Cellular Perception and Static Magnetic Fields Active Penetration Depth for Pain Magnetotherapy

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Abstract— Cellular perception concerns the process by which stimulation induces events through mechanical signaling pathways, according to a sense order whose nature is discussed by epistemology: It is supposed that the signification base at the origin of the cell behavior answers to a "being-envelope" whose physical nature can be approached in topological thermodynamics terms. In joined cells with gap-junctions, sense order can be covered by the signaling effect of calcium waves. But as it is related to the cell functional status, it can explain the biphasic response of the cell behavior after exposure to Static Magnetic Fields, SMF.

Four magnetobiological mechanisms solve the "kT paradox" about thermal agitation, (whose energy is $4 \cdot 10^{-21}$ J, at 310°K): 1/ Magnetosomes; (endogenous ferromagnetic nanoparticles can have magnetic moments of $2 \cdot 10^{-15}\,\mathrm{JT}^{-1}$). For ionic channels activation, these magnetosomes must operate two other kT independent mechanisms: 2/ Radicals' pair, and 3/ Interference in angular modes of proteins. A fourth mechanism is: 4/ Protons subsystems, (inducing topological evolution in the medium).

In these mechanisms, the SMF determining parameter is magnetic flux density, or induction B: When comparing clinical trials results about pain relief by SMF, an active induction threshold of 0.5 mT is suggested. With the field decay from the magnet surface, when B is around 0.5 mT, the lateral field gradient, dB/dx, is far under its active threshold, thus secondary. Therapy must determine the SMF Active Penetration Depth from the skin surface, as compared to the tissue receptors depth. It depends on the magnet characteristics and setting.

1. INTRODUCTION TO THE POSTULATE OF CELLULAR PERCEPTION

Cellular perception concerns the process by which the cell receptors stimulation induces biological events through mechanical signaling pathways, according to a *sense order* whose nature is discussed by *epistemology*[1]. *Cellular perception* supplements the molecular aspects of cell biology, because it includes two orders, *the causal order* which is about mechanical signaling and *the sense order* which is dependent on a more global mechanism. By example, the causal bioeffects of weak Electromagnetic Fields, EMF, may be apparently subtle [1]. But EMF gradients could offer cell guidance criteria capable of influencing cell migration, orientation and function [2]. Now articular cartilage health state depends on the functional state and differentiated functions of the cartilage matrix cells which are the chondrocytes [3]. These chondrocyte state and functions may be related to changes in the actine fibers of the cytoskeleton [4]. These spatial changes may result from transduction of signals coming from the cartilage matrix, which are associated with the control of gene expression [5]. Through changes in surface topologies, spatial changes can help to overcome the effect of inflammatory factors on chondrocyte response [6]. It is conjectured that changes could depend on a topological *sense order* in the cellular perception:

According to *epistemology* (as it results from *the philosophy of nature* [7, 8]) any independent cell without gap junction[2] is *a simple natural being* which has an intrinsic unit. In this case, its perception *sense order* is stated to be neither local nor subjective. It is asserted that the *signification base* which is at the origin of *the cell behavior* answers a "*being-envelope*"[3] whose physical nature is *global* and *topological.* Insofar as the *sense order* of the individual cell answers its *topological being-envelope,* the cell behavior can be modulated by its *surrounding topological structure.* Cell-cell contact may inhibit this individual effect: The possible Static Magnetic Fields, SMF, action on chondrocyte metabolism is thus inhibited if the concentration of cultured cells is

[1] With simplest, *epistemology* is the philosophy of sciences. But it also aims at locating science in an experiment of knowledge which overflows it and which is reduced finally to *the biological problem of perception*

[2] A *gap junction* is a local membrane vacuum acting as a ionic channel across membranes of two joint cells.

[3] In Whitehead and Merleau-Ponty doctrines of *organic mechanisms*, as Toscano [9] indicated, *life* is considered as a structure or a *being-envelope* for micro-phenomena; it is a relational *architectonic* that sets constraints on phenomena at lower scales. *Architectonic* means here: globally structuring, as by a qualitative topology envelopment effect.

too high [10]. In those *in vitro* joined cells, the lack of individual modulation by medium topology is covered by the gap-junction functioning, particularly through a calcium waves' effect [11].

Because of the cellular sense order, a same Ca^{2+} influx in cells exposed to SMF can be translated in a biphasic biological response. Xu [12], then Okano [13] described SMF enhance vasodilatation if vessels are relatively vasoconstricted and enhance vasoconstriction if vessels are relatively vasodilatated. Mayrowitz [14] suggested the local thermodynamics modulates this bioeffect. This idea agrees with the theory of the topological thermodynamics environment, presented by Kiehn [15].

Sense order in the cellular perception is epistemologically asserted to be the soil containing the root of *cell behavior*. While acting on the medium topological thermodynamics structures, then acting upon the cellular *sense order*, stimulation by EMF may indirectly modulate the *general behavior* of the cell. For cultured chondrocytes, the starting *guidance* is that of the only electrostatic structure of the medium, such as a galvanotaxis [2, 16]. Under Pulsed EMF, PEMF, stimulation, (not SMF) a *topological structuring* can translate into morphological changes [17]. More generally the topological aspect of the full organism sense order could allow perturbations in ambient EMF activity to impact on human behavior in a clinically meaningful manner [18]. And workers exposed to perturbed EMF may have an increased brain tumor incidence attested by epidemiologic data, even if EMF mechanical effects, through an increased cytosolic calcium concentration, $[Ca^{2+}]_c$, are neither mutagenic nor tumorgenic [19].

2. BIOLOGICAL INTERACTION WITH STATIC MAGNETIC FIELDS

Sense order and possible bioeffects of PEMF and SMF gradients: From 0.6 to 6 mT, SMF may inhibit apoptosis in cells hit by apoptogenic agents, by interfering with the apoptotic process through an alteration of Ca^{2+} fluxes [20]. But as calcium flux plays a role in cell shape regulation [21], a possible occurrence of morphological changes in cell surface, depending on cells type, has also to be considered [22]. Now without any modification of cell shape, a majority of hit cell types rescue from apoptosis after a 6 mT exposure, when a promotion of apoptosis may be observed in some other types of hit cells [23]. Could it be because of a SMF topological effect acting upon the cellular *sense order*, but not on the cell morphology?

Eichwald and Walleczek [24] proposed a model of EMF regulation of cell calcium dynamics through a *feed-back* leading to a modulation of calcium entry. Such a *feed-back* is linked to the cell biological-functional status, itself linked to the *sense order* in perception. This status, then *sense order*, would induce the biphasic response behavior from the same EMF action on the cell calcium signaling. But there is a big empirical difference between the PEMF and SMF possible effects on morphological changes:

The biggest difference between PEMF and SMF structuring effects concerns the time derivative of magnetic induction, the *temporal gradient*, $\delta B/\delta t$, which induces electric fields. Many PEMF clinical tests highlighted the therapeutic interest to apply pulsations with a *temporal gradient*, $\delta B/\delta t$, set between 1 and 10 mT/ms [25]. Now, applied SMF offer no *temporal gradient* in a resting body. SMF can only offer a *spatial gradient*, particularly a *lateral gradient*, $\delta B/\delta x$. With SMF produced by homopolar disk magnets, a peak gradient region exists in a limited ring, just peripheral to magnets. Such a peak gradient region is reinforced in multipolar magnets. This way, Cavopol [26] observed bioeffects in this peak region and suggested that the *lateral gradient threshold* for effective pain relief by neurone blockade, is around 0.5 mT/mm. Okano [27] showed a behavioral effect, (an endothelial tubular formation,) is promoted by SMF *lateral gradient*, 28 mT/mm, (when uniform SMF, 20 or 120 mT, did not). No effect had been shown for low intensity SMF gradients, even if they affect the medium topological structure.

Now, as showed by Kiehn [15], for non-equilibrium systems, topological dimensions of $\delta B/\delta t$ and $\delta B/\delta x$ are different. It implies the integral over time cannot be the same as the integral over space. This way, $\delta B/\delta t$ cannot be biologically equivalent to $\delta B/\delta x$, and therefor PEMF and SMF effects on topological structuring are not equivalent. However SMF may induce bioeffects where PEMF do not: Chiu [28] observed that SMF could promote osteoblast-like cell differentiation, via increasing *membrane rigidity*. With contrast, Jahns [17] supposed PEMF effects involved the *reorientation of membrane molecules*.

The most general target: The target for SMF interactions is generally assumed to be the *cellular membrane*. Ayrapetyan [29] suggested that the general target for SMF & PEMF interactions could be the *aqueous medium* bathing the membrane, then acting on the cellular membrane components. Further more, the most general target could be the *aqueous physical environment* which consist of the fields that bathe H_2O molecules and other chemical components in the environmental space.

A model of topological thermodynamics for non-equilibrium systems has been described by Kiehn [15]. A key result is that EMF interaction is a cubic curvature not involving the forces generated by the E and B fields, but the A and Φ potentials and the charge current densities. Similarly, in the quantum approach of Binhi, 2007 [30], the state of a molecular target interacting with low frequency MF can be described not through forces, E and B, but through potentials A and A_O, as in the Bohm-Aharonov effect.

Andocs [31] used this idea to demonstrate that when two charged particles create a chemical bond, their interaction could be changed by an external *magnetic vector potential A*. The effect would apply to the bifurcative phenomena of hydrogen bonds in water, bringing some topological thermodynamics changes in protons subsystems.

The four possible primal mechanisms for SMF interactions: Simultaneously, the applied magnetic induction B may interact on molecular targets only through a few physical processes. Binhi [30] demonstrated that four possible mechanisms of magnetobiological effects directly solve the kT paradox about thermal agitation, (whose energy is $4 \cdot 10^{-21}$ J at 310°K [32]):

1/ Magnetosomes. (Endogenous ferromagnetic nanoparticles can have magnetic moments of $2 \cdot 10^{-18}$ J/mT, whose reorientation, under more than 2 mT, exceed thermal agitation., for a ionic channel activation, it must be associated with a stochastic resonance and operate the two following mechanisms [33]:

2/ Interferences in angular modes of proteins. (Interference of quantum states of bound heavy ions involve natural active biophysical structures [34]. And, ion-channel gating interactions may stem from locally SMF enhanced drift velocities [35].)

3/ Spin orientations in free radicals. (There are two aspects: Radicals' pair mechanism [36] and Mechanism of enzyme reactions involving metal radical ions with large hyperfine constants, as in anti-oxidative system, easily altered by SMF [37].)

4/ Aqueous medium structuration, through proton subsystems. (Hydration structure and translocation of protons affect aqueous domains [38], and modulate some membrane-bound hydrated protein activity [39, 40].)

When these primal physical mechanisms act on cellular receptors molecules, what can be the magnetic induction threshold which induces a pain relief effect?

3. THE ACTIVE PENETRATION DEPTH OF STATIC MAGNETIC FIELDS

Free radicals mechanisms act on biological reactions through non-linear complex processes and could be preponderant when the applied SMF exceed 1 mT [33, 41, 42]. However a causal effect of SMF depends also on the other coupled mechanisms. So that Fanelli [20] showed a 0.6 mT minimal threshold in cells cultured *in vitro*. Can the calcium ion-channel gating which depend on cell receptors be acted *in-vivo* for a 0.5 mT SMF threshold?

3.1. Objective: To Check the Weintraub's SMF Active Threshold

The empirical results of Weintraub [43] suggested that the minimum threshold for MF detection by the receptors of *in vivo* biological targets is around 0.5 mT. This Weintraub minimal limit comes out from his comparison of trials of weak SMF acting upon neuropathic pain. In one of these pathologies, the receptors of the sensitized afferent pain fibers are only at few mm below the skin surface. Despite the very strong field decay, the used multipolar magnets placed at some mm over the skin could then offer more than 0.5 mT at the receptors distance. But in another trial the concerned neuroreceptors were too deeply seated in the body, at a distance exceeding the SMF 0.5 mT Active Penetration Depth, APD. For this reason, the first study results showed a significant pain relief and the second not.

3.2. Method: As Weibtraub, to Carry out Another SMF APD Comparison in Two Similar Trials

Field decay and the Weintraub limit can explain clearly the opposite results between the Alfano and Colbert trials of SMF for fibromyalgia treatment. Alfano [44] used powerful magnets, offering more than 400 mT on surface, but he sets them under mattress, well below the patient. Colbert [45] used less powerful magnets, 110 mT on surface, but she sets them closer to the patient, in upper mattress. We have calculated the field decay at a distance d from the surface of similar magnets, by checking the approximation of the square law, k/d^2, through systematic measurements at variable distances with the help of a Gaussmeter, (model HT23). The result yields two response curves, A, Colbert setting, and B, Alfano setting, drawn on Figure 1.

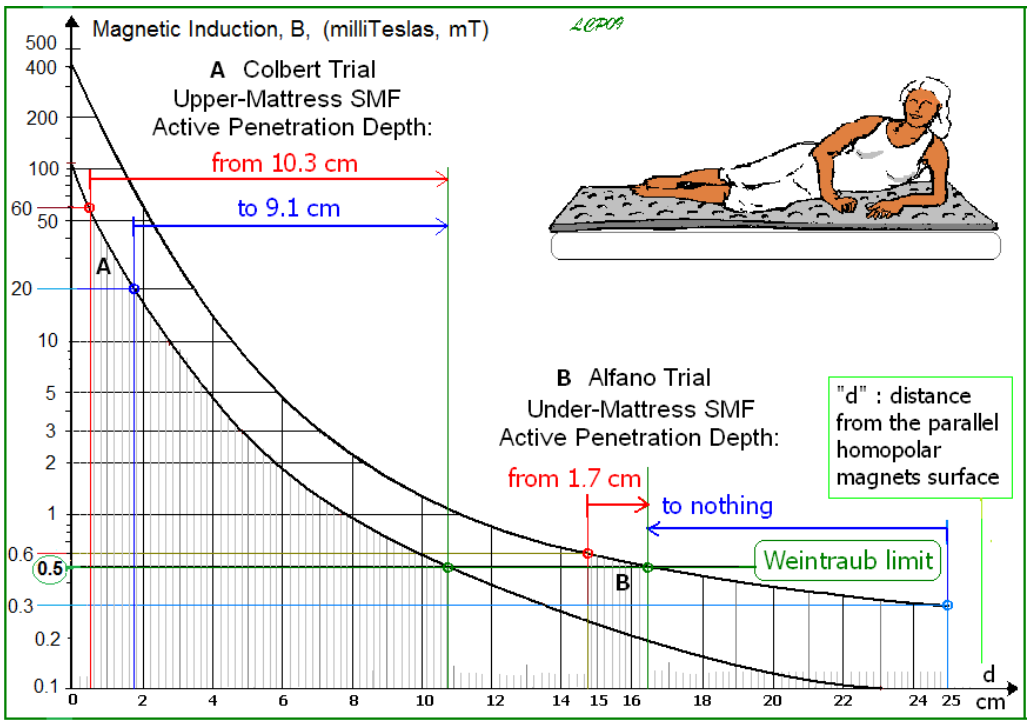

Figure 1: Static magnetic fields active penetration depth, in compared clinical trials for fibromyalgia treatment (Magnetic induction is scaled in milliTeslas, mT, with 1 mT = 10 Gauss).

3.3. Results

In the Colbert trial, the upper mattress magnetic pad offers between 60 et 20 mT at the skin surface level. For the 5 Gauss, or 0.5 mT, threshold, a graphic calculation using Figure 1 shows an active penetration depth, APD, of 10.3 to 9.1 cm, inside the patient body. This way Colbert SMF bioeffects were able to stimulate the deep peri-rachidians receptors which are relative to the pain ways.

In the Alfano study, the under mattress magnetic pad allows an active penetration offers between 0.6 and 0.3 mT at skin surface level. Graphic calculation from the Figure 1 shows an active penetration depth of 1.7 to zero cm. Alfano SMF bioeffects could thus concern only some surface receptors of the patient body.

Finally Colbert could observe a significant pain relief and a functional status improvement, when Alfano could only observe non-significant bioeffects, which is in good agreement with a 0.5 mT threshold. In the region around this threshold, the measured maximum of lateral gradient, $\delta B/\delta x$, is less than 15 µT/mm, far under the active limit of 0.5 mT/mm, thus as a secondary causal parameter for pain relief.

4. CONCLUSION

In order to obtain a pain relief in physiopathological situation, it is assumed that the causal order in the cellular perception needs SMF induction more than 0.5 mT at the receptors level. Based on this threshold, the SMF active penetration depth, SMF-APD, appears to be an important SMF therapy parameter. This parameter can be determined with the help of a Gaussmeter. Moreover, the principle of sense order in the cellular perception could explain the bioeffects of qualitative tiny magnetic fields, through an interaction within the topological thermodynamic structure of the aqueous medium.

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