Orchestrated Objective Reduction of Quantum Coherence in Brain Microtubules: The "Orch OR" Model for Consciousness

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ABSTRACT

Features of consciousness difficult to understand in terms of conventional neuroscience have evoked application of quantum theory, which describes the fundamental behavior of matter and energy. In this paper we propose that aspects of quantum theory (e.g. quantum coherence) and of a newly proposed physical phenomenon of quantum wave function "self-collapse"(objective reduction: **OR** -Penrose, 1994) are essential for consciousness, and occur in cytoskeletal microtubules and other structures within each of the brain's neurons. The particular characteristics of microtubules suitable for quantum effects include their crystal-like lattice structure, hollow inner core, organization of cell function and capacity for information processing. We envisage that conformational states of microtubule subunits (tubulins) are coupled to internal quantum events, and cooperatively interact (compute) with other tubulins. We further assume that macroscopic coherent superposition of quantum-coupled tubulin conformational states occurs throughout significant brain volumes and provides the global binding essential to consciousness. We equate the emergence of the microtubule quantum coherence with pre-conscious processing which grows (for up to 500 milliseconds) until the mass-energy difference among the separated states of tubulins reaches a threshold related to quantum gravity. According to the arguments for **OR** put forth in Penrose (1994), superpositioned states each have their own space-time geometries. When the degree of coherent mass-energy difference leads to sufficient separation of space-time geometry, the system must choose and decay (reduce, collapse) to a single universe state. In this way, a transient superposition of slightly differing space-time geometries persists until an abrupt quantum classical reduction occurs. Unlike the random, "subjective reduction"(**SR**, or **R**) of standard quantum theory caused by observation or environmental entanglement, the **OR** we propose in microtubules is a self-collapse and it results in particular patterns of microtubule-tubulin conformational states that regulate neuronal activities including synaptic functions. Possibilities and probabilities for post-reduction tubulin states are influenced by factors including attachments of microtubule-associated proteins (MAPs) acting as "nodes"which tune and "orchestrate"the quantum oscillations. We thus term the self-tuning **OR** process in microtubules "orchestrated objective reduction"("B>Orch OR", and calculate an estimate for the number of tubulins (and neurons) whose coherence for relevant time periods (e.g. 500 milliseconds) will elicit **Orch OR**. In providing a connection among 1) pre-conscious to conscious transition, 2) fundamental space-time notions, 3) non-computability, and 4) binding of various (time scale and spatial) reductions into an instantaneous event ("conscious now", we believe **Orch OR** in brain microtubules is the most specific and plausible model for consciousness yet proposed.

1 INTRODUCTION

Current neurophysiological explanations of consciousness suggest that it is a manifestation of emergent firing patterns of neuronal groups involved in either a) specific networks (e.g. Hebb, 1949, 1980; Freeman, 1975;1978), coherent 40-80 Hz firing (e.g. von der Marlsburg and Schneider, 1986; Gray and Singer, 1989; Crick and Koch, 1990) and/or attentional scanning circuits (e.g. Crick, 1984; Edelman, 1989; Baars, 1988;1993). But even precise correlation of neuronal firing patterns with cognitive activities fails to address perplexing differences between mind and brain including the "hard problem"of the nature of our inner experience (e.g. Chalmers, this Volume). In this paper we apply certain aspects of quantum theory (quantum coherence) and a new physical phenomenon described in Penrose (1994) of wave function self-collapse (objective reduction: **OR**) to specific, essential structures within each neuron: cytoskeletal microtubules. Table 1 summarizes how quantum coherence and **OR** occurring in microtubules (**Orch OR**) can potentially address some of the problematic features of consciousness.

Problematic Feature of Consciousness	**Possible Quantum Solutions**
Unitary sense: "binding problem"/TD>	1) Non-local quantum coherence; Indivisible macroscopic quantum state (e.g. Bose-Einstein condensate); 2) Instantaneous self-collapse of superpositioned states (**Orch OR**).
Transition from pre-conscious/sub-conscious to conscious processes	1) Sub-and pre-conscious occur in quantum computing mode 2) Automatic, autonomic functions occur in classical computing mode 3) Quantum classical transition. (Wave function "self" collapse - **Orch OR** -is intrinsic to consciousness).
Non-computable, non-algorithmic logic	**Orch OR** is non-computable.
(Apparent) non-deterministic "free will"	Non-computable, but non-random wave function self-collapse (**Orch OR**).
Essential nature of human experience	1) Wave function self collapse (**Orch OR**) from incompatible superposition of separated space-times; 2) Pre-consciousconscious transition; 3) Effectively instantaneous "now"(**Orch OR**) collapse.

Table 1 *Aspects of consciousness difficult to explain by conventional neuroscience and possible quantum solutions.*

Quantum theory describes the surprising behavior at a fundamental level of matter and energy which comprise our universe. At the base of quantum theory is the wave/particle duality of atoms and their components. As long as a quantum system such as an atom or sub-atomic particle remains isolated from its environment, it behaves as a "wave of possibilities"and exists in coherent "superposition"(with complex number coefficients) of many possible states.

There are differing views as to how quantum superposed states (wave functions) are "collapsed"or "reduced"to a single, classical state (Table 2). The conventional quantum theory view (Copenhagen interpretation) is that the quantum state reduces by environmental entanglement, measurement or conscious observation (subjective reduction: **SR**, or **R**). Precisely where a quantum particle is and how it is moving when observed is "indeterminate"and, according to the Copenhagen interpretation, results in random measured values. We take the view (Penrose, 1994) that, to address this issue, a new physical ingredient (objective reduction: **OR**) is needed in which coherent quantum systems can "self-collapse"by growing and persisting to reach a critical mass/time/energy threshold related to quantum gravity. In the **OR** scheme, the collapse outcomes ("eigenstates" need not be random, but can reflect (in some non-computable way) a quantum computation occurring in the coherent superposition state.

Another feature of quantum systems is quantum inseparability, or non-locality, which implies that all quantum objects that have once interacted are in some sense still connected! When two quantum systems have interacted, their wave functions become "phase entangled"so that when one system's wave function is collapsed, the other system's wave function, no matter how far away, instantly collapses as well. The non-local connection ("quantum entanglement" is instantaneous, independent of distance and implies that the quantum entities, by sharing a wave function, are indivisible.

Where and how in the brain can quantum effects occur? Warm, wet and noisy, the brain at first glance seems a hostile environment for delicate quantum phenomena which generally demand isolation and cold stillness (superconductors), or energy pumping of crystals (lasers). Nonetheless, various authors have implicated ion channels, ions themselves, DNA, pre-synaptic grids and cytoskeletal microtubules as somehow mediating "standard"quantum effects. In a dualist context, Beck and Eccles (1992) proposed that an external "conscious self"might influence the apparently random quantum effects acting on neurotransmitter release at the pre-synaptic grid within each neural axon. Stapp (1993) has suggested that (**SR**) wave function collapse in neurons is closely related to consciousness in the brain. In our view, cytoskeleta microtubules are the most likely sites for quantum coherence, **OR** and consciousness.

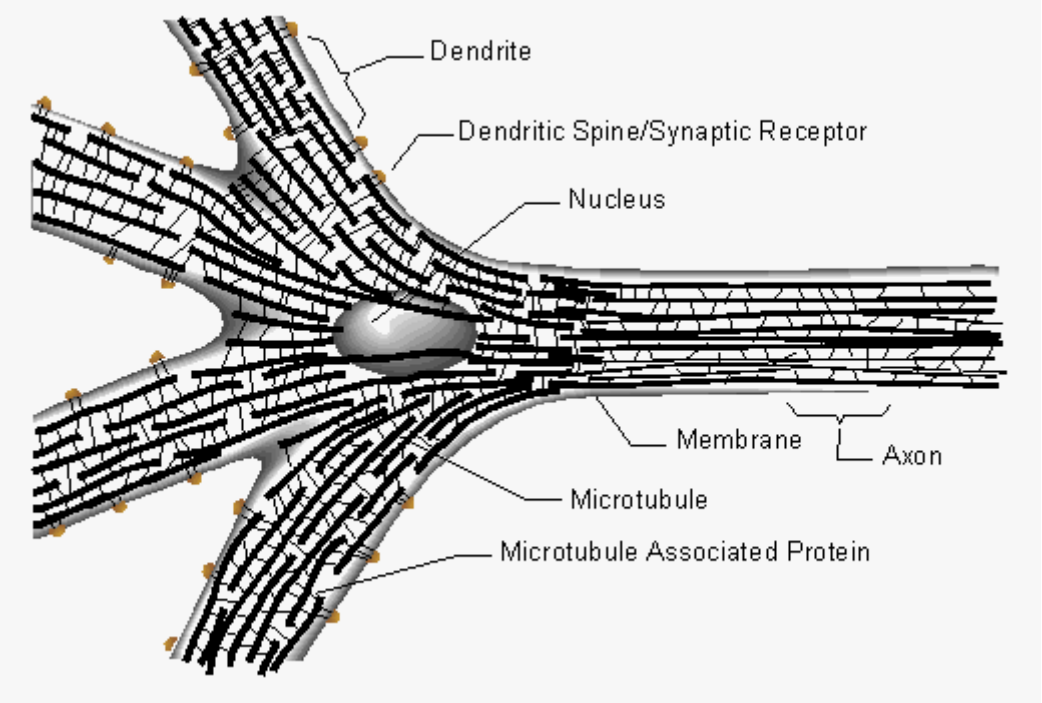

Figure 1. *Schematic of central region of neuron (distal axon and dendrites not shown) showing parallel arrayed microtubules interconnected by MAPs. Microtubules in axons are lengthy and continuous, whereas in dendrites they are interrupted and of mixed polarity. Linking proteins connect microtubules to membrane proteins including receptors on dendritic spines.*

Networks of self-assembling protein polymers, the cytoskeleton within neurons establishes neuronal form, maintains synaptic connections, and performs other essential tasks (Figure 1). The major cytoskeletal components are microtubules, hollow cylindrical polymers of individual proteins known as tubulin. Microtubules are interconnected by linking proteins (microtubule-associated proteins: MAPs) to other microtubules and cell structures to form cytoskeletal lattice networks (Figure 2).

Figure 2. *Immunofluorescent micrograph of neuronal microtububles interconnected by MAPs. Scale bar: 100 nanometers (With permission from Hirokawa, 1991).*

Traditionally viewed as the cell’s "bone-like"scaffolding, microtubules and other cytoskeletal structures also appear to fill communicative and information processing roles. Theoretical models suggest how conformational states of tubulins within microtubule lattices can interact with neighboring tubulins to represent, propagate and process information as in molecular-level "cellular automata"computing systems (e.g. Hameroff and Watt, 1982; Rasmussen et al, 1990; Hameroff et

al, 1992).

In this paper, we present a model linking microtubules to consciousness using quantum theory as viewed in a particular "realistic"way, as described in *Shadows of the Mind* (Penrose, 1994). In our model, quantum coherence emerges, and is isolated, in brain microtubules until the differences in mass-energy distribution among superpositioned tubulin states reaches a threshold related to quantum gravity. The resultant self-collapse (**OR**), irreversible in time, creates an instantaneous "now"event. Sequences of such events create a flow of time, and consciousness.

We envisage that attachments of MAPs on microtubules "tune"quantum oscillations, and "orchestrate"possible collapse outcomes. Thus we term the particular **OR** occurring in MAP-connected microtubules, and relevant to consciousness, as "orchestrated objective reduction"(**Orch OR**).

2 COLLAPSE OF THE WAVE FUNCTION

The boundary between the microscopic, quantum world and the macroscopic, classical world remains enigmatic. Behavior of wave-like, quantum-level objects can be satisfactorily described in terms of a deterministic, unitarily evolving process (e.g. state vector evolving according to the Schrödinger equation) denoted by **U**. Large-scale (classical) systems seem to obey (different) computable deterministic laws. The transition when system effects are magnified from the small, quantum scale to the large, classical scale (measurement process) chooses a particular "eigenstate"(one state of many possible states). According to the conventional Copenhagen interpretation of quantum theory, the "choice"of eigenstate is purely random. The non-computable **R** process is known in various contexts as collapse of the wave function, quantum jump, Heisenberg event and/or state reduction.

Von Neumann, Schrödinger and others in the 1930's supposed that quantum collapse, or **R** effectively occurred when a quantum system interacted with its environment, was otherwise "measured"or consciously observed. Exactly why and how collapse occurs, and how eigenstates are determined, are unknown and indicate a gap in physics knowledge: **R** is not taken to be an objectively real, independent phenomenon in the standard Copenhagen interpretation. A number of physicists have argued in support of specific models (or of general schemes) in which the rules of standard U-quantum mechanics are modified by the inclusion of some additional procedure according to which **R** does become an objectively real process. The relevant procedure of any such specific scheme is here denoted by **OR** (objective reduction). In *Shadows of the Mind*, Penrose (1994) describes **OR** in which quantum coherence grows until it reaches a critical threshold related to quantum gravity, and then abruptly self-collapses. Other schemes for **OR** include those due to Pearle (1989), and to Ghirardi et al (1986), and those which are based on gravitational effects, such as Károlházy et al (1986), Diósi (1989), Ghirardi et al (1990), and also Penrose (1989). Recent work (Pearle and Squires, 1994) lends some considerable support, on general and observational grounds, for a gravitational **OR** scheme. There are also strong arguments from other directions (Penrose, 1987;1989) supporting a belief that the appropriate union of general relativity with quantum mechanics will lead to a significant change in the latter theory (as well as in the former - which is generally accepted). There is also some tentative, but direct, evidence in favor of this union being a non-computable theory (e.g. Geroch and Hartle 1986; Deutsch unpublished; cf. Penrose, 1994). **OR** in microtubules relevant to consciousness was first considered in somewhat general terms in *Shadows of the Mind*. Here we shall adopt a fairly specific proposal for **OR** (in accordance with Penrose, 1994; Diósi, 1989; Ghirardi et al 1990) applied quantitatively in microtubules in which emergence of quantum coherence U and subsequent **OR** are "guided"and "tuned"("orchestrated" by connecting MAPs. We thus elaborate a model of "orchestrated

OR"(**Orch OR**) in microtubules which may support consciousness.

An important feature of **OR** (and **Orch OR**) is that non-computable aspects arise only when the quantum system becomes large enough that its state undergoes self-collapse, rather than its state collapsing because its growth forces entanglement with its environment. Because of the random nature of environment, the **OR** action resulting from growth-induced entanglement would be indistinguishable from the random **SR**, or **R** process of standard quantum theory.

Context	Cause of Collapse (Reduction)	Description	Acronym
Quantum coherent superposition	No collapse	Evolution of the wave function (Schrödinger equation)	**U**
Conventional quantum theory (Copenhagen interpretation)	Environmental entanglement, Measurement, Conscious observation	Reduction; Subjective reduction	**R** **SR**
New physics (Penrose, 1994)	Self-collapse -quantum gravity induced (Penrose, Diósi, etc)	Objective reduction	**OR**
Consciousness (present paper)	Self-collapse, quantum gravity threshold in microtubules orchestrated by MAPs etc	Orchestrated objective reduction	**Orch OR**

Table 2 *Descriptions of wave function collapse.*

Consciousness, it is argued, requires non-computability (Penrose, 1989; 1994). In standard quantum theory there is no non-computable activity, the **R** process being totally random. The only readily available apparent source of non-computability is OR (and **Orch OR**) self-collapse. An essential feature of consciousness might then be a large-scale quantum-coherent state maintained for a considerable time. OR (**Orch OR**) then takes place because of a sufficient mass displacement in this state, so that it indulges in a self-collapse which somehow influences or controls brain function. Microtubules seem to provide easily the most promising place for these requirements.

3 MICROTUBULES AND THE CYTOSKELETON

Ideal properties for quantum brain structures relevant to consciousness might include: 1) high prevalence, 2) functional importance (for example regulating neural connectivity and synaptic function), 3) periodic, crystal-like structure with long-range order, 4) ability to be transiently isolated from external interaction/observation, 5) functionally coupled to quantum-level events, and 6) suitable for information processing. Membranes, membrane proteins, synapses, DNA and other candidates have some, but not all, of these characteristics. Cytoskeletal microtubules do appear to have the requisite properties.

Interiors of living eukaryotic cells (including the brain's neurons and glia) are organized by

integrated networks of protein polymers called the cytoskeleton (e.g. Dustin, 1984; Hameroff, 1987). In addition to "bone-like" support, these dynamic self-organizing networks appear also to play roles as each cell's circulatory and nervous systems.

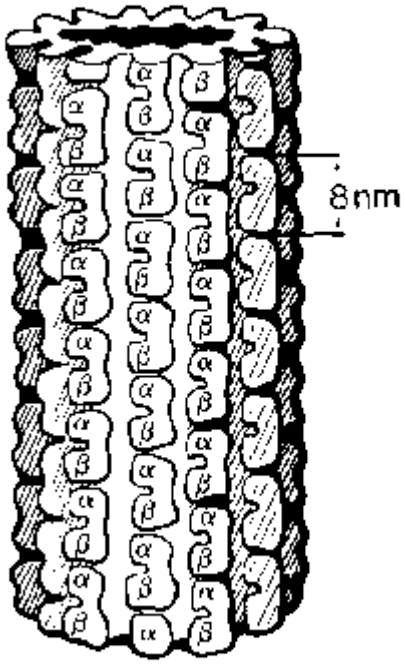

Figure 3. *Microtubule structure from x-ray crystallography (Amos and Klug, 1974). Tubulin subunits are 8 nanometer (nm) dimers comprised of alpha and beta monomers.*

The cytoskeleton consists of microtubules (MTs), actin filaments, intermediate (neuro)filaments and microtubule-associated-proteins (MAPs) which, among other duties, link these parallel structures into networks (Figures 1 and 2).

The most prominent cytoskeletal component, MTs are hollow cylinders 25 nanometers (nm = 10^{-9} meter) in diameter whose lengths vary and may be quite long within some nerve axons. MT cylinder walls are comprised of 13 longitudinal protofilaments which are each a series of subunit proteins known as tubulin (Figure 3). Each tubulin subunit is a polar, 8 nm dimer which consists of two slightly different classes of 4 nm, 55,000 dalton monomers known as alpha and beta tubulin. The tubulin dimer subunits within MTs are arranged in a hexagonal lattice which is slightly twisted, resulting in differing neighbor relationships among each subunit and its six nearest neighbors, and helical pathways which repeat every 3, 5 and 8 rows.

MTs, as well as their individual tubulins, have dipoles with negative charges localized toward alpha monomers (DeBrabander, 1982). Thus MTs are "electrets" oriented assemblies of dipoles which are predicted to have piezoelectric (Athenstaedt, 1974; Mascarenhas, 1974) and ferroelectric (Tuszynski et al, 1995) properties. Biochemical energy is provided to the cytoskeleton in at least two ways: tubulin bound GTP is hydrolyzed to GDP in MTs, and MAPs are phosphorylated. Each tubulin has a large hydrophobic region (Andreu, 1986), a non-polar pocket of amino acid side

groups which interact by van der Waals forces and can support quantum level electron delocalizability (e.g. Louria and Hameroff, this Volume).

MTs self-assemble and disassemble (e.g. Kirschner and Mitchison, 1986). The different scaffoldings they assume by their assembly and MAP attachments determine cell form and function including synaptic connections in neurons. Cell architecture (and synaptic connections) can quickly adapt by MT disassembly, and subsequent reassembly and MAP network formation in another shape or direction. Many organized cytoskeletal functions are carried out by MAPs. Some MAPs (dynein, kinesin) act as motors and carry material along microtubules (axoplasmic transport).

Several types of studies suggest cytoskeletal involvement in cognition. For example long term potentiation (LTP) is a form of synaptic plasticity that serves as a model for learning and memory in mammalian hippocampal cortex. LTP requires MAP-2, a dendrite-specific, MT-crosslinking MAP which is dephosphorylated as a result of synaptic membrane receptor activation (e.g. Halpain and Greengard, 1990). In cat visual cortex, MAP-2 is dephosphorylated when visual stimulation occurs (Aoki and Siekevitz, 1985). Auditory Pavlovian conditioning elevates temporal cortex MAP-2 activity in rats (Woolf et al, 1994). Phosphorylation/ dephosphorylation of MAP-2 accounts for a large proportion of brain biochemical energy consumption (e.g. Theurkauf and Vallee, 1983) and is involved in functions which include strengthening specific networks, such as potentiating excitatory synaptic pathways in rat hippocampus (Montoro et al, 1993). The mechanism for regulating synaptic function appears related to rearrangement of MAP-2 connections on MTs (Bigot and Hunt, 1990; Friedrich, 1990).

Other types of evidence also link the cytoskeleton with cognitive function. Production of tubulin and MT activities correlate with peak learning, memory and experience in baby chick brains (Mileusnic et al, 1980). When baby rats first open their eyes, neurons in their visual cortex begin producing vast quantities of tubulin (Cronley-Dillon et al, 1974). In animals whose brains are temporarily deprived of oxygen, the degree of cognitive damage correlates with decrease in measured levels of dendritic MAP-2 (Kudo et al, 1990). Bensimon and Chernat (1991) showed that selective damage of MTs in animal brains by the drug colchicine causes defects in learning and memory which mimic the symptoms of Alzheimer's disease (in which neuronal cytoskeleton entangles). Matsuyama and Jarvik (1989) have linkedAlzheimer's disease to microtubule dysfunction, and Mandelkow et al (1993) and others have pinpointed the axonal MAP "tau protein"as the tangle-causing defect.

How might the cytoskeleton signal and process information? Tubulin can undergo several types of conformational changes (e.g. Engelborghs, 1992; Cianci et al, 1986). Roth and Pihlaja (1977) suggested that patterns of tubulin conformation within MTs represented information. In one example of tubulin conformational change observed in single protofilament chains, one monomer can shift 27 degrees from the dimer's vertical axis (Melki et al, 1989). Whether such mechanical deformation occurs in tubulin within intact MTs is unknown; neighbor tubulins in the MT lattice might be expected to constrain movement. However, cooperativity among tubulins bound loosely in the MT lattice by hydrophobic forces could coordinate conformational changes, and support propagation of wave-like signals in MTs. Vassilev et al (1985) demonstrated signal transmission along tubulin chains formed between excitable membranes. A number of models of signaling and information processing within MTs and other cytoskeletal components have been suggested. These include propagating tubulin conformational changes (Atema, 1974), ion transfer (Cantiello et al, 1991), sequential phosphorylation/dephosphorylation along MT tubulins (Puck and Krystosek, 1992), tensegrity (Wang and Ingber, 1994), non-linear soliton waves along MTs (Chou et al, 1994; Sataric et al, 1992) and "cellular automaton"behavior due to electrostatic dipole coupling among tubulin lattice neighbors (e.g. Rasmussen et al, 1990).

4 MICROTUBULE INFORMATION PROCESSING

4.1 Protein conformation

Proteins have conformational transitions at many time and size scales (Karplus and McCammon, 1983). For example small side chains move in the picosecond to femtosecond time scale (10^{-12} to 10^{-15}), but conformational transitions in which proteins move globally and upon which protein function generally depends occur in the nanosecond (10^{-9} sec) to 10 picosecond (10^{-11} sec) time scale. Related to cooperative movements of smaller regions, hydrogen bond rearrangements and charge redistributions such as dipole oscillations, these global changes linked to protein function (signal transduction, ion channel opening, enzyme action etc.) may be regulated by a variety of factors including phosphorylation, ATP or GTP hydrolysis, ion fluxes, electric fields, ligand binding, and "allosteric"influences by neighboring protein conformational changes. Noting the extraordinary dielectric strength of proteins (their abilty to sustain a voltage), Fröhlich (1968; 1970; 1975) proposed that the various factors determining protein conformation were integrated through a quantum level dipole oscillation within each protein's hydrophobic region (Figure 4).

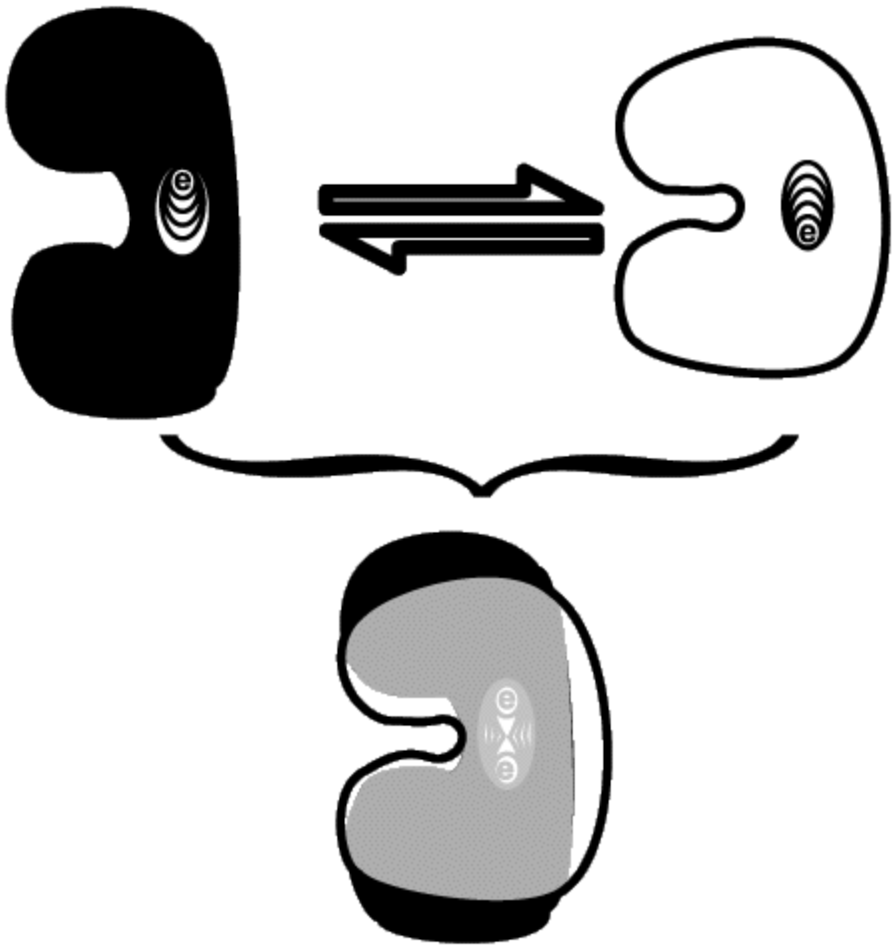

Figure 4. *Schematic model of tubulin states. Top: Two states of microtubule subunit protein "tubulin"in whichi quantum event (electron localization) within a hydrophobic pocket is coupled to*

protein conformation. Bottom: Tubulin in quantum coherent superposition of both states.

4.2 Fröhlich's coherent pumped phonons

In addition to linking protein conformation to hydrophobic quantum events, Herbert Fröhlich, an early contributor to the understanding of superconductivity, also predicted quantum coherence in living cells (based on earlier work by Oliver Penrose and Lars Onsager, 1956). Fröhlich theorized that sets of protein dipoles in a common electromagnetic field (e.g. proteins within a polarized membrane, subunits within an electret polymer like microtubules) undergo coherent conformational excitations if energy is supplied. Fröhlich postulated that biochemical and thermal energy from the surrounding "heat bath"provides such energy. Cooperative, organized processes leading to coherent excitations emerged, according to Fröhlich, because of structural coherence of hydrophobic dipoles in a common voltage gradient.

Coherent excitation frequencies on the order of 10^9 to 10^{11} Hz (identical to the time domain for functional protein conformational changes, and in the microwave or gigaHz spectral region) were deduced by Fröhlich who termed them acousto-conformational transitions, or coherent (pumped) phonons. Such coherent states are termed Bose-Einstein condensates in quantum physics and have been suggested by Marshall (1989; this Volume) to provide macroscopic quantum states which support the unitary binding of consciousness.

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

4.3 Cellular automata in microtubules

Computational systems in which complex signaling and patterns emerge from local activities of simple subunits are called cellular automata. Their essential features are: 1) at a given time, each subunit is in one of a finite number of states (usually two for simplicity). 2) The subunits are organized according to a fixed geometry. 3) Each subunit communicates only with neighboring subunits; the size and shape of the neighborhood are the same for all cells. 4) A universal "clock"provides coherence such that each subunit may change to a new state at each "clock tick" 5) Transition rules for changing state depend on each subunit's "present"state and those of its neighbors. Depending on initial conditions (starting patterns), simple neighbor transition rules can lead to complex, dynamic patterns capable of computation. Von Neumann (1966) proved mathematically that cellular automata could function as Turing machines.

In a series of simulations (e.g. Hameroff et al, 1984; Rasmussen et al, 1990) Fröhlich's excitations were used as a clocking mechanism and electrostatic dipole coupling forces as "transition rules"for cellular automata behavior by dynamic conformational states of tubulins within MTs. As in the top of Figure 4, the two monomers of each tubulin dimer are considered to share a mobile electron within a hydrophobic pocket which is oriented either more toward the alpha-monomer (alpha state) or more toward the beta-monomer (beta state) with associated changes in tubulin conformation at each "Fröhlich coherent"time step (e.g. 10^{-9} to 10^{-11} sec). The net electrostatic force F_{net} from the six surrounding neighbors acting on each tubulin can then be calculated as:

$$f_{net} = \frac{e^2}{4\pi\varepsilon} \sum_{i\ 1}^{6} \frac{Y_i}{r_i^3}$$

where y_i and r_i are inter-tubulin distances, e is the electron charge, and epsilon is the average protein permittivity. MT automata simulations (Figure 5) show conformational pattern behaviors including standing waves, oscillators and gliders traveling one dimer length (8 nm) per time step (10^{-9} to 10^{-11} sec) for a velocity range of 8 to 800 meters per second, consistent with the velocity of propagating nerve action potentials.

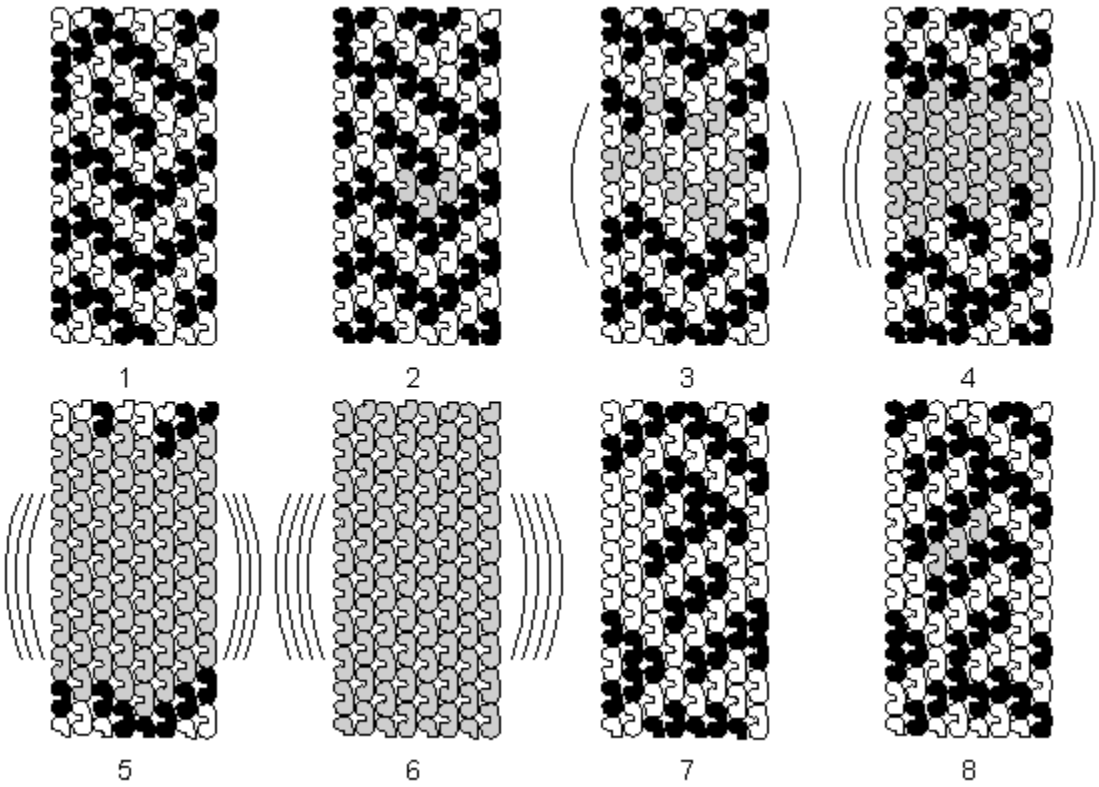

Figure 5. *Microtubule automaton simulation (from Rasmussen et al., 1990). Black and white tubulins correspond to states shown in Figure 4. Eight nanosecond time steps of a segment of one microtubule are shown in "classical computing"mode in which patterns move, evolve, interact and lead to emergence of new patterns.*

MT automata patterns can thus represent and process information through each cell; gliders may convey signals which regulate synaptic strengths, represent binding sites for MAPs (and thus neuronal and synaptic connectionist architecture) or material to be transported. Information could become "hardened"in MTs by tubulin modifications or stored in neurofilaments via MAPs.

MT conformational automata patterns provide a further level of computational complexity within each of the brain's neurons. However by considering only classical computing and local neighbor interactions, microtubule automata fail to address the problematic features of consciousness for which quantum theory holds promise.

5 WAVE FUNCTION SELF-COLLAPSE IN MICROTUBULES: OR AND Orch OR

5.1 The Collapse Criterion and Conscious Thought

Consider a quantum superposition w |A> +z |B> (where w and z are complex numbers) of two macroscopically distinguishable quantum states |A> and |B> . In standard quantum theory and in the absence of environmental entanglement, this superposition would persist forever. If, after a time ***t***, |A> would have evolved to $|A>_t$ and |B> would have evolved to $|B>^t$, then w|A> +z|B> must evolve to $w|A>_t + z|B>_t$. (This is a feature of the linear nature of **U**.)

According to the present OR criterion, such macroscopic superpositions are regarded as unstable even without environmental entanglement. Therefore the state w|A> +z|B> will decay in a certain time scale , to either |A> or |B>, with relative probabilities $|w|^2:|z|^2$. (This is analogous to the situation with an unstable radioactive particle, with a lifetime and two separate decay modes |A> or |B>, whose branching ratios are $|w|^2:|z|^2$.) The idea is that the states |A> and |B> each correspond to clearly defined energy distributions (and to well defined space-time geometries), whereas the combination w |A> +z |B> does not (and so would lead to superpositions of different space time geometries-a particularly awkward situation from the physical point of view!). According to a number of authors (e.g. Diósi, 1989; Ghirardi et al,1986;1990; Penrose, 1993;1994; Pearle, 1992), the gravitational self-energy of the difference between the mass distributions involved in |A> and in |B> will determine spontaneous reduction (at time) of the superposed combination w |A> +z |B> to either |A> or |B>.

We view |A> and |B> as representing two conformationally coupled quantum states of each tubulin within microtubules, and w |A> +z |B> as the superposition of those states (e.g. Figure 4). We envisage that time *T* at which the state w |A> +z |B> for each tubulin will decay to either |A> or |B> should relate to the transition between pre-conscious and conscious events.

We assume that pre-and sub-conscious processing corresponds with quantum coherent superposition which can perform "quantum computing"(Penrose, 1989). A number of authors (e.g. Deutsch, 1985; Deutsch and Josza 1992; Feynman 1986; Benioff, 1982) have proposed that quantum coherence can implement multiple computations simultaneously, in parallel, according to quantum linear superposition: the quantum state then "collapses"to a particular result. A state which "self-collapses"(**OR**) will have an element of non-computability, even though evolution of its quantum coherence had been linear and computable. A quantum superposed state collapsed by external environment or observation (**SR**, or **R**) lacks a non-computable element, and would thus be unsuitable for consciousness. Large scale quantum coherence occurring among tubulins (e.g. via electrons in hydrophobic pockets arrayed in the microtubule lattice, or ordered water within hollow MT cores) could take on aspects of a quantum computer in pre-conscious and sub-conscious modes.

We also assume that "non-conscious"autonomic processes correspond with classical, non-quantum computing by microtubule conformational automata. Thus an OR transition from quantum, pre-conscious processing, to classical, non-conscious processing may be closely identified with consciousness itself.

But what is consciousness? According to the principles of OR (Penrose, 1994), superpositioned states each have their own space-time geometries. When the degree of coherent mass-energy difference leads to sufficient separation of space-time geometry, the system must choose and decay (reduce, collapse) to a single universe state, thus preventing "multiple universes"(e.g. Wheeler, 1957). In this way, a transient superposition of slightly differing space-time geometries persists until an abrupt quantum classical reduction occurs and one or the other is chosen. Thus consciousness may involve self-perturbations of space-time geometry.

The extent of space-time superposition causing self-collapse is related to quantum gravity, and equal to one in "absolute units."

Absolute units convert all physical measurement into pure, dimensionless numbers (cf. Penrose, 1994-pp 337-339). This is done by choosing units of length, mass and time so that the following constants take the value of unity:

c(speed of light)=1,
h (Planck's constant divided by 2 pi)=1,
G (Gravitational constant)=1.

Physical quantities relevant to our calculations in absolute units:

second=1.9×10^{43},
nanometer=6.3×10^{25},
mass of nucleon ("dalton"=7.8×10^{-20},
fermi (strong interaction size, diameter of nucleon)=6.3×10^{19}.

Using absolute units, we can ask how many tubulins in quantum coherent superposition for how long will self-collapse (**Orch OR**)?

The gravitational self-energy for a quantum superposition of mass whose displacement for a given time sufficiently perturbs space-time for OR (**Orch OR**) is taken from the "uncertainty principle"

$E=h/T$

where *h* is Planck's constant divided by 2pi , and *T* is the coherence time.

We estimate *T* the coherence time from research by Libet (1990) and others (e.g. Deeke et al, 1976; Grey-Walter, 1953; Libet et al, 1979) who found the time scale characteristic of pre-conscious to conscious transitions to be about 500 milliseconds (msec). This is similar to other estimates in the 100-200 msec range (e.g. Koch, this Volume). Hence *T*=500 msec (half second) seems appropriate from experimental results for at least some functionally significant transitions. Similar calculations may be done using, for example, 25 msec as occurs in coherent 40 Hz excitations.

In absolute units (approximating):

$T=500ms=(0.5)1.9 \times 10^{43}=10^{43}$.

Since $h = 1$ in absolute units:

$E=T^{-1}=10^{-43}$.

This is the gravitational self-energy for which n_t tubulins displaced in quantum coherent superposition for 500 msec will self-collapse (**OR, Orch OR**). To determine $n/_t$, we calculate the gravitational displacement self energy $E/_t$for one tubulin. We assume the tubulin conformational movement displaces its mass by a distance r which is 1/10 the 2 nanometer (nm) radius of the tubulin monomer, or 0.2 nm. In absolute units:

$r=0.2(6.3 \times 10^{25})=10^{25}$.

As illustrated in Figure 6, the distribution of mass m for each tubulin conformational change may be considered as either: 1) two protein spheres, 2) two granular arrays of atoms, 3) two granular arrays of nucleons (protons and neutrons).

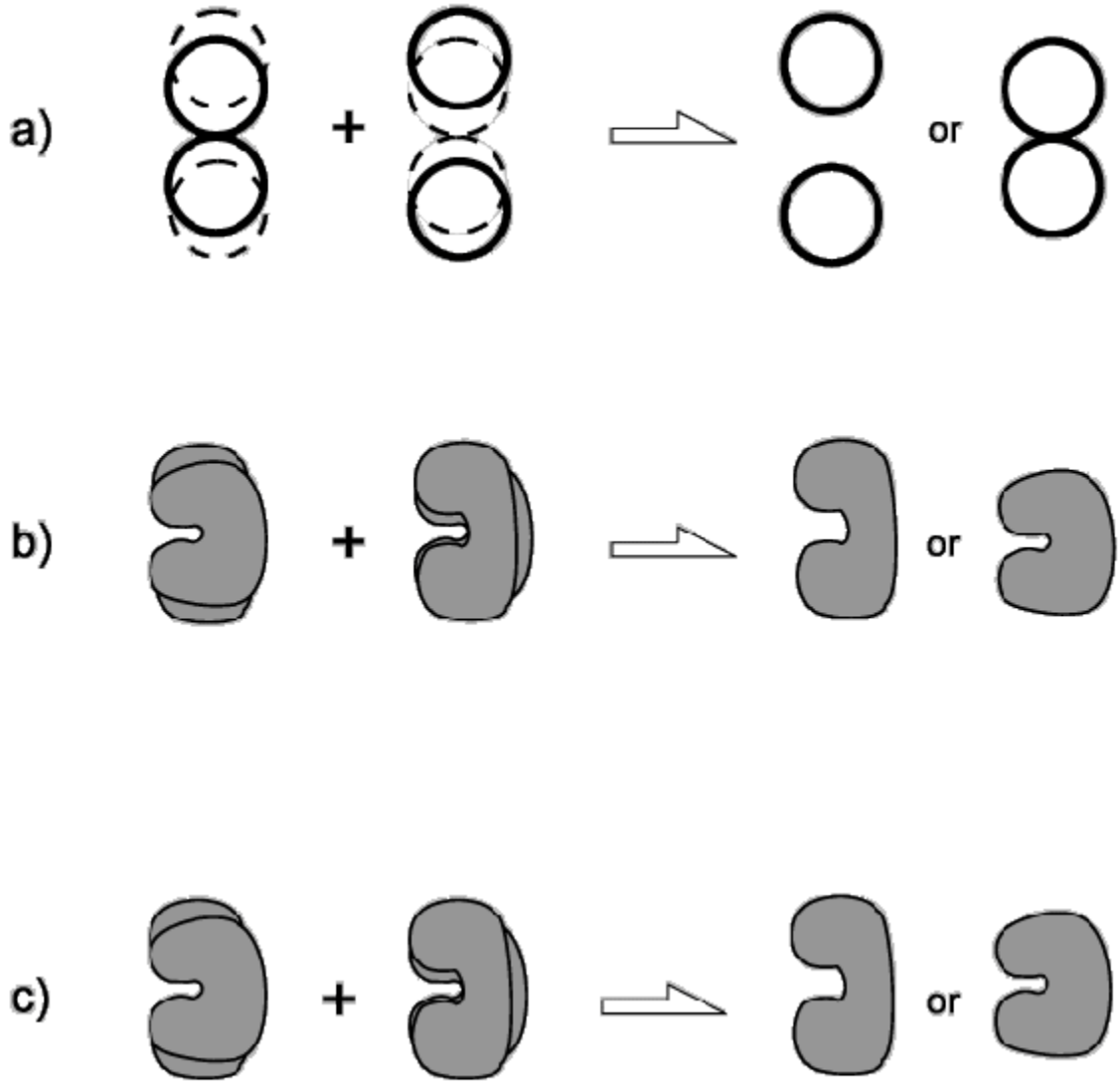

Figure 6. *Three treatments of mass distribution of tubulin. 1) 2 protein spheres, 2) 2 granular arrays of (carbon) atoms, 3) 2 granular arrays of nucleons.*

5.1.1 Protein spheres

Consider the tubulin dimer as two uniform (monomer) spheres (Figure 6a). As a reasonable approximation, the energy E_t for one tubulin dimer is twice the displacement energy of one (monomer) sphere position in the gravitational field of its other position (twice because there are two spheres per tubulin). The mass m_t of the tubulin monomer sphere is 55,000 daltons (nucleons). In absolute units:

$m_t=5.5 \times 10^{-20}=4 \times 10^{-15}$.

Since the displacement is less than the sphere radius, we need a detailed calculation to obtain the gravitational self-energy E_m of the difference between the displaced mass distributions for each tubulin monomer, considered as a uniform sphere. Taking the sphere to have a radius a and the distance of displacement to be r, we find, as the result of a double integration:

$E_m=m^2G(r^2/2a^3 - 3r^3/16a^4 + r^5/160a^6)$.

where G is Newton's universal constant of gravitation equal to one in absolute units. Here we have

$m=(1/2)m_t=2 \times 10^{-15}$ and $a=10^{26}$,

and we are taking $r=10^{25}$.

We can ignore the higher-order terms, so we obtain, in absolute units:

$E_m=m^2r^2/2a^3=(4 \times 10^{-15} \times 10^{25})^2/2 \times 10^{78} = 8 \times 10^{-58}$.

Thus, approximately,

$E_t=1.6 \times 10^{-57}$ for the gravitational self-energy of displacement for a single dimer. For n_t in absolute units (approximately):

$n_t=T^1/E_t = 10^{-43}/1.6 \times 10^{-57} = 6 \times 10^{13}$ tubulins.

Considering the tubulin mass distributions simply as protein spheres, we would thus estimate 6 x 10^{13} tubulins displaced in quantum coherent superposition for 500 msec will self-collapse (**Orch OR**).

5.1.2 Granular arrays of atomic nuclei

Consider tubulin as two arrays of (carbon) atoms (Figure 6b). The mass m_c of one carbon atom (12 nucleons) is its nuclear mass in absolute units:

$m_c=12(7.8 \times 10^{-20})=10^{-18}$.

Because the carbon nucleus displacement is greater than its radius (the spheres separate completely), the gravitational self-energy E_c is given by:

$E=Gm^2/a_c$,

where a_c is the carbon nucleus sphere radius equal to 2.5 fermi distances. In absolute units:

$a_c=2.5(6.3 \times 10^{19})=1.6 \times 10^{20}$,

$E=Gm^2/a_c=(10^{-18})^2/1.6 \times 10^{20} = 10^{-56}$

This is the gravitational self-energy in absolute units for displacement of one carbon atom nucleus (12 nucleons). To determine how many carbon nuclei n_c and tubulins n_t displaced for 500 msec will elicit **Orch OR**:

$E=n_c E_c = T_{-1}$, $n_c=T^{-1}/E_c=10^{-43}/10^{-56} = 10^{13}$ carbon atoms=12 x 10^{13} carbon atoms=12 x 10^{13} nucleons.

As one tubulin is 110,000 nucleons,

$n_t=12 \times 10^{13}/1.1 \times 10^5 = 10^9$ *tubulins*

Considering the tubulin mass distribution as atomic (carbon) nuclei, we thus estimate that tubulins displaced in coherent superposition for 500 msec will self-collapse, and elicit **Orch OR**.

5.1.3 Granular arrays of nucleons

Consider tubulin as two arrays of nucleons (Figure 6c). The mass *m(sub)n* of one nucleon in absolute units:

m(sub)n=7.8 x 10^-20.

Since the nucleon displacement is again greater than its radius (complete separation):

$E_n=Gm^2/a_n$,

where a_n is the nucleon radius , or 0.5 fermi:

$a_n=5(6.3 \times 10^{19})=3 \times 10^{19}$, $E_n=Gm^2a_n=(7.8 \times 10^{-20})^2 3 \times 10^{19} = 2 \times 10^{-58}$.

This is the gravitational self-energy for displacement of one nucleon for 500 msec. (G=1 in absolute units.) To find n_n, the number of nucleons whose displacement for 500 msec will elicit **Orch OR**:

$E=n_n E_n=T^{-1}$, $n_n=T^{-1}/E_n=10^{-43} = 2 \times 10^{-58} = 5 \times 10^{14}$.

$n_n=5 \times 10^{14}/1.1 \times 10^5=5 \times 10^9$tubulins.

Considering tubulin mass as arrays of nucleons, we thus estimate that 5 x 10^9 tubulins displaced in quantum coherent superposition for 500 msec will self-collapse, **Orch OR**.

Using the three types of tubulin mass distributions (protein spheres, atoms, nucleons), we obtain 6 x 10^{13}, 10^9 and 5 x 10^9 respectively for the required number *n(SUB>t* of quantum coherent tubulins displaced for 500 msec to elicit **Orch OR**. Although in approximation all three mass distributions contribute to **Orch OR**, that which gives the highest energy (fewest tubulins, shortest reduction time if T were not fixed) predominates. Thus, 10^9 tubulins is perhaps the best estimate. Section 5.3 considers the possible significance of this number of tubulins. As discussed in other papers in this Volume (e.g. Elitzur, Tollaksen), consciousness may be linked to creation of an instantaneous "now" and the flow of time. As **Orch OR** is instantaneous, non-computable and irreversible, it can provide "now"moments, and directionality in time. Sequential cascades of **Orch OR** events would

then constitute the familiar "stream of consciousness."The **Orch OR** process in MTs selects patterns (eigenstates of mass distribution) of tubulin conformational states. Figure 7 illustrates eight possible "eigenstates of mass distribution"for **Orch OR** occurring in 3 adjacent tubulins. The selected patterns can influence neural function by determining MAP attachment sites and setting initial conditions for MT "cellular automata"information processing. These MT activities can then govern intra-neuronal architecture and synaptic function by modulating sensitivity of membrane receptors (in, for example, dendritic spines), ion channels and synaptic vesicle release mechanisms, communication with genetic material, and regulating axoplasmic transport which accounts for delivery of synaptic material components. Microtubule associated proteins (MAPs) attached to certain microtubule tubulin subunits would seem likely to communicate the quantum state to the outside "noisy"random environment, and thereby entangle and collapse it (**SR** or **R**, rather than**OR** or **Orch OR**). We therefore presume that these MAP connections are placed along each MT at sites which are (temporarily at least)inactive with regard to quantum-coupled conformational changes. We envisage that these connection points are, in effect, "nodes"for MT quantum oscillations, and thus "orchestrate"the possibilities and probabilities for MT quantum coherence and subsequent **Orch OR** (Figure 8). MAP connection points can be regularly placed on MT lattices in super-helical patterns (Kim et al, 1986; Burns, 1978) which seems appropriate for their proposed roles as nodes. However in neural MTs, the MAP connection points appear more randomly placed. This would not prevent their acting as "nodes"because the "quantum cellular automaton"activity that we envisage could be extremely complicated, and could well appear to be random. In addition to MAPs, genetic tubulin variability (e.g. Lee et al, 1986), and "learned, experiential" (post-translational) tubulin modifications (e.g. Gilbert and Strochi, 1986) can orchestrate OR. Accordingly, we term the particular objective reduction (**OR**) occurring in MTs, self-tuned by MAPs and other factors, and relevant to consciousness as "orchestrated objective reduction"(**Orch OR**).

Because OR phenomena are fundamentally non-local, the coherent superposition phase may exhibit puzzling bidirectional time flow prior to self-collapse (e.g. Aharonov and Vaidman, 1990; Penrose 1989; 1994). As we equate the pre-collapse quantum computing superposition phase to pre-conscious processing, bidirectional time flow could explain the puzzling "backwards time referral"aspects of pre-conscious processing observed by Libet et al (1979).

5.2 How can quantum coherence in microtubules be isolated from environmental entanglement?

When the quantum system under consideration becomes entangled with another system, we must consider the entire state involved. For example $|A\rangle$ might be accompanied by the environment state $|P\rangle$, and $|B\rangle$ with the environment state $|Q\rangle$. Then, in place of the state $w|A\rangle + z|B\rangle$, we have

$$w|A\rangle|P\rangle + z|B\rangle|Q\rangle .$$

We must consider mass movement in $|P\rangle$ and $|Q\rangle$ as well as in $|A\rangle$ and $|B\rangle$, and whenever this dominates, we get, in effect, the random **SR**, or R process of conventional quantum measurement theory, rather than the non-computable aspects of **OR** (or **Orch OR**) that would be important for consciousness.

At first glance, the interiors of living cells would seem unlikely sites for quantum effects. "Noisy"thermal motions of cell water ($|P\rangle$) would seem to decohere any quantum coherence and cause random **SR**, or R collapse. However several factors could serve to isolate microtubules and sustain quantum coherence.

5.2.1 Ordered water

Water on cytoskeletal surfaces can be highly "ordered" extending up to 9 layers (about 3 nm) around each microtubule (Clegg, 1983; Watterson, this Volume). Thermal interactions which would cause decoherence involve energy coupling to oscillations in short range interactions (e.g. hydrogen bonds) among water molecules and groups of water molecules with energy of about kT (10^-12 sec). Interactions of MT surface ordered water molecules with a Fröhlich coherence in MTs are predicted to have a frequency (10^-14 sec) much higher than thermalization energy. Thus MTs may be embedded in "cages"of structured (coherent) water which can act to isolate MT quantum coherence (Jibu et al, 1994). If a quantized electric field generated by Frû…lich pumped phonons in MTs is comparable to the coherent strength of water, the field penetrates/propagates by "piercing"it (self-focusing, filamentary propagation analogous to Meissner effect in superconductivity). Del Giudice et al (1983) showed this self-focussing should result in filamentous energy beams of radius 15 nanometers, precisely the inner diameter of microtubules!

5.2.2 Isolation inside microtubule hollow core

Using quantum field theory, Jibu et al (1994; this Volume) have modeled the ordering of water molecules and the quantized electromagnetic field confined inside hollow microtubule cores. They predict a specific collective dynamics called super-radiance in which each microtubule can transform incoherent, disordered energy (molecular, thermal, or electromagnetic) into coherent photons within its hollow core. The time for super-radiant photon generation is much shorter than the time needed for the environment to act to disorder the coherence thermally.

5.2.3 Sol-gel states

Cytoplasm is comprised of two phases: sol (solution) and gel (gelatinous). Calcium ions binding to actin and other cytoskeletal polymers convert sol to gel transiently and reversibly (e.g. cytomatrix: Satir, 1984). MTs and other MT-associated proteins (i.e.calmodulin) bind/release calcium. Gelatinous phases near adjacent to microtubules could isolate them from thermal effects during quantum coherence.

5.3 The Collapse Fraction

Here we get a very rough idea of the fraction of brain required for **Orch OR**. In section 5.1 we obtained a very rough estimate that 10^9 tubulins in quantum coherent superposition for 500 msec are sufficient for **Orch OR**. Yu and Baas (1994) measured about 10^7 tubulins per neuron. Thus about 100 neurons whose tubulins were *totally* coherent for 500 msec may be the minimal number for **Orch OR**, and for consciousness. It may be more likely that only a fraction of tubulins within a given neuron becomes coherent. (Global macroscopic states such as superconductivity can result from quantum coherence among only very small fractions of components.) For example if 1% of tubulins within a given set of neurons were coherent for 500 msec, then 10,000 such neurons would be required to elicit **Orch OR**. Thus for 500 msec we get a range for minimal consciousness from hundreds to thousands of neurons. Nervous systems of organisms such as the nematode C. elegans contain several hundred neurons. Functional groups of neurons in human cognition are thought to contain thousands. Hebb's (1949) "cell assemblies" Eccles' (1992) "modules,"and Crick and Koch's (1990) "coherent set of neurons"are each estimated to contain some 10,000 neurons which may be widely distributed throughout the brain (Scott, 1995).

Rather than always being 500 msec, time and the number of tubulins may vary, and result in different types of conscious experience. A very intense, sudden input may recruit emergence of

quantum coherent tubulins faster so that **Orch OR** occurs sooner ("heightened"experience, Figure 11c). For example, 10^{10} coherent tubulins would elicit **Orch OR** in 50 msec, and so on. Lower intensity input patterns develop coherence more slowly, and **Orch OR** occurs later. An instantaneous **Orch OR** may then "bind"various coherent tubulin superpositions whose net displacement energy is T^{-1}, but which may have evolved in separated spatial distributions and over different time scales into an instantaneous event (a "conscious now". Cascades of **Orch OR**s can then represent our familiar "stream of consciousness."

6 SUMMARY: ORCHESTRATED OBJECTIVE REDUCTION (Orch OR) OF QUANTUM COHERENCE IN BRAIN MICROTUBULES

The picture we are putting forth involves the following ingredients:

A) A macroscopic state of quantum coherent superposition can exist among tubulin subunits in microtubules across a large proportion of the brain. Plausible candidates for such states include models proposed by:

1) Marshall (1989) in which Frû…lich pumped phonons induce a Bose-Einstein condensate among proteins distributed throughout the brain

2) Jibu et al (1994) in which ordered water within microtubule hollow cores is coupled to Fröhlich excitations of tubulins in microtubule walls

resulting in coherent photons ("super-radiance" 3) Kaivarainen (1995) in which quantum coherent "flickering"clusters of ordered water within hollow microtubule cores are coupled to (non-Fröhlich) tubulin conformational dynamics and generate coherent photons

4) Conrad (e.g. this Volume) in which conformational states and functional capabilities of proteins are controlled by quantum superposition dynamics of electrons and hydrogen bonds within them.

B) The quantum coherent state is weakly coupled to conformational activity taking place in tubulins within microtubules. The link occurs by changes in individual electric dipole moments within tubulins. For example movements of a single electron within a hydrophobic pocket centrally placed within each tubulin dimer may couple to the conformational state of the tubulin (Figure 4).

C) This combined quantum state among many tubulins is able to maintain itself without significant entanglement with its environment for a relevant period of time (up to 500 msec). We envisage several possible mechanisms which could serve to isolate the MT quantum state from its environment within the neuron. These include (see Section 5.2):

1. Shielding by ordered water on tubulin surfaces
2. Isolation within hollow MT inner cores
3. Shielding by gelatinous cytoplasmic layer

D) Cooperative interactions among neighboring tubulins in microtubules can signal and process information by computational mechanisms such as cellular automata behavior. We propose two types of microtubule computation:

1. Classical computing: conformational patterns propagate through the cytoskeleton to regulate synapses and perform other neural functions (Figure 5). This mode correlates with non-conscious and autonomic activities.

2. Quantum computing: large scale quantum coherence occurs among tubulins (e.g. via electrons in hydrophobic pockets arrayed in the microtubule lattice) and takes on aspects of a quantum computer (e.g. Deutsch, 1985; Deutsch and Josza 1992; Feynman 1986; Benioff; 1982) where multiple "computations"are performed simultaneously, in parallel, according to quantum linear superposition. We equate quantum computing with pre-and sub-conscious processing.

E) In the quantum computing mode, changes in dimer conformations involve the movement of mass. According to the arguments and criterion described in Section 5.1), we estimate the time scale *T* , and calculate the number *n(sub)t* (of coherent superpositioned tubulins) required for self collapse (objective orchestrated reduction: **Orch OR**) to occur. As we equate quantum computing with pre-conscious processing, we approximate the time scale to be equivalent in some cases to that found by Libet et al (1979) and others (e.g. Deeke et al, 1976; Grey-Walter, 1953) to be characteristic of the transition from pre-conscious to conscious processing (up to 500 msec). For *T =500* msec, we get a rough estimate of 10^9 tubulins required for **Orch OR**.

F) Microtubule associated proteins (MAPs) attached to certain microtubule tubulin subunits would seem likely to communicate the quantum state to the outside "noisy"random environment, and thereby entangle andcollapse it (**SR**, or R). We therefore presume that these MAP connections are placed along each MT at sites which are (temporarily at least) inactive with regard to quantum-coupled conformational changes. We envisage that these connection points are, in effect, "nodes"for MT quantum oscillations, and (along with genetic and other tubulin modifications) thus "orchestrate"MT quantum coherence and subsequent OR (Figure 8). Accordingly, we term the particular objective reduction (OR) occurring in MTs and relevant to consciousness as "orchestrated objective reduction"(**Orch OR**).

G) The **Orch OR** process selects a new set of tubulin conformational states ("eigenstates of mass distribution" within MTs which can implement and regulate neural function by determining MAP attachment sites and setting initial conditions for "cellular automata"information processing by "classical"conformational transitions. These MT activities can then govern intra-neuronal architecture and synaptic function through modulating sensitivity of membrane receptors, ion channels and synaptic vesicle release mechanisms, communication with genetic material, andregulating axoplasmic transport which accounts for delivery of synaptic material components.

H) How is a particular conformational pattern within each microtubule chosen in the **Orch OR** process? The Copenhagen quantum interpretation would suggest the selection of states upon (**SR**, or R) collapse is purely random. Effects of MAPs, genetic and other tubulin modifications can set the possibilities and probabilities ("orchestrate", but reduction within that context is non-computable. As described in Shadows of the Mind (Penrose, 1994), it remains possible that presently unrecognized OR (or **Orch OR**) quantum-mathematical logic acting on these programming influencesprovides a hidden order.

I) Because **OR** (and **Orch OR**) phenomena are fundamentally non-local, the coherent superposition phase may exhibit puzzling bidirectional time flow prior to self-collapse (e.g. Aharonov and Vaidman, 1990; Penrose 1989; 1994). We equate the pre-collapse quantum computing superposition phase to pre-conscious processing. This could explain the puzzling "backwards time referral"aspects of pre-conscious processing observed by Libet et al (1979). (Also see Tollaksen, this Volume.)

J) The persistence and global nature of consciousness is seen as a feature of large scale quantum coherent activity taking place across much of the brain. Varieties of **Orch OR** with differing

coherence times and amounts of coherent tubulin may blend into conscious thought. Very intense, sudden inputs may recruit emergence of quantum coherent tubulins faster than 500 msec so that **Orch OR** occurs sooner ("heightened"experience, Figure 11c). Lower intensity, unexciting input patterns develop coherence more slowly and **Orch OR** occurs later. An instantaneous **Orch OR** may then "bind" disparate tubulin superpositions which may have evolved in separate spatial distributions and over different time scales into an instantaneous conscious "now" Cascades of **Orch OR**s can then represent our familiar "stream of consciousness."

7 CONCLUSION

Approaches to understanding consciousness which are based on known and experimentally observed neuroscience fail to explain certain critical aspects. These include a unitary sense of binding, non-computational aspects of conscious thinking, difference and transition between pre-conscious and conscious processing, (apparent) non-deterministic free will and the essential nature of our experience. We conclude that aspects of quantum theory (e.g. quantum coherence) and of a newly proposed physical phenomenon of wave function self-collapse (objective reduction, OR, Penrose, 1994) offer possible solutions to each of these problematic features. We further conclude that cytoskeletal microtubules, which regulate intra-neuronal activities and have cylindrical paracrystalline structure, are the best candidates for sites of quantum action and OR, and of "orchestrated OR"(**Orch OR**). Accordingly, we present a model of consciousness based on the following assumptions:

Coherent excitations (Fr&ounl;hlich pumped phonons) among microtubule subunits (tubulins) support "cellular automaton"information processing in both classical (conformational) and quantum coherent superposition modes. Classical processing correlates with non-conscious, autonomic activity; quantum processing correlates with pre-and sub-conscious activity.

The microtubule quantum coherent computing phase is able to be isolated from environmental interaction and maintain coherence for up to 500 msec (pre-conscious processing).

A critical number of tubulins maintaining coherence within MTs for 500 msec collapses its own wave function (objective reduction: OR). This occurs because the mass-energy difference among the superpositioned states of coherent tubulins critically perturbs space-time geometry. To prevent multiple universes, the system must reduce to a single space-time by choosing eigenstates. The threshold for **OR** is related to quantum gravity; we calculate it in terms of the number of tubulins coherent for 500 msec to be very roughly 10^9 tubulins. Larger coherent sets will self-collapse faster, and smaller sets more slowly. Coherent sets which evolve over different time scales and in different brain distributions may be bound in an effectively simultaneous collapse which creates instantaneous "now" Cascades of these events constitute the familiar "stream of consciousness"

.Microtubule associated proteins (MAPs) and other tubulin modifications act as "nodes"to tune microtubule coherence and help to orchestrate collapse. We thus term the specific OR proposed to occur in microtubules and intrinsic to consciousness as "orchestrated objective reduction"(**Orch OR**).

.The **Orch OR** process, which introduces non-computability (Penrose, 1989; 1994), results in eigenstate patterns of tubulin conformational states which help direct neural function through the actions of microtubules.

In providing a connection among 1) pre-conscious to conscious transition, 2) fundamental space-time notions, 3) non-computability, and 4) binding of various (time scale and spatial)

superpositions into instantaneous "now" we believe **Orch OR** in MTs is the most specific and plausible model for consciousness yet proposed.

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