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A.V. CHALYI, K.A. CHALYY, E.V. ZAITSEVA, A.A. KRYSHTOPA
Department of Medical and Biological Physics and Informatics,
Bogomolets National Medical University
(13, Shevchenko Blvd., Kyiv 01601, Ukraine; e-mail: avchalyi7@gmail.com)

FEYNMAN'S CLASSIFICATION OF NATURAL PHENOMENA AND PHYSICAL ASPECTS OF 2014 NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE

This review article is devoted to the formulation of the Richard Feynman's classification of three stages in the study of natural phenomena and the application of this classification to the amazing discovery of the hexagonal grid cells that constitute a positioning system in the brain which was awarded the 2014 Nobel Prize in Physiology and Medicine. The problem of grid cells in brain is considered with accounting for (a) the experimental studies that led to the emergence of hexagons in the human and animal brains, (b) discussion of the problem of generation and propagation of an action potential along nerve fibers, (c) physical parameters of the human brain and its medical applications in the method of hyperthermia for the treatment of malignant tumors, (d) theoretical considerations using a certain analogy between grid cells in brain and the Abrikosov vortex lattice in type II superconductors, and (e) hexagonal graphene and dimensional crossover.

Keywords: Feynman's classification, grid cells, physical parameters of brain, method of hyperthermia, conduction and induction currents, Abrikosov vortex lattice.

> *"The real glory of science is that we can find a way of thinking such that the law is evident."* [1]
> Richard FEYNMAN,
> 1965 Nobel Prize winner in Physics

1. Introduction

In this review article (being a continuation of the article by one of the authors [2], while a number of new problems are considered here, and some others are discussed in more details), we will focus our attention on integration trends in science and education which are associated with interdisciplinary synergetic bonds between physics and medicine (see, e.g., [3–9]). In our opinion, the main idea of synergetics is the fundamental possibility of using quantitative results obtained by exact methods of a "simpler" science (e.g., physics) in similar (isomorphic) phenomena of a much more complex science (e.g., medicine). Such a synergetic approach unites various natural phenomena previously related to different areas of scientific knowledge, and thereby largely compensates for the differentiation processes that have been characteristic of the development of natural sciences (such as physics) for more than three centuries. To explain the fundamental reasons for the processes of ordering and formation of a new phase, we propose to use the so-called "The Feynman's classification of the three stages in the study of natural phenomena". These three stages were essentially discussed by Richard Feynman in his lectures on physics [1]. They include two obvious, one might say – generally accepted, the following stages:

the first of them is the accumulation and systematization of experimental data; then the second stage may come (or not, as in a number of scientific fields) – the creation of a theory that explains the obtained experimental data. Finally, in the third, less obvious, stage, it may happen that Feynman called as follows: "the real glory of science is that we can find a way of thinking such that the law is evident". Undoubtedly, this third stage is the most important, enabling to establish the main reason for the "first principle" underlying the theory which explains the experimental data obtained, respectively, at the first and second stages in the study and cognition of this natural phenomenon.

Here, we shall also consider the examples of using a synergetic approach to explaining the occurrence of hexagonal structures on the border of physics and medicine. It should be noted that hexagons can be found in many objects of inanimate and living nature. In the inanimate (inorganic) world, they arise in Benard cells [10], in crystals and alloys with hexagonal or other type of symmetry [11], on the surface of the Salt Lake Uyuni in Bolivia [12], in geological colonnades Giant's Causeway in Ireland [13], in the cloud structure around Saturn's North Pole [14], in such carbon modifications as fullerene C_{60} having 62.5% hexagonal faces (1986 Nobel Prize in Chemistry) [15] and graphene being a hexagonal monoatomac plane (2010 Nobel Prize in Physics) [16, 17], *etc.* In the living (organic) world, hexagonal structures appear in grid cells of brain (2014 Nobel Prize in Physiology or Medicine) [18], in beeswax honeycombs [19], in such biomedical phenomena as the spreading depression of Leao and other neurological dysfunctions [20], in the problem of cell-to-cell communication (synaptic transmission) [21–23] with regard for the porosytosis hypothesis and hexagonal synaptomers [24], *etc.* The striking geometric similarity of these structures, as well as the variaty of objects in which they appear, suggests that there should probably exist a universal explanation or, in other words, the first principle underlying their formation.

The structure of this review article is as follows. Section 2 discusses, in more details, "The Feynman's classification of the three stages of the studyi in natural phenomena" and provides relevant examples. The neurophysiological system of the so-called place and grid cells in brain providing the spatial orientation of humans and animals [18] is considered in Section 3 with accounting for such important points: (a) the experimental studies that led to the discovery of the hexagonal structures of grid cells in brain, (b) discussion of the problem of generation and propagation of an action potential (AP) along nerve fibers [25], (c) physical parameters of the human brain and its medical applications in the method of hyperthermia which is used in the treatment of malignant tumors [26–30, 8, 9], (d) theoretical considerations using a certain analogy between hexagonal structures in grid cells in brain and the Abrikosov vortex lattice in type II superconductors [18, 31–34], (e) discovery of graphene (2010 Nobel Prize in Physics) [16, 17] and dimesional crossover applications [35–37].

2. The Feynman's Classification of the Three Stages in the Study of Natural Phenomena

An outstanding American physicist Richard Feynman, receiving the 1965 Nobel Prize in Physics, has essentially discussed three stages in the study of natural phenomena in a famous textbook "The Feynman Lectures on Physics" [1]. These lectures were delivered by Richard Feynman in 1961–1963 to students at the California Institute of Technology (Caltech), taped and prepared for publication by Prof. Robert Leighton and Prof. Matthew Sands. As an example of the three stages of studying the natural phenomena, Prof. Richard Feynman chose the optical phenomenon of light refraction at the air-water interface considered in [1]. These three stages are proposed to be called ***"The Feynman's classification of the three stages in the study of natural phenomena"***, being as follows:

1st stage: ***Accumulation and systematization of experimental data.*** The optical phenomenon of light refraction was studied experimentally by Claudius Ptolemy (Claudius Ptolemaeus) about 140 AD. Richard Feynman cited a table of experimental data from Ptolemy's book "Optics", which presents the relationship between the angles of incidence and refraction of a light beam at the boundary of air and water.

2nd stage: ***Finding a law (creating a theory) explaining the experimental data.*** The law connecting the incident and refraction angles was found by the Dutch scientist Willibrord Snellius (Snell van Royen) in 1621. As is well known, the Snell's law states that the ratio between the sine of the angle of incidence ($\sin\alpha$) and the sine of the angle of refraction ($\sin\beta$) of a light beam is equal to the refractive index (n) of the medium in which the refracted ray propagates relative to the medium in which the incident beam propagates. It should be noted that there is a good quantitative agreement between the experimental data of Ptolemy and theoretical data according to Snell's law for the angles of refraction of a light beam in water, accounting for their "distance" in time, which is almost 1500 years (see Table 1 which unifies Table 26.1 and 26.2 in [1]).

It would seem that, with such agreement between experiment and theory, the problem of light refraction at the interface between two media could be considered practically solved. However, Richard Feynman believed that another final stage of the study and cognition is needed to fully understand this problem.

3rd stage: *Formulation of the first principle underlying the theory that explains experimental data.* For the optical phenomenon of light reflection, this first-principle law was discovered by the French mathematician, physicist, and lawyer Pierre de Fermat in 1662, and is called "Fermat's principle of least time". The physical meaning of this principle is that a ray of light passing from point A of one medium (e.g., air) through the interface to point B of another medium (e.g., water) chooses such a trajectory, along which the travel time will be minimal. In the mathematical language, Fermat's principle means that the following integral, which determines the time of movement of the light beam along the trajectory

Table 1. **Comparison of experiment (Ptolemy's data) and theory (Snell's law)**

Angle of incidence α of the light beam in the air	Refraction angle β of a light beam in water (Ptolemy's experiment)	Refraction angle β of a light beam in water (Snell's law)
10	8	7.5
20	15.5	15
30	22.5	22
40	28	29
50	35	35
60	40.5	40
70	45	48
80	50	49.5

AB, should take the minimum possible value:

$$\int_A^B ndS/c = t_{\min}, \tag{1}$$

where dS is the element of the trajectory length, c is the light speed in vacuum, n is the refractive index of a medium.

Another equivalent definition of "Fermat's principle of least time" is the "Principle of least optical length", according to which a ray of light between two points A and B chooses a trajectory along which the optical length takes the minimum possible value. "Principle of least optical length" can be written in the form

$$\int_A^B ndS = c\int_{t_A}^{t_B} dt = ct_{\min} = [AB]_{\min}. \tag{2}$$

Here, the notation for optical length $[AB] = \int_A^B ndS$ is used [38].

Following the classical example from geometric optics discussed by R. Feynman and related to the phenomenon of light refraction at the boundary of two media, let us consider other physical examples that illustrate the manifestations of "Feynman's classification of three stages in the study of natural phenomena" and especially the implementation of the third stage, which requires formulations of "first-priniciple laws" for a theoretical explanation of the observed data.

First of all, we turn to the laws of conservation of energy, momentum, and angular momentum. At the first stage associated with the accumulation and systematization of observed data (in the sense of Feynman's classification), these laws use a lot of experimental data, and not only of a physical nature. In this regard, the contribution of the German physician and subsequently physicist Julius Robert Mayer, who is considered one (and, possibly, the first) of the founders of the law of conservation of energy, is of interest.

In the early 40s of the XIX century, Julius Robert Mayer worked as a ship's doctor and used the method of treating diseases with the help of leeches (hirudo – in Latin) which was widespread at that time. The leeches' saliva contains the enzyme hirudin, having anticoagulant properties and being discovered in 1884. In the process of treating sailors' diseases with

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leeches (in more modern terms – by the method of hirudotherapy), Robert Mayer visually detected a change in the color of the patients' blood from bright red to darker red, which is characteristic of arterial and venous blood. Considering this fact, Mayer came to the conclusion that there must be a relationship and equivalence between the amount of heat that the human body receives (and blood, including) and the work related to the oxygen consumption in the human body. At that time, the concept of "energy" was associated with the concept of "vital forces". Julius Robert Mayer published his article "A note on the forces of inanimate nature" (Annals of Chemistry and Pharmacy, 1842) on the essence of the law of conservation of energy (his first article on this topic was sent to print in 1841, but was not published), before the publications of James Joule and Hermann Helmholtz, who are also considered by right the founders of the law of conservation of energy. Figure 1 contains the portraits of the scientists, including Julius Robert Mayer (far right), who made the significant contributions to both medicine and physics [39].

To these scientists should be added the German Professor of medicine and physics Germann Ludwig Helmholtz, who co-authored the law of conservation of energy due to his book "On Conservation of Force" published in 1847, as well as the great English physicist James Prescott Joule (his article on the measurement of the mechanical equivalent of heat was published in 1843). Another universal scientist was the French physicist and physician, Academician of the French Medical Academy Jean Louis Poiseuille, who was the first to measure blood pressure with a mercury manometer in 1828 and who experimentally proved a hydrodynamical (haemodynamical) law in 1841 that was formulated by a German physicist and hydraulic builder Gotthilf Hagen two years earlier in 1839. In accordance with this law, known as the Hagen–Poiseuille law, the volume of a fluid (blood) V, flowing per unit of time t (the so-called volumetric velocity $Q = V/t$, or minute blood flow) is directly proportional to the fourth power of the radius of the cylindrical tube (blood vessel). It is of interest that the volumetric velocity (minute flow rate) of blood in the aorta of adults is 5–6 liters per minute in a calm state and up to 20 liters per minute in a state of maximum excitement [8, 9].

The laws of conservation of energy, momentum, and angular momentum, which have received numerous experimental and theoretical justifications, are ones of the most fundamental laws of nature. From the viewpoint of Feynman's classification, one could say that these laws of concervation are themselves the first principles of nature, being necessary to explain the phenomena and processes occurring in animate and inanimate nature. However, this statement is not true, since the question remains as follows: what initial positions underlie the laws of conservation of energy, momentum, and angular momentum or, in simpler words, where these laws come from? The answer to this question is given by symmetry considerations, which were first formulated by the German mathematician Emmy Noether in [40] (the Noether's theorem) and were consistently proved in the first volume "Mechanics" of the famous textbooks "Theoretical Physics" by Lev Landau and Eugenii Lifshits [41].

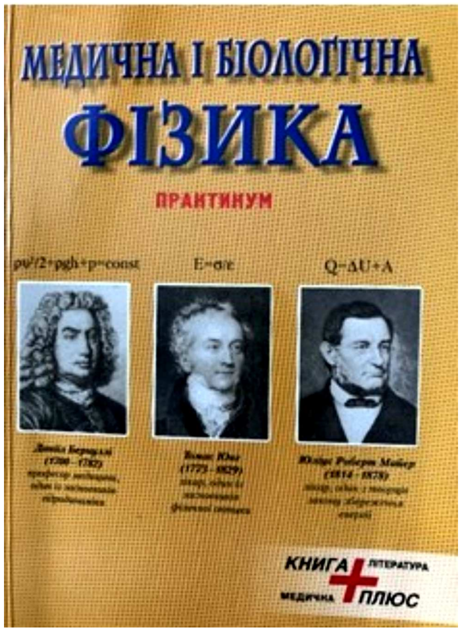

Fig. 1. Title cover of "Medical and Biological Physics. Practice" with portraits of D. Bernoulli, T. Young, and J.R. Mayer, being physicians and physicists [39]

As is known, the laws of conservation of energy, momentum, and angular momentum are based on the following first principles: 1) the law of conservation of energy is a consequence of the first principle which is related to the homogeneity of time, 2) the law of conservation of momentum is a consequence of the first principle which is related to the homogeneity of

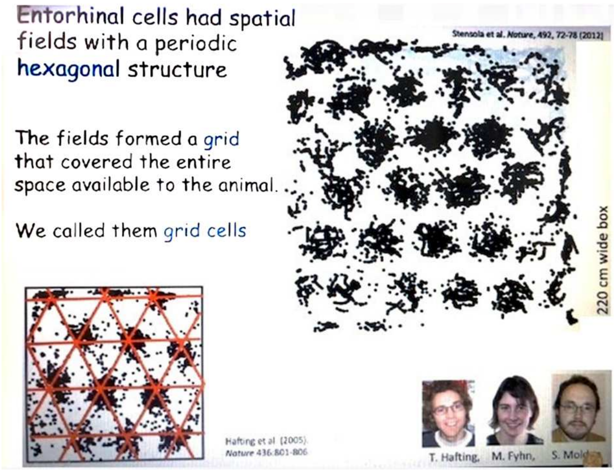

Fig. 2. Hexagonal grid cells in the entorhinal cortex of the rat's brain (from Nobel lecture by Edward Moser "Grid Cells and the Entorhinal Map of Space" [18])

space, 3) the law of conservation of momentum is a consequence of the first principle which is related to the isotropy of space.

3. Discovery of Grid Cells, Physical Parameters of Brain and Its Medical Applications, Analogy between Grid Cells and a Vortex Lattice in Superconductors

In this section, we will consider the following problems: 1) discovery of place and grid cells in brain (2014 Nobel Prize in Physiology or Medicine) [18], 2) generation and propagation of the action potential (AP) along nerve fibers (1963 Nobel Prize in Physiology or Medicine) [25], 3) physical parameters of the human brain and its medical applications [26–30, 8, 9], 4) Edwin Moser's idea of analogy between hexagonal grid cells in brain and the Abrikosov vortex lattice in superconductors [18, 31–34], and 5) discovery of graphene (2010 Nobel Prize in Physics) [16,17] and the concept of a dimensional crossover [35–37].

3.1. Discovery of place and grid cells (2014 – Nobel Prize in Physiology or Medicine)

The 2014 – Nobel Prize in Physiology or Medicine was awarded to the American and British physiologist John O'Keefe from the University College London and to the Norwegian physiologists May-Britt Moser and Edward Moser from the Norwegian University of Science and Technology "for their discoveries of cells that constitute a positioning system in the brain" [18]. Prof. John O'Keefe, being a founder of these studies, has discovered a special type of "place cells" in 1971 that are capable to create a positioning map in the hippocampus of animals (rats) [42]. Prof. Edward Moser and Prof. May-Britt Moser have found the "grid cells" in 2005, being an additional component of the orientational system that is locating in the entorhinal cortex of brain [43]. Later, grid cells were found not only in the brains of rats and other animals, but also in the brain of humans [44]. Such studies have opened up new possibilities for the understanding processes taking place in brain [45–54].

An experiment on detecting the grid cells [43] was carried out by May-Britt Moser, Edward Moser, and their students T. Hafting, M. Fyhn, and S. Molden as follows. They implanted electrodes in the entorhinal cortex of the rat's brain. Such an operation made it possible to fix the action potential (AP) occurrence or, in other physiological words, the "firing of AP" in neurons, as a result of the spatial movements of the rat in a confined space.

It turned out that the spatial distribution of grid cells is characterized by a virtual 6-sided lattice with a periodic hexagonal symmetry (see Fig. 2), which creates a coordinate navigation system and allows animals and humans to find their position in space, as well as the direction and the speed of movement. It is worth to mention that the discovery of grid cells and the study of the features of their functioning are directly related to the problem of treating Alzheimer's disease associated with disorders of the entorhinal cortex of the human brain in the early stages of this disease [42]. All the above applies to the first "experimental" stage from the point of view of Feynman's classification.

3.2. Generation and propagation of the action potential (1963 Nobel Prize in Physiology or Medicine)

In this subsection, we will focus our attention on the electrical mechanism of intercellular interaction caused by the generation and propagation of AP along the axon. A discussion of some of the physicochemical aspects of the problem of cell-to-cell communication and synaptic transmission with regard for the porosytosis hypothesis and synaptomers having a hexagonal geometry, as well as a quantative description of this problem based on nonlinear kinetic models can be found, for example, in [21–24].

First, let us discuss some theoretical considerations related to the description of grid cells in brain at the second "theoretical" stage of Feynman's classification. In this regard, we will briefly review the classic studies on the AP emergence and propagation along the nerve fibers by Alan Hodgkin and Andrew Huxley. They were awarded the 1963 Nobel Prize in Physiology or Medicine together with John Eccles, "for their discoveries concerning the ionic mechanisms involved in the excitation and inhibition in the peripheric and central portions of the nerve cell membrane" [25].

As is known (see, e.g., [46–54, 8, 9]), the AP is generated as a result of the certain external stimulus of electrical, mechanical, or some other nature, which causes the depolarization phenomenon inside an axon. The process of depolarization of the axoplasm is associated with a local shift of the electrical potential from its value given by the formula for the equilibrium Nernst electric potential for potassium ions

$$\phi_i^K = (RT/F)\ln([\mathrm{K}^+]_e/[\mathrm{K}^+]_i) \approx -70 \text{ mV} \tag{3}$$

to the threshold potential value $\phi_{\text{thr}} \approx -(40\text{–}50)$ mV. Here, R is the universal gas constant, T is the absolute temperature, F is the Faraday number, and subscripts "e" and "i" correspond to the concentrations in the environment and inside the axoplasm, respectively. As a result, sodium channels become open, and a significant increase (approximately 500 times in a giant squid axon) of the permeability for Na^+ ions occurs in 1–2 ms. The depolarization process leads to an increase in the internal potential of the axoplasm to the value of the equilibrium Nernst electric potential for sodium ions given by the following formula:

$$\phi_i^{\mathrm{Na}} = (RT/F)\ln([\mathrm{Na}^+]_e/[\mathrm{Na}^+]_i) \approx +40 \text{ mV}. \tag{4}$$

Thus, a quantitative estimate of the AP amplitude ϕ_{AP} gives an approximate value $\phi_{\text{AP}} = \phi_i^{\mathrm{Na}} - \phi_i^{\mathrm{K}} \approx 110$ mV characterizing the firing of AP in neurons.

The most important result of the Hodgkin–Huxley model is the experimental and theoretical substantiation of a nonlinear partial differential equation for the function $\Delta\phi(x,t)$, which describes the process of AP propagation along nerve fibers:

$$\frac{r}{2\rho_a}\frac{\partial^2\Delta\phi}{\partial x^2} = C_m\frac{\partial\Delta\phi}{\partial t} + g_{\mathrm{K}}n^4(\Delta\phi - \phi_i^{\mathrm{K}}) + g_{\mathrm{Na}}m^3h(\Delta\phi - \phi_i^{\mathrm{Na}}) + g_{\text{oth}}(\Delta\phi - \phi_i^{\text{oth}}). \tag{5}$$

Here, in the Hodgkin–Huxley equation (5), r is the axon radius; ρ_a is the specific resistance of axoplasm; C_m is the membrane capacity; g_{K}, g_{Na}, g_{oth} are, respectively, the conductances of the ion channels of potassium, sodium, and other ions (like chlorine Cl^-); $n(t)$, $m(t)$ are numbers of activated pottasium and sodium channels, and $h(t)$ is the number of inactivated sodium channels. We note the fundamental similarity between the AP propagation process along nerve fibers, the signal propagation process along an electrical wire, and the process of soliton propagation in nonlinear media and molecular systems, described, respectively, by the Hodgkin–Huxley equation (5), the cable (telegraph) equation, the Korteweg-de Vries equation, as well as the equations for Davydov's solitons, and corresponding equations for nonequilibrium processes in various media (see [55–58], references therein, and famous results obtained by scientists of the Bogolyubov Institute for Theoretical Physics of the NAS of Ukraine).

3.3. Physical parameters of the human brain and its medical applications in the hyperthermia method

In living nature, unique electrical processes are realized in nerve fibers (axons), depending on whether the axons are covered by the myelin sheath or not. So, the nerve bundles of the white matter of brain have, for the most part, a myelin sheath, which prevents the diffusion of the main inorganic ions of potassium and sodium and, thus, the continious propagation of the action potential along the axon.

However, in the process of biological evolution, nature has created a mechanism of transmission of an electrical signal in jumps through the so-called Ranvier interceptions, which are implemented on sections of axons not isolated from the external environment with a width of about 1μm and at distances from each other up to 1.5 mm, which do not have a myelin sheath and contain a large number of voltage-gated sodium channels in these places. Such a saltatory (jumping) mechanism of electrical signal transmission using Ranvier's interceptions has a significantly higher speed of about 25÷100 m/s, than the speed of signal propagation in unmyelinated axons, which turns out to be 1-2 orders of magnitude lower and reaches 0.7÷2.3 m/s.

Here, we will consider some physical parameters of the substance of the human brain that are useful for a further consideration. Speaking about the neurons of brain and without going into the anatomical details of its structure, it should be noted that we are talking primarily about the neurons of the gray matter of brain, since the white matter of brain consists mainly of bundles of nerve fibers (axons) covered by the white myelin sheath.

Now, we will estimate the average density of the human brain matter, using known statistical data on the average mass and volume of the human brain [2, 30, 46]. The average mass of the human brain is 1350 ± 50 g, while the average volume of the human brain is within 1400 ± 200 cm^3. Therefore, the average density of the human brain matter is 0.96 ± 0.17 g/cm^3, i.e., slightly less than the density of water $\rho_{\rm water} \approx 1$ g/cm^3, the most common and mysterious liquid in nature.

As is shown in [8, 9, 30], the numerical values of the relative dielectric permeability ϵ for such substances as water, blood, gray (gmb) and white (wmb) substances of brain are almost close to each other and equal:

$$\epsilon_{\rm water} = 81, \quad \epsilon_{\rm gmb} = \epsilon_{\rm blood} = 85, \quad \epsilon_{\rm wmb} = 95.$$

The electric conductivity of biological tissues may very in a very wide interval [8, 9]. Such biological fluids as cerebrospinal fluid (crbf) and blood (bld) are substances with a high electric conductivity and, respectively, low electric specific resistance: $\rho_{\rm crbf} \approx$ ≈ 0.55 Ohm·m, $\rho_{\rm bld} \approx 1.66$ Ohm·m. At the same time, such dense biological tissues as dry skin and bone, on the contrary, have a low electric conductivity and a very high electric specific resistance: $\rho_{\rm skin} \approx 10^5$ Ohm·m, $\rho_{\rm bone} \approx 10^7$ Ohm·m. The brain tissue has a more or less intermediate value of the electric specific resistance: $\rho_{\rm brain} \approx 14$ Ohm·m.

Table 2. **Specific electrical resistivity of various biological tissues [8, 9]**

Biological tissues	Specific electrical ressistivity ρ, Ohm·m
Cerebrospinal fluid	0.55
Blood	1.66
Muscles	≈2
Brain tissue	≈14
Adipose tissue	≈33
Dry skin	10^5
Bone without periosteum	10^7

It should be taken into account that the above low and high values of the specific resistivity of biological tissues are of fundamental imporance in the choice of physiotherapeutic methods for the treatment of oncological diseases. Conducted studies (for more details, see, e.g., [26–30]) confirm that the use of the hyperthermia method in oncology, based on heating malignant tumors, leads to a significant damage or even to the complete destruction of tumor cells and, as a result, the volume of the tumor. Hyperthermia, as a method of treating malignant tumors, is used at temperatures higher than 39.5 °C (usually at temperatures 41–45 °C) with a choice of time and temperature intervals depending on the type and location of tumors. Usually, hyperthermia in oncology is used in conjunction with methods such as chemotherapy and radiation therapy. This increases the effectiveness of a number of chemotherapy drugs, as well as provides a higher sensitivity of tumor cells to the effects of radiation during radiation therapy.

In the case of the alternating *conduction current* with density $j_{\rm cond}$, the heat effect may be evaluated by a specific quantity of heat $Q_{\rm cond}$ in unit volume V per unit time t, for which the following formula of the Joule–Lenz law in the differential form can be written:

$$Q_{\rm cond}/Vt = \rho j_{\rm cond}^2. \qquad (6)$$

This formula proves that, at a fixed conduction current density $j_{\rm cond}$, more heated will be tissues with more specific electical resistivity ρ such as bones and skin, while less heated will be cerebrospinal fluid and blood (see Table 2) [8, 9].

In the case of alternating *induction current* (other notable titles – *vortex current* or *Foucault current*), the heat effect may be evaluated by the Joule–Lenz law (6) with regard for such a formula for the amplitude of the induction current density:

$$j_{\rm ind} \sim \omega B_0/\rho, \qquad (7)$$

which gives the following expression for the amplitude of the specific heat quantity $Q_{\rm ind}/Vt$:

$$Q_{\rm ind}/Vt = k\frac{\omega^2 B_0^2}{\rho}. \quad (8)$$

Here, k is the coefficient depending on the geometric dimensions of a tissue, ω and B_0 are the frequency and the amplitude of the alternating magnetic induction, respectively.

As follows from formula (8), the use of the hyperthermia method is more effective for tissues with low specific electrical resistivity, i.e., for such biological fluids as cerebrospinal fluid, blood, and limph. Thus, both methods of hypertermia discussed above, using conduction currents and induction (vortex) currents, can complement each other at different localizations of oncological formations.

In addition to the studies mentioned above, it should be noted that the research team of the Department of Medical and Biological Physics and Informatics of the Bogomolets National Medical University in Kyiv conduct scientific reasearches on problems at the border of physics and medicine, including joint studies with scientists from the clinical departments of the Bogomolets National Medical University in Kyiv and other institutions of Ukraine (see, e.g., [21, 59–63]).

3.4. Analogy between hexagonal grid cells and a vortex lattice of superconductors

In conclusion of this section, we will focus on the theoretical studies which can be considered as an initial attempt to formulate the first principle of the emergence of hexagonal grid cells in brain in the spirit of Feynman's classification of the study of natural phenomena. In his Nobel lecture "Grid Cells and the Entorhinal Map of Space" [18], Edward Moser suggested to explain the appearance of hexagonal structures in brain using the results of the magnetic properties of superconductors [31, 32]. He proposed drawing an analogy between grid cells in brain and the vortex lattice of superconductors by Aleksei Abrikosov, 2003 Nobel Prize laureate in Physics. Actually, A. Abrikosov obtained fundamental physical results on the magnetic properties of superconductors of the second group that preserve their superconducting properties in strong magnetic fields [31], while the experimental studies by U. Essmann and H. Trauble [32] confirmed the theoretical results of A. Abrikosov, as is written in the English-language scientific literature. The idea of such an analogy between seemingly so distant fields as theoretical physics of superconductors and neurophysiological studies of human and animal brains could be explained by the fact that Edward Moser received his first scientific degree in mathematics, statistics, and programming in 1985. Five years later, he received two more degrees in psychology and neurophysiology.

The problem of superconductivity has a long, interesting, and sometimes tragic history that goes far beyond the scope of this review. Here, it seems to us necessary to emphasize the fact [33] that the first experimental studies in the field of type II superconductors were carried out in Kharkiv, at the Ukrainian Institute of Physics and Technology (UPhTI) by L.V. Shubnikov, V.I. Khotkevich,b Yu.D. Shepelev, and Yu.N. Ryabinin [34]. On the basis of these experimental studies, A.A. Abrikosov (whose scientific superviser was L.D. Landau, who together with V.L. Ginzburg created the theory of superconductivity [64] or, as it is sometimes called, the theory of type I superconductors), developed the theory of type II superconductors [31], which not only qualitatively, but also quantitatively confirmed the experimental results obtained by Shubnikov *et al.* [34]. Thus, the truth lies in the fact that, at first, the experimental data of L.V. Shubnikov with his collaborators were obtained [34]. 20 years later, the theory of type II superconductors was created by A.A. Abrikosov [31], describing these experimental data, and, 10 years later, additional experimental data by U. Essmann and H. Trauble [32] appeared, which essentially confirmed the experiments [34] and the theory [31]. Today, physicists over the world often use the term "Shubnikov phase" for type II superconductors, introduced by Pierre-Gilles de Gennes, 1991 Nobel Prize laureate in Physics for achievements in the field of soft matter physics which showed that "methods developed for studying order phenomena in simple systems can be generalized to more complex forms of matter, in particular to liquid crystals and polymers".

The creators of the theory of superconductivity, the great theoretical physicists L.D. Landau, V.L. Ginzburg, and A.A. Abrikosov became the winners of the Nobel Prize in Physics: Lev Landau – in 1962, Vitaly Ginzburg and Aleksei Abrikosov – in 2003. The great experimental physicist Lev Vasil'evich Shubnikov lived a very short 36-year life. He was shot in

1937 on charges of inviting foreign scientists to the UPhTI who allegedly engaged in espionage [33]. In connection with the above, it is necessary to mention the undoubtedly decisive influence of the Kharkiv period of the work of L.D. Landau and the Kyiv period of the work of N.N. Bogolyubov, as well as the Ukrainian theoretical schools created by them for the further development of physical and mathematical researches in the scientific centers of Kyiv, Kharkiv, Lviv, Odesa, and other cities known far beyond the borders of Ukraine, in particular, in the field of studying the influence of fluctuation effects on phase transitions in various media (see, e.g., [57, 58, 65–76]).

3.5. Hexagonal graphene (2010 Nobel Prize in Physics) and dimensional crossover

While discussing hexagons in physical systems, let us briefly mention the bright scientific discovery related to the discovery of graphene (2010 Nobel Prize in Physics), achievements of Ukrainian physicists, and the dimensional crossover. Graphene is one of the carbon modifications having a two-dimensional hexagonal crystal lattice formed by a monolayer of carbon atoms. The 2010 Nobel Prize in Physics was awarded to Andrey Geim and Konstantin Novoselov “for groundbreaking experiments regarding the two-dimensional material graphene” [16, 17]. Without dwelling in detail on the unique physical propeties of graphene, one should note the contribution of Ukrainian physicists from the Bogolyubov Instutute for Theoretical Physics (NASU, Kyiv) [77–80] to the study of these properties which are cited in the papers of Nobel laureates Aleksei Abrikosov, Andrey Geim, and Konstantin Novoselov.

Table 3. **Values of the lower crossover dimensionality D_{LCD} for real systems**

Real confined 3-dimentional systems	Corresponding limiting cases	Lower crossover dimensionality D_{LCD}
Plane-parallel layer, slitlike pore, membrane, synaptic cleft, layered graphite	Molecular plane	2
Cylindrical pore, bar, ionic channel	Molecular line	1

Using the notion of the lower crossover dimensionality D_{LCD} (see Table 3, [35–37]), it will be correct to say that graphene is layered graphite in the limit, when the value of the lower crossover dimensionality (LCD) tends to the value $D_{\mathrm{LCD}} = 2$. The value of the low crossover dimensionality D_{LCD} (3rd column of Table 3) characterizing a certain real system (1st column) corresponds to such a limiting spatial dimension of a geometric object (2nd column) at which the linear size of a system in the directions of its spatial limitation reaches the molecular size. As an example of such a $3D \leftrightarrow 2D$ dimensional crossover, a bulk sample of layered graphite takes a form of a graphene monomolecular plane.

Obviously, the transition between systems of different dimensions (say, from a 3d system to a 2d one) cannot occur adruptly, but must be a continuous and smooth transition (of course, with the exception of special cases such as mechanical chipping of bulk graphite to obtain 2d graphene samples). One of the conformations of a smooth dimensional crossover can be a result of computer experiments [81, 82] and theoretical studies [35–37] describing this dimensional crossover.

The Kawasaki’s idea from the theory of mode coupling [83] was used in [35–37] to obtain the following interpolation formula for the effective critical exponents n giving a continuous and non-jumping transition from its 3d n_3 to 2d n_2 numerical values:

$$n = n_3 + \left(\frac{2}{\pi}\,\mathrm{arctg}\,(ax - b) - 1\right)\frac{n_3 - n_2}{2}, \qquad (9)$$

where $x = L/L_0$ is the dimensionless width of a slitlike pore or the radius of a cylindrical pore; L_0 is the linear size of the system in restricted geometry at which the dimensional crossover occurs; a and b are the dimensionless parameters characterizing the slope and position of the $3D \leftrightarrow 2D$ crossover.

The shift of the critical temperature $T_{\mathrm{C}}^{\mathrm{pore}} = T_{\mathrm{C}}(H)$ for confined systems in slitlike pores, as compared with its bulk critical temperature $T^{3D} = T_{\mathrm{C}}(\infty)$, is given by the following formula (see, e.g., 81]):

$$\frac{T_{\mathrm{C}}(H)}{T_{\mathrm{C}}(\infty)} = 1 + kH^{-1/\nu}, \qquad (10)$$

where k is the coefficient of proportionality, and H is the width of the slitlike pore. This formula allows one to check the interpolation formula (9) by the results of computer experiments [81] with accounting for the size dependence of the critical exponent $\nu(H)$ for the correlation length inside the following interval: $\nu = 0.63$ for $D = 3$ and $\nu = 1$ for $D = 2$.

The curve shown in Fig. 3 was obtained in the computer experiment [81]. The size dependence of the critical temperature $T_C(H)$ in slitlike pores obtained from (10) is shown in Fig. 4. The agreement between the computer experiment data and theoretical calculations appears to be quite satisfactory. The authors of [81] pointed to the fact that the beginning of the $3D \leftrightarrow 2D$ dimensional crossover (when the effective critical exponent $\nu_{\text{eff}} \approx 1$) takes place at the thickness $H^* \approx 2.4$ nm of a slitlike pore filled by water molecules with its diameter about 0.3 nm. Thus, such a crossover thickness H^* corresponds to approximately 8 monolayers of water molecules in slitlike pores.

An interesting consequence of the $3D \leftrightarrow 2D$ dimensional crossover for the effective spatial d_{eff} and fractal d_{fr} dimensionalities in the process of layer-by-layer ordering was studied in [35, 37] and illustrated in Fig. 5. The calculation of effective critical exponents depending on the number S of molecular layers was carried out according to formula (9), while the following formulas were used to calculate the effective spatial d_{eff} and fractal d_{fr} dimensionalities, respectively:

a) the known hyperscaling relation for the spatial dimensionality

$$d_{\text{eff}} = (2 - \alpha_{\text{eff}})/\nu_{\text{eff}}; \tag{11}$$

b) the Mandelbrot formula for the fractal dimensionality

$$d_{\text{fr}} = d_{\text{eff}} - \beta_{\text{eff}}/\nu_{\text{eff}}. \tag{12}$$

In (11) and (12), the effective critical exponents α_{eff} and β_{eff} descibe, respectibely, the temperature dependence of the isochoric heat capacity and liquid/vapor densities on the coexistance curve for the liquid-vapor system near its critical point. The calculations using the interpolation formula (9) together with (11), (12), and experimental values of the critical exponents α, β, ν from papers by Mikhail Anisimov and his collaborators [84, 85] show that, as a result of the $3D \leftrightarrow 2D$ dimensional crossover, the effective critical exponents α_{eff}, β_{eff} and the fractal dimensionality d_{fr} decrease smoothly from values $\alpha_{3d} = 0.011$, $\beta_{3d} = 0.325$ and $d_{\text{fr}} = 2.482$ for 3-dimentional systems to values $\alpha_{2d} = 0$ (respectively, to a logarithmic singularity), $\beta_{2d} = 0.125$, and $d_{\text{fr}} = 1.875$ for 2-dimentional systems.

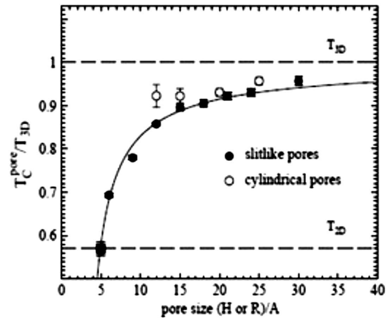

Fig. 3. Size dependence of the pore critical temperature (computer experiment [82])

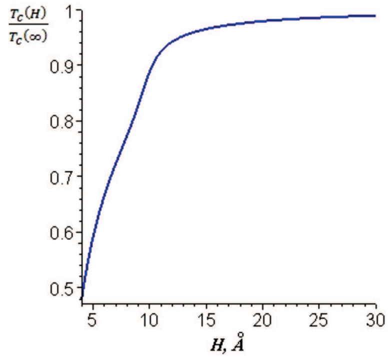

Fig. 4. Size dependence of the critical temperature in a slitlike pore (finite-size scaling + formula (9) for ν)

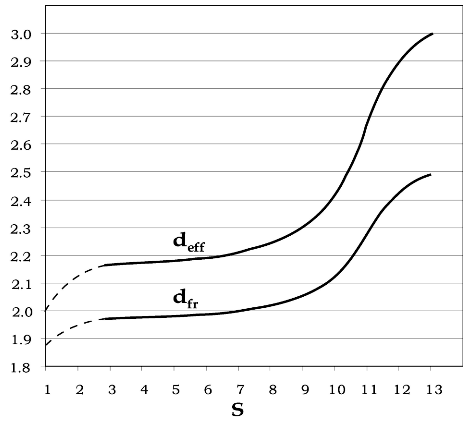

Fig. 5. The dependence of the effective spatial d_{eff} and fractal d_{fr} dimensionalities on the number S of molecular layers in a confined system

To conclude this subsection, let us consider the question of the role of order-parameter fluctuations and their dependence on the spatial dimensionality d. The role of fluctuation effects may be clarified on the basis of the Levanyuk–Ginzburg criterion [86, 87] of the applicability of the Landau thermodynamic mean-field theory which neglects fluctuation effects. In other words, the role of fluctuations can be estimated by analyzing the Ginzburg number Gi (see, e.g., [88, 89]). The Ginzburg number Gi is determined through the ratio of the average square deviation of order-parameter fluctuations $\langle \Delta\phi^2 \rangle$ to the square of the order parameter ϕ_0^2. It can be shown that the following relation holds for the Ginzburg number Gi in a d-dimensional space:

$$Gi \propto \phi_0^{d-4}/R_0^d, \qquad (13)$$

where R_0 is the radius of the intermolecular interaction. As follows directly from formula (13), the Ginzburg number $Gi \ll 1$ near the points (lines) of phase trasitions, if $d \geq 4$ and/or $R_0 \to \infty$. In this case, fluctuations of the order parameter can be neglected, and the Landau thermodynamic mean-field theory becomes valid (speaking exactly, with logarithmic precision). As is known, this fact is used in the Fisher–Wilson ϵ-expansion method, where $\epsilon = 4 - d$.

Another important cosequence of formula (13) is the fact that, as the spatial dimensionality d decreases, the role of order-parameter fluctuations is enhanced. Indeed, the order parameter tends to zero while approaching the phase transition points (lines), and the Ginzburg number Gi and, accordingly, the role of fluctuation effects grow, as the spatial dimension d decreases in (13), since $d-4$ is negative and increases in modulus. Obviously, an increase in fluctuation effects should be taken into account when studying the phase transions in two-dimensional graphene.

4. Conclusions

This review paper is aimed at formulating the Richard Feynman's classification of three stages in the study of natural phenomena and, first of all, the most important 3rd stage of cognition related to understanding the "first principles" that explain the reasons for the laws describing the experimental data. Here, we have considered Edward Moser's idea of a certain analogy between grid cells in brain and the Abrikosov vortex lattice in type II superconductors. In addition, we paid a special attention to the experimental studies, which led to the discovery of the hexagonal structures of grid cells in the human and animal brains, and to the main theoretical provisions that should be taken into account to formulate the first principle related to the proposed Feynman's classification, as well as to describe the physical parameters of the human brain and its medical applications, features of the process of generation and propagation of the action potential, and the electrical and chemical natures of the intercellular interection. It is these essential factors that will later enable us to show that the grid cells in a chemically interacting system of neurons rather belong to the universality class of real liquid-vapor systems with a scalar order parameter.

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О. Чалий, К. Чалий, О. Зайцева, А. Криштопа

ФЕЙНМАНІВСЬКА КЛАСИФІКАЦІЯ ПРИРОДНИХ ЯВИЩ І ФІЗИЧНІ АСПЕКТИ ВІДКРИТТЯ, ЗА ЯКЕ БУЛО ПРИСУДЖЕНО НОБЕЛІВСЬКУ ПРЕМІЮ З ФІЗІОЛОГІЇ АБО МЕДИЦИНИ 2014 РОКУ

Ця оглядова стаття присвячена формулюванню класифікації трьох етапів дослідження природних явищ Річарда Фейнмана та застосуванню цієї класифікації до дивовижного відкриття клітин гексагональної сітки, що утворюють систему позиціонування в мозку, яке було удостоєно Нобелівської премії 2014 року з фізіології або медицини. Проблема “grid cells” в мозку розглядається з урахуванням (а) експериментальних досліджень, які привели до появи шестикутників у мозку людини і тварин, (б) обговорення проблеми генерації та поширення потенціалу дії вздовж нервового волокна, (в) фізичних параметрів людського мозку та їх медичного застосування в методі гіпертермії для лікування злоякісних пухлин, (г) теоретичних міркувань з використанням певної аналогії між клітинами сітки в мозку та вихровою ґраткою Абрикосова в надпровідниках типу II і (д) гексагональний графен і розмірний кросовер.

Ключові слова: класифікація Фейнмана, фізичні параметри головного мозку, метод гіпертермії, струми провідності та індукції, вихрова ґратка Абрикосова.