Spatial and Temporal Electrodynamics in Acuzones: Test-Induced Kinematics and Synchronous Structuring. Phenomenological Study

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ABSTRACT

Background: So far there is no confidence in the basics of acupoint/meridian phenomena, specifically in spatial and temporal electrical manifestations in the skin.
Methods: Using the skin electrodynamic introscopy, the skin areas of 32 × 64 mm² were monitored for spectral electrical impedance landscape with spatial resolution of 1 mm, at 2 kHz and 1 MHz frequencies. The detailed baseline and 2D test-induced 2 kHz-impedance phase dynamics and the 4-parameter time plots of dozens of individual points in the St32-34 regions were examined in a healthy participant and a patient with mild gastritis. Non-thermal stimuli were used: (1) (for the sick subject), microwaves and ultraviolet radiation applied alternately from opposite directions of the meridian; and (2) (for the healthy one) microwaves to St17, and cathodic/anodic stimulation of the outermost St45, alternately.
Results: In both cases, the following phenomena have been observed: emergence of in-phase and/or antiphase coherent structures, exceeding the acupoint conditional size of 1 cm; collective movement along the meridian; reversible with a reversed stimulus; counter-directional dynamics of both whole structures and adjacent points; local abnormalities in sensitivity and dynamics of the 1 MHz and 2 kHz parameters indicating existence of different waveguide paths.
Conclusion: It is assumed that these findings necessitate reconsideration of some basic methodological issues regarding neurogenic/acupuncture points as spatial and temporal phenomena; this requires development of an appropriate approach for identifying the acuzones patterns. These findings may be used for developing new approaches to personalized/controlled therapy/treatment.

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large area of the skin to assess its 2D electrodynamics in real time.

In the context of this report, it is also worth mentioning the recently proposed concept of “acupoint sensitization,” where AP's in a sensitization state are dynamic in variability. In clinical application, only the 2-step location method, preliminary and accurate localizations (sensitive probing localization) from the Internal Classic, can localize the AP's precisely, rather than a 1-step location method such as a proportional measurement or body surface landmark localization. The nature and property of AP's are different based on the functional state, as AP's are not just in fixed locations’ [20,21].

The initiative for the project began back in the 1980s after realization that in order to reliably localize/measure an invisible, non-stationary object, it is necessary 1st to develop a method for non-invasive visualization of its entire habitat, i.e. its skin electrodynamical landscape (SEL). A series of laboratory-clinical experiments were carried out in the clinics of Kiev Research Institutes of Traumatology and Neurosurgery using an early sample of the skin electrodynamical introscopy (SEI) with a spatial resolution better than 1 mm [22]. However, among dozens of examined patients, not a single case of a point-sized AP was located, but only a few small electro-abnormal spots at least 3-4 mm in size, and only on the auricle (Fig. 1). Using an improved scanner sample, a phenomenon of test-induced wave-like propagation along the pericardium meridian (PC5 and 6) at a speed in the range of known calcium waves, and a corresponding hypothesis had been proposed [23,24]. That Ca\(^{2+}\) wave hypothesis is consistent with current concepts of the role of Ca\(^{2+}\) in the biophysics of meridians [25]. These early results went unnoticed in the TCM community, possibly due to the lack of similar tools to validate these results. Oddly enough, the device is still unique, because known impedimetric scanners [11,18,26] do not provide proper metrology (i.e., high resolution within 5-10 cm\(^2\) and sufficient speed, not yet mentioning the multiparametry) to reveal/monitor a whole dynamic structure with a size of several cm\(^2\).

These early SEI findings, unnoticed in the TCM community, predetermined the choice of malignant skin tumor (melanoma) as the next model, for which intercellular Ca\(^{2+}\) signaling disorders are generally considered an early diagnostic sign. With the aid of modern SEI sample, the new phenomena of test-induced (MF, mm-EMF, hypoxia) coherent in phase and antiphase SEL clustering in the affected tumor environment had been revealed. It was also assumed that similar cooperative processes may be characteristic of functionally abnormal areas [27,28]. The calcium signaling abnormality was not the only analogy of AZ with tumor. As reported, the accumulation of microvessels in AZ's, as well as in the tumor, was considered a clear characteristic, which could be seen in the surrounding tissues [29-31]. Thus, it may be assumed, that in AZ, as in any functionally heterogeneous living tissue, the phenomena of clusterization should also be present, and be especially pronounced in response to a proper test stimulus.

With this work, we return to the original basic problem of AZ identification using a modernized SEI sample.

**Materials and Methods**

The aim of the study was investigation of the initial and the test-induced electrodynamical landscape of the AZ's and thus identify their distinctive features as spatio-temporal structures. Fig. 2 shows a general view of the modified SEI setup, including: sensory head, tripod, measurement unit, laptop and battery power supply. A monopolar method (with a large indifferent electrode) was used, which allowed measuring of the transverse impedance of the skin. The sensory head was a matrix (2048 stainless steel electrodes of 0.6 mm\(^2\), 1 mm pitch, spanning a 32\(\times\)64 mm\(^2\) area) combined with a specially developed multiplexer. The measurement unit (Fig. 2, left) included a sinusoidal current generator of 1-20 μA at 2 kHz and 1 MHz. Four parameters: modules \(|z_k|\), \(|z_M|\) and phase angles \(\phi_k\) and \(\phi_M\) (subscripts k and M mark the kHz and MHz-frequencies) of the spectral impedance \(Z=|z|e^{j\phi}\) were simultaneously measured (further, \(z\) -without brackets). This frequency span enabled the distinction of physiological events happening at the intercellular and intracellular level. The measurement cycle for 1 pixel took 4 ms, making 8 s a full frame.

**Data analysis**

To assess SEL dynamics, we used: image differencing, correlation analysis, calculated fields of dispersion, and graphical analysis of
the temporal dynamics of chosen points/pixels. To eliminate the time drift of the mean contact impedance, if appropriate, the image matrices were normalized (MV = 0, σ = 1).

Testing means and procedure

The following devices were used: mm-EMF1 microwave generators of extremely low intensity (< 0.1 mW/cm², 54-75 GHz) (“Porog-1”); mm-EMF2 microwave generators of therapeutic intensity PTO-013 (< 10 mW/cm², 60-62 GHz, with horn antenna), both generators were approved for application by the USSR Ministry of Health, 1989); UV ultraviolet emitter (XP-UV-16 mm, 395-400 nm, 3 W) in a cylindrical mandrel (Ø20 mm, h = 15 mm): electrical stimulator ES (self-made electrical constant current generator, battery powered, ±12 V, 0-100 µA). The active electrode: stainless steel, 0.4 mm, cotton wool soaked in saline. The passive electrode: a stainless steel mesh electrode fixed on the sole. The magnitude of the current was corrected by the patient himself until a sensitive, but quite tolerable sensation was achieved, which was 20-30 µA. The potential impact of the on/off transient processes was excluded by ensuring the smooth rise and fall of the current. More information about the method has been reported [27,28].

Subjects

There were 2 volunteers: Experiment 1. A 79-year-old man, who was originally identified as a healthy subject (he was in excellent physical shape for his age), but then, according to the results of the experiment, his forgotten diagnosis “duodeno-gastric-esophageal reflux” was taken into account, and Experiment 2. A healthy 45-year-old man.

Since this study is phenomenological (with a focus on the study of various test factors), we did not initially set the goal of identifying diagnostic signs of gastritis, and so the same stimuli was not used for both subjects.

Ethics approval and consent to participate

All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Results

Experiment 1

The experiment consisted of 4, one by one stimulations of the stomach meridian from opposite directions, by UV and mm-EMF expositions: firstly, onto more distant AP’s -St17 and St45, and then, similarly, onto the 2 adjacent AP’s to the scan-area as marked with circles in Fig. 3a.

Experiment plan: “0” was the preliminary stage of 10 frames (to evaluate the process of adaptation to the measurement procedure), followed by a 10-minute resting state (with the scanner position unchanged).

The main experiment consisted of 9 stages “1st -9th” with a total duration of 8 minutes (8 s × 60 frames):

1st. - pre-stimulation resting state, series of 15 frames (2 minutes); 2nd. - UV1-exposure to St17, 5 frames (40 s); 3rd. - post-stimulation resting state, 5 frames; 4th. - mm-EMF1-exposure to St45, 5 frames; 5th. - post-stimulation resting state, 10 frames; 6th. - UV2-exposure to the near upper AZ (an extrameridian AP between St31 and St32), 5 frames; 7th. - post-stimulation resting state, 5 frames; 8th. - mm-EMF2-exposure to St33), 5 frames; 9th. - post-stimulation resting state, 5 frames.

A photo of the surveyed area is shown in Fig. 3a, where, according to the AP atlas, the St32 and the nearest extra-meridian AP’s are also approximately marked. The initial maps of impedance magnitude/modulus z and phase angle φ are depicted at Figs. 3b and 3c. Both maps are presented in normalized values, p < 0.01. The red/blue colors indicate areas of above/below average.

Since the “impedance magnitude” is customary to use in most electropuncture measurements, it is the z-map which has been chosen as a reference in the analysis of the φ-landscape, more so because, as far as we know, such a comparison between mainly capacitive and resistive SEL features was not performed earlier. The above average z-area (“1”) is marked with a contour on the φ-map. Within the latter, 2 AZ’s, apparently matching with St32 and Pn96, are marked as 1° and 1°. A quantitative comparison showed that these AZ’s differ from the background by approximately 10 and 3 times for φ and z respectively. For both zones, the palettes were similarly chosen to highlight the initial inter-parameter topological differences as a prerequisite for the following test-induced processes. Noteworthy was a noticeable difference between φ and z-maps in the zones “2” and particularly in its subsection Zone “2” (which presumably coincides with Pn94, Fig. 3a), whose reliefs even have the opposite sign. A comparison of Fig. 3b and 3c revealed other

![Fig. 3. a-c). Dynamics of some AZ 1a points. a,b) Initial z- and φ-time curves of 6 neighboring points in real parameters; c) The 4-parameter dynamics of p.8x18, p.7x17, and the frame-averages in normalized values](image-url)
noticeable differences: not only in dimensions of Zone “1”, but also in 1-2 mm mismatch of the foci in Zone 1 and 2.

Some functional peculiarities of the \( \phi_k \)-landscapes appeared already at Stage “0”. Figs. 3d and 3e showed the correlation fields calculated for each pixel time curve relative to the frame-averaged curve during “0”-stage and “1”-stage, respectively. The Zone “1” manifested itself in the very 1st frames by its antiphase response as a coherent dynamic structure of considerable size (d), which shrank to 2 small structures (e) that exactly matched the topography of St32 and Pn96 on the AP atlas. At the same time, however, one can note the existence of a 2.5 mm gap between these “functional” location and the stationary one, i.e., 1st. Similar, but less visual, the process of decreasing distant antiphase microstructures can be traced throughout the entire scanning zone in the hypothetical AZ Pcs158 (2°). The time curves of the 6 adjacent points of Zone 1a are shown in Figs. 4a and 4b. From the very beginning, one of the central points (p. 8×18) stands out with a more pronounced reaction and paradoxically opposite dynamics (the St32 candidate?). The latter is more pronounced in the \( \phi_k \)-parameters. Fig. 4c shows normalized graphs of p. 8×18, p. 7×17 and the average values of all 4 parameters throughout the experiment (other examples of the diverse dynamics in Supplement Materials, s1-s3). Hence it follows that the adaptation process was completed by the beginning of 1st stage (the downward trend of \( z_k \) and \( z_M \) is caused by gradual penetration of electroconductive cream into the epidermis). The course of the frame-averaged curves indicated that for the majority of pixels, the response to stimulation was characterized by “normal” antiphase dynamics of intra- and intercellular parameters: \( \phi_k \) vs \( z_k \), \( z_k \) vs \( z_M \), i.e., as a predominance of transmembrane ion exchange. Especially interesting was that during 6th-8th Stages, it was a kind of dynamic which was most pronounced at the p. 8×18 in comparison with the average. It can also be noted that the phase relationships between p. 7×17, p. 8×18 and \( \phi_{ka,av} \) varied to the opposite at different stages, which may indicate participation of other mechanisms. It is also interesting that this phenomenon was not observed in the \( z_M \)-dynamics of these points. However, such inter-parametric relationships can hardly be attributed to the distinctive features of only AZ, since they are presumably typical for many, if not all, micro-areas with initially antiphase dynamics, Fig. 3d.

The discrepancy between the time curves of the low-frequency and high-frequency parameters of the “strange” points (Fig. 4; Supplement Materials, s1-s3) was presumably explained by: local release of Ca\(^{2+}\) from intracellular stores, which increase only intracellular conductance, while intercellular conductance remains unchanged; and vasoconstriction, which mainly affected the phase component of the impedance, and exits to the skin surface along PVS collaterals.

It is pertinent to note that the phenomenon of antiphase dynamics, which was reported in malignant tumor surroundings using SEI [27,28], was also observed in an AP locus using just a pair of point electrodes. Wherein, the author hypothesized the existence of “an electrical wave” as an instant communicator between an internal organ and an AP, and this wave affects also impedance of the surrounding tissue [32]. We believe that such dynamics can rather be explained in terms of 2 concepts: a hydromechanical model of pore fluid flow along the meridians [33-35], according to which the incoming stimulus might shift circulation of interstitial fluid to neighboring areas; and intra- and inter-cellular signaling where calcium ions may play a pivotal role [27,28,36,37].

In this present study, only a few such “coupled points” were detected (see "Supplement Materials"). Taking into account (i) their location in the most active zones and (ii) the report [32], it seems likely that such a dynamic is a distinction criterion of AP.

The differences in sensitivity and direction of the response of the intra- and intercellular media can be presented more clearly by pairwise comparison of the curves \( \phi_{ka,av} \), \( \phi_{ka,av} \) and \( z_{ka,av} \), \( z_{ka,av} \), Fig. 5. The above assumption on the \( \phi_{ka} \)-informational significance is seemingly confirmed by its pronounced responses to the mm-EMF tests (especially to mm-EMF1 as a weakest stimulus): a noticeable response was detected in only a few of the dozens of points studied. In these cases, only the subcellular parameter \( z_{ka} \) showed maximum sensitivity. In addition, at a number of points, a 10-20 s delay in response to UV was observed, while any delays in response to mm-EMF “on” were not detected (however, the cooperative \( \phi_k \)-response to mm-EMF1 “off” clearly manifested in the spatial dynamics, Fig. 6). Taken together, these facts support the hypothesis of different communication channels/waveguides for electromagnetic waves in the microwave and optical ranges.

Spatial variations of the \( \phi_k \)-activity for all 1st-9th stages are shown in Fig. 7 as dispersion fields for each stage. In order to adequately display the dynamics in areas with small \( \phi_k \)-values of Zone 1, it turned out to be expedient to use relative units \( \sigma(\phi_k)/\phi_k \), where: \( \sigma \)
is pixel variance over the frame, \( q_k \), its magnitude. The colored side arrows indicate the type and direction of the stimulus applied.

Without going into physiological interpretation, we formally report the possibility of monitoring initial and test-induced AZ’s or neurogenic spots. Hence it becomes possible to compare/assess the spatial redistributions of activity during periods of, e.g., stimulation and relaxation which in this case occurred mainly in the Zones 1 and 2. Variations in activity within the AZ 1a and 1b, as well as those at 1s and 2s are also noteworthy. The most conspicuous event was the test-induced shift in activity to the right side (d). (Without taking into account the depth of the relief, this event would have shown greater contrast, but against its background, the dynamics in “1” would have been indistinguishable).

This dependence of the response on the direction of applied stimulus can seemingly be related to Kim’s [38] statements that stimulation often travels only to the next AP along, and sometimes to the following one.

Fig. 6 demonstrates the frame by frame spatial \( \phi_k \)-dynamics for 4th-6th stages in normalized difference images, i.e. \( \Delta \)-maps calculated in relation to the frame #23 of the III stage (Figs. 4 and 5). a) the \( q_k \)-original landscape, b) the \( \Delta \)-map between 2 last images of the 3rd stage (i.e., frame # 24- frame #23) followed by \( \Delta \)-maps of: c-v) the 4th stage; h-p) the 5th stage; r-v) the 6th stage; w) 1st frame of the 7th stage, thus showing the start of response to the UV2 off. The loci of AZ’s 1a and 1b are marked with “+” and “×”. To the left and to the right of the image sequence, line profiles crossing the AZ 1a are shown. They provide an additional idea of both: dynamics of the AZ and (ii) offset of a profile relative to the zero level. The sign +/- of this deviation determines red/blue palette, whereby indicating the boundaries of the clusters*. As seen from the profiles, the test-induced magnitudes can be, e.g., 6 times higher compared with 0 and w) and more. Since the fluctuation error was less than half of 1 scale division of the profiles, it was not taken into account when specifying the color scale.

As can be seen from Fig. 6a, there were no significant changes during the last 2 frames of the previous 3rd stage, i.e., the landscape is a relatively flat surface with just small local physiological variations against the background of minor 50Hz-interference. The mm-EMF1 on triggered immediate deformation of the entire landscape in the form of: 2 local “ridges” around, a large one in Zone “2”， and a “hollows” between them. At the same time, the “hollows” seems to be oscillatory as if around the 1st and 2nd islets. Meanwhile, the ridge “2” faded out quickly after the 3rd frame.

The mm-EMF1 off, with 1 frame delay (h), stopped these processes and launched a completely different scenario. Starting from Zone “1”, in place of the “hollows” a new structure gradually emerged and grew, propagating in the direction of 2s, i.e., along the meridian. The speed of the front propagation was approximately 0.3-0.5 mm/s, which was close to Kim’s [38] measurements (0.3 mm/s).

The response to UV2 “on” was not instantaneous as that of mm-EMF1. It became noticeable only after 1-2 frames (r, s) delay, during which the aforementioned propagation was reversed, and

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*Fig. 5. The frame-averaged 4-parameter dynamics. The two pairs of normalized curves Zk,n,av, ZM,n,av and \( \phi_k,n,av, \phi_M,n,av \) demonstrate distinctions between the extra- and intracellular dynamics throughout the experiment.

Fig. 6. The frame by frame spatial \( \phi_k \)-dynamics during IV-VI stages. All normalized difference \( \Delta \phi \)-images/maps are presented. The loci of AZes 1a and 1b are marked with “+” and “×”. To the left and to the right of the normalized difference \( \Delta \phi \)-images, the profiles for an arbitrarily selected section are shown. The radar and light bulb icons indicate the stages of mm-EMF2 and UV2 tests, respectively. a) the original landscape, b) difference image of the two frames preceding the mm-EMF2 test (i.e. frame # 24-frame #23 at Fig. 6a); c-v) the IV stage; h-p) the V stage; r-v) the VI stage; w) 1st frame of the VII stage, thus showing the response to the UV off. To the left and to the right of the frame images, profiles are shown for an arbitrarily selected section, which gives a quantitative idea of the magnitude of changes relative to the zero level and, accordingly, the formation of color patterns/clusters on the image sequence (p < 0.01).
in the next 3 frames it disappeared (reduction to the size of 1\(^a\) and 1\(^b\). This revers, on the other hand, can be characterized as the reappearance of the “hollows” (compare the neighboring maps e and s) and its progress from 2 to 1, i.e., again along the meridian, but in the opposite direction.

The spatial coherence of these processes is represented as a correlation field in Fig. 8, which was calculated relative to the dynamics of \( p \) in the 3\(^{rd}\)–4\(^{th}\) stages and which clearly revealed the antiphase synchronous dynamics of the right vs left sides with a range of \( r = \pm 1.0 \) (\( p < 0.1 \)).

The noticeable differences in the delay time of the reaction to UV and mm-EMF, which were also manifested in the graphs (Figs. 4, 5, s1–s3), show evidence in favor of the hypotheses of different waveguide paths of signal propagation. This, in principle, does not cause surprise due to the large difference in wavelengths of optical and microwave radiation. Collagen, interstitial fluids, vessels including the primary vascular system can act as such waveguides [41–46].

**Experiment 2**

The experiment consisted of 11 stages (13 minutes), during which only once was a stimulus (mm-EMF2) applied to the upper side of the meridian, whereas the next 4 stimulations were applied one by one, from the side of the lower AZ St45:

1\(^{st}\)- pre-stimulation resting state, 13 frames (100 s);
2\(^{nd}\)- mm-EMF2-exposure to AZ St17, 11 frames;
3\(^{rd}\)- post-stimulation resting state, 10 frames;
4\(^{th}\)- cathodic electrical stimulation (CES) of the lowest AZ ST45, 5 frames;
5\(^{th}\)- post-stimulation resting state, 5 frames;
6\(^{th}\)- anodic electrical stimulation (AES) of AZ St45;
7\(^{th}\)- post-stimulation resting state, 5 frames;
8\(^{th}\)- cathodic electrical stimulation of AZ St45, 10 frames;
9\(^{th}\)- post-stimulation resting state, 5 frames;
10\(^{th}\)- anodic electrical stimulation of St45, 5 frames;
11\(^{th}\)- post-stimulation resting state, 5 frames.

The investigated skin area, with AP marks according to the AP chart, is shown in the photo of Fig. 9a. The initial \( z_k \)- and \( \phi_k \)-landscapes are presented at Fig. 9b, 9c, in real values (\( p < 0.01 \)). The black and white palettes were chosen so that the AZ’s St33 and St34 looked similar. Assumed boundaries of AZ St33 and AZ St34 were marked as “1” and “2”, respectively (these boundaries were not chosen arbitrarily, but determined as shown below, in accordance with the 4\(^{th}\) test). The digit “3” denoted an additionally identified area of increased sensitivity. It can be seen that the marked zones covered areas of predominantly maximum \( z_k \) and \( \phi_k \) values. The boundaries of the zone of indeterminate origin “4” were determined in response to the anodic stimulation (6\(^{th}\) stage).

Note. Visually, this area was no different. The assumption that this initially active area (Fig. 10a) was manifested due to increased pressure of the scanner on the skin does not seem entirely reasonable. At the edges of the scanning head (they are not rounded), the pressure is maximum, which was invariably determined, in contrast to Zone 4, had higher \( z_k \) and \( \phi_k \) values (compare Figs. 9b, 9c, 10a, 10b. Presumably, this zone is a neurogenic spot or/and microcirculatory network with a predominant (compared with the surrounding tissues) connection with a lateral branch of the femoral artery.

**1\(^{st}\) stage (Fig. 9)**

To determine the possibility of detecting local functional
differences in the form of a response to the measurement procedure, i.e. still at the 1\textsuperscript{st} stage, 2 maps of the $\phi_k$-correlation field relative to $\phi_k$-frame-average time curve were calculated: over the 1\textsuperscript{st} 7 frames (Fig. 9d) and last ones (Fig. 9e), respectively. Expanding in the course of measurement, the chain of emerging microregions of antiphase activity, apparently, exactly coincided with the direction of the meridian.

\textbf{2\textsuperscript{nd}-3\textsuperscript{rd} stages (Fig. 10)}

The dispersion $\phi_k$-fields, calculated in relative units (i.e., $\sigma(\phi_k)/\phi_k$ as for the 1\textsuperscript{st} case), for 2\textsuperscript{nd} and 3\textsuperscript{rd} stages are depicted in Figs. 10a and 10b), respectfully. The meridian strip manifested itself, contrary to expectations, as a coherent zone of minimum dispersion, which was clearly manifested in the change in the landscape during the 2\textsuperscript{nd} stage (Fig. 10c). The surprise at such dynamics continued until attention was paid to the time of the experiment: 18:00-18:30, that is, exactly during the known period of minimum activity of the meridian.

\textbf{4\textsuperscript{th}-5\textsuperscript{th} stages (Fig. 11)}

In response to the cathodic stimulation, it is these areas 1-3 (Fig. 10b) of initial minimal activity that manifested themselves most actively, and, thus, now it clearly revealed the boundaries of the above-mentioned Zones 1-3. Fig. 11. Zones 1-2, according to chart (Fig. 9a), apparently matched with AZ's St33,34. Zone 3 was not marked on the known AP charts, so it can be assumed that it includes 1 or 2 new PC (Curious Point). To contrast the high dynamics at the stage of stimulation with respect to that at relaxation, the scales of Figs. 11a and 11b were chosen as the same (all the more so that, with any other choice, the aforementioned meridian strip of the minimum variance was no longer found). The $\Delta \phi_k$-map for the 4\textsuperscript{th} stage (Fig. 11c), in contrast to that of the 2\textsuperscript{nd} stage (Fig. 9c), revealed not only a smaller background shift, but
also several micro-areas with clearly opposite dynamics, of which a pair of pixels in Zone 1 was of particular interest (see Fig. 12). It was also interesting that: (i) Zone 1 was surrounded by a chain of antiphase pixels (yellow); and (ii) a similar chain-from 1 to 3 was visible along the meridian.

6th–7th stages (Fig. 13)

The anodic stimulation caused maximum dispersion (about 1.5 and 3 times greater than the cathodic and mm-EMF stimuli, respectively) and a significant spatial restructuring, which appeared as a spread of activity from right to left along the meridian (compare Fig. 13c and Fig. 10c) and, thus, uniting Zones 2 and 3, Fig. 13a, 12c. During the resting 7th stage, the variance returned to its original level.

8th–9th Stages

Fig. 12a-c represented the φk-stage-averaged modifications which occurred in 7th–8th, 9th–10th and 10th–11th stages as a sequence of corresponding ∆φk-maps. Comparing Fig. 13a with Fig. 13b, within the framework of TCM, it can be assumed that cathodic stimulation, as opposed to the anodic one, led to activation of the meridian.

In a functionally homogeneous tissue, one would expect the same type of reaction to the same stimulation. In this current case, it was repetition of the cathode/anode stimuli in the 4th/6th and 8th/10th stages. In Fig. 14, these differences were contrasted by subtracting 2 pairs of maps, i.e., Fig. 13c - Fig. 11c and Fig. 12b - Fig. 12a. Comparing the two ∆-maps: the Zone 1 was the only distinctly abnormal zone (Fig. 14a); the aforementioned meridian strip exhibited the most similarity in both cases, particularly in the 2nd one, when it stretched along the entire scanned area, Fig. 14b; and the fact that Zones 1-3 did not appear in Fig. 14b, can be interpreted as leveling the functional landscape during the 4th–6th stages.

Similarly to Case I, graphical analysis of the 4-parameter temporal dynamics of a plurality of pixels of the scanned area was carried out. In contrast to the not quite healthy subject, in the healthy one, the number of small clusters with antiphase dynamics was to be significantly smaller (compare Fig. 3d, e and Fig. 11c). In addition, as in Case I, it was not possible to display all the diversity in the 4-parameter dynamics set of pixels. In this

Fig. 12. The 2D φk–response to the anodic stimulation. a,b) Dispersion field for VI and VII stages, respectively; c) The Δφk-map – changes for VI stage. The red arrow indicates direction of the applied stimulus. The meridian stripe manifested itself as a chain of white spots in c).

Fig. 13. Similarity and difference in the φk-response to the IV/VI and VIII/X stages of the anodic/cathodic stimulation. Difference between the maps: a) Fig. 12c – Fig. 11c; b) Fig. 13b–Fig. 13a.

Fig. 14. Stages VIII-XI. a,b,c) The Δφk-maps for VII-VIII, IX-X and X-XI stages, normalized Δφk,n–between first and last frames of the whole experiment.
regard, one example of antiphase dynamics of pixels in the center of Zone 1 is presented (Fig. 15). The frame-averaged dynamics of all 4 parameters is depicted at Fig. 16; (See other examples in the Supplemental Materials, s4-s5).

As in Case I, interest lies in the fact that the distinct response to mm-EMF was clearly manifested mainly at the submembrane level. Indeed, from Fig. 15 it can be seen that the response to mm-EMF: was not noticeable at the cellular membrane level ($\phi_k$); was very weakly expressed at the level of the intercellular environment ($z_k$); was clearly visible on the $z_M$ and $\phi_M$ curves, while the latter had antiphase character. However, since such a marked response to mm-EMF was not expressed on the $\phi_M$- and $z_M$-curves of the average values (Figs. 15 and 16), it followed that such an effect was inherent only in a minority of points. The performed graphical analysis revealed a dozen such points with the same or even greater sensitivity to the mm-EMF. Noteworthy, these points were located mainly in the "meridion strip," as e.g., p. 7×12, p. 22×17 from Zones 2 and 3 (see s4, s5 in Supplemental Materials).

The above assumption for the smoothing $\phi_k$-landscape (Fig. 14b) was consistent with the noticeably smoothed dynamics of all curves in Figs 15, 16 after the 6th stage.

Noteworthy is the clear difference in the course of the averaged curves of the healthy and sick subjects (Fig. 5 vs Fig. 16). Despite the fact that much stronger stimuli were used in Case II, a noticeable divergence along the $\phi_k$- and $\phi_M$-curves was observed only at the 4th-6th stages and, at the same time, was not as pronounced as in the sick subject. (By approximating the unexpressed response of all curves to the mm-EMF test, Fig. 16, it can be assumed that the same would probably be observed for $z_k$ and $z_M$-parameters if the same weak stimuli were applied to a healthy subject.) Another distinguishing feature is likely to be differences in response delay, which were registered in both cases.

The detailed spatial dynamics of the $\phi_k$-landscape is shown at Fig. 17 a-z as a frame sequence of normalized difference images for the 4th-6th stages (frames 34-65, Figs. 15 and 16). The 2-color palette, i.e., red versus blue, corresponded to the sign of $\Delta \phi_k$ relative to zero, as can be seen on the presented profiles.

In response to the 1st CES on some noticeable changes, became noticeable only after a delay of 2-3 frames (Fig. 17e): the blue structure appeared on the right and began to spread into Zone 1. On the next 3 frames (starting with "g"), it can be seen that this is not a single structure, but an ensemble of blue islands, manifested along the line of the profile ("meridian stripe"), and which was also clearly seen from the shift of the profile towards negative values of $\Delta \phi$. With the CES off, the reverse process immediately began (j), which continued not only during the relaxation (5th stage), but also for another for 2 frames "n, o," i.e., during the 6th stage. The latter, on the other hand, meant nothing more than a 20 s delay in the response to the AES VI on. On the 3rd frame of AES, a sharp transformation of the entire landscape occurred (Fig. 17p). The two large distinctly antiphase $\Delta \phi_k$-structures appeared: the lower one precisely combined Zone 2 and the lower part of 3 (Fig. 12a), and the top red $\Delta \phi_k$-structure related to Zone 4. After the next 3 frames ("q-s"), this pattern with noticeable variations of the "meridian stripe," began to fade away without any pronounced changes either to the AES off ("w"), or to the subsequent the CES on ("z").

Note. Super threshold electrical stimulation (e.g., steep impulse fronts) did not reveal such structuring effects, but leads to an
In our opinion, it is these issues that would be of greater interest in further multimodal studies. Compared with the healthy subjects, the unhealthy one had: the elevated variance of initial parameters of the AP zone in comparison with the frame-average (in a healthy person, on the contrary, it was reduced presumably in accordance with the cycle of activity of the meridian); a wider range of test induced changes (up to 30%, 20%, 30%, 4% for phase and magnitude at 2 kHz and 1 MHz, respectively); and in response to mm-EMF: larger discrepancy in the courses of the low- and high-frequency curves.

The differences listed between the unhealthy and healthy subjects do not claim to be statistically significant because $n = 2$. These differences are given only as an optional addition to the identified phenomena, the great similarity in both subjects is of fundamental importance.

Unfortunately, as far as we know, there is still no device similar to the SEL, i.e., a device which would allow high-quality dynamic SEL mapping on a sufficiently large area of skin (i.e., at least $20 \times 40$ mm$^2$ with $1-2$ mm of spatial resolution), and could therefore test the results of this current study. Probably due to the lack of...
such devices, our publications have so far remained unnoticed by scientific community. The data obtained indicate the special importance of the sub-membrane 2D processes; however, the current parameters of the 1MHz channel are not good enough for a more thorough analysis of the sub-membrane dynamics.

Conclusion
It is assumed that these findings necessitate reconsideration of some basic methodological issues concerning neurogenic/AP spots as spatial and temporal electrophysiological phenomena. For practical medicine, the information obtained can be used to develop more adequate methods of electropuncture diagnostics and personalized therapy.

Conflicts of Interest
The authors have no conflicts of interest to declare.

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Ethical Statement
This research did not involve any human or animal experiment.

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