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A new theory of the origin of cancer: Quantum coherent entanglement, centrioles, mitosis and differentiation

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Abstract:
Malignant cells are characterized by abnormal segregation of chromosomes during mitosis ("aneuploidy"), generally considered a *result* of malignancy originating in genetic mutations. However recent evidence supports a century-old concept that maldistribution of chromosomes (and resultant genomic instability) due to abnormalities in mitosis itself is the primary cause of malignancy rather than a mere byproduct. In normal mitosis chromosomes replicate into sister chromatids which are then precisely separated and transported into mirror-like sets by structural protein assemblies called mitotic spindles and centrioles, both composed of microtubules. The elegant yet poorly understood ballet-like movements and geometric organization occurring in mitosis have suggested guidance by some type of organizing field, however neither electromagnetic nor chemical gradient fields have been demonstrated or shown to be sufficient. It is proposed here that normal mirror-like mitosis is organized by quantum coherence and quantum entanglement among microtubule-based centrioles and mitotic spindles which ensure precise, complementary duplication of daughter cell genomes and recognition of daughter cell boundaries. Evidence and theory supporting organized quantum states in cytoplasm/nucleoplasm (and quantum optical properties of centrioles in particular) at physiological temperature are presented. Impairment of quantum coherence and/or entanglement among microtubule-based mitotic spindles and centrioles can result in abnormal distribution of chromosomes, abnormal differentiation and uncontrolled growth, and account for all aspects of malignancy. New approaches to cancer therapy and stem cell production are suggested via non-thermal laser mediated effects aimed at quantum optical states of centrioles.

Key words: Cancer, centrioles, differentiation, genomic instability, malignancy, microtubules, mitosis, mitotic spindles, neoplasm, quantum coherence, quantum computation, quantum entanglement, quantum theory, stem cells

Theories of the origin of cancer: mutation, aneuploidy, genomic instability

Malignant cells divide and multiply uncontrollably. They evade built-in autodestruct mechanisms, stimulate formation of blood vessels to feed themselves, and can invade other tissues. Proper differentiation – the process by which genetic expression leads to specific cell types (phenotypes) – is lost. Despite intense efforts and recognition of predisposing factors (e.g. carcinogens, reactive oxidants, genetic/family history) cancer remains an enormous problem.

In the early 20th century German biologist Theodor Boveri observed cell division ("mitosis") in normal and cancerous cells (Boveri, 1929). Whereas normal cells exhibited symmetrical, bipolar division of chromosomes into two equal mirror-like distributions (Figure 1), Boveri noticed that cancer cells were different. Cancer cells showed imbalanced divisions of chromosomes, with asymmetrical and multipolar unequal ("aneuploid") distributions (Figure 2 and 3). Boveri suggested that aberrant processes in mitosis itself caused abnormal distribution of chromosomes and genes. He reasoned that most abnormal distributions would be non-viable, but some would lead to viable cells and cancerous differentiation with uncontrollable proliferation. But because no recurrent pattern occurred—the aneuploidy changed from generation to generation (what is now called "genomic instability")—the majority of scientists assumed the abnormal distribution of chromosomes were effects, rather than causes of malignancy and that cancer originated from intrinsic chromosomal changes. In retrospect, genomic instability is a logical consequence of abnormal mitosis. Nonetheless, the belief that cancer resulted from genetic mutations became the "standard dogma" (Gibbs, 2003).

As DNA and genetics became understood and prominent, the idea that cancer is the result of cumulative mutations became entrenched. Specific alterations in a cell's DNA, spontaneous or induced by carcinogens, change the particular proteins encoded by cancer-related genes at those spots. Two particular kinds of genes were identified as being potentially relevant to cancer. The first included tumor suppressor genes which normally restrain cells' tendencies to divide. Presumably mutations affecting these genes disabled them, removing beneficial effects of suppressors. The second group included oncogenes which stimulate growth, or cell division. Mutations leading to cancer were thought to lock oncogenes into a permanently active state.

However in the era of genetic engineering, oncogene/suppressor theory has failed to explain cancer. No consistent set of gene mutations correlate with malignancy; each tumor may be unique in its genetic makeup. In fact tremendous genetic variability occurs within individual tumors, and genomic instability—changes in the genome with subsequent cycles of mitosis—is now seen as the major pathway to malignancy (Marx, 2002).

Some specific DNA factors are indeed related to genomic instability. These include unrepaired DNA damage, stalled DNA replication forks processed inappropriately by recombination enzymes, and defective telomeres which protect ends of chromosomes. But again, inherent DNA mutation and sequelae—

the “standard dogma”—don’t explain the entire picture. Other approaches suggest that a combination of DNA defects and other problems are responsible for genomic instability and malignancy.

One approach is called “modified dogma” which revives an idea from 1974 by Lawrence A. Loeb and colleagues (Loeb et al., 1974) who noted that random mutations, on average, would affect only one gene per cell in a lifetime. Some other factor—carcinogen, reactive oxidants, malfunction in DNA duplication and repair machinery—is proposed to increase the incidence of random mutations (Loeb et al., 2003). Another approach is “early instability” (Nowak et al., 2002) which suggests that master genes are critical to cell division—if they are mutated, mitosis is aberrant. But master genes are still merely proposals.

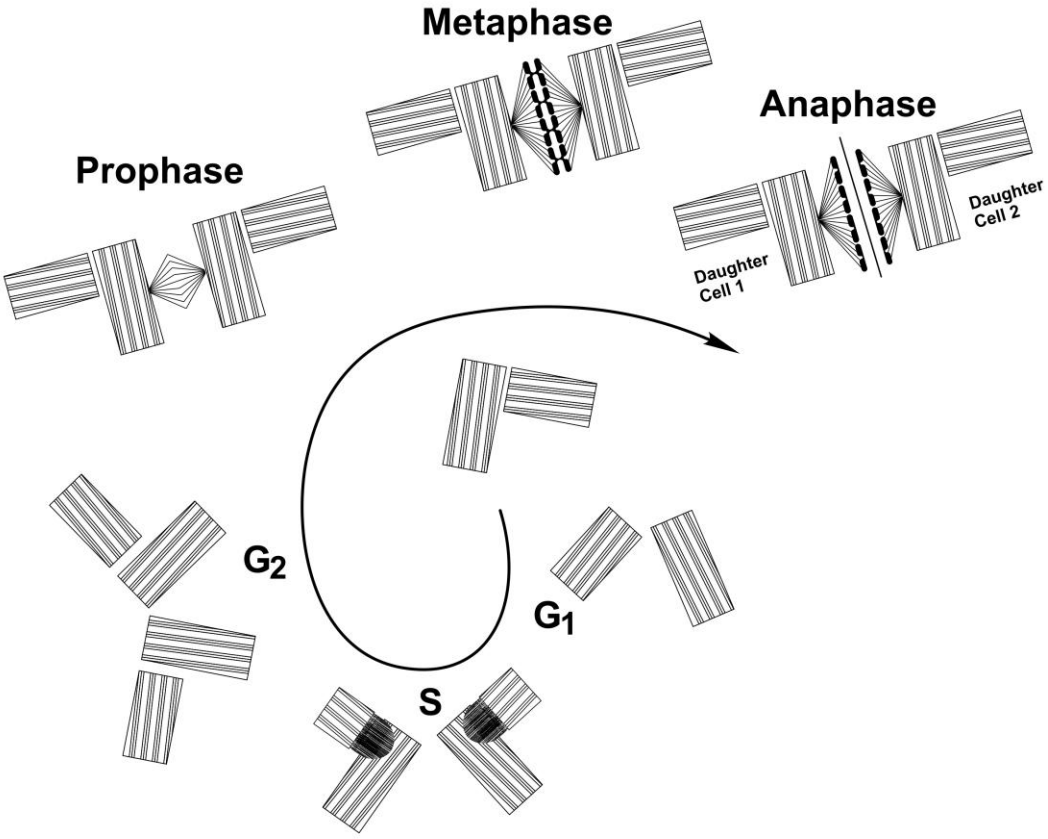

Figure 1. Modifications to the centriole in the normal cell cycle and mitosis (not to scale: centrioles are ~750 nanometers in length and 200 nanometers outer diameter, much smaller than mitotic spindles). Center: centriole as two perpendicular cylinders. Clockwise from center (G1, S and G2 occur during “Interphase” which precedes and follows mitosis): in G1 phase centriole cylinders separate. In S phase centrioles replicate, each cylinder forming a new perpendicular cylinder via connecting filamentous proteins. G2 phase: centrioles separate and begin to migrate. Prophase: centrioles move apart and microtubules form the mitotic spindles between the centrioles. Metaphase: mitotic spindles attach to centromeres/kinetochores on opposite sides of each paired

chromosome (only 4 of which are shown). Anaphase: Paired chromosomes separate into sister chromatids and are moved by (and move along) mitotic spindles to newly forming daughter cells. Modified from Hagan et al. (1998) by Dave Cantrell.

Another idea returned to Boveri's suggestion that the problems lie with the molecular machinery of mitosis which, under normal circumstances, results in precisely equal separation of duplicated chromosomes. The "all-aneuploidy" theory (Duesberg et al., 2000) proposes that cells become malignant before any mutations or intrinsic genetic aberrancy. With the exception of leukemia, nearly all cancer cells are aneuploid. Thus malignancy is more closely related to maldistribution of chromosomes than to mutations on the genes within those chromosomes. Experiments show that genomic instability correlates with degree of aneuploidy.

What causes aberrant mitosis? Asbestos fibers and other carcinogenic agents are known to disrupt normal mitosis. Certain genes trigger and regulate mitosis, and experimentally induced mutations in these genes result in abnormal mitosis and malignancy. However such mutations in mitosis-regulating genes have not been found in spontaneously occurring cancers. Thus mitosis *itself*, the dynamical, ballet-like mechanical separation of chromosomes into two perfectly equal paired sets, may be at the heart of the problem of cancer. However the organization of mitosis is not understood.

Mitosis and differentiation

Under normal conditions chromosomes replicate into "sister chromatids" which remain attached to each other at a single point via a structure called a centromere/kinetochore. Chromatids are then separated and pulled apart into two identical sets by remarkable molecular machines called mitotic spindles which attach to the chromatid centromere/kinetochore (Hagan et al., 1998). The spindles are composed of microtubules (centromere/kinetochores also contain microtubule fragments). Once separated, sister chromatids are known as daughter chromosomes.

The microtubule spindles pull the daughter chromosomes toward two poles anchored by microtubule organizing centers (MTOCs), or centrosomes (as they are known in animal cells). Centrosomes are composed of structures called centrioles embedded in an electron-dense matrix composed primarily of the protein pericentrin. Each centriole is a pair of barrel-like structures arranged curiously in perpendicular tandem (Figures 4 and 5), and (like mitotic spindles) are comprised of microtubules, self-assembling polymers of the protein tubulin. In centrioles, microtubules are fused longitudinally into triplets; nine triplets are aligned, stabilized by protein struts to form a cylinder which may be slightly skewed (Dustin, 1984). New cylinders self-assemble/replicate perpendicular to

existing cylinders, and centriole replication involves self-assembly of two new cylinders from each pre-existing cylinder of the pair which constitutes the centriole (Figure 1-3, G1, S and G2 phases). The two perpendicular pairs then separate resulting in two centrioles.

Centrioles are the specific apparatus within living cells which trigger and guide not only mitosis, but other major reorganizations of cellular structure occurring during growth and differentiation. Somehow centrioles have command of their orientation in space, and convey that information to other cytoskeletal structures. Their navigation and gravity sensation have been suggested to represent a "gyroscopic" function of centrioles (Bornens, 1979). The mystery and aesthetic elegance of centrioles, as well as the fact that in certain instances they appear completely unnecessary, have created an enigmatic aura "Biologists have long been haunted by the possibility that the primary significance of centrioles has escaped them" (Wheatley, 1982).

The initiation of mitosis ("S" of interphase into prophase) involves centriole replication, separation and migration to form the mitotic poles to which spindles attach (Nasmyth, 2002). The opposite end of each spindle affixes to centromeres/kinetochores on specific

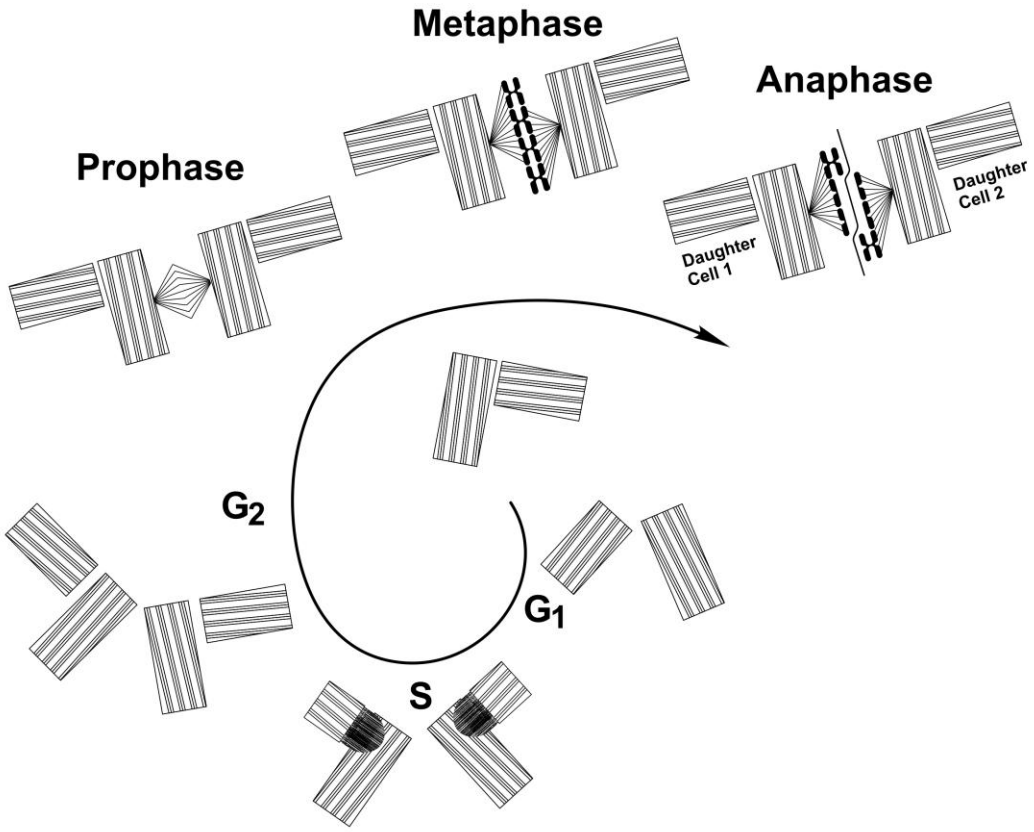

Figure 2. Abnormal centriole activities in mitosis leading to aneuploidy. As in Figure 1 except that during metaphase the centriole/spindle binding of chromatids is defective and asymmetrical leading to maldistribution of chromosomes in the anaphase daughter cells. Each daughter cell is missing an entire chromosome and has an extra chromatid, hence an abnormal genotype. By Dave Cantrell.

chromatids, so that proper separation of centrosomes/centrioles results in separation of chromosomes into equal sets forming the focal point of the two daughter cells (Figure 1).

There are a number of questions regarding mitosis, but one compelling issue is how all the intricate processes are coordinated in space and time by centrioles to generate a geometric structure that maintains itself at steady state. Indeed, the mitotic apparatus resembles a crystalline structure, however it is also a dynamic, dissipative system. A review in *Science* concluded: "Robustness of spindle assembly must come from guidance of the stochastic behavior of microtubules by a field" (Karsenti, 2001). Without any real evidence some conclude that chromosomes generate some type of field which organizes the centrioles and

spindles. However Boveri and later Mazia (1970) believed the opposite, that spindle and centrosome/centriole microtubules generated an organizing field or otherwise regulated the movement of chromosomes and orchestration of mitosis.

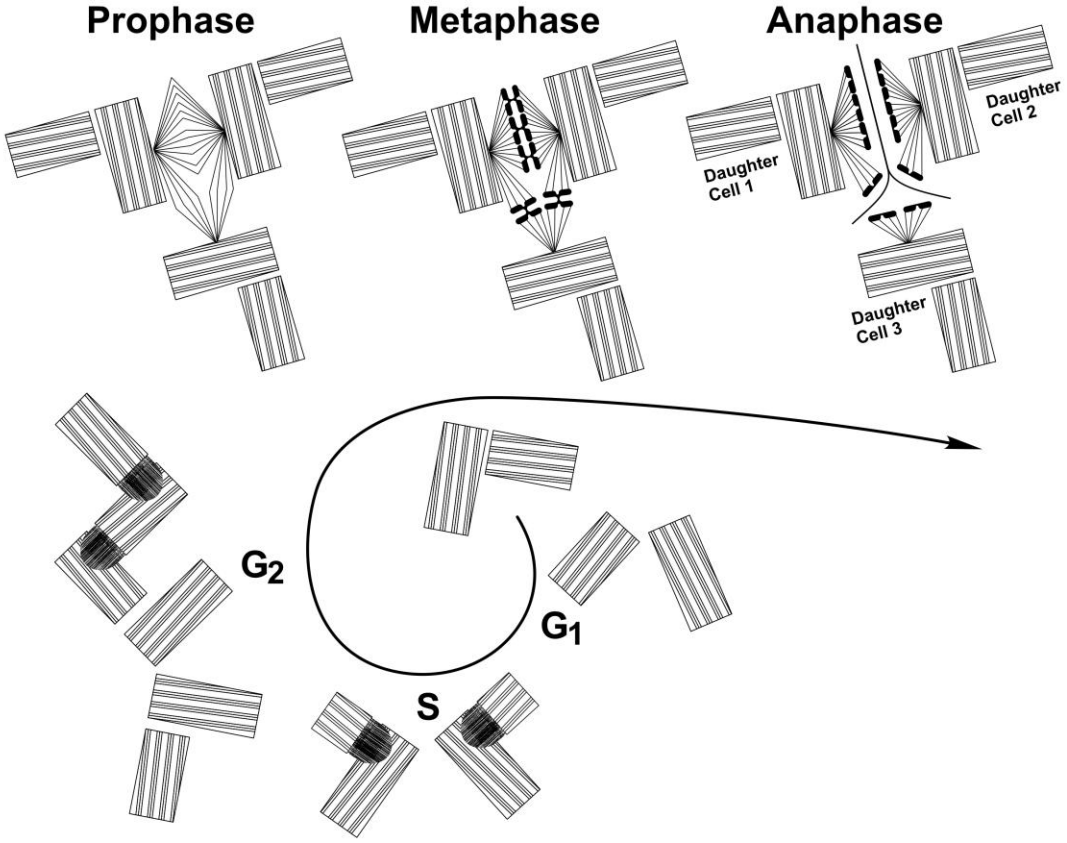

Figure 3. Abnormal centriole activities in mitosis leading to aneuploidy. As in Figures 1 and 2 except that defective centriole replication continues in G2 producing 3 centrioles which form abnormally distributed spindles in prophase and abnormal chromosome distribution/genotypes in metaphase and anaphase. This results in chromosomes maldistributed among 3 daughter cells. By Dave Cantrell.

As centrosomes/centrioles organize the spindles (which anchor in the pericentrin matrix surrounding centrioles), it seems most likely that centrosomes/centrioles are the primary organizers of mitosis.

Cultured cells in which centrosomes are removed by microsurgical techniques, leaving the cell nucleus and cytoplasm, are called karyoplasts. Maniotis and Schliwa (1991) found that karyoplasts reestablish a microtubule organizing center near the nucleus and form mitotic spindles. Karyoplasts can grow but do not undergo cell division/mitosis.
Khodjakov et al. (2002) destroyed centrosomes by laser ablation in cultured cells and found that a random number (2 – 14) of new centrosomes formed in clouds of pericentrin.

In any case centrosomes/centrioles are essential to normal mitosis (Marx, 2001; Doxsey, 1998; Hinchcliffe et al., 2001) and impairment of their function can lead to genomic instability and cancer (Szuromi, 2001; Pihan, 1999). Multiple and enlarged centrosomes have been found in cells of human breast cancer and other forms of malignancy (Lingle et al.,1998; 1999; Pihan et al., 2003). Wong and Stearn (2003) showed that centrosome
number, hence centriole replication, is controlled by factors intrinsic to the centrosome/centrioles (i.e. rather than genetic control). Referring to the centrosome as the "cell brain", Kong et al (2002) attributed malignancy to aberrant centrosomal information processing.

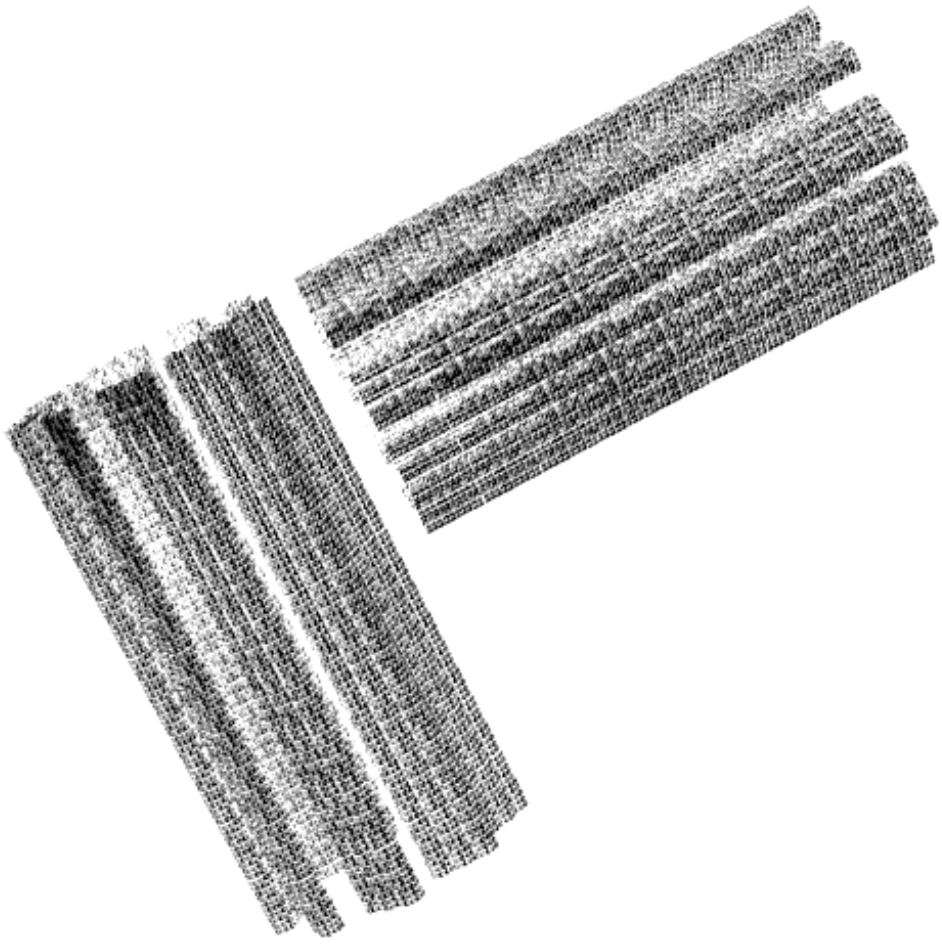

Figure 4. A centriole is comprised of two cylinders (as shown in Figure 5) arranged in perpendicular tandem. Each cylinder is 750 nanometers (0.75 microns) in length. By Dave Cantrell.

In other forms of intracellular movement and organization, microtubules and other cytoskeletal structures are the key players. So it is logical that they also organize mitosis. But something is missing. What type of organizational field, information processing or principle might be occurring in mitosis? Recent attempts to explain higher brain functions have suggested that microtubules within neurons and other cells process information, and may utilize certain *quantum* properties. If so, these same properties could also explain aspects of mitosis and normal cell functions lost in malignancy.

Subsequent to mitosis, embryonic daughter cells develop into particular types of cells ("phenotypes"), e.g. nerve cells, blood cells, intestinal cells etc., a process called differentiation. Each (normal) cell in an organism has precisely the same set of genes. Differentiation involves "expressing" a particular subset of genes to yield a particular phenotype. Neighbor cells and location within a particular tissue somehow convey signals required for proper gene expression and differentiation. For example an undifferentiated "stem cell" placed in a certain tissue will differentiate to the type of cell in the surrounding tissue. However the signaling mechanisms conveyed by surrounding cells to regulate differentiation are unknown.

Cancer cells are often described as poorly differentiated, or undifferentiated – lacking refined properties characteristic of a particular tissue type, and unmatched to the surrounding or nearby normal tissue. Abnormal genotypes (e.g. from aberrant mitosis or mutations) can disrupt normal differentiation, but again the mechanisms of normal differentiation (genotype to phenotype) are unknown.

It seems likely that centrioles play key roles in differentiation. Situated close to the nucleus, centrioles can transduce intra-cellular signals to regulate gene expression (Puck and Krystosek, 1992). As "commander" of the cytoskeleton, centrioles can determine cell shape, orientation and form. And centrioles have the information storage and processing capacity to record the "blueprints" for a vast number of phenotypes, all possible states of differentiation in a specific organism. The key question in differentiation is how signals/communication from neighboring and surrounding tissues mediate gene expression. While chemical messengers and chemical gradients are possible mechanisms (e.g. Niethammer et al., 2004), a more elegant, efficient and practical method may involve nonlocal quantum interactions (e.g. entanglement) among microtubules and centrioles in neighboring and nearby cells.

Microtubules and centrioles

Interiors of eukaryotic cells are structurally organized by the cell cytoskeleton which includes microtubules, actin, intermediate filaments and microtubule-based centrioles, cilia and basal bodies (Dustin, 1984). Rigid microtubules are interconnected by microtubule-associated proteins ("MAPs") to form a self-

supporting, dynamic tensegrity (definition: synergy between balanced tension and compression components, DW added) network which, along with actin filaments, comprises a negatively-charged matrix on which polar cell water molecules are bound and ordered (Pollack, 2001).

Microtubules are cylindrical polymers of the protein tubulin and are 25 nanometers (nm = 10^{-9} meter) in diameter (Figure 6). The cylinder walls of microtubules are comprised of 13 longitudinal protofilaments which are each a series of tubulin subunit proteins (Figure 6). Each tubulin subunit is an 8 nm by 4 nm by 5 nm heterodimer 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 the cylinder wall are arranged in a hexagonal lattice which is slightly twisted, resulting in differing neighbor relationships among each subunit and its six nearest neighbors (Dustin, 1984). Pathways along neighbor tubulins form helices which repeat every 3, 5 and 8 rows (the “Fibonacci series”).

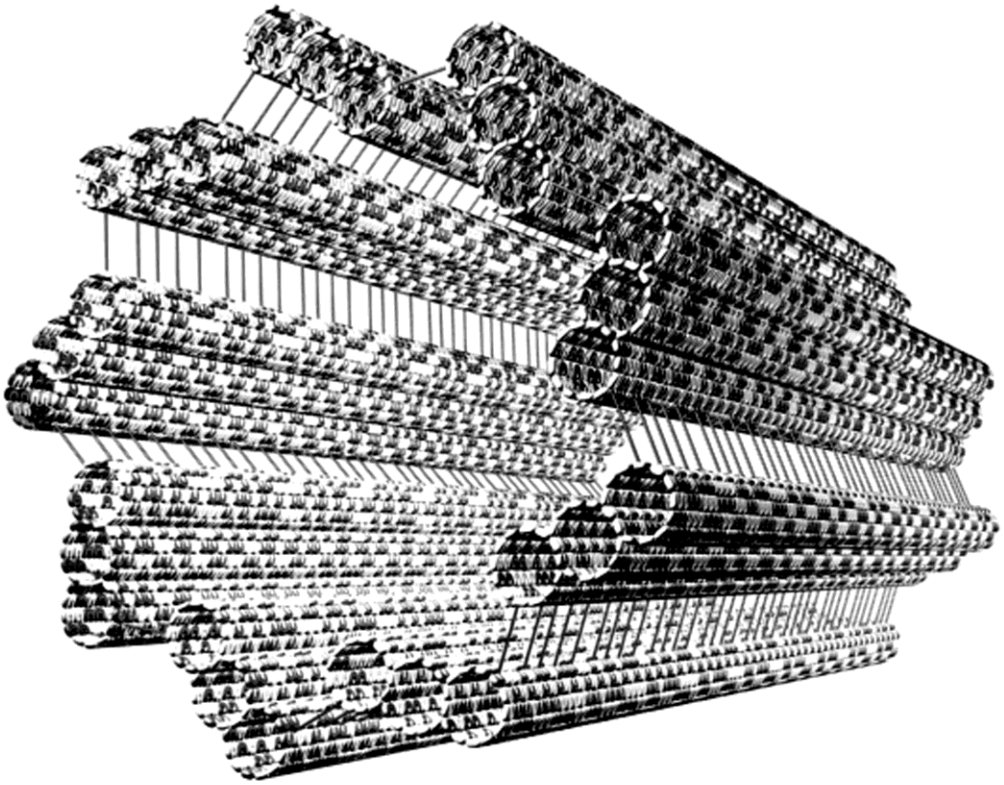

Figure 5. Centriole cylinder (one half of a centriole) is comprised of 9 microtubule triplets in a skewed parallel arrangement. Each microtubule is comprised of tubulin proteins (Figure 6), each of which may be in one or more possible conformational states (illustrated as e.g. black or white). The cylinder inner core

is approximately 140 nanometers in diameter and the cylinder is 750 nanometers in length. By Dave Cantrell.

Each tubulin has a surplus of negative surface charges, with a majority on the alpha monomer; thus each tubulin is a dipole (beta plus, alpha minus). Consequently microtubules can be considered ”electrets”: oriented assemblies of dipoles which are predicted to have piezoelectric, ferroelectric and spin glass properties (Tuszynski et al.,1995). In addition, negatively charged C–termini “tails” extend outward from each monomer, attracting positive ions from the cytoplasm and forming a plasma-like “Debye layer” surrounding the microtubule (Hameroff et al., 2002).

Biochemical energy is provided to microtubules in several ways: tubulin-bound GTP is hydrolyzed to GDP in microtubules, and MAPs which attach at specific points on the microtubule lattice are phosphorylated. In addition microtubules may possibly utilize nonspecific thermal energy for “laser-like” coherent pumping, for example in the GigaHz range by a mechanism of “pumped phonons” suggested by Fröhlich (1968; 1970; 1975). Simulation of coherent phonons in microtubules suggest that phonon maxima correspond with functional microtubule-MAP binding sites (Samsonovich et al., 1992).

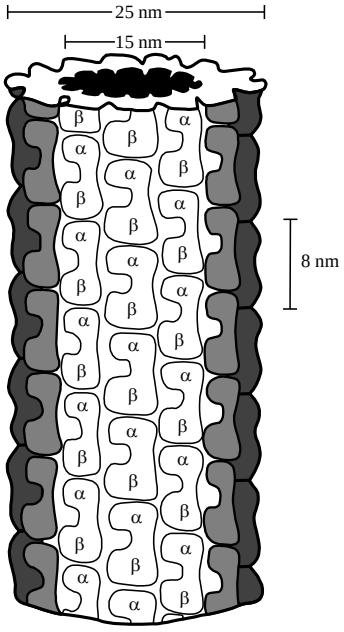

Figure 6. Microtubules are hollow cylindrical polymers of tubulin proteins, each a “dimer” of alpha and beta monomers.

In centrioles (as well as cilia, flagella, basal bodies etc.) microtubules fuse into doublets or triplets. Nine doublets or triplets then form larger barrel-like cylinders (Figure 5) which in some cases have internal structures connecting the doublets/triplets. The nine doublet/triplets are skewed, and centrioles move through cytoplasm by an "Archimedes screw" mechanism.

Albrecht-Buehler (1992) has shown that centrioles act as the cellular "eye", detecting and directing cell movement in response to infra-red optical signals. (Cilia, whose structure is nearly identical to centrioles, are found in primitive visual systems as well as the rod and cone cells in our retinas.) The inner cylindrical core of centrioles is approximately 140 nanometers in diameter and 750 nanometers in length, and, depending on the refractive index of the inner core, could act as a waveguide or photonic band gap device able to trap photons (Figure 8). Tong et al (2003) have shown that properly designed structures can act as sub-wavelength waveguides, e.g diameters as small as 50 nanometers can act as waveguides for visible and infrared light.

Historic work by Gurwisch (1922) showed that dividing cells generate photons ("mitogenetic radiation"), and recent research by Liu et al (2000) demonstrates that such biophoton emission is maximal during late S phase of mitosis, corresponding with centriole replication. Van Wijk et al.(1999) showed that laser-stimulated biophoton emission ("delayed luminescence") emanates from peri-nuclear cytoskeletal structures, e.g. centrioles. Popp et al (2002) have shown that biophoton emission is due to quantum mechanical "squeezed photons", indicating quantum optical coherence. The skewed helical structure of centrioles may be able to detect polarization or other quantum properties of photons such as orbital momentum.

Unlike centrioles, cilia and flagella bend by means of contractile proteins which bridge between doublets/triplets. The coordination of the contractile bridges are unknown, however Atema (1973) suggested that propagating conformational changes along tubulins in the microtubule doublet/triplets signaled contractile proteins in an orderly sequence. Hameroff and Watt (1982) suggested that microtubules may process information via tubulin conformational dynamics (coupled to dipoles) not only longitudinally (as Atema proposed) but also laterally among neighbor tubulins on the hexagonal microtubule lattice surface, accounting for computer-like capabilities. Rasmussen et al (1990) showed an enormous potential computational capacity of microtubule lattices (and microtubules interconnected by MAPs) via tubulin-tubulin dipole interactions, with the dipole-coupled conformational state of each tubulin representing one "bit" of information. The regulation of protein conformational states is an essential feature of biological systems.

Tubulin conformational states

Within microtubules, individual tubulins may exist in different states which can change on various time scales (Figure 7). Permanent states are determined by genetic scripting of amino acid sequence, and multiple tissue-specific isozymes of tubulin occur (e.g. 22 tubulin isozymes in brain: Lee et al., 1986). Each tubulin isozyme within a microtubule lattice may be structurally altered by "post-translational modifications" such as removal or addition of specific amino acids. Thus each microtubule may be a more-or-less stable mosaic of slightly different tubulins, with altered properties and functions accordingly (Geuens et al., 1986).

Tubulins also change shape dynamically. 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) with associated changes in the tubulin dipole ("open versus closed" conformational states). Hoenger and Milligan (1997) showed a conformational change based in the beta tubulin subunit. Ravelli et al. (2004) demonstrated that the open versus closed conformational shift is regulated near the binding site for the drug colchicine (definition: inhibits microtubule polymerization-> acts as poison to cancer cells, DW added). Dynamic conformational changes of particular tubulins may be influenced, or biased, by their primary or post-translational structures.

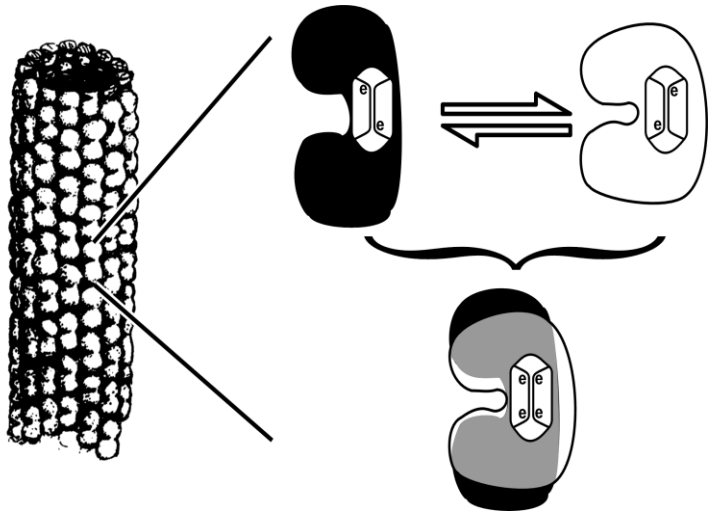

Figure 7. Tubulin protein subunits within a microtubule can switch between two (or more) conformations, coupled to London forces in a hydrophobic pocket in the protein interiort. Right (bottom): Each tubulin is proposed to also exist in quantum superposition of both conformational states

(Penrose has written controversial books on the connection between fundamental physics and human consciousness. In *The Emperor's New Mind* (1989), he argues that known laws of physics are inadequate to explain the phenomenon of human consciousness. Penrose hints at the characteristics this

new physics may have and specifies the requirements for a bridge between classical and quantum mechanics (what he terms correct quantum gravity, CQG). He claims that the present computer is unable to have intelligence because it is a deterministic system that for the most part simply executes algorithms, as a billiard table where billiard balls act as message carriers and their interactions act as logical decisions. He argues against the viewpoint that the rational processes of the human mind are completely algorithmic and can thus be duplicated by a sufficiently complex computer -- this is in contrast to views, e.g., Biological Naturalism, that human behavior but not consciousness might be simulated. This is based on claims that human consciousness transcends formal logic systems because things such as the insolubility of the halting problem and Gödel's incompleteness theorem restrict an algorithmically based logic from traits such as mathematical insight. These claims were originally made by the philosopher John Lucas of Merton College, Oxford.

In 1994, Penrose followed up The Emperor's New Mind with *Shadows of the Mind* and in 1997 with The Large, the Small and the Human Mind, further updating and expanding his theories. Penrose's views on the human thought process are not widely accepted in scientific circles. According to Marvin Minsky, because people can construe false ideas to be factual, the process of thinking is not limited to formal logic. Furthermore, he says that AI programs can also conclude that false statements are true, so error is not unique to humans.(Penrose and Stuart Hameroff have constructed a theory in which human consciousness is the result of quantum gravity effects in microtubules, which they dubbed Orch-OR (orchestrated object reduction). But Max Tegmark, in a paper in Physical Review E, calculated that the time scale of neuron firing and excitations in microtubules is slower than the decoherence time by a factor of at least 10,000,000,000. The reception of the paper is summed up by this statement in his support: "Physicists outside the fray, such as IBM's John Smolin, say the calculations confirm what they had suspected all along. 'We're not working with a brain that's near absolute zero. It's reasonably unlikely that the

brain evolved quantum behavior', he says." The Tegmark paper has been widely cited by critics of the Penrose-Hameroff proposal. It has been claimed by Hameroff to be based on a number of incorrect assumptions (see linked paper below from Hameroff, Hagan and Tuszyński), but Tegmark in turn has argued that the critique is invalid (see rejoinder link below). In particular, Hameroff points out the peculiarity that Tegmark's formula for the decoherence time includes a factor of in the numerator, meaning that higher temperatures would lead to longer decoherence times. Tegmark's rejoinder keeps the factor of for the decoherence time. DW added from wikipdia) Penrose and Hameroff (1995; c.f. Hameroff and Penrose 1996a; 1996b).

In general, conformational transitions in which proteins move globally and upon which protein function generally depends occur in the microsecond (10^{-6} sec) to nanosecond (10^{-9} sec) to 10 picosecond (10^{-11} sec) time scale (Karplus and McCammon, 1983). Proteins are only marginally stable: a protein of 100 amino acids is stable against denaturation by only ~40 kiloJoules per mole (kJ mol^{-1}) whereas thousands of kJ mol^{-1}
are available in a protein from amino acid side group interactions. Consequently protein conformation is a "delicate balance among powerful countervailing forces" (Voet and Voet, 1995).

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
3) Induced dipole - induced dipole

Type 3 induced dipole - induced dipole interactions are the weakest but most purely non-polar. 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 (in some cases) spherically symmetrical, nevertheless

have instantaneous electric dipoles due to asymmetry in their electron distribution: electrons in one cloud repel those in the other, forming dipoles in each. 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, the London forces which regulate tubulin states are quantum mechanical and subject to quantum uncertainty.

In addition to electron location, unpaired electron spin may play a key role in regulating tubulin states. Unpaired electron spin is basically a tiny magnet and microtubules are ferromagnetic lattices which align parallel to strong magnetic fields, accounted for by single unpaired electrons per tubulin. Atomic structure of tubulin shows two positively charged areas (~100-150 meV) near the alpha-beta dimer “neck” separated by a negatively charged area of about 1.5 nanometers (Hameroff and Tuszynski, 2003). This region constitutes a double well potential which should enable inter-well quantum tunneling of single electrons and spin states since the energy depth is significantly above thermal fluctuations (kT=25 meV at room temperature). The intra-tubulin dielectric constant is only 2, compared to roughly 80 outside the microtubule. Hence neither environmental nor thermal effects should decohere quantum spin states in the double well. Spin states and superposition of unpaired tunneling electrons should couple to excess tubulin electrons and global tubulin conformational states including tubulin quantum superposition states. Tubulin subunits within microtubules may be regulated by quantum effects.

The strange world of quantum reality

Reality seems to be described by two separate sets of laws. At our everyday large scale classical, or macroscopic world, Newton's laws of motion and Maxwell's equations for electromagnetism are sufficient. However at small scales in the "quantum realm" (and the boundary between the quantum and classical realms remains elusive) paradox reigns. Objects may exist in two or more states or places simultaneously—more like waves than particles and governed by a "quantum wave function". This property of multiple coexisting possibilities, known as quantum superposition, persists until the superposition is measured, observed or “decoheres” via interaction with the classical world or environment. Only then does the superposition of multiple possibilities "reduce", "collapse", "actualize", "choose" or "decohere" to specific, particular classical states.
The nature of quantum state reduction—the boundary between the quantum and classical worlds— remains mysterious (Penrose, 1989; 1994).

Another quantum property is entanglement in which components of a system become unified, governed by one common quantum wave function. The quantum states of each component in an entangled system must be described with reference to other components, though they may be spatially separated. This leads to correlations between observable physical properties of the systems that