On the Origin of Space

Part 3E: Quantum Spatial Development
- Cell Proliferation

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Abstract
Quantum space manifolds sustained by the cell nuclear envelope are seen here as being the required physical entity allowing cell proliferative multiplication in metazoa. They are a prerequisite for cell differentiation, the complement process leading to organism development.

Keywords: cell nucleus, centromere, telomere, centrosome, Rabl axis, bouquet axis, mitosis, meiosis, quantum space manifolds

Introduction
Can we apply the understanding of quantum dynamical spaces, i.e. space being built by its contents, as developed in [1] through [4], to the set of evolving biological cells called eggs, oocytes, zygotes and embryos, i.e. to the beginnings of living organisms? If we can do that in a meaningful way, we would obtain a strong confirmation about the existence of physical phenomena in Life not found anywhere else, as well as additional insight on how such processes run and are applied by Life. We have looked at the oocyte of the fruit fly and its early embryo in earlier articles as examples of development. Now it is time to look at the question of cell proliferation and differentiation in general, as this was found to be the key physical problem of early multicellular development, and Drosophila was quite peculiar in that area. We will concentrate here on the proliferative aspect, leaving differentiation for another article. The role of the cell nuclear system and its physical interactions with the cytoplasmic MT/centriole/centrosome system appear to be paramount in this matter.
Proliferative cell division

Strange as it may seem, knowing how modern biology portrays itself as “advanced,” the simple “proliferative division” of a cell, which is the developmental base of a typical multicellular organism, is a phenomenon that has to this day no overall physical or chemical explanation: [5] for example points out that in the physical division experienced by the cell cytoplasm, “the manner in which the mitotic apparatus [chemically] signals the actin and actin-based motor molecules in the cell cortex to assemble into a contractile ring [to cut the cytoplasm in two parts] is completely unknown.” The quantum space approach proposed in [1] through [4] at least tells intuitively and directly what is physically going on (as well as tells what is missing from the experimental data so we can go find that missing data instead of fishing in an empirical manner), but this concept is entirely outside classical physics and so we still need to ensure it applies to the cell nucleus as development certainly depends on that aspect of the cell. Let's look at the proliferative mitotic cell division process in a schematic way:

![Diagram of proliferative cell division](image)

In Fig. 1a, (cell division interphase) we have a centrosome standing right next to the cell nucleus. This by itself has no known reason to be so. Why is the centrosome not standing anywhere else in the cytoplasm at random? We will advance that it can only be so because the centrosome “feels” the presence of space manifolds generated by the nucleus, and places itself at their intersection, being stopped from going inside the nucleus only by the reticulum surrounding the nuclear membrane. (Let’s remember here that a cell depleted in energy cannot maintain that relative location.)
Nuclear quantum space manifolds

Indeed, we get an idea that such manifolds do exist first from pictures of the endoplasmic reticulum surrounding the nucleus, with the relative position of centrosomes and nuclear pores added. (Fig. 2)

Looking inside the nucleus, we see further order: Chromosomes in interphase are decondensed and their centromeres are on one hemisphere of the nuclear envelope and telomeres on the opposite side (Fig. 3A). They are not intertwined, and instead occupy distinct regions (outside the nucleolus), with motion restraints in the form of a series of discrete loci connecting them with the nuclear envelope (Fig. 3B).

Such regions are seen in the literature as defining the repressed and permitted transcription areas of genes, and thus the character of a cell, with (1) the heterochromatin region (where centromeres form) as a repressive (“gene silencing”) area, and (2) only loci of genes in overlapping regions being capable of interacting for mRNA production.

A deeper knowledge about this nuclear order is obtained by looking at what is happening in the zygotene stage of meiosis in plants (rye, maize), where a realignment of telomeres happens, called the “bouquet.” [8, 9] We quote [8]:

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**Fig. 3 – Nuclear order** ([7], Fig. 1)

**Fig. 4 – Centrosome location vs. the Rabl nuclear axis and bouquet axis** ([8], Fig. 10 – with in C centrosomes and metaphase plate added – see later)
“Fig. 4a: Telomeres (circles) are polarized to one hemisphere of the nucleus, creating a ‘Rabl axis.’ Nuclear pores (ovals) are distributed uniformly. [Layout for interphase.]

Fig. 4b: At the leptotene-zygotene transition, unknown mechanisms polarize both nuclear pores (top arrow) and telomeres (bottom arrow) in opposite directions. If movement of the nuclear envelope causes the difference in polarity between telomeres and nuclear pores, there must be differential movement at each membrane (arrowheads in top and bottom insets).

Fig. 4c: The result is a ‘bouquet axis’ that is independent of the original Rabl axis.”

[10] adds the key fact that the base of the bouquet is juxtaposed to the MT organizing center, be it a centrosome or spindle pole body, and this prior to the centrosome duplicating and moving at opposite ends of the nucleus perpendicular from that axis in meiosis I (which is otherwise similar to mitosis in normal cell duplication - Fig. 1b). We have thus added information in Fig. 4C for later discussion, using the fact that the nuclear pore complexes are in the region of the centromeres at that point. The above geometrical moves demand the concept of quantum space manifolds, not only in relation with the MT system as [1] through [4] already developed, but for the nuclear system as well. We can strengthen further this requirement by looking at the details of the nuclear components relocation during mitosis.

The very specific nuclear order above is maintained throughout mitosis (Figs. 1c and 1d – [11]), and this can only obtain through a built-in spatial topography: The order of centromeres perpendicular to the spindle axis is preserved via a simple linear projection onto the metaphase plate, and the anaphase chromatin regions destined to be the child nuclei. (Fig. 5) The difference in timing of sister chromatids separation at anaphase maintains the position of the chromosomes along the spindle axis in the child nuclei vs. the parent nucleus. Sisters destined for a more poleward position (distal from the cleavage

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**Fig. 5 - Transmission of chromosome order along the mitotic spindle** ([11], Fig. 6D) - x-y projections of the trajectories from the centromeres superimposed on the segmented prophase nucleus (dark gray), metaphase plate (light gray), anaphase chromatin regions (dark gray) and G1 daughter nuclei (light gray).
furrow) in the child nuclei (green in Fig. 5B) separate prior to ones that are to be less poleward (closer to the cleavage furrow). Subsequent expansion of child nuclei occurs isometrically without long-range centromere movements, thus preserving relative neighborhoods. **Position inheritance from one cell generation to the next in proliferative cell divisions is then implemented via specific timing differences of sister chromatid separation at anaphase onset coupled with the absence of any whole chromosome movement in interphase.**

Physically, in order for this to work at all, **the axis of the spindle has to be perpendicular to the Rabl nucleus axis, or close to it**, with centrosomes/centrioles located on that axis so that the projection of the centromeres location retains a positional meaning. We take here the Rabl axis instead of the bouquet axis in the absence of data in the literature about centrosome relative location vs. the nuclear axis in interphase. (This will be justified below.) The centrosomes must be then able to sense the topography of the telomeres/centromeres inside the nucleus at all times, and, further, have a means to move vs. this topography. However, **it stands to reason that no chemical process can produce such correlated large scale relocations and precise non-random movements.**

To add to the extent of the coherence involved, we add Fig. 6. This is a schematic drawing that [12] describes as depicting the process of nuclear envelope lamina “stretching and tearing” during mitotic nuclear envelope breakdown (NEBD), where the MT system is somehow helping **in a holistic way** through molecular “motors.” We have removed the motor force arrows from the figure, and added nuclear/centrosome-generated space manifolds so we can detail our alternative explanation. Quoting [12]: “Surprisingly, microtubule-dependent forces not only deformed the envelope but also mechanically **stretched** the nuclear lamina before NEBD, demonstrating pulling forces in the plane of the envelope... The tearing site would thus be determined by the geometry of the mitotic spindle and chromosome-envelope

![Figure 6. Nuclear envelope breakdown ([12], Fig. 7)](image)
contacts... In the absence of microtubules, NEBD did occur—but ... nuclear shrinking was followed by permeabilization through many small holes that did not expand.” The mechanical forces mentioned by the reference is in fact a speculation limited by classical physics, while their description of a “surprising” expansion is telling us what’s really going on: the expansion of a space manifold.

Starting with Fig. 6C, the centrosomes are expanding the space manifolds they took over from the nucleus in Fig. 6B (see below for an explanation of this take-over). In Fig. 6D there is a collapse of the nuclear envelope inside the manifolds since no longer sustaining a manifold (and thus being absorbed by the endoplasmic reticulum). In Fig. 6E the centrosomes further inflate the manifolds to start the anaphase separation (as [1] through [4] described). The nuclear centromeres gather at the intersection of the centrosome manifolds, thereby giving the observed metaphase plate - in the same way they were congregating at the intersection of the nuclear manifolds in the interphase nucleus, i.e. at the Rabl axis pole in Fig. 6A. Their motion was studied earlier through Fig. 5, and we saw this move as a straight linear projection from the nuclear location.

As Figs. 5 and 6 testify, nuclear disassembly and formation of the mitotic spindle/metaphase plate are highly coordinated spatial processes, and on top of this, a number of biochemical processes are also coordinated in time with these overall processes (e.g. nuclear pore complexes disassemble then in discrete steps). Such a coordination is just too extent to see it as a chemical happening between many separate things – the observed holistic aspect cannot be obtained that way. This lacuna is similar to the one found in textbook explanations of mitosis.

Since there is no physical field around to fix the axis of the mitotic spindle vs. the nuclear axis, and since centrioles have been already understood to generate quantum space manifolds per [1] through [4], there must be also manifolds generated by the nuclear envelope (and most likely by the nuclear pore complexes since they are relatives of centrioles). The intersection of these manifolds must be setting the location of the centrosomes and must influence their direction of separation, i.e. the mitotic metaphase plate orientation.

When comparing Figs. 6A and 4C, we see further that,

1) In order to properly realize the x-y projections described earlier about Fig. 5, the paired centromeres must act as one block, acting independently of the envelope in their sensing of the new intersection of manifolds set by the centrosomes, and thus must be generation a space manifold of their own - the break of the nuclear envelope needs not start from the Rabl pole;

2) In order to record the relative distances it had to the Rabl axis pole, the heterochromatin area on the nuclear envelope must have a gradient of thickness from that pole, with the farthest being the thinnest, so that heterochromatin must physically sense the manifolds from the nuclear pore complexes meeting at the Rabl axis pole while in an intact envelope.
Remark: As a reminder here from [1] through [4], the existence of leptonic quantum space manifolds generated outside the nucleus by centrioles and MTs, has a number of experimental (indirect) confirmations. One of such is the very simple “glass bead experiment,” [13] where a bead has been mechanically inserted in the cytoplasm of a cell (Fig. 7A) so that the division portrayed by Fig. 1 gets modified in an obvious way: During the division (Fig. 7B), no furrow appears above the bead as the left and right manifolds generated below the bead by the asters and MTs on each side of the bead cannot meet above due to the cytoplasm being kept away from the asters at that location. (The manifolds being sustained by MTs have the metaphase plate as intersection and can only cover the neighborhood of the asters containing the centrioles.)

An actin cleavage furrow can appear above the bead only in the second division process (Fig. 7C) because then the new asters generate new manifolds above the ones created in the first division and thus around and above the bead, leading to a connection between two perpendicular leptonic space manifolds at that point above the bead, allowing actin to accumulate there at last, sensing the connection between manifolds, to form an observable furrow (something which cannot be explained via chemical processes). Due to the furrow disconnecting the manifolds in Fig. 7B as a result of the initial presence of the bead (giving an artificial asymmetry to the cytoplasm), the resulting 4 cells in Fig. 7D can connect only above the bead, unlike the natural case of Fig. 1.

Coordination of evolution between quantum space manifolds

But how can the two space manifold systems, nuclear and MT, coordinate their evolution? As quantum space manifolds, the only way they can is through their material contents. It has been observed that a number of molecules move from the centrosome to the nucleus and conversely, and their concentration peaks correlate with the NEBD. The only physical way that such directed motion of molecules can happen is through the “cell cycle system.” Such a system cannot
be of chemical origin, even though we can only observe its shadows from the molecules concentrating at one area or another. Chemical affinity is a statistical process that can only work through local interactions in a medium allowing random motion of molecules, and the typical mediums of Life do not allow a full random motion by far. Indeed, as other parts of the cell, the nucleus is filled with a nuclear matrix of microfilaments that strongly hinder such random motions. [14] We have here a very precise process leaving little room for randomness.

We have also seen in [1] through [4] that space is an electromagnetic entity with a non-local character. Here we are dealing with very small spaces compared to cosmological spaces. This means that the frequency modes of space production are narrowly defined, so specific molecular arrangements will generate specific spatial modes. If there is a process such as the one evolving in centrioles, and maybe in centromeres/kinetochores/nuclear pore complexes, that can create a oscillating timer via the concentration of a given molecule where a space mode is shut down while another is started, the origin (source) of that space can be switched from one generating system to another. The MT system space origin is the centrosome (centriole) while the nuclear system has several space origins in the nuclear envelope (i.e. the nuclear pore complexes) as well as the heterochromatin. Then any molecule, which, by its presence in a space, shuts down the mode of production of that space, will then see the space being generated through another mode, such as via the centrosome, and will then relocate at the new origin of the space, until its presence shuts down that new source of space again, sending the molecule back to the “center of mass” of its original source, i.e. inside the nucleus.

**Conclusion**

We have then a generic principle using non-local spaces instead of their local contents as classical mechanics does, provided we see spaces as generated by their contents, which is an eminently quantum aspect of reality ([1] through [4]). Relocation of molecules via non-local means is the stuff of Life.

The cell cycle is just one of many space source switching processes. [15, 16] give excellent examples of molecules shuttling between the nucleus/nuclear pore complexes and the centrosome to effect the needed cell cycle timing process. Then the full details of the observed cell cycle can be physically obtained through the quantum program in the centrosome/centriole receiving inputs from the nucleus via genetic products at specific times to develop its own division.

We will see in a future article that this kind of quantum spatial relocation of molecules is also at the origin of cell differentiation, the other key physical process that allows multicellular Life besides cell proliferation.
References


