

CONSCIOUSNESS, FREE WILL AND QUANTUM BRAIN BIOLOGY – THE ‘ORCH OR’ THEORY¹

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1. Introduction – Consciousness and its place in the universe

We know what it is like to be conscious – to have awareness, phenomenal experience (composed of what philosophers term ‘qualia’), a sense of ‘self’, feelings, sensations, emotions, apparent choice and control of actions, memory, a model of the world and one’s body, thought, language, and, e.g. when we close our eyes, or meditate, internally-generated images and geometric patterns. But what consciousness actually is, how it comes about and its place in the universe remain unknown.

Science generally portrays consciousness as an emergent property of complex computation among brain neurons. In this view, consciousness first appeared during evolution of biological nervous systems. On the other hand, some philosophical, spiritual and quantum physical approaches suggest consciousness depends on a fundamental property intrinsic to the universe, and that consciousness has, in some sense, been in the universe all along. Could both views be true?

The very existence of consciousness seems highly unlikely. Cosmologists tell us that if specific values for the twenty or so fundamental numbers which characterize the universe (precise charge and mass of particles, values for gravitational and other constants, etc.) were just slightly different, life and consciousness—at least as we know them—would be impossible. The universe is seemingly ‘fine-tuned’ for life and

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consciousness. Why this may be so is approached by several versions of the ‘anthropic principle’. In the ‘strong’ version (Barrow, and Tipler 1986), the universe is somehow compelled to harbor and enable consciousness, as if consciousness were engaged in its development, organizing the universe. The ‘weak anthropic principle’ (Carter, 1974) suggests that only our particular universe is capable of consciousness, and only this one universe, a privileged version of a multitude of universes, can be observed and wondered about. The question again boils down to whether consciousness is intrinsic to the universe, or an emergent property of brain computation.

The conventional wisdom in neuroscience and philosophy tells us consciousness emerges from brain computation, specifically complex synaptic computation among ‘integrate-and-fire’ (‘Hodgkin-Huxley’) brain neurons. The foundation for attempts to understand consciousness is that the brain is a computer. Consciousness is a computation. Some proponents further believe that when the brain’s computational wiring diagram—the ‘connectome’—is unraveled, mapped and replicated in silicon, brain functions including consciousness will be downloaded and recreated (Kurzweil, 2013). Consciousness would become a commodity. Huge resources are aimed at ‘mapping the brain’.

But consciousness isn’t necessarily computation. Physicist Sir Roger Penrose (1989) points out that while computers surpass humans in many information capacities, they don’t really ‘understand’ anything. And as philosopher David Chalmers’ (1996) ‘hard problem’ illustrates, phenomenal ‘qualia’ like redness, joy, the taste of mustard and the smell of lilac may involve some added feature, some ‘fundamental’ entity or process intrinsic to the fine scale structure of the universe, akin to mass, spin or charge, perhaps embedded with fundamental values which work to anthropically optimize the universe for consciousness.

Unable to account for consciousness through strictly neuronal computational approaches, prominent neuroscientist Christof Koch (2012) has appealed to panpsychism, the notion that material particles are endowed with subjectivity, or experiential ‘qualia’, intrinsic to the universe as a property of matter. But matter itself, at tiny scales, is continuously ‘materializing’, i.e. reducing, or collapsing to definite states from multiple quantum possibilities. At the scale at which biomolecules

govern neuronal activity, the strange laws of quantum mechanics come into play, and materialism is a mirage. Consciousness seems related to the boundary between quantum and material worlds.

Physical reality is ruled by two sets of seemingly incompatible laws. In our everyday material ('classical') world, Newton's laws of motion, Maxwell's equations, the gas laws and others accurately predict behavior of particles and energy. However at tiny scales, and the size cutoff, or boundary between the two worlds is variable and unknown, the laws of quantum mechanics rule. Particles can exist in multiple locations or states simultaneously ('quantum superposition'), become spatially separated from one another, but remain connected ('entanglement'), and condense into unitary objects ('quantum coherence').

This strangeness isn't observed in our material world. Attempts to measure quantum superpositions cause them to collapse to definite states. The mystery of why this happens, why there exists some boundary, or edge between quantum and classical worlds is known as the 'measurement problem' in quantum mechanics.

Several interesting solutions to the measurement problem have been put forth. Decoherence is the notion that quantum systems which interact with the classical environment are disrupted by thermal interactions. What about isolated quantum systems?

One proposal from the early days of quantum mechanics is that the very act of conscious observation causes quantum possibilities to materialize, or reduce to definite states - consciousness 'collapses the wave function' (e.g. Wigner, von Neumann, Stapp). This view is also known as the 'Copenhagen interpretation' due to the Danish origin of Niels Bohr, one of its early proponents. But this view led to a major dilemma about unobserved, isolated quantum systems, as illustrated by Schrödinger's famous thought experiment in which the fate of an isolated cat is tied to a quantum superposition. According to Copenhagen, the cat is both dead and alive until observed by a conscious human. Absurd it was, but the question persists. Why aren't quantum superpositions seen in our material world?

The 'multiple worlds' hypothesis suggests that with each superposition, the universe separates at a fundamental level, each possibility evolving into its own universe (Everett, 1957). Thus there exists an infinite number

of co-existing, 'parallel universes'. This view has been linked to the weak anthropic principle, in which we live in the one universe, of a multitude of universes, most conducive to life and consciousness.

These approaches are flawed. But each may each hold part of an answer. The Copenhagen/conscious observer approach has its Schrödinger's cat problem, and places consciousness outside science as the external cause of collapse/reduction. But it does directly link consciousness to quantum state reduction.

'Multiple worlds' is untestable, non-falsifiable, energetically unfavorable, and doesn't deal with consciousness. But it does deal with the nature of superposition. It implies that a particle in two places at the same time is equivalent to separation, bifurcation, in the fine scale structure of the universe—spacetime geometry (irrespective of whether the separated spacetimes evolve to their own universes). Each particle location has its own spacetime geometry.

Another proposed solution to the measurement problem with concepts similar to these two features is Penrose 'objective reduction' (OR) in which quantum superpositions evolve by the Schrödinger equation until reaching an 'objective' threshold for reduction, or collapse. Similar to 'multiple worlds', Penrose OR portrays quantum superpositions as spacetime separations (due to alternate curvatures), but are unstable due to properties inherent in spacetime geometry. Before each spacetime branch evolves its own new universe, the separation reaches OR threshold by the uncertainty principle $E_G = h/t$ (E_G is the magnitude of separation, h is the Planck-Dirac constant, and t the time at which OR occurs). At that instant, spacetime geometry reconfigures, quantum possibilities choose particular material states, and, according to Penrose, a moment of conscious experience occurs. Penrose OR turns the Copenhagen/conscious observer approach around. Rather than consciousness *causing* collapse/reduction, consciousness is collapse/reduction, a process on the edge between quantum and classical worlds.

Generally, OR can be taken as equivalent to decoherence, the process by which a quantum system is said to be disrupted by its random environment. Superposition/separations E_G arising continuously will entangle other such random superpositions and quickly reach OR threshold by $E_G = h/t$. In such cases, the conscious experience would be

primitive qualia without cognitive meaning, described as ‘proto-conscious’, intrinsic to the universe, accompanying OR events ubiquitously shaping material reality. This approach is similar to the ‘Ground of Being’ concept in Eastern philosophical terms.

OR ‘protoconscious moments’ are also similar to Buddhist concepts of discrete conscious moments, and to an approach to consciousness as ‘occasions of experience’ by philosopher Alfred North Whitehead (1929, 1933) who saw consciousness, and the universe, as a process, as sequences of events. Leibniz (1768) had ‘quantized’ reality, describing fundamental ‘monads’ as ultimate entities, but Whitehead transformed monads into ‘actual occasions’ occurring in a “basic field of proto-conscious experience”. Whitehead occasions of experience are intrinsic to the universe, spatiotemporal quanta, each endowed, usually, with only low level, “dull, monotonous, and repetitious [...] mentalistic characteristics”. Abner Shimony (1993) observed how Whitehead ‘occasions’ resemble quantum state reductions.

How do we get from simple proto-conscious moments, or occasions, to full, rich meaningful consciousness? In panpsychism, simple particles with simple experience must be somehow organized, or combined into a cognitive, meaningful arrangement—the ‘combination problem’. Whitehead considered this problem for his ‘occasions’, or events, rather than particles, and described how ‘highly organized societies of occasions permit primitive mentality to become intense, coherent and fully conscious’.

How can Penrose OR events be so organized, and occur in the context of brain function? The Penrose-Hameroff ‘Orch OR’ theory suggests OR events are ‘orchestrated’ into full, rich conscious moments. This paper describes how Orch OR can occur in structures called microtubules inside brain neurons, how it addresses the particular issue of free will, and discusses ‘brain tuning’, the possibility of addressing mental states and disorders through microtubule quantum vibrations. Consciousness is seen as intrinsic to the universe.

2. Where in the brain does consciousness occur?

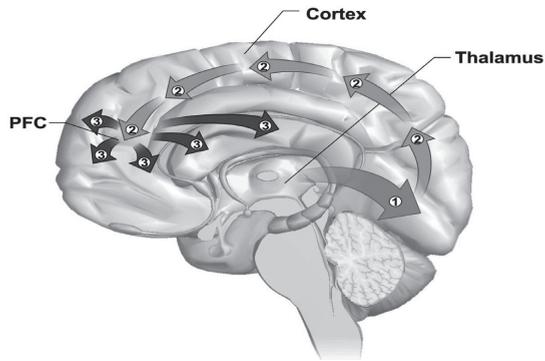


Figure 1. Three waves in sensory processing. Sensory inputs from spinal cord and cranial nerves to thalamus result in primary projections (1) to primary sensory cortex, e.g. visual area 1 (V1) in occipital cortex in the back of the brain. From these areas, feed-forward projections (2) go to secondary associative and ‘executive’ areas cortex, e.g. pre-frontal cortex (PFC) from which tertiary projections (3) go to other brain regions whose content then becomes conscious.

The general architecture for conscious sensory processing in the brain is shown in Figure 1. Sensory inputs to thalamus result in (1) projections to primary sensory cortex, e.g. visual area 1 (V1) in occipital cortex in the back of the brain. From primary sensory areas, (2) secondary feed-forward projections go to associative and ‘executive’ e.g. pre-frontal cortex (PFC). From there, (3) tertiary projections go to other cortical regions whose content then becomes conscious.

The notion that this ‘third wave’ feedback is conscious, and first and second waves are not conscious, is consistent with philosophical approaches called ‘higher order thought’ (‘HOT’), and neuroscientific cortical feedback models for conscious vision (Lamme & Roelfsma, 2000). Experimental evidence for the association of the ‘third wave’ with consciousness is provided through studies of anesthesia. Despite the fact that neurotransmitters, receptors and other neurophysiology appears identical among the three waves, all three types of anesthetic molecules (volatile gas anesthetics, propofol and ketamine) selectively inhibit third wave activity while sparing primary and secondary projections (Lee et al, 2013).

There are two clarifications with this anatomical scheme. First, although the brain’s medial surface is shown in Figure 3, sensory-based

cortical projections may occur more toward outer dorsal surfaces. Second, internally-generated conscious states, e.g. mindwandering, meditation and dreams, possibly mediated through default mode networks, will have different pathways, though their end targets (layer V cortical pyramidal neurons, see below) may be identical.

Third wave activity within cortex seems to also be composed of three waves, successively, and maximally, integrating information. Cortex is arranged in 6 horizontal layers, and sensory inputs from thalamus go (1) to layer 4, and thence (2) from layer 4 to layers 1, 2, 3 and 6. (3) Projections from these layers converge on layer 5 giant pyramidal neurons, the most likely site for consciousness in the brain. Apical dendrites from pyramidal neurons ascend vertically to the cortical surface, and are most directly responsible for measurable electro-encephalography (EEG), e.g. '40 Hz' gamma synchrony, the best neural correlate of consciousness. Axonal firing outputs from layer V pyramidal neurons descend, e.g. to implement behavior, exerting causal efficacy in the world. Third wave integration in cortical layer V pyramidal neurons is the most likely site for consciousness in the brain.

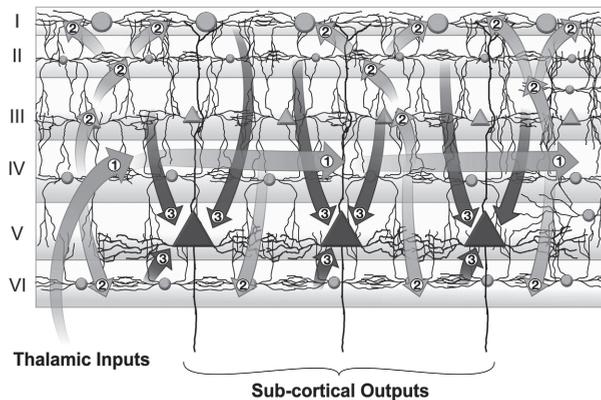


Figure 2. Three waves of sensory processing in cerebral cortex, a thin mantle on the very top of the brain composed of 6 hierarchical cellular layers. Primary sensory projections from thalamus (1) arrive in layer IV which projects secondary activity (2) to layers I, II, III and VI. These areas then project tertiary (3) activity to giant pyramidal neurons in layer V, where consciousness is most likely to occur. Outputs from layer V pyramidal neurons project sub-cortically, e.g. to manifest 'conscious' behavioral actions. Activity in apical dendrites from pyramidal neurons which ascend to cortical surface are most directly responsible for measurable electro-encephalography (EEG).

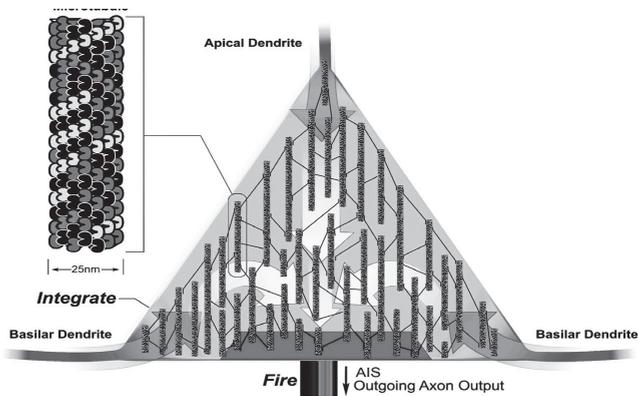


Figure 3. Layer V pyramidal neuron with internal networks of microtubules connected by microtubule-associated proteins ('MAPs'). Inputs from apical and basilar dendrites are integrated in pyramidal neuronal membranes and cytoskeletal microtubules. On left, a single microtubule is shown comprised of individual tubulin proteins, each in 3 possible states.

'Integrate-and-fire' layer V pyramidal neurons are the final, and maximal, integrator for sensory processing, providing a neurobiological basis for 'Integrated information theory' (Tononi, 2012). Their firing outputs control behavior, but neuroscience considers pyramidal neurons (indeed all neurons) according to the Hodgkin-Huxley (HH) standard model. In HH, each neuron is a threshold logic device in which dendrites and cell body (soma) receive and integrate synaptic inputs via excitatory and inhibitory membrane potentials to a threshold at the proximal axon (axon hillock, or axon initiation segment— 'AIS'). When AIS membrane potential reaches a critical threshold, the axon 'fires' to convey signals to the next synapse and layer of neurons.

Integration implies merging and consolidation of multiple disparate information sources. At the level of an individual neuron, integration is approximated as linear summation of synaptic membrane potentials. However integration in branching dendrites and soma requires logic, amplification of distal inputs, branch point effects, and signaling in dendritic spines and local dendritic regions. Nonetheless, according to HH, all such factors are reflected in membrane potentials, and thus the HH neuron is completely algorithmic and deterministic. For a given set of inputs, synaptic strengths and firing threshold, a fixed output in

the form of axonal firings, or spikes will occur. Networks of integrate-and-fire neurons regulated by synaptic strengths and firing thresholds can integrate at various anatomical scales, providing highly nonlinear functional processing. But in the end, such processes are algorithmic and deterministic, leaving no apparent room for consciousness or free will.

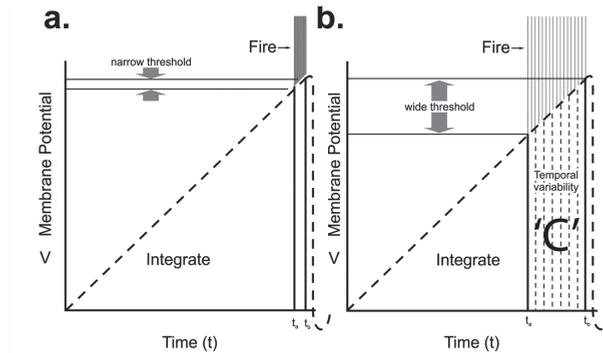


Figure 4. Integrate-and-fire neuronal behaviors. a. The Hodgkin-Huxley model predicts integration by membrane potential in dendrites and soma reach a specific, narrow threshold potential at the proximal axon (AIS) and fire with very low temporal variability (small $t_b - t_a$) for given inputs. b. Recordings from cortical neurons in awake animals (Naundorf et al. 2006) show a large variability in effective firing threshold and timing. Some additional factor, perhaps related to consciousness ('C') exerts causal influence on firing and behavior.

However, real neurons differ from idealized HH neurons. For example Naundorf et al. (2006) showed that firing threshold in cortical neurons in brains of awake animals vary spike-to-spike. Some factor other than inputs, synaptic strengths and the integrated membrane potential at the AIS contributes to firing, or not firing. Firings control behavior. This integration 'x-factor' deviation from HH behavior, modulating integration and adjusting firing threshold e.g. in layer V pyramidal neurons, is perfectly positioned for consciousness, causal action and free will, yet is in some way divorced from membrane potentials. What might it be?

3. A finer scale?

Interiors of neurons and other cells are organized and shaped by the cytoskeleton, a scaffolding-like protein network of microtubules, microtubule-associated proteins (MAPs), actin and intermediate filaments.

Microtubules (MTs) are cylindrical polymers 25 nanometers (nm = 10^{-9} meter) in diameter, comprised usually of 13 longitudinal protofilaments, each chains of the protein tubulin. MTs self-assemble from the peanut-shaped tubulin, a ferroelectric dipole arranged within microtubules in two types of hexagonal lattices (A-lattice and B-lattice), each slightly twisted, resulting in differing neighbor relationships among each subunit and its six nearest neighbors. Pathways along contiguous tubulins in the A-lattice form helical pathways which repeat every 3, 5 and 8 rows on any protofilament (the Fibonacci series).

Each tubulin may differ from among its neighbors by genetic variability, post-translational modifications, phosphorylation states, binding of ligands and MAPs, and dipole orientation. MTs are particularly prevalent in neurons (109 tubulins/neuron), and uniquely suitable, especially in dendrites and cell bodies, for information processing, encoding and memory. In cell division, MTs dis-assemble, and then re-assemble as mitotic spindles, which separate chromosomes, establish daughter cell polarity and then re-assemble for cellular structure and function. However neurons are unlike other cells; once formed, they don't divide, and so neuronal MTs may remain assembled indefinitely, providing a stable potential medium for memory encoding.

MTs in neuronal soma and dendrites are unique in other ways as well. Each tubulin dimer (composed of slightly different alpha and beta monomers) has a dipole, a net positive charge at the beta monomer, and a net negative charge at the alpha monomer. So MTs assembled from parallel arrayed tubulin dipoles also have a net dipole, positive toward its beta monomer end, and negative toward the alpha end. In axons, and in all non-neuronal cells throughout biology, MTs are arrayed radially, like spokes in a wheel, extending continuously from the centrosome near the nucleus, outward toward the cell membrane. These radially arrayed MTs all have the same polarity, the beta plus end outward toward the cell membrane, and alpha negative end inward at the hub, anchored to the centrosome/centriole near the nucleus.

However unlike axons and all other cells, MTs in dendrites and cell bodies/soma are short, interrupted and of mixed polarity, some with their beta plus ends outward, and the rest inward, all interconnected by MAPs into local networks. Dendritic-somatic MTs are also stabilized

against depolymerization by special MAP capping proteins, and are thus particularly suitable for memory encoding.

The mechanism by which memory is encoded, stored and processed in the brain remains largely unknown. The standard explanation is through synaptic plasticity, i.e. sensitivities at particular synapses guide activity and create patterns through neuronal networks. However synaptic membrane proteins which determine sensitivity are transient and continuously recycled, lasting only hours to days, and yet memories can last lifetimes. Some other factor, or factors, must be involved.

Synaptic proteins are synthesized in neuronal cell bodies/soma, and transported to synapses by 'dynein' and 'kinesin' motor proteins traveling along MTs, which appear to act as passive guides, like railroad tracks. In dendrites and soma where MTs are short, interrupted and of mixed polarity, the motor proteins must jump from MT to MT, and, at dendritic branch points, choose particular pathways to deliver their cargo to the proper synapses. How they do so seems to depend on tau, the microtubule-associated protein (MAP) thought to stabilize MTs, that also seems to serve as traffic signals, instructing motor proteins precisely where to disembark and deliver their cargo. Thus specific placement patterns of tau on MT lattices subserves synaptic function related to memory, and implies specific tau binding locations are encoded in MTs. Tau displacement from MTs results in neurofibrillary tangles, microtubule instability and cognitive dysfunction in Alzheimer's disease.

Thus memory-related synaptic function depends on information encoded in MT lattices, e.g. tau placement. As the origins of memory must reach MTs from the outside world, the question then becomes how synaptic-based inputs may encode information in MTs.

The prevalent synaptic model for memory is long term potentiation (LTP) in which brief, high frequency pre-synaptic stimulation results in long-term post-synaptic potentiation (increased synaptic sensitivity), able to influence neuronal network patterns. At the intra-neuronal level in LTP, synaptic excitation causes influx of calcium ions which convert the hexagonal enzyme calcium-calmodulin to an insect-like calcium-calmodulin kinase II holoenzyme ('CaMKII'). Each of six extended kinase domains on either side of CaMKII are able to phosphorylate (or not phosphorylate) suitable protein substrates, thus providing up

to 6 'bits' of information per CaMKII, with hundreds to thousands of CaMKII activation per synaptic excitation. Protein substrates for CaMKII phosphorylations are likely sites for memory encoding, storage and processing. What might they be?

Craddock et al (2012) showed the hexagonal CaMKII kinase array precisely matches hexagonal tubulin lattice spatial geometry in microtubules, and that each kinase domain can reach intra-tubulin amino acids suitable for phosphorylation (Figure 5). CaMKII tubulin phosphorylation may alter dynamical properties, and lead to post-translational modifications resulting in memory 'hardwiring'. Dendritic-somatic microtubules are likely sites for memory encoding.

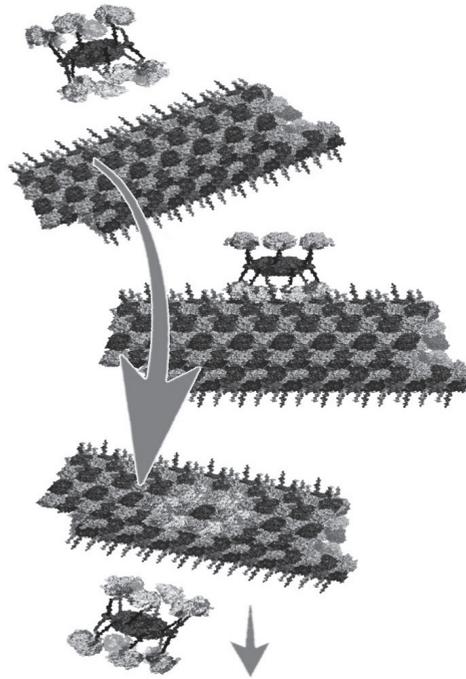
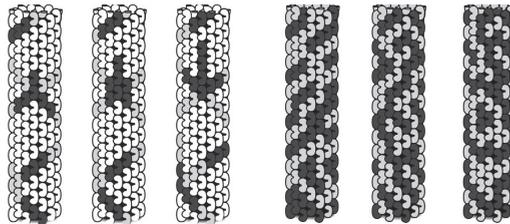


Figure 5. Memory trace - Calcium-calmodulin kinase II ('CaMKII'), a hexagonal holoenzyme activated by synaptic calcium influx extends 6 leg-like kinase domains above and below an association domain. The 6 kinase domains precisely match hexagonal size and geometry in both A-lattice and B-lattice microtubules.

Due to their lattice structure and organizational roles, MTs have long been suggested to function as information processing devices. Observing and wondering at the intelligent behavior of single cell organisms (lacking synapses), famed biologist Charles Sherrington said (1957): “of nerve there is no trace, but the cytoskeleton might serve”. Early descriptions of MTs as computer-like devices (Hameroff, and Watt 1982; Hameroff 1997; Rasmussen et al. 1990) suggested that (1) individual tubulins act as binary bit-like information units (e.g. flexing between two conformations, or dipole states), and that (2) the microtubule lattice acted as a computational matrix or cellular (‘molecular’) automata. In the latter case, tubulin states interact with hexagonal lattice neighbor tubulin states by dipole couplings, synchronized by biomolecular coherence as proposed by Fröhlich (1968, 1970, 1975; Smith et al. 1984, Rasmussen et al. 1990). Simulations of microtubule automata based on tubulin states show rapid information integration and learning. If the MT memory proposal is correct, information processing relevant to cognition



and consciousness would be occurring precisely in the medium in which memory is embedded, a highly efficient and logical proposition.

Figure 6. Three time-steps (e.g. at 10 megahertz) of two types of microtubule automata. (a) Dipole paths or spin currents interact and compute along spiral lattice pathways, for example generating a new vertical spinwave (a ‘glider gun’ in cellular automata). (b) A general microtubule automata process.

Models of MT information processing developed in the 1980s and 1990s considered fundamental information units to be a bit-like binary state of an individual tubulin, interacting/computing with states of its six surrounding tubulin lattice neighbors. However, subsequent models have considered, instead, topological pathways of like tubulin states through two types of MT lattice geometry. In the A lattice with Fibonacci geometry (Figure 7), pathways through adjacent tubulins follow pathways

which (1) travel upward/rightward, repeating every 5 tubulins on any single protofilament, and another upward/leftward, repeating every 8 tubulins. Dipole orientations along these pathways may also represent information, interact and compute, perhaps coupled to MT vibrations along these pathways.

In any case, MT-based information processing implies enormous capacity and speed. Based on tubulin binary switching and 10 megahertz processing (see below), MT-based information capacity is roughly 10^9 tubulins per neuron oscillating at e.g. 10 megahertz (10^7 Hz) for 1016 operations per second per neuron.

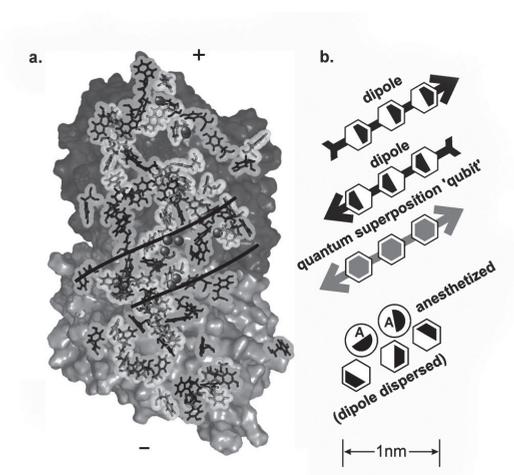


Figure 7. (a) Molecular modeling of tubulin dimer shows aromatic amino acids tryptophan, phenylalanine and tyrosine in non-polar, hydrophobic regions. Spheres are anesthetic binding sites. Curved lines enclose rings in particular aligned orientation along 5- and 8-start helical channels, containing anesthetic binding sites (with permission from Craddock et al. 2012). (b) Schematic of 5-start helical pathway of aromatic ring dipoles as suggested in Figure 7a. Top 2 pathways show alternate dipole orientations, and 3rd shows quantum superposition of both orientations. Bottom shows how anesthetics disperse dipoles, acting to erase consciousness.

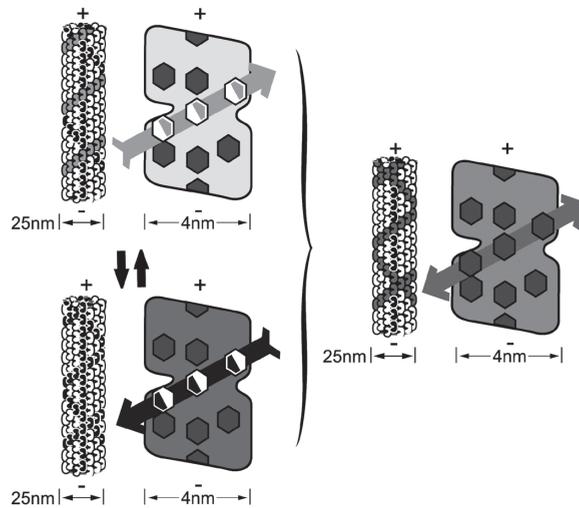


Figure 8. Dipole qubit in microtubule, with classical and quantum dipole information states for the '5-start' helical pathway in tubulin and microtubules. Left: The '5-start' helix in microtubule A-lattice aligned with dipoles in intra-tubulin aromatic rings (Figure 7). Top: 'upward' dipole, bottom: '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.

Dendritic-somatic MTs regulate synapses in several ways. They serve as tracks and guides for motor proteins (dynein and kinesin) which transport synaptic precursors from cell body to distal synapses, encountering, and choosing among several dendritic branch points and many MTs to find the right location. The navigational guidance seems to involve the MAP tau as a 'traffic signal' (specific placement of tau on microtubules being the critical feature). In Alzheimer's disease, tau is hyperphosphorylated and dislodged from destabilized microtubules, forming neurofibrillary tangles associated with memory loss (Matsuyama & Jarvik, 1989; Craddock et al., 2012a). In Downs syndrome dementia, post-operative cognitive dysfunction (POCD) and other cognitive disorders, MTs are also destabilized and partially disrupted.

Information integration in dendritic-somatic MTs, influenced by encoded memory, may cause deviation from Hodgkin-Huxley neuronal

behavior, exerting causal agency. A deeper order, high capacity, finer scale process, e.g. at end-integration in cortical layer V pyramidal neuron dendritic-somatic MTs is a likely site for consciousness. But such a process would still be algorithmic, deterministic, and fail to address phenomenal experience—the ‘hard problem’. Something is still missing. Penrose OR provides non-algorithmic (non-computable) processing, causality and addresses the hard problem. In the mid-1990s, Penrose and Hameroff teamed up to apply OR to biology, specifically OR-terminated quantum computations in brain neuronal MTs ‘orchestrated’ by synaptic inputs, memory and intrinsic MT resonances.

4. Penrose ‘Objective Reduction’ (‘OR’) and the ‘Orch OR’ qubit

Penrose OR is one proposed solution to the ‘measurement problem’ in quantum mechanics, the problem of why quantum superpositions—particles existing in multiple states or locations at the same time, and described by a quantum wave function—are restricted to microscopic scales, not seen in the ‘classical’ world we experience. Other suggestions include (1) proposals by Bohr, Wigner, von Neumann, Stapp and others (the ‘Copenhagen interpretation’, after Niels Bohr’s Danish origin) in which conscious observation causes the wave function to collapse (e.g. Schrödinger’s cat), but putting consciousness outside science, and (2) decoherence, which suggests that interaction with the random, classical environment disrupts quantum states. (3) ‘Multiple worlds’ (Everett, 1957) proposes that each possibility evolves its own spacetime geometry, resulting in an infinite number of co-existing universes. And (4), objective reduction (OR) models specify thresholds for quantum state reduction. Among these is Penrose OR.

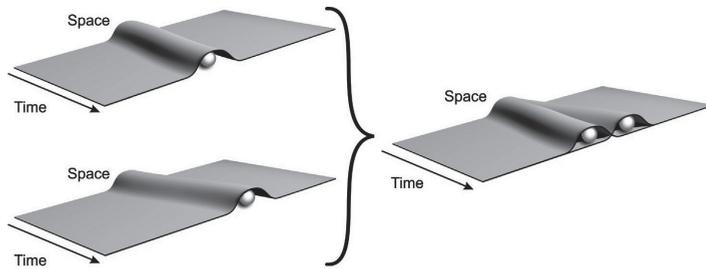


Figure 9. Spacetime geometry schematized as one spatial and one temporal dimension in which particle location is equivalent to spacetime curvature. Left: Top and bottom show spacetime histories of two alternative particle locations. Right: Quantum superposition of both particle locations as bifurcating space–time depicted as the union (‘glued together version’) of the two alternative histories (adapted from Penrose 1989, 338).

To approach superposition, Roger Penrose first equated particle states to particular curvatures in spacetime geometry, and superposition to simultaneous, alternate curvatures. Superposition may then be seen as a Planck scale separation, or bubble in the fine scale structure of the universe (Figure 1). In the ‘multiple worlds’ proposal, each such possible curvature would evolve its own universe. However Penrose suggested spacetime separations were unstable, and would reduce (collapse) due to an objective threshold given by a form of the uncertainty principle $E_G = \hbar/t$. E_G is the gravitational self-energy of the superposition, \hbar is the Planck-Dirac constant, and t the time at which OR occurs, accompanied by a conscious moment, and selecting particular states of reality (Figure 2).

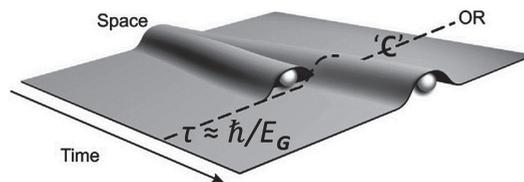


Figure 10. As superposition curvature E_G reaches threshold (by $E_G = \hbar/t$), OR occurs. One particle location/curvature is selected and becomes classical. The other ceases to exist.

Generally, such OR events occur in a random environment (identical to decoherence), the accompanying subjective experience lacking cognitive

function or meaning. The Penrose-Hameroff 'Orch OR' theory proposes that biology evolved specific mechanisms to isolate and 'orchestrate' OR events ('orchestrated objective reduction' - 'Orch OR'), giving full, rich conscious experience with cognitive meaning and volitional choice. Specific Orch OR mechanisms involve a form of quantum computing in the brain, specifically via structures called microtubules found in all animal and plant cells.

In quantum computers, information is represented not just as, e.g., binary bits of 1 or 0, but also as quantum superposition (quantum bits, or 'qubits') of both 1 *and* 0. Qubits can entangle, interact and compute with other qubits non-locally, and highly efficiently, according to the Schrödinger equation. (In topological quantum computing, qubits are states of particular pathways through lattices, rather than states of individual subunits comprising those pathways.)

Two basic issues limit implementation of quantum computers. First, interaction with the classical environment disrupts the quantum superposition ('decoherence'), and must be avoided long enough for useful computation to occur. Laboratory quantum computers are hampered by decoherence due to the 'random' thermal environment, and thus constructed at extremely cold temperatures. (Topological qubits are more resistant to decoherence.)

Conceptually, Penrose OR by $E = h/t$ replaces decoherence. Without isolation, in a random environment, OR occurs rapidly, with random outcomes. The combined EG of the system and its environment quickly reach threshold at h/t , and OR occurs with a non-cognitive, random moment of subjective experience. Presumably, this is occurring continuously, ubiquitously, throughout the universe.

If, however, superposition EG is isolated from the random environment, 'orchestrated' in a computational register (e.g. a microtubule) by inputs, memory and resonances, and follows the Schrödinger equation to perform cognitive quantum computing, then the orchestrated process will reach OR threshold by $E_G = h/t$, with EG being composed entirely of orchestrated states. Orch OR then occurs with meaningful cognition and full, rich conscious experience. Sequences of such Orch OR conscious moments provide our familiar 'stream of consciousness'. Tubulin states selected in each Orch OR event (e.g. in layer V pyramidal neuron soma

and dendrites) can exert influence on triggering, or not triggering, axonal firing. Orch OR can be the source of ‘conscious’ deviation from Hodgkin-Huxley behavior.

Orch OR also directly addresses the second issue hampering technological quantum computing, akin to the ‘halting problem’ in classical computing. If E_G is isolated, premature OR/decoherence is avoided, and the quantum computation proceeds, what then stops it to cause reduction, or collapse to a set of classical values as the solution? In technological quantum computers, the isolated quantum process must, at some point, be ‘measured’, i.e. the system is observed, causing environmental decoherence, collapse or premature OR. This introduces randomness, and some quantum computers are intended to run the same process repeatedly to average out randomness in measurement/decoherence.

Orch OR offers a direct solution, the quantum computation ‘halting’ by an objective threshold $E = h/t$. Moreover the specific states (conscious perceptions, actions, tubulin dipoles) selected in each Orch OR event are not randomly chosen, but a product of the quantum computation influenced at the instant of Orch OR by ‘non-computable’ Platonic factors inherent in spacetime geometry.

Orch OR thus proposes a conscious connection between brain biology and behavior, and the fine scale structure of spacetime geometry through the gravitational self-energy E_G of the superposition separation of tubulin in $E_G = h/t$.

According to Orch OR, tubulin states are governed by electronic (and perhaps magnetic) dipoles in non-polar electron clouds, such as aromatic resonance rings of tryptophan, tyrosine and phenylalanine. 32 such rings occur in tubulin, aligned in ‘quantum channels’, which may align with those in neighboring tubulins, and pathways, in the MT lattice (Figures 7 & 8). These same quantum channels are where anesthetic gas molecules bind by weak, quantum-level London forces to selectively erase consciousness, sparing non-conscious processes. Superposition of tubulin dipole orientations may enable tubulins to act as qubits, and helical pathways through microtubules to act as topological qubits. But electrons have extremely low mass, and E_G for their superposition separation would be very small, requiring extremely long values of t .

However, electron movements of one nanometer shift nearby atomic nuclei by femtometers (Mossbauer recoil and charge attraction), so superposition of electron cloud dipole orientations should result in femtometer superposition separation in tubulin atomic nuclei, sufficient for significant E_G and brief t .

E_G for tubulin superposition separation in Orch OR was calculated in three ways: (1) as separation of 10% of the protein dimer length (~1 nanometer), (2) as separation at the level of the atomic nuclei within each atom of tubulin (femtometer, 10^{-15} meter for carbon), and (3) as separation at the level of nucleons, i.e. protons and neutrons within nuclei (10^{-16} m). The dominant effect was determined to occur at (2) femtometer separation at the level of atomic nuclei. This implies electronic (or magnetic) dipole movements and superpositions in intra-tubulin 'quantum channel' electron cloud resonance rings correspond with femtometer movements and superpositions of nearby atomic nuclei.

Gravitational self-energy E_G of a superpositioned tubulin is then given by $E_G = Gm^2/ac$ where G is the gravitational constant, and ac is the superposition separation distance, a carbon nucleus sphere radius equal to 2.5 fermi distances (2.5 femtometers, 2.5×10^{-15} meter). If t is assumed to correspond with a neurophysiological event, say 40 Hz gamma synchrony EEG (the best neural correlate of consciousness), then E_G is calculated to be roughly 1010 tubulins. With 109 tubulins per neuron, estimating 0.1% tubulins as quantum coherent (the percent of quantum active molecules in superconductors), requiring 10,000 neurons for $t = 25$ msec gamma synchrony. But premature OR/decoherence would need to be avoided for 25 msec, a long time in the seemingly 'warm wet and noisy' intra-neuronal environment. Indeed, quantum approaches to brain biology and consciousness have seemed unlikely because of environmental decoherence.

Physicist Max Tegmark (2000) published a critique of Orch OR based on a formula he developed which calculated microtubule decoherence at brain temperature to occur at time τ of 10^{-13} seconds, far from 25 msec. But something was rotten in Tegmark's formula for τ , specifically a term in the denominator for superposition separation. In Orch OR, this is the femtometer diameter of atomic nuclei, however Tegmark described a superpositioned soliton separated from itself by 24 nanometers (3

tubulin lengths) along the microtubule. This gave a decoherence time τ 7 orders of magnitude smaller than it should have been, i.e. from 10^{-13} sec to 10^{-6} sec. Hagan et al. (2001) used Tegmark's same formula, correcting for Orch OR stipulations (superposition separation distance, permittivity etc.) and recalculated microtubule decoherence times to be 10^{-4} sec, suggesting topological resonances would sustain quantum coherence in microtubules for 10^{-1} to 10^{-2} sec. Tegmark's critique, and Hagan et al.'s reply, pitted theory versus theory.

In 2006, experimental research began to show that photosynthesis, the mechanism in plants by which sunlight is converted to chemical energy for food, and without which life could not exist, utilizes quantum coherence at ambient temperatures, i.e. in sunlight. Energy from each photon absorbed in one region of a plant cellular complex is transported as electronic excitations ('excitons') to another region of the complex through a series of 'chromophores', light-absorbing molecules composed of electron resonance clouds. What was surprising—stunning, really—was that the excitons propagated through the chromophores by all possible pathways, essentially a quantum superposition of excitonic pathways. Further work suggested the quantum coherent superposition was aided by coupling to mechanical vibrations in the protein complex. But because the propagation distance was so short, i.e. a few nanometers within the cellular complex, the coherence persisted only for very brief periods of time, e.g. femtoseconds.

What about microtubules? Using nanotechnology, the group of Anirban Bandyopadhyay at the National Institute of Material Science in Tsukuba, Japan was able to apply 4 electrodes to a single MT at room temperature. Two electrodes were used to apply very low levels of alternating current (AC) at varying frequencies, and the other two electrodes used to record conductance through the MT. Without AC stimulation, MTs were non-conductive, their resistance extremely high. However at a number of applied AC frequencies across a wide spectrum (gigahertz, megahertz, and as low as 10 kilohertz), MT resistance dropped, and the MT became significantly conductive (Sahu et al. 2013a, 2013b). More recent studies using nanoprobe inside active neurons also show megahertz and kilohertz coherent vibrations. Particular resonant frequencies may correlate with conductance and vibrations along specific helical pathways through MT lattices.

Quantum resonances as low as 10 kilohertz indicate MT coherence times as long as 10^{-4} seconds, the same MT coherence time calculated by Hagan et al. (2001) using Orch OR stipulations. If t in $EG = h/t$ is set to 10^{-4} secs, EG of tubulins in 10 million neurons would be required. For 10^{-7} secs, 10 MHz (also proven) EG of tubulins in 10 billion neurons (or higher involvement per neuron) would be required. Indeed, Orch OR may be seen to occur at different frequency ranges, e.g. akin to different scales in music. But $t = 10^{-4}$ secs is still too brief for physiological effects, such as gamma synchrony EEG at 25 msec.

In Hameroff and Penrose (2014) it was proposed that EEG rhythms are ‘beat frequencies’ of faster oscillations in microtubules. For example MT megahertz vibrations of slightly different frequencies, or energies, would interfere to give much slower ‘beats’, e.g. in the 1 to 100 Hz range seen in EEG. Indeed, consciousness may be more like music than computation, sequences of events, at different frequencies, in some cases harmonically related. Quantum vibrations in brain MTs punctuated by Orch OR events are also ripples, or rearrangements in fundamental spacetime geometry. Orch OR connects conscious brain activities to processes in the fine scale structure of the universe.

Each Orch OR conscious moment, e.g. occurring in dendritic-somatic MTs in layer V cortical pyramidal neurons, also selects tubulin states which govern neuronal activities including axonal firing, thus exerting causal action and conscious control of behavior. Can Orch OR account for free will?

5. Free will - Is consciousness too late?

Free will implies conscious agency – that ‘we’ have conscious causal control and choice of our actions. Indeed, ‘we’ do seem to have conscious control, but do we really? First, who, or what exactly is ‘we’, or ‘I’? There is no agreed-upon mechanism for consciousness nor conscious agency in neuroscience and philosophy. However Orch OR does offer a mechanism for conscious causal action – tubulin states selected in each Orch OR event may trigger, or not trigger, axonal firings to implement behavior (deviation from Hodgkin-Huxley).

A second issue involves determinism, the notion that all processes in the world, and in our minds, are algorithmic and our choices inevitable

and predetermined, with perhaps a dash of randomness. Determinism implies that conscious perceptions and actions follow a complex script written by the laws of nature and history of the universe. Penrose OR avoids determinism by ‘non-computable’, non-algorithmic influence on selection of particular states at the instant of reduction. According to OR, the quantum wave function of superposition E_G evolves algorithmically according to the Schrödinger equation up until the moment of OR at time t ($E_G = h/t$). At that instant, according to Penrose OR, non-random, ‘non-computable Platonic values’ embedded in the fine scale structure of spacetime geometry influence choices selected in the OR process. Whether such Platonic values are themselves algorithmic and deterministic are unknown. But to some extent at least, Orch OR dodges determinism.

A third issue with free will pertains to the timing of conscious action, in that consciousness, in some cases, appears to come too late. Neural correlates of conscious perception occur 150 to 500 milliseconds (msec) after impingement on our sense organ, yet we often consciously respond to those perceptions within 100 msec after sensory impingement. For example (Velmans 1991) analysis of sensory inputs and emotional content, phonological and semantic analysis of heard speech, preparation of spoken words and sentences, forming memories, and performing voluntary acts all occur, seemingly consciously, before the stimuli to which the responses were aimed are processed. The conclusion among neuroscientists and philosophers (Dennett & Kinsbourne 1992; Wegner 2002) has been that we act non-consciously, and have belated, false impressions of conscious causal action. This implies that free will does not exist, that consciousness is epiphenomenal, and that we are, as T.H. Huxley bleakly summarized, “merely helpless spectators”.

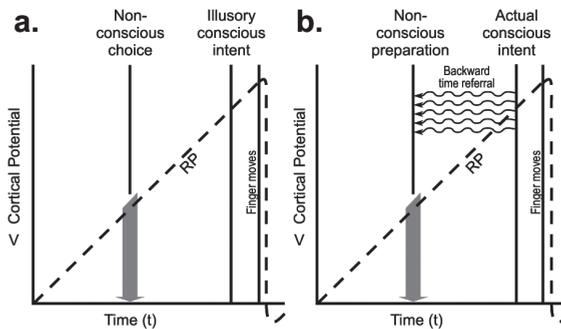


Figure 11. The “readiness potential (RP)” (Libet et al. 1983). (A) Cortical potentials recorded from a subject instructed to move his/her hand whenever he/she feels ready, and to note when the decision was made (Conscious intent), followed quickly by the finger actually moving. (Time between Conscious intent, and finger moving is fixed.) Readiness potential, RP, preceding Conscious intent is generally interpreted as representing the Non-conscious choice to move the finger, with Conscious intent being illusion. (B) Assuming RP is necessary preparation for conscious finger movement, Actual conscious intent could initiate the earlier RP by (quantum) temporal non-locality and backward time referral, enabling preparation while preserving real time conscious intent and control.

Some evidence appears to support the epiphenomenal contention. Kornhuber and Deecke (1965) recorded electrical activity over pre-motor cortex in subjects who were asked to move their finger randomly, at no prescribed time. Gradually-increasing brain electrical activity preceded finger movement by ~800 msec, termed the *readiness potential* (‘RP’). Benjamin Libet and colleagues (1983) repeated the RP experiment, except they also asked subjects to note precisely when they consciously decided to move their finger. (To do so, and to avoid delays caused by verbal report, Libet et al. used a rapidly moving clock and asked subjects to note when on the clock they consciously decided to move their finger). The ‘conscious decision’ came ~200ms before actual finger movement, hundreds of milliseconds after onset of the RP. Kornhuber, Deecke, Libet and others concluded the RP represented a non-conscious causal action of the finger movement, that many seemingly conscious actions are initiated non-consciously, and that conscious intent is an illusion. Consciousness apparently comes too late.

But does it? Strangely, apparent backward time effects are observed in brain biology related to consciousness, and theoretically allowable in quantum physics. Could quantum backward time effects rescue conscious free will?

In physics, the ‘arrow of time’ implies a flow of time in one direction, toward increasing entropy according to the second law of thermodynamics. However, other laws of physics are generally ‘time reversible’, working quite well in both directions. In principle, there’s no reason for an exclusively unidirectional arrow of time. In the Wheeler-Dewitt equation, which attempts to mathematically reconcile quantum mechanics and general relativity, time plays no role from an external viewpoint. However in the Wheeler-Dewitt equation, conscious observers within the universe do perceive a flow of time and events, the unidirectional flow of time being exclusively related to consciousness (c.f. Hameroff, 2003). However consciousness may utilize backward time effects.

A principal hallmark of quantum physics is quantum entanglement which implies complementary quantum particles (e.g. electrons in coupled spin-up and spin-down pairs) remain entangled when separated spatially (or temporally). Einstein initially objected, as it would require signaling faster than light, and thus violate special relativity. He famously termed it ‘spooky action at a distance’, and (with colleagues Podolsky and Rosen – ‘EPR’) described a thought experiment in which an entangled pair of superpositioned electrons (EPR pairs) would be sent in different directions, each remaining in superposition (Einstein et al, 1935). When one electron was measured at its destination and, say, spin-up was observed, its entangled twin miles away would, according to the prediction, correspondingly reduce instantaneously to spin-down which would be confirmed by measurement. The issue was unresolved at the time of Einstein’s death, but since the early 1980s (Aspect et al. 1982, Tittel et al. 1998) this type of experiment has been repeatedly confirmed through wires, fiber optic cables and via microwave beams in the atmosphere. Entanglement is an essential feature of quantum information technologies such as quantum cryptography, quantum teleportation and quantum computers. How does it occur?

Penrose (2004; cf. Bennett, and Wiesner 1992) proposed that measurement and reduction of one twin of the EPR pair sends quantum information backward in time to when the particles were spatially together, then onward to the second twin. According to this scheme, apparent backward time effects are necessary for entanglement, and thus ubiquitous. Aharonov has proposed that quantum state reductions send

quantum information both forward and backward in time. In his 1989 book *The emperor's new mind*, Penrose (1989) suggested quantum effects could mediate the brain's backward time referral of subjective information reported by Benjamin Libet.

In the late 1970s and 1980s, Libet and colleagues (in addition to their RP 'move your finger' research, described above) studied the timing of conscious sensory experience in awake, cooperative patients undergoing brain surgery with local anesthesia. This allowed stimulation and recording of somatosensory cortex (e.g. of the hand), periphery (e.g. hand) and direct report of the timing of conscious experience. (To avoid delays due to reporting, subjects observed a fast moving clock, and noted precisely when a sensory perception occurred.) Two types of sensory stimulation were used, one type involving direct stimulation of the skin of the hand, recording the sensory activity from somato-sensory 'hand area' of cortex, and obtaining the subject's report of the precise time of the conscious experience (via the fast-moving clock). Generally, stimulation of the hand resulted in (1) a cortical sensory-evoked potential (EP) at 30 msec after stimulation, and (2) conscious sensory experience also occurring at 30 msec, 30 msec being roughly the time required for neural signals to reach the brain from the hand. In these same subjects, Libet and colleagues also directly stimulated the 'hand area' of somato-sensory cortex. They found no EP, and discovered that 500 msec of continuously-induced cortical activity was required for conscious sensation of the hand to occur at 500 msec. Libet concluded that 500 msec of cortical activity was required to reach threshold for conscious 'neuronal adequacy'. This requirement for several hundreds of msec of direct cortical stimulation to produce conscious experience ('Libet's half second') was subsequently confirmed by Amassian et al. (1991), Ray et al. (1999), Pollen (2004) and others. It was also consistent with the subsequent work of Velmans (1991), Dennett, Kinsbourne and others who maintained that consciousness occurred several hundred msec after sensory impingement, and after seemingly conscious responses. But then, how can conscious experience occur at 30 msec with hand stimulation and the EP?

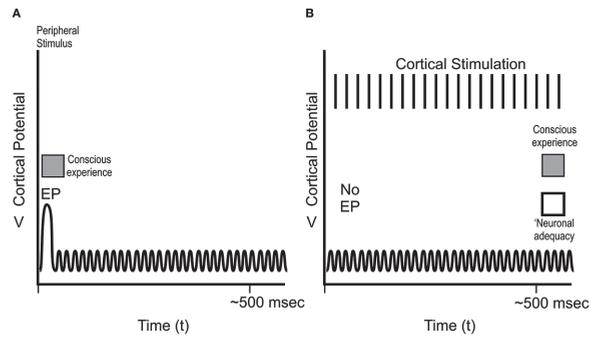


Figure 12. Cortical potentials in Libet's sensory experiments. (A) Peripheral stimulation, e.g., at the hand, results in near-immediate conscious experience of the stimulation, an evoked potential EP at ~30msec in the "hand area" of somatosensory cortex, and several 100 msec of ongoing cortical electrical activity. (B) Direct cortical activity of the somatosensory cortical hand area for several 100msec results in no EP, ongoing cortical activity, and conscious sensory experience of the hand, but only after ~500msec. Libet termed the 500msec of cortical activity resulting in conscious experience.

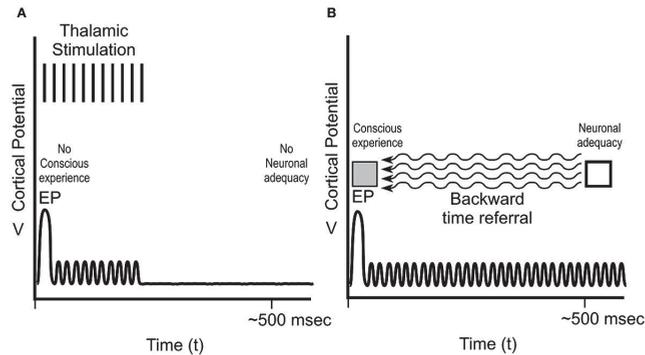


Figure 13. Libet's sensory experiments, continued. (A) Libet et al. stimulated medial lemniscus of thalamus in the sensory pathway to produce an EP (~30ms) in somatosensory cortex, but only brief post-EP stimulation, resulting in only brief cortical activity. There was no apparent "neuronal adequacy," and no conscious experience. An EP and several 100 msec of post-EP cortical activity (neuronal adequacy) were required for conscious experience at the time of EP. (B) To account for his findings, Libet concluded that subjective information was referred backward in time from neuronal adequacy (~500msec) to the EP.

To address this issue, Libet and colleagues did further studies in human subjects stimulating medial lemniscus of thalamus, the primary relay station between, e.g. hand and sensory cortex. Stimulating thalamus, they observed a cortical EP at 30 msec, and ongoing cortical activity for as long as they stimulated thalamus. If the stimulation and ongoing

cortical activity persisted for ~500 msec, the subjects reported conscious experience at 30 msec, the time of the EP. If, however, stimulation and cortical activity were stopped after the EP, but prior to ~500 msec, no conscious experience occurred. Somehow, the brain 'knew' whether or not cortical activity would continue for hundreds of msec after the EP for consciousness to occur at the time of the EP. Libet concluded that subjective information was referred 'backward in time' from neuronal adequacy at ~500 msec to the time of the EP at 30 msec. Libet's backward time assertion was disbelieved and ridiculed (e.g. Churchland, 1981; Dennett & Kinsbourne 1992) but never refuted. Indeed, several types of experiments have continued to show backward time effects in the brain.

Electrodermal activity measures skin impedance, usually with a probe wrapped around a finger, as an index of autonomic, sympathetic neuronal activity causing changes in blood flow and sweating, in turn triggered by emotional response in the brain. Researchers Dean Radin and Dick Bierman have published a series of well-controlled studies using electrodermal activity to look for emotional responses to images presented at random times on a computer screen. They found that emotional images elicited responses half a second to two seconds before the images appeared. They termed the effect pre-sentiment because the subjects were not consciously aware of the emotional feelings; non-conscious emotional sentiment (i.e. feelings) appeared to be referred backward in time.

In 2011, Daryl Bem published "Feeling the future: Experimental evidence for anomalous retroactive influences on cognition and affect" in the mainstream *Journal of Personality and Social Psychology*. The article reported on 8 studies showing statistically significant backward time effects, most involving non-conscious influence of future emotional effects (e.g. erotic or threatening stimuli) on cognitive choices. Mossbridge et al. (2012) published a meta-analysis of 26 reports published between 1978 and 2010 showing backward time effects, and concluded the results were valid. Moreover they pointed to findings in mainstream neuroscience which show backward time effects but are not reported.

In the famous double slit experiment in quantum physics, quantum entities (e.g. photons, electrons) can behave as either waves, or particles, depending on the method chosen to measure them. John Wheeler described a thought experiment in which the measurement choice

(by a conscious human observer) was delayed until after the electron or other quantum entity passed through the slits, presumably as either wave or particle. Wheeler suggested the observer's delayed choice could retroactively influence the behavior of the electrons, e.g. as waves or particles. The experiment was eventually performed and confirmed Wheeler's prediction; conscious choices can affect previous events, as long as the events were not consciously observed in the interim.

In 'delayed choice entanglement swapping', originally a thought experiment proposed by Asher Peres (2000), Ma et al. (2012) went a step further. In entanglement swapping, two pairs of unified/entangled particles are separated, and one from each pair is sent to two measurement devices, each associated with a conscious observer ('Alice' and 'Bob', as is the convention in such quantum experiments). The other entangled particle from each pair is sent to a third observer, Victor. How Victor *decides* to measure the two particles (as an entangled pair, or as separable particles) determines whether Alice and Bob observe them as entangled (showing quantum correlations) or separable (showing classical correlations). This happens even if Victor decides after Alice's and Bob's devices have measured them (but before Alice and Bob consciously view the results). Thus Victor's conscious choice affects behavior of previously measured, but unobserved, events. Entanglement apparently includes not only spooky action at a distance, but spooky action on past events. Anton Zeilinger, senior author on the Ma et al. study, said: "Within a naïve classical worldview, quantum mechanics can even mimic an influence of future actions on past events".

Such influences in the brain can allow real-time conscious control of our actions, seen as deviation from Hodgkin-Huxley neuronal behavior (Figure 14). With quantum brain biology, consciousness does not come too late. Free will is possible.

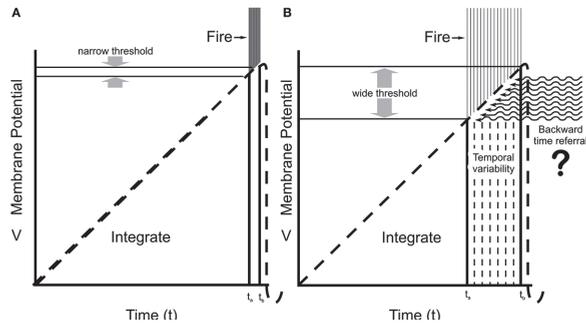


Figure 14. As in Figure 4, Integrate-and-fire neuronal behaviors. a. The Hodgkin-Huxley model predicts integration, narrow threshold potential and low temporal variability in firing at the proximal axon (AIS) b. Recordings from cortical neurons in awake animals (Naundorf et al. 2006) show a large variability in effective firing threshold and timing. Some additional factor, perhaps related to consciousness ('C') exerts causal influence on firing and behavior, and may include backward time referral.

6. Tuning the brain

Orch OR has been skeptically viewed on the basis of 'decoherence' (i.e. random, 'un-orchestrated' OR). Technological quantum computers require extreme cold, near absolute zero temperature, to avoid thermal vibrations which appear to disrupt delicate quantum effects. Critics said the brain is simply too 'warm, wet and noisy' for functional quantum effects.

Orch OR countered theoretically that coherence akin to Bose-Einstein condensation, and described for biological systems by Herbert Fröhlich, converted thermal energy to coherent vibrations, somewhat like a laser. Quantum spin transfer through aromatic rings was shown to be promoted by heat, not disrupted (Ouyang & Awschalom, 2003), and beginning in 2006, evidence began to accrue for warm temperature quantum coherence in photosynthesis proteins (Engel et al, 2007). Recently, room temperature Bose-Einstein condensation has been demonstrated (Plumhof et al 2014). The brain is not too 'warm' for functional quantum effects.

Orch OR also suggested microtubule quantum coherence originated in isolated, non-polar, 'hydrophobic' regions within tubulin ('quantum channels'), shielded from polar, aqueous interactions. At such quantum sites, anesthetic molecules selectively erase consciousness, acting by quantum London forces. The brain is not too 'wet' for functional quantum effects, at least not in 'dry' quantum channels.

Is the brain too ‘noisy’? Seemingly random electrical fluctuations occur continuously throughout the brain, embedded as background in the EEG. The fluctuations emanate mostly from neuronal post-synaptic membrane potentials which don’t reach threshold for axonal firing. According to standard neuroscience doctrine, such activity is irrelevant, as firings are all that matter, and dendritic-somatic ‘noise’ (though it constitutes ‘integration’) is ignored as irrelevant. Is it really?

The ‘noise’ is seen at all levels—neuronal, network, and the entire brain. While appearing locally random, brain electrical noise, or ‘ongoing activity’, is highly synchronized, or correlated (Arieli et al, 1996). The fluctuations are precisely the same everywhere. In pyramidal neurons, simultaneous recording of ‘noise’ in soma and apical dendrite (micron separation) show ‘isopotentiality’, near-perfect correlation (Yaron-Jakoubovitch et al 2008). Could correlated ‘noise’ have a function? Perhaps dendritic-somatic ‘noise’ is essential, or at least related to, cognition and consciousness (Pockett, 2000; McFadden, 2002). Perhaps brain noise is, as it has been said, “the brain orchestra warming up”. Orch OR suggests correlated brain ‘noise’ originates from deeper level, finer scale quantum vibrations in microtubules inside neurons.

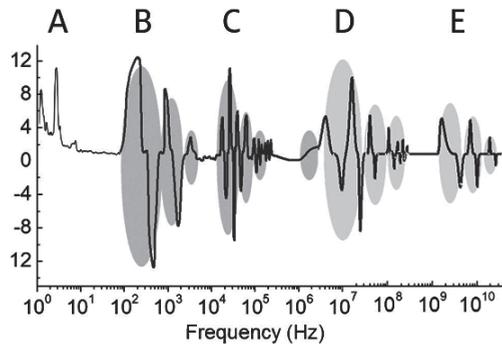


Figure 15. Five frequency bands of microtubule and brain activity plotted on a log scale. Starting at right, E and D are gigahertz and megahertz resonance frequencies found in individual microtubules (Sahu et al. 2013a, 2013b). B, C and D are kilohertz, tens of kilohertz and megahertz resonance frequencies detected from microtubule bundles inside active neurons (Bandyopadhyay 2014). A is the EEG spectrum put in ‘by hand’. The 5 bands are self—similar and separated evenly by ~ 3 orders of magnitude, suggesting a harmonic system. EEG (A) may be derived as inverse harmonics, or ‘beats’ of higher frequency microtubule vibrations.

Brain noise (and measurable EEG) derive from local field potentials due to post-synaptic trans-membrane potentials of roughly 100 millivolt fluctuations, mediated by ion fluxes through membrane protein channels. (Axonal firing potentials, or 'spikes', contribute only in a small way to noise and EEG.) Bandyopadhyay's megahertz and kilohertz electric field fluctuations from microtubule bundles inside neurons of 40 to 50 millivolts are sufficient to influence and regulate membrane potentials. Hameroff and Penrose (2014) suggested interference between microtubules vibrating at slightly different megahertz, or kilohertz, frequencies would give rise to slower 'beat' frequencies, seen as membrane potential fluctuations in EEG or brain noise. EEG is the tip of an iceberg of brain activity.

Thus brain activity relevant to cognition and consciousness may occur at various spatiotemporal scales, moving and combining, like music. Sequences of events at different frequencies, in some cases harmonically related, appear to be anchored by resonances inherent in microtubule lattice geometry. By Penrose OR, Orch OR events are also ripples, or rearrangements in fundamental spacetime geometry. Orch OR connects conscious brain activities to processes in the fine scale structure of the universe.

Within the brain, neuronal and microtubule vibrations span 10 orders of magnitude (Figure 15), and may be directly relevant to mental states. Microtubule vibrations inside brain neurons offer therapeutic opportunities for mood, cognition and neurological disorders.

Modern psychopharmacology aimed at modulating mental states, mood and cognitive function, based on the standard computationalist approach in neuroscience, has as its targets neuronal membrane receptor and channel proteins, and thus may be somewhat misguided. For example the antidepressant Prozac aims to prolong action of the neurotransmitter serotonin at its synaptic receptors (by inhibiting its 'reuptake'). The membrane-mediated effect is immediate, but mood improves only after several weeks, apparently allowing dendritic-somatic microtubules to reorganize (Bianchi et al, 2009).

Anti-anxiety benzodiazepine drugs such as Valium, Versed and Xanax are said to act by enhancing binding of GABA (gamma-amino-butyric acid), the brain's primary inhibitory neurotransmitter, to its membrane 'GABA receptor' proteins. But benzodiazepine molecules have several

non-polar rings, directly inhibit microtubules in mitosis (Troutt et al. 1995), and are likely to enter neurons and bind in microtubule quantum channels. Similarly, opiate drugs which cause euphoria bind to opiate receptors, but also enter neurons and likely bind in microtubules. While receptor binding occurs, mood-altering drugs may act to tune microtubule vibrations and mellow the music.

Psychedelic drugs are also highly non-polar, contain indole electron resonance rings, and able to enter neurons. Potency of such molecules correlates with their ability to donate electron resonance energy (Kang, and Green; Snyder, and Merrill), thus perhaps promoting microtubule quantum vibrations at higher frequencies, and vibrational resonances over many scales.

Anesthetics have opposite effects, selectively erasing consciousness while sparing non-conscious brain functions. They include numerous gas molecules whose potency correlates precisely with solubility in a non-polar, 'olive oil' medium, e.g. as found in lipids, and protein hydrophobic interiors. Franks and Lieb (1984) showed that anesthetics act in non-polar, hydrophobic regions of proteins (not in lipids), presumably membrane proteins, with receptors for acetylcholine, serotonin, glycine and GABA the most likely candidates. But despite decades of widespread searching, particular membrane receptors or channels mediating anesthetic action have not been found.

In 2006, Rod Eckenhoff's lab at University of Pennsylvania showed that anesthetics such as halothane bind to ~70 proteins in brain neurons, roughly half membrane proteins, and half cytoskeletal proteins including tubulin. Following anesthetic exposure, genetic expression of tubulin, but not of any membrane proteins, was altered. Genomic and proteomic evidence point to microtubules as the site of anesthetic action. Emerson et al. (86) used fluorescent anthracene as an anesthetic in tadpoles, and showed cessation of tadpole behavior occurs specifically via anthracene anesthetic binding in tadpole brain microtubules. Despite prevailing assumptions, actual evidence suggests anesthetics act on microtubules, not membrane receptors and channels to erase consciousness.

Thus modern psychopharmacology may be aiming at the wrong targets, thus explaining why it isn't more successful in treating mental state disorders. A primary reason membrane receptors and channels

are studied is that their effects (drug binding, conformational change, channel opening) are measurable. Until recently, there was no assay for microtubule function other than polymerization states of assembly/disassembly. Now however resonance vibrations, e.g. in megahertz, have been discovered, and drugs may be assayed for their effects on microtubule resonance spectra inside neurons. New vistas await in the study of drug effects on microtubule vibrations.

Another avenue to treating mental states and cognitive dysfunction comes through noninvasive brain stimulation techniques. Among these are transcranial magnetic stimulation ("TMS"), transcranial electrical direct current stimulation ("TDCS") and transcranial ultrasound stimulation ("TUS"), all of which have shown promise and interesting effects. Among these, only TUS can be narrowly focused to target specific, deeper brain regions (Legon et al. 2014).

Ultrasound consists of mechanical vibrations above human hearing threshold (~20,000 Hz), and is usually used in the low megahertz (10^6 to 10^7 Hz) for medical imaging, passing through the body and echoing back off surfaces. TUS consists of low intensity, sub-thermal levels of ultrasound administered at the scalp which safely penetrates skull and reaches the brain sufficiently to be echoed back to provide an image of the brain surface and sulci. As microtubules have megahertz vibrational resonances, TUS with proper settings might be expected to enhance microtubule resonance, and thereby affect microtubule functions related to cognition and mental states. Indeed, focused TUS enhances sensory discrimination in human volunteers (Legon et al, 2014), and unfocused TUS improved mood in chronic pain patients (Hameroff et al. 2013).

At the cellular level in embryonic neurons, ultrasound promotes growth of neurites leading to formation of axons, dendrites and synapses (Raman). At the level of tubulin, ultrasound promotes microtubule assembly. As traumatic brain injury involves disrupted microtubules, synapses and circuits, and as Alzheimer's disease and post-operative cognitive dysfunction (cognitive decline after anesthesia in elderly), TUS may be useful for all these disorders.

Traumatic memory is an important factor in psychotherapy (e.g. post-traumatic stress disorder). Some suggest eliciting a traumatic memory and then over-writing it at that time with a positive memory (Lane et

al). Since synaptic membrane proteins are too short-lived to store and encode memory, and microtubules appear likely to do so, psychotherapy combined with TUS aimed at microtubule vibrations may be optimal.

To erase or over-write traumatic memory, to change the music and re-tune the tubules, combinations of pharmacology, psychotherapy and TUS (e.g. aimed at microtubule vibrations in amygdala, hippocampus and pre-frontal cortex) may be optimal. As the Beatles sang, “Take a sad song and make it better”.

7. Conclusion

The mainstream materialist approach to brain function in neuroscience and philosophy suggests that consciousness and cognition emerge as higher order network effects from complex computation among relatively simple neurons. The fine grain of conscious and cognitive information is conveyed at the neuronal level by axonal firings and synaptic transmissions mediated entirely by membrane proteins.

This approach has failed. Neuronal computational networks fail to account for (1) cognitive phenomenal aspects of single cell organisms like *paramecium* which swim, learn, find food and mates and have sex, all without synaptic connections, using their cytoskeletal microtubules for sensory processing and motor actions, (2) phenomenal subjective aspects of consciousness (the ‘hard problem’), (3) free will as real-time conscious control, neuronal activity correlating with perception occurring after seemingly conscious response, relegating consciousness to epiphenomenal ‘helpless spectator’, (4) memory, as membrane proteins determining synaptic sensitivity are transient, and yet memories can last lifetimes, (5) molecular mechanisms for drugs affecting consciousness including anesthetics, which selectively erase consciousness, but despite popular belief, do not act on membranes, and (6) scientific plausibility for non-locality, e.g. so-called telepathy, pre-cognition, near death/out-of-body experiences, and afterlife. These are generally stated to be impossible because they cannot be scientifically explained by the mainstream view based on neuronal-based computation. But the mainstream materialist view can’t really explain anything about consciousness. And materialism itself is illusory, as particles repeatedly coalesce from quantum possibilities.

In spiritual and idealist approaches, consciousness has in some sense always existed in the universe, being in some way intrinsic to its very makeup. Some such views place consciousness as primary, omnipresent, with matter and the world manifesting within an all-pervading consciousness. But such approaches themselves are as yet untestable and unfalsifiable, essentially putting consciousness outside science.

Orch OR is based on deeper level quantum vibrations in microtubules inside neurons, quantum vibrations which occur in the fine scale structure of spacetime geometry. Orch OR provides a bridge between the two approaches, and an opportunity to treat mental disorders by tuning microtubule quantum vibrations

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