degree of quantum coherence that is 'just right' for attaining maximum efficiency."

From Schrödinger to 2-D spectroscopy

The idea that evolution may have used quantum mechanics as a control knob isn't new. Talks on quantum biology inevitably pay homage to Erwin Schrödinger's classic 1944 book *What Is Life?*, which argued that quantum mechanics could underlie the processes of heredity. (Schrödinger even predicted aspects of the then-unknown molecule that encoded genes—ideas that would influence James Watson and Francis Crick, who nine years later would be credited with unveiling the structure of DNA.)

In a recent review of quantum biology's origins, Al-Khalili and his Surrey colleague, biologist Johnjoe McFadden, trace back the discipline's roots further, particularly to ideas articulated in the 1930s by the German physicist Pascual Jordan, who coined the term *Quantenbiologie*. Jordan's reputation suffered, however, owing to his association with the German Nazi state. That association, McFadden and Al-Khalili suggest, plays



Coherence and photosynthesis

In the semi-classical view of photosynthesis, a photon of sunlight stimulates an exciton that "hops" from pigment to pigment until it reaches the reaction center. In the quantum view, coherence observed in 2-D spectroscopy experiments points to electronic-vibrational resonances that may facilitate energy transfer.

Illustration by Phil Saunders

"an important role in explaining why the field did not flourish further after the war ended."

Yet even as molecular biology and biotech thrived along resolutely classical lines in the postwar years, a handful of scientists remained fascinated by biology's possible quantum side. In 1966, for example, Don DeVault and OSA Fellow Britton Chance at the University of Pennsylvania, USA, saw the possible signature of quantum effects in pulsed-laser experiments with photosynthetic bacteria. In 1978, Klaus Schulten of the Max Planck Institute in Germany proposed that the magnetic-field-based navigation of some organisms could rely on sensing coherent electron spins. And Judith Klinman, a chemist at the University of California, Berkeley, USA, helped establish, in the late 1980s and 1990s, the now widely accepted view that proton tunneling holds one key to the reaction-speeding work of biological enzymes.

In the past decade or so, interest in quantum effects in biology has mushroomed, in part because of new photonic tools to study them. Lasers can now produce pulses with widths on the order of femtoseconds, narrow enough to hit the time and length scales at which quantum effects become important. And an ultrafast-enabled technique pioneered by OSA Fellow David Jonas, 2-D electronic spectroscopy, has opened a window into how biological systems might leverage one of the most fundamental quantum properties, quantum coherence.

Coherence and photosynthesis

Photons are particularly convenient quantum objects for study. So it's not surprising that much of the recent action in this field has revolved around biology's quintessential light-based process, photosynthesis—the process by which plants convert sunlight into stored energy, ultimately responsible for all life on Earth.

A typical organism's photosynthetic equipment includes an antenna complex—hundreds of thousands of light-absorbing pigment molecules, arranged at carefully tuned distances on a protein scaffold—linked to a reaction center. At that center, the captured solar energy is processed into a charge-separated state to drive further chemical reactions. In the common, semi-classical view of the process, a photon of sunlight, absorbed by one of the antenna pigments, stimulates an excited state—an electron-hole pair, or exciton—that "hops" from pigment to pigment until it reaches the reaction center for charge separation.

An intriguing feature of the process is its incredible quantum efficiency. It turns out that almost every photon absorbed by the plant's light-harvesting antennae causes an electron transfer further down the chain in the photosynthetic reaction center. How does the energy captured from the photon "know" the most efficient route to take through the maze of pigment molecules to find the reaction center? The answer, some believe, could lie in quantum coherence and superposition—which, in effect, could allow the energy to travel multiple paths at the same time.

In a landmark 2007 experiment, Gregory Engel and others, working in the lab of Graham Fleming at the University of California, Berkeley, used the then-new technique of 2-D electronic spectroscopy to study a protein-chlorophyll complex in photosynthetic green sulfur bacteria. They found evidence for coherent quantum "beats" in the spectroscopy signal that seemed to match the relevant electronic energy gaps—and that persisted for a surprisingly long 660 fs.

This, they argued, suggested that, rather than hopping, particle-like, from pigment to pigment, the exciton exists as a long-lived, delocalized, wavelike energy distribution across multiple pigments in the antenna complex, allowing the energy flow to find the most efficient path. "The 2007 experiments really

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spurred a huge amount of renewed interest in quantum biology," says Jennifer Ogilvie.

Additional work since then in a variety of labs, including those of Ogilvie and Olaya-Castro, has deepened the picture. It turns out that the quantum beats appear not to stem from long-lived electronic coherences, as originally interpreted. Instead, Ogilvie says, a majority of the observed quantum beats have been found to arise from pigment vibrations—and some reflect specific resonant nuclear vibrations that match energy gaps between the electronic transitions. This "vibronic" state, according to Ogilvie, could be "a critical part of defining how energy moves through the system," a problem her group and numerous others are working on. And, adds Olaya-Castro, the interaction between electronic and nuclear motion is a key place to look for nontrivial quantum effects that might actually help drive photosynthesis. "It has no classical analog," she says.

Tunneling: Enzymes, olfaction, mutation

Vibrations also have a key role in the biological systems that may rely on another quantum effect, tunneling. One area where tunneling is widely agreed to play a part, for example, is enzyme catalysis, essential for speeding up important biochemical reactions. In this catalysis, it's thought that thermal "jiggling" of the enzyme molecules can bring specific electron donors and acceptors into a distance where their wavefunctions overlap. That puts them into a "tunneling-ready" state, where hydrogen transfer can take place, kicking the targeted biochemical reaction into high gear.

In a talk at a recent U.S. National Science Foundation meeting on quantum biology in Washington, D.C., the chemist Judith Klinman referred to this phenomenon as "donor-acceptor distance sampling." And she suggested that proteins have evolved to fine-tune these distances so that enzyme catalysis proceeds with maximum efficiency. "The encounter with quantum mechanics has taught us a great deal about how enzymes work," Klinman said at the meeting. "Nature *does* use quantum mechanics."

Vibration and tunneling have also cropped up as a possible explanation for olfaction, the ability of organisms to distinguish among thousands of different smells. At Surrey, meanwhile, Al-Khalili and McFadden have been looking into whether thermally assisted tunneling could underlie one of life's most fundamental processes: the genetic mutations that drive evolution.

When they first approached the problem, says Al-Khalili, "we were thinking in terms of two strands of DNA, hydrogen-bonded together." Under this view, "protons can jump from one strand to the other, leading to a mutation when the DNA replicates." Since then, he says, they have recognized that this simple model is "quite naïve."

"I'm gradually coming to appreciate the sheer complexity of biochemistry," Al-Khalili notes. "Luckily for my Ph.D. students, they've got several years ahead of them to investigate these problems!" His team is now focusing on computationally modeling the system more realistically, using sophisticated density-functional theory.

Entanglement: Birds, bacteria and beyond

One of the more remarkable examples of a biological quantum effect might just be visible in the sky every spring. It's been suggested that some birds find their way across long distances using a system that relies on yet another bit of quantum weirdness—entanglement.

In the early 1970s, the German ornithologists Wolfgang and Roswitha Wiltschko showed that European robins navigate using an internal compass that senses the inclination of Earth's magnetic field, which varies with latitude. Subsequent experiments revealed that the process is light-dependent—the birds can't orient themselves unless their retinas are first struck with photons of short-wavelength (blue) light. The light dependence suggested a quantum explanation, and the magnetic-field dependence pointed to one quantum parameter in particular: electron spin, the same property that underlies the technology of nuclear magnetic resonance imaging.

The model that has evolved since then, called the radical-pair mechanism, begins with a photon striking one of the blue-light-sensitive molecules in

It's been suggested that the European robin's ability to navigate long distances comes from sensing the effect of Earth's magnetic field on light-activated electron spin states in the bird's retina.

Francis C. Franklin/Wikimedia Commons

the bird's retina, cryptochrome-4. Under the model, the photon energy triggers an electron transfer that forms two molecules with unpaired electrons and quantum-correlated electron spins—a so-called radical pair. The entangled pair oscillates between mixed singlet and triplet spin states before recombining, with the recombination rate dependent on the magnetic-field inclination felt by the radical pair. The recombination produces a quantum beat that the bird's nervous system interprets as navigational information.

Intriguing as the radical-pair model is, many researchers believe it will take considerably more work to put it on firmer ground. Meanwhile, several groups have played with entanglement in other biological systems in the lab. Scientists at Oxford University, for example, were recently able to achieve a highly entangled state between living green sulfur bacteria, injected into a microcavity, and quantized light. And OSA Fellow Prem Kumar of Northwestern University, USA, has used four-wave mixing and photon-pair measurement to establish entanglement of single photons from green fluorescent protein, a light-emitting biomolecule widely used in biotechnology.

More experiments needed

Whether these lab demonstrations point to a role for entanglement in living organisms is far from clear. Indeed, Kumar—whose interest in biological quantum effects initially stemmed from the possibility of using them to improve human-made quantum devices—sounds a note of general caution on interpreting such effects. "There's no reason to assume that nature didn't take advantage of fundamental principles of all kinds, including quantum," he says. "But how that works, and how they affect the processes we have, are largely not understood."

One reason, says Kumar, is that while his experiments and some others deal with single quantum objects (photons), much of the work in this field has involved measuring correlated wavelike behavior in ensembles of biological particles, which provides an averaging effect. "Seeing coherence is not indicative of quantum effects, because coherence also exists in classical systems," he maintains. "You can say it's consistent with the theoretical quantum model, but it doesn't prove it."

For that reason, many researchers, particularly on the physics side, believe that the next steps forward in the field lie in taking it to the study of single biomolecules and even single photons. Luca Sapienza, a researcher in quantum photonics at the University of Southampton, U.K., became interested in quantum biological effects precisely because of his discipline's potential to shed light on these problems. "Even though we don't have expertise in making photosynthetic biomolecules," he says, "we have the expertise to work with single-photon sources, and to carry out single-photon spectroscopy experiments."

Quantum optics' well-tested ability to boost the brightness of single-photon emitters via optical cavities should also come in handy, he notes, by enhancing the otherwise faint signal available from single biomolecules. "And we can cool them down to cryogenic temperatures … to study the molecules when they're much more stable." Sapienza admits that conditions of 5 to 10 K aren't exactly the sweet spot for living organisms. But starting there, where the molecules are protected from vibrations and interactions, opens the possibility of temperature-resolved measurements that will help in understanding the physics behind these complex systems.

Olaya-Castro, too, sees the combination of quantum optics and single biomolecules as "a very fruitful area" that "can give us complementary information on these systems." And she finds considerable promise in another optical technique that has experienced phenomenal growth—optogenetics. The ability to genetically encode how individual cells emit and respond to light signals, she says, adds a layer of control for setting up new experiments and tests. That could not only aid investigation of light-based systems like photosynthesis, but also offer ways to dig into other quantum biological phenomena, such as enzyme catalysis, that currently aren't amenable to probing with light.

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Potential payoffs

Such experiments could illuminate whether the quantum effects thus far detected in biological systems have significant relevance to how those systems actually work. That kind of insight, if gained, would have obvious implications for improving biomedicine and drug design.

Many also see a potential payoff in the opposite direction, taking cues from how nature has fine-tuned quantum effects to up the game of human-made quantum technologies. Kumar hopes to use genetically engineerable systems such as GFP as a control knob for optimizing sources of quantum light, and is currently working with geneticists at a number of institutions to take the next steps. Other systems, too, could be ripe for bio-inspired quantum engineering. "If you manage to understand how recombination mechanisms occur in biosystems," points out Sapienza, "you can reverse-engineer them, for instance, to enhance absorption in photovoltaic devices."

Researchers attempting to develop artificial photosynthesis—human-engineered systems that capture sunlight and convert it to biofuels—also have a natural interest. Such systems, which will rely heavily on efficient solar energy capture and charge separation, could benefit handily from an improved understanding of the process at the quantum level.

"There are plenty of people trying to develop artificial light-harvesting materials by changing donors and acceptors, and trying to find the right chemistry and the right way to mix them together," notes Ogilvie. "If there are other design principles we could find [from the study of quantum effects], that could accelerate the development of better materials."

The surprisingly long-lived coherence effects seen in ostensibly warm and noisy photosynthetic systems could even have relevance to quantum information and quantum computing. "I'm very interested in how a quantum coherent process could survive at room temperature in a living medium," says Sapienza. "One of the problems with single-photon sources is to preserve or increase their coherence time. If you can understand how biological systems do it, maybe that can also be useful in quantum technology applications."

Finding a common language

One significant challenge, and opportunity, for this emerging field is its interdisciplinary nature. As always, the interdisciplinary nexus offers fertile ground for potential new knowledge. But tending that ground requires finding a common language among scientists from very different communities in physics, chemistry and biology. "We need people in the middle," says Kumar, "who can explain things to each other."

One possible avenue for boosting mutual understanding lies in conferences such as this month's OSA Incubator Meeting on quantum biophotonics, hosted by Engel, Olaya-Castro and Sapienza. Sapienza believes that the meeting's small format, and its focus on open discussion, offer particular advantages for this interdisciplinary area. "It's a very nice opportunity," he says, "to bring together biologists, quantum physicists, experts in engineering, nanofabrication, energy harvesting, and discuss where we are and what interdisciplinary opportunities can be followed to shine light on this field."

Another route toward better mutual understanding, adds Surrey's Al-Khalili, will be laid out by the students coming of age studying these interdisciplinary problems. Surrey, for example, has recently set up a new doctoral training center for quantum biology. Within that environment, "you have students who are graduates from biology, from chemistry, from physics, all talking to one another," Al-Khalili observes.

Bridging those disciplinary gaps, difficult as it sometimes is, could bring significant rewards, according to Olaya-Castro. The study of quantum effects in living systems "takes quantum science out of its comfort zone, and it also takes biology out of its comfort zone," she says. "And whenever a field is taken out of its comfort zone, it's a source of new development, of creativity and of scientific advancement." OPN

Stewart Wills is OPN's senior editor.

References and resources are at **www.osa-opn.org/bio-quantum.**