A SPACE GENERATION FORMULATION OF BIOLOGICAL PROCESSES

ABSTRACT

A previous exploratory study reviewed works by Everett, Feynman and others dealing with the nature of the quantum in light of an hypothesis by Bruno, Leibniz and Einstein about the origin of space. A common thread was identified within that line of thought, allowing to discern an alternate conceptual approach for the problem of the elements making up our reality. The obtained formulation on the relation between the quantum and space was found to have verifiable consequences in Particle Physics and Astrophysics. In the present study a third field is identified for the purpose of verification, the Life Sciences. Physical hypotheses advanced in that field are first reviewed. From there an hypothetical process originally designed by Penrose to effect a quantum mind is replaced by a space generation process where a local space manifold structure is generated by the quantum, a key concept identified in the earlier study about the origin of space. An organizing principle based on this concept is then found to apply to biological systems in general and nervous systems in particular. Through the envisioned phenomenon of quantum space generation (1) the classical approach to embryo development followed by Turing, Wolpert and Kauffman may be augmented, or in some cases replaced, by an approach involving non-local quantum effects, and (2) known biomolecular structures may be able to support an infinite computational process via non-local quantum cellular automata. Several experiments in embryo development are suggested to confirm the validity of the approach. A formal dynamical analysis based on previous work about quantum computation provides part of the theoretical basis for the physical processes involved, while Everett's formulation of the quantum, as clarified by the earlier study, is found necessary to properly evaluate their physical and computational characteristics. However, a complete formalism suitable for the envisioned quantum-generated local space structures cannot be provided within the confines of this review due to the intrinsic novelty of their elements for Mathematical Analysis. Additional theoretical work is also required to formalize the kind of computational processes identified. This study and the earlier one on the origin of space are examples of a priori conceptual searches. An overall conclusion then addresses the nature of a scientific quest, with arguments presented against the approach of logical positivism with its emphasis on formal methods, and in favor of first seeking conceptual understandings regardless of the availability of a corresponding formalism.

Keywords: artificial intelligence, artificial life, cellular automata, composite quantum, computation, creativity, darwinism, embryo development, many-worlds, mind, mitosis, monads, morphogens, multiple-realities, neuron, paradigm, quantum, quantum computation, turing test

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I. INTRODUCTION

This study completes a falsifiable formulation of the quantum origin of space that was begun in an earlier study (Gouin, 1999), addressing here biological processes. Overall, through these two studies, three *a priori unrelated* areas are found with predictable experimental consequences, Particle Physics, Astrophysics and Biophysics. Each of the evidences has its limitations, but when considering them together they ought to be able to establish the validity of the formulation.

In the earlier study, without addressing the matter, I identified a key barrier against our understanding of reality to be the origin of sentience, i.e. our awareness. This matter can of course only be addressed if something is known about the *physical* makeup of a mind, *a system that apparently forms a whole* out of a very large collection of microbiological elements that are yet to be identified. I reviewed in the earlier study how "elementary" particles may act as wholes extended in space thanks to the multiple-reality make-up of our universe envisioned by Everett, and developed since the 1960s through studying the puzzling "non-local," "contextual" and "counterfactual" characters of the quantum. However, there is a large chasm between elementary particles and biomolecules, and quantum effects have been found so far only in very cold places with very tiny things, while Life appears to be "hot" and "macroscopic," an appearance that has suggested up until now an entirely classical approach to the causal description of biological processes (Section II). In order to bridge such a chasm, Penrose recently hypothesized a quantum phenomenon that would have the required characteristics for supporting the physical makeup of a mind, but this phenomenon seems to relate only to brain-related effects (Penrose, 1994; Hameroff, 1998), and since living organisms, *a priori* and undeniably, have an extended whole aspect besides minds, a realistic physical formulation ought to apply to a wide range of biological processes.

Section III proposes such a formulation by replacing Penrose's picture with a quanta-based space generation process inspired from the earlier study on the origin of space. This alternate approach envisions a *macroscopic* process existing through the extended whole the quantum would construct *by building its own space* out of individual bioelements. An experimental backing appears to have existed well before such a phenomenon could be identified, but the meaning of the observations could not be grasped earlier having no suitable theoretical framework, especially when taking into account the Classical Physics context that was selected from the start by the Life Sciences. Due to this context, and until now, Life has been considered a priori unlikely to display "hard" *new* physical effects, so Appendix A reviews the literature

pointing out the *need for them* in order to obtain a true causal description of many known biological processes. Between this appendix and the corresponding Sections (III and IV) there ought to be enough to consider the *theoretical* existence of such effects, but *new experiments identified through the formulation* are essential to confirm their *physical* existence.

Section IV then gets to where experiments should focus by first analyzing how the basic function of a typical living cell may be physically carried out. In that line, there is a potential for *contextual* structural changes and motions with collective exchanges of quanta between known supramolecular structures. Their self-assembly and relative motion are looked at through well-known and so far unexplained experimental facts. The results of this analysis are subsequently applied to higher levels of processes in order to evaluate their generality and importance, as well as their fitness for experimentation. Nature appears to have found how to implement "extended computations" through supramolecular structures on top of the ones it may be effecting at the nuclear and atomic levels as the earlier study envisioned. A formal analysis (Appendix B) describing the evolution of observed supramolecular structures evaluates the physical basis for such computations presenting them as examples of *quantum conformational dynamics*. The section ends with potential experimentation in the various areas analyzed, thereby providing the looked-for other set of experimentally verifiable consequences for the quantum space-generation formulation.

With this background established, Section V can at last address the key barrier against our understanding of reality presented by the existence of our awareness, as the characteristics of the previously identified biological computational processes may be telling us something physical about this elusive feature of reality. However, due to the sketchy state of our present knowledge in that area, this section only intends to provide a very preliminary *physical* ground upon which the next century could potentially build to deal with the physical aspect of minds.

The conclusion applies to both the present study and the earlier one on the origin of space. It examines the basis these studies have for seeking a conceptual and physical understanding verifiable through experiments while leaving the search for formal methods to a future task. A discussion of this kind is necessary because sensible ideas have been regarded *in this century* as only possibly coming from ones that can be immediately formalized, and there sometimes regardless of their physical value. This philosophical stand, which originates from logical positivism, has lately put the very function of Physics in question when it came to identify the elements of our reality, *as these elements may not correspond to any possible formalism*. In this respect, a short list of potential analyses is provided in Appendix C to outline the extent of the formal work that would need to be done if the space generation formulation is indeed found experimentally supported.

II. THE ORIGIN OF THE PRESENT CLASSICAL APPROACH TO LIFE

Schroedinger (1943) asked "What is Life?" as he thought that the basic features of the quantum were then known enough to permit the next fertile field of discoveries to be Biology, now that it could be equipped with the new knowledge of the quantum. But biologists so far don't known the main reason Schroedinger was known, they only found out from him that Chemistry was no longer an empirical science as a result of quantum mechanical discoveries, and thus it was time to dig the more complex aspects of Biological Reality through Chemistry. In effect, Schroedinger made his belief in the bright future of Microbiology come true, inspiring, among many others, such milestones as the discovery of DNA. Later, Monod (1971) dreamed that Life was nothing more than a classical "tinkering" ("bricolage" in French) through the phenomenon of genetic Darwinian evolution while Schroedinger's quantum was absorbed in Chemistry as only providing local processes, and the route of Classical Physics with its separated and distinguished features was taken. The quantum and its holistic non-local effects have since not been considered in the biological realm as a result of Physics seeing non-local effects only at extremely cold temperatures and at the atomic level. Schroedinger himself back in the 1940s thought from what was

known then that Life was based on classical statistical phenomena,[1] and the key to Life's special character could be explained through "aperiodic crystals," later called DNA, *themselves based on the quantum*, and thus for him the unknowable product of a deity that would be responsible for the order observed, a thought right out of Mach's logical positivist ideas. So the description of Life has been made since in terms of chemical substances (hormones, proteins, etc.), neural networks, etc., all that one thinks necessary but only "well-known" chemico-physical "macroscopic" parameters, with all their mysterious quantum origins set aside. The laws of classical electromagnetism, thermodynamics, chemical kinetics have been taken as enough to predict the evolution of Life's physical systems *in principle*, enough for *setting up an accurate simulation on a computer*.

In order to explain (if not explain away) the undeniably *holistic* aspect of Life and the corresponding "ubiquitous tendency of Nature to coordinate things" (Kelso, 1995, p.27, and *create* things, I may add), Maturana and Varela (1987) have then thought in the 1970s and 80s that Life arises as "autopoietic" entities, vortices born from Irreversible Thermodynamics, a field studied by Prigogine[2] in the 1950s and derived from 19th century classical Statistical Mechanics. But contrary to the expectations of fifty years ago, when we had a superficial idea about the details of Life processes, Life has been found in fact to rarely depend on statistics, and even to fight them. In order to address such a discrepancy, Kauffman and others studying Artificial Life[3] have thought in the 1990s that the order Life creates from statistical disorder (Kauffman, 1993) arises "for free" from a few rules of operation in a classical system programmed at the genetic level. But is this all that Life is about? Aren't we confusing "coordination" with "creation"? Aren't we discounting the possibility of the quantum non-local aspect to be involved *somehow* in Life, not only organizing but also creating the whole systems called "living organisms"? Shouldn't it be the job of Physics to realize something strange indeed is going on in Life now that we have details about it?

Earlier this century, D'Arcy Thomson (1917), and recently Brian Goodwin (1994), have attempted to identify, through the set of constraints and features arising from the *limited set of possible physical phenomena*, a "playing field" that had to be used by Darwin's classically-limited trial and error process.[4] Having been conceived at a time the quantum was unknown, this process was understood from the start as part of Classical Mechanics, and thus has been seen as a *computable* search utilizing the features available from physical reality within the evolution of living organisms. This hypothesis is at the origin of the Artificial Life research agenda, an agenda which then really belongs to the 19th century. But physical reality features are potentially uncomputable as I described in the earlier study (it is only an article of faith by the logical positivists that the world covered by Science should be computable[5]), so *it is yet to be demonstrated that Darwin's search is indeed entirely (classically) computable*. And according to the point made by Thomson and Goodwin, if an organizing and creative principle existed through the quantum that Life could use, we could be certain that Darwin's process would have taken full advantage of it, *including its uncomputable aspect*. Is there such a principle?

Indeed Physics has so far failed to identify a quantum process that could run at room temperature over macroscopic distances, and thus could apply to biological systems. The various experiments on non-locality (Gouin, 1999, Section VII) done in the 1980s and 90s identified several fundamental aspects of the quantum describing quanta as non-local whole entities, including "contextuality" between remote actions when multiple reality choices are made across space instantaneously, but such experiments involved elementary particles, not biomolecules.

Yet a process with the required characteristics has been recently imagined by the mathematician-physicist Roger Penrose for neural tissues.[6] As he described (Hameroff and Penrose 1996a, 1996b), assuming conventional quantum theory in the background, with large assemblies of atoms forming molecules that can be reshaped by the change of state of a single electron within themselves, one set of such molecules, or a polymer of them, may evolve quantum mechanically shapewise without "interference" with the random surrounding medium (made out of tiny water molecules). The giant leverage that the internal single electrons state changes would have in the conformation (shape) of such molecules would then allow single transition quanta to change the relative positions of an *inertially significant set of atoms*, significant

in the sense that Heisenberg's time-energy uncertainty would permit quantum coherent processes existing in cycles lasting sizeable fractions of seconds at macroscopic scales (on the order of the size of an organ such as the brain) and room temperature, long enough to have a "contextual" conformational behavior across distant molecules and cells.[7]

However, as described, such a process is not applicable to most living materials due to its cycle requirement, and due to the assumed layout in the brain, which cannot be generalized to other organs. So Penrose's hypothesis as presented would go against the key Thomson/Goodwin principle identified earlier requiring physical processes once used to be used over and over again by Life. But the molecular arrangement assumed in the hypothesis is common in Life, so the process Penrose alluded to may indeed be applicable to any system containing this kind of arrangement, provided it is understood properly. A revision to Penrose's description then is in order.

III. LIFE'S SECRET CONNECTIONS?

When using the monadic spaces concepts of Gouin (1999) I am led to a behavior for the electron-set of atoms identified by Penrose quite different from the one he thought. The set of biomolecules being able to exist in two different conformations corresponding to their dual electron state (alpha and beta parts of a "dimer") must create a parallel layer for the common space manifold in order to minimize the energy required for the electron shuttling process (see Fig. 10 of Gouin, 1999). I have of course no data at this point on such an energy requirement, but it seems that at least a "ground state" for the electrons shuttling process must be reached. Then the common space manifold layering would sustain *a coherent macroscopic whole quantum system creating a separate space (the "inertial" space) through the evolution of the monadic spaces forming its electrons*. Such a feature would exist at temperatures found in living materials because *the electrons would have then enough available energy (enough realities) to be in their ground state and exchange enough quanta to create the needed inertial space*. Transition quanta (photons) and virtual quanta in this picture would be an essential part of the non-local quantum dynamical system.

While it has been shown (Del Giudice *et al*., 1986, 1988) that water is an excellent medium to keep photons focused and coherent across mesoscopic distances while attracting biomolecules with a dual electron state, this effect is not relevant to the definition of the envisioned separate space because water molecules are not involved in it, and neither is their stochastic thermal energy.

The envisioned inertial space *content* must be naturally "coherent" at macroscopic distances (seen through its connections with ordinary space), and the coherent quantum system building up this space can only be limited in extent by the masses and locations of the biomolecules making up its connections with ordinary space, and by how many realities (how much energy) the shuttling electrons have in order to build the space manifold. Section IV will discuss the possibility that, through their "cytoskeleton," biological cells support a duplicate layer of the common space manifold at their location, thereby sustaining a whole *unobservable* quantum system. Then such a system would spread through cell duplications in an embryo all the way up to complete organs, with the nervous system completing the whole at the level of the organism, the mind being but only one of the features of the resulting whole.

Even though unobservable, the quantum system and its associated space must create observable effects in ordinary space. For an example of such observable effects, the duplication of supramolecular structures from Fig. 12 (from Appendix B discussion) could be seen as the result of inertial space building itself into a 3-D manifold from an initial 2-D cylindrical one. A duplicated complementary structure would assemble *close to and perpendicular to* the existing structure by molecules in the surrounding medium being attracted via the photonic process generated by the existing structure. Section IV will provide further details on this process.

Sheets of polymers using biomolecules of the cell cytoskeleton have been recently made to identify their structure (Nogales *et al.*, 1998), but "in vitro" studies of their conformational evolution and the duplication of their supramolecular structures have yet to be done.

I would not reject the existence of quantum non-local phenomena in living materials just because we supposedly have not yet observed them. We may just have turned our eyes and mind away from them by not having the theory to understand what was being observed. Also the envisioned quantum process would give effects in ordinary space that are mere "shadows" of the full process, so not only knowledge but educated imagination would have to be used here! So I am now going to take another look at the approach of today's Science to see if indeed there is room for such quantum non-local effects in Life.

A. Is Penrose's hypothesis (quantum minds) having any chance to be correct?

The present idea of "Complexity,"[8] itself resulting from Chaos theory (Gleick, 1987), a 20th century side development of Newton's cosmology inaugurated by Poincaré (Diacu and Holmes, 1996), seems at first sight to be insufficient for explaining the origin of minds and the complexity of the organization built into their physical support, the brain. Our billions of neurons don't even come close to forming some fancy ant colony a la E. O. Wilson,[9] or using any classical "cooperative" phenomena. Behaviorists[10] earlier this century have attempted to deny we have something common to all these neurons, something called by various terms, one of them being "consciousness," another being "mind," but we know such a thing does exist by an immediate introspection.[11] It is not because we know next to nothing physically about it that we can deny its existence, at least within a Science that wants to see itself as "respectable"! It is thus undeniable that our billions of neurons do produce a mind. Likewise, such a mind is undeniably a single *non-local* physical entity in some way. The key then is what is meant by the adjective "non-local." Its meaning seems to be quite different in Biology from the one found in the quantum, but is it really that different?

Experimentation does confirm that a mind (the "self") has its physical support *somehow* "spread out" within our brain in a manner that does not make full sense within the natural phenomena part of Classical Physics. Among the many reports testifying on this matter, I shall cite four kinds to clarify the meaning of non-locality when it comes to the physical brain: (1) surgical operations show that the various distinguishable functionalities of the brain (Calvin and Ojemann, 1994) are supported by rather imprecise and *extremely variable locations*, and the "self" itself does not disappear as a result of the physical removal of most of the brain (as extreme cases such as Phineas Gage's demonstrated - Damasio, 1994, Part I), (2) there is experimental evidence[12] for common operating principles between the brain and holographic images, utilizing in some fashion the Fourier transform effected by the ganglion cells in the retina of the eye, (3) strong anesthesiological evidence (Hameroff and Penrose, 1996a, 1996b) identifies specific electrons in cytoskeletal biomolecules within brain cells as having a disruption of their quantum evolution correlated with the temporary interruption of consciousness, so elementary particle phenomena are definitely involved in the creation of a mind, with the holographic effects above coming then most likely from the quantum realm, not the classical field of coherent optical phenomena, (4) recent studies of the brain cortex function using *direct optical imaging* of millions of individual neurons activity[13] show that "an individual response [to a visual stimulus] is the sum of two components: the *reproducible* response and the ongoing activity [of the brain]. Thus, the effect of a stimulus might be likened to the additional ripples caused by tossing a stone into a wavy sea [itself not noise at all but many independent superposed non-random activities]." This description is a perfect metaphor for a quantum mechanical phenomenon with its characteristic non-locality and superposition features existing behind the electrical signals, themselves "localized" happenings appearing like "shadows" of non-localized effects, as Schroedinger thought about Physics elementary particles (Moore, 1989).

With such a flexible and seemingly non-local (in the quantum sense) behavior of the mind's physical support it is very hard to imagine such a support, the brain, as some fancy ("massively parallel") classical computer. However, Churchland and Sejnowski (1992) and many others believe the brain to be such a computer. Neither is it likely to be some sort of "quantum computer" as conceived by Feynman, Deutsch, Lloyd and others. Within this last concept, a *fixed* classical serial logic process a la von Neumann, not very flexible and "natural" in itself, is retained (Feynman, 1985), and the brain is manifestly not a serial linear device.

Reports in the line of the ones above are not a proof of the quantum nature of minds, and neither is Penrose's hypothesis, of course. Only experiments can give such a proof. Section IV will look then into potentially verifiable facts on this critical matter.

B. Is then Life in general purely classical?

But if a mind is a non-local quantum phenomenon, then an area of critique opens up for the stand on Life in general as purely classical. Life must have other places besides the brain where the quantum has a role, and a corresponding significant effect. From D'Arcy Thomson and Brian Goodwin's point that Nature uses a playing field of physical effects for its tinkering, it would not make any sense at all for the mind to be the lone feature of Life with such a type of physical support. But, so far, as mentioned earlier, for today's Science, Life is nothing but a classical happening. So no thought has been given on looking *within biological processes in general* to see whether non-local quantum physical processes are at work. However, if I dig under the surface of today's Science classical phenomena stand on Life, there are conclusions or approaches that may not hold under experimental scrutiny, or at least may be interpreted with a double meaning, while the quantum meaning is of course never considered. As a result of this position there is a corresponding lack of experimentation specifically done to find non-local quantum phenomena in Life. However, as I shall identify in Section IV, supplemented with Appendix A, there is a plethora of well-known experimental data that tell big chunks of the story for anybody who would have the theoretical background to make sense out of them. So the key of this study will be to convey the necessary understanding.

1. Embryo development

Under the leadership of Lewis Wolpert (1991), present Embryology sees the development of living organisms as a chemical clockwork process classically programmed through the genes to direct the *cells differentiation process* implemented through series of macromolecular reactions ("pathways"), in effect a computational process as understood by today's Computer Science. A key problem in such a subject is how *the "unfolding"*[14] *in real time of a body 3-D shape* is directed through the body development, certainly at first sight a "non-local" process since it definitely has a sequence and many parallel subprocesses operate as if under an overall control. The key hypothesis in this field is the existence of "morphogens" doing the directing from data in the genes ("homeobox" genes - Goodwin, 1994) providing a "positioning system" (Wolpert, 1969, 1991) for defining the kinds of cells in the embryo that are differentiated, at least in the early stages when differentiation and partitioning has not yet occurred. This hypothesis was first thought about in the 1950s, not by a biologist but by a computer scientist, Alan Turing.[15] Turing's goal was to identify a living organism as a *self-constructing computer* in line with his concept of computation that anticipated our modern computers. John von Neumann, also in the 1950s, contributed to this search, and recently the Artificial Life "movement" has taken the relay. Kauffman (1993), following Wolpert and Turing, describes morphogens as elements involved in classical stochastic reaction-diffusion density gradient phenomena.

However, what is seen in the *drosophila melanogaster*'s initial division into segments[16] may not come only from Statistical Mechanics.[17] Experiments have yet to show how the genes of a cell modify their "program" according to the concentration of morphogens at their location. What is known is that certain molecules *present* around a cell can trigger or inhibit the production of other gene products. What is not known is how such external molecules could affect via their *concentration* the internals of the cell nucleus through two isolation membranes.[18] There is no indication on how the cells that are part of the choreography described can change or trigger an ongoing program among many different programs available in the DNA, *and somehow run by it, in synchronization with other cells*. For such a program to run in parallel across cells at least some kind of synchronization must be present between these cells, at least all the cells involved in one function, maybe one organ. What is this non-local clocking mechanism?

Also, molecules such as "Sonic HedgeHog" (a gene product with a weird name) have been found as the closest thing to morphogens.[19] But they appear in the development process more like "initiating a cascade of local cell-signaling responses"[20] or as inhibitors of other programs to implement a small part the 3D blueprint in the genes, appearing at specific stages and in which their presence (*not their concentration*) is in effect "directed" by other molecules via "signal pathways" for their "activation" as the chemists describe, *with no attempt to get into the physics part of the thing*.

Recent observations (Vogel, 1999) have shown that Hedgehog and other *such products, that supposedly "regulate" growth and "decide" on cell fate, are in fact being transported in the embryo via "cytonemes," very thin threads of cytoplasm thrown by individual cells from one side of the embryo to the other to pick up "messages" from the source cells by using transport vesicles going along MTs* (see later and Appendix A for details on MTs). The formation of such cytonemes is a big mystery, but they were produced "in vitro" by the mere presence of target cells nearby. So the "regulation" and the "decisions" on embryo development *may not be a chemical process at all*. Separately, egg rotations have been observed as being directed by *MTs transporting a protein in vesicles from one side of the egg to the other, and this protein "turns on a host of genes."* In the reference news article it is advanced that "developing embryos may actively ship key signaling molecules from place to place, instead of relying on diffusion to carry the messages," and the processes observed "may show the way to solve the long standing mystery of how signaling molecules orchestrate development so precisely." Apparently it was known all along that *diffusion is not a precise enough phenomenon to account for embryo development*.

2. Statistical mechanics and Life

In general, there are only few signs of the influence of Statistical Mechanics principles in embryo development as Turing, Wolpert and Kauffman[21] assumed. Where it seems to have an influence such an origin may be misidentified in lieu of other unknown processes simply because of that fact. Below are a few relevant observations about this fleeting role of statistical processes in Life in spite of the theoretical wishes to the contrary (Science has to have an explanation!).

a. Template matching

Biochemical reactions for the most part seem to be driven by individually directed physical motions and precise reorientations of molecules versus each other to match "templates" sites on each of them (Kauffman, 1993, p. 324), a very unlikely process if it is classical knowing the complexities of biomolecules. Template matching is extremely important in Biochemistry, but Biochemistry does not fully address the *dynamics* of this process, i. e. how it physically occurs. From many papers in the literature, it appears that this dynamics is taken as a stochastic process within the confines of a box helped by latching mechanisms. Yet few justifications for such a hypothesis are given in light of the complexity of the matching processes. In that line, the assembly of large molecules such as dendrimers looks to be

unexplained due to the intricacy, and resulting improbability, of the *3-D assembly* of each piece (notably such an assembly cannot be simulated via macroscopic wedges of wood shaken in a 2-D box[22] per Hosokawa *et al*., 1995). Locking mechanisms in the O. Penrose (1959) fashion may play a role in certain cases, but this classical view seems far from hitting the mark when *coordinated* multiple and separate assemblies are required.

b. Subcellular morphogenesis

In that line there are many phenomena which show the incredible propensity of Life for self-assembly, especially in *subcellular morphogenesis*. For example, a *bacterial flagellum*[23] is made of precise supramolecular structures that build themselves from parts produced by the DNA somewhere at the opposite end of the cell. The produced parts come together there making for example *a propelling motor with exact dimensions out of dozens of parts*! How about that for angels dancing on the head of a pin? Not only that, the resulting product is astonishingly sturdy even when supposedly only weak van der Waals bonds are present. The literature as usual treats the matter as a Rube Goldberg tinkering via sequential chemical releases from the DNA or from the partially assembled multi-parts structure returning as a feedback to the DNA. But how do these chemical releases move with such a purpose? In the meantime the complex structure is still precisely self-assembling with no help in sight from anybody, and nobody really knows how.

The biochemists put out the descriptions by filling in the blanks with metaphors such as "sending through the channel" or "coming down the pipeline" *as if there was a physical track from the DNA to the structure* (this sort of expression can be found everywhere in the microbiological literature). *But there is no physical basis for such tracks in a classical world where molecules are individual entities, especially if they are subject to statistical mechanical effects*. One could only advance that flagella are part of a MT system, and such systems seem to have very peculiar *physical* properties (Section IV). The referenced literature does look for a new "paradigm" to explain things and at last fill in the covered-up blanks.

c. "Contextual" motions

To corroborate the above point on self-assembly, macro-molecules have been reported as moving apparently *contextually*, i. e. non-randomly to a certain long-range destination that looks to be appropriate for their use. In one case,[24] a *single* molecule just made by a gene is heading out of the nucleus for use within the cytoplasm of the cell. With only very small portholes in the nucleus membrane compared to its size, how does it find its way out, and why would it go out in the first place? The corresponding report says nothing on that matter. In two other cases[25] (among many others) a molecular complex produced by the nucleus is found to locate itself around a specific component of the cell, with very little spreading around as expected if diffusion was the means to reach its destination.

d. Lack of Brownian motion.

Living tissues have very little randomness in their behavior, as there is not much Brownian motion in Life due to the extremely structured arrangements at the molecular level through the gel-sol makeup of the cells cytoplasm, and through the intimate and complex organization of a cell interior in general, as it is observed in everyday Biology (Hameroff, 1987 and Appendix A). How could diffusion work in a medium as partitioned as a living tissue all the way down to the cytoplasmic microtrabecular matrix inside a cell, not to mention the intricate separate parts within the cell that originated from very different organisms through symbiosis? (Margulis, 1993) If Brownian motion was allowed how could replication and transcription, the "engine" of the DNA program in the crowded cell nucleus, occur where such delicate and precisely sequenced processes are constantly occurring in very large numbers below the micrometer range[26]

while the MT system (Section IV) does its "pulling apart" process outside the nucleus? There is order all the way down the scale, no "chaotic" behavior here.

C. Non-local processes

Many examples of long-range processes ("non-local" in the biological sense) can be found in individual cells functions as well as for overall body maintenance, such as mitosis, meiosis, the Golgi system maintenance operation within a cell, apoptosis (cell deciding on its own death for the good of the organism[27]), even molecules dealing with the circadian rhythm of the entire body. In order to perform their *organized* functions cells must migrate throughout the developing embryo, and such a migration cannot be stochastic. Where is the true origin of that three-dimensional movement? What directs it? Are neurons just following a local "scent"? If yes, where is the command system distributing this scent? How are the commands defined and *directionally* propagated? The makeup of the brain shows *much more data needed there for its construction than is available in the genes*. How is such data generated in real time? Where is the mighty computer performing all these synchronized and parallel non-local jobs?

Appendix A reviews the literature to find out whether available experimental data does leave room for such non-local processes. It finds indeed not only room but *a basic need for them*. However, the corresponding dynamics would be unapproachable via chemical effects due to (1) the molecules' individual and distinguished aspect coming from Chemistry's classical approach, and (2) the limited applicability of statistical phenomena in Life processes. Such a well-synchronized and choreographed dynamics then appears to be simply not addressed. This gap in the approach exists not only for processes involving the whole organism, but also for cell-bound ones, such as the "simple" duplication of a cell.

D. A lesson from Evolution

As I mentioned earlier, Schroedinger answered his question on Life (Schroedinger, 1943, Chapter 7) by identifying DNA as its key, and added that "we must be prepared to find Life working in a manner that cannot be reduced to the ordinary [classical] laws of Physics" *due to DNA's quantum origin*. He concluded that these "aperiodic crystals" would be the source of the order found in Life due to their non-classical origin (in Schroedinger's mind, following Mach, the quantum was unknowable and thus the sign of a deity's work), even though, he assumed, statistical phenomena were ruling that realm.

But in his time there were not much details on Life processes, especially on how they originated. We have found since, including through the study of its Evolution, that order in Life does not in fact entirely come from DNA, and this by far. A drastic change occurred eons ago resulting in Life going multicellular (Appendix A), and DNA does not seem to be the instigator of such a change. It may have come instead from *a symbiotic agent that ended up reproducing without DNA*, using physical effects *essentially not displayed* by DNA. As I shall describe in the next section, this (relatively) new agent may originate from and use the quantum like DNA, but via effects Schroedinger could not have known.

E. Conclusion

Are the classical laws failing in living materials? And why would they be failing?

At first sight, the answer is: No, the laws are not failing if we see the quantum non-local character of reality as not applicable to Life, and thus classical effects *must* do the job being the only ones around (after all, we need an explanation no matter how contrived it can be!). But *after giving a second look*, in order for

Life to exist at all, and *a fortiori* to exist in its extended multicellular form, *non-local feats and contextual motions* seem to be needed that go well beyond what Classical Mechanics and Chemistry can do due to their separated and distinguished nature. When considering the *self-assemblies and the extended whole systems* that look to be created right in front of our eyes (and are us!), knowing that DNA is burdened by delivering its data, another (symbiotic) agent must be providing the needed collective non-local effects to build larger entities. However, a proof of the non-local quantum function displayed by this agent can only be obtained through experimentation. But planning experimentations first requires finding a few facts, so far unknown, about this agent that can be predicted from theoretical considerations. Next section will address this matter.

IV. THE CASE OF THE MISSING ORGANIZING PRINCIPLE

A. Introduction

Could it be possible that a key process known to occur in living materials with no explanation whatsoever as to its origin *for over a century* can be explained now through a fundamental *physical* phenomenon that has yet to be recognized to exist? To find out I am going to proceed in a logical fashion through Life quintessential operation of *cell replication*, where I shall meet the phenomenon in the well-known but unexplained behavior of a supramolecular structure, and obtain thereby a few of the phenomenon attendant features. Then I shall go to the higher levels of Life processes to see the consequences of such features appearing again and again, as it ought to be, knowing the propensity of Nature to tinker with available physical effects (Section III). In that area the experimental evidence has been also well-known for many years. There it happens to have already an explanation in the literature, albeit incomplete. However, I find such an explanation likely to be mistaken in light of the analysis I provide at the lower level.

1. Introduction to “mitosis”

A well-observed process with a *fixed sequence* in a biological eukariotic cell is “mitosis” (Hyams and Brinkley, 1989), the splitting of the cell into two new cells, a fundamental process in eukariotes.[28] The present literature assumes some chemical sequence is at work for defining the various stages of mitosis (and this looks to be indeed the origin of the stages), but nothing is mentioned about *why* the suprastructures involved behave the way they do physically. Mainly the existing knowledge is about the *description* of their relative physical motions. A key feature of the process is its coordinated character throughout the cell. A statistical effect cannot be involved as very precise relative positions of the structures are observed. Chemistry looks to be only a side show in that process. Even in the nuclear material, non-local physical effects may be involved in its evolution for coordinating the very complex replication process happening there (Cook, 1999), but such a matter will not be pursued in this study outside the function of chromosomal *kinetochores*, molecular complexes which look to be critical for mitosis and are understood in the literature as being part of the microtubular (MT) system. Unlike the mainly chemically-based (local quantum effects) DNA reproductive function in the cell nuclear material, the mitotic process seems to have an exclusively physical origin. So let’s examine the various phases of this process, looking for such an origin.

2. A preamble to the analysis

Microbiology and Biophysics are not like Physics. We do not set up the experiments there most of the time, Nature does. So we are looking at a lab that has many experiments going on at the same time in the same "apparatus," the cell or the organism, and for which we are not told what principle is being used in each observed intermixed effect. So the picture obtained through the literature that observed these experiments is pretty messy, especially when the large number of workers in the field is considered. What I am going to present is the centriolar system without other components, as such components look to be "old" systems that were there well before centrioles appeared, and can confuse the description if they are not separated out. I shall add the old system picture in remarks at the appropriate locations in the description. Appendix A provides an analysis of the data found in the literature that I used for the description and remarks below.

B. The mitotic process as a monadic spaces evolution

1. The process of centriole replication.

The observed starting point (Vandre and Borisy, 1989) of mitosis is when the pair of *centrioles* in the cell breaks up. Each centriole subsequently replicates itself into another centriole *perpendicular to the axis of the original one*. *So far how and why this happens remain deep mysteries in today's Science*. I shall advance that the physical clue is in fact the relative position of the child versus the parent, for, when I think in terms of monadic spaces (Gouin, 1999), *another dimension appears to be added to a space manifold* through that replication process. Indeed, as I shall describe later on in the analysis, the common space manifold layering and its 2-D "inertial" space manifold envisioned at the start of Section III, if effected by the tubulin molecules making up the centrioles, would give a non-local background for the mitotic process, as well as the physical means for its control through an internal quantum "program."

Through such a program the original centriole would emit photon pulses in dimension 2 of its inertial space, which is common with the ordinary space manifold according to Fig. 1, attracting MT biomolecules present in the cell medium to that manifold through the photonic effect mentioned in Section III (an effect which will receive a new understanding later on). The striking one-sided aspect of the duplicated structure location versus the original would come from the initial location of the first biomolecules reaching the site, localizing the photon pulse set in ordinary space (in the sense of localizing monadic spaces reality sets - see Gouin, 1999) somewhere within the common space manifold dual layer area around the original centriole, thereby fixing the location of the child cylinder axis in ordinary space (Fig. 2a). The duplication then would go layer by layer of molecules outward from the center of the system, guided by the location of the previous expansion of the inertial space manifold in that dimension (Fig. 2b). The resulting structure would then extend the ordinary (common) space manifold layering in a direction orthogonal to the original structure, and also extend thereby its inertial space manifold in a third dimension becoming then a 3-D manifold (Figs. 1 and 2).

2. The trigger of mitosis

In that picture, the separation between the parent and the child centrioles at the start of mitosis (Fig. 3 - step 2) occurs as a result of the structures "inertial" evolution (in the inertial space) stopping their photon exchanges in their common inertial dimension, which is one of the ordinary space dimensions as seen earlier (dimension 2 in Fig. 3). This appears to be the key to the relation between the DNA replication timing and the MT replication process. The messaging between the two systems seems to be obtained through the production by the nucleus of cyclin-dependent kinase 2-cyclin E (Cdk2-E) complex (Hinchcliffe *et al*., 1999) that, in the monadic spaces picture, would be attracted by the quanta exchanged between the two

centrioles in the inertial space common dimension (in ordinary space) and would block it. Cdk2-E is shown in the referenced paper as being localized in very specific areas of the cell, so it is extremely unlikely it moves by statistical diffusion, more like by following unobservable inertial space tracks laid out between the nucleus and the centrioles (see Section III for the matter of statistical processes in general).

REMARK.

- Besides the production of Cdk2-E by the nucleus, there are correlated *changes of conformation* in certain molecules within the cell[29] which may provide a messaging system, but there is no experimental hint on how the mitotic process sequence relates physically to such reshapings. It is not known whether these changes of conformation affect the centrioles inertial space evolution as well as the nucleus membrane and chromosomal support, or are themselves directed from the centrioles.

3. Centrioles separation, replication, moving apart and spindle production.

With one of its dimensions eliminated, the 3-D inertial space manifold identified with the centriole pair splits into two 2-D manifolds thereby "disconnecting" the two structures within ordinary space (they merely drift apart there), but not through inertial space dimensions 1-3, as I shall discuss later.

Subsequently, once new child centrioles are built out of the separated centrioles, the new pairs have each a rebuilt 3-D inertial space manifold. Being kept connected via inertial space 1-3, the two pairs are still quantum coherent with each other in their evolution. Then they are able to exchange photons through the inertial dimension 2 they have again in common with ordinary space when their common program reaches that stage.

Such 1-D quantum coherent photon exchanges "inflates" their individual 3-D inertial manifold. This inflation sends the two pairs of centrioles at opposite locations in the cell. Then MT polymerization *between* the centriole pairs induced by the quanta exchanges forms the well-known mitotic "spindle" (Fig. 3 - step 3 and Fig. 4). As I shall identify later, these MTs have different sets of inertial dimensions (1-2 or 2-3) according to which centriole pair emits the photons.

REMARKS.

- As described in Appendix A there is "pericentriolar material" (PM) accumulating around the parent centriole. This PM can exist in cells without centrioles, and can "nucleate" MTs by itself. All spindle MTs come from the PM, not from the centrioles. Centrioles appear to be an add-on to earlier cells which had such localized accumulations. The PM was called "centrosome" before centrioles were known to exist.
- From the fact the accumulation is only around the parent I can deduce that a PM sustains an inertial space in the same dimensions as the parent centriole it surrounds. This material in fact *accumulates on the centriole itself* when only small amounts of MTs nucleation occur. After child separation, a PM accumulates on the child, and that PM must have its inertial dimensions according to the child's dimensions.
- Centrioles are using the dual layer areas of the common space manifold initially created by the PMs, and add to that existing system their ability to produce quanta in inertial space and thereby coordinate the mitotic process much better, as I shall describe later. The "old" system does not seem capable of such a feat, but *still creates the majority of the spindle threads* by sustaining a dual layer area for the common space manifold. However such threads do not seem to have any function when centrioles are present except extending the dual layer via MT polymerization.
- When there is no centriole in the cell, PMs act as the poles of a MT spindle which is generated then by cell nuclear material as this material is apparently also sustaining a dual layer (see later).

- Energy is required to assemble MTs and keep them assembled. As Appendix A mentions, a cell with depleted energy becomes disorganized and shows MTs dissolving. Also *the energy consumed by MTs is not accounted for*. This could be an indication of the presence of a dual layer in the common space manifold as it requires energy to be maintained (see Section III).

4. Cell separation

The separation of the cell into two cells after the completion of chromosomes duplication is described in the literature (see for example Kuchel and Ralston, 1998) as effected through MTs polymerizing in-between the centrioles, and between them and the cell cortex, a "pulling force" being seen as generated by a "treadmill effect" of the MTs helped with dynein "motors" attached to them. The MTs evolution is observed to occur in concert with all the components of the cell, including the nucleus components which replicate in their own way, helped by the MTs segregating somehow the replicated chromosomes. I shall note that the coordinating agent for this *non-local* so-called "pulling apart process" (which can only be seen as *miraculous* when considering all the other coordinated events happening in the nuclear material) cannot be found described in the literature.

Let's now turn to the monadic spaces picture of the system. MTs are mostly produced in the period starting before the "pulling apart process" begins, and ending with the start of the cell splitting into two cells (Vandre and Borisy, 1989). This indicates that *the dual layer common space manifold with its associated inertial space manifold connects to the entire cell up to and including the cell cortex molecules through MTs that go from the centrosome to that cortex* (Fig. 3 - steps 3 and 4). The *3-D connection* of the inertial space manifold with the common space manifold at the pair of centrioles would be reflected by the *so far unexplained* large inertia that has been observed associated with centrioles.[30] This inertia would come through the inertial space tying the location of the centrioles to the location of the entire cell (thus the name for that space). Such a feature would also explain the *sturdiness* of the centrioles even though they are made of nine seemingly unconnected parts (Fig. 11 related to Appendix B - see later for more on this).

REMARK.

- The "pulling apart process" using dynein motors may exist as a help in parallel with the inertial space ebbing for separating *larger* chromosomes. The question of synchronization and coordination of the motors operation will be discussed later.

The chromosomes in the cell nucleus include molecular complexes called *kinetochores*. Their replication would end up with 2-D inertial space manifolds in separate dimensions 1-2 and 2-3, probably through principles similar to the ones of centrioles replication. Such manifolds would be included in the corresponding MT system manifolds through the photon exchanges between centriole pairs *according to the extent of their inertial dimensions*, and thus attach the chromosomes they hold to the corresponding threads of the spindle (Fig. 3 - step 4 - more on this later).

Then, as it happened for centrioles separation, the photon exchange ends, forcing the second dimension of the centriole pairs inertial space to *recede* between them. What makes the photon exchange end here? From many reports this looks to be effected by the kinetochores, as *they must all attach in order to stop all the photon exchanges in inertial space dimension* 2, thereby breaking the 3-D inertial space manifold of the cell into two 2-D manifolds.

REMARKS.

- The literature (see Appendix A) has identified a chemical "gate keeper" that would be emitted

by the kinetochores while not attached to the spindle threads to signal the other kinetochores to wait before going to "anaphase" (separation of chromosomes). This signal in fact tells the "anaphase promoting complex" (Appendix A Section 4.c) to wait for chemically dissolving the bonds between chromosomes so they are free to move with the ebbing of the inertial space. Kinetochores individually have no means to know they are all attached and thus cannot perform this *non-local* function.

- The literature fails however to explain how all the kinetochores of one set align toward the same spindle pole, as well as why they *physically* align in an "equatorial plate," even though a MT system molecule has been found implicated in that process.
- There are many more threads in the spindle than there are kinetochores. This is explained from the fact the pericentriolar material around the centrioles (Appendix A) naturally nucleates MTs *as a result of being in a dual layer area of the common space manifold* (they attract MTs that way, thereby explaining their MT nucleation property), but the resulting threads do not carry quanta exchange paths between the two centriole pairs, and thus do not participate in the breakup of the inertial space manifold.

But the above matching process would require the number of quanta exchange paths connecting the two centrioles (not the number of spindle threads) to equal the number of kinetochores. I shall investigate later a physical process that would result in such a fixed function. The subsequent receding inertial space then segregates and pulls apart the two sets of chromosomes, as well as the other parts of the cell that were duplicated in parallel with the nuclear material.

REMARKS.

- As Appendix A identifies, mitosis may not involve centrioles at all, centrioles being an "add-on" in the evolutionary process of Life. The physical separation of the chromosomes then occurs from the kinetochores side. In this older version of the mitotic process quanta exchanges would not be involved (Fig. 5). With centrioles the kinetochores are attracted to the spindle threads by the centrioles quanta exchanges and thus are not in control of the mitotic process except for breaking up the chromosomes as seen earlier. Without centrioles and quanta exchanges around they provide the separation on their own. By sustaining themselves a local dual layer of the common space manifold (DLCSM), their replication would produce two separate inertial space manifolds, one in dimension 1-2 and the other in dimension 2-3, connected in dimension 2 via the chromosomes forming the spindle equatorial plate in normal space. Attracted by the presence of the dual layer in the common space manifold at the equatorial plate the MTs threads nucleate in a barrel fashion. Their polymerization then extends this dual layer from the plate. By stacking themselves farther and farther away from that plate until they run out of material in the medium (if barrel shaped) or thin out to nothing (if a full spindle), *the overall shape they get into results from the MTs having no lateral support out of the equatorial plate to maintain the DLCSM spread out*. Coordination between kinetochores would solely come from the MTs accumulation rate out of the equatorial plate. The separation of chromosomes would then be done via the chemical process identified earlier dissolving their bonds and allowing the breakup of the 3D inertial manifold into two 2D manifolds subsequently receding toward the pole ends of the DLCSM area. (Again the dimension 2 connections being only at the kinetochores, other threads generated at the equatorial plate would not participate in that breakup.) Since there would not be a synchronization of the MTs formation across all the kinetochores this alternate process appears less reliable. Centrioles would provide a precise fixed overall control over the manifolds separation process through their quanta exchanges.
- Further, there are chromosomes separations that do not even involve kinetochores (Appendix A, Section 4.e). Then the chromosomes themselves would have to sustain a dual layer of the common space manifold. This makes sense when considering the normal location of the centrosome next to the

cell nucleus (a location coordination lost when the cell energy is depleted). Duplicated chromosomes would have complementary inertial manifolds that attract fibers (not necessarily MTs) in a spindle and would allow them to separate. This method would require that *chromosomes be rather small* in order for them to maintain a minimum of coordination based solely on chromatin accumulation rate. This would have been the physical method used by prokariotes in their split for reproduction without MTs. As Margulis said, this crude method originating *from the beginnings of Life* would not have allowed them to increase the size of their chromosomes.

- This point is very important for the dual layer manifold theory because *such a simple phenomenon would have very naturally effected the* ***physical separation*** *of a replicated system in the beginnings of Life, and would have made the sophisticated systems observed today unnecessary.* The only requirement would have been to find a molecular replication process creating complementary inertial manifolds, apparently a common feature of biomolecules assuming the monadic spaces picture. It would also have made symbiosis (Appendix A) possible through the natural spatial coordination of wildly different organisms it could provide, something now being observed via *the nucleus and centrosome close spatial coordination*, with DNA naturally gathering into the nucleus as a result of the combined mitotic process.

Since the cell membrane itself is connected to inertial space[31] the inertial space ebbing process ultimately results with a separation into two cells (Fig. 3 - step 5).

REMARKS.

- The final separation of the daughter cells involves the transient formation of an actin "cleavage furrow" ring seen in the literature as "squeezing apart" the cytoplasm (Appendix A, Section 6.c4). The localization of actin may be an indication this component of the cytoplasm senses inertial space manifolds connections. It then locates itself at the connection of the two cell submanifold where they form a 3D border due to their different MT dimensions, thus forming a ring in the spindle equatorial plate plane.
- Actin coating of the nuclear membrane in a "geodesic dome," as referred by Appendix A, would be another instance of this phenomenon. This dome would identify the nuclear envelope as sustaining a set of inertial space manifolds with their connections located at the vertices of the dome, being common to six manifolds alternating in their dimension 1-2 or 2-3. Margulis did identify the nuclear envelope as a *filiation* of the MT/nuclear material symbiosis that resulted in the eukariotes, so the material making this envelope has to reflect the properties of its parents. Such an arrangement would also induce the cell cytoplasm layout into an actin *microtrabecular matrix* of domains as Appendix A mentions. The cell membrane would provide anchor points through its receptors (see later) for MTs in-between the actin filaments.

C. A monadic spaces extended computational process?

How are the photon exchanges in inertial space dimension 2 triggered? How can a specific number of threads be generated? The answer to these questions within the monadic spaces picture requires understanding the quantum process occurring within the postulated inertial space. I attempt to obtain part of this understanding in Appendix B, and I shall address it further below. The appendix examines a generic cylindrical supramolecule and deduces that *its surface arrangement must have symmetrical and asymmetrical features like the ones displayed by the MT system and centrioles in order to sustain a 2-D quantum non-local cellular automata evolution.*[32] The system as presented there assumes an evolution in normal space, but of course the quantum coherence can only come from the system evolving in inertial

space, with the photons emitted by the structure through one dimension of this inertial space "along" normal space. The postulated phonons (more on them later) represent the changes of conformation *as seen from the electronic system part of the inertial space* when they switch according to the rules of Fig. 13 (related to Appendix B) from one layer of the common space manifold to the other through two dimensions of inertial space making thus 4 layers available as I shall explain further below. The required number of photon pulses generated across two pairs of centrioles to form the spindle would then come from the computation occurring through the electronic shuttling inside the centriole inertial space, itself sustained by quantum conformational dynamics of the MTs biomolecules while lining up the layers of the common space manifold (again, more on this below).

Through the split of the inertial space manifold into two 2-D manifolds in different dimensions at step 2 of mitosis, the computation on the centrioles is stopped, with the electronic states frozen at the instant of separation since only one inertial dimension is available for their shuttling. For the computation to restart the centrioles must drift apart far enough so that the dual layer of the common space manifold is limited to the neighborhood of each centriole, thereby allowing a sufficient localization of photons in dimension 2 to start the child construction described earlier (Fig. 2a). The computations on the two centrioles then become separate in their evolution even though they are coherent evolutions by themselves. They just will have to exchange quanta through conduits provided by MTs from then on in order to obtain a common computation (realizing then a composite quantum system - see later for more on this matter).

In step 5 of mitosis, once the cells are separated in ordinary space, quanta exchanges can exist through the cells MTs, membrane and extracellular matrix, allowing their centrioles to continue evolving with some input from their neighbors *provided they remain in sufficient contact*, but a common computation can no longer be sustained as it happened in mitosis. Input from neighbors may involve synchronizing their replications, among other things, through quanta exchanges with their own nucleus kinetochores. The importance of cell contact will be discussed further later.

D. The physical computational principles

1. Non-local cellular automata

I shall start with Fig. 13 related to the analysis in Appendix B. There are 8 triangular configurations for the near-neighbor biomolecules electron states operating as cellular automata rules. This set can be divided into *two sets complementing each other's conformation* (Fig. 6). One centriole of the pair has its inertial space in dimension 1 while the other has it in dimension 3 as a result of the construction of the child from the parent I described earlier. The two centrioles have then a *complementary configuration of biomolecular conformations. They line up the ordinary space manifold through dimension 2 of the inertial space manifold while being superposed in that manifold* (Fig. 6). The electrons in the two centrioles can then shuttle within inertial space dimensions 1 and 3 through the 4 layers of the common space manifold in effect provided by the two centrioles. They can then evolve as described in Appendix B, in a non-local cellular automata according to the rules of Fig. 13. *The two centrioles then support a single computationally evolving composite quantum system within one inertial space* ***dual*** *cylindrical manifold*.

Appendix B describes also the automata evolution in forward and backward "computational fronts." Then the "slat" construction of the centrioles forces a given centriole to sustain only a forward or a backward front because each slat can "observe" (as an Everett Observer, per Appendix B of Gouin, 1999) only the previous slat photon pulses emitted in dimension 2 (ordinary space) by the corresponding slats on *both* centrioles, each centriole again being in its own dimension 1 or 3, thereby making a ratchet fashion one-way non-local coherent evolution on both centrioles (Fig. 7a).

2. Coherent phonons and self-assembly

In the monadic spaces picture, the critical asymmetry in the slats arrangement must be the result of the collective quantum *mechanical* evolution (*phonons* - see Appendix B) occurring in the slats dual layer common space manifold *connection* with their inertial space while they are being originally produced by the DNA. Phonon exchanges *between slats* would occur because (1) one-way ballistic mode propagation is available through an asymmetrical arrangement (the other way the phonons have nowhere to go - Fig. 7a) allowing a *stable larger evolution*, a two-way evolution creating resonances destroying the system, thus the needed odd number of slats, and (2) the slats inertial spaces are produced by the DNA all with dimensions 1-2 or with dimensions 2-3, allowing then a *common* manifold.[33] Then they *extend* the slats inertial space across them effecting a single 2-D cylindrical manifold out of the original set of individual slat manifolds. The resulting *stable larger* space manifold in turn prevents the structure from falling apart. The original assembly of the slats out of the DNA must thus occur "naturally" as soon as they are produced near each other.

This *self-assembly* could be seen as (1) an example of *Life originating from monadic spaces searching for larger collective evolutions*[34] and (2) a beautiful example of a set of monadic spaces finding a *possible, stable, larger* arrangement for their *collective* (non-local and unseparable) evolution, with their search including modifications to the ordinary space manifold! Maybe the process happening in sink holes (Gouin, 1999) is of the same kind: Monadic spaces would rearrange themselves there also to find possible *stable* arrangements *as large as possible*, thereby defining all the *necessary asymmetries* found in elementary particles as well as the needed "constants of Nature" to accomplish their collective goal.[35]

Question: Centrioles assembly seems to be a good set-up for a monadic spaces formalism. Can such be found, especially if the assembly is an uncomputable process? (Gouin, 1999)

The phonons above are *coherent* as a result of the biomolecular nuclei supporting them being part of the connection of the common space manifold with an inertial space manifold. *Such collective connections cannot be affected by ordinary space thermal effects since thermal effects can only come from localized evolutions, so only coherent collective phenomena can be present.*[36]

3. Two-dimensional quantum computation

When I tack the electrons evolution described earlier onto the phonons evolution I obtain a pure mechanical/electronic forward (or backward) evolution on both centrioles. Since complementary biomolecular patterns are on the two centrioles *the combined evolution on their superposed surfaces in inertial space exists in only one direction of propagation, and thus is a* ***deterministic two-dimensional quantum computation***.

I shall note here that Feynman thought of spin waves as possibly sustaining a quantum computation (Feynman, 1985). But he could not get away from the fact both directions in the spin chain were allowed, making the time to complete the potential computation *undetermined*. His computation was also only one-dimensional (this is the origin of the "quantum computers" of today's vintage, using only interfering realities through the present quantum theory formalism - see Appendix B of Gouin, 1999, and Section V for more on this matter). In the centrioles arrangement Nature seems to have solved the problem by allowing only one direction for the evolution through its asymmetrical slat construction.

Also, due to the slats construction out of three small cylinders, each slat can "observe" the previous one *in more than one direction* (Fig. 7b - see Appendix B of Gouin, 1999, for the notion of a quantum observer as Everett envisioned). Since each cylinder strip holds *non-commuting variables* according to the Appendix B analysis, the evolution of the automata ends up branching in as many realities as the automata patterns computation can have choices in its evolution, *each reality following its own evolution path* ***non-interfering*** *with each other on the centriole surface in inertial space* (this feature is also discussed in

Appendix B of Gouin, 1999). Present quantum theory cannot consider this kind of composite quantum system, being able to formalize only interfering realities through its statistical formalism. On the other hand, Everett's interpretation of the Schroedinger equation characteristics identifies in fact such a feature, but fails to clearly point out it is a generic composite quantum system feature, and Appendix B of Gouin (1999) fills up that gap. Since we are dealing with an exponential branching of realities we have not only a 2-dimensional computation (a non-local cellular automata), we also have a quasi-infinite number of such happening in parallel.

While being deterministic in the sense of Physics through the monadic spaces understanding (not through present quantum theory! See Gouin, 1999), the computation is then also ***"non-deterministic" in the sense of Computer Science***.[37]

I shall note that, due to the localizations effected by the strong forces (atomic nuclei - see Gouin, 1999) present in the biomolecular nuclei and the finite number of biomolecules on the centrioles, there is not an uncountably infinite set of *computations*. However, each involves monadic spaces sets "states" evolutions, so *the process is in fact about an* ***uncountably infinite set*** *at the monadic spaces level*. The creation of the inertial space occurs because the number of photons and electrons monadic spaces in that space is uncountably infinite (Gouin, 1999). Their grouping via localized quanta, and thus "states," allows the evolution to be *described as* a finite multi-realities computation through such "states" evolution as quanta, but it is really involving an uncountably infinite number of elements, a feature that will have a very important consequence as I shall discuss in Section V.

4. Computational output and spindle formation

A *computational output* occurs when electrons simultaneously shuttle in dimension 1 and dimension 3 at the same corresponding location along their slat on both centrioles, thereby emitting photon pulses in dimension 2 common with ordinary space. Such pulses have a circular polarization in inertial space dimensions 1-3 and thus do not interact with ordinary space content manifolds (water, etc.). They are thus *unobservable*. They attract biomolecules because they "connect" with them through their inertial space *in the process of extending a space manifold* (a key feature of monadic spaces - see Gouin, 1999). They contain a set of photon realities simultaneously emitted from a set of computation realities from the entire length of the slats, forming a parallel train of photons crossing dimension 2 superposed with each other.

The other pair of centrioles being coherent (synchronized) with the first one will emit at the same time a corresponding pulse (Fig. 3). But the centrioles in that second pair result from the prior pair that split. A 90 degree rotation was made to create a complement pattern in dimension 3 during the original pair build-up. Another rotation was made for the construction of the present pairs so the initial pattern is again in dimension 1 but rotated 180 degrees (Fig. 8). Then the present second pair has its computation running in the opposite direction *in dimension 1* from the first pair, thereby emitting the photon pulse in the opposite direction from the pulse emitted by that pair, and thus towards it.

Dimension 2 of the inertial space between the two pairs is of course a single dimension of that space manifold while a curve in 3-D through ordinary space. The pulses generate two "spindle threads" between the pairs of centrioles, one thread having its inertial space in dimensions 1-2 and the other in 2-3 according to the source dimensions that emitted the photons, and the attracted biomolecules sense ("observe") the photon pulses polarization in inertial space through their electron shuttling orientation.

The spatial separation between threads at the equator of the spindle is created by the presence of the nucleus kinetochores creating a dual layer in the common space manifold as I described earlier (Fig. 5). As experiments with *mitosis without chromosomal material* showed the spindle reduced to straight parallel lines (Margulis, 1993, p.229). The set of duplicated kinetochores have their inertial manifolds in dimension 3 if the originals have theirs in dimension 1, thus *together* they form a 3D inertial manifold in two submanifolds connected in dimension 2 at the kinetochores themselves. The kinetochores are attracted

selectively by the photons on their way to the other centriole pair according to their inertial space manifold orientation.[38]

When the photon pulses meet the corresponding slats in the other centrioles pair, they do it in the same way they were emitted (thinking in more than 3D is here also important!). At that point, each pair of centrioles in effect receives back ("observes") its own photon pulse (undistiguishable set of monadic spaces) as if it was reflected in a mirror. The computation then runs as if a time reversal occurred until a new set of photon pulses is generated by the computation. Therefore the computation must generate a fixed even number of threads through processing its automata pattern program generating the same pulses again and again until this cycle is stopped by the kinetochores as we have seen earlier, allowing the computational process at that time to go further in its evolution.

As a result of the above analysis, I can infer that, when alone in a cell, a pair of centrioles generates MTs either all with inertial dimensions 1-2 or all with dimensions 2-3, depending on whether the pair was the "first" or the "second" one in the mitosis they come from. In other words, the 3-D inertial space manifold of the cell is basically a 2-D layer "lining up" the ordinary 3-D cell space except for the centrioles area which has a stub in a third dimension (here again thinking in more than 3D is important). The inertial space of the cell will be fully 3-D only during mitosis when the spindle threads intermix to pick up the chromosomes as seen earlier.

5. Synchronized molecular motions along MTs

In the picture drawn above, the MTs generated by the centrioles cannot perform a computation since only two complementary conformational configurations through either inertial dimensions 1 or 3 are available[39] (see the left side of Fig. 6). The electrons have then a fixed dual state to shuttle between in inertial space. These states correspond to molecular conformations forming a *fixed* 3-D pattern in *ordinary space*. This pattern is dynamic as it propagates through the phonons "computational waves" described in Appendix B, except that no computation is performed here. *This non-local dynamic pattern of conformations propagating in waves can be seen as at the physical origin of the synchronized motions observed for dynein and kinesin "motors" used in intra-cellular transports along MTs.*

REMARK.

- Appendix A Subsections 5 and 6 and their references identify directed molecular transport as a vital function of cells, and the function of MTs there is central for coordination of the processes. But without a coordinating factor through quanta it is wishful thinking to envision the realization of such a coordination in a classical system. Kinesin and dynein motors movement must be synchronized, and this over macroscopic distances. Even though MTs cannot perform a computation, they sustain an inertial space through photons produced by the coherent electronic evolution over such distances. Overall control of the process would come from the centrioles computation selecting the state of the electronic evolution pattern in the MTs (in the cell or from out of the cell in the case of neurons - see later).

These dynamic patterns have other functions: They can be modified either by multiple reality photon pulses from the centriole pair or from (classical) ion translation in the cytoplasm. They are therefore *the "memory" of the cell quantum system* as well as its *input/output versus the outside classical reality*.

6. Application to mono-cellular organisms (ciliates such as paramecia)

In the case of a mono-cellular organism, ion motions are triggered through motion of the entire cell or through an impact from the outside. The motion of the cell is then effected by a repatterning of the photon pulses from the centrioles computation that relocates the MTs. This computation thereby *directs as well as effects* the motion and shape of the cell.

The input to the computation then looks to be coming from many sources, chemical as well as radiation, but all from the classical reality affecting the dynamic conformational state pattern of the cell MTs biomolecules. Such sources may be internal to the cell, via chemical factors emitted from the nucleus, and/or external to it via the cell membrane and its cilia (which are part of the MT system - Chap. 8 in Margulis, 1993, and Appendix A). It has been advanced that the centriole pair may act as the eye of the system. Such a function is doubtful in the picture above. Radiation most likely affects the MTs dynamic pattern, which the centrioles then sense. In that respect it would be interesting to find the cell response to focused beams versus wide beams. The cell reaction will depend on its program, so some of the characteristics of that program may be determined in that manner. Then the centrioles quantum system "observes" its memory, which, as I mentioned earlier, is in an inertial manifold "lining up" normal space, scanning it via its photon pulses in inertial space, and acting from it according to its ongoing multiple reality computation.

One question that would need an answer in the monadic spaces picture: Where in the DNA of the cell can the initial pattern of the centriole (its "program") be found? Such a pattern would determine the generic physical *behavioral characteristics* of the organism.

E. Multi-cellular organisms - The Puppet Master Hypothesis

1. The hypothesis

Margulis formulated a hypothesis about the origin of multicellularity: "The failure to solve the problem of reproduction and motility on the single-cell level led, in several groups, to the origin of multi-cellularity." (Margulis, 1993, p.260) I shall advance a modified hypothesis, explaining also multi-cellularity as a consequence of the evolutionary dead-end of ciliates, in light of (1) reproduction being in fact a simple function to *merely help* effect (MTs are not needed to effect it), (2) such a function is *not* helped by going multicellular since each cell still needs to divide individually in that case. On the other hand, the single-cell MTs had to both *control* and *realize* cell motion, which are each an enormous task. They must be split if the organism has to increase its *choices of behavior*, being an immediate tool for survival. Then my hypothesis will be that ***the MT system found a way to split these two functions through multicellularity***. From (1) this consideration, (2) Margulis' description of symbiotic operations between the MT system and the nucleus in a cell, where the *form* as well as motility of cells are the original MT system functions, and (3) the fact neurons do not have centrioles, I shall advance the

Puppet Master Hypothesis:

The computation generating the MTs in neurons must be occurring in the numerous glial cells abutting each neuron, which do contain centrioles.[40] *The neurons then are, shapewise and motionwise,* ***behavioral puppets*** *of a non-local computation occurring within and across glial cells.*

During organism development neurons would provide the physical motion and means to shape the nervous system while glial cells provide the directions how to proceed. It would be interesting to find how the glial cells at some point take over the control of neurons when they lose their centrioles.

REMARK.

- Appendix A examines the question of neural development. A coordination of MT and actin cytoskeleton functions with some guidance from local chemicals to produce axonal "growth cones." (See Appendix A, Subsections 5.b and 6.d). As mentioned earlier, actin seems to sense the boundaries of inertial space manifolds. MTs sustaining such manifolds would then localize actin, which would in turn produce the growth cones through additional localized polymerization upon influence from gene products (see Appendix A). But this scheme still does not address the question of system overall development control. See below for this matter.

Subsequently, when the organism is completed, neurons would become the sensors data and controls transmission medium to the motor parts of the organism, which then are in turn puppets of the neurons. In such a scheme *the goal of the glial cells is to pool their computational power to increase the versatility of the organism behavior*. Then the neural MTs would be "remote spindles" between glial cells centrioles to provide the quanta exchange paths needed to create a common computation as it was effected in mitosis. But how would such spindles *physically* relate to the centriole pairs that generate them *from outside the neurons* (thereby shaping the neurons) and/or exchange quanta through them?

2. The origin of synapses

In order for two "separate" glial cells centriole pairs to have a quantum computation common to both, a 3-D inertial space manifold common to the neurons and glial cells is needed for their quanta exchanges. However, in the physical picture of mitosis outlined earlier, neurons have their MTs inertial space in either dimensions 1-2 or 2-3 as all cells were found to have earlier. Therefore *a connection with ordinary space in dimension 2 must complement the neurons inertial manifold dimensions 1-2 and 2-3*. The need for such a 3-D manifold connection then gives a physical reason for neural *synapses* (Fig. 9), as *the MTs within the neurons would be then able to provide the quanta exchanges paths between glial cells centrioles pairs* as they were providing in mitosis within a single cell.

In that picture, each glial cell pair of centrioles emits a photon pulse in dimensions 1-2 or 2-3 *through the synapse of the nearest neuron* (Fig. 10b), *maybe using neurons cytoplasm elements such as the vesicles "coated" with the supramolecular structure clathrin*[41] *enclosing cell membrane receptors*. Such vesicles would then be involved not only in releasing neurotransmitters in the synapse cleft for subsequent classical ion pulses (see below), but more importantly act as a *photon pulses redirector* between inertial space submanifolds, by themselves *effecting a 3-D connection with inertial space as centriole pairs would do*. This function would come from the cell membrane receptors put in a quasi-spherical arrangement inside the clathrin *triskelion* structures forming the vesicle clathrin coat. Such receptors holding "hydrophobic pockets" would sustain a spherical common space manifold dual layer, creating an *orthogonal* 3-D inertial space connection through the pocket electrons shuttling in separate layers (Fig. 10a). *To experimentally confirm such a feature (and thus give a strong confirmation of the Puppet Master Hypothesis), the inertia of synapses should be measured, in the same way the centrioles inertia was done earlier*.[42] The glial cells attached to the neuron would then direct the formation of synaptic connections (and modify them as called for by the computation) through forming the MTs in the neuron (themselves directing actin for the needed growth cone) via its clathrin-coated vesicles, which would in a sense provide the pulling strings of the puppet master.

REMARKS.

- Such an arrangement would be common in cell functions in general (Appendix A), such as in the Golgi and Endoplasmic Reticulum maintenance systems where *directed* and collective motions of vesicles are observed (Appendix A). Such vesicles would sustain a dual layer of the common space

manifold, and thus would allow quanta exchanges coordinating their motion along MTs by forming a whole system via inertial space.

- As Margulis pointed out, the evolutionary origin of the cell membrane receptors, through cilia for protozoa, points to relatives of centrioles.

3. Quantum links

The 3-D inertial space connections would then provide the glial cell photon pulses with a route to the inertial space of the neural MTs in their various directions of dimension 2 (within my convention that this dimension is 3D in normal space). The neural MTs electrons would then interact with the photon pulses, changing their state (resulting in the neuron being "activated"). This would be just a variation on what the single cell ciliate would do for scanning its memory, except here a neuron would be common to many glial cells. Then here, beside providing an input/output with classical reality, *the memory would act also as a quantum link between the processors*.

This link is described in Fig. 10b. The system without input/output keeps on processing and modifying the data in the neurons, an *ongoing process*[43] by its inherent nature. In a multicellular organism the exchanges of quanta through the nervous system are then part of a coherent whole and non-local quantum computational system across many cells evolving in inertial space, the centrioles in glial cells being its processing subsystems. Through its evolution as a multiple-reality computation, such a system then effects a macroscopic-size "many-worlds" as Everett envisioned (albeit for reality at large). A "wave function collapse" as Penrose hypothesized is nowhere in sight, all the realities of the computation existing in parallel. This matter will be evaluated further in Section V.

4. Quanta exchanges, ionic pulses and the input/output principles

The ionic impulses (classical "nerve impulses") observed in and across neurons then contain no data, as they merely are *side effects* of coherent photon pulses in the neural "spindles" that exchange quanta between the centriole pairs of the glial cells. The ions would be collectively moved in a statistical fashion by the conformational state changes in the MTs biomolecules. The ionic impulses observed travelling along neural axons MTs would be "shadows" of quanta travelling in the dimensions 1-2 or 2-3 of the MTs 2-D cylindrical inertial space manifold parallel to their hollow core. At the synapses, the photon pulses would be received by glial cells centriole pairs, which would retransmit them to the next neuron via an output of their computation. These pulses being relayed through the neural/glial cells chain would be ultimately received by glial cells subsequently storing the data in nearby neurons as patterns within their MTs 3-D inertial space, thereby effecting the input/output memory of the central computation. The MTs in neurons then would hold the input/output memory of the central computation as well as memory used by the computation for itself.

An input to the ongoing process in the central computation can be then provided via a chain of neurons/glial cells transmitting the result of a computation done at the sensory part of the system. The sensory part may be acting as a separate quantum computation effecting a Fourier transform of the input data as a pattern of multiple reality coded photon pulses in inertial space (again, shadowed by classical ion pulses which would contain no data). The information would then spread in a holographic fashion[44] to a set of glial cells that would in turn process and store it in neural MTs biomolecular states holding the data until it is picked up by the central computation. This pickup would be done by the inertial space photon pulses exchanges between the glial cells in which the photon realities would be modified by the MTs electrons that had their states changed.

The output to the outside classical reality would occur in a reverse fashion, but with a twist. The glial cells photon pulses would, through a chain of neurons/glial cells, trigger ion pulses at the motor part of the system. There the shadow ion pulses would at last become of value as they would produce classical effects on the motor parts.

5. Implications for Neuroscience

In the picture above, the function of neurons is to (1) provide the medium for the *physical interconnections* between the various glial cells subsystems to complete a whole macroscopic composite quantum system existing in a space separate from ordinary space with exchanges of quanta (not ionic pulses!) between subsystems performed in fixed one-dimensional ways through the neural synapses, and (2) provide conduits and hold the outside classical world inputs and outputs as patterns in a 3D fashion to be picked up by the quantum computations occurring on the centrioles of the glial cells in their inertial space.

The various kinds of synapses observed[45] would then not come from classical effects at all, they would instead correspond to variable characteristics coming from the unobservable computations in the nearby glial cells. For example, "synaptic strength" would be a change of behavior in the computation of the glial cell associated with that synapse from prior inputs to the computation. Quanta exchanges characteristics would likely be influenced by the chemistry occurring in the neurons and at the synapse through the vesicles function there, and thus involve correlated chemical effects back to the computational process. But the classical ion pulses called "nervous impulses" would be still side-effects of the quantum process, and would only result in *mitigating reactions by the local neural chemistry and consequent design of neural features (myelin sheath, etc.) to counter the effects of such inevitable ionic transport processes*. These classical reactions would be then seen by today's Neuroscience as the "prime moving" process, not being able to observe the quantum phenomena occurring in inertial space. *The well-known non-local coordinated and synchronized aspects of the observed classical process, the only one immediately accessible to experiments, is still a deep mystery*, (See for example Crick, 1994, Chapter 17) a situation which, I shall advance, may be a consequence of the above mistaken identity.

6. Cancer and inertial space

Appropriate cell-to-cell contact, thought so far in the literature as regulated in some mysterious way through the cytoskeleton, appears to be critical in preventing cells from becoming cancerous (Kuchel and Ralston, 1998). Within the monadic space concept picture above, I have identified earlier the cell cortex (including the membrane) as in effect supporting the boundaries of the inertial spaces between cells in the dual-layer common space manifold. Therefore cell-to-cell contact must be present to maintain the common inertial space covering the cells and the cross-cell postulated quantum system it contains. *The inertial space must be then maintained between cells for the tissues to function properly through such (unobservable) whole evolving quantum system, as it may allow synchronizing and coordinating living tissues division processes* (see Fig. 4 - step 5). So we need to know what could disturb the boundaries of this inertial space, and find the details of how the cytoskeleton quantum mechanically evolves within that space.

Separately, the origin of the organism's cancerous disruption has been traced recently *also* to either centrioles pair replication malfunction (multiple duplications instead of one) or "aneuploidy," the misdistribution of chromosomes in duplicated cells (Duesberg, 1999). As I described earlier (step 4 of mitosis) the segregation of the chromosomes being an inertial space physical effect, which would have nothing to do with the genetic makeup, the misdistribution would be purely of physical origin, the inertial space manifold receding process, itself dependent on having the proper number of MTs in the spindle (and

maybe other things), and thus may involve a "bad" program on the cell centrioles. So we need to find where this program is located in the cell DNA[46] and analyze it for defects (once we know how to analyze it!). Multiple centriole pairs (leading to aneuploidy also) on the other hand appear to come from a malfunction of the DNA program affecting the division messaging to the MT system.

F. Experimentation

1. Introduction

As I mentioned in the intoduction to this section, the key experimental data is already known. Centrioles construction and behavior can be seen through any electron microscope. There is nowhere in sight a construction apparatus around these large structures, which are quite obvious ***sturdy*** *structures that seem suspended in mid cell medium without support of any kind, made out of parts that don't even touch each other,* ***which reproduce and move without any visible causal means***. In other times it would have been called a *miracle*. Section III discussed the question of self-assembly in Microbiology and there too miracles are everywhere to find. So here is only a typical case for everyone to see, as well as to find described in the literature in minute details *but without an explanation*. I shall emphasize that it is not because phenomena have been known to occur for ages without an explanation that somehow the very knowledge of their existence reduces the importance of the message they contain. In other words the experiments proving the theory were done well before the theory could be formulated. This does not render these experiments useless for such a demonstration, now that the explanation may at last be available. Since there was no rational explanation for what was being observed, the matter was taken as just a fact that somehow could be blended with what was known. The field of Biology to this day is replete with examples of that sort. In the early times of Physics there were many cases similar to the present experience in Biology. The lesson of the past is that the importance of physical facts cannot be appreciated without a theory. A well-known example was the question of weights falling at the same rate, a matter which took hundreds of years for a theory to come up and finally identify its importance. In the meantime, people (including Newton!) said "So what?"

So here the key to the success of the previous analysis is not only about having at last a *rational explanation* but about being able to bring out the theoretical importance of the explanation. This is why this study needs the support of one like Gouin (1999) which approaches the matter from a very general conceptual angle so that the phenomenon can be fitted in a much larger understanding. The key again is to identify the *explanatory worth of the physical concepts* in spite of them giving results that have been taken for granted for so long without an explanation.

So how could the unobservable monadic space manifolds involved in mitosis be confirmed besides through the well-known and *direct* evidence of self-assembly phenomena if such are not convincing enough by themselves (i.e. for believers in miracles)?

2. Experiments on centrioles

New experiments I can think of about centrioles would be to

- analyze their duplication process through interrupting it by a local temperature change collapsing the common space manifold layering - centrioles should fall apart as well as the surrounding PM (proof of dual layer),

- redo the centriole inertia experiment as well as measure the inertia of synapses to identify their 3-D connection with inertial space via the large inertia resulting from such a connection (proof of dual layer),
- destroy the centrioles of a cell and, if the cell still functions, observe the next mitotic spindle starts from the kinetochores area instead of the centrosome (proof of a centriolar role in mitosis),
- during mitosis, right before anaphase in a cell with centrioles, remove one set of sister chromosomes and their kinetochores (i.e. reduce the number of chromosomes) and verify that the next mitosis does not go into anaphase even though chromosomes detach (proof of centriolar computation in mitotic process),
- evaluate how sturdy the centriole structure is versus a typical London/van der Waals bond based structure (proof of structural connection with inertial space).

3. Experiments on spindle

Two more experiments with less precise results should give additional background on the phenomenon:

- verify *using shields* that photons are *not* detected in the process of building the mitotic spindle (or a centriole), yet MT biomolecules accumulate on the shields, showing that they are moved by the presence of photons in inertial space, and so act as *detectors of such unobservable photons*,
- verify that the spindle buildup is not affected by electromagnetic phenomena in ordinary space unless such phenomena affect molecular position/existence.

4. Experiments on dual layer

A set of experiments about the existence of dual layer areas in the common space manifold within a cell would be

- Move the centrosome away from the nucleus (if possible) and observe it returns back close to it. Redo with a low energy cell and verify this does not happen.
- Verify that the microtrabecular matrix domains disappear (random matrix) after the nucleus is removed.
- Verify that a low energy bacterium cell becomes disorganized (the DNA material spreads out).
- Remove the nucleus from one incompletely separated child cell during mitosis just before the cleavage furrow is established and verify that the furrow does not form and the division does not reach completion.

5. Experiments on development

Studies already performed (Keynes and Stern, 1988) indicate that (1) the development process goes by *cell adhesions* (see the previous section on cancer) that *simultaneously* increase in a segment *a fixed number of cell cycles* into the segmentation process, (2) the increase in cell adhesion always takes place at the same time point of the same cell cycle, (3) ***heat shock*** *transiently arrests the development clock at some critically sensitive phase of the cell division cycle.* These are indications the development process has a clock covering the entire embryo based on the number of cell divisions. An experiment for this area could be:

- *If the quantum non-local process across cells envisioned here effects this clock*, it could be stopped by temperature changes that would partially collapse the common space manifold layering. Verify that these heat shocks affect only the cells membrane and extracellular matrix, and if it goes deeper into the cells it literally *kills* the process, and thus Life, through an observable disorganization of cells.

In order to prove the Puppet Master Hypothesis, experimentation would have to involve (1) the developmental process feature whereby entire cells are seen moving versus each other in a seemingly purposeful manner, such as in the nervous system development, and (2) in the developed organism, the formation of new synapses. Experiments in that area could be:

- observe the effect of temperature changes or anesthesiological products on glial cells in a very specific area of a tissue *under development* results in disturbing "contextual" evolutions occurring in the MTs, growth cones and vesicles of the corresponding neurons,
- destroy all centrioles of glial cells attached to an *acentriolar* neuron, and verify neuron stops moving or "functioning" (it is no longer "activated"),
- the motion of vesicles in developing neurons while forming a synapse should be correlated with the dendrites growth cones formations and with the neuron cytoplasm (actin/MT) motion.

REMARK.

- "In vitro" experiments are not envisioned at this point due to the lack of information on the conditions required for the common space manifold dual layer formation, conditions which would have to be identified if the experiments above have positive results.

G. Conclusion

If or when at last the monadic spaces manifold layering process existence is accepted as a fact (i. e. miracles are no longer believed), a generic physical study of biomolecules regarding their ability to sustain an inertial space would then need to be conducted. In that respect, from knowledge about MTs, kinetochores, cell membranes and bacterial flagellum assemblies, the existence of "hydrophobic" areas in a macromolecule seems to be one of the prerequisites for such an ability. The resulting phenomenon would have immediate technological applications (outside Life) from the "macroscopic" quantum processes it could allow.

Biological "information processing" would then include (in an extended computational way) much more than DNA-related local sequencing functions, and the corresponding new concepts would allow us not only to understand but also to *plan* experiments in that light, experiments which otherwise could not even be thought about.

V. MEETING THE HYPOTHETICAL PUPPET MASTER

The generic characteristics of the quantum computational system identified in the previous section remain to be discussed. I am now in a position to evaluate Penrose's hypothesis of a mind based on the quantum, the hunch that started my discussion on Life in Section III, through the principles outlined earlier, and also to evaluate the worth of the alternate monadic spaces picture (1) as an explanatory tool concerning the basic principles of Cognitive Science, a discipline that has considered so far only classical concepts, and (2) as a paradigm for future Computer Science research if the realm of the quantum is to be at all

approached there in a direct way instead of through the present patch on classical concepts called "quantum computation," a misnomer by its very restrictive scope definition, as I shall discuss.

A. Extended Computations

1. The unstated part of Penrose's hypothesis

Penrose's hypothesis as discussed in Section II was part of a thesis about the *uncomputability* of certain quantum physical processes that may be involved somehow in the mind's physical support.[47] Such processes would require new physics coming from an unknown connection between the quantum and gravitation. According to this thesis, the inertia of the large number of atoms making up certain biomolecules would enter in the picture as the means by which a quantum computation in the brain would provide its results. The "reduction" of Schroedinger's quantum wave functions would be then self-generated by the system in an uncomputable fashion, in contrast with the reductions ("wave function collapses") in the outside world, which would originate from "decoherence" (Gouin, 1999), and thus be computable, being based on statistical phenomena involving large numbers of systems. Then our mind function would be uncomputable through our perception as quantum entities of the external world while the rest of reality would be computable (if we neglect its non-deterministic aspect!).

In contrast, Section IV has identified the possibility of a quantum system providing its input/output through a multiple reality internal observation in the manner identified by Everett, without any need to consider wave function collapses, and Gouin (1999) has discussed the possibility that all quantum processes may be in general uncomputable, giving a corresponding non-deterministic character to the wave function "reduction." But there an "extended computation" was envisioned because a step process was involved.

But even though Penrose's views seem to be then ultimately incompatible with the monadic spaces picture, they may bring a new twist to that framework. Penrose's thesis could be seen as hinting at *a quantum system observing and acting on the classical world* instead of the usual quantum theory where the classical world measures and acts on the quantum. When considering such a way of seeing things, *our instruments would be communicating to us, quantum multiple reality beings, a classical set of facts* that we would *choose* to consider.

2. How to use extended computation

How about applying the idea of "extended computation" available through the monadic spaces concept? For this to be accomplished two things need to be done: (1) obtain a formal understanding of such extended computations, (2) go beyond the barrier of non-determinism brought about by the formalism of the quantum wave function.

For requirement No. 1, Gouin (1999) described an extended computation at the monadic spaces level as involving an uncountably infinite process in a "structured" continuum. When dealing with the molecular level, as investigated in Section IV, the extended computation may be reduced to an evolution described through a finite (even though quasi-infinite) process thanks to the localizations provided by atomic nuclei. Such a computation then uses patterns as input processed in a multiple-reality non-local cellular automata fashion, a process which needs a future theoretical evaluation to identify its features and capabilities. It cannot be dealt with through the classical notion of computation defined by Turing since such a notion is derived from a Classical Mechanics world that inherently requires separability and distinguishability.

As a consequence of requirement No. 2, when the non-determinism is assumed (through the monadic spaces concept) to result only from the passage to the classical world, the computation, including the

handling of its inputs and outputs, must remain within the quantum system, with no intervention from an outside world "observer" as present quantum theory envisions. The computation would then observe and act on the classical world.

Could I imagine then *composite quantum systems that could discretely observe the classical world and act on it, as a whole*? Could such self-contained quantum systems (SCQS) be the key to our use of extended computation?

B. What is a SCQS?

Definition:

A SCQS is a composite quantum system made out of electrons and photons, its "physical support," where, instead of interacting with photons from all directions at any time, electrons within a given processing subsystem (a quantum processor) would only interact discretely in one-dimensional ways with other processing subsystems electrons through a separate space within a dual layer region of the common space manifold.

Then such electrons are *separated* from the rest of reality by having their infinite sets of monadic spaces selected by the external common reality as *one separate set of monadic spaces*, in effect brought together through the evolution of the common monadic space manifold into two layers as envisioned at the start of Section III. This set of monadic spaces would then have limitations in its evolution through the SCQS layout into separate processing subsystems using quantum non-local cellular automata such as the one identified in Appendix B. Even though the electronic evolutions within each processor would be separate, exchanges of quanta with other processors would create and mantain a separate space, thereby making the SCQS *a whole coherent quantum system undisturbed and separate from ordinary space and its content.*

To bring this kind of physical system in the perspective of reality at large as I have discussed in Gouin (1999), I shall make a correspondence with the nuclei of atoms. Each nucleus generates a space by itself out of quarks/gluons monadic spaces evolution *within the space* generated by the leptons/photons monadic spaces evolution, which was described as the "electromagnetic space." There is a coupling between these spaces because the elements part of nuclei can have electromagnetic interactions due to the nature of nuclear monadic spaces geometry versus electromagnetic monadic spaces geometry (as it has been detailed in Gouin, 1999). A SCQS space (which I called earlier "inertial") would be also loosely coupled to the electromagnetic space. But the *computational isolation* of the SCQS from this outside reality would be effected differently from the isolation of atomic nuclei. Nuclei are isolated in their computational steps from the surrounding electromagnetic space due to the large difference in the frequencies involved with electromagnetic monadic spaces updating (Gouin, 1999). The SCQS would evolve as any composite quantum system can evolve, that is, as a multiple reality with exchanges of quanta between its various subsystems, but would have the extra benefit of being in its own space, thereby remaining undisturbed by the rest of reality. The time in that space would be coordinated with the outside time through the biomolecular systems connecting ordinary space with that space. The SCQS computation would be then related to the normal space monadic computation only through the records effected by input/output "states" which would then be the "memory" of the SCQS, its information interface with the outside reality.

C. The SCQS world

1. Subjective time

A SCQS would have an overall reality computation that would "observe" its other computations occurring within different realities. This overall computation would "experience"[48] a "subjective" time from the output of a specific ongoing computation taking as input the amount of processing done by the rest of the system.[49]

2. Qualia

Also, in analogy with a mind,[50] a SCQS would experience objects such as "feelings"[51] (needs, colors, etc.) collectively also called "qualia" in Cognitive Science. Within the monadic spaces picture these would be objects built out of (*created from*) elements within the SCQS spacetime through its uncountably infinite (extended) computational process.

3. The creative evolution

They would exist because the SCQS internal evolution is a fundamentally *creative* process: Instead of the "contiguous" arrangements of classical systems, which cannot create anything except large scale patterns (with, granted, their own features too, as a classical computation can provide[52]), the objects existing in the SCQS spacetime would have new features *not part of the computation* original data (the outside world input). In a sense this would be like passing at the continuum limit from a series for an integration process, where, for example, the volume obtained is an entirely new feature of the set of elements obtained through an *uncountably infinite process*.

Even though the computation identified in Section IV is finite, it runs through "states" of monadic space sets (electrons and photons) which are themselves uncountably infinite (Gouin, 1999). Then such a computation is in fact an uncountably infinite process. This is a fundamentally foreign concept for the Classical Mechanics originated view of present Computer Science, as the "decoherence" process separating and distinguishing things within the composite quantum system making up the classical world renders it discrete, if not finite, but this is not how our reality at large seems to be built (Gouin, 1999).

I describe below, with the superposition effects, something that can be personally experienced to demonstrate[53] this fundamental *creativity* of the quantum in a mind setting. Again, *such phenomena are* ***created*** *through the sets of monadic spaces formed through the evolution of its physical support (electrons/photons)*, the SCQS own kind of "particles," "trajectories" as well as extended (spacewise) objects that could be seen as the "condensed matter" of that world, i. e. the patterns in the memory of the SCQS. These extended objects have recognizable multiple features and patterns (including a "feel," which is also a created object) that the SCQS can experience (1) by *recording its own evolution as part of the external reality*, and (2) through the structured relations built across the subsystems making up the composite system (see Section IV), relations that would be modifiable by the computation itself, thus potentially realizing *not only a self-constructing computer as Turing envisioned, but also a self-modifying one*.

Hameroff[54] brought out the idea that, within the quantum mind picture, since the wave function collapses from the distortion of space geometry according to Penrose's hypothesis, then our psychological life would be able to be explained from the nature of that space. But in present-day physical theory there is no description of how space comes itself into being, thus a fortiori such a theory cannot explain the internal space of the mind with its objects we all experience. The *creative aspect* of monadic spaces and the quantum has been missed from the beginnings of quantum theory with the unstated assumption that space is merely an arena and not created by its content. This feature appears now to be a fundamental necessity for our understanding about the creativity of the mind. Within the monadic spaces picture of a SCQS, our

dreams, imagination and concepts are objects generated by such a creative process within a space coming also from that process.

4. An isolated world

Such objects would exist through the SCQS physical support evolution, but, unlike for the outside reality monadic spaces and quanta, they would not be separated within the SCQS space through a mechanism of localization for the monadic spaces, and thus would remain as non-local data in the memory of the SCQS. In contrast, the external reality connects undistinguishable units to create separate, distinguishable things extended in both its space and time through the *creation* of classical features from the quantum via localizations that can happen thanks to the localized quanta (atomic nuclei) existing in the external reality, as Gouin (1999) describes. The localized quanta of the SCQS are the states of its electrons in the biomolecules effecting its memory *as well as certain states of its computation that would effect a sort of dynamic memory*. As in the case of the nuclei parts, the quarks and gluons, these phenomena would never be able to be seen by themselves in our classical reality, being in an entirely different space. They could not even interact with the monadic spaces constituting the external reality. Only the SCQS itself would be able to experience them.

For a mind, nervous impulses would only reflect quanta exchanges occurring at the biomolecular memory level, not the internal computational world of the mind in any way. The evolution of a SCQS would be able to affect the external reality by the computation selecting which among its internal realities is to act on its input/output memory, and, conversely, the evolution of some of its realities would be able to be affected by the external reality. In the case of a mind, unobservable photon pulses in inertial space would produce classical ion impulses that would act on the classical world (Section IV), and, conversely, the external reality would affect part of the subsequent evolution of the SCQS through changing its memory.[55]

D. SCQS features

But how can these internal objects be experienced if they are all part of the same system that experiences it? Isn't there a need for some kind of "information transfer" between the various parts of this system for such experiences to occur?

Questions like these raise the matter of SCQS internal features, which can of course vary according to the complexity of the composite system arrangement. At this point, through Cognitive Science, we can obtain only a very cursory knowledge of such features. But there seems to be a few that may be identified. Future studies will have to discover the precise physical configurations effecting them in a SCQS.

1. The "Being"

As a general feature, a SCQS "knows" the state of its various parts instantaneously in its space through the *"observation" by the computation* of one of its internal realities among the quasi infinite set of its other ones (as an Everett Observer within a many-realities world, not via a wave function collapse). The SCQS individual processors constantly scan its input/output memory, so the knowledge is locally updated but is available globally. This "information" is similar to the differentiated localities and directions that are created by the strong forces defining nuclei of atoms (Gouin, 1999). These localized quanta allow our common reality to differentiate its parts through its virtual quanta ("field") giving a non-local "presence" in the common space manifold. In that sense nuclei provide the information needed for the differentiation. In a SCQS there is no information transfer, as "information," the character of a *differentiated* set of entities,

can only be defined by the states of its various memories, and thus there is only information *available to* the system through its non-local memory banks. Of course there is no conflict with the speed of light as a barrier for information transfer since there is no "long-range" transfer within the SCQS, being a non-local system.

On its "side," in the case of a mind, the classical world sees appreciable time lapses for the mind to be informed through its various *sensory parts*. But this is only due to Nature's limited choice of means through Evolution to keep the central computation informed. In that case it had to go through a chain of neurons (Section IV). There could be alternatives to such a method. On the other hand, the classical world could experience "contextual" choices made by a SCQS, i. e., if a *SCQS extended in space* is considered, with corresponding sensory-motor parts, these choices may then be made in the lightcone spacelike portion of Relativity, whereby the external classical observers of such a SCQS would have no clue on the contextuality character of its choices. The SCQS switch of internal reality in its computation, as a well-known fundamental monadic spaces quantum feature (Gouin, 1999), would be *instantaneous* across space. Of course, the maintenance of an inertial space manifold connection across large distances would be then required, but it would not be impossible if means different from the one Nature found are used. In this respect, the two halfs of the brain seem to have such connections, via its "commissures," and these cover pretty large distances to form a single mind when considering biomolecular scales.

2. The "Focus of Attention"

The quantum system *may* be able to shift its "focus of attention"[56] on external or internal events as Dennett describes. Such a process is separate from the generic design above. It would be a computational feature that provides the ability to select a set of memories (either affected by the external world, the internal world, or both) in the space of the SCQS through an *overall evolutionary state* of the system modified by all the inputs from its memory. It does not seem to be a Darwinian search as Dennett proposes.[57] In a quantum perspective, it would be using a much quicker method, more like a change of drumbeat as a result of a computation result on the frequency and mode of the membrane vibration from the screws tightening around the drum corresponding to the total qualia experienced by the system (Feynman would have liked this analogy!).

3. The "Self"

The quantum system *may* experience its own self[58] and the state of its subsystems by *exchanges between undistinguishable parts of the computation*, creating an infinitely recursive process since the result of a power of monadic spaces sets process, and thus *creating* the self. Such a phenomenon may use a quantum superposition effect when the self *observes* (in the Everett sense) sub-quantum systems, very much as stereoscopic vision appears to be a quantum superposition effect *creating* the depth "sensation" through *creating a subspace in the inertial space*. The fact that stereovision may not be a mere pre-existing mapping of reality but *a continuous creation of a subspace out of the recognition of its content,* in the way external reality creates its own space (Gouin, 1999), is supported by the mental experience obtained through staring at single 2D images constructed in a special manner.[59] In the case of minds, schizophrenia and other mental disorders, such as split personalities, point to the splitting of the inertial space, and may then point to the origin of the phenomenon of "self" creation by identifying how the reflection effect can break down. *Exchanges of quanta between undistinguishable entities* would still effect unseparable wholes, but then such wholes would be connected *only via the outside single reality* through separate SCQSs biomolecular memories, and thus would be distinguishable (either internally through perceived "internal voices" or externally via split personalities).

4. Coordinated sequential motility

The SCQS internal quantum process would be able to act on the classical world *at the level of the entire system* only when certain records in the biomolecular conformations are modified in a e-m spacetime time-wise linear fashion. In a mind this would allow a *speech stream* as a variation of *coordinated sequential body movements*. Such a conclusion may be clarified through examining prehistoric records. In this respect Calvin[60] provides some ideas on the role of motion sequential coordination with speech. He goes back to prehistory using records (tools, etc) before homo sapiens sapiens existed and tries to identify how the language capability may have evolved, *assuming that language is a telltale of self-awareness*.

5. Language vs. self-awareness

This last connection is in turn questioned by Jaynes (1990) through a controversial approach. He understands consciousness as another word for *self-awareness*, and he estimates it to be no more than 3000 years-old in the Old World and as recent as the time of the Incas in the New World. From the "evidences" he selects the homo sapiens sapiens mind would have been split until such times in a paleo-schizophrenic sort of way (labeled a "bicameral mind" to disconnect the concept from a mental illness). Under such a view the language ability would be a prerequisite of, but would not necessarily correspond to self-awareness. Self-awareness would then be a clearly added feature that a mind may display, separate from the rest of its functions, *inferring the existence of a corresponding specific configuration of the physical system*. In Nature it would have taken hold only by giving a sharp survival advantage. Of course, before it could give real clues on the physical design of SCQSs, the would-be science of "paleopsychology"[61] would have to work out reliable definitions and much more complete evidential backing in order to resolve the differences in approaches and conclusions among its protagonists.

6. Consciousness vs. self-awareness

As a point of comparison, Hameroff (1998a) thinks from his views on the quantum character of the mind and as an anesthesiologist, that consciousness (he makes no difference with self-awareness!) is a clinical state existing in animal life at large that would have appeared 540 million years ago (we were worms back then!). If I follow such a line of approach, I would then advance from my analysis in Section IV that paramecia are self-aware. It looks like Hameroff's understanding of consciousness is to be the "Being" feature I identified earlier. Clearly if consciousness results from a basic quantum computation, then self-awareness demands a very special kind of composite system.

7. The reference reality

As Gouin (1999) described, the outside reality evolution may be made out of infinitely multiple realities within a "structured" continuum *decohering as a single reality due to the impossibility to maintain coherence among many composite quantum systems in differentiated localities (through the existence of the strong forces) within a single reality of the common space manifold*. Then a SCQS would be infinite in that manner. But, unlike for reality at large, it would be able to keep its multiple realities coherent thanks to its generation of a *separate space without strong forces differentiating localities*. Unlike for other pieces of the common reality, a brain would have physical properties utilizing the multiple

aspect of reality to define its function as a *whole system*. As Everett assumed for the external world (not knowing about decoherence), "wave function collapses" would not occur in the physical support of a mind, not having differentiated localities. The outside reality would be then the *reference reality* used by the monadic spaces making up this support to collectively structure their multiply parallel computations.

8. "Free Will"

A mind would be then able to choose from such multiple realities in an "extended computation" way, thereby presumably expressing a *free will*, something impossible in any classical system, and thus in computers, as Laplace centuries ago pointed out,[62] even when 20th century deterministic chaos is considered, and something that would not be left to "chance" either as present quantum theory assumes.

E. Physical behavior and computational capabilities

A computer as conceived in today's technology is finite because it is inherently a *classical being*, having shed all multiple realities, by construction. Then there would be no way under such a picture that a computer could completely and genuinely reproduce the *physical behavior* of a mind, including its internal physical processes as discussed earlier. However, "physical behavior" and "computational capabilities" are qualitatively two very different things as I describe below, so hasty conclusions on such a matter must not be drawn.

1. "Human-level intelligence"

I shall stress at this point that I have been discussing *physical behaviors* that SCQSs may have from comparison with our present limited knowledge of the human mind behavior when assumed coming from quantum physics. "Human-level intelligence" as known in Computer Science is a completely unrelated subject and concept, where the physical support of the mind is taken as irrelevant to its behavior in general. It was developed by Turing through the idea of a test, known as the "Turing Test," where a computer is pitted against a human subject and *the comparison of **behavior** between the two is made via a language*. Turing then assumed that the behaviors of the two can be accurately and completely compared that way, which is not obvious at all and thus the matter of much philosophical discussions (Searle, 1992). Mainly, it looks like Turing was confusing physical behavior and computational capabilities, and this because *Turing was unaware of the quantum*. If comparisons are made between classical systems, comparisons via language ought to be sufficient as a consequence of the Universal Turing Machine theory. But when considering minds as quantum systems, knowing that the quantum has physical characteristics fundamentally different from the ones of classical systems, and behaviors accordingly as seen earlier, there cannot be any connection between the *physical behaviors* of minds and our classical (discrete) computers (or "quantum computers" for the matter).

Penrose has argued against Turing's claim that "human-level intelligence" can be in principle attained with computers using finite and discrete means available from Classical Physics. ("Intelligence" here is a term referring to *computational capabilities*, not physical behavior, since tied to the theory of Turing machines.) But, as Turing was disconnecting the mind from its physical support after Descartes' philosophy, Penrose made his stand as philosophical as Turing's by missing the crucial fact that there is no way with our present technology to access the physical makeup of a mind as a quantum device,[63] so there is right now no way to make any comparison in ***potential*** capabilities (behavioral or computational). He attempts to connect the uncomputability of the quantum wave function collapse (which I find lacking in

SCQSs) with a supposedly *extra computational* capability of a mind, but he can't address how this physical feature could be such an extra since *he has no idea about the **overall** physical design of a mind*. His "Orch-OR model" describes the principles of a semi-local physical process based on an assumed wave function collapse but he fails to incorporate it into a computational system.

Further, if Penrose had considered the details of the needed computational configuration he would have had to envision *composite quantum systems*. But present quantum theory (the theory he uses, of course) cannot address such systems (see Appendix B of Gouin, 1999), so he could not possibly reach the conclusions he wanted to obtain about non-quantum computers.[64] Deutsch[65] in fact looked at the theoretical aspect of computation using the notion of "quantum computer," a misnomer since covering a very restrictive definition as I describe below, and found out that the quantum has then its own problems when the details of the *conventional quantum formalism* are applied.

On top of this, a SCQS evolution does not involve wave function collapses as Penrose assumed, so the key on capabilities in that kind of system is about one computational reality observing other such realities (Appendix B of Gouin, 1999), and thus its capabilities must depend at least in part somehow on this feature, which of course Penrose did not address.

The physical features of the system configuration and the corresponding physical effects are what determines its capabilities. If these features are not known nothing can be advanced about such capabilities. In order to go further in this field, *there seems then to be no other way but to identify composite quantum system configurations that may provide a computation, and analyze their computational capabilities **and their behavior** from the specifics of the system layout, not from an outside means as then a classical world link such as a language would be used, which could not represent the quantum.* Any generic a priori conclusions on such capabilities must be then invalid *in principle*.

2. "Quantum computers"

As Appendix B of Gouin (1999) explains, the "quantum computation" theory does not use *composite quantum systems* where *non-interfering realities* may be grouped separately, since that theory is grafted onto the von Neumann classical *serial* computational process by applying the conventional wavefunction formalism. *Being able to use only interfering realities through a serial set-up, such a computation skips most of the advantages quantum parallel realities could otherwise* provide (Bennett *et al*., 1997), except for special cases such as factoring numbers.[66] Non-interfering realities on the other hand require the use of composite quantum systems using definite, one-dimensional and discrete-in-time interfaces between their subsystems (in other words, SCQSs), a "technology" which may have been stumbled upon by Nature eons ago thanks to the possibility for space to be generated by its content (Section IV).

3. SCQS computational capabilities

The question of computational capabilities as of now can be asked only from a classical computation viewpoint, as numbers and "variables," the objects of the computation understood in the term "capabilities," are distinguishable things. For example, solving any of the NP-complete problems of Computer Science in polynomial time (Garey and Johnson, 1979) cannot be *in general* addressed. *Distinguishable* variables are a foreign concept for the quantum. So the question has no direct answer. There has to be a subsystem that, for the input, "deserializes" things to make them whole *continuous* entities, then "fits" patterns (this is not a discrete data matching as "pattern recognition" in Computer Science understands!) with others in memory and, then, upon finding what to do next, *distinguishes* things and "serializes" them for the output. These tasks can only be done via successive pattern "resonances," which may be very hard tasks for a quantum system.

However, since the system would be using deterministic parallel processing generating realities as it goes along its computation, it may be a "non-deterministic" computation in the sense of Computer Science (Section IV), and thus *may* have a chance to be superior to classical systems in certain tasks. Separately, the creation of the "self" and other *creative* processes are capabilities of SCQSs that are a priori unreacheable by classical means. Yet for a definite capabilities score from such features a formalism for "extended computation" must be first found, as I indicated earlier. But can creativity be formalized?

F. Conclusion

Penrose's approach seems not to fit as a description of a computational system, and it is very incomplete for other purposes. It could only be used as an initial hunch to bridge the gap between the monadic spaces concept and the apparently fundamental quantum aspect of Life, which would have been unreachable from present quantum theory. SCQSs seem to be the key to our use of extended computation, but a lot of theoretical work will need to be done, including developing physical features that could support a system awareness, a subject which could only be dimly approached at this point.

VI. CONCLUSION

Now that this study has sketched the worth of the understanding established in Gouin (1999) and its potential experimental evidence from the Life Sciences, I am in the position to address the last question identified in that earlier study, the origin of the storm over the modern approach of Physics. This I shall address by establishing this study and the previous one as following a scientific approach even though they are *informal*. Such an issue has nothing to do with its scientific accuracy, and everything to do with the *kind* of description it provides, very much as the *functioning* of Physics is now in question, not its content. Undeniably this study does not proceed as "normal science" would according to Thomas Kuhn's definition (Kuhn, 1996, p.5):

"Normal science is predicated on the assumption that the scientific community knows what the world is like."

Indeed this assumption could not be taken here knowing the nature of the clouds that are now present over this knowledge. The difficulty faced by this study then stems from being categorized as "extraordinary science" within Kuhn's world. *I shall argue then that Kuhn's picture of a scientific work as being merely a formal "puzzle-solver," on top of the previous doctrines of Mach and Bohr* (Gouin, 1999), *in effect brought the present storm in the function of Physics.* The question on the scientific suitability of the informal approach followed by this study comes from the same source. It will be answered by evaluating the suitability of the question itself for Science.

A. The Thomas Kuhn affair

Kuhn, as a young *physicist-in-training* fed up with the textbook knowledge he was being asked to assimilate, especially the ones reflecting Bohr's philosophy, grew to hate Science, and ended up abandoning it with the intent to work out a philosophy that would bring it down from its pedestal as a provider of truths. Even though he presented this philosophy as a reaction from logical positivism, it ended up completing the work of Mach and Bohr that led to the present storm in Physics. Kuhn's 1962 doctrine of "paradigms" and "paradigm shifts" was pulled out of the specialized views of the gestalt psychology acquaintances he knew back then. Science as an institution, a role given to Science following World War II, was to rely upon this doctrine as a guidance for its proceedings. Science fell in love with Kuhn's views, even though they were profoundly anti-Science from the start.

The irony of this relationship can be immediately seen from the definition of "normal science" that Kuhn provided. It implied that the scientific community is striving to be the holder of the *truth* about the world. But Kuhn played carefully with words, as he did throughout his historical essay, covering up his feelings toward Science, and Science loved such words, as they fitted its new function. But Kuhn hijacked the term "paradigm" out of the common language to convey his wish that Science be incapable of providing truths about our world, and only function as a *seeker of puzzle-solving methods*. He later denied that the term was portraying *Science as subjective and irrational*, even though its connotation was obvious. In fact Kuhn ended up flat out admitting he denied Science the ability to know the truth. "Paradigm" as an *ersatz of truth* was then perfect for covering up that meaning while it did its deed in everyday parlance. He thus denied Science's real goal and progress through the hidden message contained in a redefined word. A *scientific revolution*, which was earlier identified with real progress, would be from there on merely a gestalt switch of viewpoint, a "fundamental paradigm shift," as he put it. In his 1969 postscript he suggested replacing "paradigm" with "disciplinary matrix." The term "discipline" still connotates a regimentation. He could have used the term "field," but he did not. So the alternative still reflects his feelings about Science, as he could not get away from them. He also proposed "examplar" as a replacement term when "paradigm" was understood as the set of tools to learn a particular field of Science. But such tools are hardly the gut of a theory, only the means to acquire its *understanding*, which is certainly not an ersatz of truth.

The idea of Science being incapable of providing truths, and truths being unknowable, are at the base of the earlier logical positivist philosophy (Gouin, 1999). Since these times, metaphysics, a. k. a. the search for truth, has no longer been part of Physics, and this against its most well-known practitioners (such as Einstein and Schroedinger). Mach's philosophy was essentially an attempt to dissociate Physics from imagination, reducing it to the invention of formalisms, or "puzzle-solving methods," to explain and predict the outcome of experiments. The example of Feynman looking at gravitons as an alternative to Einstein's notion of curved space is a prime example of this new attitude brough in by logical positivism.[67] Kuhn's philosophy was intended to deliver the knock-out punch: Through Mach Physics gave up the goal to find truths about Nature, and was thus emasculated; now, with Kuhn, it became a *zombie* by being left as a pathetic puzzle-solver. Numerous scientific papers and books published nowadays testify to the love of Science for this idea! The term "paradigm" can be found repeated ad nausea in some of the works referenced in this study. Two cases in points[68] are the studies of the bacterial flagellum and the discovery of cytonemes (Section III).

Science in effect no longer seeks real progress, only an ersatz of progress in the sense Kuhn described. Of course, the author of the philosophy that killed its *elan vital* defended himself against such a conclusion. Expressing outright his real intent (and feeling) would have made him an instant outcast. So Kuhn described in his 1969 postcript (epitaph for Science?) "later scientific theories are better than earlier ones for solving puzzles *in the often quite different environments to which they are applied*." There he identifies his doctrine as limiting Science to that zombie state, no longer progressive *in the absolute*, just another tool of the trade for developing new technologies (Science and Technology are equated), right in line with Bohr's philosophy. *This purpose indeed fitted Science as the institution it became after WWII*. But effecting that shift in purpose destroyed the basic scientific thrust that produced the wonders of the 20th century. Science had been up until then a set of individuals; so now, by its transformation as an institution, it could no longer take individuality and its unruly imagination. Wild Science was too dangerous, it had to be tamed. The deed is everywhere to be seen in Kuhn's essay.

Kuhn also clearly identified his thesis as backed up by the deeds or words of earlier scientists. He selected Bohr of course for that duty when he wrote: "There is no theory-independent way to reconstruct phrases like 'really there', the notion of a match between the ontology of a theory and its 'real' counterpart in nature now seems to me illusive in principle." This selection of facts was quite see-through. I shall cite only one small example he missed: When Einstein saw DeBroglie's thesis for the first time, he exclaimed

"He has lifted a corner of the great veil [of Nature]!" (Moore, 1989, p. 187) Einstein was certainly not conveying the idea that DeBroglie just thought of another method for solving puzzles!

The clincher of Kuhn's stand can be found in the last two pages of his essay: He claimed there to base unprogressive Science *on a scientific discovery, namely* ***Darwinism***. Science would be a "survival of the fittest" kind of process, thus *without any ultimate goal in sight*. Of course, a better theory and its attendant understanding would bring methods fitting the facts of Nature better. But identifying the discovery process with a mindless Darwinian struggle to find methods is in effect *banalizing* Science, making it nothing but a *computable* process. This replacement of *goals* with the means to pursue the goal, i. e. *methods*, looks to have been intended to eliminate the human factor of Science, what I called in Section V the uncomputable aspect of the mind. This Kuhn did in effect by equating the human mind with a computer (in line with the ideas of the time and Turing), thereby denying the existence of imagination, understanding, creativity and individuality, especially making any knowledge *relative to the background of the scientist*, no longer natural truths. In that line Kuhn did find linguistics to be his career, thinking that language could be handled by a computer, thus could be knowable, much preferable to pursuing Nature, the unknowable! Kuhn thus fitted his time well, and his success was no surprise. But success is not a sign of correctness.

Then, very much as Cardinal Bellarmine took Galileo for a recant of his truths as mere hypotheses, Kuhn joined Mach and Bohr as the 20th century equivalent, inducing Science to recant its goal of finding the truths of Nature. Apparently the Pope judged about their collective success, and returned the favor by pardoning Galileo in 1993. Kuhn could die satisfied (1996), the deed was done.

B. The point of this study

So is there any point now in looking for a larger meaning in Nature that Science would be interested in, especially if this meaning could not be a formalism as Mach understood Science to only provide?[69] Apparently the answer by Mach, Bohr and Kuhn is a resounding No! Science is not interested in truths any more, especially the ones that can only be found through the imagination. Science is looking for feeding its puzzle-solving needs, and certainly not to advance toward a goal since there would be then a danger of reaching that goal. Also, with a goal, Science would be revolutionary and thus totally unacceptable as an institution.

Against such a background I must emphatically deny that the present study is about "puzzle-solving." *Its purpose is to develop a new understanding of Nature, hoping thereby to obtain a larger truth about it.* As Einstein (1929) pointed out, *an understanding involves qualitative things that only the imagination can grasp*. Formal methods can only come later, if at all possible. So I must defend this study as *indeed making sense for Science* by questioning the boundaries Mach, Bohr and Kuhn put on it. Since such boundaries were apparently defined within the context of Darwinism, then I must look at Darwinism for being the *whole truth* as this line of philosophy understood (and in effect contradicting itself right there!). Natural truths do exist, but they are not of the kind philosophers can understand, and the case of Darwinism will describe why.

C. A larger meaning?

Answering an editorial by Stephen Jay Gould in the June 25th, 1999 issue of Science magazine[70] permits me to address this matter directly. Gould as a well-known biologist and president of the American Association for the Advancement of Science, described Darwin's Theory of Natural Selection (Darwin, 1859) as something of the upmost importance (the title of the editorial was "Darwin's More Stately Mansion") and having the required qualities for its knowledge to be spread around, as "the truth can only make us free."

Such a goal is very commendable and needs to be pursued, *especially since a truth was indeed found by Science!* But there ought to be a loud caveat identified in the message, as when a scientific truth is to be spread we must first be certain the *complete* truth is provided. A partial truth presented as complete may in fact enslave us (and this is what Kuhn in effect did by defining the boundaries of Science through it!). First of all, Darwin's work is a *contribution* to Science, and as such can only be partial, no matter how important it is and how long it has been known. The problem that Science has had through the ages is that the knowledge it obtains for Humanity is always potentially incomplete. For example, we must remember that Darwin's theory was formulated at a time we believed the world was fully determined, a la Pierre Simon Laplace (1814), through Classical Mechanics, which was an unquestionable truth, but partial, as the 20th century demonstrated, and thus its *meaning* was simply incorrect, even though its truth is still there.[71]

The completeness of Darwinism has not been questioned for more than a century because Physics has not been able to know the elements that make our World, and thus could not evaluate Darwin's theory in a larger scheme of our reality. Einstein's Relativity and Schroedinger's Quantum Physics are both theories of principles that do not tell us what is behind the pictures they have drawn of Reality. So are the truths of the Life Sciences, incomplete, and in a big way. We still don't know what makes a living organism a whole entity, in spite of what is normally pictured from available experimental data. As an example, we are compared to an ant colony by the Complexity theorists (Section III), but where is the "super-ant" in such a metaphor? Also, we are told that Life arises in a "vortex" of some sort thanks to chaotic effects, even though Life displays little of such effects.

The immediate fact about Darwin's world (raising suspicion about its completeness) is that it features a classical trial and error process, a tinkering at a grand scale as Jacques Monod called it. It then begs the questions: Did Nature have no other choice but this mindless way knowing the existence of the Quantum? If Nature could ever have a better choice, what is it waiting for to use it? That alternate way may be right in front of our eyes, or rather, in-between them, while we are still looking at our World in a Classical Physics way, with its individualities and separabilities! The Quantum is undistinguishability and unseparability, something very new indeed on the scene of Science, to the point that Mathematics may not yet have caught up after 70 years of having heard about it (Gouin, 1999). The Classical World has lost both of these features, as the whole gave way to the many. Life may have started from the Quantum just because of that, as Life seems to be made of unseparable wholes. Darwin specifically identified that area as not part of his theory, and he certainly had no knowledge of the Quantum. Yet, to this day, we are still looking for Life's classical origin, thanks to our interest with 19th century ideas as a result of not fully understanding the Quantum. Can't our minds be in fact a quantum effect, being quite an obvious whole unreacheable via classical means? If so, then Life in general must also be somehow based on the Quantum, knowing how evolution proceeded in its discovery process, tinkering around with physical effects (Section III). We just don't have these truths yet.

But if they are truths, then Nature's trial and error ways were only a long running last resort after Life reached sizes where whole systems could no longer exist by themselves, and classical means had to be used from then on with their extremely slow ways (classical computation), thus the eons of Evolution. This does not mean quantum effects were not used to build Life in that process, and Life may very well have done so, still unbeknownst to us as a result of our blindness about really new things thanks to Kuhn's philosophy (Sections III and IV). Then Nature discovered the Mind! (Section V) Darwin called it the "Descent of Man" (Darwin, 1871). The "Ascent of Mind" sounds to be a much more appropriate term, as, with our ability to self-reflect and see and act logically on our world, we have in effect ended this miserable trial and error process at last, and this through unknowingly using the Quantum, very much as Life would have originated from! Then Nature may have at last found the alternative it was looking for to continue its construction. We would be then its spearhead, not animals any more if we learn how to use our minds for the improvement of our condition and our world, instead of its destruction. But, as for all breakthroughs, such a tool has of course two edges, and must be used extremely carefully. Indeed, as a witness of its power, we are alone with it. We seem to have destroyed all the others with any feature even remotely

resembling it (Lewin, 1993). We apparently needed to do that in order to start Nature's new way of constructing reality on this planet. But now Nature misses the diversity any self-creating and self-reflecting world requires.

The Book of Nature may be telling us what our purpose is, but it seems that we have not read it enough, and so we are not in a position to give a verdict on the situation of Humanity versus the World, especially by presenting Darwin's work as the complete truth about how the evolution of the World did *and thus can* proceed. We could only say in that regard that some of the things Science has found about the procedures of this world *before* Humanity arrived are pretty sad, but now that we are here we (and Science - refer here to Kuhn's thesis!) are not compelled to proceed in the same way. Nature looks to have at last found us, and to have thereby delegated to us the goal, and the choice, to complete this reality in a more expedient, reasonable and kind way than it could do without our minds.

If the concepts identified in this study were established as truths, we could add: Now we know via the Quantum that there is an Organizing Principle that exists behind classical Life which may give our World new means how to proceed in that goal. Knowing the limitations of classical systems, and provided we really dig deep into what we are, the Quantum may even allow us[72] to at last reach the diversity waiting out there far in the sky, thereby fulfilling a basic need to know that Nature ***as a set of monadic entities*** (Section IV) has ingrained in us to further its own need to construct *a better, larger and meaningful reality*.

But even if such a path was found possible there is now the phalange of scientists unknowingly following Mach, Bohr and Kuhn who are there in the way, unlike the small minority at the end of the previous century, who would say: So what? There is nothing out there that can be really new, we already have experienced everything that needs to be experienced, and the truth cannot be found anyway as only a deity can know it. Besides, really new things may be very dangerous as the past has shown. When it comes to our loneliness we can always think about dolphins as being conscious like us. So why bother? What we know now provides enough to maintain our World as it is, let's just complete the details of our knowledge about it to be sure we do the best job possible at our maintenance assignment, let's continue on the safe road we are following in the tradition of our philosophers who told us how far we could go, and reserve our imagination for making fairy-tales.

But then, what is the purpose of the Scientific Enterprise, if not *realizing* such fairy-tales, and allowing us to dream of new ones that are impossible to dream of due to our ignorance?

"Have something to say, say it, and stop."
Santiago Ramon Y Cajal

APPENDIX A: NON-LOCAL SPATIAL EFFECTS IN CELL FUNCTIONS - A REVIEW OF THE LITERATURE

1. Introduction

I identify some of the basic non-local physical effects found in living organisms, starting with the cell duplication function, mitosis, since it is a process encompassing the entire cell, then going to some other non-local functions that seem inherent to Life, as least in its more evolved versions. The emphasis is on making sense of what is being described.

Among the many articles, books and monographs on *mitosis* and the related cell components published in the past ten years I have selected two texts that are from the early 1990s for their careful description without overwhelming biochemical details, even though they are of course not the most up-to-date in all aspects of the field. What is important in the present task is to distinguish the basics out of the details, and these texts give a good base in that regard. The Vandre-Borisy (VB) work concentrates on the *centrosome*

and mentions many variations on the "typical" behavior and form of the organelle. The work by Margulis gives a wide view of where this organelle belongs to in Microbiology at large, adding to the previous text the background needed to understand and follow the meaning of the events observed.

However, neither of these texts identifies the relationship between the chromosomal *kinetochores* and the centrosome even though they are partners in mitosis. I only obtain the idea that kinetochores may be an older separate system which happens to connect to the dynamics of the centrosome and its newer centrioles. In Section 4 I try to find additional data on kinetochores through a set of more recent papers. The physical origin of the spatial and dynamical relations between these two systems is still not described in these newer texts, outside some allusions to local chemical actions by molecules without a physical description how the actions are performed and how the molecules find themselves at the proper locations.

Section 5 reviews a few articles that identify molecules as guides and relocators of other molecules and organelles in a cell. The question there is about how such molecules locate themselves, and then how they know where to go from there. It is a matter that puts the centrosomes/kinetochores function in the proper perspective in the sense that they may not have the exclusivity in displaying physical effects involving non-local spatial actions at the biomolecular level.

In the last section, I review the information Hameroff put out some years ago on the nature of the cytoplasm as it seems to be the fundamental level of Life, and looks to be performing non-local functions too, in the mitotic process as well as in other processes.

2. The centrosome cycle in animal cells (Vandre and Borisy, 1989)

a. Introduction.

The centrosome is identified as made of two parts, the pericentriolar material (PM) and one or two *centrioles* located at its center. The PM is identified as a random set of unidentified molecules that give a "fine electron-dense matrix." Two centrosomes form the "poles" of the mitotic *spindle*. Plant cells and lower eukariotes do not contain centrioles in their mitotic spindle poles, and centrioles are dispensable in the mitosis process. Centrioles and flagellar *basal bodies* are a "manifestation of the same organelle" (see Margulis' text on this matter also). So centrioles do have a background for helping the *motility* (movement) of a cell while also helping in the mitotic spindle process through somehow "organizing" the microtubules (MTs) making the spindle.

But kinetochores on the cell chromosomes have also the ability to organize MTs, and so do basal bodies and the nuclear membrane. There are also other sites in the cell cytoplasm that "nucleate" (originate) MTs. The centrosome is however clearly the *preferred* site of MT nucleation in mitosis (however not in meiosis).

b. The microtubule cycle: a reflection of centrosome dynamics

Before centrioles were known to exist, the MTs polymerization was described as starting from a focal point in the cytoplasm near the nucleus membrane (subsequently turning into two poles), not from the kinetochores. I shall see in Section 4 that the kinetochores neighborhood may induce the polymerization also, but then straight out in a barrel pattern. VB identify that MTs have a "turnover rate" of about 30 minutes, so they are not stable structures in mitosis. The reason why is not known. In fact we don't know how assembly-disassembly of MTs *in non-local fashion* (across the cell) is "regulated" (a chemistry term). Similarly, the chromosomes attached to the MT threads of the spindle through the kinetochores are moving to the spindle pole, and again we really don't know why. A "cytoplasm environment favoring MT assembly" is though as the driving force. But how can it be spatially selective in the mitotic spindle if only

local and chemical?

c. Ultrastructure of the centrosome

The changes in the centrosome structure (centriole replication with parent-child orthogonal relationship) has only been known by 1982 from "ultrastructural" studies (electron microscope). A network of thin filaments was then reported surrounding each centriole. The PM surrounds only the parent. The parent has an associated cilium (from its origin as a flagellum basal body). There is material that deposits on the parent centriole slats. This deposit is called "centriolar feet." The PM surrounding the parent centriole expands during mitosis with concomitant loss of the centriolar feet and the majority of the satellite structures while there is a ten-fold increase in MTs nucleating capacity in an astral array. The primary cilium is resorbed (disappears) and its dense sheath is less prominent.

d. Centrosome composition

There VB indicate that DNA is not present in the centrosome. Margulis reports the "uni-group" DNA in the nucleus corresponding to the origin of centrioles (such DNA group was found around 1990). PM has been found at the acentriolar barrel-shaped spindle poles of mouse oocytes and higher plant cells. It is suggested that phosphorylated components in the PM are involved in the MT nucleating activity.

e. The centrosome replication cycle

The centriole replication cycle has been known only since 1985. By 1960 it was known that the centrosome was "duplex" in nature, i. e. has two spindle poles forming units, but centrioles were not observed. A *quadripartition* experiment was done in 1985 using a chemical that stopped the centriole replication. Then two spindles formed from 4 mono-centriolar poles. Then the cell split as a clover-leaf fashion into 4 cells. From then on mitosis occurred with single poles! Separately, *the PM association with the child centriole was found to occur only after the splitting of the pair*. Centriole replication and DNA replication are events coordinated in time, but are independent processes. There are *acentriolar* centrosomes (plant cells and early embryos) which operate normally in the spindle formation process.

f. Centrosome function

The origin of the generation of a centriole child and the origin of the MTs generation by the PM are unknown. Again, here MTs are identified as growing from the centrosome, not the kinetochore system on the chromosomes. The PM is the site of MT nucleation. The end of the centriole pair has the greatest amount of PM. Centrioles without PM do not nucleate MTs. *Fragments of PM can nucleate MTs without centrioles around*. A polypeptide in that material seems responsible for the nucleation. The MT nucleating capacity of the centrosome is tied to the mitotic cycle, not the centriole cycle. The centrosome controls the electrical polarity of the MT, the plus end being distal to the centrosome. The nucleating sites within the PM serves as a template to nucleate MTs into a fixed geometry of 13 filaments. *The organization of a focused region of microtubule growth may precede the accumulation of PM at that site*. The centrioles, just by their presence, seem to organize the PM, which in turn nucleates MTs. Then the reproduction of the centrioles is assumed to ensure that a critical amount of PM is assembled at each pole around the pairs of separated centrioles.

Finally, chromosomes *kinetochores* as a system can function as spindle-organization center instead of centrosomes. So centrosomes are not required for spindle formation. See Section 4.

g. Regulation of centrosome function

Here VB write that "the increase in [MT] nucleating activity is correlated with an increase in the amount of PM," a statement qualified with the possibility that, instead, the material is altered to produce more MT initiating sites. So here an unknown "regulating agent" (i.e. a chemical) may do the job. It was demonstrated though that the onset of mitotic protein dephosphorylation coincided with the onset of anaphase (the start of chromosomes separation). So phosphorylation of PM may trigger the MT nucleation increase. But how about the *direction* of this nucleation toward the chromosomes? VB don't say anything on this matter. At that point VB look to be losing sight of the overall physical picture by concentrating on chemicals.

h. The centrosome cycle: an overview and future perspectives

This is a series of questions: (1) What regulates the reproduction of centrosomes (centrioles)? [This was only recently answered via the CDK2-E complex produced by the nucleus to synchronize mitosis.] (2) Why are there two centrioles? [This was answered by Margulis via the ancestry of centrioles - see Section 3.- I would ask instead why the child is orthogonal with the parent!] (3) What are their relationship with the PM, and how is the PM maintained (spatially)? (4) What is the composition of the PM, and why does it find itself around the centrioles? (5) How is its *spatially directed* initiation of MTs controlled? (6) What does the centrosome do with the MTs, i. e. polymerize, depolymerize them?

i. General comments on the Vandre-Borisy text

Right from the introduction nothing is mentioned about how MTs find themselves in a *spindle shape* between the centrosomes containing the centrioles. This text ignores the obvious coordination with the kinetochores system. As Margulis shows from Cleveland's work, the shape of the spindle (its width at the equator) depends on the chromosomes presence by holding the kinetochores. So the spindle *width* must come from the spatial requirement created by the presence of the chromosomes (their bulk dimension).

3. Symbiosis in cell evolution (Margulis, 1993)

a. Chapter 8: nuclei, mitosis, and undulipodia

a1. *Nuclear Origins.* Margulis argues here that the nucleus with its "double membrane enigma" is the basic organism which had to create a membrane to protect itself against attacks by surface spirochetes (microtubular or MT organisms?) that ended in eukariotes as the MT system and its mitotic apparatus. "Mitosis is then a chimeric [composite of several systems] process, the establishment of which involved symbiosis as well as direct filiation through the new nuclear membrane." The symbiosis with MTs was the one that led to multicellularity, while prokariotes (bacteria) remained as "dust."

a2. *Protoctist Cell Division.* "No one who sees mitosis fails to marvel at its living elegance. Lacking physicochemical explanation, mitotic phenomena is fascinating because of its intrinsic logic." In the text here there is a confusion between centrosomes and centrioles. "*Kinetosomes*" are the "basal bodies" of

undulipodia, the *undulating* protrusions out of cells, such as cilia and sperm tails, and are shown as identical to centrioles except that shafts ("*axonemes*") are "attached" to them. In Fig. 8-3, there is a drawing of how a kinetosome reproduces. It is very much like the VB description for centrioles, except additional microtubules appear to "hang out" parallel to them somehow "dangling" in mid-medium and the axoneme looks to be an extension of some of the small cylinders of the centriole, with an added small double cylinder at the center of the shaft. In Fig. 8-5 we see a drawing of a rather special single-cell organism with the MT system clearly operating by itself in the cell effecting mitosis with the chromosomes having been chemically deleted (but the kinetochores are left intact). The representation (from Cleveland, 1985) shows that "motility" is provided by cilia protruding from special kinds of centrosomes. However, nothing identifies what provides the overall *coordination* of the cilia "oar movement" that is supposedly separating the (inexistent) chromosomes.

a3. *Centriole-Kinetosomes and Microtubules*. Microtubules are somewhat described here. One characteristic is that *they dissolve by cooling them to about 4° C*, which is kind of strange for the type of bonds involved (London/van der Waals). MTs form sensory parts and organs. They effect chromosomes movement, asymmetrical shape of cells, intracellular transport, undulipodial movement and intracellular communication (but we don't know how they *physically* perform these functions!). In the ciliate mating process, "the cytoplasmic parent, not the nuclear parent, determines the transmission of certain cortical traits." A description is given via picture how centrioles are formed in development originally from a "generative DNA complex," without of course any details how several centrioles seem to assemble *in an orthogonal fashion* with the spheroidal looking DNA complex (Fig. 8-10). "The genetic determinants are of a size below the power of resolution of the electron microscope." *Kinetochores*, the spindle attachment of the chromosomes, are identified as part of the MT system, not the chromosomes. Chromosome movement is identified here as only coming from their association with MTs in a spindle. The Golgi bodies are identified as part of the MT system too. Margulis then cite a hypothesis by someone else: "The kinetochore proteins themselves *probably* comprise the motor for poleward chromosome movement in anaphase." This hypothesis seems to have never been really substantiated (see Section 5). Then Margulis hypothesizes that "mitosis evolved by deployment of parts of symbiotic spirochetes."

a4. *Toward Mitosis*. The question now is asked: "What kind of selection pressures gave rise to mitosis?" A hypothesis is given as answer: "In the absence of efficient mechanisms for ensuring the equal distribution of newly synthesized DNA to progeny, the genetic complexity of the earliest eukariotes must have been limited." Then "the interactions of populations of the surface spirochetes that became undulipodia underlie the species-specific patterns and *the autonomous genetic behavior of the ciliate cortex*." This leads to the hypothesis that the nuclear membrane evolved also from spirochete genes, and that "the precise distribution of genes led to the final refinement of mitosis," all derived from spirochetes. Here Margulis assumes "mitotic movements are the direct consequence of the polymerization of tubulin into elongating MTs," while "other movements involve MT-associated 'motility proteins', such as kinesin and dynein." "An incomplete distribution of genes exerted continuing pressure for improved mechanisms of chromatin segregation." Then Margulis goes over her set of steps that led to present mitosis, showing that the present centrioles are the descendants of spirochetes that superposed their DNA division system with the host system where the spindle starts from the centrosome instead of the nuclear material, presumably giving a much more reliable segregation knowing the rigors of natural selection. Also she cites the facts ciliates have (1) micronuclei with intranuclear spindles, (2) *the numerous kinetosomes of their cortex reproduce independently of nuclear division*, and (3) the macronuclei contain large number of copies of short pieces of DNA, the pieces of chromatin there still segragate via a spindle "by some [undescribed] idiosyncratic system."

Then examples of single-cell organisms with centrioles connected to an axoneme are given, followed with examples of single cells with *axopods* that lose them, and thus their motility, during mitosis. That way Margulis leads to her hypothesis that "the failure to solve the problem of reproduction and motility led to the origin of multicellularity" and hypothesizes that the genome from spirochetes provided cell

differentiation in metazoa.

a5. *Centriole-Kinetosome DNA*. A discussion added in the second edition on possible DNA ("or at least RNA") *inside* centrioles is provided. VB dismissed this in their text. Margulis needs it to get more backup on her thesis on the spirochetal origin of the MT system. I think this is wishful thinking at this point because it is not seen in the "child" centriole, and so would be lost after cell division. The nuclear DNA "uni group" looks to contain the MTs DNA. The reproduction of centrioles is still an unexplained phenomenon.

b. Chapter 9: undulipodia from spirochetes

I shall mention only one set of important facts identified by Margulis herself that goes against her DNA hypothesis for centrioles: The search for kinetosomal DNA ended with the realization that kinetosomes (and thus centrioles!) do not divide: They "develop" *somehow* in the centrosomes. There is a case where a ciliate (*stentor*) has 20,000 kinetosomes all *synchronously* reproducing in less than 2 hours, and DNA synthesis does not accompany the production of this enormous amount of MT material. Further, the synchronization of this development process on such a scale (considering the size of the single-cell organism) is totally unexplained.

Synchronism is a big theme in spirochetes motion. This has been explained (or explained away) through hydrodynamics. Yet in *stentor* above, the reproduction being an internal process, hydrodynamics can't explain that phenomenon.

c. General comments on Margulis' text

Margulis does not identify the pericentriolar material identified by VB but she gives a good reason for the existence of centrioles: The improvement of mitosis reliability in chromosomes separation. She portrays centrioles as exclusively supporting the MT spindle in mitosis. No mention is made of mitosis without centrioles in metazoa (multicellulars) early in embryo development. She takes the synchronization between centrioles "emitting" MTs as granted even though it is an unexplained immediately observable phenomenon. This theme of synchronism is brought clearly in the description of spirochetes motion and stentor cilia duplication. What kind of phenomenon are we looking at?

4. The role of kinetochores

a. The spindle assembly checkpoint (Elledge, 1996)

As several articles in this section are, this article is a chemist's set of metaphors. Mitosis is first described either as a precise sequencing with checkpoints "like building a house," or "positive or negative regulatory circuits," with the last metaphor indicated as the appropriate one, knowing as a chemist presumably does, nothing else but "molecular logic." The article is heavily concerned with the "DNA damage checkpoint," with one third added for "the spindle assembly checkpoint." Under that heading, there is an introduction and four sections.

a1. *The introduction*. The only checkpoint identified here is the onset of *anaphase*, the separation of chromosomes moving toward opposite spindle poles. So, apparently, for this chemist, that's the only mitotic checkpoint that exists dealing with the mitotic process outside the nuclear material!

a2. *Spindle assembly signals and sensors*. First, the various unknown "sensors" about the anaphase checkpoint are guessed at. Mention is made of a possible sensor for "the tension generated on the

kinetochores" to detect attachment, an inadequate concept since it does not include the collective aspect across the kinetochores, and a concept found incorrect one year later. Indeed the article was written right before the discovery of the "wait" signal emitted by the kinetochores (next article). Mention is made of micromanipulation ending up with two sister chromosomes at the same pole, most likely because one kinetochore was destroyed before the chromosomes detached. This one example points to where ignorance about theoretical possibilities behind the phenomena observed and the resulting tinkering (the brute force ways of modern science) leads to a lot of wasted time (and money) in research. So this section is a bunch of chemistry guesses which are found all useless in next article.

a3. *Signal transducers in the spindle assembly*. There is a long discussion on the various genetic products correlated with the anaphase checkpoint, with no firm ideas presented. MAD2 is mentioned through "its localization to the unattached kinetochores," but no question is asked how this could physically happen. A discussion on how tension on kinetochores would be the separation signal identifies "microtubules inhibitors" as if molecules could have a mind of their own. Metaphors are ok as long as they are not taken as an explanation, as I have seen too often done in this field.

a4. *The Remainder of the Article.* The remainder of the article is made of chemical guesses with no firm facts.

b. Cell division gatekeepers (Pennisi, 1998)

This article comes one year after the one above. It reports the discovery that kinetochores emit a chemical that signals the other ones to "wait." The key here is: to wait for what? The researchers think it is to wait for starting the separation of chromosomes. But the description only shows that the kinetochores when all attached simply emit a solvent that removes the bonds between the sister chromosomes, with no description on what makes them move away from each other. Also an experiment is mentioned where a last unattached kinetochore is destroyed with a laser, resulting in the chromosomes separation. This drastic method may do other things besides destroying a kinetochore. Another key experiment is observing a gene product, MAD2, which "concentrates at the kinetochores before they are attached to the spindle, but leaves by the time they are aligned." Two pictures are provided, and even though the caption says that MAD2 concentrates at the kinetochores, the picture shows them *mostly at the spindle poles*, with only some of them at the kinetochores! Then it is said that MAD2 copies "continuously migrate into the cytoplasm [from the nucleus] where they somehow broadcast the wait signal throughout the cell." Then CENP-E is mentioned. It is a "molecular motor" which is known from helping transport cellular components along microtubules. It associates here with the kinetochores and helps them achieving accurate chromosome alignment at the spindle equatorial region. Without it the chromosomes separate before lining up in that region. A third protein BUB that links up with CENP-E at the kinetochore, somehow leading to the disabling of MAD2 located there. When all the kinetochores are attached, MAD2 is disabled somehow throughout the cell! How about that for a non-local effect! (Since MAD2 was so localized, how does it spread the word everywhere?)

c. The anaphase promoting complex (Elledge, 1998)

Less than one month later, an article discusses the regulation of the "anaphase-promoting complex" or APC (also called "cyclosome"). The article does not mention where this APC is located (this must not be important for chemists!). Apparently the APC mainly deals with the DNA side of mitosis. This complex, wherever it is (probably in the nuclear area), only appears to be a relay which, upon MAD2/BUB disappearance produces dissolving agents disconnecting the chromosomes between the kinetochores so anaphase can start.

d. Meiotic spindle control by kinetochores and chromatin (McKim and Hawley, 1995)

This article is very important because it attempts to prove that the phenomenon of spindle formation is a chemically based effect, and kinetochores generate traction forces to pull apart the chromosomes. It fails to prove both cases. Notably there does not seem to be any force involved with kinetochores in spite of the arguments advanced by the authors.

d1. *Introduction.* The following hypotheses are proposed:

(1) "Molecular motors" are moving the chromosomes during mitosis and meiosis,

(2) In many meiotic cells the divisions take place on *acentrosomal* spindles organized *solely* by the chromosomes and their kinetochores.

The first hypothesis will be defended by the authors but their case appears undefensible. The second hypothesis raises the question of what kind of non-local physical phenomenon is at play here, since the reasons given by the authors are found wanting.

d2. *Chromosomal Control of Meiotic Spindle Formation.* This is an important description of a meiotic spindle formation. The pictures provided tell the story better than the words. MTs are nucleating out of and around both kinetochores and chromatin. *There is no centrosome around*. A single chromosome can form its own spindle! So it appears that the spindle formation around the bundle of chromosomes is a *collective* effect where the kinetochores arrange themselves toward the proper pole. *This phenomenon has strictly no explanation!* But the authors are unfettered and go on showing "presumably" MTs "captured" by the chromosomes. What they do show is that, *when* there are centrosomes, the spindle formation is a joint process, *somehow*. It looks like the presence of the centrosome suppresses or "outcompetes" the MT "gathering ability" by the chromosomes. What physical phenomenon can provide such a non-local effect?

Then there is the interesting observation that chromatin itself "attracts" MTs. So it looks like the orientation in space of the chromosomes is affected also by the unknown physical effects the authors avoid to mention. They do this avoiding by identifying "chromokinesins" molecules localizing as if by magic along the arms of the chromosomes! (How do they localize there? How would they do the chromosomes reorientation? Do they know their position in space? Etc. etc.) Another chemical (NOD) is added to provide a "force" to keep the chromosomes in the equatorial plate. All this seems very contrived. Not that there may not be these chemicals, rather that they can't as *individual* molecules provide a collective effect as they are wished they do. This is not a statistical mechanics vortex we are observing here! The very shape of the spindle tapering off should be telling us something. But what?

d3. *Chromosomal Control of Prometaphase Movement.* The introduction to this section describes the attachment of kinetochores to the spindle threads as a stochastic process thus prone to errors, and thus there must be error correction mechanisms. But then they state that an incorrect connection is "unstable" without identifying why! This whole part makes then no sense. What they certainly fail to identify is how the matching kinetochores attach to the proper pole! The reason indeed appears to be a big mystery.

Then they go to describing movement of shorter chromosomes as happening sooner than longer ones. There they explain the difference in timing via one of the "motor molecules" *breaking the motion* that would be more numerous on the longer ones. Well, if they waited one year (Section 4.b above) they would have learned that it is a matter of dissolving more or less numerous bonds between sisters, and their meandering story about forces would have fallen apart.

d4. *Kinetochore-Mediated Control of Anaphase Chromosome Movement.* This section opens with a statement about an earlier "traction" hypothesis where the *centrosomes* were doing the pulling apart of chromosomes. Now the authors advance this was incorrect, and they propose that instead the kinetochores do the tracting. Well, it looks like there is no traction from there too!

First, they state that the kind of chromosome segragation (two kinds in meiosis) is selected by the kinetochores. Well, I would have guessed so from the fact only the nuclear material knows about itself!

Why would the spindle know? So this part of the text has no bearing on the issue of force.

Second, they talk at last about an assumed pulling force generated by the kinetochores. The problem with that hypothesis is stated by the authors themselves: In the case of *natural* trivalent (3 kinetochores per chromosome) there is no difference in location of the chromosome at the equatorial plate versus the two poles!

So here is a true mystery: *If there is no force, how do the chromosomes move to the poles?*

d5. *Chromosome-Mediated Cell Cycle Control*. This section goes at length on anaphase checkpoint control through the assumed tension on the kinetochores. This has been proven to be an incorrect view in 1998 (see Section 4.b above). This section is nevertheless interesting to read to see how an incorrect hypothesis was verified as right so many times! I can only conclude that there is a lot of wishful thinking going on in this area. Also, it looks like most micro-manipulations lead to wrong conclusions because they disturb unseen things.

e. Kinetochores are dispensable (Ersfeld and Gull, 1997)

Here the single cell organism (tripanosome) has two kinds of chromosomes. The large kind uses kinetochores in mitosis, while the small kind does not. The article emphasizes that the segregation between sister chromosomes is reliable and precise in spite of the absence of kinetochores. So again here it looks like the segregation process does not depend on molecular force action. Something invisible provides for the segregation. (Note: tripanosome cells have a spindle shape themselves)

f. General comments on the articles above

The kinetochore system can generate the spindle instead of the centrosomes, but in turn chromosomes are found to be able to do that themselves. As a result of this dual ability to generate MTs from one region or the other of the cell, the chromosomes separation method looks to be somehow *spatially* and collectively related with the centrosome. To the point that, as in the mouse oocytes, the spindle looks to be *generating* the centrosomes (of course without centrioles then) via the "gathering" of MTs (do they gather or form at that location collectively?). This spatial coordination cannot come from electrical effects since all the MTs have the same electrical polarity. Also, no force is being generated by the kinetochores on the threads (*some segregations happen in fact without kinetochores*). So what physical non-local effect are we facing here which segregates and pulls apart the chromosomes without visible means?

5. About molecules that spatially guide and relocate things

a. Molecules that guide axons (Strauss, 1998)

"Molecular logic" is wished to be the theme of the article, but it falls short of its goal. I quote: "Developmental biologists have discovered in the last several years how growing axons find their way to the [embryo] midline: They are drawn in by attractive molecules, among them the proteins called netrins, released by midline cells." But once the midline is crossed "neurons forever ignore the signal that most strongly attracted them early in life." The papers mentioned by this news article supposedly have shown that "a dynamic interplay of both attractive and repellant signals between the midline and the neurons directs axon movements." Then "an axon has to integrate multiple kinds of guidance cues, some positive and some negative." The hope is that such an approach "will eventually lead to a better understanding of how neurons know where to go as they set up the entire nervous system, including the brain and neuronal

connections in the periphery." One question in an approach based on chemical attractors and repellants for such a precise and complex process, which in effect assumes neurons are guiding themselves, is "delving into the inner workings of the axon tip to understand how receptors influence the filaments [actin, per next article] of the neuron to cause an axon to turn."

This is indeed a good question, for which no answer seems to be on the horizon. A neuron does not seem to have the means to do that job by itself, having no "actin organization center" as MTs do (the centrosomes). See below.

b. The actin cytoskeleton and chemotaxis (Hall, 1998)

The description of the *actin* cytoskeleton (the MTs are not discussed here) is prefaced as "mediating a variety of essential biological functions in all eukariotic cells, and their dynamic properties providing the driving force [the prime movers!] for cells to move and to divide." I was told elsewhere that this was the MTs role. Oh well. The following text does not live up to what it introduces actin as doing. From what the text does say, actin looks more like a *filler* in-between the MT cytoskeleton system, which does the cell shape control.

In the early 1990s it was found that *Rho,* a gene product, acts as a "molecular switch" to somehow control the link between *cell membrane receptors* with the actin cytoskeleton. *Rac,* another gene product, acts on that skeleton to make it produce cell peripheral lamellipodia and cell membrane ruffles (of course at random). A third product generates filopodia.

These earlier findings are then linked to axonal growth and guidance studies (previous article), as such growths look to be driven by actin polymerization with filopodial and lamellipodial protrusions that would be controlled by these gene products, then "possibly" under the control themselves of local attractants and repellants from the outside of the cell in order to realize the genetic body design. Here I shall remark that there is *a lot more details in the brain than is available in data from the genes*, so some sort of computation is needed to "unfold" the detail design, and no local action as envisioned in the article is likely to do the job. But that's another story.

Then the article mentions that actin is not the only thing acted upon by the gene products in question. There are also *integrin* complexes on the surface of cells for *adhesion between cells*, but no detail is given on this last matter.

The article arrives at the subject of *directed* cell movement, requiring "discrete," i.e. localized, intracell coordinated action as specified by local cues external to the cell. Here it is said that we don't know how to measure the presence (or concentration) of the gene products that would do the controlling. Also, how the actin cytoskeleton interacts with mitosis is unknown, especially how the cell "contractile ring" cuts the cell into two cells. Of course no extracellular "signals" are involved there. The conclusion of that part of the text is then that we don't know anything about localized intracell actions. From reading this text, it tells me in fact that we only know actin polymerizes at random upon introduction of the gene products discussed. There is no clue how the cell controls its local form or motion from there.

Finally, embryo development is talked about. Genetic analysis in that area shows the need for *rho* and *rac* and a third item, but nothing else. The presence at a *budding site* does not tell why that site is chosen! No clue is given how the actin cytoskeleton is regulated *spatially* via these products to define cell shapes, motions, and behavior. Again here the hope is to find molecules somehow concentrating *by themselves spatially as if apparently they knew where to go,* but nothing is offered in the way of experiment to prove the worth of this hypothesis. From other texts, MTs seem to provide the system directing such cell shapes, not actin. And also, where is the *collective physical organizing means* which is obviously needed here for such cell shape and motion?

c. Kinesin and dynein - organelle transport (Hirokawa, 1998)

Here we switch to the MT system and its *helpers* to see its role in transporting things within a cell, as actin manifestly can't do that function either. "MTs serve as rails on which motor proteins, such as kinesin and dynein proteins, convey their cargo." This is a cute metaphor (with cartoons), but a very incomplete one: How do they move physically? Why do they choose a specific cargo? How do they know where to go? How do they locate themselves in the first place? What makes them move on the rails? Not putting such questions in the research agenda makes it quite unsound. So the text is an assembly of data about all the chemicals involved. Nothing is advanced about what makes them all work together. But living organisms behave as whole moving systems, not as a bunch of parts in a bag! Something physical and *essential* is missing from this picture. So here I went to another text to find answers. It is reviewed in Section 6.

d. Endocytosis and the Golgi system (Marsh and McMahon, 1999)

Here we meet the key structural component participating *somehow* in intra-cell transport, *clathrin*. Its parts, the *triskelions*, make a "coat" that clings on the inside of the cell membrane and *curves it inward* to make *vesicles*. The key here is that the terminals of the three branches of a triskelion attach to *receptors* complexes in the membrane containing "*hydrophobic pockets*." This means that such pockets are then finding themselves *inside* the vesicle, and thus are placed in a *quasi-spherical arrangement*. Knowing the mitotic role of MTs in physical actions the potential for physical effects due to the hydrophobic pockets here may be in the line of the ones found with MTs, which have such pockets but in a *cylindrical arrangement*. Could this quasi-spherical characteristic be the source of key physical effects such as in the Golgi precise maintenance system and in neural synapses, where *directed* vesicle motions *specific for their purpose* are required and observed?

e. The molecules that effect the body circadian rhythm[73]

This last article deals with a key way of seeing things, or rather way of skipping things in present Microbiology. This news report and the accompanying article tell about molecules that find their way to the nucleus in a cell starting from outside the cell, and furthermore go to a specific place in the DNA to shut down a specific sequencing process there! How can we imagine such a thing happening without calling it a miracle? Pictures in the article do show that a *specific* protein (CRY) *allows* another protein (TIM) to go into the nucleus of the cell and act on the DNA. Without CRY, TIM cannot go there. Now, as I have seen earlier, the cell medium is very partitioned, it is not by any means an open Petri dish where stochastic processes could do the job somehow. Specific transport systems have been proven to be needed to go from one part of the cell to another (see Section 5.c above and Section 6 below). So here, with this phenomenon about CRY/TIM directed motion, we are then facing another unknown non-local *physical* effect, and such an effect appears to be not specifically identified in the research agenda of today's Microbiology even though it looks to be a fundamental Life process.[74]

6. The nature of the cytoplasm (Hameroff, 1987 - Chapter 5)

This book is in general misleading due its speculative nature, but there is a number of facts identified that give a reasonable picture of where we are in our cellular functions understanding (or lack of it). Chapter 5, which I review here in part, is important in that regard. Even though it is now over 10 years old, the book is not obsolete as to some of the questions it raises.

a. The MT cytoskeleton

After going through a short history of the discovery of microtubules, Hameroff quotes someone else saying that "when MTs are required by a cell for a particular function, MTs assemble in the appropriate part of the cell, with the necessary orientation, and, as MTs are no longer needed, they depolymerize." He sees MTs as "real time executives of dynamic activities within living cells." He fails to mention that MTs themselves appear to be "organized" around a centrosome.

a1. *Microtubules*. Then Hameroff goes into the description of MTs, failing there to identify the fact the structure of tubulin was not fully known when he wrote the book (we had to wait more than 10 years after the book for such data). He points out their alpha and beta tubulin monomers are "held together by water-excluding hydrophobic forces" with an electronic dipole. He identifies that various forms of tubulin exist (he fails though to identify gamma tubulin). Their functions are (1) cell support, (2) cell motion coordination and shape, (3) actin neural growth cones coordination, (4) molecular transport "rails," and (5) sensory perception via cilia and modified forms making receptors.

a2. *Microtubules in the Cell*. MTs assemble not only from the centrosome but also by themselves "like viruses" (Hameroff must be referring here to neurons and to other cells where there is no centriole). They are stable in cilia and flagella, and unstable in mitotic spindles. *In energy depleted cells random assembly prevails instead of organized assembly*. The energy from phosphate bond hydrolysis used by MT polymerization is *unaccounted for (unexplained)*. Hameroff guesses that it is used for MT lattice vibrations such as solitons (see Section 6.c2 below). MT assembly is affected by calcium ion concentration and binds 16 ions per dimer. An excess of ions disassembles them. Unstable MTs, as in mitosis, experience a "treadmill" effect from disassembly at one end and assembly at the other. MAPs (see below) stabilize MTs in the growing phase. Cell "polarity" occurs because "signals" outside the cell cause an asymmetry of the MTs. Then Hameroff asks: How can a peripheral clue lead to reorganization deep in the cell? He hypothesizes that either a signal is relayed through the MTs to the centrioles, leading somehow to *a change in the nucleation orientation out of the centrosome*, or that a local signal acts like a domino effect to affect the entire cell, maybe both, resulting in a particular *overall functional role* for the cell.

a3. *Centrosome and Centrioles.* Here Hameroff presents DeBrabander's theory of how the mitotic spindle works. It assumes that the *electrical polarity* of the MTs is important, even though we are in an aqueous medium and spindles can occur without centrosome! Also a "cartwheel filamentous pinwheel structure" is mentioned as being present at one end of centrioles even though many photographs in Margulis book don't show such. Hameroff does say that the reason for the very peculiar *perpendicular* reproduction of centrioles is unknown. Hameroff adds that the delicate array of the two centriole pairs, with their connected MT spindles, and the projections to the cell cortex have suggested to many observers some type of electromagnetic field pattern. But since such can't be possible in such a medium, what physical effect are we looking at?

a4. *MT Associated Proteins (MAPs)*. MAPs are proteins which generate cross-bridges between MTs and other cytoskeletal filaments (IF and MTL below) and organelles. They are separate from kinesin and dynein, which are discussed later (such provide relative motions between MTs as well as motions of other structures along MTs). MAPs enhance MTs polymerization and stabilization. The pattern of their attachment on MTs can be either regular or irregular. Irregular ones happen in the brain. Studies in rats show an increase in number and altered distribution of the various forms of tubulin and MAPs which correlate with brain development and learning. MAPs are concentrated in body and dendrites of neurons, and absent in glial cells. Different MAPs are in axons. It is hypothesized that MAPs affect the calcium ions motions effecting nerve impulses.

b. Other cytoskeletons

First, Hameroff gives a short review of the *intermediate filaments* (IF). They are keratin, desmin, vimentin, neuro-filaments, and glial filaments. Neurofilaments are seen as providing axons structural strength. However their existence is unexplained in neurons in general.

Second, there is the *actin cytoskeleton*. Here only its *cell background* form, called the *microtrabecular lattice* (MTL), is discussed (amoeboid feelers, axonal growth cones and tensegrity gels are discussed in the next subsections). The MTL is the lowest level of the cytoskeleton, with actin mixed with various types of *myosin* filaments. It is a filler between the other cytoskeleton components, forming a sort of *cytomuscle* creating patterns dividing the cell into *domains*. Upon trigger by calcium ions waves the MTL would switch domains between their "gel" and "sol" state. This switching would effect amiboid movements, as well as release neurotransmitter vesicles.

Diffusion in the cell cytoplasm is much slower than expected knowing the cytoplasm aqueous phase occupies 4/5 of its volume. Such a discrepancy is explained by molecules like RNA being dynamically bound to the cell MTL "solid state." This feature would also account in general for the efficiency of various enzymatic processes. The MTL vast surface being lined up with "ordered" and "vicinal" water would account for the lack of Brownian motion in cells.

c. Cytoskeletal motility (chemotaxis)

Hameroff quotes Albrecht-Buehler (1985): "Cell movement appears to be determined by some kind of chemical computer, the nature of which is beyond our present understanding." Then he adds: "Internal movement such as streaming of the cytoplasm, secretion of cell product vesicles, engulfment of matter, and the separation of paired chromosomes in cell division are routine functions whose complexity, organization, and precision generally boggle biologists."

c1. *Cytoplasmic Probing*. First he shows drawings describing the various cell components located along MTs coming from the centrosome. *Without MTs the cell becomes totally disorganized*. Then he describes how an amoeba moves using "feelers." These protrusions made of *actin* are sensory elements responding to lack of stickiness or presence of obstacles. So there is a *chemical regulatory system* at work realizing the motion process. But every few hours the cell changes direction for no reason. Why? Only a random thing? The cell motion has a front-rear axis, an overall motion coordination, and rules for changing direction. Therefore there is need for coordination of many MTL domains and navigation commands which involve assessment of the environment. It appears that the MTs provide this coordination, and the MTs in turn receive orders from the centrosome (centrioles). But how? Finally, two percent of a fibroplast can be torn out and move on its own protrusions, so each cell compartment is a physico-chemical system by itself capable of autonomous movement (random, of course)!

c2. *Bending Sidearms*. Muscle cell function is described, showing it is a local system using *myosin* appendages coordinated by waves of calcium ions released by membrane electrical activity, so a very classical process with no mystery. Then *axoplasmic transport* is discussed, showing the mechanical arm process of moving vesicles as similar to muscle action processes, but using *kinesin* or *dynein* arms instead. However, unlike for muscles, the origin of the *coordination* is here unknown, especially considering that neurons have no centriole! (The mitotic "pulling apart" process also needs coordination.) Separately, it is unclear how the energy delivered to the system is used to produce the motion. Hameroff suggests a *soliton* wave process may use this energy.[75]

c3. *Ciliary and Collective Movement.* A MT removed from a cell will "glide" on a glass due to the synchronized action of its *kinesin* and *dynein* arms, so the motility is still there "in vitro." This happens also for cilia taken out of a cell. The origin of the synchronization is unknown, and so is the origin of the motion direction command. Hydrodynamics was thought to account for this effect in spirochetes (see

Margulis), but a "gliding" MT on glass proved the explanation invalid. Even though these effects were identified in the early 1970s they are not yet explained 30 years later!

c4. *Geodesic Tensegrity Gels*. *Actin* filaments with *tropomyosin* in a cell support the nucleus in its position versus the membrane. They attach to the vertices of a polyhedral actin gel coat on the nuclear membrane. How is this built? Also, when the cell is in the final stage of division, a "ring of constriction" or "cleavage furrow" encircles the equator of the cell and constricts the cytoplasm until it is divided into two cells. What makes actin locate precisely there and act like that? Something physical must be at work.

d. The cytoskeleton and development.

Here neural "growth cones" are described. This activity is similar to movement in amoeba (see above). They continually probe their surroundings by sending out and then retracting delicate ruffles known as lamellipodia, and finger-like projections called filopodia. These dynamic appendages are a meshwork of actin filaments. MTs and neurofilaments splay into the growth cones, but generally stop short of the actin-rich areas. MTs are necessary for the growth of neurites, while actin filaments are essential for growth cone protrusions. A complex interplay between actin and MTs is then required there. Hameroff hypothesizes that the MT cytoskeleton is in charge of such process. But how could it know what to do? The same question would be asked from an outside "scent" the cytoplasm would receive. This is a fundamental problem for present Microbiology.

7. Conclusions

VB do not describe a specific function for centrioles. In mitosis they are dispensable and a single centriole can be the pole of a spindle. The location of centrioles at the center of the PM is also unexplained. Centrioles seem to be an add-on to a system that can operate without them. Yet centrioles are in a cell to provide a cell function of some sort. From examining Evolution, Margulis advances that centrioles make mitosis much more reliable simply on the basis their symbiosis was selected for in that evolution. From their past history they are very unlikely to just follow the ride in mitosis without doing anything. Margulis presents the centrioles as emitting MTs, but the PM does that job according to VB. My conclusions are as follows on this matter of centriole role:

In a partnership with the chromosomal kinetochores, they seem to at least bring more reliability to the mitotic process through helping the cell to split by moving the centrosomes to opposite sides of the cell, a physical event that does not occur without centrioles. The *quadripartition* experiment reported by VB showed that centrioles as pairs are *associated more with the splitting process of the cell than with the spindle formation*.

Margulis also suggested that they may allow the cell to maintain its motility during that critical phase of the cell life. However, such a function could be performed only by *sensing somehow the overall cell condition* as a single-cell eukariote seems to do (and needs to do!), and influencing, somehow with a purpose, the shape and motion of that cell, including its division.

By their central location, reproduction and motion within the cell (physical actions that are by themselves unexplained) centrioles appear to provide at least some physical coordination. This coordination does not seem to be effected via chemical processes, as such processes, by their local nature, cannot provide a true differentiated spatial action involving the entire cell. In other words centrioles would then use non-local physical effects. But what are such effects?

Also, centrioles seem to work in cooperation with the nuclear material, and kinetochores in particular, thus superposing on top of an older system that can work all by itself. What is the origin of this cell-wide synchronism? Synchronism and collective behaviors have been known for a long time as prominent features

in flagella and spirochetes, the relatives of the MT system and centrioles, but such features remain unexplained. Hameroff emphasizes further synchronism, self-assembly, localization and coordination of motion as being all unexplained phenomena in MTs, while looking to be the key to extended (multicellular) Life.

The review of the literature for the rest of Life on physical effects is very disappointing when it comes to explaining what makes Life develop and maintain itself. Mostly local chemical facts are found, with only very few principles of organized causal spatial motion identified. Some classical notion of local "force" is advanced in the case of kinetochores, but, after reviewing all the diverse ways of separating chromosomes, from simple to sophisticated, and the precise coordination required to do the job, such an explanation does not seem to fit reality. So, taking the big picture, the physical effects that put Life together look to be just simply missing, even for basics such as cell division. For now fifty years we have followed Schroedinger's suggestion to use the *local* aspect of the quantum or Chemistry. Even though we did find quickly DNA as he guessed, along with an enormous amount of chemicals that are part of and affect Life, we still have not found the *physical non-local coordinating principles* that make Life possible.

> There is not so much Life as talk of Life, as a general thing. Had we the first intimation of the definition of Life the calmest of us would be lunatics.
>
> E. Dickinson, circa 1880

APPENDIX B: QUANTUM CONFORMATIONAL DYNAMICS

1. Introduction

The well-known configuration of microtubules (MT) sprouting around centrioles is a configuration so far without a theoretical explanation (Figures 1 and 2 of Hameroff *et al*., 1988 and Figures 2.1 and 2.2 of Vandre and Borisy, 1989). Such a configuration could be taken as evidence of the spatial coordination influence of the centrioles through photon pulse emission from their surface.

Separately, the classical cellular automata dynamics described in Hameroff *et al*. (1988) and Rasmussen *et al*. (1990) concern themselves with individual microtubules and assume the applicability of a quasi-classical theoretical treatment.[76] However, the criterion for this applicability is that the wavelengths of the phenomena considered must be small compared to the characteristic dimensions of the field potentials involved. This is not the case here in light of the size of the postulated automata cells versus the diameter of the cylinders. The soliton wave treatment of Tuszynski *et al*. (1995) on the other hand is warranted under that criterion to explain the long-range construction of the cylinders. But this last phenomenon cannot start the polymerization of the MTs itself as it requires the prior existence of a classical electric field along the small long cylinders, which can only exist once the cylinders have at least begun to be built. It is thus yet to be shown that a process within the centrioles can in fact start the photon emission process creating the MT network in the first place.

As Penrose (1994) has identified, the microtubular conformation may be able to be treated quantum mechanically as a result of the large number of atoms making up one tubulin dimer, and therefore the inertia involved. The conformation dynamics would be quite uninteractive with the surrounding medium (tiny "vicinal" water molecules), and yet would be determined by the evolution of a single electron state within each molecule.

If coherence is assumed, it then behooves me to look at the dynamics involved to see what kind of evolution can be quantum mechanically predited out of such an arrangement.

2. The Physical Set-up

Hameroff (1988), Margulis (1993), Vandre and Borisy (1989) describe centrioles as cylindrical aggregates of identical molecules containing an electronic dipole related to two molecular conformations and assembled in a way that differentiates clockwise and counterclockwise rotations versus the surrounding medium in a "ratchet" fashion (Fig. 11).

A chemical sequencing from the DNA in the microtubule organization center builds initially these supramolecular structures (Margulis, 1993). Separately, such structures have also been reported to duplicate themselves through a process described by Figure 8-3 of Margulis (1993) and Figure 2.4 of Vandre and Borisy (1989). This well-known process has no attendant explanation as to what physical phenomenon drives its execution (Fig. 12). From the observed make-up of a microtubule, I can take the molecular grid on the surface of the centriole as a *weakly bonded triangular lattice* made out of parallel filaments built out of identical large molecules (tubulin) each having two conformational states linked to an electron effecting an electric dipole shifting orientation with the change of conformational state.

The filament construction results in one of the grid triangle vertices being differentiated from the other two, and the weak lattice allows only near-neighbors interactions.

3. The Quantum Theory

a. The molecular triangle subsystem logic

The Hamiltonian of a given molecular triangle, as an isolated subsystem within the grid, must reflect the symmetries of the electric field of the dipoles held by the molecules, notably the one vertex weak interaction mentioned above. Because the dipole fields are anisotropic, the strength of the interactions among the 3 molecules depends upon the relative orientation of their dipoles. When the two dipoles opposite the weak one are oriented the same way their fields add. A symmetrical configuration, thus with the same energy and reversible (Fredkin and Toffoli, 1982), will be obtained through inverting all three orientations. On the other hand, when these two dipoles have different orientations their fields subtract. A configuration with the same energy will be then obtained by exchanging their orientation as they will leave the third dipole unaffected. I have therefore four eigenstates for the triangle in four degenerated energy levels each with two basis states, with possible transitions between basis states as shown in Fig. 13.

b. The grid evolution

Due to its own symmetry the grid experiences traveling waves of rearrangements of the molecules conformation within the triangle subsystems at various moments of its evolution. Then, when "hit" by the wave, the mechanical supports of the three dipoles of a given subsystem are moved and switch to their dual conformational state (and corresponding dipole orientations) depending on which hamiltonian the subsystem has at the start of this conformation "update." Each subsystem in effect operates as an electronic "bistable," not being able to transit between its states of equal energy unless the rearrangement wave is present to free up molecular motion. In quantum mechanical terms, an internal triangle system state transition could be expressed as the result of interactions with the grid phonons (Jones and March, 1973). However the phonons occurring here correspond to the two non-linear conformational states of the molecules instead of the continuously varying molecular positions expected with "normal" phonons.

When placed in the grid, the molecules of a triangular subsystem will mechanically interact with it. In terms of creation and annihilation operators p^+_l , p^+_m , p^+_n , p_l , p_m , p_n for molecular state (conformational/dipole) quanta, the Hamiltonian of triangle 'lmn' will be:

$$\boldsymbol{H_{lmn}} = P_{lmn} + P^+_{lmn} \tag{B1a}$$

where P_{lmn} is either

$$J^1 p_l p^+_m \quad , \quad J^2 p^+_l p_m \quad , \quad J^3 p^+_l p^+_m p_n \quad \text{, or} \quad J^4 p_l p_m p_n \tag{B1b}$$

depending on which state the subsystem is in at the start of a conformation update, the J coefficients being operators reflecting its energy. The variability of this local Hamiltonian reflects the interactions with the nearby triangles as they can flip one or more of the subsystem dipoles (through the corresponding molecular conformations) during the evolution of the grid outside the update that includes the subsystem.

The interactions between the subsystems effect elementary logical connections, within which each subsystem acts as a logic gate for the data bits realized by the electronic dipoles held by its triangle vertices. This logic gate is capable of handling eight states:

$$A = \begin{pmatrix} -1 \\ -1 \\ -1 \end{pmatrix} \quad B = \begin{pmatrix} 1 \\ 1 \\ 1 \end{pmatrix} \quad C = \begin{pmatrix} 1 \\ 1 \\ -1 \end{pmatrix} \quad D = \begin{pmatrix} -1 \\ -1 \\ 1 \end{pmatrix} \quad E = \begin{pmatrix} 1 \\ -1 \\ -1 \end{pmatrix} \quad F = \begin{pmatrix} -1 \\ 1 \\ -1 \end{pmatrix} \quad G = \begin{pmatrix} -1 \\ 1 \\ 1 \end{pmatrix} \quad H = \begin{pmatrix} 1 \\ -1 \\ 1 \end{pmatrix} \tag{B2}$$

through two unitary step (evolution) operators U and V such that $B=UA$, $A=UB$, $D=UC$, $C=UD$, $F=VE$, $E=VF$, $H=VG$, $G=VH$, with U and V reflecting the symmetries of the subsystem as described above:

$$U = \begin{pmatrix} 0 & -1 & 0 \\ -1 & 0 & 0 \\ 0 & 0 & -1 \end{pmatrix} \qquad V = \begin{pmatrix} 0 & 1 & 0 \\ 1 & 0 & 0 \\ 0 & 0 & 1 \end{pmatrix} \tag{B3}$$

Using the Schrödinger equation, the corresponding Hamiltonians can be obtained through:

$$U = e^{iH^{(1)}_{lmn}} \qquad V = e^{iH^{(2)}_{lmn}} \tag{B4}$$

In order to represent the grid evolution, the Hamiltonians obtained from (4) need to be tensorially multiplied by a set of grid phonons creation and annihilation operators. Such a formulation will then reflect the ability of the local subsystem to "freeze" its state from one update to the next within the context of the grid evolution as a result of mechanical constraints between the molecules.

c. The conformational clock waves

I have a set of triangle mechanical "excitations" which can propagate along any direction $\boldsymbol{r_n}$ as well as anywhere on any row of the grid along that direction, in other words in the entire plane. In time-dependent form, a grid *one-dimensional* mechanical vibration wave quantum state (phonon) vector can be expressed by (Jones and March, 1973):

$$\boldsymbol{u_k}(\boldsymbol{r}) = \boldsymbol{\varepsilon_k}\, exp\, [\, i(\boldsymbol{k.r} - \omega_{\boldsymbol{k}}\, t)\,] \tag{B5}$$

where $\omega_{\boldsymbol{k}}$ is the frequency of the wave, $\boldsymbol{k}$ the wave vector, $\boldsymbol{\varepsilon_k}$ its polarization, $\boldsymbol{r}$ the position considered, and t the time. Such state vectors as formulated are *independent from each other*. However, the one-dimensional waves interact among themselves in the plane of the grid. An anharmonic term in the Hamiltonian of the system (Jones and March, 1973) needs then to be included, built out of a tensor product of state vectors such as (5). Such a term corresponds to the energy of dynamically, locally interacting, non-linear conformational states of the molecules forming the grid. In *second quantization* form, taking Planck's constant as unity, a state vector of interacting one-dimensional harmonic waves has the form:

$$\boldsymbol{u_{kl}} = (2\, \omega_{\boldsymbol{k}})^{-1/2}\, (\, \boldsymbol{a_k} + \boldsymbol{a^+_{-k}}\,)\, \boldsymbol{\varepsilon_k}\; exp\, (i\boldsymbol{k.l}) \tag{B6}$$

where $\boldsymbol{a_k}$ and $\boldsymbol{a^+_{-k}}$ are the annihilation and creation operators for wave vector $\boldsymbol{k}$.

I get the corresponding two-dimensional interaction state tensor at site '***lmn***':

$$\boldsymbol{s}_{lmn} = \sum_{k_1 k_2 k_3} \boldsymbol{C}_{lmn} (\boldsymbol{a}_{k1}+\boldsymbol{a}^{+}_{-k1}) (\boldsymbol{a}_{k2}+\boldsymbol{a}^{+}_{-k2}) (\boldsymbol{a}_{k3}+\boldsymbol{a}^{+}_{-k3}) \, exp[i(\boldsymbol{k}_1.\boldsymbol{l} + \boldsymbol{k}_2.\boldsymbol{m} + \boldsymbol{k}_3.\boldsymbol{n})] \quad \text{(B7)}$$

where $\boldsymbol{C}_{lmn}$ is a parameter characteristic of the interaction.

The clock wave system Hamiltonian is then expressed as:

$$\boldsymbol{H}_{\text{int}} = \sum_{k_1 k_2 k_3} \left(\sum_{lmn} \boldsymbol{A}_{lmn} \boldsymbol{e}^{i(k_1.l+k_2.m+k_3.n)} \right) (\boldsymbol{a}_{k1} + \boldsymbol{a}^{+}_{-k1})(\boldsymbol{a}_{k2} + \boldsymbol{a}^{+}_{-k2})(\boldsymbol{a}_{k3} + \boldsymbol{a}^{+}_{-k3}) \quad \text{(B8)}$$

with $\boldsymbol{A}_{lmn}$ being an operator representing the strength of the interactions at site '***lmn***'.

The total momentum ***K*** of the grid at the site of the interactions must be unchanged and equal to zero since the grid itself is not affected by such interactions. If only two waves were to interact, the sum of their two vectors ***k*** could not be zero unless they were equal in length and opposite in direction, therefore I would have in fact a single wave interacting with itself, and a two-wave interaction would not occur. A minimum of three waves will need then to interact.

The tensor $\boldsymbol{s}_{lmn}$ can represent a two-dimensional stepwise process clock wave provided:

1. only one wave polarization exists, so there will be only one kind of wave interacting (which is the case of the non-linear phonons identified above),
2. only 3 neighboring sites interact throughout the grid, all with the same interaction energies among themselves, so the interactions will be restricted to only one set of wave vectors ***k***'s lengths, and to three quanta created or three quanta annihilated, not a mix of creations and annihilations, otherwise there would be more than one set of resulting wave numbers possible (a weakly bonded filament lattice has this characteristic),
3. the grid spacings are not equal, so that, knowing ***K*** = 0, the wave vectors of the quanta created are equal and opposite to the vectors of the ones annihilated.

With the above conditions met, expression (8) becomes:

$$\boldsymbol{H}_{\text{int}} = \sum_{k_1 k_2 k_3} \left(\sum_{lmn} \boldsymbol{A}_{lmn} \boldsymbol{e}^{i(k_1.l+k_2.m+k_3.n)} \right) (\boldsymbol{a}^{+}_{k_1} \boldsymbol{a}^{+}_{k_2} \boldsymbol{a}^{+}_{k_3} + \boldsymbol{a}_{-k_1} \boldsymbol{a}_{-k_2} \boldsymbol{a}_{-k_3}) \quad \text{(B9)}$$

Now since the molecules are mechanically "on-off" through their conformational *dual* states (*non-linear* phonons) I can define *individual* triangle vertex "excitation" annihilation and creation operators (similar to the case of 3-D spin waves - Jones and March, 1973):

$$\boldsymbol{a}_l = \sum_k \boldsymbol{a}_{-k} e^{\,ik.l} \qquad \boldsymbol{a}^{+}_l = \sum_k \boldsymbol{a}^{+}_k e^{ik.l} \quad \text{(B10)}$$

which allow the elimination of the wave vectors from expression (9):

$$\boldsymbol{H}_{\text{int}} = \sum_{lmn} \boldsymbol{A}_{lmn} \ (\boldsymbol{a}_l^{+} \boldsymbol{a}_m^{+} \boldsymbol{a}_n^{+} + \boldsymbol{a}_l \boldsymbol{a}_m \boldsymbol{a}_n) \quad \text{(B11)}$$

The individual terms can be then regrouped in odd and even sets of indices along a given grid direction. $\boldsymbol{A}_{lmn} \boldsymbol{a}_l^{+} \boldsymbol{a}_m^{+} \boldsymbol{a}_n^{+}$ can be interpreted as an even triangle *excitation operator* and $\boldsymbol{A}_{lmn} \boldsymbol{a}_l \boldsymbol{a}_m \boldsymbol{a}_n$ an odd triangle *de-excitation operator*. Together they act then as a *forwards step operator* for the clock wave. In the same manner, $\boldsymbol{A}_{lmn} \boldsymbol{a}_l \boldsymbol{a}_m \boldsymbol{a}_n$ for an even triangle and $\boldsymbol{A}_{lmn} \boldsymbol{a}_l^{+} \boldsymbol{a}_m^{+} \boldsymbol{a}_n^{+}$ for an odd triangle together act as a *backwards step operator*. Now let's consider states of the clock wave with only triangles excited within a single "wavefront," i. e. on a straight line. The wavefront forwards step operator of the system will be:

$$\boldsymbol{F}_l = \sum_{mn} (\boldsymbol{A}_{lmn} \boldsymbol{a}_l^{+} \boldsymbol{a}_m^{+} \boldsymbol{a}_n^{+} + \boldsymbol{A}_{l\text{-}1mn} \boldsymbol{a}_{l\text{-}1} \boldsymbol{a}_m \boldsymbol{a}_n) \quad \text{(B12a)}$$

with '***mn***' indexing here the triangles in the wavefront while ***l*** indexes the step itself, and the corresponding backwards step operator:

$$F^{+}_{l} = \sum_{mn} (A_{lmn}\, a_l^{+} a_m^{+} a_n^{+} + A_{l\text{-}1mn}\, a_{l\text{-}1}\, a_m\, a_n) \qquad \text{(B12b)}$$

By imposing different and single energies for different directions of propagation, the third condition stated earlier forces an element of the wavefront to continue propagating in the same direction on the grid, limiting its choice at each step to only forwards or backwards propagation from the previous step, *with no change of direction possible*. Therefore the clock wave *wavefront states* then form invariant subspaces in the Hilbert space product of the triangles vertices state spaces, each subspace corresponding to a propagation direction while the system evolves according to the Schroedinger equation.

d. The grid evolution complete Hamiltonian

A complete wavefront step operator is then defined as a wavefront step operator from expressions (12) with each element tensorially multiplied by a "logical" operator corresponding to the operators (4) effecting the wavefront triangular subsystems internal state transitions as described earlier. The subsystems complete hamiltonian will be then:

$$H_{comp} = \sum_{lmn} D_{lmn} (a_l^{+} a_m^{+} a_n^{+} + a_l\, a_m\, a_n) \qquad \text{(B13)}$$

where D_{lmn} includes the variable reversible logic operator corresponding to the operators (4) following the logic of Fig. 13. Due to this variability of the operators, such a Hamiltonian is itself variable, reflecting the changing pattern of the molecules on the grid with the propagating clock wave.

When identified by Hilbert subspaces with wavefront steps operators F and F^{+}, it can be expressed as:

$$H_{comp} = \sum_{l} (F_l + F^{+}_{l}) + \sum_{m} (F_m + F^{+}_{m}) + \sum_{n} (F_n + F^{+}_{n}) \qquad \text{(B14)}$$

e. The "computational" front

I shall rename the wavefront as a "computational" front because its steps do not happen all at once, and perform a logic from the rules of Fig. 13. To see why let's assume an interaction just created three waves packets propagating away from their origin. It will take them the same time to propagate in direction d to two parallel-going computational front blocks either side of the origin, because it is $k.d/\omega_k$ either way from expression (7). On the other hand, to go to two computational front blocks going in different directions, they have to go themselves in two different directions, each with a different time formula $k.d/\omega_k$. Since the grid spacings are not equal, these two time formula give different results, and the crossing computational front blocks are not in phase, i. e. not simultaneous. Their corresponding incompatible logics can affect differently their common data sites by acting at different moments.

Each computational front itself will have to be then a sequence of elemental steps, each step acting on all the triangles with the same set of wave vectors. Because of the tensorial connection between all the triangles within a computational front from expression (7), the timing of the sequence is fixed, making the front an indivisible quantum obeying computational front step operators, with its states remaining in a given Hilbert subspace.

Since the front operators are sums of products of triangle excitation operators defined in equations (10) coming themselves from harmonic wave operators which are bosons (Jones and March, 1973), they are also bosons, and follow bosons commutation relations. With l, m, n representing here wave vectors:

$$[a_l a_m a_n,\ a_u^{+} a_v^{+} a_w^{+}] = \delta_{lu}\delta_{mv}\delta_{nw} \qquad \text{(B15)}$$

When part of the same Hilbert subspace, front step operators (12) do not commute because their one-to-

one corresponding component triangles have identical sets of wave vectors.

f. Computational wave analysis

In order to study the various sets of front steps in expression (14) I have to turn to a graphical analysis that follows the general topological requirements imposed by the definitions of the formalism, as well as (12) and (14). I take the alternate picture of fronts active at the same time throughout the plane so that the analysis covers the plane instead of a single strip:

- Forwards and backwards steps within an orbit are then represented as alternating to reflect the inherent symmetry of the Hamiltonian in that picture.
- Two forwards (or backwards) step blocks cannot 'touch', because they cannot have one of their vertices in common as they would then have to follow incompatible rules at the same time.
- At least two different orientations for valid computational orbits must be used in the layout, otherwise all steps of the fronts would operate simultaneously.
- Two synchronous blocks cannot touch, again because the update of the corresponding common data bits would have to obey two different sets of rules simultaneously.
- A computational front must contain adjacent blocks with different phases for their update clocks.

I first lay out in Fig. 14 a lattice with:

1. a lattice cell (triangular subsystem) using one of three orientations,
2. triangles having a distinguishable vertex, per the discussion about Fig 13,
3. different triangles so at least two orbits can exist.

Figure 14 is drawn as a "sieve" of shaded triangles representing triangular subsystems that are active during one time segment of the wavefront step. The simplest way to meet the second requirement above is to have one side of all the triangles aligned on parallel lines (horizontal lines in Figure 14), i.e. the molecular filaments postulated earlier for the physical layout. I then choose one of the various possible sieves represented by expression (14) in accordance with the above topological requirements. I select the forwards 'F' and backwards 'B' steps and identify the corresponding computational "orbits" (Hilbert subspaces) directions.

The shaded triangles without a designation are disjoint from each other, therefore do not support a computational orbit. Also, even though there are three kinds of triangles, two are so far mirror images of each other (triangles ABC and BDE). The phase of the two orbits they belong to are the same since the sum of vectors inner products in the exponent of expression (7) gives the same result for both triangles. *I need then to add a slant, a skew, to the grid to allow the blocks to be "distinguishable" by the clock wave components*, i. e. have different phases for the two different directions of orbits. The computational fronts are then identifiable as going up following the added skew. Since adjacent front blocks belong to different orbits, their updates happen at different moments, making the fronts valid as constructed and *a computational sequence is therefore supported by the sieve obtained.*

g. The other phases of the computation - cylindrical arrangement

I am now examining the grid of Fig. 14 at different moments of its evolution. First, the 'blank' triangles can be chosen as making the active sieve. The clock wave components of this sieve have phases

different from the ones of the shaded sieve because its triangles are not the mirror image of the shaded sieve triangles. These other computational steps can then happen with the shaded sieve steps interspersed with them.

I can also translate horizontally the shaded sieve by the distance between two grid vertices (I to J in Fig. 14). The new sieve obtained corresponds also to different phases of the clock wave. In order to see this relationship it is easier to take the point-of-view of a grid *wrapped around a cylinder*. The grid then has not only a translation symmetry in its plane but also a rotation symmetry in the third dimension. Let's assume to fix further the mind that the cylinder has a 13 rows circumference and a three-elementary-cells skew[77]. With these parameters, the computational front will have to go around the cylinder twice in order to be back exactly on the same rows of the grid, and the corresponding clock wave will experience a complete period or 360 degrees phase shift (Fig. 15). The computational steps in the translated sieve can then happen at moments interspersed with the ones of the previous sieves.

A translation from I to K in Fig. 14 yields another sieve with similar features. I have thus so far found six sieves (with the selected parameters) working in parallel at different moments of the system evolution giving 12 groups of simultaneous elemental steps to complete a given computational front step. An analysis of a translation along one of the two inclined axis of the grid gives 12 other sieves. Combining all three clock wave propagation axes of the grid, the system evolution then has the possibility to go through a total of 30 sieves for the parameters I have assumed.

h. Selection of a direction of propagation

The selection of an evolution will be accomplished through the layout of the grid in separate parts. Here I use Feynman's view on quantum computation. Feynman's idea (Feynman, 1982, 1985) was to use a one-dimensional *finite* spin wave system, assuming a "ballistic" mode of propagation for a spin "cursor" wave packet. Then the observer waits for the cursor to come out of the chain at the opposite end of its start, *leaving the time for the completion of the computation undetermined*. The idea works the same way in a two-dimensional set-up as I have here, but with a clock wave "strip cursor" instead. Feynman's finite chain is replaced with a "ratchet" slat cylinder surface (Fig. 11) where the symmetry of the wave propagation is broken, allowing a set of waves to evolve in only one direction, the propagation between slats being through photons emitted from one to the next as a result of molecular conformational transitions. Unlike for Feynman's set-up, the computation would be here fully determined.

i. Non-local cellular automata

Let's consider a single cylinder evolution. Once started from one strip the computation runs following clock wave fronts updating the entire grid strip by strip and completes a generational update of the triangles data sites after two full turns around the cylinder arrangement assuming the parameters given earlier. Within a classical automata generation, the new state of each cell is computed from the nearest neighbors states that came out of the previous generation (Wolfram and Packard, 1985). Here in contrast the grid generational computation is done in computational fronts, each with a fixed number of non-local steps updating simultaneously a group of triangles vertices scattered throughout the length of the grid. The resulting cells new states then depend on the pattern obtained by the previous non-local step, not the previous generation. As a result, I have a globally parallel update as opposed to the classical automata locally parallel one.

For example, in order to determine the patterns of the 24 steps in Fig. 16 (showing two successive fronts with the sequence followed by their elemental steps) I have to assume a computational front no longer than the sites shown, with left and right being the end of the grid. In a classical automata, I can draw

an initial pattern in an arbitrary fraction of the automata grid, and compute the next generation of that fraction. Here I need to know the pattern of an entire longitudinal section of the grid from one end to the other in order to compute each set of three neighbors, and then I have to wait for two revolutions of the front around the cylinder to get to the next update, the new generation.

As there are notable patterns in classical automata such as "gliders," "flashing beacons," etc., the above automata will most likely get into special stationary patterns for a certain number of generations. Such patterns would then allow an output of the computation toward the medium surrounding the cylinder through the emission of photons by the electric dipoles displacement during the rearrangement of the molecules (Del Giudice *et al*., 1983, 1986, 1988).

4. Conclusion

It has been shown here that a specific triangular grid can indeed run a two-dimensional quantum computation thanks to the asymmetrical mechanical interactions between its molecules. Such a process was identified earlier as impossible for rectangular grids (Margolus, 1986, 1990) and *the generic theoretical question about the possibility of two-dimensional quantum computations was left open by the referenced papers.*

Because of the close resemblance of the obtained grid layout asymmetries with MTs and centrioles surfaces arrangements, such biological systems may be able to sustain a quantum computation. Of course they would need to be somehow maintained coherent versus the surrounding medium.

The properties of the non-local cellular automata require a separate analysis.

APPENDIX C: SUMMARY OF POTENTIAL THEORETICAL STUDIES

1. Physics

---Identify parameters allowing molecular arrangements that could sustain an "inertial" space (study such spaces dynamics at large) (Section IV)
---Collective quantum phenomena associated with space manifolds connections using examples such as the described self-assembly of centrioles (Section IV)
---The SCQS physical realization of a "nondeterministic" computer (Section V)

2. Computer Science

---Define a "non-deterministic" pattern logic processing using quantum non-local cellular automata (Section IV and Appendix B)
---Determine the equivalent of "intractable" problems in the above processing scheme (Section V)

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List of Figure Captions

Notes

[1] See Chapter 6 of Schroedinger (1943).

[2] Prigogine (1980), Prigogine and Stengers (1984), and background found in Gleick (1987), Lewin (1992) and Waldrop (1992).
[3] For a background on Artificial Life see Langton (1989, 1992, 1994).
[4] Artificial Life experiments have all the common problem of identifying the "world" the cyber organisms have to evolve in, which is of course limited by the imagination of the experimenter, not by Physics.
[5] By Science providing only formalisms. This matter will be discussed in the Conclusion.
[6] See Penrose (1991, 1994), Hameroff and Penrose (1996a, 1996b).
[7] See Penrose's description of Kochen-Specker contextual process analysis in Penrose (1994).
[8] For a history of the complexity "movement" see Lewin (1992) and Waldrop (1992).
[9] As described by Lewin (1992) and Waldrop (1992). In a metaphor of that sort, where is the "super-ant" created as a whole that would make the mind?
[10] See an introduction in Hampden-Turner (1981) - Map 6. Behaviorism was an application of logical positivism (Miller, 1996, Chap. 8).
[11] Let's remember Descartes' *cogito ergo sum* here!
[12] See Hampden-Turner (1981) - Map 25 for further references on K. Pribam's holographic mind hypothesis.
[13] The optical imaging is based on staining the cortex with voltage-sensitive dyes which attach to neurons and act as transducers transforming changes in the neuron's *electrical* activity into flashing lights. 50 years ago people wondered about how much easier it would be to understand the brain if neurons would light up when they "talked" to one another. Well, now we know. Can we understand? See Arieli *et al*. (1996) and an example of use in Baraniga (1999a).
[14] A term used by Christopher Alexander (1979), the guru of "design patterns" in Computer Science.
[15] See description of Turing (1952) in Kauffman (1993) and Goodwin (1994).
[16] Nuesslein-Volhard and Wieschaus (1980), Ingham (1993).
[17] And so for vertebrates, see Keynes and Stern (1988).
[18] For extensive examples of such influence see for example Metzger and Krasnow (1999).
[19] Lee *et al*. (1992), Fan *et al*. (1995), Jiang and Struhl (1995), Basler and Struhl (1994), Lepage *et al*. (1995), Li *et al*. (1995), Strutt *et al*. (1995), Eberlein *et al*. (1995).
[20] Heemskerk and S. DiNardo (1994), Perrimon (1995).
[21] See also Kauffman (1995) for a conceptual elaboration.
[22] However the cytoplasm large surface area (Appendix A) may restrain the motions to 2D, yet the specific orientation of the molecules is not accounted for.
[23] Shapiro (1995), Jones and Aizawa (1991), Manson (1992).
[24] See Femino et al. (1998) and the cover of the corresponding magazine issue.
[25] See Hinchcliffe *et al*. (1999) for one example (Section IV), and Appendix A, Subsection 4.b for another.
[26] See one description among many in Cook (1999).
[27] "Death domains" are present in the internal part of two cell membrane-traversing receptor proteins. Receptor proteins *aggregation* (grouping together through self-association and hetero-association) in these domains has been found essential for passing death molecules into the cell. Again, here there is a *complex assembly* with no construction apparatus in sight. See Wallach et al. (1995).
[28] See Appendix A and its references for the features of both cell nuclear and microtubular systems.
[29] Vogel (1997) identifies the evolution of a set of kinases, enzymes that add phosphate groups to a variety of cell proteins as correlated with the mitotic sequence, and this evolution involves molecular reshapings.
[30] Bornens (1979). This article assumed that the large inertia observed comes from *an extremely fast rotation* of the centrioles. Such an apriori unlikely conclusion is made impossible by close observation done since that paper, in particular the fact "satellite bodies" are next to centrioles as Vandre and Borisy (1989) describe.
[31] This connection appears to happen via the *receptors* in that membrane. See later for more details.

[32] I start from the work by Margolus (1986, 1990), which comes from Feynman's understanding about "quantum computers." Margolus indicated in his papers that he was not able to find an arrangement that would sustain a 2-D quantum computation. Nature would have found it eons ago!
[33] Appendix A Subsection 3.a3 mentions an *orthogonal* construction too out of a spherical DNA area.
[34] Maybe I could then envision quantum *groupish monads* controlling Richard Dawkins' *classical* selfish genes as puppets. (Dawkins, 1989).
[35] Schroedinger (Moore, 1989) would have been pleased as he despised the individuality that he thought came with the idea of finite monads as he obtained it from Leibniz's understanding, not Bruno's infinite kind (Gouin, 1999).
[36] Herbert Froehlich guessed in the 1980s (Froehlich, 1988) that there may be collective quantum coherent phenomena in biological materials due to the large electrical potentials present in a cell.
[37] A "nondeterministic" Turing machine (NDTM) is a hypothetical computer that can simultaneously follow an unlimited number of parallel computation paths. Given a state and symbol that is observed on its tape, the NTDM can "choose" from a finite set of choices for its next move, where each choice involves a next state, an output symbol, and a move of its tape head. A NTDM then makes every possible choice available to it, and in parallel simultaneously follows every possible computation path. See Aho *et al*. (1974).
[38] The literature speculates (Appendix A) that there may be duplicated kinetochores connected to the same pole. It is hard to see how in the monadic spaces picture.
[39] From the theoretical reasons given at the beginning of Appendix B, *the **classical** cellular automata envisioned by Hameroff to occur on the surface of MTs* (e.g. Rasmussen *et al*., 1990) *do not seem to be a possibility either*.
[40] There are several types of glial cells (covered also under the name of "astrocytes"). See Hameroff and Penrose (1996a, 1996b) and Churchland and Sejnowski (1992), p. 307-308.
[41] See Appendix A Subsection 5.d and Penrose (1994), p. 365.
[42] See Note 30.
[43] Its sea-wave-like "shadow" has been experimentally found to exist through observing the "activity" of millions of neurons, see Arieli *et al*. (1996) and Section III (Note 13).
[44] See Note 12. Note that since nervous impulses contain no data, the literature such as Crick (1994) will discount the holographic hypothesis, the characteristics of the process not being available for measurement by happening in inertial space.
[45] See Alkon (1992), Churchland and Sejnowski (1992) and Rose (1992).
[46] This DNA may not reside in the cell nucleus according to Margulis.
[47] See Penrose (1991, 1994). Penrose does not agree with Everett's parallel universes view (I do not know his opinion on a multiple-reality interpretation of it). His spacetime view is also incompatible with the concept of space as generated by its content.
[48] The SCQS will be called an "observer" when it can observe itself with a "focus of attention" as will be discussed later - if the SCQS does not have these features the term "experience" will be used as it just interfaces the outside reality and its own reality in many ways, with no such focus of attention.
[49] In contrast, Hameroff and Penrose "subjective" time would be defined versus the e-m spacetime by how often the wave function collapses in the input/output biomolecular memory arrangements due to the warping limitations inherent to that e-m spacetime reflected by Heisenberg's time-energy uncertainty.
[50] A SCQS may or may not relate to a mind, but since there is no other example of SCQS than minds at this point I shall look at what minds experience from our own introspection. For an introduction to the concepts see Part II, Section 6 and Part III, Section 12 of Dennett (1991).
[51] Schroedinger (1958), Chapter 6 addressed this subject.
[52] See for example Ball (1999). Within the monadic spaces understanding, these patterns are ***not*** seen or recognized by the computation, only the human observer who sees the result sees the patterns and thus

creates them. ALife experiments depend on the human observer to make sense of the "emergence." Emergences all ultimately originate from the quantum, starting with "simple" chemical reactions, which are of course localized quantum phenomena.

[53] Of course such an experience will not replace a mathematical demonstration.

[54] Penrose (1994), Hameroff (1998), Hameroff and Penrose (1996a, 1996b).

[55] This is the answer to the old conundrum of Descartes about the relation between mind and matter (Descartes, 1997, p. 339).

[56] This feature is **not** in the definition of SCQSs I gave earlier. It is an addition corresponding to a physical layout of the quantum system components which still needs to be theoretically identified. I present here only clues to where the feature may come from.

[57] Dennett sees the human mind as a classical system, of course. This Darwinian search hypothesis was tested on a computer (Ullman et al., 1995). The results were very slow in coming. As other ALife experiments, this may not prove much about Life. See Note 4.

[58] Note 56 applies here too.

[59] Bela Julesz's 3-D perceived 2-D computerized images experiments of 1971 as reported in p.117-119 of Casti (1994). For vivid color examples see Thing (1993).

[60] Calvin (1991) also thinks the mind uses a Darwinian search.

[61] This is my coinage. There are several psychologists who have been looking into this matter as Calvin and Jaynes did. One example is Donald (1993). There the idea is that the use of *external memory* (pictures, symbols and writing) changed the "cognitive makeup" of the mind to enable it to self-reflect over generations. It is not clear whether he thinks that this was like a Baldwin effect. Such matters were discussed at the conference "Einstein meets Magritte" in Brussels, Belgium May 29-June 3, 1995.

[62] P. S. Laplace (1814) had a universal determining equation in mind, the first "Theory of Everything," in the early 19th century.

[63] I discount here all attempts at examining the function of a brain in a classical manner as I have identified the potential inadequacy of such an approach in Section III.

[64] Penrose maintains however that his best argument is based upon the metamathematical operations a mind would be capable of doing in light of Goedel's results.

[65] See Deutsch (1985) and Appendix B of Gouin (1999).

[66] The factorization problem (Schor, 1994) identifies the location of components of a whole in the space of the whole *without distinguishing them*, so it is a relatively easy problem for the quantum.

[67] Which was really a very old attitude, as Pope Urban VIII expressed it early in the 17th century through a comment at the end of Galileo (1997) p. 307. Simplicio (representing the Pope) said: "He [God] would have the power and the knowledge to do this [the tides] in many ways, some of them even inconceivable by our intellect." Drake (1990, p. 190) paraphrased this sentence as "God had always many ways to produce any phenomena that men can observe," an understanding followed by Feynman through Mach. Finocchiaro points out that the theological argument "also has a nontheological analogue" describing it as a "purely methodological and logical terms," i. e. the "problem" of induction, without referring to logical positivism, a. k. a. Mach's philosophy, and thus showing the direct connection of logical positivism with religious interests. Such a "problem" is the problem of *finite* logic, the only kind found in a Classical World, which encumbered Human reasoning since Antiquity. The truths of Science go beyond finite logic as Science now uses (uncountably) infinite logic in quantum theory (QED).

[68] Vogel (1999), Shapiro (1995), Jones and Aizawa (1991), Mansson (1992).

[69] As Dugas (1988, p. 444) put it: "In the terminology of modern philosophy Mach, reducing Science to a well-formed language, would be called a pan-mathematician."

[70] This reply also addresses E. Schroedinger's concerns expressed in Schroedinger (1958) Chapter 2.

[71] Another truth that will need reinterpretation in light of the Quantum is the entropy law of Thermodynamics that led to Clausius' vision of doom called the "heat death," another "mal du siecle" present at the end of last century which is still with us (for a review see Miller, 1996, Chap. 4).
[72] See hints on this in Section V and Gouin (1999) Section VII.
[73] Barinaga (1999) has a good set of references on circadian rhythms. See also Ceriani *et al*. (1999).
[74] See for example the consequences for gene therapy and HIV in Amado and Chen (1999).
[75] He published a paper on this recently (Tuszynski *et al*., 1995), but there is no mention of the influence of the surrounding medium, both mechanical and electrical, so it remains to be proven the effect exists.
[76] See for example Schiff (1968), §34 and Chapter 11.
[77] These parameters are typical of biological eukariote cell microtubules (Margulis, 1993; Hameroff *et al*., 1988; Rasmussen, 1990), the subunits that form the surface of MTs and centrioles.