Stuart Hameroff

Consciousness, Microtubules, & 'Orch OR'

A 'Space-time Odyssey'

Abstract: *In the 20 years of the Journal of Consciousness Studies (JCS) I've been deeply involved with the conference series 'Toward a Science of Consciousness' (TSC), and the 'orchestrated objective reduction' (Orch OR) theory of consciousness with Sir Roger Penrose. Thanks in large part to JCS and TSC, an interdisciplinary field of Consciousness Studies has emerged. Regarding the science underlying consciousness, most theories view neuronal membrane and synaptic activities in the brain as its essential currency. However, in Orch OR, consciousness derives from deeper-order, finer-scale quantum computations in microtubules inside brain neurons which 1) regulate neuronal membrane and synaptic activities, and 2) connect brain processes to fundamental space-time geometry, the fine-scale structure of the universe. Here I tell the story of my 40-year obsession with consciousness, and conclude, confidently, based on new evidence, that the biology, biophysics, and neuroscience of Orch OR are largely correct, and that consciousness occurs due to quantum vibrations in brain microtubules. If the connection to fundamental space-time geometry is also validated, Orch OR may provide a bridge between neuroscience and more spiritual approaches to consciousness.*

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1. Introduction — The Road to Microtubules

I'm drawn to big questions. This is likely due to my grandfather, Abraham, a Russian intellectual whose surname was changed from Gamerov to Hameroff at Ellis Island at the turn of the twentieth century. In grade school, he gave me books on the Big Bang, expanding universe, Einstein, and Freud.

As a pre-med I took 'Philosophy of Mind' and became interested in consciousness. In medical school I gravitated toward neurology, but did research in a haematology/oncology lab. There, I peered through microscopes at mitosis — cell division — in which filamentous spindles, anchored by mysterious barrel-like centrioles, teased apart and separated chromosomes into identical, mirror-like sets. If the separation wasn't perfect, abnormal genotypes and cancerous cells could ensue (Boveri, 1902; *cf*. Duesberg *et al.*, 1998; Hameroff, 2004). Everyone else in the lab became enamoured of chromosomes and genetic roots of cancer (this was the early 1970s, the dawn of genetic engineering), but I fixated on the elegant choreography of spindles and centrioles. How did they 'know' where to go, what to do, and when to do it? Was there, at that level, intelligence? Consciousness?

I learned three key points: 1) Spindles and centrioles were composed of microtubules (Dustin, 1985); 2) Microtubules were hollow cylindrical lattice polymers of the protein 'tubulin', with spiral geometry matching the famous Fibonacci sequence (3, 5, 8, 13, etc.); 3) Brain neurons were full of microtubules.

Computers were also new, and I learned about Boolean switching matrices and logic gates. Were microtubules computers? Did tubulin states represent interactive information 'bits'? I raised these notions at lab meetings to dumbstruck looks and rolling eyes. Upon graduation, I found a medical internship in Tucson, Arizona.

There I met the chair of anaesthesiology at the new University of Arizona medical school, Dr Burnell Brown, who was starting a residency programme and needed physician bodies. He invited me into surgery, going from room to room, supervising residents, cracking jokes, and quoting Shakespeare. Upon learning of my interests, he handed me a paper showing anaesthetics depolymerized microtubules (Allison and Nunn, 1968) and said: 'If you want to figure out consciousness, study how anaesthetics act. And anaesthesia pays well.' My path was clear.

It was known that all anaesthetic gases followed the 'Meyer-Overton correlation' (Meyer, 1899; Overton, 1901) whereby anaesthetic potency depends on solubility in a lipid-like, non-polar, (hydro-

phobic') medium akin to olive oil, or benzene. Accordingly, anaesthetics were originally thought to act in membrane lipids, but Franks and Lieb (1982) showed instead that anaesthetics acted directly on proteins, in non-polar, 'lipid-like' hydrophobic pockets inside them.

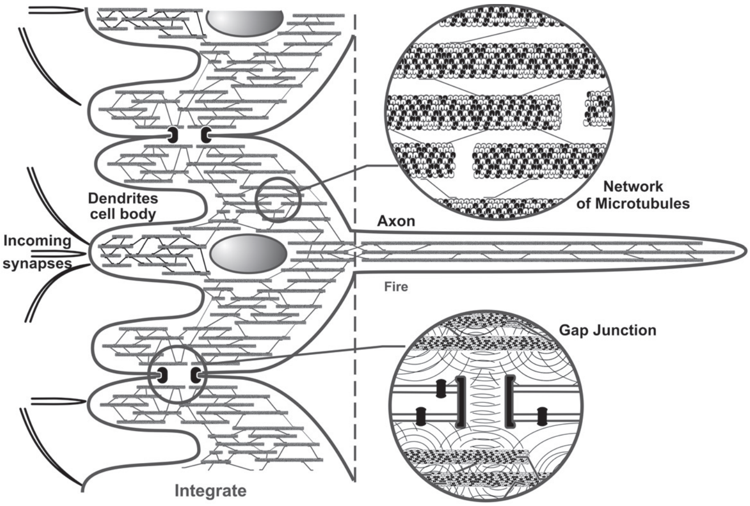

Figure 1. An 'integrate-and-fire' brain neuron and portions of other such neurons are shown schematically with internal microtubules interconnected by microtubule-associated proteins (MAPs — upper circle, right). Gap junctions synchronize dendritic membranes, and may enable entanglement and collective integration among microtubules in adjacent neurons (lower circle right). In Orch OR, microtubule quantum computations occur during dendritic/somatic integration, and the selected results regulate axonal firings which control behaviour.

As oil separates from water, non-polar groups separate from polar ones, and stick together by van der Waals forces. In protein folding, this creates non-polar (but polarizable) 'hydrophobic pockets', e.g. regions containing π electron resonance clouds of phenyl and indole 'aromatic' rings of amino acids phenylalanine, tyrosine, and tryptophan (Figures 6 and 7). Anaesthetic molecules are also non-polar, and bind in these same pockets by 'dipole dispersion' van der Waals 'London' forces.

Thus anaesthetics acted in a way that was completely different from all other (polar, charge-based) drug actions I had learned about in pharmacology. (At the time I didn't appreciate that London forces were also quantum interactions.) And anaesthetics were fairly selective, erasing consciousness while sparing non-conscious brain

activities. Non-polar, but polarizable, electron clouds inside brain proteins seemed somehow related to anaesthesia and consciousness.

An engineer colleague, Rich Watt, mentioned electron clouds were a plasma, or corona, of mobile electrons, and that we could make a corona chamber to test anaesthetic effects. So we did, and found a Meyer-Overton correlation for corona discharge — the more potent an anaesthetic, the more potent it was in inhibiting the corona (Hameroff and Watt, 1983). We suggested anaesthetics act by direct inhibition of electron mobility, in a corona chamber, or in hydrophobic pockets in neuronal brain proteins. But two questions loomed: 1) which proteins, and 2) how was electron mobility in hydrophobic pockets in these proteins related to consciousness?

Rich and I also modelled microtubules as Boolean switching circuits (Hameroff and Watt, 1982), and I soon learned about 'cellular automata', grid-like lattices of fundamental units interacting at discrete time steps, able to 'compute'. With physicist colleagues (Smith *et al.*, 1984; Hameroff *et al.*, 1988; Rasmussen *et al.*, 1990), we modelled 'microtubule automata' in which tubulins interacted with neighbour tubulins by dipole coupling forces. Patterns of dipole states representing information were able to 'learn' and perform computation (Figure 2a and b).

For discrete time steps in our 'microtubule automata', we applied 'Fröhlich coherence'. Herbert Fröhlich (1968; 1970; 1975) showed how inducible dipoles in a common geometry and voltage would oscillate coherently ('condense to a common state'), due to non-coherent energy. He pointed to dipoles in non-polar (but polarizable) regions within proteins for the proposed coherence, precisely where anaesthetics acted to erase consciousness. (I appreciated years later that Fröhlich coherence, or condensation, was a quantum effect.)

As biological sites for his proposed coherence, Fröhlich had considered primarily membrane proteins, but I convinced him (when we met in Stuttgart in 1986) that microtubules were worthy candidates (Hameroff, 1988). Applying Fröhlich coherence as discrete time steps in microtubule automata, Danish colleague Steen Rasmussen and I (Hameroff *et al.*, 1988; Rasmussen *et al.*, 1990) realized that information processing by Fröhlich coherence at the microtubule level had enormous computational capacity, far, far greater than networks of individual neurons.

Artificial intelligence (AI) and neural network researchers calculated brain capacity based on 100 billion neurons as fundamental units, each with a thousand synapses, switching 100 times per second, to be roughly 10^{16} operations per second. When a computer could

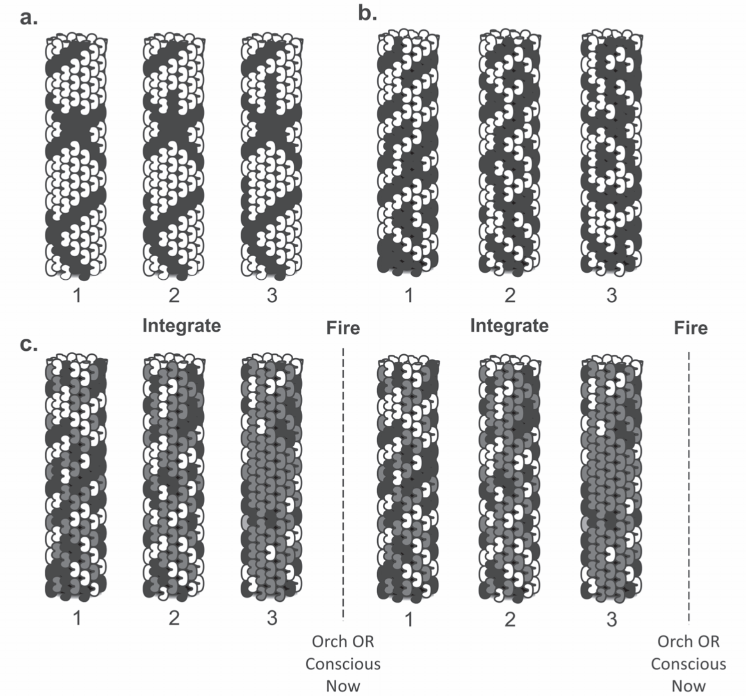

Figure 2. Microtubule automata sequences (e.g. at 10 megahertz). Tubulin subunit dipole states (black, white) represent information. (a) Helical dipole patterns compute a new vertical pattern. (b) A general microtubule automata process. (c) Two Orch OR events in which superpositioned (grey) tubulins reach threshold, with moments of conscious experience, and selection of specific tubulin states.

achieve 10^{16} operations per second, they claimed, it would do whatever brains do, including production of consciousness. I annoyed them by saying relevant information processing extended inward, to intra-neuronal microtubules. I talked about *paramecium*, single cell organisms which could swim nimbly, find food and mates, avoid obstacles and predators, learn, and have sex, all without synapses, using their microtubules. For information capacity we calculated a billion tubulins per neuron switching at, for example, 10 megahertz, giving 10^{16} operations per second *per neuron*, 10^{27} 'ops/sec' in the brain. This pushed the AI target for brain equivalence in computers far into the future. 'Simulate a paramecium before worrying about a brain!', I insisted — I became unpopular among AI people, and remain so.

But one day someone said: 'Let's say you're right, there's all this computation in microtubules. How would that explain consciousness?… feelings, phenomenal experience, love, pain…?' (This was the 'hard problem' later articulated by David Chalmers, 1996.) I didn't know. I was slightly shaken. Consciousness had slipped away, and I was a reductionist. Fortunately, that same person recommended I read *The Emperor's New Mind: A Search for the Missing Science of Consciousness* by British physicist Sir Roger Penrose (1989). And so I did.

2. The Quantum Leap

The Emperor's New Mind was many things: a slap in the face to AI, an argument through Gödel's theorem against consciousness-as-computation, a suggested solution to the quantum measurement problem, a merging of general relativity and quantum mechanics, and a specific proposal for a mechanism of consciousness. The latter involved a quantum computation ruled by a type of quantum state reduction connected to the fine scale structure of the universe. This was the first, and remains the only, specific physical mechanism ever proposed for consciousness.

In quantum computation, information states (e.g. binary 'bits' of 1 or 0) exist in superposition, wave-like coexistence of multiple possible states, e.g. quantum bits, or 'qubits' of both 1 *AND* 0. But we don't see quantum superpositions in our perceived world (the 'measurement problem' in quantum mechanics). Quantum pioneers Niels Bohr, John von Neumann, Eugene Wigner, and later Henry Stapp suggested that quantum superpositions persisted until observed by a conscious human, commonly termed the 'Copenhagen interpretation' after Bohr's Danish origin. At that instant, quantum superposed possibilities reduced to definite states — the wave function 'collapsed'. This approach pragmatically allowed quantum experiments to successfully continue, but put consciousness outside science. Does consciousness collapse the wave function?

To show how absurd was the notion, Erwin Schrödinger (1935/1983) designed his still-famous thought experiment known as 'Schrödinger's cat'. Imagine a cat in a box with a vial of poison whose release is coupled to a quantum superposition outside the box. According to Copenhagen, Schrödinger concluded, the cat would be both dead and alive until a conscious human opened the box and observed the cat. Absurd it was, but the measurement problem persists.

Alternatives include the multiple worlds hypothesis (Everett, 1957/1983), that every possibility evolves its own new universe, and decoherence — interaction between a quantum system and its classical environment disrupts superposition. But how can any quantum system truly be isolated?

Some assume an objective threshold for reduction — 'objective reduction' ('OR'). Penrose (1989; 1994; 1996) based OR on superposition separation in underlying space-time geometry. From Einstein's general relativity, a particle's location is equivalent to a curvature in space-time geometry, with superposition as simultaneous alternative curvatures, essentially bubbles or blisters in the fine scale structure of the universe (Figure 3). If these separations were to evolve, each would give rise to an alternate universe, as in multiple worlds. But Penrose considered space-time separations to be unstable, reaching an objective threshold for 'self-collapse', or objective reduction/OR at time $\tau \approx \hbar/E_G$, where $\hbar$ is Planck's constant over 2π, and E_G the gravitational self-energy of the separation.

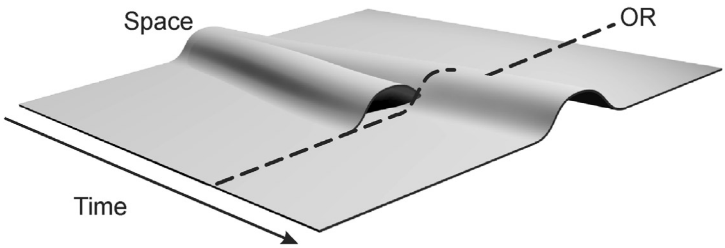

Figure 3. 4-dimensional space-time depicted as a 2-dimensional sheet (3 spatial dimensions condensed to one). A superpositioned particle separating from itself correlates with two space-time curvatures E_G which reach threshold at time $\tau \approx \hbar/E_G$. OR occurs, one location/curvature is selected and becomes classical, and the other ceases to exist. A moment of conscious experience is proposed to occur at the instant of OR.

Roger added two significant features. 1) Each OR event is a moment of conscious experience, a process in the fine scale structure of the universe. 2) Particular space-time curvatures in each OR event were not chosen randomly, but rather influenced by what Penrose termed 'noncomputable Platonic values' embedded in fundamental space-time geometry.

I was impressed. Roger had turned the observer effect upside-down, putting consciousness back into science, precisely on the edge between quantum and classical worlds. And the connection to space-

time geometry, non-locality, and non-computable influences seemed almost spiritual (though Roger avoids such comparisons). Intuitively, it felt right, and was maybe 'crazy enough'. But Roger lacked a biological candidate for OR-terminated quantum computing in the brain. He had a mechanism for consciousness, but not a biological structure. In microtubules I had a biological structure, but not a mechanism.

I wrote to Roger suggesting microtubules could be his quantum computers in the brain. I included some articles and mentioned I would be in the UK, and was pleasantly surprised to receive his reply, inviting me to meet him in Oxford. It was the autumn of 1992.

We cleared two chairs in Roger's cluttered office. He asked many questions, e.g. about the microtubule Fibonacci geometry, and mentioned he was going to a consciousness conference at Cambridge with philosophers Daniel Dennett and Patricia Churchland. After several hours we shook hands and said goodbye.

Two weeks later, before flying home, a friend said he had been to the Cambridge conference, and that Roger Penrose was talking about me and my microtubule ideas. Soon thereafter I was invited to a memorable meeting in northern Sweden with Roger Penrose, Daniel Dennett, Petra Stoerig, Herman Haken, Robert Rosen, and several Swedish scientists.

3. Toward a Science of Consciousness

The study of consciousness was stirring. After William James, behaviourists banned consciousness from science, but in the late 1980s a shift occurred, with books about consciousness not only by Roger Penrose, but also Nobel laureates Francis Crick and Gerald Edelman.

In the summer of 1992 I attended a consciousness conference at the Holiday Inn in Sierra Vista, Arizona, organized by a local physician named Gordon Olson. Tragically, Gordon's daughter had been injured and lay comatose, and he obsessed about consciousness. A few months later Gordon phoned to suggest another conference, this time with my help at the University of Arizona.

At that time, the internet had appeared, with a discussion group Psyche-D. There I learned of the *Journal of Consciousness Studies* (*JCS*) begun by Keith Sutherland and others, and administrated by Anthony Freeman and Joseph Goguen. After some consideration, I agreed with Gordon to organize an academic, interdisciplinary consciousness conference at the University of Arizona (UA) in 1994.

We needed help. I approached Alfred ('Al') Kaszniak, a friend and UA professor of psychology, psychiatry, and neurology. 'Al K'

meditated, studied eastern philosophy, and knew an enormous amount about the brain. He agreed. I also asked Alwyn ('Al') Scott, another friend and UA professor of mathematics who was writing *Stairway to the Mind* about consciousness, nonlinear dynamics, and emergence (Scott, 1995). He also agreed. And Jim Laukes, a UA conference management specialist, came on board. We scheduled it in early April 1994, when Arizona hotel rates dropped, and college basketball season had concluded. We reserved the UA Hospital Duval Auditorium with 350 seats for plenary sessions, and space at the Arizona Inn a block away for posters and parties. We called it 'Toward a Science of Consciousness' (TSC), put a notice on Psyche-D, an ad in *Scientific American*, and invited speakers, nearly all of whom said yes. Keith Sutherland at *JCS* wanted to attend and promote the new journal, and we were delighted to accommodate.

A few submitted abstracts were selected for plenary, the rest posters. Among the submitters was an unknown philosopher named David Chalmers. His abstract talked about how conscious experience was the real 'hard problem', while learning, memory, behaviour, etc. were relatively 'easy'. It was audacious, but made sense. We needed one more philosophy plenary speaker, and Dave was it.

The room was filled when the conference opened with philosophy of mind. The first two philosophers read their talks without slides, and the interdisciplinary audience grew restless and bored. Then Chalmers took the stage, strutting like Jagger, talking about the hard and easy problems. The crowd settled in. At the coffee break I listened as they buzzed about the hard problem. At that moment, we all knew why we were there.

After the conference, on a trip to the Grand Canyon, Roger and I spoke about how quantum computing could occur in microtubules and terminate by $E_G \approx \hbar/\tau$. We set τ to a physiological time, e.g. 25 msec for gamma synchrony 40 Hz oscillations. We could then solve for E_G in terms of the number of superpositioned tubulins, microtubules, and neurons for a particular conscious event.

Gravitational self-energy E_G for superposition — a protein separated from itself — could be calculated in 3 ways. One was the entire protein separated, e.g. by about 10 percent of its volume (~1 nanometer). Second was separation at the level of each atomic nucleus (e.g. carbon nuclei, ~5 femtometers) comprising the protein. Third was separation at the level of even smaller nucleons, i.e. protons and neutrons within nuclei (~1 femtometer). Roger gave me equations for each situation using the dimensionless constants he had described in *The Emperor's New Mind*.

Happily feeling like Roger's student, I came up with numbers for E_G for separation at the three levels. Roger noted the highest E_G, the greatest energy, occurred with separation at the level of atomic nuclei, not the larger or smaller separations. 'That effect will predominate', he said. We then knew how to calculate E_G. For τ equal to 25 msec (40 Hz), E_G would be about 2 x 10^{10} tubulins separated at the (femtometer) level of their atomic nuclei. Neurons each have about 10^9 tubulins, and, as Roger said, superconductors use only about 0.1 percent of their components in quantum states, so we calculated that microtubules in about 20,000 brain neurons were needed for a 25 msec OR event. I smiled and told Roger that neural assemblies of tens to hundreds of thousands of neurons had been estimated as the size required for consciousness by Crick and Koch (1990), Alwyn Scott (1995), and others. We were in the game (Figure 4).

Microtubules are interconnected by microtubule-associated proteins ('MAPs'), and I suggested that MAPs provide synaptic inputs into microtubules, essentially 'tuning' their quantum states and OR, like frets in a guitar. Roger smiled, and asked 'what shall we call this process?' Sticking with musical metaphors I suggested 'orchestration'. Synaptic inputs (and embedded memory) would 'orchestrate' microtubule quantum computation, leading to threshold for OR. 'Orchestrated objective reduction', 'Orch OR' for short. We agreed, and committed to develop a publication. Roger's wife Vanessa advised me to be patient, as Roger was overcommitted and very meticulous. I nodded and thanked her. I was prepared.

At the first TSC conference, a society was proposed that eventually grew into the Association for the Scientific Study of Consciousness (ASSC). Two San Francisco Bay area groups offered to organize a follow-up TSC conference, but couldn't agree on an interdisciplinary agenda. I concluded a much-needed broad approach would be difficult unless we did it ourselves.

But every year was too much. Al Kaszniak, Al Scott, Jim Laukes, and I planned a second TSC conference in April 1996. We moved downtown to the Tucson Convention Center, using the stately Music Hall for plenary sessions. We expanded the Programme Committee, adding Dave Chalmers, Christof Koch, Petra Stoerig, Keith Sutherland, and Marilyn Schlitz.

An Italian colleague of Al Kaszniak named Chloe Taddei-Ferretti asked us to co-sponsor a TSC conference in 1995. We agreed, and TSC 1995 took place on the island of Ischia (near Naples and Capri), with historic and enjoyable hot spring baths. As Tucson TSC conferences have continued in even-numbered years, co-sponsored TSC

conferences have occurred in odd-numbered years elsewhere (1995 Italy, 1997 Denmark, 1999 Japan, 2001 Sweden, 2003 Czech Republic, 2005 Denmark, 2007 Hungary, 2009 Hong Kong, 2011 Sweden, 2013 India). TSC 2015 will be held in Helsinki, Finland, organized by Paavo Pylkkanen. Overall, TSC conferences have run annually since 1994.

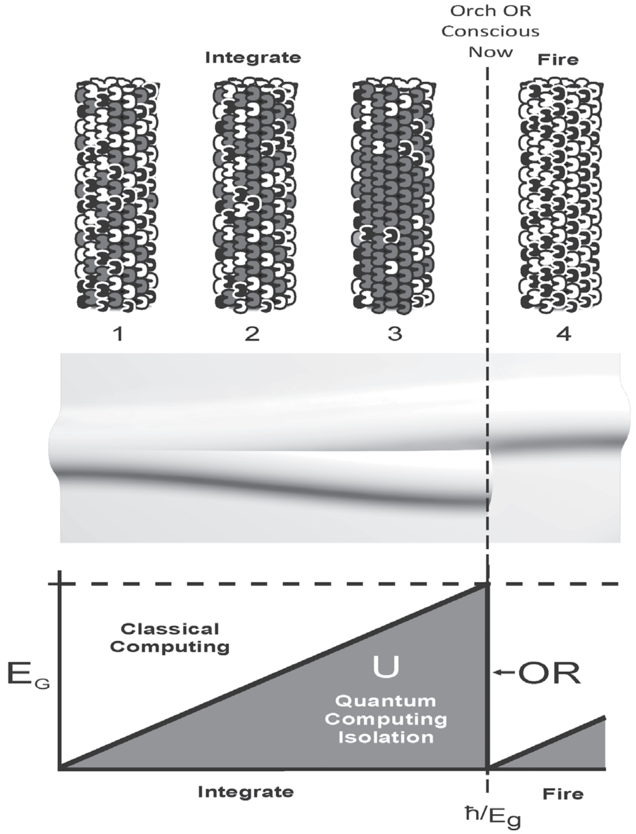

Figure 4. Three views of Orch OR. Top: three steps in a proposed Orch OR conscious event in a single microtubule, grey tubulins signifying quantum superpositions which evolve, compute, and reach threshold for Orch OR (Figure 2c). Middle: corresponding separated space-time curvatures ('top' view from Figure 3) reaching threshold. Bottom: schematic of Orch OR event by $\tau \approx \hbar/E_G$ (see Figure 8).

4. A Fortuitous Ambush in *JCS*

The Orch OR paper with Roger was very slow going. But in early 1995 we heard from Keith Sutherland at *JCS* that philosophers Rick Grush and Patricia Churchland had written a derogatory piece attacking Orch OR, based on what we had presented online and at conferences. Their paper's title, 'Gaps in Penrose's Toilings', referred to Roger's famous work on geometric tilings covering a plane (Grush and Churchland, 1995). The first half attacked Roger's use of Gödel's theorem to assert non-computability in conscious understanding. The second half was biological, aimed at the necessity of microtubules for consciousness. Grush and Churchland ('G&C', as we called them) noted that colchicine, a drug used to treat gout, causes microtubules to depolymerize (thus immobilizing inflammatory cell migration into joints by microtubule-dependent movement). They smugly remarked that patients taking colchicine don't lose consciousness, and, comparing us to *Alice in Wonderland*, concluded our theory was 'no better supported than one-in-a-gazillion caterpillar-with-hookah hypotheses'.

Ouch. Keith said Roger and I could reply in the next issue, but that he would need the manuscript in two weeks. Two weeks?! It had been almost a year without a manuscript describing Orch OR. But fortunately G&C had significantly annoyed Roger. We decided to combine two half-papers, his addressing Gödel, and mine addressing microtubules.

Regarding gout, I said (1) colchicine doesn't cross the blood brain barrier, and doesn't affect brain microtubules, (2) colchicine acts only on microtubules in cycles of assembly/disassembly, whereas neuronal microtubules are uniquely stable, without such cycles, and (3) colchicine injected into brains of mice caused profound impairment (Bensimon and Chermat, 1991). We had a paper in two weeks, calling it 'Gaps? What Gaps? Reply to Grush and Churchland' (Penrose and Hameroff, 1995). We closed by responding to the *Alice in Wonderland* crack: 'It's not that we're in Wonderland, but p'raps their heads are in the sand!' Keith commissioned a famous cartoonist to capture the moment (Figure 5 — reprinted from *JCS*).

The 1996 TSC conference was big. New ideas, interdisciplinary cross-fertilization, contentiousness, passion, media, personalities, and excitement were all around. Intellectual battle lines were drawn, traditions were born (Poetry Slam, Zombie Blues, End-of-Consciousness party). Afterwards, I took Roger and Vanessa on a houseboat trip on Lake Powell in southern Utah. We discussed Orch OR at length,

Roger concerned about how quantum coherence could survive in the warm neuronal environment.

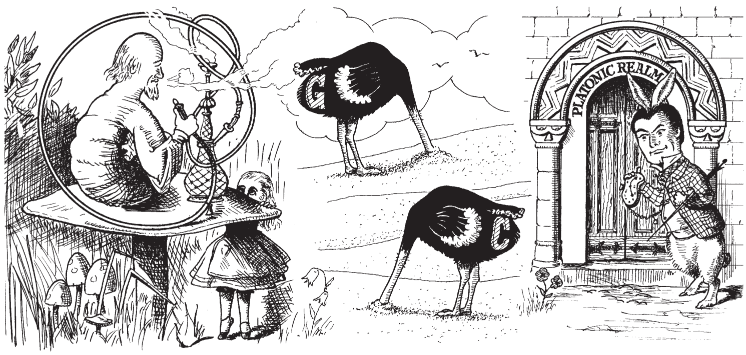

Figure 5. 'It's not that we're in Wonderland, but p'raps their heads are in the sand', by Jack Buckmaster, after Sir John Tenniel. Courtesy of *Journal of Consciousness Studies*.

I suggested Fröhlich coherence of electron cloud dipoles in non-polar hydrophobic pockets inside each tubulin avoided decoherence. These regions — quantum channels — would be where anaesthetics acted to prevent consciousness. Years later we found them (Craddock *et al.*, 2012; Figures 6 and 7).

We published our Orch OR article (Hameroff and Penrose, 1996a). Soon thereafter *JCS* had a special issue on the 'hard problem', and Roger and I wrote another paper in which we suggested that qualia, the raw components or precursors of conscious experience, were embedded in the fine scale structure of the universe, e.g. Planck scale space-time geometry (Hameroff and Penrose, 1996b). Our view, it turned out, was similar to that of process philosopher Alfred North Whitehead (1929; 1933) who described 'occasions of experience' occurring in a 'wider field of protoconsciousness'. Abner Shimony (1993) had observed that Whitehead occasions were comparable to quantum state reductions, and thus Orch OR events (Figure 4).

Following the 1996 TSC conference, with funding from the Fetzer Institute, Jim Laukes, Al Kaszniak, Al Scott, and I put together an integrated Center for Consciousness Studies (CCS) within the University of Arizona, established in 1997 with Al Kaszniak as Director. Dave Chalmers soon joined the UA philosophy faculty, and took over as CCS Director. When Dave left for the Australian National University (ANU) in 2007, the Directorship fell to me. Jim Laukes also left,

and was replaced by Abi Behar-Montefiore, the current Assistant Director. At this writing, Abi, Dave (now at both ANU and New York University), and I are preparing for the 20-year TSC anniversary conference, April 2014. TSC, *JCS*, and Orch OR are 20-year-old triplets!

5. 'Something is rotten in Tegmark's Formula'

With three Orch OR papers published, Roger invited me to speak at his 65th birthday 'Festschrift' at Oxford in 1997. It was a 'Who's Who' of notable scientists, primarily physicists, and I was truly honoured (Hameroff, 1998a). Stephen Hawking opened, dramatically wheeling centre stage. He flicked his pinky to start, the computerized voice saying on his behalf: 'I just hope that when I reach Roger's age, I look as good as he does.'

Roger also invited me to a quantum information conference at the Royal Society in London (Hameroff, 1998b). A big issue was entanglement, how things could connect non-locally, instantaneously — Einstein's 'spooky action at a distance'. Most of the speakers were young, and at the very end, Roger wrapped up. He drew the famous EPR (Einstein-Podolsky-Rosen) experiment on the blackboard. Two entangled, superpositioned particles go their separate ways, and a measurement is made on one of them — spin down, lets say. Instantaneously, at another location, the other one collapses to spin up. How could that happen? Roger said that everyone had been hinting at the answer, but were reluctant to say it. He drew a line from the measured first particle *backward in time* to where the pair was together, then onward to the second particle. Roger closed by saying that he alone could say something so outlandish because, among the speakers, he alone was already a member of the Royal Society.

Apparent backward time effects (time symmetry) have indeed been reported in the brain, for example in the famous Libet *et al.* (1979) sensory experiments. In *The Emperor's New Mind* Roger suggested that quantum mechanisms explained Libet's backward time effects, now shown in psychological (Bem, 2012; Bierman and Radin, 1997) and so-called 'quantum erasure' experiments (Ma *et al.*, 2012).

Measurable brain activity corresponding to stimulus perception apparently occurs after we respond to that stimulus. Accordingly, consciousness is thought to occur after-the-fact, as an epiphenomenon, and real-time conscious action is considered illusion. Initiated by Dan Dennett (1991), epiphenomenalism is the party line in mainstream cognitive science and philosophy. But Orch OR, quantum brain

biology, and time symmetry can rescue conscious free will (Hameroff, 2012).

The main scientific issue we faced was decoherence. Technological quantum computers were built near zero temperature to avoid thermal disruption. Nearly everyone said the brain was too 'warm, wet, and noisy' for delicate quantum effects. We asserted Fröhlich coherence, but there was no evidence either way.

In 2000 a rising physics star named Max Tegmark (2000) challenged Orch OR on the basis of decoherence time, which we were suggesting to be tens to hundreds of millieconds (10^{-1} to 10^{-2} secs), as in gamma synchrony EEG (40 Hz, hence 25 msec decoherence times). Tegmark developed a novel formula to calculate microtubule decoherence time as a mere 10^{-13} seconds, far too brief for physiological effects and Orch OR. The journal *Science* ran a damning commentary: 'Cold Numbers Unmake Quantum Mind' (Seife, 2000). It was a major blow, considered devastating to Orch OR.

But 'something was rotten in Tegmark's formula'. Soon thereafter I met Roger in Washington for talks at the Rand Corporation. I gave him a copy of Tegmark's paper which he read, scoffed at, and tossed back, saying 'according to this, quantum states of any kind are impossible!'

Physicist colleagues Scott Hagan and Jack Tuszynski and I noticed Tegmark's decoherence formula had temperature in the numerator, meaning that decoherence time should lengthen with heat. That was odd. We also noticed the superposition separation in the denominator was of a soliton separated from itself by 24 nanometers, not femtometer separation of a carbon atom nucleus as proposed in Orch OR. This meant Tegmark's calculated decoherence time should have been seven orders of magnitude (a million times) longer, closer to what we needed. Hagan, Tuszynski, and I replied in the same *Physical Reviews E* journal a year later (Hagan *et al.*, 2001), saying Tegmark had refuted his own microtubule model, not Orch OR. Using Tegmark's formula, we recalculated microtubule decoherence times of 10^{-4} seconds, now demonstrated (see below, Sahu *et al.*, 2013a,b), though still too brief for the tens of milliseconds we had called for. The solution to that problem came later.

I always looked at Max Tegmark going after Roger Penrose like a punk Wild West gunslinger ambushing Wyatt Earp. Max missed, and shot himself in the foot.

But how are quantum resonances mediated in microtubules? Beginning in 2002, with colleagues Jack Tuszynski, Travis Craddock, and others, we used molecular modelling to locate electron resonance

rings within tubulin, forming 'quantum channels' which can extend through microtubules, support Orch OR, and act as sites of anaesthetic binding (Figures 6 and 7; Hameroff *et al.*, 2002; Craddock *et al.*, 2012).

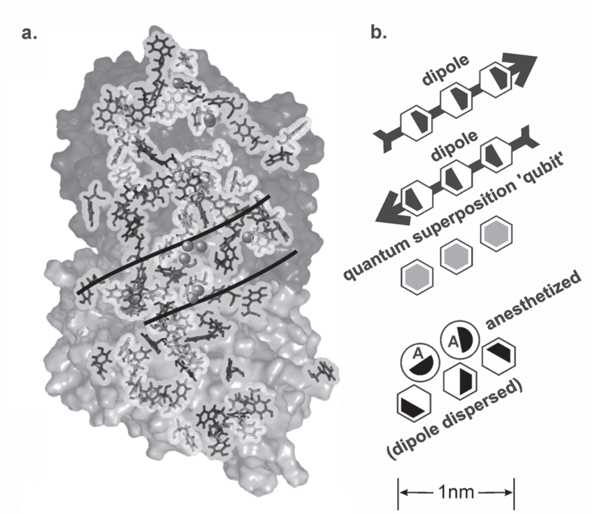

Figure 6. (a) Molecular model of tubulin dimer shows tryptophan, phenylalanine, and tyrosine resonance rings clustered in non-polar, 'quantum' channels. Spheres are anaesthetic binding sites (with permission from Craddock *et al.*, 2012). Black curved lines show intra-tubulin pathways which align with those in neighbouring tubulins in microtubule lattice (see back cover for colour version). (b) Schematized 5-start helical quantum dipole pathways of rings of tubulin. Top two pathways show alternative dipoles, and third pathway (grey) shows quantum superposition of both (quantum bits, or 'qubits'). Bottom: anaesthetic gas molecules (A) form their own (van der Waals London force) dipole couplings, dispersing collective dipoles and disrupting quantum dipole computations.

When asked why he robs banks, famous criminal Willie Sutton answered, 'because, that's where the money is'. Anaesthetics must surely act at, or very near, where consciousness originates. Nearly everyone assumes anaesthetics act on membrane proteins, but the tide is turning to microtubules. Sophisticated research in genomics, proteomics, and optogenetics (Xi *et al.*, 2004; Pan *et al.*, 2007; Emerson *et al.*, 2013) all point to tubulin as the target for anaesthetic action in preventing consciousness.

In addition to Tegmark, there were other criticisms. Christof Koch (2004) dispensed with Orch OR in a footnote on page 5 of his book

The Quest for Consciousness, and later wrote a silly paper in *Nature* with Klaus Hepp (Koch and Hepp, 2006) about a thought experiment combining Schrödinger's cat and binocular rivalry. With one eye, an observer sees a cat in superposition of dead and alive. Where in the observer's brain does the collapse/reduction occur, choosing either dead or alive?

It's a trick question. A superposed cat of ~10 kilograms would, by $E_G \approx \hbar/\tau$, self-collapse in less than the Planck time of 10^{-43} secs, essentially instantaneously. In conscious vision of any classical object, Orch OR would occur in microtubules in the visual cortex and other areas, with sequences of Orch OR conscious moments over several hundred msec for a visual gestalt. Thus consciousness according to Orch OR occurs in the same neurons as recognized in conventional neuroscience, just inside those neurons at a deeper level.

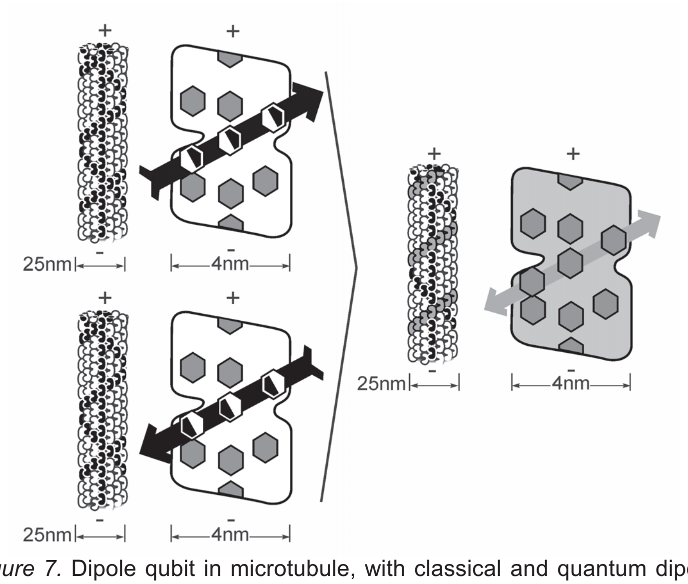

Figure 7. Dipole qubit in microtubule, with classical and quantum dipole information states for the '5-start' helical pathways in tubulin and microtubules. Left: the '5-start' helix in microtubule A-lattice aligned with dipoles in intra-tubulin aromatic rings. Top: 'upward' dipole; bottom: 'downward' dipole. Right: quantum superposition of both upward and downward helical paths coupled to dipole orientations, i.e. 'qubits'. Dipoles may be electric dipoles due to charge separation, or magnetic dipoles, e.g. related to electronic (and/or nuclear) spin. Similar qubit pathways may occur along 8-start pathways, or other pathways.

Orch OR can account for the related issue of bistable perceptions (e.g. the famous face/vase illusion or Necker cube) better than conventional approaches. Non-conscious superpositions of both face and vase evolve in brain microtubules, and then reduce by OR at time $\tau \approx \hbar/E_G$ to a conscious perception of face or vase.

I like Christof personally, and appreciated his late collaborator Francis Crick who once grilled me about microtubules at a private meeting in San Diego with Christof and Pat Churchland, after which Pat reluctantly admitted that I 'bore up rather well'. As a neuroscientist, Christof has been supportive of the study of consciousness and the Tucson conferences. But we've butted heads on other matters, such as whether axonal firings, 'spikes', are the fundamental currency of consciousness, of 'qualia', as he claims.

In my view, Orch OR and consciousness happen at end-of-integration phases in microtubules within dendrites and cell bodies of brain neurons (e.g. pyramical cells). The result of each integration and Orch OR can then trigger (or not trigger) axonal firings, or 'spikes', as messengers.

Christof maintains spikes mediate consciousness, and also espouses, with Giulio Tononi, 'Integrated Information Theory' (IIT; e.g. Koch, 2012). But integration happens in dendrites and cell bodies/soma, not axons. And integration happens in a thermostat. The degree of consciousness in IIT is based on a complexity measure, 'Phi', derived from EEG, but without relation to specific biological activity. I'm not sure what's complex about a toothache, but in my opinion, attributing consciousness to complexity *per se*, to 'Phi', without testable predictions or biomolecular connections, is 'idolatry'. IIT doesn't add up to consciousness. Christof and Giulio have now embraced panpsychism to rescue IIT, but not in any useful way, attributing primitive consciousness to quantum particles without considering their quantum aspects.

The most organized assault against Orch OR came from a group of Australian scientists who wrote papers in *PNAS* and *Physical Reviews E*. In *PNAS*, Reimers *et al.* (2009) described three types of Fröhlich coherence (weak, strong, and coherent). They validated 8 MHz coherence in microtubules (Pokorný *et al.*, 2001; Pokorný, 2004) as weak coherence, but, based on simulation of a 1-dimensional linear chain of 'tubulin' oscillators to approximate a 3-dimensional microtubule, concluded that microtubule coherence was insufficient for Orch OR. Clearly microtubule coherence depends on 3-dimensional cylindrical lattice vibrations. Unbeknownst to Reimers *et al.*, Samsonovich *et al.* (1992) simulated microtubules as 2-dimensional lattice planes with

toroidal boundary conditions (approximating 3-dimensions). They found strong Fröhlich coherence at super-lattice patterns which precisely matched attachment sites for microtubule-associated proteins (MAPs). With their 1-dimensional microtubule, Reimers *et al.* are like the Troglodytes in Plato's cave, mistaking 2-dimensional shadows for 3-dimensional reality.

Following Reimers *et al.*, the second paper from the Aussie 'hit squad' (McKemmish *et al.*, 2012) declared that Orch OR was not only wrong, but irreparably wrong, that despite any possible future modification, it could not be fixed. They gave two reasons.

1) Orch OR characterizes tubulin switching by London force dipoles of π electrons in indole and phenyl rings. McKemmish *et al.* pointed out that π electrons in a single ring are completely delocalized, and cannot switch, nor exist in superposition of both states. I agree completely. London force dipole couplings occur between two or more π electron clouds (32 such clouds per tubulin). It takes two (or more) to tango. We now know tubulin has contiguous arrays of phenyl and indole rings in quantum channels (Figure 6 and 7). And efforts to synthesize quantum systems utilize contiguous arrays of these same rings (Hayea *et al.*, 2013). McKemmish *et al.* missed the point entirely.
2) Based on early Orch OR schematic cartoons of tubulin flexing, McKemmish *et al.* asserted that energy required for switching would be enormous, and generate heat. Again, I agree. Orch OR doesn't assert flexing, just electric or magnetic dipole switching, accompanied by femtometer movement of atomic nuclei (six orders of magnitude smaller than flexing). Early Orch OR cartoons showing tubulin nanometer flexing were admittedly, but unintentionally, misleading. All Orch OR calculations are based on electronic dipole coupling and superposition separation in femtometers.

Reimers *et al.* and McKemmish *et al.* completely whiffed on both attacks (*cf.* Hameroff and Penrose, 2014c; *cf.* Hameroff and Penrose, 2014a,b). But, in any case, these debates merely pitted theory versus theory.

In 2006 experiments began to show quantum coherence in warm living systems. Photosynthesis in plants turns out to use quantum coherence (e.g. Engel *et al.*, 2007; Hildner *et al.*, 2013). Captured photon energy is transferred along chromophores containing non-polar electron clouds, the propagation occurring through all possible

paths simultaneously, apparently promoted and maintained by coherent mechanical vibrations (e.g. Chin *et al.*, 2013). If a tomato or rutabaga can utilize quantum coherence, shouldn't our brains be able to manage it?

6. 'Good vibrations'

At the 2009 TSC conference in Hong Kong, I met Anirban Bandyopadhyay PhD, working in Tsukuba, Japan's 'science city', who said he had evidence supporting Orch OR. His team assembled microtubules (from animal brain tubulin) on an insulated surface at various temperatures and conditions. Using nanotechnology, they attached four electrodes to single microtubules, two from which to record and two to stimulate across a spectrum of alternating current frequencies. At specific stimulation frequencies, microtubules became highly conductive — resistance dropped precipitously, even at room temperature in air. 'Is that quantum conductance? Superconductivity? Fröhlich coherence?', I asked Anirban. 'Now we can only say that it's some kind of resonance' he replied, explaining that the inherent resistance in the electrode interfaces showed in the results. He now has clear evidence for warm quantum coherence in microtubules, e.g. resistance through an entire microtubule is lower than through single tubulins, and conductance is temperature-independent (Sahu *et al.*, 2013a,b).

Anirban's microtubule resonances range from kilohertz through megahertz and gigahertz frequencies, and may be fractal-like, repeating over many spatio-temporal scales. In our Orch OR review (Hameroff and Penrose, 2014a), Roger and I suggest that time τ in Orch OR events occurring by $\tau \approx \hbar/E_G$ may correlate with Anirban's coherence, e.g. at 10 megahertz, much faster than we had previously suggested. This means decoherence need be avoided for only 10^{-7} seconds, and coherence times as long as 10^{-4} seconds have already been demonstrated, putting Orch OR on firm ground. We also suggested that interference between sets of coherent microtubule vibrations (e.g. in megahertz) results in much slower 'beat frequencies', e.g. at 30 to 90 Hz gamma synchrony. Indeed, well known (but poorly understood) electro-encephalographic (EEG) rhythms may be 'beats' of much faster vibrations in microtubules inside neurons (Figure 8).

With resonances, orchestration, beats, and different scales, or octaves, microtubules are looking like musical instruments, at least metaphorically. In Orch OR, microtubule vibrations also correspond with fluctuations in the fine scale structure of space-time geometry, so in some sense, consciousness is the 'music of the universe'.

Microtubules are piezoelectric, so megahertz electromagnetic resonance implies mechanical megahertz vibrations, which is ultrasound. We use ultrasound in anaesthesiology for imaging, so I wondered if ultrasound applied to the brain could affect consciousness. I found studies showing brain ultrasound altered behaviour and electrophysiology in animals (Tyler *et al.*, 2008), and suggested to my fellow anaesthesiologists we try it on volunteer patients in our pain clinic. 'We try this on ourselves first', insisted my colleague Dr John Badal. 'Hammer' (my 'nickname' in the operating room), he said, 'It's your idea. You got a shaved head. You're first.'

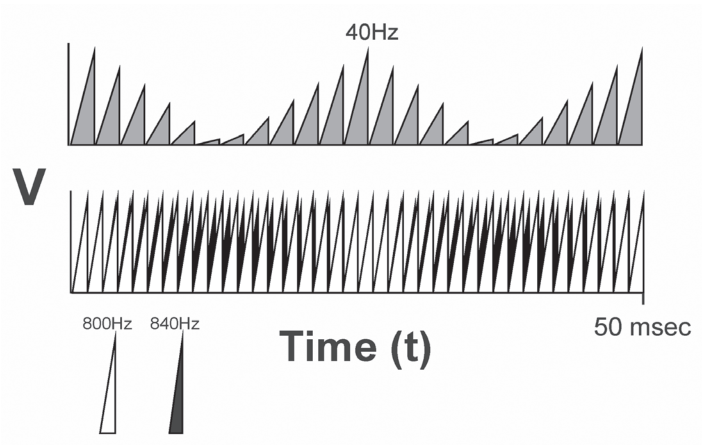

Figure 8. 50 msec of Orch OR activity, 'beat frequencies', and EEG. Two (one whole, and two half) 40 Hz gamma synchronized EEG waves/Orch OR events (top) are interference 'beats' from higher frequency microtubule vibrations near 800 Hz (bottom), from Hameroff and Penrose (2014a).

And so I was. I placed some gel on the transducer probe of our GE Logiq$_e$ ultrasound imaging machine, turned it on at 8 megahertz and put it to my temple. Nothing. I felt nothing, heard nothing. After 15 seconds I stopped, and checked to make sure the device had been on. It had. 'Oh well', I thought, disappointed. But then, after about a minute, I felt a buzz, a gush of energy, focus, and good feelings, a pleasant ringing through my brain that lasted an hour. Was it placebo? Or were my microtubules really humming?

We did the study, applying 8 megahertz (or placebo) to the temple of subjects for 15 seconds, and found improved mood for 40 minutes after ultrasound, publishing the first human trial of 'transcranial ultrasound' ('TUS', Hameroff *et al.*, 2013). TUS is also the airport code for Tucson.

Further ultrasound studies with colleagues Jay Sanguinetti, John JB Allen, Uma Raman, and Sourav Ghosh have shown even better mood with 2 megahertz, and accelerated neurite sprouting in embryonic neurons, suggesting TUS trials on traumatic brain injury, Alzheimer's, PTSD, depression, and entertainment. Quantum vibrations in microtubules might be the answer to nearly everything.

Psychedelic drugs, which may be considered 'mind expanding', bind in non-polar hydrophobic regions within proteins, and enhance electron resonance and quantum dipoles (Snyder and Merril, 1965; Shulgin *et al.*, 1969; Kang and Green, 1970). Although psychedelic drugs (like anaesthetics) are considered to act at membrane receptors, they also get inside cells and can bind in quantum channels in tubulin where they may increase frequency of microtubule quantum dipole resonances and Orch OR events, driving consciousness more deeply into the quantum world, thereby 'expanding' consciousness. As the Beatles sang, 'the deeper you go, the higher you fly; the higher you fly, the deeper you go!'

When I first read *The Emperor's New Mind*, I thought Roger touched on spirituality, as consciousness was occurring in the fine scale, non-local structure of the universe, where everything is, in some sense, connected, and in which Platonic values can influence conscious perceptions and choices. This sounded vaguely like 'divine guidance', or 'the way of the Tao', though Roger has always avoided references to religion and spiritual beliefs.

Patients who survive cardiac arrest often report 'near-death' and 'out-of-body' experiences with a consistent phenomenology, e.g. a 'white light, tunnel, life review and sense of serenity' (Van Lommel *et al.*, 2001; Parnia *et al.*, 2001).

Conventional explanations focus on hypoxia and ischemia — lack of oxygen and blood supply to the brain. But I've seen many hypoxic patients, and (if they remain conscious) they are agitated, confused, and fearful. Lack of blood flow and oxygen may prevent energy-dependent membrane activities, but spare lower energy, deeper level quantum processes in microtubules which may persist, and perhaps dissipate to non-local space-time geometry in the universe at large, remaining entangled as a 'quantum soul' (Hameroff and Chopra, 2012). I don't claim any proof for this, but Orch OR provides a plausible mechanism if it does occur. Sceptics who deride such possibilities can't explain consciousness in the brain, so they cannot exclude consciousness out of the brain.

7. Conclusion

In 40 years studying consciousness, the last 20 involving *JCS*, TSC, and Orch OR, I've encountered many, many wonderful and famous people, places, and ideas. It seems I've found the right people in the right places at the right times to help develop the right theory. I feel like the 'Forrest Gump' of the science of consciousness.

The right theory is Orch OR, a comprehensive integration of molecular and cell biology, neuroscience, cognitive science, pharmacology, philosophy, quantum physics, cosmology, and spiritual traditions. Orch OR generates testable predictions, some validated, none significantly refuted, and has withstood 20 years of sceptical criticism without a scratch. Other theories have come and gone, or pale in comparison.

Sir Roger Penrose is far more modest and polite than I am in this regard. Indeed, when defending Orch OR, I'm told I can be brash, abrasive, and foul-mouthed (perhaps a by-product of nearly 40 years fighting for patients' lives in a busy trauma hospital). So in addition to being the Forrest Gump of the science of consciousness, I sometimes identify with its 'Lenny Bruce', the profane social critic and comedian of the 50s and 60s.

Sir Roger and I have published an Orch OR update, 'Consciousness in the Universe — Review of the Orch OR Theory' (Hameroff and Penrose, 2014a). Its key points:

1) Proto-conscious processes (Penrose objective reduction, 'OR') have been in the universe all along, occurring in the fine scale structure of space-time geometry, shaping the material world.
2) Microtubules evolved in biology to compute and 'orchestrate' OR events into rich conscious experience and causal action (Orch OR), sequences of which give rise to our 'stream of consciousness'.
3) Microtubules have quantum vibrational resonances (e.g. in megahertz) blocked by anaesthetics and enhanced by psychoactive drugs. Interference of microtubule vibrations results in slower 'beat frequencies', accounting for electroencephalography (EEG) rhythms.
4) Therapies aimed at brain microtubules may be useful in a variety of neurological and psychiatric disorders.
5) Consciousness is self-organization in the fine scale structure of space-time geometry, the 'music of the universe'.
6) Orch OR is the most comprehensive, rigorous, and successful theory of consciousness ever put forth.

For Orch OR, *JCS*, and TSC the future is bright. Congratulations and thanks to *JCS*, its readers, and to TSC participants, colleagues, critics, and students of consciousness everywhere.

In the end, consciousness is all that really matters.

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