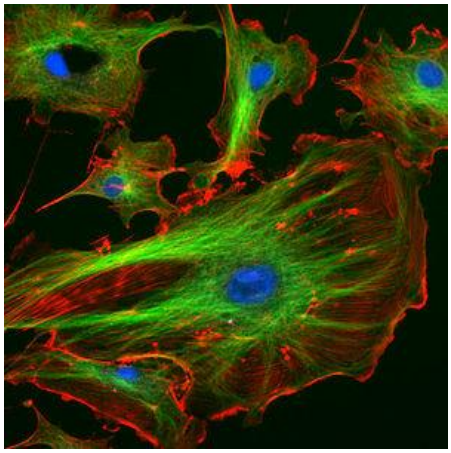
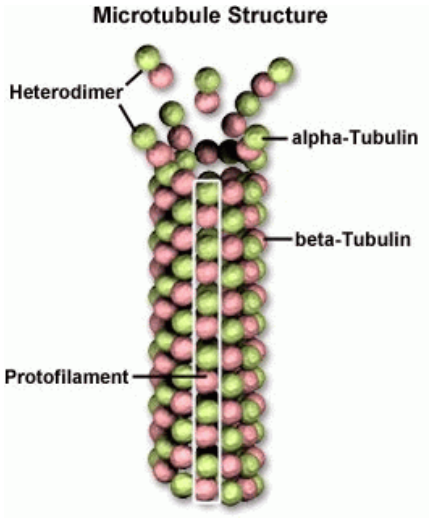
By Krishnashish Bose

Interiors of living cells are functionally organized by webs of protein polymers – the Cytoskeleton. The cytoskeleton has a dynamic structure which reorganizes continually as the cells change their shape, divide, and respond to their environment. The cytoskeleton is composed of intermediate filaments, actin filaments (or microfilaments), and microtubules. The filaments and the microtubules are mutually connected and form a three-dimensional network in the cell. The cytoskeleton is the main component which organizes the cell, mediates transport of molecules, organelles, and synaptic vesicles. The cytoskeleton possibly receives signals from the cellular environment mediated by the membrane of proteins and participates in signal transmission to the neighborhood of the cell.



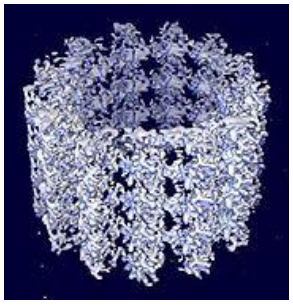
The Eukaryotic Cytoskeleton.
Microtubules are shown in green. Actin filaments are shown in red. The blue sphere at the centre is the nucleus.

Major components of the cytoskeleton are microtubules. These paracrystalline Cytoskeletal structures play a fundamental role in the cell *mitosis*, as well as in the transfer of electric signals and, more general, for dissipation-free energy transfer in the cell, according to ideas of Fröhlich (1986).



These are self-assembling hollow crystalline cylinders of polymers of α- and β-tubulin dimers with cross-sectional diameter 25 nm. The tubulin dimers polymerize end to end in protofilaments. The protofilaments then bundle into hollow cylindrical filaments. Typically, the protofilaments arrange themselves in an imperfect helix with one turn of the helix containing 13 tubulin dimers each from a different protofilament. The arrangement of the dimers is such that, if one ignores their size, they resemble triangular lattices on the MT surface. Each dimer consists of two hydrophobic protein pockets, and has an unpaired

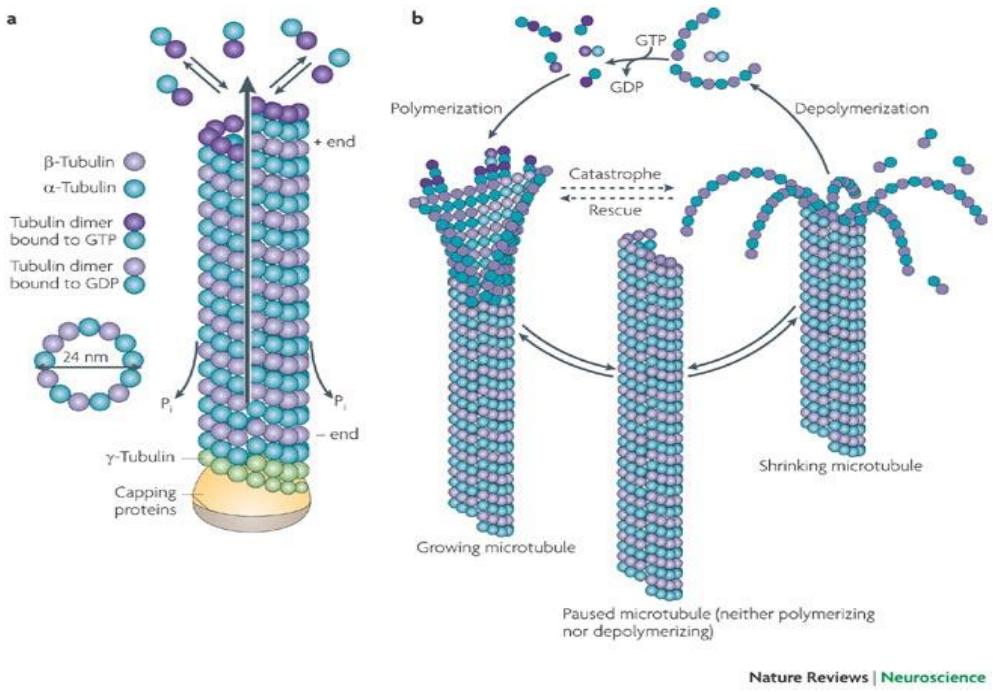
electron. There are two possible positions of the electron, called α and β conformations. When the electron is in the β-conformation there is a 29° distortion of the electric dipole moment as compared to the α-conformation.



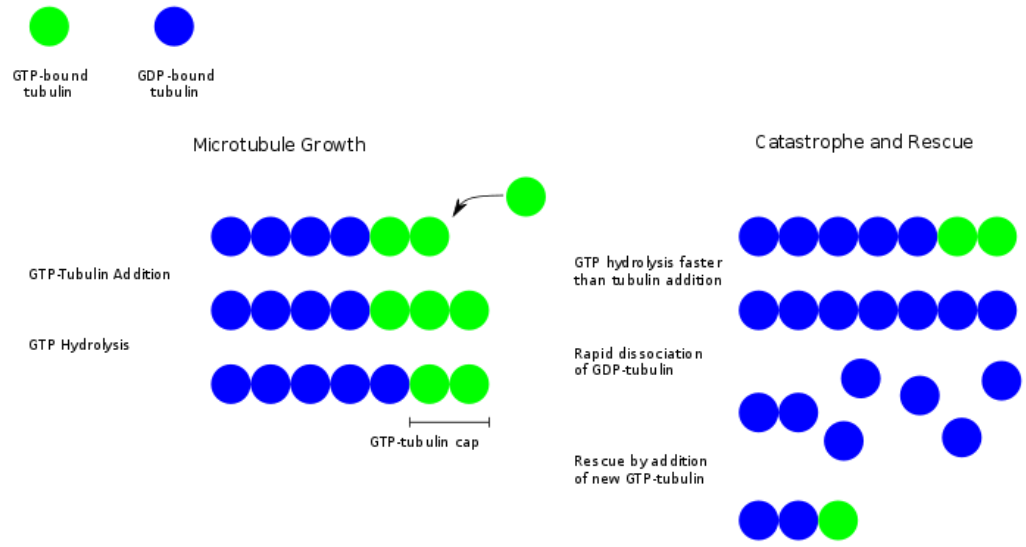
The MT interior works as an electromagnetic wave guide, filled with water in an organized collective state, transmitting information through the brain. A gelatinous state of water in brain cells could boost these communication effects. The electromagnetic field can transfer information through the environment among the systems like a communication channel. The charge separation of the MTs is wide enough to store information. Due to its dynamic coupling the information can be stored as mechanical energy and chemical events.

Another important feature of microtubule structure is polarity. The interior of the cylinder (of cross-section diameter 14 nm) contains ordered water molecules, which implies the existence of an electric dipole moment and an electric field. Tubulin polymerizes end to end with the α subunit of one tubulin dimer contacting the β subunit of the next. Therefore, in a protofilament, one end will have the α subunit exposed while the other end will have the β subunit exposed. These ends are designated the (–) and (+) ends, respectively. The protofilaments bundle parallel to one another, so in a microtubule, there is one end, the (+) end, with only β subunits exposed while the other end, the (–) end, only has α subunits exposed. The MTs thus represent a dipole due to individual dipolar charges of each tubulin monomer. The microtubule dipole produces a fast growth at the plus end towards the cell periphery and a slow growth at the minus end. The MT polarity is closely connected with its functional behavior which can be regulated by phosphorylation and dephosphorylation of microtubule-associated protein (MAP).

During polymerization, Guanosine triphosphate molecules (GTP) are bound to both tubulins in the heterodimer. While the GTP bound to α-tubulin is stable, the GTP bound to β-tubulin may be hydrolyzed to GDP shortly after assembly. The kinetics of GDP-tubulin is different from those of GTP-tubulin; GDP-tubulin is prone to depolymerization. A GDP-bound tubulin subunit at the tip of a microtubule will fall off, though a GDP-bound tubulin in the middle of a microtubule cannot spontaneously pop out. Since tubulin adds onto the end of the microtubule only in the GTP-bound state, there is generally a cap of GTP-bound tubulin at the tip of the microtubule, protecting it from disassembly. When hydrolysis catches up to the tip of the microtubule, it begins a rapid depolymerization and shrinkage.



This switch from growth to shrinking is called a catastrophe. GTP-bound tubulin can begin adding to the tip of the microtubule again, providing a new cap and protecting the microtubule from shrinking. This is referred to as rescue. After polymerization, when the heterodimer is attached to the microtubule, the GTP bound to the β-tubulin is hydrolyzed to the guanosine diphosphate (GDP). On the other hand, the GTP molecule of the α-tubulin is not hydrolyzed. The microtubules present a calm dynamic instability which is their principal feature. The pulses generated by the free energy in the GTP hydrolysis propagate along the MTs through an elastic coupling or through electric field propagation between tubulin dimers.



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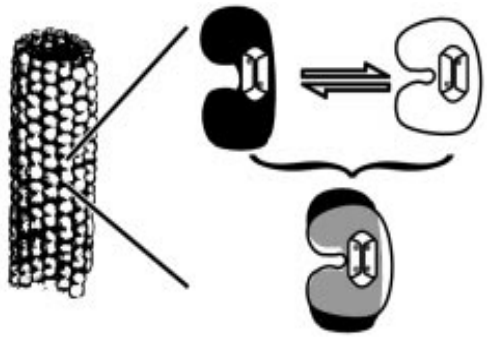
Microtubules are essential for a variety of biological functions including cell movement, cell division (mitosis) and establishment and maintenance of cell form and function. They are found throughout the plant & animal kingdom. In neurons, microtubules self-assemble to extend axons and dendrites and form synaptic connections; microtubules then help maintain and regulate synaptic strengths responsible for learning and cognitive functions. While microtubules have traditionally been considered as purely structural components, recent evidence has demonstrated mechanical signalling and communication functions (Glanz 1997; Maniotis et al .1997a; b; Vernon & Wooley 1995). Microtubules interact with membrane structures and activities by linking proteins (e.g. fodrin, ankyrin) and `second-messenger' chemical signals.



Widely recorded observations of Gamma Synchrony indicate that information may propagate through the brain much faster than a chemically mediated neural network would physically permit. In the Orch-OR theory of consciousness, Roger Penrose and Stuart Hameroff postulate that microtubules in neurons conduct quantum-level manipulations of matter which produces consciousness. The MT networks can sustain *macroscopic* coherent quantum mechanical states, identified with the *preconscious states*. Coupling the latter to space-time quantum (fluctuating) gravitational degrees of freedom triggers an *organized collapse* down to a specific or *conscious* state.

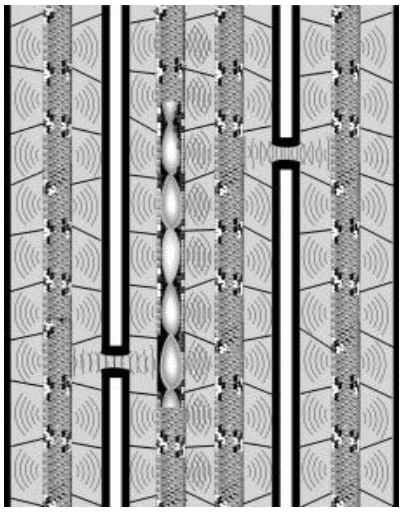
Theoretical models propose that microtubule subunit tubulins undergo coherent excitations, for example, in the gigahertz range by a mechanism suggested by Fröhlich (`pumped phonons'). Experimental evidence for Fröhlich-like coherent excitations in biological systems includes observation of gigahertz-range 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). Fröhlich excitations of tubulin subunits within microtubules have been suggested to support computation and information processing (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* exhibiting information processing, transmission and learning (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 (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, which 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.

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.

But if isolated cytoplasmic quantum states do occur within neuronal cells, could they traverse membranes and synapses to spread macroscopically throughout the brain & constitute a Giant Brain Wave function? One possibility involves quantum tunnelling through gap junctions between neurons and glia. 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 tunneling. 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.



Schematic diagram of proposed quantum coherence in microtubules in three dendrites interconnected by tunneling 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 tunneling among dendrites in macroscopic quantum states.