

Life of Alexander G. Gurwitsch and his relevant contribution to the theory of morphogenetic fields

LEV V. BELOUSSOV^{1*}

and additional commentary by JOHN M. OPITZ² and SCOTT F. GILBERT³

¹*Department of Embryology, Faculty of Biology, Moscow State University, Moscow, Russia,*

²*Pediatrics, Human Genetics and Obstetrics and Gynecology, University of Utah, Salt Lake City, UT and*

³*Department of Biology, Martin Biological Laboratories, Swarthmore College, Swarthmore, PA, U.S.A.*

Alexander Gavrilovitch Gurwitsch was born on 26 September, 1874 in Poltava, not far from Kharkov in the Ukraine. His father was a lawyer and the whole atmosphere of this "provincial" Jewish family (with some roots in the Baltic states) was highly intellectual. Music and painting were priorities; Alexander's beloved step-sister was a professional pianist. Music was for him the best and probably the only relaxation from scientific work; even in his last years he was happy to play piano arrangements of Beethoven symphonies and quartets. No one in his family or among his friends was a natural scientist or a physician, and his gifts as a painter were such that after graduating from the classical gymnasium, he decided to become a professional artist and went to Munich to enrol in its famous Art Academy for professional training. However, he failed the entrance examination, and on that same day he made an impulsive life-decision by entering the medical faculty.

Nevertheless, artistic and, more importantly, aesthetic consideration continued to play an important and probably a decisive role in his further work. In his own words, it was the beauty of histologic structure, of mitotic figures and of embryonic preparations which

determined his interest in these very events. During his third or fourth year of medical training he rotated through the laboratory of the great histologist, Kupffer, together with his young American colleague, Herbert Niel, his best friend in those years. Soon, however, Gurwitsch developed a primary interest in embryology, an unusual thing to do in those days, and in 1895 he published his first paper on the action of different chemicals in gastrulation in the frog, being the first to describe the phenomenon of lithium-induced exogastrulation. Much later, in his unpublished "Autobiographical Remarks" he stated that "while observing for the first time developmental processes, I had that deep feeling of wonder, which, as rightly noted by Aristotle, is the mother of science: the appreciation of embryonic development as a miracle never left me the rest of my life and determined the direction of all my research work."

After graduating from Munich University in 1897 (as the student of A.A. Boehm), Gurwitsch worked until 1904 in the histology laboratories of the Universities of Strasbourg and Bern. In Bern he was Privatdozent and met his future wife, also medically trained, the Russian-born Lydia Felicine, who became his life-long devoted research collaborator. In those early years Gurwitsch gradually obtained an international reputation as a skilful and well-trained histologist, having completed in 1904 the important monograph "Morphologie und Biologie der Zelle". However, these early publi-

In searching for relatives/descendants of Gurwitsch in Moscow in 1994, one of the authors (J.M.O.) was privileged to meet Professor Belousov, grandson of Alexander G. Gurwitsch.

*Address for reprints: Fac. of Biology, Moscow State University, Vorob'evy ory, Moscow, 119899, Russia. e-mail: lbelous@embr.bio.msu.su

cations barely indicate his future interests and scientific originality. What was quite unusual for a medical histologist was his deep interest in and knowledge of physics. One of his closest friends was a relative of the same age, Leonid Mandelstamm, later on a famous physicist and member of the Soviet Academy of Sciences, the founder of the so-called Moscow school of theoretical physics. It was Mandelstamm who explained to Gurwitsch Einstein's newly published theory of relativity and other developments in physics; without such an influence Gurwitsch would probably not have created his later biological field theory.

In his reminiscences, Gurwitsch records a breakthrough in his mind in 1904 when he was in the depths of Russia, far from scientific centers and having been drafted into military service as a surgeon. He describes his shift in thinking as follows:

"Suppose we have detailed knowledge of a biologic process, such as spermiogenesis. This, however, is very far from giving us the full satisfaction of 'understanding' the process. But, what does it mean 'to attain understanding?'" For Gurwitsch it was nothing less than the formulation of a *general* law explaining the *entire* process *without* reducing it into its individual parts, even being possible to establish a causal link between them. Many years later, Gurwitsch expressed this conviction, which formed his subsequent scientific career, in the following words:

"... An invagination of a germ layer may be explained on a basis of a pressure difference between the two surfaces (or sides) or by cell movements, and so forth. This can be considered as an 'explanation' until we ask about the origin of pressure differences, or the mechanisms involved in cell movement, etc. However, questions of this kind become trivial when a larger process, rather than its individual components becomes the main problem. Suppose for a moment that each element in the succession A, B, C... can be explained separately, e.g. A as a swelling, B as a chemical reaction, etc. Interesting as they may be, these explanations are of subordinate importance when related to the main question: Why indeed is a *regular* (emphasis added) succession of these obviously quite different processes taking place at all?... Most biological problems are of this kind and all of embryogenesis is just such a single problem. Here we require a peculiar or, maybe, original explanatory principle... A process may become accessible to explanation only insofar as one can succeed in substituting [understanding of] a purely phenomenological multiplicity and diversity of events [for understanding] of a less diverse and less arbitrarily created picture correctly reflecting reality. The main aim of such a construction would be as follows. The entire process should be accessible for analysis into a finite, not very large number of stages, each stage being represented as a monotonic function of some definite initial conditions and a single variable such as time, or distance, etc. If this cannot be realized, we consider a given set of events as scientifically inaccessible. On the other hand, even a partial success of such an enterprise is an obvious step forward." (Gurwitsch, 1944).

Such an unusual view made the young histologist an isolated person among his descriptively minded colleagues, but also among the experimentalists who tried, following Wilhelm Roux' *Entwicklungsmechanik*, to discover one after the other those elementary causes of the developmental processes, which, according to Gurwitsch, were not *per se* of general importance. This, however, did not affect in the slightest way the close and friendly personal relationship between Gurwitsch and Roux who was

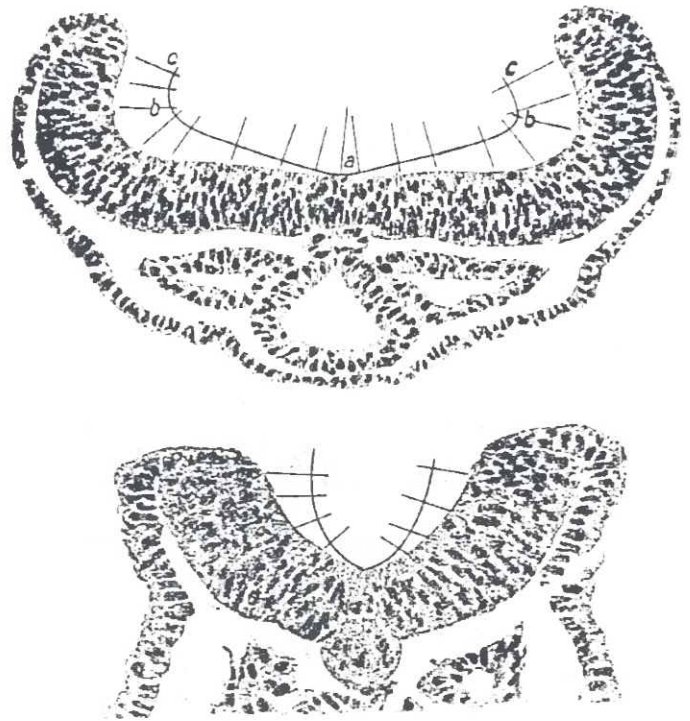


Fig. 1. "Prognostic" orientation of longitudinal nuclear axes in Selachian neural plate. (Top) The prediction based on theory as to where the surface of the neural plate will move morphogenetically is represented by the line *cbac*, the contour of the line being based on the lines drawn perpendicular to the surface of the neural plate through the long axis of representative nuclei in corresponding mirror image sides of the neural plate. Exactly this line will be reached in about 1 h of further development. **(Bottom)** Predicted surface of the neural plate at a somewhat later stage of Selachian neural tube formation.

always glad to accept his papers into his famous *Archiv für Entwicklungsmechanik*, and who recommended the young scientist as "einen eigenen Denker, der manches anderes sieht und bewehrt als andere" (as an original thinker who sees much more and evaluates better than others). Gurwitsch's *Atlas and Outline of Embryology of Vertebrates and of Man* (1907) was a beautifully illustrated and highly regarded text on that subject prepared for his course at the St. Petersburg Women's University. In the 1920s when Roux invited Gurwitsch to take his chair at the University of Berlin, Gurwitsch refused politely, but firmly, linking his fate again with Russia, then already under Soviet leadership.

However, let us return for a moment to the first decade of the century. Some 40 years later Gurwitsch once told me that Roux had asked him: "Lieber Kollege, warum experimentieren Sie nicht?" (Dear colleague, why don't you experiment?) In reply, Gurwitsch explained to him the details of his original approach to development which consisted in a thorough quantitative (often statistical) analysis of morphogenesis. This resulted in the major papers which he published, mostly in German, between 1910 and 1914 while Gurwitsch was (until 1918) Professor of Histology at the St. Petersburg Women's College (in those times women in Russia could not attend the other universities of the empire). The most important papers are: "Premises and causes of cleavage and cell

division," "Determination, normality and stochastic aspects of ontogeny," "Heredity as a process of realization," and "Heredity of form" (paraphrases of German titles, JMO). Let us briefly review the main ideas and findings reported in these papers.

The main task Gurwitsch set himself was not only to trace a general outline but also to evaluate quantitatively the influence of a whole (embryo or its parts) on its components (cells). Here, Gurwitsch followed the way outlined by Hans Driesch who, in turn, paid great tribute to Gurwitsch, characterizing him as "...the original thinker and profound Russian investigator (Driesch, 1921). Stimulated by the beautiful work of Driesch, Gurwitsch wrote: "I consider the properties and manifestations of 'the whole' as a reality, and think, that they should be studied in a manner similar to those of any other natural object...I am trying to study the participation and the mode of action of these factors on the commonest and best-studied of all subjects: in biology." (Gurwitsch, 1922).

The main theoretical step forward as compared to the ideas of Driesch was to consider "the whole" not as a static entity (or as a reflection of some unique experimental situation), but as an invariant dynamic law pertaining to the entire process of development. Gurwitsch moved step-by-step in that direction, trying never to lose contact with real biological data.

A first step in this research program was a statistical study of the distribution of mitotic division in several different but always geometrically precise objects such as the sea-urchin gastrula, chick optic cup, or onion root. Gurwitsch found that even in apparently symmetrical objects, the number of cell divisions occurring simultaneously on the two opposite halves were far from equal; instead, they related to each other either as members of a Gaussian (*Normierung*, "normality") or a super-Gaussian (*Obernormale*) distribution. Thus, the individual cell divisions appear to be related to each other more or less randomly and effect their end result only in relation to a supra-cellular ordering or integrating factor (Gurwitsch, 1910). This was the first investigation in biology documenting the stochastic aspects of a very regular developmental process; presently it is virtually impossible to make a complete list of such examples. This landmark paper may rightly be considered the earliest example of a powerful trend in science dealing with "deterministic chaos."

In his next, most theoretical paper in this series (Gurwitsch, 1912), the author made an attempt to formulate empirically verified criteria of involvement of a supra-cellular ordering factor in morphogenetic processes. Thus, he hypothesized that the determination of developmental fate of an embryonic part by a supra-cellular ordering principle would be more probable than its determination by the attributes of the individual elements (cells) if: 1) the dependence between cell properties and their positions with respect to a common set of coordinates is precise and mathematically simple; 2) a gradual increase of the regularity and in the precision of the arrangement of the cells is observed within the course of development; 3) the outlines of a part or a whole embryo can be formulated mathematically more precisely than the shape and the arrangements of its (internal) parts. This is the first paper in which Gurwitsch introduces explicitly the idea of a "field" as a supracellular ordering principle governing the fate of cells; he referred to this principle or effect as a *Kraftfeld* or *Geschehensfeld* (field in which a force is exerted or in which *Geschehen*, events, occur in an integrated, coordinated manner).

The next step in this program was made in the 1914 paper devoted to the morphogenesis of the shark brain. Here Gurwitsch



Fig. 2. The Gurwitsch Laboratory in Simferopol (1923-1924).

First Row (left to right): Dmitry Hukovsky, Alexander Gurwitsch, Lydia Gurwitsch, Wolf Ravvin, Alexander Levin. Second Row: Georgy Petsky, Zinaida Yaretskaya, Elizaveta Zabolot'naya, Rebecca Ravvin, Ruzinov, Alexander Karpas, Semen Zalkind, Natalya Temnikova, Gleb Frank, N. Gurwitsch, Fridrich Bezler (Photograph from archives of L. Beloussov.)

documents his most successful histological demonstration of a "law" that seems to be universal for all epithelial morphogenesis: in the epithelial layers destined to change their shape, the long axis of the nuclei (and, as became evident later, the lateral cell walls as well) are oriented perpendicularly not to the transient surface of the layer, but to that to be established some time later (say, after several hours of further development) (Fig. 1). Gurwitsch spoke of this phenomenon as "prognostic nuclear orientation" and considered it as evidence for the existence within a space surrounding the embryo of a field of force with its equipotential surface(s) coinciding with the configuration to be reached eventually by the embryonic parts/layers during morphogenesis. The synonym for this surface field of force was "dynamically preformed morphae." The epithelial layer was situated, in a manner of speaking, in a *Kraftfeld* the

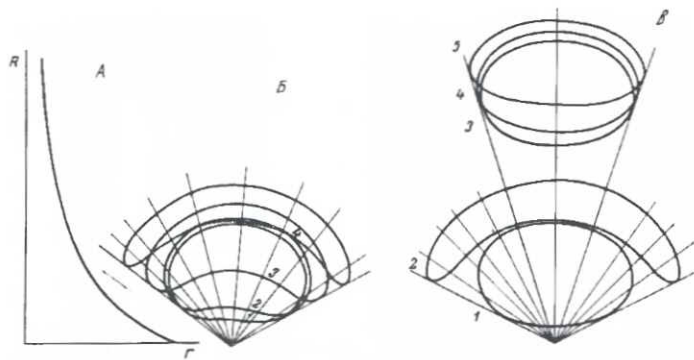


Fig. 3. Prechondrogenic condition of mesenchyme in the developing limb of *Ambystoma*, the so-called Anikin patterns. **Right:** Modeling of the deformations of prechondroblast nuclei in the rudiments of forelimb phalanges of *Triton* larvae. The nuclear surfaces are postulated to be deformed by a force exerted from the geometrical center *O* of the entire rudiment. For each point on the surface of a nucleus, the rate of centripetal movement is found to be inversely proportional to the distance of the point from the center *O*. **Left:** 1-4 are the successive stages of deformation of the same nucleus. The results predicted by theory correspond exactly to the observed progressive changes of shape of the nuclei (after Anikin, 1929, from Gurwitsch, 1944). (Figure courtesy by Dr. Neil H. Shubin, University of Pennsylvania).

intensity of which stood in an "inverse relationship to the distance between the cells involved and the surface of the force effect" (Gurwitsch, 1914). This then was a true field construction permitting predictions related not only to the orientation of the nuclei, but also to the relative rates of the cell movements and the relative orientation of the cell axis in different regions of the brain.

It is characteristic of Gurwitsch that the word "hereditary" (*Vererbung*) is used in the title of his 1912 and 1914 papers in spite of their purely embryological content. It is a fact that Gurwitsch firmly considered "heredity" and its effects during embryogenesis as a single, indivisible phenomenon; therefore, the hereditary factor ought to behave exactly as the supra-cellular field forces which he studied. Consequently, he became a stubborn opponent of a particular genetics as it emerged in those years from Morgan's laboratory. Apparently this added much to Gurwitsch's non-acceptance by his colleagues in Russia. However, it is important to record in this context that many years later in 1948, when Russian geneticists became victims of Lysenko and some colleagues urged him to strengthen his stand on Mendelism by reminding him of his previous public disagreement with geneticists, he rejected such a suggestion with indignation and publicly joined the side of the persecuted. But, let us return to the second decade of the century.

The intensive labors of Gurwitsch were interrupted first by WWI, during which he worked as a military surgeon in one of St. Petersburg's hospitals, and then by the revolutions of 1917. Having lost all possibility for scientific study and suffering from hunger, Gurwitsch accepted in 1918 an offer to work at the newly established Tauric University in Simferopol (Crimea) together with a group of first-class Russian scientists including the outstanding geologist and geochemist, Vladimir Vernadskii, a former member of the Imperial Academy of Sciences and good friend of Hans Driesch and Gurwitsch. The trip across Russia and the Ukraine, already deeply involved in a civil war, lasted all winter, being

interrupted by a severe infectious disease of himself and his family. Luckily, Gurwitsch survived and in the spring of 1919 reached Simferopol. Despite many deficiencies and food shortages, Gurwitsch considered the years spent in Crimea (1919-1924) the happiest of his life. These were the early post-revolutionary years, full of hope for the future and for greater democracy, at that time not yet suppressed by Bolshevik ideology. He was, for him, socially unusually active, in the University, and he was happy to live in this beautiful land (Fig. 2). Here, in 1923 he made his famous discovery of the (invisible ultraviolet) mitogenic rays that stimulate cell division in onion roots. This began the long and dramatic study of the mitogenic rays which will not be considered here in detail. Let us only mention that this story had its ups and downs. After initial world-wide recognition in the 1920s and 1930s, some claims appeared that the phenomenon did not exist at all. Because of that and the subsequent political cataclysms in Europe and Russia, work on this phenomenon dropped almost to zero level. However, that was not the end of the story by any means. In recent years the existence of ultra-weak radiation from living organisms was confirmed numerous times by physical methods and interest is being renewed in this phenomenon (see for example Popp *et al.*, 1992 and Belousov *et al.*, 1997). For Gurwitsch the main task for the rest of his incredibly productive and energetic life was the study of mitogenic rays and their pertinence to medicine. The theoretical work on developmental fields had to be put aside momentarily, although Gurwitsch continued to regard it of fundamental importance.

The next work on this subject and the first one with the word "field" in its title was published by Gurwitsch in 1922. This time the analysis involved the development of the flower of composites and the fruiting body of a fungus. In both cases, he showed that these developing parts manifested a gradually increasing exactness of their overall shape, in spite of considerable fluctuation in shape and rate of growth of its constitute parts similar to his previous work on the developing shark brain. Gurwitsch interpreted these observations as evidence for an overall field of force governing the behavior of the components. In contrast to the work of 1914, he makes the important step forward by suggesting that somehow "such a field is produced by the developing body itself, rather than appearing in an unknown way in the space surrounding the developing organism."

In 1924 Alexander Gurwitsch, now a famous scientist, was appointed Professor of Histology at Moscow University. Here he worked until 1929 when the ideological conflict with the Communist administration (provoked by an assistant of Gurwitsch, namely the notorious Olga Lepeshinskaia, q.v. Soyfer, 1994) forced him to leave his chair¹). While continuing his studies of mitogenic rays, Gurwitsch was less able to attend to the field problem. However, an important piece of work on that subject was produced, under Gurwitsch's direction by his pupil A.W. Anikin (1929). In this work Anikin formulated a general law on the deformation of the nuclei of mesenchymal (prechondroblast) cells in the primordial phalanges of *Triton* embryos. The formulation of this law appeared to be quite simple: All of the observed deformations could be described by assuming that the elements, all parts, of a nuclear surface are "repulsed" from a geometrical center of the primordium in a

¹) Lepeshinskaia was never Gurwitsch's protégée; he had to endure her as an influential Party member at his Department in Moscow University (LVB).

hyperbolic manner (force decreasing in inverse proportion to the distance from the center of the primordium) (Fig. 3). This work aroused considerable interest and was discussed more than 30 years later in the important book *"New Patterns in Genetics and Development"* by Conrad Waddington (1962). "Anikin" fields or patterns are now a normal part of the language of, theoretical, biologists dealing with the evolutionary aspects of development of limbs (q.v. Shubin and Alberch, 1986; Alberch and Hinchcliffe, 1991; Shubin, 1991).

Until the beginning of WWII, intense studies on mitogenic radiation allowed Gurwitsch almost no time to further elaborate the field theory. But, he always kept it in mind. The apparent involvement of molecular events in the processes of mitogenic radiation gradually convinced him that the principles of supra-molecular ordering should also be extended to this level as well. Already in the early 1930s, we find in his papers and the important book *"Die histologischen Grundlagen der Biologie"* (The Histological Foundations of Biology), the beginnings of the concept that ordered structure at a molecular level is far from a thermodynamic equilibrium. He called these structures "non-equilibrium molecular constellations" (NEMC) and interpreted the data from some of his laboratory experiments on mitogenic radiation (so-called degradational radiation, detectable immediately after reversible tissue damage) as evidence for the existence of NEMC. Gurwitsch's NEMC may be considered the earliest formulation of the "dissipative structures" of modern self-organization theory (see for example Nicolis and Prigogine, 1977).

As of 1930, Gurwitsch worked in Leningrad (former and future St. Petersburg) directing a large laboratory in the famous All-Union Institute of Experimental Medicine (where Ivan Pavlov and many other outstanding scientists worked during those years). Those were the years of greatest recognition of his work (Fig. 4). In 1934, Gurwitsch opened the International Congress of Radiobiology in Venice and after the Congress lectured in several European countries. In 1941, he was awarded a Stalin Prize for his mitogenic radiation work related to cancer (at that time for the diagnosis of cancer). In the same year Russia entered WWII and soon Leningrad became the object of German air bombardment and artillery shelling with increasing food shortages.

Alexander Gurwitsch, his wife, Lydia and their daughter, Anna, a Doctor of Science and his assistant, stayed in the besieged town until December with indomitable spirit and extraordinary courage. Without an opportunity to do experimental work, he wrote a diary, devoted almost exclusively to science. However, an occasional entry (e.g. November 7, 1941) gives an indication of their personal condition: "Situation deteriorating; worsening of undernutrition", (what a restrained expression of mortal hunger!... and then: "Returning to equilibrium structures, etc.")

Fortunately the Gurwitsch family was evacuated safely from Leningrad in December 1941, first by plane over the German frontlines and then in a medical train (not cattle car as was usual in those times) to Kazan on the Volga. Here, the Gurwitsch family (including Lev Belousov, a 6-year-old boy) spent the winter in a little wooden house in a room of 9 square meters. The atmosphere was highly intellectual, since most of the staff of the Soviet Academy of Sciences was evacuated to the same town, and many came to visit Gurwitsch. Never in Lev's life had he seen so many Academy members packed so densely in one room. The topics of discussion varied enormously, one of the most mysterious and

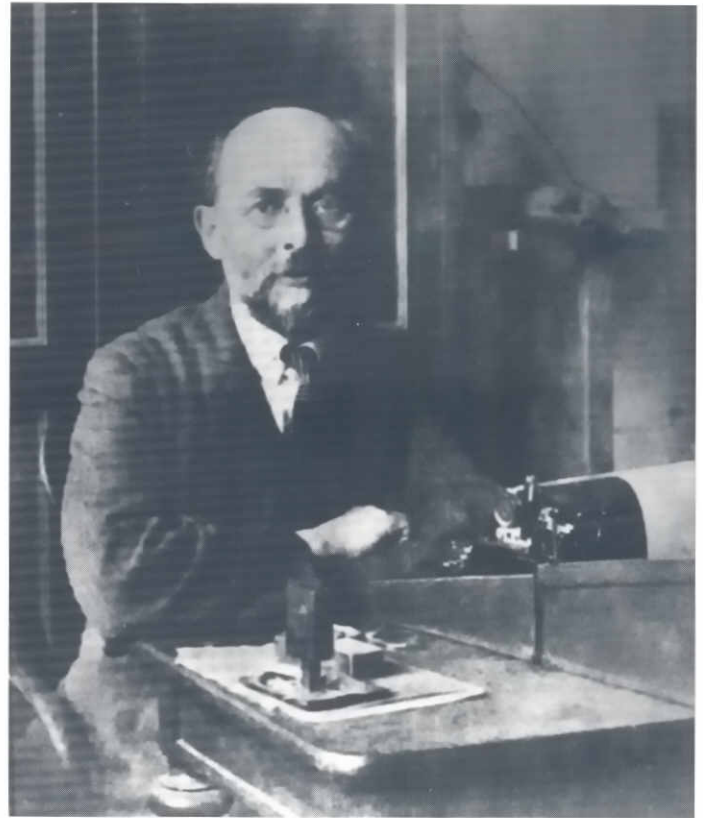


Fig. 4. Alexander Gavrilovich Gurwitsch (1874-1954). (From archives of L. Belousov.)

serious being the "uranium bomb," as it was called at that time (the Russian atomic bomb project having had its start in Kazan). And when there were no guests, grandfather Gurwitsch liked to tell him something of world history (the fall of the Roman Empire, Napoleon's wars, etc.), a subject Lev recalled in perfect detail.

Under these circumstances, Gurwitsch began to elaborate a completely new, final version of the field theory which was published as a small book in Russian in 1944 and in French in 1947. In it Gurwitsch undertook the task of formulating a general law governing the outcome of biological processes (instead of a number of particular laws, such as the one formulated by Anikin in 1929), and of extending this law toward the realm of molecular processes. In this connection it is of interest that Gurwitsch was one of the first to use the term "molecular biology"; he was also among the first opponents of extending classical cytology towards a molecular level.

The main postulates of the new version of the field theory were as follows (Gurwitsch, 1944):

"The field acts on molecules. It creates and supports in living systems a specific molecular orderliness. This means, in our opinion, any spatial arrangement of the molecules which cannot be derived from their chemical structures, or from equilibrium states such as chemical bonds, van der Waals forces, etc. Consequently, molecular orderliness generally is a non-equilibrium phenomenon..."

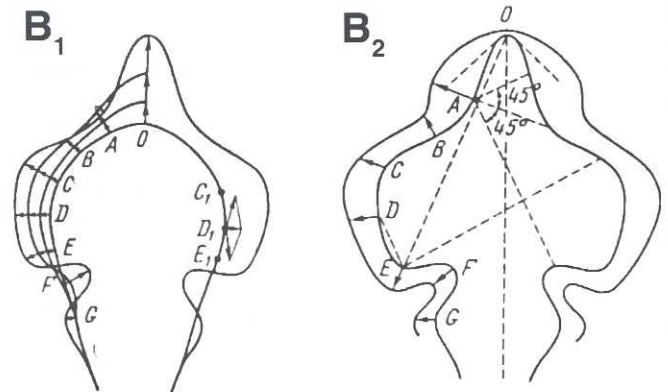
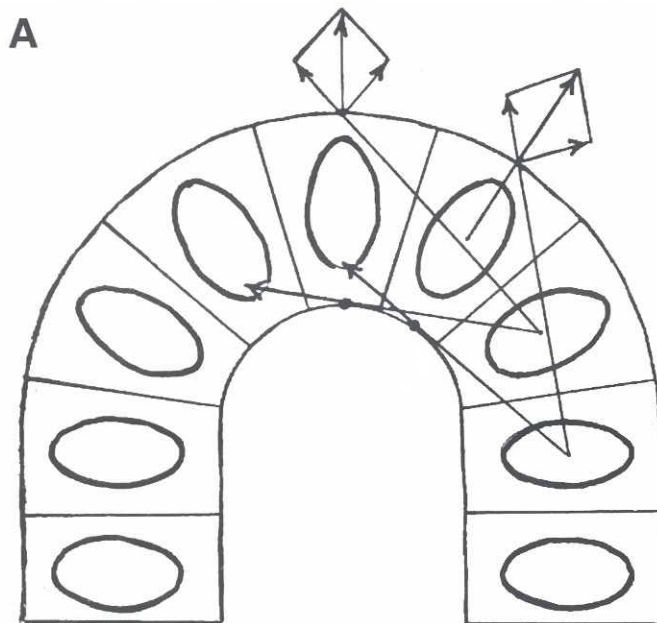


Fig. 5. Illustrations of the "curvature-increasing rule" based on the 1944 version of Gurwitsch's field theory. (A) Field vectors at the tip of archenteron invagination of the sea-urchin (Gurwitsch, 1944, Fig. 23). (B1 and B2) Application of the curvature-increasing rule to the morphogenesis of hydroid polyp *Obelia loveni*. In B1 the shift of points O and A-G on the initial contour are assumed to occur along a path perpendicular and proportional to the original contour of the curve. In B2, the interactions

between the opposite walls of the primordium are introduced (dotted lines) in a manner suggested by Gurwitsch (1944). As a result, rather realistic changes of shape are modeled (Belousov, 1968). Later, another model for the same changes of shape was introduced (Belousov and Lakirev, 1991).

The field is anisotropic... The field is continuous and successive... During cell division the cell field divides as well ...

A cell creates a field around it, that is to say, the field extends outside the cell into intracellular space... Therefore, at any point of a group of cells there exists a single field being constituted of all of the individual cell fields... Hence, the properties of this aggregate field will depend, besides other factors, also on the configuration of the multicellular whole. Rather than postulating independently existing supracellular fields, we now attribute their function to a field representing the vectorial addition of the individual cell fields...

A field is somehow associated with the molecules of chromatin, but only while they are chemically active... A postulated field continuity may be understood molecularly in the following way: If in the vicinity of chromatin molecule A, which is at the given moment a field "carrier", an active chromatin molecule B is synthesized, the field of molecule A induces the field of molecule B losing at the same time its own field....

The field employs the energy released during exothermic chemical reactions in living systems to endow molecules (proteins, peptides, etc.) with ordered, directed movement... A point source of a cell field coincides with the center of the nucleus, hence, the field is, in general, a radial one... The direction of the field vectors is centrifugal (i.e. the vectors are directed from a field center to the periphery)".

For the author, one of the main advantages of this version of field theory was the ability to model the successions of changes of shape of embryonic rudiments. For any non-spherical multicellular configuration, the field theory postulates rather definitive successive changes of shape, which, in the simplest cases, could be visualized with "pen and paper models." The main one repeatedly exploited by Gurwitsch may be called the "curvature-increas-

ing role." This derives from the postulate that the "morphogenetically active" cell is unstable and reacts to any small local curvature inequalities by tending to enhance them. Gurwitsch applied this concept to sea urchin gastrulation (Fig. 5A) and to the formation of the embryonic brain. I remember vividly how excited I was applying in the 1960s the curvature-increasing rule to the development of the buds of hydroid polyps, and getting, as a result, quite exact predictions of subsequent shape (Fig. 5 B1,B2). My first reaction was that the field theory must be absolutely true, and it required a long time for me to realize that these postulates are only formally correct (not a mean feat after all, considering there are several of them) while the underlying mechanisms may be quite different from (and much simpler than) those postulated by Gurwitsch.

Alexander Gurwitsch continued to elaborate his field theory until his last days. As a result of Lysenko's coming to power in 1948, Gurwitsch was expelled from the directorship of the large Institute of Experimental Biology of the USSR Academy of Medical Sciences (Fig. 6). At that time he began to write his last book, tentatively entitled: "*Analytical Biology*." In some sections of this large unfinished manuscript published in Russia only 40 years later (Gurwitsch, 1991), the author approached rather closely the much later established self-organization theory. Thus, Gurwitsch stated that the central problem in biology was the "irrepressibility" of the coming-into-being process and he expressed a "viewpoint, different from a common one, that from a really adequate analysis of any given developmental stage, its passage into the next one should follow inevitably" (Gurwitsch, 1991, p. 124). He paid particular attention to interactions of processes at different levels and even formulated a concept of a closed-feedback loop between the morphogenetic field and its morphogenetic consequences. In his diary, he considered the main goal of his field theory to be a model



Fig. 6. Gurwitsch laboratory in Moscow, 12 June, 1948. First Row: Alexander Gurwitsch, second from the right. The third from the right is daughter Anna Gurwitsch. (From archives of L. Belousov.)

of a synergistic, non-additive interaction between the elements. Unfortunately these sometimes profound and prescient insights into developmental biology were tightly bound to the other unacceptable postulates of his 1944 theory.

In the view of Professor D. Chernavsky (personal communication), which I share in general, on the inadequacy of the last field theory of Gurwitsch, the roots of this true scientific tragedy lie in attempting to solve essentially non-linear problems of biological organization with the use of quasi-classical linear fields. Gurwitsch was correct and very much ahead of his time in stressing non-equilibrium orderliness and vectorization of molecular processes essential in living organisms. But he certainly could not foresee that a modern, largely non-linear self-organization theory (i.e. Nicolis and Prigogine, 1977; Haken, 1978; Prigogine, 1980, etc.) such vectorization does not require at all the existence of some kind of repulsive field with a definite source.

The main difference between Gurwitsch's and the more modern point of view can be briefly formulated as follows: Gurwitsch believed (in classical traditions), that the presence of NEMC indicate the existence of a field which is external to them and is required for maintaining NEMC. Meanwhile, according to a more modern point of view of non-equilibrium structures, they are self-maintained and generate themselves a kind of non-linear field.

As I remember, Gurwitsch never held his field theory as a dogma. One day I found him in a brown study in his armchair with an embryology text in his hand. When I asked him what was bothering him, he replied: "Oh, but I cannot derive the pattern of sea-urchin cleavage from my field theory. And sometimes I doubt whether this theory is really true."

The last years of Alexander Gurwitsch were sad. In 1951 Lydia, his beloved wife and lifetime research collaborator died, and the general political and scientific atmosphere was very gloomy. The research on mitogenic radiation was reduced to a minimal scale and continued only due to the enthusiasm of his daughter, Anna, with a small staff and minimal facilities. Since 1948 it was impos-

sible for him to publish his theoretical studies. When I entered the Faculty of Biology of Moscow University in 1952, my grandfather asked me whether some of my friends might be interested in attending a private lecture course in biology he might like to give, not realizing that such attendance of a course by a man persecuted by the powerful Lysenko was quite unsafe for all involved. Only one person joined me, my close friend, Michael Lipkind, now a Professor of Virology at Jerusalem University. During the entire winter 1953/4, Gurwitsch read lectures to both of us, covering a wide variety of problems, including Mendel's laws, officially forbidden to be taught at this time. He mentioned his field theory only tentatively, "being afraid," he said, "to infect you with these heretical ideas."

Alexander Gurwitsch died on July 27th, 1954, at the age of 79 of heart disease. His mind was completely clear until his last day. Several days before his death I returned to Moscow from field work in Botany. "Well?" asked grandfather, already severely ill, with his usual demanding voice, "What else have you discovered now?" I told him something about a budding pattern in a plant. "And what is the scientific name of the plant?" he asked. "*Azarum*..." I started, "Oh, *Azarum europaeum*" he continued, "and do you really think no one ever noticed that before?" Those were the last words which I ever heard from him. And this exactness of utterance was very typical of him, an exactness directed by this truly outstanding man first of all to himself.

Interest in Gurwitsch and his intellectual contributions is increasing. In 1991 Gurwitsch's last book was published-with a 40 year delay! In 1994, on the occasion of the 120th birthday of Gurwitsch, Moscow State University held the first International Alexander Gurwitsch Conference on Non-Equilibrium and Coherent Systems in Biology, Biophysics and Biotechnology. This Conference was attended by several dozen investigators from Russia, Germany, China, Italy, The Netherlands, New Zealand, and other countries who discussed several of the scientific problems worked on by Alexander Gurwitsch (qq.v. Belousov and Popp, 1995).

COMMENTARY

by John M. Opitz and Scott F. Gilbert

The formulation of field concept by Gurwitsch and Spemann occurred independently. Gurwitsch began work on the subject in 1910, completed his manuscript at Simferopol and submitted it on November 29, 1921. It was published in 1922. Spemann's "field of organization" was also published in 1921.

Paul Weiss (1923) derived his concept of the field from that of Gurwitsch, and from his own experiments on regeneration. Paul Weiss' textbook *Principles of Development* (1939) summarized the field concept and used it as an organizing concept for all of embryology. Weiss noted that "the field concept has been extensively adopted by embryologists," and he proposed a series of postulates to identify and characterize such fields. He saw fields as having the following properties:

1. Field activity is invariably bound to a material substratum.
2. A field is an entity and not a mosaic.
3. The structure of the field varies in three dimensions, and usually there is an axis to the field's effect.
4. Like the poles of a magnet, none of the component elements of a field district can be identified with any particular component of the field.
5. When the mass of a field is reduced, the structure of the field is not affected.
6. The splitting of a field district leaves each half in possession of a complete proportionate field equivalent in structure to the original single field.
7. The fusion of two field districts can produce results based on the orientation of their axis.

The concept of the field was based on empirical evidence, and the field attributes of individuality, heteropolarity, and gradation were reconstructions from observed experimental results. To Joseph Needham (1950), the concept of the field was the central concept of embryology, giving "powerful aid to the codification of *Gestaltungsgesetze*," the research program that sought the laws of ordered form. Embryologist and historian Jane Oppenheimer (1966) concurred, noting that the concept of the morphogenetic field was assumed by embryologists of the 1930s and 1940s.

Spemann (1938; pp. 298-317) discussed three concepts of the field, and he did so in a developmental series: *From Gurwitsch to Weiss to Spemann*. Spemann related his concept to that of embryonic induction, and emphasized chemical influences in addition to "physical factors such as tension, electrical states, and rays which are extensively thought of in the physical field conception." The other two concepts of the field were seen as inferior and leading up to his. He viewed Weiss' fields as just more examples of Driesch's "harmonious equipotential systems" and did not see Weiss' field as a conceptual advancement. (Weiss [1935] had already interpreted Spemann's experiments in terms of fields — instead of organizers — and had found them wanting). Gurwitsch's field is dismissed as being independent of the embryo and not necessarily linked to a physical substrate. (Although Spemann acknowledges that he may be wrong in this interpretation, his extensive quotation from Gurwitsch suggests Gurwitsch's taking the physical metaphor of electromagnetic fields too literally).

The concept of the morphogenetic (or embryonic) field was extremely robust in the 1930s, as is evidenced by the debates concerning the structure of the fields. Huxley and deBeer (1934) popularized the notion of the "gradient field," extending the work of Morgan and Child on regeneration, while Weiss' 1939 book put forth a more ecological and interactive notion of the field (see also Schmalhausen, 1938; Filatov, 1943). However, after World War II, the concept of fields went into dramatic decline. There were several reasons for the decline. First, biochemical methods (such as those employed by Needham) were not adequate to enable embryologists to analyze field properties such as limb polarity, neural patterning, and lens induction. Second, there was the decline of the scientific infrastructure in Germany and other European countries. The Spemann laboratory, for instance, had scattered around the world. Third, Morgan and other geneticists were in direct opposition to the morphogenetic field which they saw as a rival to the explanation for heredity. They actively blocked the publication of materials by those investigators (especially C.M. Child and his students) who favored field explanations (see Haraway, 1976; Mitmann and Fausto-Sterling, 1992; Gilbert *et al.*, 1996). Fourth, the field concept had been made extensively holistic and refractile to the scientific analyses of its time. Although Weiss and Spemann vehemently claimed that embryonic fields were real, physical entities, they could not be analyzed by the techniques of their day. Indeed, Weiss' fourth postulation in his characterization of morphogenetic fields made it doubtful that fields could ever be reduced to biochemical analysis. This was seen by many geneticists as evidence of poor science.

The notion of the field persisted, especially in studies of limb generation and of *Drosophila* imaginal discs (see Huettnner, 1948; Gilbert *et al.*, 1996). The last theoretical exposition of the embryonic fields prior to the 1980s was probably that of Curt Stern (1954). In this remarkable article, he equated embryonic fields with the prepattern of the embryo. After analyzing the data concerning the ability of genes to regulate where and when they are expressed, he noted, "Yet this astonishing result fits perfectly well into existing concepts of the embryologist. He has discovered the existence of prepatterns which he calls embryonic fields... Under normal circumstances, the differentiation takes place in only a limited part of the whole field, at a peak, figuratively speaking. Once differentiation has set in on the peak, no other differentiation occurs within the larger field ...The prepatterns of the embryonic tissue in *Drosophila*, which call forth a response of genes involving the differentiation of bristles, are embryonic fields of larger dimensions than the limited points of normal location of bristles."

Stern also hypothesized that the fields were themselves the products of genes. From here on, the fields are considered (when considered at all) as epiphenomena of gene expression. As part of the genetic explanation of embryology, genes were considered primary. Fields, if they existed, were merely gene products.

During recent years, there has been a re-appreciation of morphogenetic fields as units of developmental and of evolution (see Goodwin, 1982, 1995; De Robertis *et al.*, 1991; Opitz, 1993; Gilbert *et al.*, 1996). Interestingly, Stern (1954) hinted that changes in embryonic fields might allow for evolutionary novelties to arise.

Acknowledgments

J.M.O. is deeply grateful to colleagues in the Institute of Medical Genetics in Moscow, who made it possible to meet Professor Belousov. We are also grateful to Ms. Melanie Callahan for expert secretarial collaboration.

References

- ALBERCH, P. and HINCHCLIFFE, J.R. (1991). The developmental basis of limb evolution. In *Developmental Patterning of the Vertebrate Limb*. (Eds. Hinchcliffe, J.R., Hurlle, J.M., Summerbell, D.). Plenum Press, New York, pp. 439-442.
- ANIKIN, A.W. (1929). Das morphogene Feld der Knorpelbildung. *W. Roux Arch Entwmech. Org.* 114: 549-577.
- BELOUSSOV, L.V. (1968). Interpretation of a succession of morphogenetic processes in a hydroid, *Obelia loveni*. *Biol. Nauki* 7: 21-27.
- BELOUSSOV, L.V. and LAKIREV, A.V. (1991). Generative rules for the morphogenesis of epithelial tubes. *J. Theor. Biol.* 152: 455-468.
- BELOUSSOV, L.V. and POPP, F.A. (1995). *Biophotonics - The Non-Equilibrium and Coherent Systems in Biology, Biophysics and Biotechnology*. BiolInform Services, Moscow (in English). International Institute of Biophysics Station Hombroich Vockrather Swasse, Neuss, Germany.
- BELOUSSOV, L.V., VOEIKOV, V.L. and POPP, F.A. (1997). Gurwitsch mitogenetic rays (in Russian). *Priroda N3 (979)*: 64-80.
- DE ROBERTIS, E. A., MORITA, E. M., and CHO, K. W. Y. (1991). Gradient fields and homeobox genes. *Development* 112: 669-678.
- DRIESCH, H. (1921). *Philosophie des Organischen*. Engelmann, Leipzig, p. 153.
- FILATOV, D. P. (1943): Developmental mechanics as a method for study of some of the problems of evolution. *Zh. Obshch. Biol.* 4: 28-46.
- GILBERT, S. F., OPITZ, J. M., and RAFF, R. A. (1996). Resynthesizing evolutionary and developmental biology. *Dev. Biol.* 173: 357-372.
- GOODWIN, B. (1982). Development and evolution. *J. Theor. Biol.* 97: 43-55.
- GOODWIN, B. (1995). "How the Leopard Changed Its Spots: The Evolution of Complexity." Scribner, New York.
- GURWITSCH, A.G. (1907). Atlas und Grundriss der Embryologie der Wirbeltiere und des Menschen. J.F. Lehmann, Munich, pp. 345.
- GURWITSCH, A.G. (1910). Über Determinierung, Normierung und Zufall in der Ontogenese. *Arch. Entw. Mech.* 30: 133-193.
- GURWITSCH, A.G. (1912). Die Vererbung als Verwirklichungsvorgang. *Biol. Zbl.* 22: 458-486.
- GURWITSCH, A.G. (1914). Der vererbungsmechanisms der form. *W. Roux Arch. Entwmech. Org.* 39: 516.
- GURWITSCH, A.G. (1922). Über den Begriff des embryonalen Feldes. *Arch. Entw. Mech.* 51: 388-415.
- GURWITSCH, A.G. (1922). Weiterbildung und Verallgemeinerung des Feldbegriffes. *Arch. Entw. Mech.* 122: 433-454.
- GURWITSCH, A.G. (1930). "Die histologischen Grundlagen der Biologie." Fisher, Jena, pp. 310.
- GURWITSCH, A. (with the collaboration of Gurwitsch, L) (1932). *Die mitogenetische Strahlung, zugleich zweiter Band der 'Probleme der Zellteilung*. Julius Springer, Berlin, pp. 383.
- GURWITSCH, A.G. (1944). *A Biological Field Theory*. Sovietskaya Nauka; Moscow, pp 156. (Russian).
- GURWITSCH, A.G. (1947). *Une théorie du champ biologique cellulaire*. Bibliotheca Biotheoretica, Series D.V., Leiden.
- GURWITSCH, A.G. (1948). A concept of whole as related to the biological field theory. In *Works on Mitogenesis and the Theory of the Biological Field*. USSR Acad. Med. Press; Moscow, pp. 141-147 (in Russian).
- GURWITSCH, A.G. (1991). *Principles of Analytical Biology and the Theory of Cellular Fields*. Nauka, Moscow, pp. 288.
- HAKEN, H. (1978). *Synergetics*. (Eds. Springer-Verlag) Berlin, Heidelberg, New York.
- HARAWAY, D (1976). *Crystals, Fabrics, and Fields: Metaphors of Organicism in Twentieth Century Developmental Biology*. Yale University Press. New Haven.
- HUETTNER, P. (1948). *Textbook of Vertebrate Embryology*. MacMillan, New York.
- HUXLEY, J. and DEBEER, G.R. (1934). *The Elements of Experimental Embryology*. Cambridge University Press, Cambridge.
- MITMAN, G. and FAUSTO-STERLING, A. (1992). Whatever happened to Planaria? C. M. Child and the physiology of inheritance. In *The Right Tool for the Job: At Work in Twentieth-Century Life Sciences*. (Eds. A. E. Clarke and J. H. Fujimura). Princeton University Press, Princeton.
- NEEDHAM, J. (1950). *Chemical Embryology*. Cambridge University Press, Cambridge.
- NICOLIS, G. and PRIGOGINE, I. (1977). *Self-organization in nonequilibrium systems*. John Wiley and Sons. New York, London.
- POPP, F.A., LI, K.H., and GU, Q. (eds) (1992). *Recent advances in biophoton research and its applications*. World Scientific. Singapore, New York, London, Hong Kong, p. 504.
- PRIGOGINE, J. (1980). *From being to becoming*. Freeman and Company, New York, p. 272.
- OPITZ, J. M. (1993). Blastogenesis and the primary field in human development. *Birth Defects: Orig. Art. Ser.* 29 (1): 1-34.
- OPPENHEIMER, J.M. (1966). The growth and development of developmental biology. In *Major Problems of Developmental Biology*. (Ed. Locke, M). Academic Press, pp. 1-27.
- SCHMALHAUSEN, I. I. (1938). *Organism as a Whole in Individual and Historical Development*. Acad. Sci. SSR Press, Moscow.
- SHUBIN, N.H. and ALBERCH, P. (1986). A morphogenetic approach to the origin and basic organization of the tetrapod limb. *Evol. Biol.* 20: 319-387.
- SHUBIN, N.H. (1991). The implications of "The Bauplan" for development and evaluation of the tetrapod limb. In *Developmental Patterning of the Vertebrate Limb*. (Eds. Hinchcliffe, J.F.; Hurlle, JM; Summerbell, D). Plenum Press, New York, pp. 411-421.
- SOYFER, V.N. (1994). *Lysenko and the Tragedy of Soviet Science*. Rutgers University Press. New Brunswick.
- SPEMANN, H. (1921). Die Erzeugung tierischer Chimaeren durch heteroplastische embryonale Transplantation zwischen Triton cristatus u. taeniatus. *Roux Arch. Entwmech. Org.* 48: 533-570.
- SPEMANN, H. (1938). *Embryonic Development and Induction*. Yale University Press, New Haven.
- STERN, C.M. (1954). Two or three bristles. *Am.Sci.* 42: 213-247.
- WADDINGTON, C.H. (1962). *New Patterns in Genetics and Development*. Columbia University Press, New York, p. 178.
- WEISS, P. (1923). *Naturwissen.* 11: 669.
- WEISS, P. (1935). The so-called organizer and the problem of organization in amphibian development. *Physiol. Rev.* 15: 639-674.
- WEISS, P. (1939). *Principles of Development*. Cambridge University Press, Cambridge.