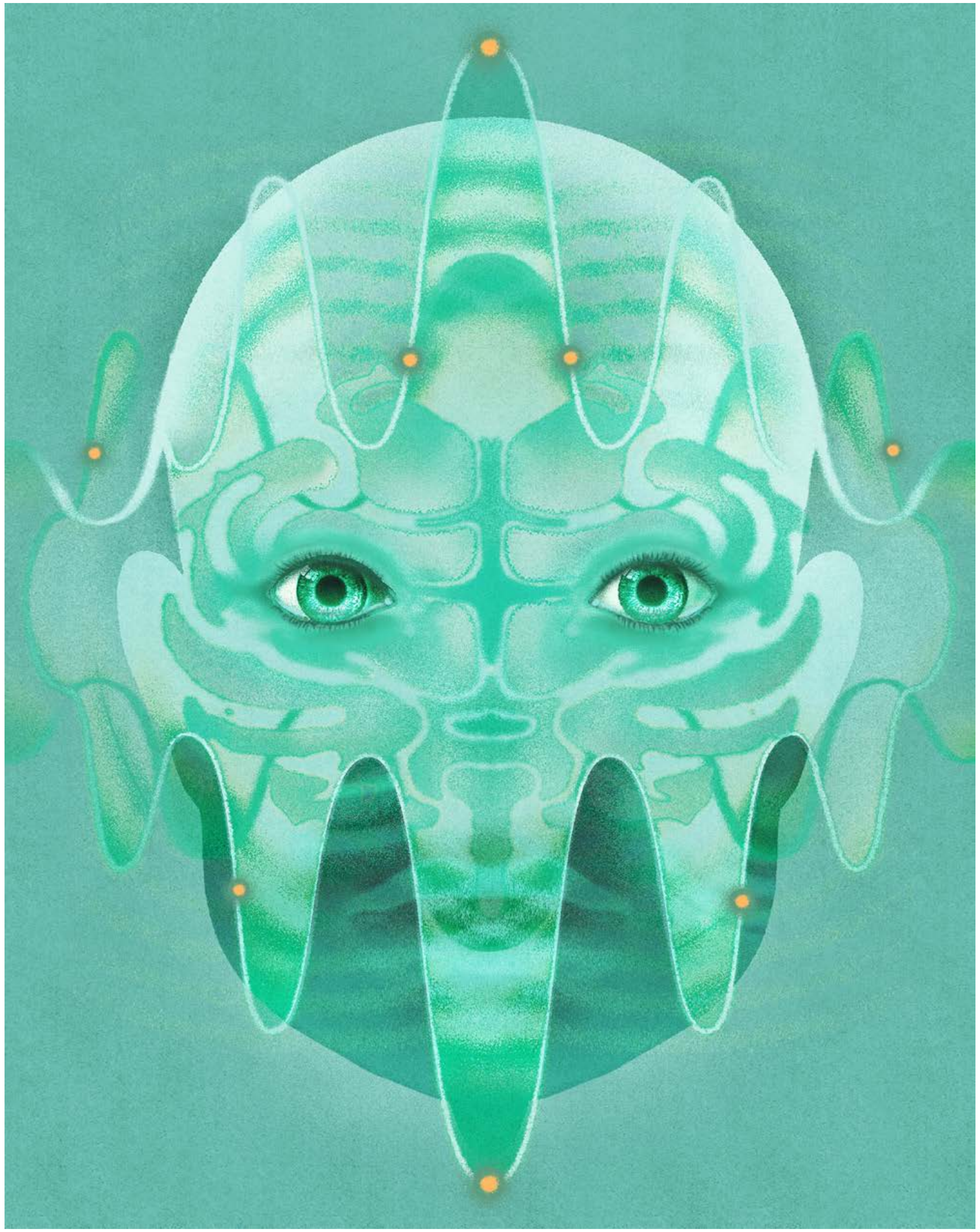


EOIN RYAN

The quantum mind

With anaesthetics and brain organoids, we are finally testing whether quantum effects can explain consciousness. We may have misunderstood this long-derided idea, says **George Musser**

TWO weeks before the pandemic lockdown in March 2020, I flew to Tucson, Arizona, and knocked on the door of a suburban ranch-style house. I was there to visit Stuart Hameroff, anaesthesiologist and co-inventor, with Nobel prize-winning physicist Roger Penrose, of a radical proposal for how conscious experience arises: namely, that it has its origins in quantum phenomena in our brains.

Such ideas have existed, in various guises, on the fringes of mainstream consciousness research for decades. They have never come in from the cold because, as their critics argue, there is no solid experimental evidence that quantum effects occur in the brain, never mind a clear idea of how they would give rise to consciousness. "It was very popular to bash us," Hameroff told me.

But after a week interrogating the concept with him, I realised that his version of quantum consciousness, at least, is widely misconstrued. Partly, I think that is Hameroff's fault. He creates the impression of a single take-it-or-leave-it package. In fact, his idea is a series of independent proposals that each force us to confront important questions about the relationship among fundamental physics, biology and that ineffable thing we call consciousness.

Moreover, having seen some experiments that Hameroff was proposing during my visit come to fruition, it has become clear that his ideas can submit to experimental investigation. Researchers have now produced tentative evidence to suggest that fragile quantum states can endure in the brain, and also that anaesthetics have an impact on them.

So is it time to start taking the idea of quantum consciousness more seriously?

Hameroff and Penrose's proposal is known as orchestrated objective reduction, or Orch OR. In short, it says that consciousness arises when gravitational instabilities in the fundamental structure of space-time collapse quantum wave functions in tiny structures called microtubules that are found inside neurons – and, in fact, in all complex cells. But a statement like that requires some serious unpacking, starting with quantum mechanics.

Quantum theory, in its textbook formulation, says that a particle exists in a cloud of probabilities – where it can appear both here and there, say, simultaneously – until it is snapped into a definite, "classical" state upon observation. This is what physicists refer to as the collapse of the quantum wave function, a mathematical entity that describes all possible states of a particle before it is observed. But we don't know what, if anything, induces collapse, and there are all manner of interpretations of what is going on.

Igniting experience

In the late 1980s, building on earlier ideas, Penrose proposed that "objective" wave function collapse is a result of the inherent incompatibility of quantum theory and general relativity, which describes gravity as the result of mass warping space-time. Unlike quantum fields and the particles they manifest, gravitational fields don't exist in an uncertain state – at least as far as we can tell. Penrose's idea, then, was that any observation of a quantum particle forces an interaction with the classical gravitational field associated with the apparatus, creating a conflict that drives the quantum particle to collapse into a definite state.

It was a big leap, to say the least. But Penrose went further, postulating that each time a quantum wave function collapses in this way in the brain, it gives rise to a moment of conscious experience.

This is where Hameroff entered the picture. Since the 1970s, he had been studying proteins called tubulin and the hollow, cylindrical microtubule structures they form, trying to figure out their role in cell division. Crucially, they seemed to be affected by anaesthetics, which cause loss of consciousness. This led Hameroff to posit that microtubules inside neurons could be exploiting quantum effects, somehow translating gravitationally induced wave function collapse into consciousness, as Penrose had suggested.

Penrose and Hameroff published their Orch OR paper in 1996, to much incredulity. On the one hand, here was an audacious attempt to bridge the quantum and classical worlds, while explaining the origin of our moment-to-moment experience. On the other, critics complained that they had committed the fallacy of minimising mysteries: just because consciousness and quantum mechanics are both mysterious doesn't mean that those mysteries must have a common source. And although Penrose, Hameroff and their collaborators developed the concept in more detail over the following decades, without solid experiments to back their ideas up, Orch OR remained beyond the pale of mainstream consciousness research.

Now, several groups have begun to demonstrate that it is possible to test one cornerstone of Orch OR, the idea that quantum effects could exist in the brain, and the early results are intriguing.

During my stay in Tucson, Hameroff was applying for a grant to conduct some experiments, and the results of one came out in early 2023. Aarat Kalra and Gregory Scholes, physical chemists who were both then at Princeton University, led a study into how energy – absorbed in the form of light – propagates through microtubules. They tagged these structures along their length with a fluorescent dye in order to observe this. To their surprise, energy diffused about five times further than expected according to classical calculations, suggesting a quantum phenomenon was at play in the microtubules. "It's likely some kind of quantum resonance," says Scholes.

Quantum traces

Remarkably, when they doused the microtubules with two general anaesthetics, etomidate and isoflurane, the diffusion length fell slightly but significantly, from 7 to 6 nanometres. "These anaesthetics do interact with microtubules, which is interesting," says Scholes, since it would link the quantum effects to consciousness.

The trouble is this experiment was done on isolated microtubule compounds in test tubes – a far cry from the complexities of actual neurons inside brains. Physicist Max Tegmark has argued that even if quantum effects do exist somewhere in biology, the brain is too wet, warm and noisy for them to persist long enough across a sufficient number of neurons to sustain the kind of quantum processing that could plausibly explain our consciousness.

Yet there are tantalising hints that they do persist. In 2018, a team led by Na Li at Huazhong University of Science and Technology in Wuhan, China, anaesthetised 80 mice using four different isotopes of xenon gas. By definition, isotopes are chemically identical – as they have the same number of protons in their nucleus, but a different number of neutrons – so you would expect them to have identical effects. But the isotopes that contained an odd number of neutrons in their nucleus, giving them a quantum property called "spin", were found to be about 20 per cent weaker in their anaesthetic effects. Among other things, spin makes the nuclei act like tiny bar magnets, and in general such behaviour can only be explained using the equations of quantum mechanics. So Li and colleagues argued that their result, by implicating spin in the action of the anaesthetics, suggests that consciousness relies on quantum phenomena.

Many remain unconvinced. "This may just be wrong," says Hartmut Neven, vice president of engineering at Google, who in 2017 was part of a team that looked for differences in the action of neurotransmitters altered to give their atomic nuclei the quantum property of spin, and found none. Nevertheless, Neven remains sufficiently intrigued that he has assembled another team to examine the result reported by Li further, which is taking two approaches.

In the first, Luca Turin, a biophysicist at the University of Buckingham, UK, will use fruit flies to study the anaesthetic strength of different xenon isotopes. Meanwhile, neuroscientist Kenneth Kosik at the University of California, Santa Barbara, will do the equivalent test on brain organoids. These mini-brains, comprising several million cells in a ball about the same size as a lentil, are grown in a lab by mimicking what happens during the natural growth of embryos.

Brain organoids are much easier to poke and probe than a natural brain. "We have a really great recording system, with 20,000 electrodes" that monitor patterns of neural activity, says Kosik. Moreover, despite their artificial origins, the organoids are uncannily brain-like. Their neurons wire themselves up spontaneously, says neuroscientist Alysson Muotri at the University of California, San Diego. "As far as we can tell, they make the connections they would do in the brain," he says. In 2019, Muotri's group found that brain organoids exhibit brain waves of similar complexity to electroencephalogram readings from a newborn human baby's brain.

In other ways, they are quite different. Organoids model only one part of the brain and they aren't embedded within a body, so don't receive any sensory input. These differences suggest an organoid isn't sentient. "I would say it's not conscious – pretty firmly," says Kosik. Muotri, however, is less sure.

Whether or not organoids have inner experience, their electrical activity gives consciousness researchers something tangible to measure. And it is already clear that these bundles of neurons respond to anaesthetics. In 2022, Kosik and his colleagues found that diazepam – which has a sedating, anxiety-relieving effect by enhancing the effect of a neurotransmitter called GABA – made the organoids' electrical bursts more regular. In the same year, Muotri and his group found that the electrical activity of brain organoids implanted in mice was dampened by isoflurane anaesthetic.

Kosik and others in Neven's group plan to do much the same with xenon anaesthetic. "Let's measure all the different activity signals that they normally look at [in brain organoids] and see how they are differentially suppressed by the different isotopes," says Neven.

If they do confirm a difference, the challenge would be to figure out why it arises. "Where, within a biological system, is that difference being detected?" asks Kosik, who suspects it would entail some kind of quantum effect.

Biological computer

One possibility lies in something called a "radical pair" mechanism, which features in the poster child of quantum biology: a bird's inbuilt compass. Here, the idea is that a chemical bond in a cell ruptures, creating a pair of chemically reactive entities known as radicals that each has an odd, unpaired electron. Electrons have the quantum property of spin and so act like bar magnets that are sensitive to Earth's magnetic field. When these radicals eventually react, the outcome will depend on the strength and orientation of the magnetic field. The thinking is that the bird is sensitive to this in a way that allows it to tell north from south. The process is highly quantum as the radical pair electrons are entangled, which means that they act as a single quantum object, even though they are some distance apart.

In anaesthetised brains, the magnetic field that steers the outcome for the radical pairs would be generated by the xenon atomic nuclei – rather than Earth's iron core. "It provides a way for the nuclear spin [of an anaesthetic] to influence an electron spin and then for the electron spin to influence chemical reactions," says Christoph Simon, a physicist at the University of Calgary, Canada. In 2021, Simon and his colleagues modelled this quantum effect in computer simulations with anaesthetic xenon isotopes. Peter Hore, a chemist at the University of Oxford who studies the biological compass, deems it "interesting but very speculative", as the model makes various uncertain assumptions.

Such a spin-dependent mechanism would be hugely consequential for medicine, as it would behove doctors to consider magnetic interactions when administering anaesthetics and other drugs. "That is our main experimental prediction," says Simon. But it could have deep implications for how we understand the source of consciousness, too.

If the action of anaesthetic in brain organoids proves to be partly quantum in nature, it would make Penrose and Hameroff's proposal more plausible. First, it would show that quantum effects do operate in the brain, countering Tegmark's influential critique. Second, those effects evidently have some relation to consciousness, as the involvement of anaesthesia suggests. And third, the specific mechanisms that are being proposed may even make contact with Penrose and Hameroff's conjectures. Simon and Hadi Zadeh-Haghighi, also at the University of Calgary, argued in 2022 that a similar radical pair mechanism might occur in microtubules.

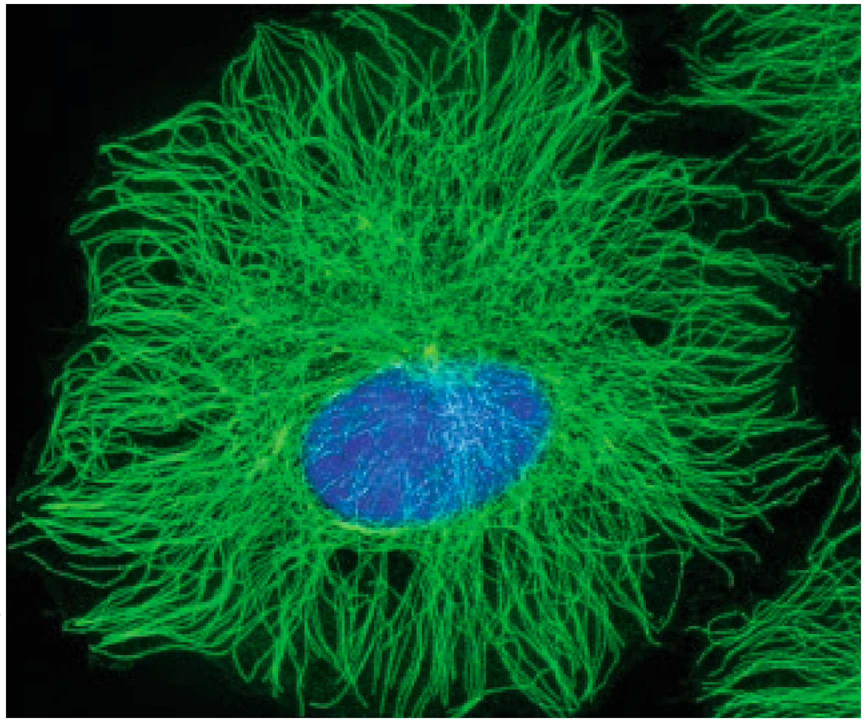
But even then, these experiments still fall short of what Penrose and Hameroff have in mind when it comes to Orch OR. It is a long way from a weakening of anaesthetic potency to a full-blown microtubule quantum computer that assembles all our sensory input and memories into a rich stream of consciousness. Furthermore, these neurobiology experiments say nothing about Penrose's physical theory of "objective" wave function collapse. "The collapse model can be tested independently from the biological system," says Cătălina Curceanu at the Italian National Institute for Nuclear Physics, who has performed just such a test. Though her work hasn't ruled out objective collapse – and may never, since the models contain plenty of wiggle room – Penrose's hypothesis is yet to be corroborated.

In fact, the legacy of Hameroff's experiments, and others pursuing the possibility of quantum consciousness, may have little to do with Orch OR and the purported quantum behaviour of microtubules. By searching for answers, researchers have realised that the brain may make use of fragile quantum effects despite the hurly-burly inside a living organism. This would suggest that life evolved ways to shield those effects from disruption. "Multicellular organisms have been relentlessly optimised over 600 million years," says neuroscientist Christof Koch at the Allen Institute in Seattle, Washington.

One tantalising idea, which Scholes explored in a recent paper, is that evolution came up with a different model of quantum computing from an engineered system with its own version of qubits. Imagining these possibilities may suggest new experiments to search for quantum effects in the brain. "What we really want to know is what to look for," says Scholes. He credits Penrose and Hameroff with driving science forward regardless of whether their proposal is vindicated: "Even if it turns out not to be exactly correct, but it inspires a field, then there's going to be advances."

Koch agrees. Although he considers Penrose and Hameroff's idea a long shot, he says it is still worth exploring: "They push us to think much harder about the limits between the classical and the [quantum] world and to what extent these limits apply to biology." ▮

"There are tantilising hints that quantum effects do persist inside the brain"



THOMAS DEERINCK, NCMIR/SCIENCE PHOTO LIBRARY

Quantum effects could be occurring in cells' microtubules (green)

SHUTTERSTOCK/ANJO KAN

Migrating birds may use quantum effects as a kind of compass

George Musser is a writer and editor. He is the author of *Putting Ourselves Back in the Equation*. @gmusser.bsky.social