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A Review of Electromagnetic Activity in Cellular Mechanics

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Abstract

This is a review of recent literature concerning electromagnetic effects on cellular mechanics. "Recent" refers primarily to papers published in this (the 21st) century. The review shows that there are relatively few papers on cellular electromagnetics as compared with those on proteins, biochemistry, and cellular anatomy. The principal finding of the reviewed papers is that cellular electromagnetic fields appear to arise from longitudinal vibrations of the filaments making up the walls of the microtubules. Microtubules are long hollow cylinders which form the overall structure of the centrioles. The microtubules, and therefore the centrioles themselves, are arranged in nine sets of parallel blades with each blade having three microtubules. The centrioles occur in pairs perpendicularly to each other. During mitosis (cell division) the centriole pair becomes two pair which then separate and divide the cell into two. It seems that electromagnetic forces play a central role in this division. Electromagnetic activity in wound healing and in the imaging and treatment of tumors is discussed.

Keywords

Centrioles, Microtubules, Cellular Electromagnetism, Cancer

1. Introduction

This is the third in a series of review papers on centriolar cellular mechanics with the focus here being on electromagnetic effects. The first two papers reviewed: 1) the literature on centrioles in general and then 2) the centriolar microtubules—the principal structural components of the centrioles [1] [2].

The research and findings cited herein, and in the two earlier papers, are primarily those documented to date in this, the 21st century. As with many reviews, important writings are either inadvertently omitted or are not given the attention they deserve. I sincerely regret such omissions and/or under-emphases.

The implication of the title is that electromagnetic effects are not only important but also essential in cellular mechanics. Unfortunately, however, the electromagnetic effects are often omitted, or not discussed in depth, in biology papers and books. But upon a close examination of intracellular mechanics, and in particular with the centrioles, the presence of electromagnetic forces is evident. Perhaps the most persuasive evidence is the observed forces exerted at a distance during centriole pair separation and during mitosis via the kinetochores [3]-[6].

Also, it has long been known that there is a voltage change across different sides of an open wound [7] [8].

How do these electromagnetic fields and their associated forces arise? There is now considerable agreement among researchers that vibrations of filaments of the microtubules (MT filaments) establish oscillating magnetic and electric fields.

As noted above, the microtubules form the structure of the centrioles: specifically, each centriole consists of nine "blades" of microtubule triplets (thus a total of 27 microtubules per centriole). The microtubules themselves are hollow cylinders whose walls are composed of 13 longitudinal filaments. The filaments are strings of α/β tubulin dimers connected end-to-end.

Figures 1-4 provide sketches of the structures of the centrioles, the microtubules, and the α/β dimers.

The α/β tubulin dimers have positive and negative charges at their ends. Thus when they are stacked together end-to-end in a microtubule filament, they are analogous to a series of batteries connected end-to-end, as in a long flashlight. During filament movement via their vibration oscillation these charged dimers produce an electromagnetic field [9]-[12].

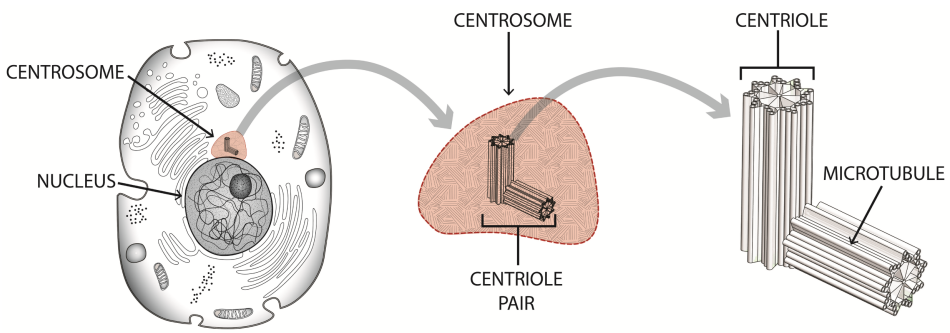

Figure 1. The structures of the centrioles.

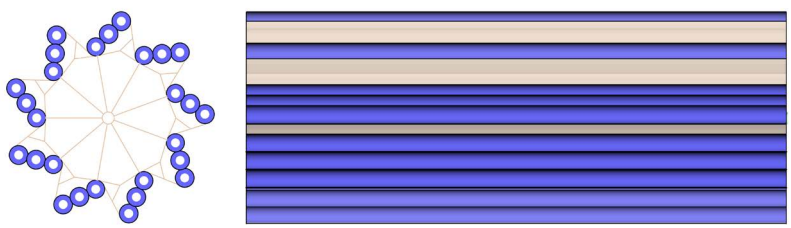

Figure 2. The structures ofthe microtubules.

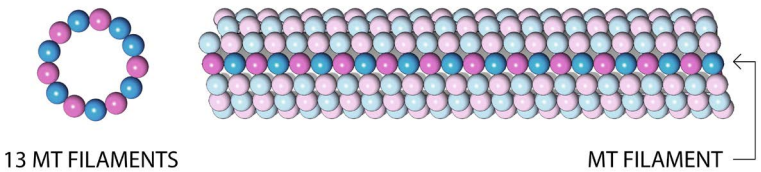

Figure 3. The structures of MT filaments.

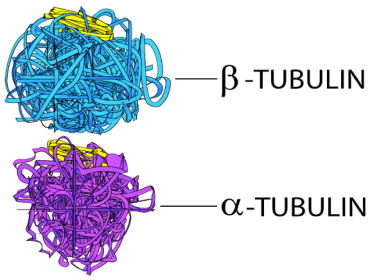

Figure 4. The structures of the α/β dimers.

The balance of the paper is divided into four sections with the first of these providing a background review for the sequel. The next two sections present evidences of electromagnetic effects and their magnitudes. The paper concludes with a brief discussion and envisions of applications of the findings.

2. Preliminary Considerations: Review of Centriole Duplication and Microtubule Development

The centrioles form a pair of perpendicular cylinders lying adjacent to the nucleus in all eukaryotic (human and animal) cells. The centrioles are hollow cylinders approximately 400 to 500 nm in length and 200 nm in diameter. Structurally they consist of nine blades of triplets of microtubules–themselves hollow cylinders approximately 25 nm in outer diameter and 15 nm inner diameter.

Of all the organelles and organs of the body the centrioles are unique in that they have straight-line geometries and no membrane cover. Also, their perpendicularity to each other is maintained since one of the pair (the "daughter") grows from the surface of the base of the other (the "mother"). The axis of the daughter thus intersects the axis of the mother at a right angle.

Although the details of centriole duplication and development are still under investigation, the generally accepted process is as follows [3]-[6]: During an intermediate time in the cell cycle ("interphase")—specifically, the "S-phase," a protein known as "asterless" attaches itself to one of the outside microtubules at the base of the about-to-become mother centriole. The asterless then recruits protein Plk4 ("polo-like kinase four") to form a base and govern the construction of a new centriole [85]. Plk4 is also known as (aka) "SAK".

Plk4 then distributes itself like a patch or base at the lower end of the mother centriole. Next with the aid of another protein STIL (aka "SIL") the Plk4 and SIL recruit yet another protein SAS6 atop the Plk4 patch.

At this point, the SAS6 expands symmetrically by developing nine spokes growing away from its center. The outer ends of these spokes form the seats of the microtubules with each spoke supporting three microtubules.

The microtubule bases and the microtubules themselves are composed of tubulin proteins: The bases consist of rings of gamma tubulin. These however are not flat (or planar) but instead their ends overlap so that they have the appearance of a lock washer [13]. Also, the rings are not uniform along their circumference but instead there are 13 equally spaced pores (or channels) through which the α/β tubulin dimers pass to form the filaments making up the walls of the microtubulin.

Surrounding the centrioles is a pool of as many as 100 proteins, an abundance of which are the α/β, and γ tubulins. This protein pool is known as the "centrosome" and also as the "microtubule organizing center" or MTOC.

The MTOC is believed to be "electron dense" [14]-[16] and thus the base of the centrioles is negatively charged and the distal ends are then positive.

3. Evidence of Electromagnetic Effects

As noted earlier there is a charge difference between either side of an open wound. This has long been known: It was discovered as early as 1860 by duBois-Raymond [7].

More recently in the 1960s and 1970s, Paul Schafer, while studying esophageal cancer cells, discovered disruptions in centriole geometries and also that similar centriolar geometric disruptions could be caused by strong electromagnetic fields [14]-[17]. Correspondingly, in 2008 and 2013 Pokorný, *et al.* reported that electromagnetic fields can cause cancer [18] [19].

In 1990 Weiss, *et al.* reported that animals with amputated limbs have a strong negative polarity on the stump [8].

The interest in electromagnetic fields both within biosystems and the effects of electromagnetic fields on biosystems greatly increased at about the turn of this the 21st century. Many investigators have identified the source of cellular electromagnetic fields as due to longitudinal vibration of microtubular filaments (e.g. [9] [12] [20]-[27]).

The most impressive evidence of cellular electromagnetic activity occurs during mitosis: First as a centriole pair is duplicated, the resulting two pairs push against each other and separate. Next, as the centriole pairs are pushed apart, the newest (or youngest) of the two pairs is driven around the nucleus to the diametrically opposite side, while the older of the centriole pair remains in place. Finally, the oppositely positioned centrioles send forth microtubules toward each other about the surface of the nucleus, thus making up the "mitotic spindle". At the same time the membrane of the nucleus between the opposing centriole pairs begins to soften and shrink. Microtubules emerging from the kinetochores, within the nucleus, extend and join the microtubules of the mitotic spindle and in this way separate the cell into two cells.

Figure 5 provides a representation of this event.

In elementary mechanics a "force" is often defined as a "push or a pull" [28]. In the foregoing description of mitosis, there is evidence of both pushing and pulling—and

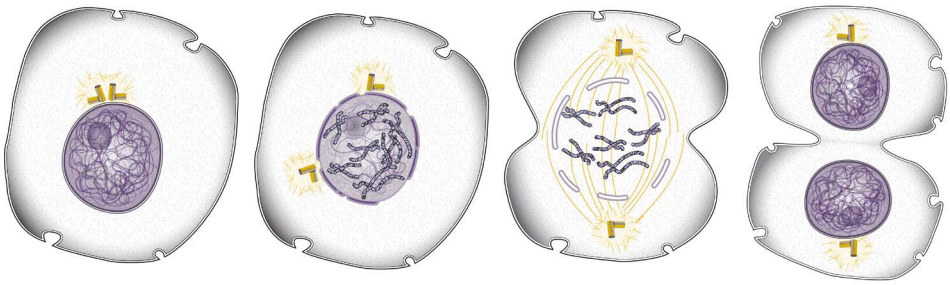

Figure 5. A representation of cell separation (mitosis).

also at a distance. Aside from gravity, only electromagnetism exerts forces at a distance.

Tumors composed of cancer cells provide additional expressive evidence of electromagnetic cellular activity. For example, breast cancer tumors produce a charge that can be measured externally [29] [30]. Correspondingly there is a voltage gradient between cancer tissue in tumors and neighboring normal tissue [31]-[34].

It is believed that the enhanced electromagnetic fields of cancerous tumors attract blood vessels which then expand and also become malignant [35].

Cancer cells are known to have supernumerary centrioles [26] [36]-[70]. These centrioles tend to cluster together [71] and these clusters are believed to be the source of the enhanced electromagnetic fields associated with cancerous tissue.

Other evidence of cellular electromagnetic effects is the aligning of chromosomes along the axis of the electric field [11], and as noted earlier, electromagnetic fields enhance blood vessel growth [35] [72].

Finally, some have suggested that the vibrating filaments within the microtubules are ferromagnetic [73]-[75].

4. Experimental Findings and Data

Unfortunately, due to the minute size of cellular tissue, there is a paucity of available recorded data about the magnitudes of cellular electromagnetics. However, improvements in microscopy and measurement techniques are likely to produce new findings in both the geometrical and physical characteristics of centrioles and their microtubules.

Here are some approximate data:

First, for wounds: in 2004 Zhao, *et al.* [30] reported that there is a voltage drop of 40 to 200 millivolts per millimeter (mv/mm) across open skin wounds. Also in 2004, Mycielska and Djamgoz [76] reported that transepitheliel potentials range from a few millivolts to tens of millivolts.

Next, at the other extreme, in the small, the data is even less precise. For example, Stracke, *et al.* [77] found the charge on a tubulin dimer to be 0.19e where e is the charge on an electron $\left(1.6\times10^{-19}c\right)$. Alternatively, other models based upon chrystallographic data predict values 50 times or more as large.

In like manner researchers have measured the tubulin dimer dipole moment (opposite end charges times separation distance) to be approximately 100 Debye [22] [78]

[79]. (A "Debye" is 10^{-29} cm.) Others have indicated the moment to be as large as 6000 Debye [80].

Although these are small numbers, Pokorný [81] indicates that the electric field near a microtubule can be as large as 10^8 v/m.

Finally, with electromagnetic fields being created by accelerating charges there is interest in the frequencies of microtubule filament vibration. These numbers range from kHz to THz with a typical value of 465 MHz [22] [82] [83].

5. Discussion and Applications of the Findings

Of all these findings, that of greatest interest is the role of electromagnetic fields in tumors and in tumorigenesis. As noted earlier tumors (particularly malignant tumors) appear to have greater magnetic fields than normal tissue. This increased field strength with tumors is believed to be due to the magnetic field strengthening by the supernumerary centrioles occurring in cancer cells. The field strengthening is believed to arise due to the resulting large number of vibrating microtubules. Also, as noted earlier, the supernumerary centrioles tend to cluster together [71].

The supernumerary centrioles, the clustering, and the enhanced electromagnetic field of cancer cells thus provide a biomarker for imaging and treatment.

A promising approach currently being pursued by a number of researchers is to use magnetically charged nanoparticles to be attracted by the enhanced magnetic field of the centrioles. The envisioned nanoparticles would be small enough to penetrate the cell membrane and then adhere to the centriole clusters. At this point the nanoparticles could achieve targeted drug delivery to cancer cells; alternatively the nanoparticles could be vibrated externally, also killing the cell via heating; or taken as a group, the nanoparticles could be used to image the tumor for precise surgical or radiation treatment.

There are two principal advantages of using magnetically charged nanoparticles for cancer treatment: First, normal tissue cells, having only a pair of centrioles, and thus a low magnetic field would not attract the charged nanoparticles. Second, the charged nanoparticles could be sufficiently numerous so that *all* tumor cells could eventually be eliminated.

A difficulty with using magnetically charged nanoparticles however is that they tend to cluster together and thus lose their effectiveness in reaching and penetrating the cancer cells. To overcome this problem, some have suggested using superparametric nanoparticles which can become magnetized in the vicinity of an electromagnetic field [84].

Much remains to be done before these concepts can be developed and tested.

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