Quantum Computation in Brain Microtubules? The Penrose-Hameroff 'Orch OR' Model of Consciousness [and Discussion]
Author(s): Stuart Hameroff and P. Marcer
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Quantum computation in brain microtubules? The Penrose–Hameroff 'Orch OR' model of consciousness

By Stuart Hameroff

Departments of Anesthesiology and Psychology, The University of Arizona, Tucson, AZ 85724, USA

Potential features of quantum computation could explain enigmatic aspects of consciousness. The Penrose–Hameroff model (orchestrated objective reduction: 'Orch OR') suggests that quantum superposition and a form of quantum computation occur in microtubules—cylindrical protein lattices of the cell cytoskeleton within the brain's neurons. Microtubules couple to and regulate neural-level synaptic functions, and they may be ideal quantum computers because of dynamical lattice structure, quantum-level subunit states and intermittent isolation from environmental interactions. In addition to its biological setting, the Orch OR proposal differs in an essential way from technologically envisioned quantum computers in which collapse, or reduction to classical output states, is caused by environmental decoherence (hence introducing randomness). In the Orch OR proposal, reduction of microtubule quantum superposition to classical output states occurs by an objective factor—Roger Penrose's quantum gravity threshold stemming from instability in Planck-scale separations (superpositions) in spacetime geometry. Output states following Penrose's objective reduction are neither totally deterministic nor random, but influenced by a non-computable factor ingrained in fundamental spacetime. Taking a modern panpsychist view in which protoconscious experience and Platonic values are embedded in Planck-scale spin networks, the Orch OR model portrays consciousness as brain activities linked to fundamental ripples in spacetime geometry.

Keywords: consciousness; quantum computation; objective reduction; orchestrated objective reduction (Orch OR); microtubules; brain

1. Quantum computation and consciousness

Proposals for quantum computation rely on superposed states implementing multiple computations simultaneously, in parallel, according to quantum linear superposition (see, for example, Benioff 1982; Feynman 1986; Deutsch 1985; Deutsch & Josza 1992). In principle, quantum computation is capable of specific applications beyond the reach of classical computing (see, for example, Shor 1994). A number of technological systems aimed at realizing these proposals have been suggested and are being evaluated as possible substrates for quantum computers (e.g. trapped ions, electron spins, quantum dots, nuclear spins, etc. (see table 1, Bennett (1995) and Barenco (1996))). The main obstacle to realization of quantum computation is the problem of interfacing to the system (input, output) while also protecting the quantum state from environmental decoherence. If this problem can be overcome, then present day classical computers may evolve into quantum computers.

The workings of the human mind have been historically described as metaphors of contemporary information technology. In ancient Greece memory was like a 'seal ring in wax' and in the 19th century the mind was seen as a telegraph switching circuit. In this century the classical computer has been the dominant metaphor for the brain's activities. If quantum computation becomes a technological reality, consciousness may inevitably be seen as some form of quantum computation. Indeed enigmatic features of consciousness have already led to proposals for quantum computation in the brain.

Conventional explanations portray consciousness as an emergent property of classical computer-like activities in the brain's neural networks (e.g. functionalism, reductionism, physicalism, materialism, computationalism (Churchland 1986; Dennett 1991; Churchland & Sejnowski 1992)). The current leading candidate for a computer-like 'neural correlate' of consciousness involves neuronal circuits oscillating synchronously in the thalamus and cerebral cortex. Higher-frequency oscillations (collectively known as 'coherent 40 Hz') are suggested to mediate temporal binding of conscious experience (see, for example, Singer *et al.* 1990; Crick & Koch 1990; Joliot *et al.* 1994; Gray 1998). The proposals vary, for example as to whether coherence originates in the thalamus or resonates in cortical networks, but 'thalamo-cortical 40 Hz' stands as a prevalent view of the neural-level substrate for consciousness.

But how do neural firings lead to thoughts and feelings? Conventional ('functionalist') approaches fall short on the mind's enigmatic features. These include (1) the nature of subjective experience, or qualia, our 'inner life' (see, for example, Nagel 1974; Chalmers 1996); (2) 'binding' of spatially distributed brain activities into unitary objects in vision and a coherent sense of 'self'; (3) transition from preconscious processing to consciousness; (4) non-computability (Penrose 1989, 1994, 1997); and (5) free will.

Functionalist approaches generally assume that conscious experience appears as a novel property at a critical level of computational complexity. On the surface this would seem to deal with issues (1) and (3); however, a conscious threshold has neither been identified nor predicted, and there are no apparent differences in electrophysiological activities between non-conscious and conscious activity. Regarding the nature of experience (why we are not unfeeling 'zombies'), functionalism offers no testable predictions. Problem (2) of 'binding' in vision and self is often attributed by functionalists to temporal correlation (e.g. coherent 40 Hz), but it is unclear why temporal correlation *per se* should bind experience without an explanation of experience. As functionalism is based on deterministic computation, it is also unable to account for Penrose's proposed non-computability (4), or free will (5). Something may be missing.

To address these issues, various proposals have been suggested in which macroscopic quantum phenomena are connected to the brain's known neural activity. For the problem of unitary binding, Marshall (1989) suggested that coherent quantum states known as Bose–Einstein condensation occurred among neural proteins (cf. Penrose 1987; Bohm & Hiley 1993; Jibu & Yasue 1995). Preconscious-to-conscious transitions were identified by Stapp (1993) with collapse of a quantum wave function in presynaptic axon terminals (cf. Beck & Eccles 1992). In another proposal, protein assemblies called microtubules within the brain's neurons are viewed as self-organizing quantum computers ('orchestrated objective reduction—Orch OR': see, for example, Penrose & Hameroff 1995; Hameroff & Penrose 1996*a*, *b*; cf. Hameroff 1997, 1998*a*–*d*).

At first glance the possibility of macroscopic quantum states in biological systems seems unlikely, appearing to require either extreme cold (to avoid thermal noise) or laser-like energetic pumping to achieve coherent states. And as in technological proposals, perfect isolation of the quantum state from the environment (and/or quantum error correction codes) would be required while the system must also somehow communicate with the external world. Living cells including the brain's neurons seem unsuitably warm and wet for delicate quantum states which would seem susceptible to thermal noise and environmental decoherence. However, specific conditions supporting quantum states in microtubules may have evolved (see § 3).

In addition to its biological setting, the Orch OR proposal differs significantly in another regard from technologically envisioned quantum computers. The latter would arrive at output states through reduction ('collapse') of quantum superposition to classical states by environmental decoherence—the quantum state would be interrupted by the external world. The outcome states in technological quantum computers would therefore reflect deterministic processing influenced at reduction by some probabilistic randomness.

On the other hand, Penrose (1989, 1994, 1996) has proposed that isolated quantum systems which avoid environmental decoherence will eventually reduce nonetheless due to an objective threshold ('objective reduction' (OR)) related to an intrinsic feature of fundamental spacetime geometry (see below). Unlike the situation following environmental decoherence, outcome states which reduce due to Penrose's objective reduction are selected by a non-computable influence on the deterministic pre-reduction quantum computation. Non-computability implies a non-algorithmic process which is neither deterministic nor random, a property which Penrose (e.g. 1997) also attributes to conscious thought and understanding. This clue suggests that quantum computation with objective reduction may somehow be involved in consciousness.

The objective factor in OR is an intrinsic feature of spacetime itself (quantum gravity). Penrose begins from general relativity with the notion that mass is equivalent to spacetime curvature. He concludes that quantum superposition—actual separation (displacement) of mass from itself—is equivalent to simultaneous spacetime curvatures in opposite directions, causing 'bubbles', or separations in fundamental reality (figure 1). Penrose views the bubbles as unstable, with a critical objective degree of separation resulting in instantaneous reduction to classical unseparated states. Objective reductions are therefore events which reconfigure the fine scale of spacetime geometry. As described in § 5, modern pan-psychists attribute protoconscious experience to a fundamental property of physical reality. If so, consciousness might involve self-organizing OR events rippling through an experiential medium.

Could OR events be occurring in the brain? If so, they would be expected to coincide with known neurophysiological processes with recognized time-scales. The critical degree of spacetime separation causing Penrose's objective reduction is related to quantum gravity by the uncertainty principle

$$E = \hbar/T,$$

where E is the gravitational self-energy of the superposed mass (displaced *from itself* by, for example, the diameter of its atomic nuclei), $\hbar$ is Planck's constant over 2π and T is the coherence time until OR self-collapse. The size of an isolated superposed system is thus inversely related to the length of time until self-collapse.

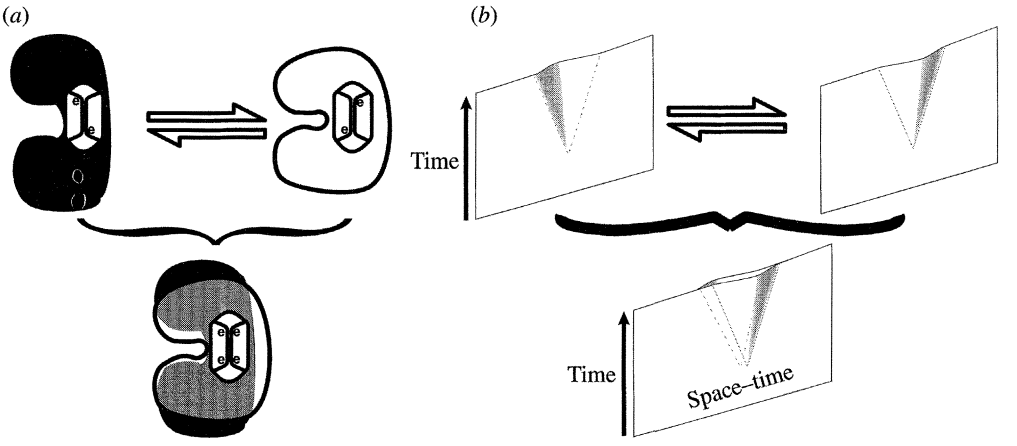

Figure 1. (*a*) Schematized protein (tubulin) capable of switching between two conformational states governed by London force interactions in a hydrophobic pocket. (Tubulin may actually have multiple, smaller, collectively governing hydrophobic pockets and more than two possible states. For simplicity a one-pocket two-state protein is illustrated). Top: protein switching between two conformational states coupled to localization of paired electrons (induced dipoles) within a hydrophobic pocket (see § 2). Bottom: quantum superposition (simultaneous existence in two distinct states) of the electron pair and protein conformation. (*b*) Four-dimensional spacetime may be schematically represented by one dimension of space and one dimension of time: a two-dimensional 'spacetime sheet'. Mass is curvature in spacetime, and the two spacetime curvatures in the top of the figure represent mass (e.g. a tubulin protein) in two different locations or conformations, respectively. Mass in quantum superposition (mass separated from itself) is simultaneous spacetime curvature in opposite directions, a separation, or bubble in spacetime. At a critical degree of separation, the system becomes unstable and must select either one state or the other (from Penrose (1994), p. 338).

Large superposed systems (e.g. Schrödinger's mythical 1 kg cat) would self-collapse (OR) in only 10^{-37} s; an isolated superposed atom would undergo OR only after 10^6 years! If OR events occur in the brain coupled to known neurophysiology, then we can estimate that T for conscious OR events may be in a range from 10 to 500 ms. This range covers neurophysiological activities such as 25 ms 'coherent 40 Hz', 100 ms EEG rhythms and Libet's (1979) 500 ms sensory perceptions. OR events coupled to roughly 100 ms activities would require a few nanograms of superposed mass.

Biological materials best suited for quantum computation and objective reduction are proteins, particularly assemblies of proteins called microtubules.

2. Proteins and qubits

Proteins are versatile macromolecules which perform a variety of functions by changing their conformational shape. Such functions include muscle movement, membrane firing via openings and closings of protein ion channels, molecular binding, enzyme catalysis, metabolism, movement and phase of cytoplasm. Life is organized by changes in protein shape.

Individual proteins are synthesized as linear chains of hundreds of amino acids which 'fold' into three-dimensional conformation. The precise manner of folding for each protein depends on attractive and repellent forces among its various amino acid

side groups, and a current view is that many possible intermediate conformations precede the final one (Baldwin 1994). Although complete linear sequences of amino acid chains are known for many proteins, predicting their final three-dimensional folded shape using computer simulation has proven difficult if not impossible. This conundrum is known as the 'protein folding problem' and so far appears to be 'NP complete': the answer can be calculated in theory, but the space and time required of any classical computer is prohibitive. Perhaps protein folding is a quantum computation (L. Crowell, personal communication)?

The main driving force in protein folding occurs as uncharged non-polar groups of particular amino acids join together and avoid water. Repelled by solvent water, 'hydrophobic' non-polar groups attract each other (by van der Waals forces—see below) and bury themselves within the protein interior. As a result, intraprotein hydrophobic pockets occur, composed of side groups of non-polar (but polarizable) amino acids such as leucine, isoleucine, phenylalanine, tryptophan, tyrosine and valine. Volumes of the pockets (*ca.* 400 Å^3, or 0.4 nm^3) are roughly $\frac{1}{30}$–$\frac{1}{250}$ the total volume of a single protein, and their physical solvent characteristics most closely resemble olive oil.

Though small, hydrophobic pockets may be critical to protein function. For example, anaesthetic gas molecules which reversibly ablate consciousness exert their effects in hydrophobic pockets of neural proteins (see, for example, Franks & Lieb 1982, 1985). Anaesthetics bind in hydrophobic pockets by weak physical interactions called London dispersion forces, a type of van der Waals force. Why are these weak localized interactions so important to protein function and consciousness?

Proteins in a living state are dynamical, and only marginally stable. A protein of 100 amino acids is stable against denaturation by only *ca.* 40 kJ mol^{-1}, whereas thousands of kJ mol^{-1} are available in a protein from side-group interactions including van der Waals forces. Consequently protein conformation is a 'delicate balance among powerful countervailing forces' (Voet & Voet 1995).

Transitions in proteins occur at many time- and size-scales. For example, small amino acid side chains move in the pico–femtosecond time-scale (10^{-12}–10^{-15} s), and conformational transitions in which proteins move globally and upon which protein function generally depends occur in the nanosecond (10^{-9} s) to 10 picosecond (10^{-11} s) time-scale (Karplus & McCammon 1983). These global changes (e.g. as schematically represented in figure 1*a*) appear to involve collective actions of various intraprotein activities (e.g. hydrogen bond rearrangements, dipole oscillations, van der Waals forces).

The types of forces operating among amino acid side groups within a protein include charged interactions such as ionic forces and hydrogen bonds, as well as interactions between dipoles—separated charges in electrically neutral groups. Dipole–dipole interactions are known as van der Waals forces and include three types: (1) permanent dipole–permanent dipole; (2) permanent dipole–induced dipole; and (3) induced dipole–induced dipole. Induced dipole–induced dipole interactions are the weakest but most purely non-polar forces. They are known as London dispersion forces, and although quite delicate (40 times weaker than hydrogen bonds) are numerous and influential. The London force attraction between any two atoms is usually less than a few kilojoules; however, thousands occur in each protein. As other forces cancel out, London forces in hydrophobic pockets can govern protein conformational states.

London forces ensue from the fact that atoms and molecules which are electrically neutral and spherically symmetrical nevertheless have instantaneous electric dipoles due to instantaneous asymmetry in their electron distribution. The electric field from each fluctuating dipole couples to others in electron clouds of adjacent non-polar amino acid side groups. Due to inherent uncertainty in electron localization, London forces which govern protein conformation are quantum effects which apparently couple to 'zero-point fluctuations' of the quantum vacuum (London 1937; Milloni 1994).

Quantum-level dipole oscillations within hydrophobic pockets were proposed by Fröhlich (1968) to regulate protein conformation, and Conrad (1994) suggested proteins use quantum superposition of various possible conformations before one is selected. Roitberg *et al.* (1995) showed functional protein vibrations which depend on quantum effects centred in two hydrophobic phenylalanine residues, and Tejada *et al.* (1996) have evidence to suggest quantum coherent states exist in the protein ferritin. Could proteins be using quantum superposition ('qubits') in determining their conformational states (bits)†?

The possible situation may be characterized as in figure 1*a* using the microtubule protein tubulin as an example. Tubulins are peanut-shaped dimers with two connected monomers and they undergo several types of conformational changes (see, for example, Cianci *et al.* 1986). For example, one monomer can shift 30° from the tubulin dimer's vertical axis (Melki *et al.* 1989; cf. Yagi *et al.* 1994). At the top of figure 1*a* a tubulin protein switches between two such states, governed by hydrophobic pocket electron pairs coupled by London forces. (Tubulin may actually have several hydrophobic pockets and occupy more than two states; however, for simplicity we consider one pocket and two states per protein.) The two possible states in the top of figure 1*a* may be viewed as representing one bit of information. If, however, the hydrophobic pocket electron pair is superposed (figure 1*a*, bottom), then protein conformation (if isolated from the external environment) is also superposed and exists in both states simultaneously ('qubit'). A properly configured and isolated array of interactive protein qubits could constitute a quantum computer.

3. Microtubules

Interiors of living cells are functionally organized by webs of protein polymers—the cytoskeleton (figure 2). Major components of the cytoskeleton are microtubules, self-assembling hollow crystalline cylinders whose walls are hexagonal lattices of subunit proteins known as tubulin (figure 3). Microtubules are essential for a variety of biological functions including cell movement, cell division (mitosis) and establishment and maintenance of cell form and function. In neurons, microtubules self-assemble to extend axons and dendrites and form synaptic connections; microtubules then help maintain and regulate synaptic strengths responsible for learning and cognitive functions. (For a more complete description of the role of microtubules and other cytoskeletal structures in cognitive functions, see Dayhoff *et al.* (1994), Hameroff & Penrose (1996*a*) and Hameroff (1994).) While microtubules have traditionally

† If so, the mechanism of anaesthetics may involve disruption of electron mobility required for quantum superposition in hydrophobic pockets of neural proteins. Experimental evidence has shown that anaesthetics inhibit mobility of free electrons in a non-biological corona discharge (Hameroff & Watt 1983).

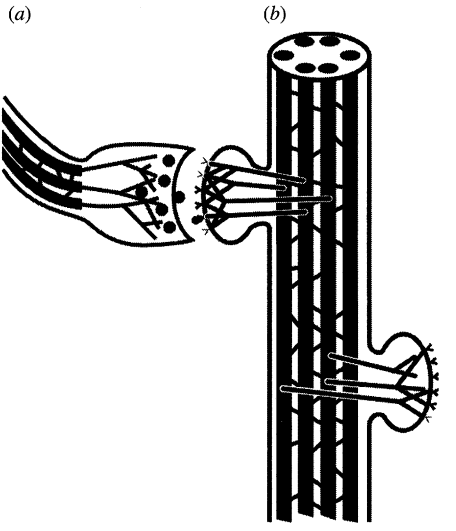

Figure 2. Schematic of neural synapse showing cytoskeletal structures within two neurons. (*a*) Presynaptic axon terminal releases neurotransmitter vesicles (spheres) into the synaptic cleft. Thick rod-like structures within the axon are microtubules; thinner filaments (e.g. synapsin) facilitate vesicle release. (*b*) Dendrite on post-synaptic neuron with two dendritic spines. Microtubules in main dendrite are interconnected by microtubule-associated proteins. Other cytoskeletal structures (fodrin, actin filaments, etc.) connect membrane receptors to microtubules (based on Hirokawa (1991)).

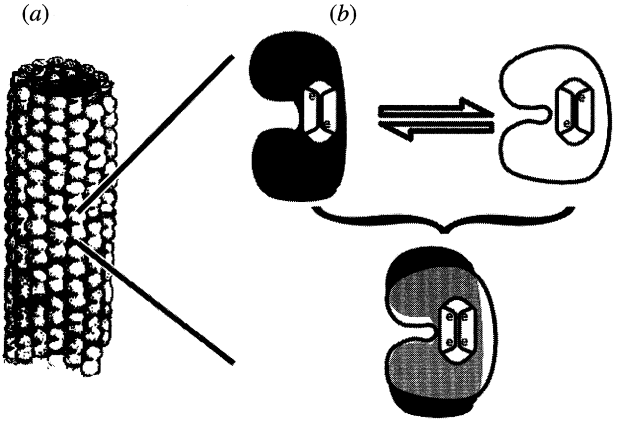

Figure 3. (*a*) Microtubule (MT) structure: a hollow tube 25 nm in diameter, consisting of 13 columns of tubulin dimers arranged in a skewed hexagonal lattice (Penrose 1994). (*b*) Top: each tubulin molecule may switch between two (or more) conformations, coupled to London forces in a hydrophobic pocket; bottom: each tubulin can also exist in quantum superposition of both conformational states (figure 1*a*) (cf. Hameroff & Penrose 1996*b*).

been considered as purely structural components, recent evidence has demonstrated mechanical signalling and communication functions (Glanz 1997; Maniotis *et al.* 1997*a*, *b*; Vernon & Wooley 1995). Microtubules interact with membrane structures

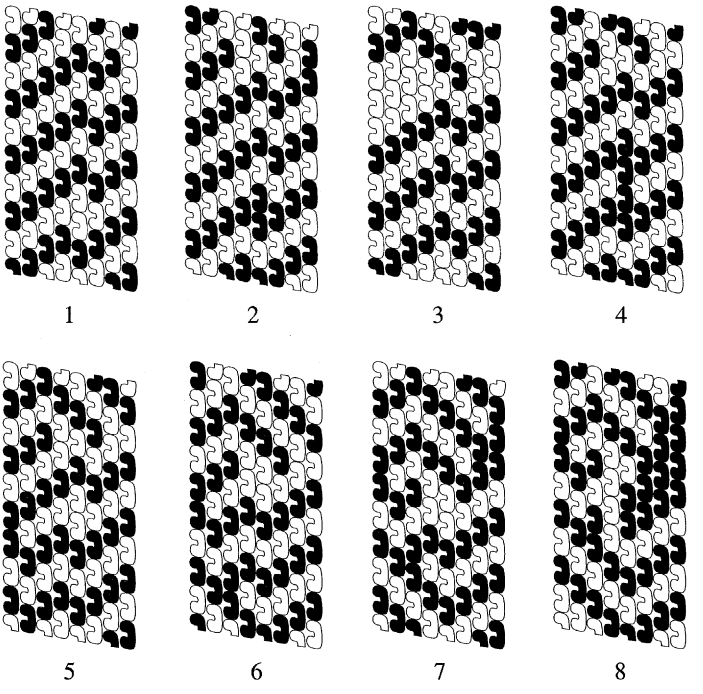

Figure 4. Microtubule automaton simulation (from Rasmussen *et al.* 1990). Black and white tubulins correspond to black and white states shown in figures 1*a* and 3. Eight nanosecond time-steps of a segment of one microtubule are shown in 'classical computing' mode in which conformational states of tubulins are determined by dipole–dipole coupling between each tubulin and its six (asymmetrical) lattice neighbours calculated by $f_{\text{net}} = (e^2/4\pi\varepsilon)\sum_{i=1}^{6}(y_i/r_i^3)$, where y_i and r_i are inter-tubulin distances, e is the electron charge, and ε is the average protein permittivity. Conformational states form patterns which move, evolve, interact and lead to the emergence of new patterns.

and activities by linking proteins (e.g. fodrin, ankyrin) and 'second-messenger' chemical signals.

How could microtubules implement classical information processing? Theoretical models propose that microtubule subunit tubulins undergo coherent excitations, for example, in the gigahertz range by a mechanism suggested by Fröhlich ('pumped phonons') (Fröhlich 1968, 1970, 1975; cf. Penrose & Onsager 1956)†. Fröhlich excitations of tubulin subunits within microtubules have been suggested to support computation and information processing (see, for example, Hameroff & Watt 1982; Rasmussen *et al.* 1990). The coherent excitations are proposed to 'clock' computational transitions occurring among neighbouring tubulins acting as 'cells' as in molecular-scale 'cellular automata'. Dipole couplings among neighbouring tubulins in the microtubule lattice act as 'transition rules' for simulated *microtubule automata*

† Experimental evidence for Fröhlich-like coherent excitations in biological systems includes observation of gigahertz-range phonons in proteins (Genberg *et al.* 1991), sharp-resonant non-thermal effects of microwave irradiation on living cells (Grundler & Keilman 1983), gigahertz-induced activation of microtubule pinocytosis in rat brain (Neubauer *et al.* 1990) and laser Raman spectroscopy detection of Fröhlich frequency energy in biomolecular systems (Genzel *et al.* 1983; Vos *et al.* 1992).

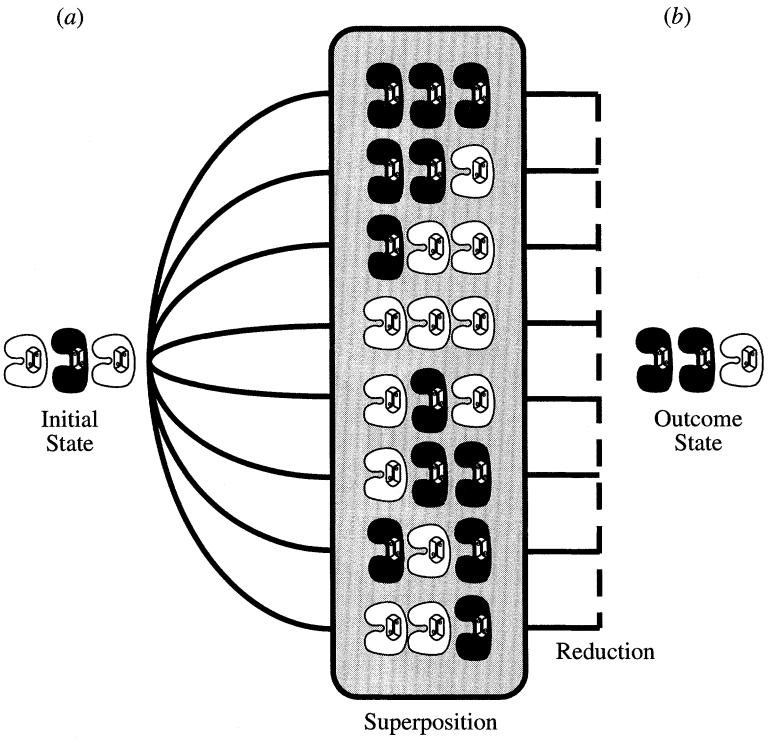

Figure 5. Schematic of quantum computation of three tubulins which begin (*a*) in initial classical states, then enter isolated quantum superposition in which all possible states coexist. After reduction, one particular classical outcome state is chosen (*b*).

exhibiting information processing, transmission and learning (figure 4) (Rasmussen *et al.* 1990).

Classical microtubule automata switching in the nanosecond scale offer a potentially huge increase in the brain's computational capacity. Conventional approaches focus on synaptic switching (roughly 10^{11} brain neurons, 10^3 synapses per neuron, switching in the ms range of 10^3 operations per second) and predict about 10^{17} bit states per second for a human brain (see, for example, Moravec 1987). However, as biological cells typically each contain approximately 10^7 tubulins (Yu & Bass 1994), nanosecond switching in microtubule automata predicts roughly 10^{16} operations per second per neuron. This capacity could account for the adaptive behaviours of single-cell organisms like *Paramecium*, for example, who elegantly swim, avoid obstacles and find food and mates without the benefit of a nervous system or synapses. As the human brain contains about 10^{11} neurons, nanosecond microtubule automata offer about 10^{27} brain operations per second.

However, even a vast increase in computational complexity will not by itself address the difficult issues related to consciousness. Quantum coherent states and quantum computation with objective reduction (Orch OR) could possibly do so. Figure 5 illustrates the general idea for quantum computation with tubulins: three tubulins are shown in initial states, in isolated superposition of possible states during which quantum computation occurs and in single post-reduction outcome states. Figure 6

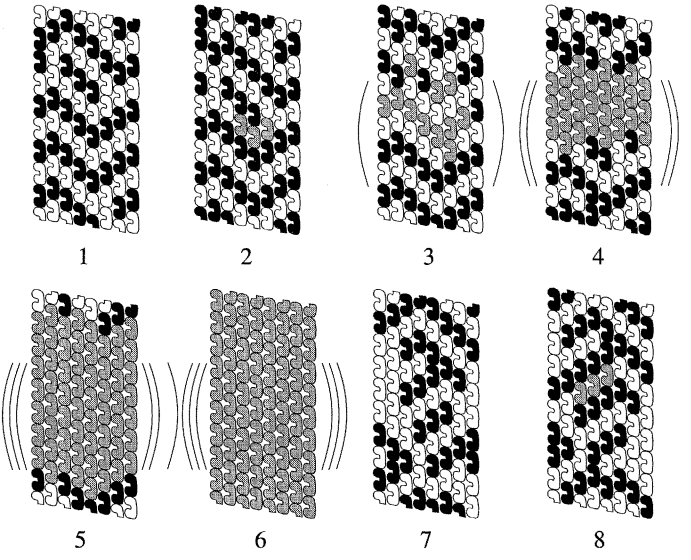

Figure 6. Microtubule automaton sequence simulation in which classical computing (step 1) leads to emergence of quantum coherent superposition (steps 2–6) in certain (grey) tubulins due to pattern resonance. Step 6 (in coherence with other microtubule tubulins) meets critical threshold related to quantum gravity for self-collapse (Orch OR). Consciousness (Orch OR) occurs in the transition from step 6 to 7. Step 7 represents the eigenstate of mass distribution of the collapse which evolves by classical computing automata to regulate neural function. Quantum coherence begins to re-emerge in step 8.

shows microtubule automata entering the quantum computation mode (grey) and meeting objective reduction threshold (between steps 6 and 7) for self-collapse to non-computably chosen outcome states. As described in figure 7, pre-reduction quantum computation is suggested to correlate with preconscious processing, and the objective reduction process itself to a conscious moment. A series of such moments can give rise to a stream of consciousness (see § 5 for a more complete description).

Macroscopic quantum states in brain microtubules would have to somehow avoid environmental decoherence and still communicate with the environment. Nature may have solved this problem with alternating phases of isolation and communication.

Microtubules and other cytoskeletal components are embedded in cytoplasm which exists in alternating phases of (1) 'sol' (solution, liquid); and (2) 'gel' (gelatinous, solid). Among the most primitive of biological activities, 'sol–gel transformations' within neurons and other living cells are caused by assembly and disassembly of cytoskeletal actin (e.g. regulated by calcium ions through the protein calmodulin, in turn regulated by microtubules). Sol–gel transformations are essential in basic cellular activities such as ('amoeboid') movement, growth and synaptic formation and neurotransmitter vesicle release (Miyamoto 1995; Muallem *et al.* 1995). Transitions can occur rapidly (e.g. 40 sol–gel cycles per second), and some actin gels can be quite solid, and withstand deformation without transmitted response (Wachsstock *et al.* 1994). Cyclical encasement of microtubules by actin gels may thus be an ideal quantum isolation mechanism (figure 8)†. A biphasic cycle of microtubule computing

† An additional mechanism may also shield microtubules. Dan Sacket at the National Institutes of

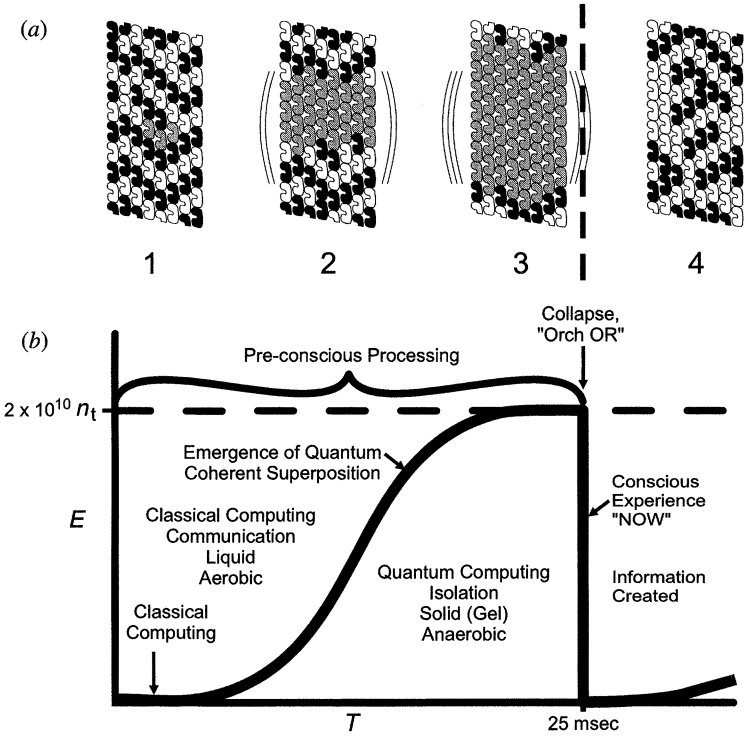

Figure 7. An Orch OR event. (*a*) Microtubule simulation in which classical computing (step 1) leads to emergence of quantum coherent superposition (and quantum computing (steps 2, 3)) in certain (grey) tubulins. Step 3 (in coherence with other microtubule tubulins) meets critical threshold related to quantum gravity for self-collapse (Orch OR). A conscious event (Orch OR) occurs in the step 3 to 4 transition. Tubulin states in step 4 are non-computably chosen in the collapse, and evolve by classical computing to regulate neural function. (*b*) Schematic graph of proposed quantum coherence (number of tubulins) emerging versus time in microtubules. Area under curve connects superposed mass energy E with collapse time T in accordance with $E = \hbar/T$. E may be expressed as N_t, the number of tubulins whose mass separation (and separation of underlying spacetime) for time T will self-collapse. For $T = 25$ ms (e.g. 40 Hz oscillations), $N_t = 2 \times 10^{10}$ tubulins.

is thus suggested: (1) a 'sol' liquid communicative phase of classical computation; and (2) a 'gel' solid-state isolated quantum computing phase.

Key quantum events may also be shielded either in hollow microtubule cores or

Health has shown that microtubules are surrounded by a pH-dependent condensed phase of charge and counter ions which can protect them from thermal noise. The phase is produced by the C-terminal end of the amino acid chain which comprises tubulin and which protrudes externally with a surplus of eight negative charges. Cations (calcium, magnesium, etc.) balance the negative charges producing a plasma-like isolation of sufficient 'Bjerrum length' (*ca.* 0.7 nm) to defeat kT, the energy of thermal background. The pH dependence may explain the evanescent nature of the 'clear zone' surrounding microtubules (Stebbings & Hunt 1982).

Microtubules could also implement quantum error-correction codes. The structure of microtubules involves helical pitches which repeat at Fibonacci series periodicities of 3, 5, 8 and 13 rows. Error-correction mechanisms could propagate along these pathways, operating on qubits following longitudinal or other pathways.

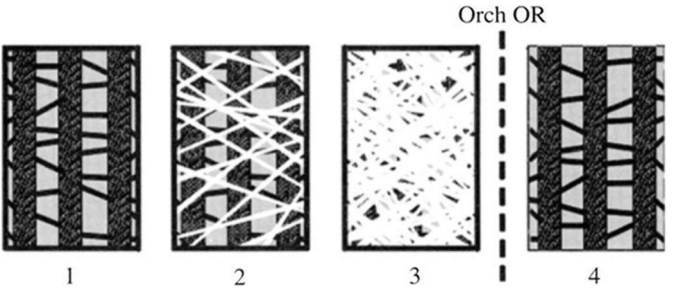

Figure 8. Three interconnected microtubules (1) enter phase of (white) actin gelation–quantum isolation (2–3) alternating with phase of solution–environmental communication (1,4). Cycles may occur rapidly, e.g. 25 ms intervals (40 Hz).

intraprotein hydrophobic pockets (where anaesthetic gases are known to act). Feasibility of quantum coherence in the internal cell environment is supported by the observation that quantum spins from biochemical radical pairs which become separated retain their correlation in cytoplasm (Walleczek 1995).

But if isolated cytoplasmic quantum states do occur within neuronal cells, could they traverse membranes and synapses to spread macroscopically throughout the brain? One possibility involves quantum tunnelling through gap junctions, primitive electrotonic windows between neurons and glia (figure 9). Cells interconnected by gap junctions form networks which fire synchronously, 'behaving like one giant neuron' (Kandel *et al.* 1991), and possibly accounting for synchronized neural activity such as coherent 40 Hz (Jibu 1990). Unlike chemical synapses which separate neural processes by 30–50 nm, gap junction separations are 3.5 nm, within range for quantum tunnelling. Widespread, but unevenly distributed, high levels of gap junctions appear in the thalamus and cortex (Micevych & Abelson 1991). Thalamo-cortical networks of gap junction-connected neurons with sol–gel phases coupled to synchronized 40 Hz activity could transiently isolate quantum states across large brain volumes.

4. Quantum computing with objective reduction: the Penrose–Hameroff Orch OR model

Full rationale and details of the Orch OR model are given in Penrose & Hameroff (1995) and Hameroff & Penrose (1996*a*, *b*). Key points are listed here.

(1) Conformational states of individual tubulin proteins in brain microtubules are sensitive to internal quantum events (e.g. London forces in hydrophobic pockets) and able to cooperatively interact with other tubulins in both classical and quantum computation (figures 3–6). Classical phase computation (microtubule automata) regulates chemical synapses and other neural membrane activities (e.g. figure 2).

(2) Quantum coherent superposition supporting quantum computation emerges among London forces in hydrophobic pockets of microtubule subunit tubulins (e.g. in a manner described by Fröhlich (1968, 1975)). In this phase, quantum computation among tubulins evolves linearly according to the Schrödinger equation (quantum microtubule automata). Actin gelation and a condensed charge phase surrounds, isolates, and insulates microtubules during the quantum phase.

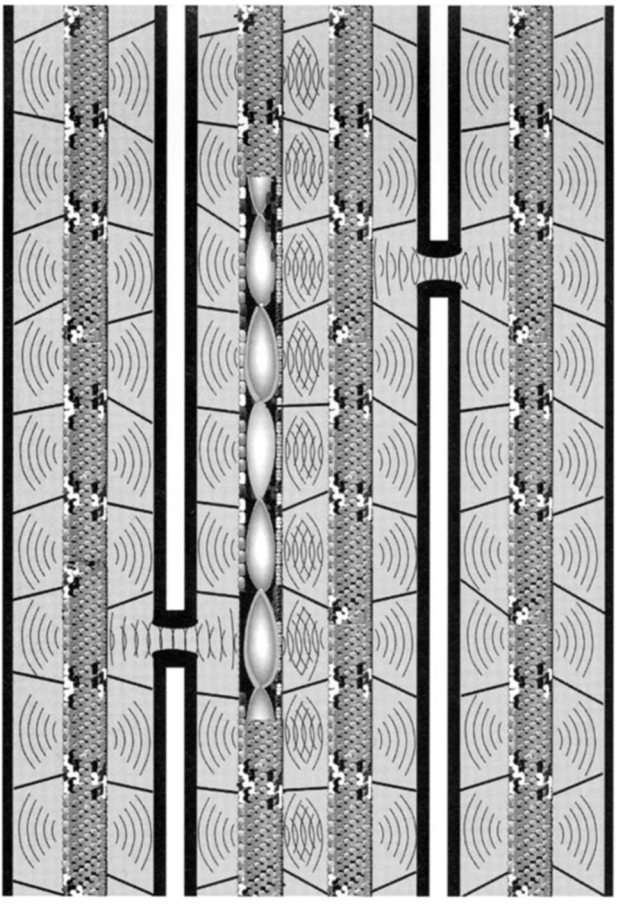

Figure 9. Schematic diagram of proposed quantum coherence in microtubules in three dendrites interconnected by tunnelling through gap junctions. Within each neuronal dendrite, microtubule-associated protein (MAP) attachments breach isolation and prevent quantum coherence; MAP attachment sites thus act as 'nodes' which tune and orchestrate quantum oscillations and set possibilities and probabilities for collapse outcomes (orchestrated objective reduction: Orch OR). Gap junctions may enable quantum tunnelling among dendrites in macroscopic quantum states.

(3) The proposed quantum superposition/computation phase in neural microtubules corresponds to preconscious (implicit) processing, which continues until the threshold for Penrose's objective reduction is reached. Objective reduction (OR)—a discrete event—then occurs (figures 5–7), and post-OR tubulin states (chosen noncomputably) proceed by classical microtubule automata to regulate synapses and other neural membrane activities. The events are suggested to be conscious (to have qualia, experience) for reasons that relate to a merger of modern physics and philosophical pan-experientialism (see § 5). A sequence of such events gives rise to a stream of consciousness.

(4) Microtubule quantum states link to those in other neurons and glia by tunnelling through gap junctions (or quantum coherent photons traversing membranes (Jibu & Yasue 1995; Jibu *et al.* 1994, 1996)). This spread enables macroscopic quan-

tum states in networks of gap junction-connected cells (neurons and glia) throughout large brain volumes (figure 9).

(5) Probabilities and possibilities for preconscious quantum superpositions are influenced by biological feedback including attachments of microtubule-associated proteins ('MAPs'), which tune and 'orchestrate' quantum oscillations (figure 9). We thus term the self-tuning OR process in microtubules' 'orchestrated' objective reduction—Orch OR.

(6) Orch OR events may be of variable intensity and duration of preconscious processing. Calculating from $E = \hbar/T$, for a preconscious processing time of, for example, $T = 25$ ms (thalamocortical 40 Hz), E is roughly the superposition/separation of 2×10^{10} tubulins. For $T = 100$ ms (alpha EEG), E would involve 5×10^9 tubulins. For $T = 500$ ms (e.g. shown by Libet *et al.* (1979) as a typical preconscious processing time for low-intensity stimuli), E is equivalent to 10^9 tubulins. Thus 2×10^{10} tubulins maintained in isolated quantum coherent superposition for 25 ms (or 5×10^9 tubulins for 100 ms, or 10^9 tubulins for 500 ms, etc.) will self-collapse (Orch OR) and elicit a conscious event.

(7) Each brain neuron is estimated to contain about 10^7 tubulins (Yu & Bass 1994). If, say, 10% of each neuron's tubulins became coherent, then Orch OR of tubulins within roughly 20 000 (gap junction-connected) neurons would be required for a 25 ms conscious event, 5000 neurons for a 100 ms event, or 1000 neurons for a 500 ms event, etc.

(8) Each instantaneous Orch OR event binds superposed information encoded in microtubules whose net displacement reaches threshold at a particular moment: a variety of different modes of information is thus bound into a 'now' event. As quantum state reductions are irreversible in time, cascades of Orch OR events present a forward flow of time and 'stream of consciousness'.

In the following section, applications of the Orch OR model to enigmatic issues of consciousness will be examined.

5. Orch OR and enigmatic features of consciousness

Five enigmatic features of consciousness were described in § 1: (1) the nature of subjective experience; (2) 'binding' in vision and sense of 'self'; (3) transition from preconscious processing to consciousness; (4) non-computability; and (5) free will. Can Orch OR address these issues?

The problem (1) of subjective experience is the most difficult. How does the brain produce 'qualia', raw feelings and sensations? There have always been two types of answers. Socrates argued that consciousness was created by the cerebrum, whereas Thales, Plotinus and other 'pan-psychists' saw conscious experience as a fundamental feature of reality.

Modern functionalists/computationalists generally follow Socrates: consciousness emerges from complexity in the brain's neural networks. However, others find this view alone unable to accommodate subjective experience, and are driven to embrace some form of pan-psychism, or pan-experientialism.

Following after ancient pan-psychists, Spinoza (1677) assigned rudimentary consciousness to all particles and objects, and Leibniz (1766) saw the universe as an infinite number of fundamental units ('monads'), each having a primitive psychological being. Whitehead (1929) was a process philosopher who saw the universe as

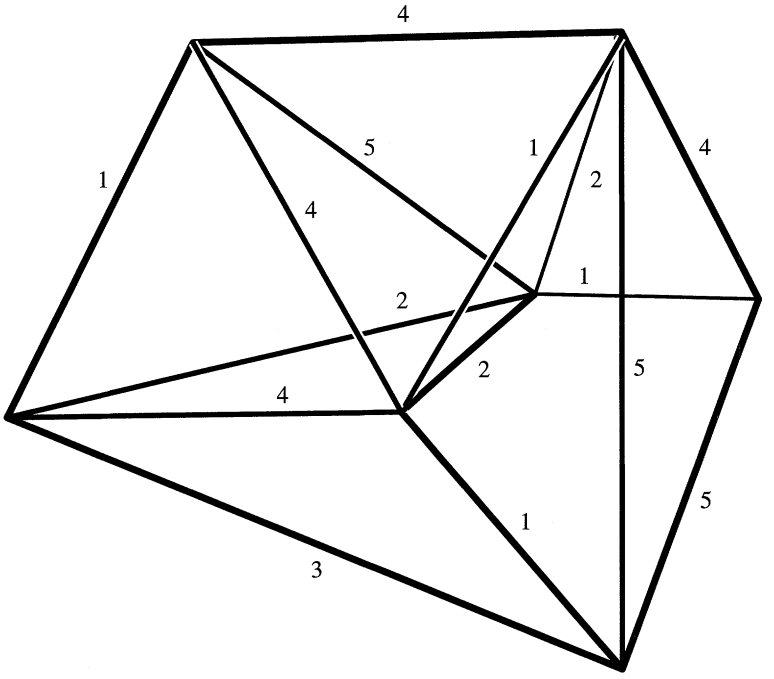

Figure 10. A spin network. Introduced by Penrose (1971) as a quantum-mechanical description of the geometry of space, spin networks describe a spectrum of discrete Planck-scale volumes and configurations (with permission from Smolin (1997) and Rovelli & Smolin (1995*a*, *b*)). Average length of each edge is the Planck length (10^{-33} cm). Numbers indicate quantum-mechanical spin along each edge. Each quantum state of spacetime is a particular spin network (Smolin 1997).

being comprised fundamentally of events. He described dynamic monads with spontaneity and creativity, interpreting them as mind-like entities of limited duration ('occasions of experience'). Each occasion, according to Whitehead, bears a quality akin to 'feeling' by virtue of occurring in a 'wider field of protoconscious experience'. Could this 'wider field' be the universe itself? Could protoconscious experience exist in empty space?

What is empty space? Democritus described empty space as a true void, whereas Aristotle saw a background 'plenum' filled with substance. Maxwell's 19th-century 'luminiferous ether' sided with Aristotle, but attempts to detect the ether failed and Einstein's special relativity agreed with Democritus: empty space was an absolute void. However, Einstein's general relativity with its curved space and distorted geometry reverted to a richly endowed plenum—the spacetime metric.

At very small scales spacetime is not smooth, but quantized. Granularity occurs at the incredibly small 'Planck scale' (10^{-33} cm, 10^{-43}s) which Penrose (1971) portrays as a dynamical spider-web of quantum spin networks (figure 10) (Rovelli & Smolin 1995*a*, *b*; Smolin 1997). Spin networks describe spectra of discrete Planck-scale volumes and configurations which dynamically evolve and define spacetime geometry. Planck-scale spin networks could provide Whitehead's basic field of protoconscious experience. Shimony (1993) has suggested Whitehead occasions are quantum state reductions. As described in § 1, Penrose's objective (quantum state) reductions are bubble-like separations and collapse in fundamental spacetime geometry extending

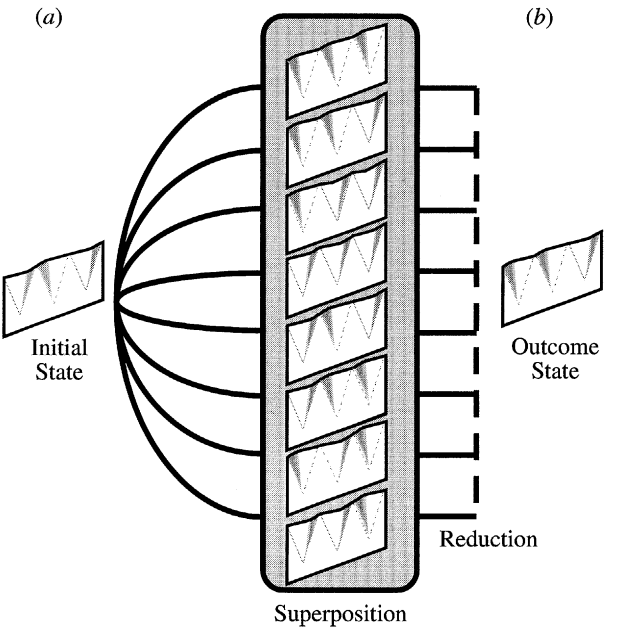

Figure 11. Schematic quantum computation in spacetime curvature for three mass distributions (e.g. tubulin conformations in figure 5) which begin (*a*) in initial classical states, then enter isolated quantum superposition in which all possible states coexist. After reduction, one particular classical outcome state is chosen (*b*).

downward to the level of spin networks. Figure 11 illustrates quantum superposition and objective reduction of spacetime geometry. Orch OR events could be Whitehead occasions of experience.

In a pan-psychist view consistent with modern physics, Planck-scale spin networks encode protoconscious ('fundamental') experience (qualia) as well as Platonic values. Particular configurations of quantum spin geometry convey particular varieties of protoconscious experience, meaning and aesthetics. The proposed Orch OR events occur in the brain, extending downward to processes in an experiential Planck-scale medium. The basic idea is that consciousness involves brain activities coupled to self-organizing ripples in fundamental reality.

How can near-infinitesimal protoconscious information link to macroscopic biology? As described in § 6, the Orch OR process may be an emergent phenomenon in quantum geometry mediated through London forces in hydrophobic pockets of tubulin and other proteins.

The second difficult issue related to consciousness is (2) binding, and it is potentially resolved by the unitary nature of quantum states (see, for example, Penrose 1987). Marshall (1989) suggested that binding was a feature of Bose–Einstein condensates among certain of the brain's neural proteins. In the Orch OR model, an instantaneous event binds superposed information whose net mass/spacetime displacement reaches threshold at a particular moment: different modes and time-scales of information are bound into a unitary 'now' event.

Problem (3) is the transition from preconscious processing to consciousness itself.

In Orch OR, preconscious processing is equivalent to the quantum superposition phase of quantum computation. Potential possibilities interact and then abruptly self-collapse, a slight quake in spacetime geometry. As quantum state reductions are irreversible, cascades of Orch OR events present a forward flow of subjective time and 'stream of consciousness'.

Quantum computation with objective reduction is potentially applicable to cognitive activities. Functions like face recognition and volitional choice may require a series of conscious events arriving at intermediate solutions. For the purpose of illustration consider single Orch OR events in these two types of cognitive activities (figure 12).

Imagine you briefly see a familiar woman's face. Is she Amy, Betty or Carol? Possibilities may superpose in a quantum computation. For example, during 25 ms of preconscious processing, quantum computation occurs with information (Amy, Betty, Carol) in the form of 'qubits'—superposed states of microtubule tubulin subunits within groups of neurons. As threshold for objective reduction is reached, an instantaneous conscious event occurs. The superposed tubulin qubits reduce to definite states, becoming bits. Now, you recognize that she is Carol! (an immense number of possibilities could be superposed in a human brain's 10^{19} tubulins).

In a volitional act possible choices may be superposed. Suppose, for example, you are selecting dinner from a menu. During preconscious processing, shrimp, sushi and pasta are superposed in a quantum computation. As threshold for objective reduction is reached, the quantum state reduces to a single classical state. A choice is made. You'll have sushi!

How does the choice actually occur? Can the selection criteria be described by a deterministic algorithm? These questions relate to problems (4), non-computability, and (5), free will.

The problem in understanding free will is that our actions seem neither totally deterministic nor random (probabilistic). What else is there in nature? As previously described, in OR (and Orch OR) the reduction outcomes are neither deterministic nor probabilistic, but 'non-computable'. The microtubule quantum superposition evolves linearly (analogous to a quantum computer) but is influenced at the instant of collapse by hidden non-local variables (quantum-mathematical logic inherent in fundamental spacetime geometry). The possible outcomes are limited, or probabilities set ('orchestrated'), by neurobiological feedback (in particular, MAPs (figure 9)). The precise outcome—our free-will actions—are chosen by effects of the hidden logic on the quantum system poised at the edge of objective reduction.

Consider a sailboat analogy for free will. A sailor sets the sail in a certain way; the direction the boat sails is determined by the action of the wind on the sail. Let's pretend the sailor is a non-conscious robot-zombie run by a quantum computer which is trained and programmed to sail. Setting and adjusting of the sail, sensing the wind and position and so forth are algorithmic and deterministic, and may be analogous to the preconscious quantum computing phase of Orch OR. The direction and intensity of the wind (seemingly capricious, or unpredictable) may be analogous to Planck-scale hidden non-local variables (e.g. 'Platonic' quantum-mathematical logic inherent in spacetime geometry). The choice, or outcome (the direction the boat sails, the point on shore that it lands upon) depends on the deterministic sail settings acted on repeatedly by the apparently unpredictable wind. Our 'free will' actions could be the net result of deterministic processes acted on by hidden quantum logic at

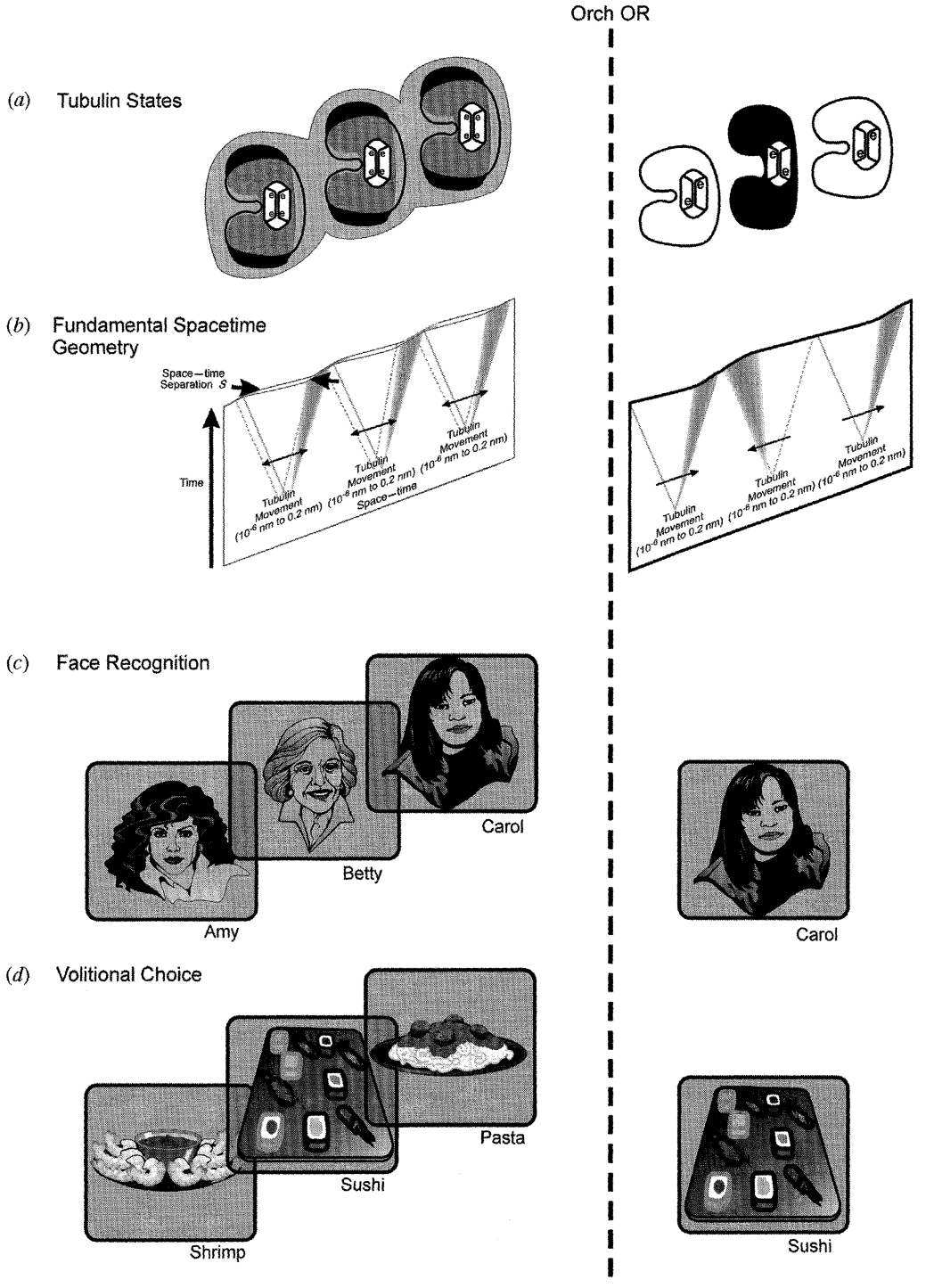

Figure 12. For description see opposite.

each Orch OR event. This can explain why we generally do things in an orderly, deterministic fashion, but occasionally our actions or thoughts are surprising, even to ourselves.

Biological quantum computation intrinsic to brain function such as the proposed Orch OR model can in principle address difficult issues related to consciousness.

6. Are microtubules quantum computers?

The idea of biological quantum computation connected to fundamental geometry seems far-fetched. The Planck length is 24 orders of magnitude smaller than the diameter of an atom. Approximately 10^{78} discrete Planck-scale volumes correspond to the space occupied by one protein, and 10^{105} such volumes to a brain. The energy of one proposed Orch OR (e.g. 25 ms) is only 10^{-28} J, or 10^{-10} eV, whereas the energy of thermal noise (kT) is much larger at 10^{-4} eV. How could near-infinitesimally small, weak and fast processes have macroscopic effects in biological systems? Orch OR may be viewed as a nonlinear phenomenon in which particular configurations of 10^{88} Planck-scale volumes emerge 40 times per second to influence protein conformation through delicately balanced London forces. Conditions supporting quantum states and primitive consciousness would favour survival and have naturally evolved (Hameroff 1998*b*).

In another paper in this volume, Tuszyński & Brown review the physics of microtubules and provide a critique of the Orch OR proposal. They raise several issues which are discussed in Appendix A.

Here similarities are sought between microtubules and technological proposals for quantum computation. A 'potentially realizable' quantum computer has been described by Lloyd (1993) as '... arrays of weakly coupled quantum systems. Computation is effected by ... a sequence of electromagnetic pulses that induce transitions between locally defined quantum states ... in a crystal lattice'.

In the Orch OR model, the microtubule assembly corresponds to Lloyd's crystal lattice. Rather than trapped ions or nuclear spins, quantum superposition is proposed to occur at the level of conformational states of tubulins, and the role of pulsed transitions played by coherent Fröhlich excitations.

The Orch OR proposal may be compared to technological schemes in terms of a 'figure of merit M' (table 1) (Barenco 1996; DiVincenzo 1995). M is the time T_{decohere} until decoherence divided by the time t_{elem} of each elementary operation, and gives the number of operations allowable per computational unit before decoherence. With t_{elem} of 10^9 s (Fröhlich frequency) and T_{decohere} of, for example, 100 ms (EEG alpha),

Figure 12. An Orch OR event (continued from figure 4). (*a*) (left), three tubulins in quantum superposition prior to 25 ms Orch OR. After reduction (right), particular classical states are selected. (*b*) Fundamental spacetime geometry view. Prior to Orch OR (left), spacetime corresponding with three superposed tubulins is separated as Planck-scale bubbles: curvatures in opposite directions. The Planck-scale spacetime separations S are very tiny in ordinary terms, but relatively large mass movements (e.g. hundreds of tubulin conformations, each moving from 10^{-6} to 0.2 nm) indeed have precisely such very tiny effects on the spacetime curvature. A critical degree of separation causes Orch OR and an abrupt selection of single curvatures (and a particular geometry of experience). (*c*) Cognitive facial recognition. A familiar face induces superposition (left) of three possible solutions (Amy, Betty, Carol) which 'collapse' to the correct answer Carol (right). (*d*) Cognitive volition. Three possible dinner selections (shrimp, sushi, pasta) are considered in superposition (left), and collapse via Orch OR to the choice of sushi (right).

Table 1. *Figure of merit M for different proposed quantum computing technologies and microtubules (modified from Barenco (1996) and DiVincenzo (1995))*

technology	t_{elem} (s)	T_{decohere} (s)	M^{a}
Mossbauer nucleus	10^{-19}	10^{-10}	10^{9}
electrons GaAs	10^{-13}	10^{-10}	10^{3}
electrons Au	10^{-14}	10^{-8}	10^{6}
trapped ions	10^{-14}	10^{-1}	10^{13}
optical cavities	10^{-14}	10^{-5}	10^{9}
electron spin	10^{-7}	10^{-3}	10^{4}
electron quantum dot	10^{-6}	10^{-3}	10^{3}
nuclear spin	10^{-3}	10^{4}	10^{7}
superconductor islands	10^{-9}	10^{3}	10^{6}
microtubule tubulins	10^{-9}	10^{-1}	10^{8}

[a]In 'units' of predecoherence operations per qubit.

the Orch OR model yields a respectable M of 10^8 operations per tubulin before a conscious event occurs.

According to the proposals put forth in the Orch OR model, microtubules seem to be well designed (perhaps ideally designed) quantum computers. If so, technological efforts can possibly mimic some of nature's design principles such as cylindrical lattice automata and alternating phases of isolation and communication. The massive parallelism and specific microtubule lattice geometry (e.g. helical patterns following the Fibonacci series) may also facilitate quantum error correction. However, technology will be hard-pressed to emulate objective reduction which, it is argued, is required for consciousness. Presently envisioned technological quantum computers will implement superposition of ions, electrons, nuclei or other small entities. To achieve objective reduction in a reasonable and useful time-scale, a fairly large superposed mass (i.e. nanograms) will be required. While such a task seems formidable, it is possible. Quantum computation with objective reduction may hold the only promise for conscious computers.

Regardless of whether or not the Orch OR proposal turns out to be correct (and unlike most theories of consciousness it is testable; Appendix B), it is the type of multilevel transdisciplinary approach needed to address the problem of consciousness.

Thanks to Roger Penrose, who does not necessarily endorse the newer proposals, Dave Cantrell for illustrations and Carol Ebbecke for expert assistance.

Appendix A. Reply to Tuszyński & Brown

In another article in this volume, Tuszyński & Brown review the physics of microtubules and give a critique of the Orch OR proposal. They raise several issues discussed here.

Gravitational effects should be entirely overshadowed by the remaining processes. The energy from an Orch OR event is indeed very small compared to thermal noise (kT) and would seemingly drown in an aqueous medium. Isolation/insulation mechanisms are thus required to shield microtubules from thermal noise or any type of environmental decoherence. The Orch OR model suggests that quantum-coherent

superposition occurs in microtubules which are immediately surrounded by an insulating charge condensation and encased (cyclically) in actin gelation (§ 3). Cyclical isolation allows for alternating phases of communication (input–output) and isolated quantum computation.

In addition to isolation, microtubule subunits (tubulins) must also be sensitive to quantum influences from other superposed tubulins and non-computable influences in Planck-scale geometry. In questioning the robustness of proposed quantum effects, Tuszyński & Brown ascribe the gravitational energy for a tubulin protein in Orch OR to be the attraction between two masses given by the standard Gm^2/r, where G is the gravitational constant, m is the mass of tubulin and r is the distance between the two masses which Tuszyński & Brown take to be the radius of tubulin. This would accurately describe the gravitational attraction between two adjacent tubulins (or tubulin monomers), and yields an appropriately small energy of 10^{-27} eV. However, the relevant energy in Orch OR is the gravitational self-energy E of a superposed mass m separated from itself by distance a, given (for complete separation) by $E = Gm^2/a$. In Hameroff & Penrose (1996) we calculated this energy for three cases: (1) partial separation of the entire protein by one-tenth its radius; (2) complete separation at the level of each protein's atomic nuclei ($a = 2.5$ fermi lengths); (3) complete separation at the level of each protein's nucleons ($a = 0.5$ fermi lengths). Of these, highest energies were for separation at the level of atomic nuclei, roughly 10^{-21} eV per tubulin (although separation at the level of, say, atoms or amino acids may yield higher energy). As roughly 2×10^{10} tubulins are involved in each proposed Orch OR event (e.g. for superpositions lasting 25 ms) the energy is in the order of roughly 10^{-10} eV, or 10^{-28} J, still extremely tiny (kT is about 10^{-4} eV). However, the 10^{-28} J energy emerges abruptly, e.g. within one Planck-time of 10^{-43} s. This may be equivalent to an instantaneous jab of 10^{13} W (J s^{-1}), roughly 1 kW per tubulin.

The size of the tubulin protein is probably too large to make quantum effects easily sustainable. Nanometre size proteins such as tubulin ($8 \times 4 \times 4$ nm^3) may be the optimal scale for a quantum/macroscopic interface (Watterson 1991; Conrad 1994). Smaller biomolecules lack causal efficacy of structural protein conformational changes responsible for a host of biological functions. Larger molecules would be insufficiently sensitive to quantum effects.

Conformational effects are expected to involve distances of 10 Å (1 nm), larger than those called for in the Orch OR model. The superposition separation distance (e.g. one atomic nucleus, 10^{-6} nm in the case cited) is indeed much smaller than conformational changes which may approach 1 nm. As described in § 2, proteins are relatively unstable, and their conformation is regulated through nonlinear 'quakes' mediated through quantum-level London forces.

Physiological temperature requirements make it extremely difficult to defend the use of the quantum regime due to the persistence of thermal noise. A biological quantum state must be isolated/insulated from thermal noise, a feature nature may have evolved in cytoplasmic actin gelation and condensed charged layers (§ 3). Some evidence supports biological quantum states (e.g. Tejada *et al.* 1996; Walleczek 1995). According to the Fröhlich mechanism, thermal energy in biological systems may condense to a coherent mode.

... microtubules are extremely sensitive to their environment ... we doubt that microtubules can be shielded. As described in § 3, nature may have solved the problem

of both isolation and communication by alternating cytoplasmic phases of solution ('sol', liquid, sensitive to environment, classical) and gelation ('gel', solid, shielded/insulated, quantum). Thus microtubules can be both sensitive to their environment ('sol' phase) and isolated/shielded ('gel' phase).

... two (or possibly more) conformational states of tubulin are separated by a sizable potential barrier which again requires an external stimulus (such as GTP hydrolysis) to overcome it. Tubulin has numerous possible conformations which can interchange without GTP hydrolysis (§ 2). The two-state tubulin model is a simplification. The structure of tubulin has recently been clarified (Nogales *et al.* 1998) so molecular simulations will soon be available.

... the 500 ms preconscious processing time may be directly related to the action potential travel time along the axon plus the refractory lag time in synaptic transmission rather than to the quantum collapse time. In the Orch OR model the 'quantum collapse time' T is chosen to match known neurophysiological time-intervals related to preconscious processes; the gravitational self-energy E and related mass may then be calculated. For example, we have used 25 ms (e.g. in coherent 40 Hz oscillations), 100 ms (e.g. EEG alpha rhythm) and 500 ms (e.g. Libet's preconscious threshold for low-intensity sensory stimuli).

If quantum superposition correlates with preconscious processing, then dendritic activities (more than axonal firings) are likely to be relevant to consciousness (e.g. Pribram 1991). Microtubules in dendrites are of mixed polarity (unlike those in axons), an arrangement conducive to cooperative computation.

Tuszyński & Brown raise valid objections; quantum states in a biological milieu appear at first glance to be unlikely. However, nature may have evolved specific conditions for isolation, thermal screening and amplification. Life itself may be a macroscopic quantum state.

Appendix B. Testable predictions of the Orch OR model

Here major assumptions (bold) and corresponding testable predictions (numbered) of the Orch OR model are listed.

Neuronal microtubules are directly necessary for consciousness.

(1) Synaptic sensitivity and plasticity correlate with cytoskeletal architecture/activities in both pre-synaptic and post-synaptic neuronal cytoplasm.

(2) Actions of psychoactive drugs including antidepressants involve neuronal microtubules.

(3) Neuronal microtubule-stabilizing/protecting drugs may prove useful in Alzheimer's disease, ischaemia and other conditions.

Microtubules communicate by cooperative dynamics of tubulin subunits.

(4) Laser spectroscopy (e.g. Vos *et al.* 1992) will demonstrate coherent gHz Fröhlich excitations in microtubules.

(5) Dynamic vibrational states in microtubule networks correlate with cellular activity.

(6) Stable patterns of microtubule/cytoskeletal networks (including neurofilaments) and intra-microtubule diversity of tubulin states correlate with memory and neural behaviour.

(7) Cortical dendrites contain largely 'A-lattice' microtubules (compared to 'B-lattice' microtubules, A-lattice microtubules are preferable for information processing (Tuszyński *et al.* 1995)).

Quantum coherence occurs in microtubules.

(8) Studies similar to the famous 'Aspect experiment' in physics (which verified non-local quantum correlations (Aspect *et al.* 1982)) will demonstrate quantum correlations between spatially separated microtubule subunit states on (a) the same microtubule; (b) different microtubules in the same neuron; and (c) microtubules in different neurons connected by gap junctions.

(9) Experiments with SQUIDs (superconducting quantum interference devices) such as those suggested by Leggett (1984) will detect phases of quantum coherence in microtubules.

(10) Coherent photons will be detected from microtubules.

Microtubule quantum coherence requires isolation by cycles of surrounding actin-gelation.

(11) Neuronal microtubules in cortical dendrites and other brain areas are intermittently surrounded by tightly cross-linked actin gels.

(12) Cycles of gelation and dissolution in neuronal cytoplasm occur concomitantly with membrane electrical activity (e.g. synchronized 40 Hz activities in dendrites).

(13) The sol–gel cycles surrounding microtubules are regulated by calcium ions released and reabsorbed by calmodulin associated with microtubules.

Macroscopic quantum coherence occurs among microtubules in hundreds/thousands of distributed neurons and glia linked by gap junctions.

(14) Electrotonic gap junctions link synchronously firing networks of cortical neurons and thalamocortical networks.

(15) Quantum tunnelling occurs across gap junctions.

(16) Quantum correlation occurs between microtubule subunit states in different neurons connected by gap junctions (the microtubule 'Aspect experiment' in different neurons).

The amount of neural tissue involved in a conscious event is inversely proportional to the event time by $E = \hbar/T$.

(17) The amount of neural mass involved in a particular cognitive task or conscious event (as measurable by near-future advances in brain imaging techniques) is inversely proportional to the preconscious time (e.g. visual perception, reaction times).

An isolated, unperturbed quantum system self-collapses according to $E = \hbar/T$.

(18) Isolated technological quantum superpositions will self-collapse according to $E = \hbar/T$. (Preliminary discussions of such experiments involving superposition of crystals have begun between Roger Penrose and Anton Zeilinger.)

Microtubule-based cilia/centriole structures are quantum optical devices.

(19) Microtubule-based cilia in rods and cones directly detect visual photons and connect with retinal glial cell microtubules via gap junctions.

A critical degree of cytoskeletal assembly, coinciding with the onset of rudimentary consciousness, had significant impact on the rate of evolution.

(20) Fossil records and comparison with present-day biology will show that organisms which emerged during the early Cambrian period with onset roughly 540 million years ago had critical degrees of microtubule–cytoskeletal size, complexity and capability for quantum isolation (e.g. tight actin gels, gap junctions (see Hameroff 1998*b*)).

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Discussion

P. MARCER (*BCS Cybernetic Machine Group, Keynsham, UK*). I welcome the Penrose–Hameroff hypothesis concerning microtubules as candidate natural systems possessing both classical and quantum computational modes. This is a testable hypothesis which should not be dismissed out of hand at this very early stage of understanding of the nature of quantum computational systems.

S. HAMEROFF. Naturally, I agree. Let me reiterate my belief that, even if Orch OR turns out to be incorrect, it is the type of multidisciplinary approach spanning physics, biology and philosophy that will be required to understand consciousness. Technological efforts toward quantum computation may be well served by studying the fine details of brain microtubules.