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Nicolas Rashevsky's Mathematical Biophysics

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Abstract. This paper explores the work of Nicolas Rashevsky, a Russian émigré theoretical physicist who developed a program in "mathematical biophysics" at the University of Chicago during the 1930s. Stressing the complexity of many biological phenomena, Rashevsky argued that the methods of theoretical physics – namely mathematics – were needed to "simplify" complex biological processes such as cell division and nerve conduction. A maverick of sorts, Rashevsky was a conspicuous figure in the biological community during the 1930s and early 1940s: he participated in several Cold Spring Harbor symposia and received several years of funding from the Rockefeller Foundation. However, in contrast to many other physicists who moved into biology, Rashevsky's work was almost entirely theoretical, and he eventually faced resistance to his mathematical methods. Through an examination of the conceptual, institutional, and scientific context of Rashevsky's work, this paper seeks to understand some of the reasons behind this resistance.

Keywords: Mathematical biology, Neurophysiology, Nicolas Rashevsky, Physiology, Rockefeller Foundation, Theory, University of Chicago, Warren Weaver

Introduction

The migration of physicists into the biological sciences during the early 20th century has been a topic of interest in the history and philosophy of biology, with associated issues of the disciplinary authority of physics, the autonomy of biology, and the reduction of biological phenomena to physical terms.[1] Most often, these migrations

[1] The relationship between physics and biology has occupied Anglo-American philosophers of science in the 20th century, as they inherited a set of questions posed by logical positivists during the 1930s. In postpositivist philosophy of science, the extent to which biology possesses laws and generalizations was a test of whether biology differed significantly from physics. The issue evolved into debates about the autonomy of biology from the physical sciences, with the earliest explicit works in philosophy of biology treating the question (Ruse, 1973; Hull, 1974).

resulted in the importation of instruments – such as electrophoresis and X-ray diffraction – that aided in the quantitative analysis of organisms. As several historians have noted, many of the stunning achievements of molecular biology have been intimately tied to the role that physics and physicists have played in biology.[2] The focus of this paper is another "migration" story, one that stands in striking contrast to the fairly clear-cut success stories of physicists and molecular biology. I will examine the work of Nicolas Rashevsky, a Russian émigré theoretical physicist who developed a program in "mathematical biophysics" at the University of Chicago during the 1930s. A conspicuous figure in American physiology during the 1930s and early 1940s, Rashevsky participated in several Cold Spring Harbor meetings and received several years of funding from the Rockefeller Foundation. Stressing the complexity of biological phenomena, Rashevsky argued that the methods of theoretical physics – namely mathematics – were needed to simplify complex biological processes such as cell division and neural activity. Rashevsky was initially drawn to problems in physiology, and was attempting to bring physical principles to the very branch of the life sciences that at the time was the most mechanistic, most dominated by physical instrumentation, and in a conceptual sense treated organisms as physico-chemical systems.[3] However, in contrast to work in "mainstream" physiology during the period, which was highly empirical, Rashevsky's approach to biological problems was almost entirely theoretical, full of idealizations and mathematical equations, and had little contact with experimental work. In light of this, Rashevsky's story will be treated here less as a story of a physicist moving into biology, and more as an example of attempts to use theoretical and mathematical methods in a discipline that for the most part involved experimentation. Admittedly, Rashevsky's background in physics is relevant here – the use of theoretical methods had long been common in the physical sciences and was rather rare in life sciences during the early

[2] Molecular biology is often seen as a paradigmatic case for biology being a province of physics, and indeed historical studies dealing with physics and biology have largely focused on the role that physicists have played in the development of molecular biology (e.g. Keller 1990; Kay 1992, 1993; Beyler, 1996).

[3] For discussions of experiment, measurement, and instrumentation in early 20th-century physiology, see Allen (1975), Maienschein (1986), Borell (1987) and Pauly (1987).

20th century.[4] What was striking about Rashevsky, however, was his use of a highly deductive, formal method in a field that primarily relied on observation and experiment. It was in part because of this that his work met with mixed reaction from physiologists.

The first half of this paper will characterize Rashevsky's research and method, and set it against the backdrop of work in cell physiology and nerve physiology during the early 20th century. I will begin with a brief look at Rashevsky's early work in physics and his eventual turn from physics to biology. I will then examine his published work on cell division and nerve conduction in the 1930s, and compare this with more mainstream research in physiology and neurophysiology. Following this, I will discuss some of the rhetoric that Rashevsky presented to describe and defend what he saw as a new and important field: "mathematical biophysics," and place his project within the context of other work that used mathematics in the biological sciences. The second half of the paper will primarily examine the reception of Rashevsky's work, both institutionally and scientifically, and will tell the story of Rashevsky's initial rise and eventual demise with the Rockefeller Foundation and the University of Chicago. Rashevsky's project in mathematical biophysics has a mixed legacy. On the one hand, Rashevsky may arguably be seen as an important initiator of theoretical and mathematical studies in the life sciences, an area that has now become a major field of study. Indeed, several prominent figures in the fields of theoretical neuroscience and artificial intelligence have cited Rashevsky as a pioneer or influential in their own intellectual development.[5] On the other hand, others in contemporary mathematical

[4] The use of theoretical and mathematical methods in the life sciences has been the focus of a number of historical investigations. Abir-Am (1985, 1987) has examined some of the rhetoric surrounding physics and biology during the 1930s, as well as the contemporaneous ill-fated attempt by some biologists and philosophers to develop a theoretical biology that integrated mathematical, physical, chemical, and biological approaches. Kingsland's work (1985, 1986) on the history of population ecology chronicled the development of theoretical and mathematical methods in population ecology during the 20th century. And Keller (2002) has examined the use of theoretical and mathematical methods in 20th century attempts to explain biological development. Keller briefly discusses Rashevsky (pp. 83–89), however, my analysis will delve deeper into Rashevsky's story, and will more closely examine Rashevsky's relationship with the Rockefeller Foundation and his situation at the University of Chicago.

[5] I have argued elsewhere that Rashevsky's story highlights an important element in the collaboration of Warren McCulloch and Walter Pitts, who developed a logical theory of neuron activity (Abraham, 2002). Among those who have listed Rashevsky as playing a role in their intellectual development are Marvin Minsky, Anatol Rapoport, Robert Rosen, Herbert A. Simon, and Alvin Weinberg.

biology keep Rashevsky's work at arm's length, and are quick to distinguish what they do from what Rashevsky did, often regarding his research with disdain.[6] This contempt, and the difficulties Rashevsky faced during his career, primarily stemmed from his lack of familiarity with biology and the experimental life sciences (he did little or no laboratory work) and his strong rhetoric that mathematical simplicity should be valued in a theory over any connection it might have to reality. While empiricists resisted Rashevsky's approach because it ignored the complexity of biological phenomena, Rashevsky, in contrast argued that it was this awesome complexity, this "messiness" that justified a mathematical approach based on idealization and approximation. Ultimately, several physiologists perceived a gap between Rashevsky's idealizations and work they did in the laboratory. Related to this was Rashevsky's ignorance of an epistemological goal that was in fact a prominent element in theoretical physics, one which seemed to make other attempts to use mathematics in biology more successful: predictive power. Rashevsky saw a role for his models and theories that was outside the framework of most biologists and physiologists. Theory within this context was valued to the extent that it could inform future research and predict the outcome of future experiments. Rashevsky, in contrast, saw the worth of his theories in their ability to simplify complex phenomena and aid in the development of general, fundamental biological principles. Without some sort of empirical foundation, the extent to which Rashevsky's "general principles" could relate to or be useful for particular experiences was difficult for many biologists to see.

From Physics to Physiology

Nicolas Rashevsky was born in Chernigov, Ukraine in 1899. In 1919, he obtained his doctorate in theoretical physics from the University of Kiev, and taught there as an assistant in physics.[7] It has been reported that in light of the fact that Rashevsky had fought in the White Navy during the Revolution, his academic progress inside the nascent Soviet Union was difficult.[8] He soon emigrated and from 1920 to 1921

[6] Leah Edelstein-Keshet, pers. Commun.; Lewontin, 2003.
[7] Rashevsky Resumé, Nicolas Rashevsky Biographical File, Department of Special Collections, University of Chicago Library, Chicago, IL; hereafter UC.
[8] Rosen, 1972.

worked as an instructor in physics and mathematics at Robert College in Constantinople, and between 1921 and 1924 lectured in physics at the Russian University in Prague.[9] The subjects Rashevsky dealt with during this period were in the vanguard of theoretical physics, and most of his papers were published in the *Zeitschrift für Physik*. However, between 1919 and 1926, he tackled a fairly broad range of topics (relativity theory, electrodynamics, photomagnetism, matrix mechanics, and the thermionic effect) in a relatively short period of time, never making significant inroads into any specific area. Furthermore, in contrast to much of the work being done by theoretical physicists, most of Rashevsky's conclusions were mathematical. Mathematics was the primary tool of the theoretical physicist during this period. As theoretical physicist Edward U. Condon observed in 1938, the terms "theoretical physicist" and "mathematical physicist" were often used interchangeably.[10] Yet for many theoretical physicists during the early 20th century, physical understanding took priority over mathematical understanding.[11] Although mathematics was commonly used, most work in theoretical physics involved *conceptual* analysis, a focus on the qualitative as well as the quantitative aspects of physical phenomena. The goal was to simplify existing phenomena, unify and order experimental results, and to predict new phenomena.[12] In contrast to theoretical physicists, strictly speaking, mathematical physicists resembled "applied mathematicians," and did not generally feel the need for their work to be in direct contact with experimental work.[13] When viewed within this framework, Rashevsky was more of a mathematical physicist than a theoretical physicist. He seemed to view many of the topics he dealt with as mathematical exercises. In this sense, his conclusions were often related to the logical consistency of the problem expressed in mathematical terms, and referred to variables solely as mathematical variables, devoid of their meaning within a physical system. Rashevsky's emphasis on mathematical conclusions was also to dominate his work in the biological sciences.

[9] Rosen, 1972; Landahl, 1965; Rashevsky Resumé, Nicholas Rashevsky Biographical File, UC.

[10] Condon, 1938, p. 258.

[11] Jungnickel and McCormmach, 1986, Vol. II, p. 347.

[12] Schweber, 1986, p. 57.

[13] Schweber, 1986, p. 70, after Pestre, 1984, pp. 110–111. The attitude of theoretical physicists toward mathematics, however, did vary: see Sigurdsson, 1996; Jungnickel and McCormmach, 1986, Vol. II.

The Dynamics of Cell Division

So what made Rashevsky turn to biology? In August 1924, he delivered two lectures on aspects of relativity theory at the Washington Square Laboratory at New York University,[14] and later that year immigrated to the United States, where he began working as a research physicist in the Research Department of the Westinghouse Electric and Manufacturing Company in East Pittsburgh and as a lecturer in physics at the University of Pittsburgh.[15] Although his early work at Westinghouse dealt with relativity theory and quantum mechanics, Rashevsky's research was soon devoted to the theoretical aspects of problems in industrial physics, primarily, the thermionic effect and the thermodynamic properties of colloids and polydispersed systems.[16] Between 1927 and 1929, he published seven papers on the dynamics of colloidal particles and one of his first papers on the subject addressed the problem of size distribution of particles in a colloidal solution, based on thermodynamic considerations involving volume, pressure, energy, and temperature.[17]

Rashevsky viewed the colloidal solution as "thermodynamically similar" to solutions that contained dissolved molecules of various kinds, and began to see a resemblance between the process of division in a physical system and the division of living cells.[18] As colloidal particles increased in size, they spontaneously divided. Thermodynamic restrictions, Rashevsky argued, caused such a drop to necessarily assume a spherical shape. In a resting state, such a particle will not divide, but if there is chemical interaction between the interior of the drop and the surrounding medium, the amount of liquid in the drop will increase, and

[14] "Scientific notes and news," *Science* (1924) 60: 175.

[15] Following the First World War, research at the Laboratory became more scientifically oriented, and space at the Laboratory more than tripled during 1929 and 1930. However, the Great Depression resulted in paycuts and layoffs and many researchers were forced to pursue their work in university settings.

[16] E.g. Rashevsky and Rashevsky, 1927; Rashevsky 1928a. During the first decades of the 20th century, applied colloid chemistry was directed toward understanding the properties of glues and dyes, and was an important branch of research at Westinghouse. The thermionic effect, or "Edison effect," occurred in a vacuum tube when an electrode is placed near an electrically heated electrode and not directly connected to the circuit of the heated electrode. The unheated electrode eventually develops a negative charge with respect to the hot electrode. The effect played a role in the amplification of electrical signals. For more on applied physics in the context of early 20th century industry, see Wise, 1985, particularly Chapter 5.

[17] Rashevsky, 1928a.

[18] Rashevsky, 1928b. Rashevsky based his theory on Max Planck's theory of ordinary dilute solutions (Planck, 1917).

upon reaching a certain size, the drop will divide. Rashevsky later told his student, Robert Rosen, that at some point during this period, he met a biologist at the University of Pittsburgh at a "social occasion." As Rosen recalled, "[Rashevsky] asked the biologist whether the thermodynamic mechanism on which he was working was the way biological cells divided. He was told (a) nobody knew how biological cells divided, and moreover, (b) nobody *could* know how biological cells divided, because this was biology [original emphasis]."[19] Challenged by this, Rashevsky was motivated to try to account for the process of cell division by developing differential equations that governed the process and expressed how the magnitudes of particular variables in the system are functionally related to one another and change over time. He began studying biological literature on the subject and apparently did some "informal" laboratory work with Davenport Hooker, a professor of anatomy at Pittsburgh's School of Medicine.[20]

In his published work, Rashevsky drew an analogy between physicochemical systems in a state of equilibrium, like the colloidal solutions he was used to dealing with at Westinghouse, and the living cell. He conceived of hypothetical aggregates of living cells in a surrounding medium, whose division would depend on the same thermodynamic principles as those that governed spontaneous division in colloidal particles.[21] The general problem for Rashevsky involved the factors affecting the spontaneous division of a growing cell when it reached a critical size.[22] He began with a hypothetical system: a small droplet, containing liquid A that was suspended in a different liquid, liquid B. He then supposed that liquid B contained several substances C, D, E, F, that interacted in some way to form substance A, which was insoluble in liquid B. He reasoned that in this system, the interaction of C, D, E, and F to form A would cause the droplets of A already in existence to increase in size. In the simplest case, when one "food substance" C, somehow through a reaction is converted to A, the amount of product A that diffused into the drop from the surrounding medium will depend

[19] Rosen, 1991, p. 110.

[20] According to Herbert D. Landahl, one of Rashevsky's earliest collaborators at Chicago, Rashevsky seemed driven at this stage to educate himself in practical biology, once recalling "how he brought a human brain back with him to the Westinghouse labs, to the consternation of the night-watchman" (Landahl, 1965). There is also evidence that Rashevsky had spent some time working with bacteriologist Ralph R. Mellon at the Institute of Pathology at Western Pennsylvania Hospital in Pittsburgh. ("Photograph onion light; rays stimulate growth," *New York Herald Tribune*, 28 December 1928, p. 7).

[21] Rashevsky, 1928a, b, 1932a, b.

[22] Rashevsky, 1929.

on the surface area of the droplet as well as the concentration of C already existing in the drop, according to the following expression:

$$4\pi r_0^2 h(n_0 - n),$$

where r_0 is the radius of the droplet, n_0 is the concentration of C in the surrounding medium, n is the concentration of C inside the droplet, and h is a constant.[23] The amount of C transformed into A per second will depend on the volume of the droplet and the concentration of C within the droplet:

$$\frac{4}{3}\pi r_0^3 qn,$$

where q was a constant and n, again, the concentration of C inside the drop.[24] Rashevsky then developed equations that expressed the rate of the change of mass of the droplet, which, related to its surface tension, would determine the point at which it would spontaneously divide. His theory was based on thermodynamic principles: the system needs a minimal free energy, and thus it moves from one state of relatively minimal energy to a lower one. With further idealizing assumptions, Rashevsky then developed mathematical expressions for the rate of change of the mass M of the drop. He continued to develop equations for increasingly more general cases until he arrived at the hypothetical conditions of diffusion rate, mass, size, and surface tension in which the drop would spontaneously divide. Rashevsky examined several *hypothetical cases*, and his goal, essentially, was to devise equations that would allow one to calculate the critical size at which a growing cell would spontaneously divide.[25]

That Rashevsky drew an analogy between colloidal particles and living cells was not entirely outside the conceptual framework within which a number of physiologists studied the cell. Cell studies during this period were characterized by a diversity of methods and motivations, but experimental studies of the cell largely employed biochemical and physical methods.[26] Many physiologists who tackled cell division treated the cell as a physico-chemical system that existed in equilibrium with its chemical environment, and framed their experimental studies in terms of the permeability of the cell membrane and the reactivity of the cell to external stimuli. When a stimulus acted on protoplasm, chemical

[23] This expression is based on the standard formula for the surface area of a sphere, $S = 4\pi r^2$.

[24] This expression is based on the formula for the volume of a sphere, $V = 4/3\pi r^3$.

[25] Rashevsky, 1931a. See also Rashevsky, 1932a, b.

[26] Maienschein, 1991.

reactions within the cell were modified in part because the stimulus changed reaction rates. General physiologists who focused on cell division expressed the problem in terms of surfaces, interfaces, tensions, osmosis, permeability, colloids, and dynamics.[27] Experimental studies of cell division, for example, often involved exposing cells *in vivo* to chemical or osmotic stimuli, using chemical solutions and electrical instrumentation to measure changes in potential across the cell membrane.

The early work of physiologist Ralph S. Lillie was typical of this approach. Long allied with the Marine Biological Laboratory at Wood's Hole, Lillie examined the physical and chemical conditions for initiating cell division in unfertilized sea urchin or starfish eggs and the factors governing division in fertilized eggs.[28] For Lillie, the cell was in equilibrium with its environment, and his studies focused on how cells reacted to a changing environment.[29] Lillie also discussed the analogy of the cell as a "suspended oil droplet" and likened a cell system to a colloidal system.[30] In this way, cell division could be ascribed to changes in surface forces. Lillie described the experimental results one would *expect* based on the hypothesis of the cell as a drop of viscous fluid based on the idea that cell division is connected to changes in surface tension. He then performed experiments to test this hypothesis – exposing sea urchin eggs to chemical and physical stimuli such as hypotonic seawater, cyanide in seawater, salt solutions of various concentrations, and extreme heat.[31] He examined the resistance of the cell to these injuries at different times in the cell cycle, which often occurred when the cell form was changing. The change in cell form was seen to accompany a change in the surface tension of the cell membrane, which Lillie reasoned could result from an increase in the permeability of the cell membrane to electrolytes. His method was to form a hypothesis based on previous experimental results, and perform a large number of measurements to test the hypothesis. In many of these experiments, Lillie was looking at the effects of osmotic pressure, and his data were both quantitative and descriptive – for example, the proportion of burst eggs at various levels of dilution, detailed observations of the size and state of the eggs at various times after exposure to dilute seawater (i.e.

[27] For an account of the development of general physiology in the early 20th century, see Pauly, 1987.

[28] See, for e.g. Lillie 1910, 1916. For biographical information on Lillie, see Gerard, 1952.

[29] Lillie, 1924.

[30] Lillie, 1923, pp. 98–101; 106–107.

[31] Lillie, 1916, pp. 373–376.

intact, swollen, etc.), and comparison of observations using different chemical stimuli such as sodium chloride. Following the presentation of data and calculations on the data, Lillie would draw conclusions about the nature of cell division and the role of chemical stimuli in the process. To the extent that mathematics entered the picture in these studies, it was mostly to arrange experimental data in quantitative terms.

On a conceptual level, Rashevsky's treatment of cell division in terms of diffusion rates and chemical reactions was not dramatically different from that of Lillie and other cell physiologists. However, methodologically speaking, Rashevsky's method was distinct in several ways. In contrast to the empirical studies of physiologists, Rashevsky's studies, which were riddled with numbers and formulae, had no references to specific cases, only to idealized "cell systems." Rashevsky would develop an equation relating variables such as osmotic pressure, volume, forces of attraction and repulsion between chemical molecules, and rates of reaction. He would then "solve" the equation, interpret the solution, and draw conclusions: for example, this variable will vary with respect to this other variable according to this mathematical expression. Rashevsky's published work on cell division was not based on experiments he performed himself, but rather, to the extent that his starting assumptions were informed by actual observations, they were gathered from the publications of others. In several of his papers on the subject, the meat of the argument began like a thought experiment: "Consider a physical system…"; "Consider a spherical aggregate of tightly packed cells…"[32] Rashevsky's use of mathematics was not to address the quantitative aspects of a problem, but rather formed the core of his methodology. Although he worked within the same conceptual framework as Lillie, often citing his work, his method was formal and deductive. Rashevsky was not merely applying mathematical formulae after the accumulation of data, he was using the mathematical method to idealize the cell and re-conceptualize the entities that played a role in its function.[33] Rather than view the cell as part of an experimental system, Rashevsky's concept of the cell was mathematical from the outset. This approach carried through to Rashevsky's work on excitation and conduction in nerves, a key problem in neurophysiology during the early decades of the 20th century.

[32] Rashevsky, 1933c, 1934b.

[33] Rashevsky presented related work on cell dynamics at the Cold Spring Harbor Symposium on Growth in July 1934. See Keller (2002, pp. 84–87) for a discussion of this event and the reactions of more empirically minded attendees to his work.

Theory and Experiment in Studies of Nerve Function

Physiology was arguably the branch of the life sciences that most resembled physics during this period.[34] This connection existed on both conceptual and methodological levels: many physiologists treated organisms as physico-chemical systems and framed their explanations in terms of physics and chemistry, and their studies focused on electrical phenomena and involved the use of electrical recording instruments. Since the mid-19th century, physiologists who studied the process of excitation in nerve focused on the quantitative relations they could observe when they applied an electric current to excitable tissue.[35] As Robert Frank has argued, instrumentation, as part of an experimental system involving technological, conceptual, and material elements, was crucial to many discoveries concerning the nature of the nervous impulse during the first three decades of the 20th century.[36] Electrical instruments that recorded action currents, such as the string galvanometer and electrometer, and amplifiers such as the cathode ray oscilloscope, facilitated the characterization of nerve conduction during this period.[37] The nervous impulse was characterized in terms of quantitative relations between stimulus, threshold, and response. Using these measurements, experimental neurophysiologists drew conclusions about the relations between quantitative aspects of nerve conduction.

In addition to this, theories were developed that proposed mechanisms underlying the observable electrical impulse that traveled along the nerve. Essentially, all of these theories were forms of a "membrane theory," based on the idea that a polarized membrane leads to a difference in electrical potential between in inside and outside of the nerve cell, and that this difference in voltage played a role in the conduction of the nerve impulse. The mechanisms proposed involved changes in membrane permeability, chemical reactions, and ion diffusion.[38] Many

[34] As geneticist Thomas Hunt Morgan noted in a 1926 address on the relation between biology and physics, if a physiologist had been asked to deliver the address on the relation between *physiology* and physics, "…the physiologist would have had an easy and even a delightful time, for physiology has long…been wedded to both physics and chemistry. A modern physiological laboratory is scarcely to be distinguished from a physical laboratory, having borrowed its instruments, at least, from the former [*sic*]." (Morgan, 1927, p. 213).

[35] See Lenoir, 1986.

[36] Frank, 1994. See also Marshall, 1983, 1987; Kevles and Geison, 1995.

[37] E.g. Forbes and Thatcher, 1920; Gasser and Erlanger, 1922.

[38] See Katz, 1939.

of the more theoretical accounts of nerve conduction were mathematical. Mathematical theories of nerve conduction had had a place in neurophysiology ever since the work of theoretical chemist Walther Nernst, who presented a mathematical expression of a physical theory of electric excitation in living tissues, based on changes in ion concentration and diffusion gradients.[39] Nernst had argued that the application of an electrical current can alter the concentration of ions at a membrane and that when this concentration reached a critical level or exceeded it, excitation would take place. According to Nernst's theory, if an electric current passed through a membrane that is impermeable to dissolved ions, it will set up differences in concentration at and near the membranes. These differences in concentration, when sufficiently large, caused an excitation. Nernst solved the diffusion equation,

$$\frac{\mathrm{d}y}{\mathrm{d}t} = k\frac{\mathrm{d}^2 y}{\mathrm{d}x^2},$$

that described the rate of change in concentration of the two ions based on their initial concentrations (x and y) and a diffusion constant k, and arrived at a formula,

$$\text{const.} = i\sqrt{t},$$

that connected i to the "least current required to excite," with its duration, t. The relation between the strength or intensity of the current necessary for excitation and its duration became the focus of several physical theories of nerve conduction, which attempted to propose a mechanism that would be consistent with the observable strength–duration relation.[40] Many of these models used differential equations to describe the relations between intensity of stimulus and concentration of ions (in some cases, exciting and inhibiting "substances"), postulating their movement along gradients of concentration and electrical charge.[41]

[39] Nernst, 1908.

[40] Electrophysiologists such as Jan L. Hoorweg, Keith Lucas, and Louis Lapicque found that when a current was passed through a nerve, the longer the pulse, the smaller the threshold intensity. See e.g. Hoorweg 1892; Lapicque and Lapicque, 1903; Lucas, 1906.

[41] E.g. Hill, 1910; Blair, 1932a, b; Rashevsky, 1933a. The introduction of the squid giant axon by John Z. Young, as part of an experimental system developed to measure the differences between resting membrane potential and the action potential, facilitated the characterization of the nerve impulse and the ion gradients believed to be responsible for its propagation along the axon (Young, 1936; Hodgkin and Huxley, 1939; Cole and Curtis, 1940).

Throughout the early 1930s, Rashevsky published several papers on a mathematical theory of nerve conduction, which built directly on his work on cell division.[42] In 1933, he presented a detailed theory of nerve excitation and inhibition based on the notion of diffusing substances and electrochemical gradients.[43] He began by reviewing previous theories, classifying them into two groups, and Rashevsky's perspective on these theories can reveal much about how he viewed his own theory. The first group included the theories of Nernst and Archibald V. Hill.[44] In 1910, Hill had introduced hypotheses based on Nernst's view of excitation, and compared calculated results with experimental results. These theories, argued Rashevsky, began with definite assumptions about the role of ions, their distribution, and their movement in the field of an electric current. They assumed that a critical concentration of ions is necessary for excitation, and arrived at expressions for the strength–duration relation upon stimulation by an electric current. The second group of theories, which included those of Jan L. Hoorweg, Louis Lapicque, and Henry A. Blair, displayed what Rashevsky called the phenomenological method, that is, they established mathematical equations without attempts at their physical interpretation.[45]

For his own part, Rashevsky aimed to present a phenomenological method that could also be subject to physical interpretation. He noted that both groups of theories assumed the existence of *one* type of exciting substance, which had to reach a critical level for excitation to occur. However, Rashevsky argued that since the nerve protoplasm contains many different ions, it is better to postulate that it is not the absolute concentration of one substance that is responsible for excitation but rather the ratio of concentrations of "antagonistic" ions. At the outset, however, Rashevsky said nothing about the nature of these substances.[46] He assumed that there are two factors in excitation and inhibition: an "excitatory factor," whose concentration is represented by e, and an inhibitory factor, whose concentration is i. The ratio between these concentrations, e/i, determines excitation. If e/i becomes greater than a certain constant h (i.e., if the concentration of exciting substance is sufficiently greater than that of the inhibitory substance), then excitation will occur. Rashevsky set h at 1, and the concentrations

[42] Rashevsky, 1930, 1931a, b, c, 1933a, b. For more on this work in with context of the development of electromechanical machines, see Cordeschi (2002, Chapter 3).
[43] Rashevsky, 1933a.
[44] E.g. Nernst, 1908; Hill, 1910.
[45] E.g. Hoorweg, 1893; Lapicque, 1926; Blair, 1932b.
[46] Rashevsky, 1933a, p. 43.

in resting nerve at e_0 and i_0, where $e_0 < i_0$. Assuming the simplest case, Rashevsky reasoned that the rate of change of concentrations of e and i at the cathode due to the current is proportional to the current, on the assumption that when a current flows along the axon, both ions are transported:

$$\frac{\mathrm{d}e}{\mathrm{d}t} = KI - k(e - e_0),$$

$$\frac{\mathrm{d}i}{\mathrm{d}t} = MI - m(i - i_0),$$

where K, M, k, and m are constants; $m \ll k$; $K/k \leq M/m$; and I is the current. These equations describe the rate of change over time of each ion as proportional to the current applied as a stimulus and the amount of increase (i.e. if $e - e_0$ is positive) or decrease (if $e - e_0$ is negative) of each ion. Rashevsky admitted that these equations were both "first approximations," since for high values of I in this case, e and i become negative. Eventually, Rashevsky developed an equation that described the relation between strength of current, duration, and the various concentrations of e and i:[47]

$$Kt = \log \frac{KI}{KI - k(i_0 - e_0)}.$$

Here, t is the time during which the applied current, given certain initial concentrations of e and i, will cause an excitation. Rashevsky was making approximations – deriving approximate formulae that hold, for example, for only "very small" values of t or m or k. Rashevsky was not entirely ignorant of empirical work on nerve conduction. In this same paper, he incorporated more of the current experimental work being done on nerve conduction, particularly that of Ralph W. Gerard, and compared calculated values with those observed by Lapicque.[48] Other physiologists who had previously taken similar mathematical approaches had presented their work along with experimental data.[49] In a comparison of Rashevsky's (1933a) and Hill's (1936) theories, neurophysiologist Bernard Katz saw little fundamental difference, except that Hill had included "extensive experimental study of its predictions."[50]

[47] In fact, as Rashevsky acknowledged in this paper, this equation was the same as that proposed by Blair in 1932 for the time–intensity relation (Blair, 1932a).
[48] Lapicque, 1926.
[49] E.g. Blair, 1932b, 1934.
[50] Katz, 1939, p. 12.

It is arguable that a strict dichotomy between theoretical and experimental studies of nerve function did not exist during the 1920s and 1930s. While some investigators were concerned with strictly empirical, phenomenological studies of the nerve impulse and the strength–duration relation, many attempted to work out theories that proposed an underlying mechanism to explain these observations. Mathematics was also not completely foreign to many physiologists at the time. As the University of Oregon zoologist Oscar W. Richards noted in 1925, the use of calculus in physiology was common: "…anyone who even idly turns the pages of the Journal of General Physiology must be forcibly reminded of his calculus text."[51] However, for the most part, the mathematical treatments were for *prediction*.

By the late 1930s, Rashevsky's work was appearing almost exclusively in life sciences journals, and with his increased exposure to biologists and physiologists, he began to take part in the activities of the biological community, most notably, the Cold Spring Harbor (CSH) Symposia on Quantitative Biology. In 1936, he was invited to the fourth Cold Spring Harbor meeting on "Excitation Phenomena." It is arguable that Rashevsky's approach found more resonance with the work of neurophysiologists: although their work was largely based on experimental investigations, many incorporated mathematical and theoretical analyses in their published papers and differential equations were frequently used to relate different variables in the experimental system.[52] However, certain neurophysiologists at the 1936 Cold Spring Harbor meeting questioned the "general assumptions" that Rashevsky made, and brought empirical facts to bear on his theories. For example, Rashevsky had derived a formula for the velocity of the nerve impulse (from Blair's theory) that included a constant, k. It was known that the value of this constant could be determined experimentally. However, physiologist Harry Grundfest of the Rockefeller Institute for Medical Research pointed out that depending on the type of stimulus used and the nature of the experimental setup, this constant could vary and presumably, Rashevsky's theory did not take this into account since it had little connection to experimental work.[53] Generally, those who commented on Rashevsky's paper brought up specific

[51] Richards, 1925, p. 31.
[52] E.g. Cole and Curtis, 1936.
[53] In Rashevsky, 1936b, p. 96.

experimental situations and were rather skeptical that Rashvesky's general theory could account for them.[54]

"Mathematical Biophysics," Physics, and Mathematics in the Biological Sciences

Beyond the application of mathematical methods to specific problems in the life sciences, Rashevsky had visions for the creation of a new discipline, which he called "mathematical biophysics." "Biophysics" at the time generally meant "the physics of living matter" – that is, the use of quantitative, physical methods in biological work and the analysis and explanation of biological phenomena in terms of physical principles.[55] Despite Rashevsky's use of the term "mathematical" to describe his new field, he was not referring to quantitative methods. These methods, such as measurement, were exemplars of experimental physics, and it was this aspect of the physical sciences that was admired by physiologists.[56] Rashevsky's argument was that mathematics had been successfully used in the exact sciences, and thus should be successful in the biological sciences, since biological systems are physico-chemical systems. Just as physicists used mathematical analysis to understand the "intimate details of atomic phenomena," he argued, in a physiological context, one must "*infer*, from the wealth of known, relatively coarse facts, to the much finer, not directly accessible fundamentals."[57] Rashevsky believed that mathematical biophysics stood to experimental biology in the same way that mathematical physics stood to experimental physics. He believed that the mathematical method, not experiment, was the best way to address the organized complexity inherent in biological systems:

> A simple phenomenon can be understood by mere "inspection," but it requires mathematical analysis to see through a complex system. The main thing is to apply mathematics methodologically

[54] Rashevsky, along with Landahl, was also invited to present work on cell permeability at the 1940 Cold Spring Harbor Symposium on Quantitative Biology (Rashevsky and Landahl, 1940). Landahl was absent, but the presentation was an attempt to treat permeability quantitatively and to find for it a general mathematical definition. In the discussion following the presentation, many asked Rashevsky what the implications of the theory would be for concrete specific cases, in light of all the simplifying assumptions he had made.

[55] Forbes, 1920.

[56] See, e.g. Bronk, 1938.

[57] Rashevsky, 1935a, p. 528; original emphasis.

> correctly, by first studying the abstract, over-simplified cases, which may even perhaps have no counterpart in reality. Afterwards the various complexities of the case have to be taken into account … as second, third, and higher approximations. This use of abstract conceptions in the beginning is *the* characteristic of the physico-mathematical method. Violation of this rule, and all attempts to start with actual cases in all their complexity, will result in failure…[58]

How accurate was Rashevsky's characterization of the physico-mathematical method and the epistemological standards of early 20th century physics? For Edward U. Condon, two objects of physics were simplification and organization of past experience, and mathematical physics, he argued, allowed one to pursue these goals.[59] From the data obtained through experiment, generalizations were possible only through theory and mathematics. Data from experiments, Condon argued, were usually "particular quantitative statements of relations between numbers obtained in experimental observations. From these particulars, one must try to infer a general relation structure (i.e. relations between variables) embracing the expected result of all similar observations which might have been made but were not, and suggesting an expected result of other experiments which might be made in the future. Pure mathematics is the science of abstract relation structures… It follows that pure mathematics is the chief tool of the theoretical physicist."[60]

The use of mathematics did allow theoretical physicists to simplify phenomena, and Rashesvky was correct in pointing to simplification as a motivation for applying the physico-mathematical method. Further, theoretical physicists did aim to produce general laws, and Rashevsky cited this as one aspect of his "mathematical biophysics."[61] However, Condon alluded to another goal of theoretical physics: prediction. Predictive power was something that Rashevsky rarely mentioned in his work. Any practical or predictive implications of Rashevsky's theories were not important for him. From the late 19th century, theoretical physics and experimental physics generally existed as two separate cultures, that is, theoretical physicists were rarely involved in experimental work.[62] However, by 1920, at least within the American context, theoreticians and experimentalists were often members of the same

[58] Ibid.

[59] Condon, 1938, p. 257. See also Einstein 1956 [1934], p. 219; Jungnickel and McCormmach, 1986, Vol. II.

[60] Condon, 1938, p. 258.

[61] Einstein, 1956 [1934], p. 219.

[62] Schweber, 1986.

university departments, and many theoreticians were involved in analyzing and interpreting experimental results. Thus, in a sense, Rashevsky was only partly accurate in his characterization of the method of theoretical physics.

Rashevsky's rhetorical defense of his apparent disdain for empirical work was perhaps prompted by some of the criticism he faced at the CSH meetings in 1934 and 1936. In his first publication in the journal *Philosophy of Science*, he sounds more like a mathematician than a physicist: "A characteristic of mathematical method is that it is applied to specific problems for its own sake, regardless of immediate contact with reality. The contact may not come sooner or later, but the value of a mathematical investigation is not affected. Euclid said, 'There is no royal road in geometry,' and this applied to any mathematical science. To ask of the new science of mathematical biophysics results that would lead immediately to tangible experimental verifications, would be to require it to take such an impossible royal road."[63] In 1936, Rashevsky went so far as to say that he saw little need for his theoretical work to have any use for empirical work: "Like any other theoretical science, mathematical biophysics has a right to existence of its own, and its interest lies not merely in the number of empirical facts which it can explain, but in its internal logical consistency and beauty."[64]

How did Rashevsky's notion of mathematical biophysics compare to other contemporary applications of mathematics to biological phenomena? At the time, there were several areas of biology where mathematical methods were used in a systematic way: in the biometrics of Karl Pearson,[65] in the population genetics of Ronald A. Fisher, J.B.S. Haldane, and Sewall Wright,[66] and in Alfred Lotka's and Vito Volterra's mathematical work on species interaction in populations of organisms.[67] Trained in mathematics, Karl Pearson's application of statistics to human populations was related to his aim of subjecting evolutionary concepts to quantitative analysis.[68] Through the development of biometry, Pearson developed the fundamental methods of statistical analysis of populations. It was a technique used to assess present populations, to determine the rate of change in a species and thus provide an aid to prediction.

[63] Rashevsky, 1934a, p. 180.
[64] Rashevsky, 1936a, p. 1.
[65] E.g. Pearson, 1894.
[66] E.g. Fisher, 1930; Haldane, 1924; Wright, 1931.
[67] Lotka, 1925; Volterra, 1931.
[68] Kingsland, 1985, pp. 56–57.

The mathematical population genetics of Fisher, Haldane, and Wright played a role in the modern evolutionary synthesis.[69] For all, the mathematical method meant beginning with simple, idealized cases, exploring general possibilities, and then returning to particular cases, after which the model could be modified. Although they made important contributions to the biological sciences, both Pearson and Fisher were trained in mathematical and physical sciences, and their work arguably formed the basis of modern mathematical statistics.[70] Fisher, Haldane, and Wright studied the mathematical consequences of Mendelian inheritance and provided mathematical models for hereditary change in a population of organisms, reconciling Mendelian heredity with natural selection.[71] The models analyzed distributions of gene frequencies that one would expect from a large, randomly breeding population, and analyzed changes in these frequencies from generation to generation, the population being exposed to such factors as selection, dominance, linkage, and mutation. Fisher, Haldane, and Wright would then develop hypotheses about the relationship between these variables and would introduce simplifications in order to enable mathematical analysis. Following this, they would develop "simplified descriptions" which had "testable consequences" in natural populations.[72] In this and other ways, the models differed from Rashevsky's, having explanatory and predictive power. For Provine, their theories complemented existing field research and stimulated new research, entered a somewhat controversial field and solved several existing problems, and lent a firm theoretical basis to Darwinian natural selection. The theories were highly influential, but they were not without their critics – many naturalists of the time had little training in mathematics.[73]

Like Rashevsky, both Lotka and Volterra were trained in the physical sciences. Viewing the natural world – both organic and inorganic – as a system, Lotka used the framework of physical chemistry to treat the kinetics, statics, and dynamics of living systems. Lotka's application of physical principles to biological systems, in his own opinion, was distinct from the biophysics of the time, which in his view studied the morphology and physiology of the individual organism.[74]

[69] Provine, 1978.

[70] Porter, 1986, Chapter 9.

[71] Provine, 1971, 1978.

[72] Provine, 1978, p. 174. As Haldane wrote in his 1924 paper, "…we shall only deal with the simplest possible cases." He went on to make simplifying assumptions such as completely random mating, complete dominance, and no interbreeding between generations (Haldane, 1924, p. 19).

[73] Provine, 1978.

[74] Kingsland, 1985, p. 25.

Lotka expressed the relations of organisms in terms of energy and matter, using thermodynamic principles, and aimed to find a law of evolution for biological systems with a degree of generality like that of the second law of thermodynamics. Like Rashevsky, he had a dream of discipline building, and also looked at hypothetical situations.[75] Lotka would describe the interactions between predator and prey species as a set of differential equations, based on the method used for the mathematical description of the dynamics of chemical reactions. Volterra had a background in classical mechanics, and brought a mechanistic approach to his work on predator–prey interactions. His predator–prey equations relied on the kinetic gas theory model. Volterra based his model on a physical analogy between the collision of gas molecules in a closed container and the interaction of two species. In statistical mechanics, the number of collisions between particles of different gases is proportional to the product of their densities. Volterra likened encounters between individuals from two populations to these collisions. Thus, the probability of an encounter would be proportional to the product of the number of both species. Volterra made several simplifying assumptions: that the prey is only destroyed by being eaten, and that the predator only eats one prey species. In a sense, Volterra had a similar attitude toward theory as Rashevsky. He would begin with initial hypotheses based on sometimes unrealistic assumptions, represented mathematically. Following this, for Volterra, one would determine how well the mathematical predictions accorded with reality, adjusting the starting hypothesis as needed.[76] For Volterra, this move from the general to the particular was aligned with what he called the rational and applied phases.[77]

What value was seen in the use of mathematics within this context? According to Sharon Kingsland, those studying interactions of organisms in a population turned to mathematics when "their attempts to unravel the causes of population change made them realize that purely descriptive methods could not easily cope with nature's complexity."[78] Lotka and Volterra and others had both theoretical and practical motivations for using mathematics. Practically speaking, they wanted to understand the fluctuation of populations related to agriculture and fisheries. Their theoretical motivation was to treat the "struggle for

[75] Lotka envisioned a broad research program in "physical biology". Lotka, 1925, pp. 49–54.

[76] Kingsland, 1985, p. 124.

[77] Gasca, 1996, p. 353; Kingsland, 1985, p. 124.

[78] Kingsland, 1986, p. 237.

existence'' using the methods of physics, in order to increase the status of ecology. According to Kingsland, despite the differences between Lotka and Volterra, they had the same general objective, ''…to show that theoretical, mathematical approaches had a place in biology…that theory could guide experiment and research, and that it was not worth waiting until all the facts were in before engaging in speculation with the help of mathematical models.''[79] However, unlike Rashevsky, Volterra rejected the formulation of mathematical models that could not be verified by experimental data.[80]

Rashevsky viewed his project as distinct from these efforts. In Rashevsky's view, Lotka's and Volterra's work dealt with biological *systems* and the ''general relations'' between organisms, whereas his own applications of mathematics in biology dealt with the details.[81] Indeed, their emphasis was on population dynamics and biological associations *between* organisms: Lotka and Volterra generally focused on several species living in the same milieu, where the quantitative aspects of populations are expressed as variations in the number of individuals that constitute different species. In contrast, Rashevsky's mathematical biology dealt largely with subcellular or intercellular phenomena. He also went further in his comparison: he saw his own ''mathematical biophysics'' as analogous to mathematical or ''atomic'' physics. In this sense he was accurate, to the extent that mathematical physics resembled applied mathematics and had little contact with experimental work. For Rashevsky, Lotka's and Volterra's approach was analogous to the use of mathematics in thermodynamics.[82] In fact, Rashevsky's use of mathematics was also akin to that used in thermodynamics. More accurately, Rashevsky on the whole was dealing with microscopic phenomena – whereas Lotka and Volterra were dealing with macro-

[79] Kingsland, 1985, p. 126.

[80] Israel, 1993, p. 490.

[81] This characterization might have been influenced by Lotka's own description of his program of ''physical biology'': ''…the writer would suggest that the term *Biophysics* be employed…to denote that branch of science which treats of the physics of the individual organism (e.g., conduction of an impulse along nerve or muscle); and that the term Physical Biology be reserved to denote the broader field of the application of physical principles in the study of life-bearing systems as a whole. Physical biology would, in this terminology, include biophysics as a subordinate province [original emphasis]'' (Lotka, 1925, p. 49, n. 1).

[82] In fact, Rashevsky's work depended heavily on thermodynamic principles. Although it might appear that he was casting his own work as superior to theirs, he did see their work and his as constituting two branches of the same discipline: mathematical biology (Rashevsky, 1938, p. viii).

scopic phenomena. In some senses, Rashevsky's project was distinct, but for different reasons than he himself alluded to. At first glance, Rashevsky's work appears similar to Lotka's and Volterra's, yet in the end, since the Lotka–Volterra equations could be solved to predict the nature of interaction between two species, and their theories had something that Rashevsky's did not: predictive power.

Institutional Reception: The Rockefeller Foundation and the University of Chicago

Rashevsky's application of methods from the exact sciences in a biological context initially attracted the interest of Warren Weaver, who was director of the Natural Sciences Division at the Rockefeller Foundation (RF) between 1932 and 1955. As Robert Kohler and Lily Kay have documented, Weaver aimed to foster interdisciplinary approaches in biology.[83] His program for the Natural Sciences Division favored enterprises that appeared to transcend the divide between physics and the life sciences: general physiology, experimental and chemical embryology, "molecular" biology, and biophysics. Indeed, it is likely that both Rashevsky's motivation for developing "mathematical biophysics" and Warren Weaver's initial backing of Rashevsky's work were in part connected to what were seen as highly successful applications of methods of the exact sciences to biological problems. Although Rashevsky continued to publish work in physics journals, by 1933, he had published 12 papers in life sciences journals, thus exposing his work to the biological community. As the Depression hit, he was forced to leave Westinghouse, but fortunately, had made some initial contacts that would bring him to the University of Chicago.[84] In July 1933, Rashevsky wrote to his former Westinghouse colleague Francis O. Bitter that he had just spent 2 weeks in Chicago and had made the

[83] Kohler, 1991; Kay, 1993.

[84] Rashevsky was laid off in March 1934, and was desperate to find work in an academic setting. He wrote to his friend and former colleague Francis Bitter that "the Chicago group of biologists" was making efforts to have him there. (Rashevsky to Bitter, 1 March 1934, Francis O. Bitter Papers, Box 1, Correspondence Q-R, 1931-38. MC 77, Institute Archives and Special Collections, MIT Libraries, Cambridge, MA; hereafter MITSC). Later that week, Rashevsky wrote to Bitter that the Chicago people had approached the RF and that he was now in "direct contact" with the director of the Foundation (Rashevsky to Bitter, 5 March 1934, Francis O. Bitter Papers, Box 1, Correspondence Q-R, 1931-38. MC 77, MITSC).

acquaintance of several "interesting" European scientists.[85] In March 1934, Rashevsky wrote to Bitter that the "Chicago group" of biologists were making efforts to bring him there, and that he had been in direct contact with the director of the Rockefeller Foundation.[86] That April, after losing his position at Westinghouse, Rashevsky came to the University of Chicago as a Special Fellow of the General Education Board – a body established by John D. Rockefeller in 1903 to aid education in the U.S., providing grants for colleges and universities. The 1-year fellowship was for a project on "physico-mathematical methods and biological problems."

Rashevsky's association with Chicago is not surprising in certain respects: By this point, he had published several papers on conduction in nerves, and Chicago was a major center of neurophysiological research.[87] Louis L. Thurstone, who was then Chairman of the Department of Psychology, was instrumental in bringing Rashevsky to the school. It has been reported that several other Chicago researchers, most likely those he had been in contact with the previous year, also facilitated his transfer: the physiologist Ralph S. Lillie, the geneticist Sewall Wright, the Nobel-prize-winning physicist Arthur H. Compton, and the experimental psychologist Karl S. Lashley.[88] However, from early on, it was clear that Rashevsky's lack of experience in biology would become a target of criticism. Simon Flexner, physician and Director of the Rockefeller Institute for Medical Research, had written to Weaver in September of 1934, regarding a paper Rashevsky had recently published in the journal *Philosophy of Science*.[89] Weaver had sent Flexner a copy of this article, and had also given a copy to W.J.V. Osterhout, a member of the Division of Physiological Chemistry at the Rockefeller Institute. Osterhout reported to Weaver that in the paper, Rashevsky

> …is so ignorant of biology that he falls into frequent error. The important question is whether, in spite of this, he makes useful suggestions. I am inclined to think that he does, but cannot be certain, since only future investigation can decide…his exuberant imagination leads him to make extravagant claims. In this respect

[85] Rashevsky to Bitter, 7 July 1933, Francis O. Bitter Papers, Box 1, Correspondence Q-R, 1931–38. MC 77, MITSC.

[86] Rashevsky to Bitter, 1 March 1934; Rashevsky to Bitter, 5 March 1934, Francis O. Bitter Papers, Box 1, Correspondence Q–R, 1931-38. MC 77, MITSC.

[87] Blustein, 1992.

[88] Landahl, 1965.

[89] Rashevsky, 1934a.

> he is poetic, rather than scientific. In claiming that Nature must act in a certain way he shows immaturity. Had he said that his equations may be useful in pointing out possibilities which should be investigated, he would be on safer ground…I have devoted much time and effort to interesting mathematicians, physicists, and chemists in biology, and the results have been very helpful…I should, therefore, favor the idea of encouraging a man like Rashevsky, provided he can work with a competent biologist who understands what Rashevsky is about, and provided Rashevsky can subject his imagination to sufficient criticism to make it really useful.[90]

Despite Osterhout's caution to Weaver, Rashevsky already had his Rockefeller funding, and was able to find a niche at Chicago. In January 1935, Rashevsky wrote to Bitter, reporting that he had begun a weekly seminar series on "mathematical biophysics," and that "the audience is very diverse: physicists, chemists, mathematicians, physiologists, and psychologists…"[91] However, his excitement about the seminars was tempered: "What will happen with respect to my future is not entirely certain. The 'big-wigs' still don't take my mathematical biophysics so seriously. Rather more like amusing brain-gymnastics. The followers, who are enthusiastic, as yet have no influence. Hopefully this will change…"[92] Notwithstanding this uncertain climate, in 1935 Rashevsky was appointed Assistant Professor of Mathematical Biophysics in the Department of Psychology, and eventually joined the Department of Physiology, at the invitation of Swedish émigré physiologist Anton J. Carlson, the department's chairman and a staunch empiricist. Although Carlson was initially sympathetic with Rashevsky's approach, he later dismissed him as being too theoretical. Dwight Ingle has recalled that Carlson's dictum was "Keep your mouth closed and your pen dry until you know the facts."[93] Carlson's stress on a practical, empirical approach to physiology led to a conflict with Rashevsky, and eventually he

[90] Quoted in Flexner to Weaver, September 10, 1934, Simon Flexner Papers, B F365, Folder "Weaver, Warren," American Philosophical Society, Philadelphia, PA; hereafter APS. Lewis G. Longsworth studied the measurement of mobilities of ions and molecules in liquid media, as well as the diffusion on neutral molecules in solution. He studied at the Rockefeller Institute with chemist Duncan A. MacInnes and Theodore Shedlovsky, and together they created a center for electrolyte research.

[91] Rashevsky to Bitter, 15 January 1935, Francis O. Bitter Papers, Box 1, Correspondence Q-R, 1931–38. MC 77, MITSC.

[92] Rashevsky to Bitter, 15 January 1935, (in German, my translation), Francis O. Bitter Papers, Box 1, Correspondence Q-R, 1931–38. MC 77, MITSC.

[93] Ingle, 1979, p. S123.

was forced to return to the Department of Psychology.[94] But Weaver and the RF continued to support Rashevsky's research, and his work was becoming well known internationally, at least within communities of other theoretically oriented biologists.[95] For example, in a proposal to the RF for the creation of the interdisciplinary, ill-fated "Institute for Chemical-Morphology," embryologist Joseph Needham listed Rashevsky's name as a potential contributor to the "Division of Theoretical Biology" envisioned in the program.[96] However, in December 1935, Henry M. Miller, the Foundation's Assistant Director for the Natural Science Division, reported on a meeting he had with Honor B. Fell, who was Director of the Strangeways Laboratory in Cambridge, England, and in contact with Joseph Needham and other members of the British "Biotheoretical Gathering." Fell told Miller that "either Waddington or Needham expressed the opinion that [Rashevsky] could probably profit greatly if he could have a period of contact with the various groups in experimental biology."[97] Although Needham and Waddington advocated a theoretical approach to biological phenomena, and initially saw a place for Rashevsky's work in their research program, they were both trained experimentalists. Their apparent problem with Rashevsky seems not so much that his work was theoretical, but that he was so far

[94] As Jack D. Cowan recalled, "Carlson, who was a very famous physiologist, threw him out after a year because he never did any experimental work. The story is that Carlson went into Rashevsky's office, and there was a desk and a chair and Rashevsky, sitting there with a pencil…Carlson said, 'Where is your apparatus?' And Rashevsky said in his Russian accent, 'What apparatus? I am a mathematical biologist'" (Cowan, 1998, pp. 104–105). Carlson, according to Taliaferro, had "always actively disliked and mistrusted" Rashevsky, however, a few years later, Taliaferro pointed out to him that this was "self-defeating," since a rejection of Rashevsky's inclusion in the Department of Physiology would force Taliaferro to set up a separate "Department of Biophysics" for Rashevsky. Carlson then agreed to have Rashvesky return to the Department of Physiology, although in separate quarters, in another building (Weaver Interviews, June 18, 1940, Record Group 1.1, Series 216D, Box 11, Folder 147, Rockefeller Archive Center, Sleepy Hollow, New York; hereafter RAC).

[95] By the spring of 1935, the General Education Board entered into a co-operative agreement with the University of Chicago, and the university appointed Rashevsky to an Assistant Professorship for a 3-year period; with the Board paying Rashevsky's salary for the first year, and a fraction of the salary for the subsequent 2 years. The University would pay the remainder. "Agreement for Rashevsky's Grant-in-Aid," Record Group 1.1, Series 216D, Box 12, Folder 160, RAC.

[96] "Sketch of the Biotheoretical Gathering's Joint Proposal for an Institute for Physico-Chemical Morphology," Needham Archive, Cambridge, UK; reprinted in Abir Am, 1987.

[97] Henry M. Miller Diary, December 4, 1935, Record Group 1.1, Series 216D, Box 12, Folder 160, RAC.

removed from empirical work in biology that the relevance of his mathematical treatments was questionable.

Rashevsky and Philosophy of Science

Although Rashevsky's convictions about the use of mathematics and idealization in biology met with mixed reaction within the scientific community, philosophers, at the peak of the unity of science movement, seemed to view Rashevsky's work as an example of how the methods of physics could be applied to biological problems. Logical positivism, a view that dominated the journal at its inception, had as a central tenet the legitimacy of using the methods of physics in nonphysics disciplines. Simply put, the logical positivists, particularly Moritz Schlick, Rudolf Carnap, and Otto Neurath, advocated the development of a "scientific philosophy," a field which took science as its object of study – involving the logical analysis of the concepts, hypotheses, theories, and proofs of science.[98] Early logical positivists aimed to purge science of metaphysics, had an empiricist tendency, a "bias for the methodological intervention of logic," and advocated the mathematization of all the sciences.[99] In the first issue of *Philosophy of Science*, appearing in 1934, Carnap had declared that "the philosophical problems of the foundation of biology refer above all to the relation between biology and physics."[100] The unity of science was a central aim of the logical positivists – primarily on the level of language – that is, a common language was sought to unify various sciences, and "physical language," or the language of physics, was seen as best suited for this purpose. This was the key claim of the physicalist thesis: that every sentence of every branch of science is "translatable" into some expression in physical language, and thus, in a sense, physicalism was the doctrine of the unity of language in science. Thus, to be scientifically respectable, biology, like physics, would need laws or law-like statements that should be expressed in the language of physics.[101]

With Rashevsky's strong arguments about the importance of using the methods of theoretical physics in the life sciences, and his search for the "fundamentals" of biological phenomena, it is not surprising that he

[98] Carnap, 1934.
[99] Joergensen, 1937, p. 279. The work of Joseph H. Woodger is the most prominent example of the application of logical positivist principles to biology (Woodger, 1937).
[100] Carnap, 1934, p. 18.
[101] Neurath, 1931; Carnap, 1937.

engaged the interest of this community. In January 1936, RF officer Frank Blair Hanson discussed with Rashevsky the upcoming International Congress on the Unity of Science in Copenhagen. In conversations with Charles Morris, who was in Chicago's philosophy department and on the organizing committee for the congress, Rashevsky decided to attend the meeting. He requested a grant-in-aid from the General Education Board to cover the expenses of the trip, citing his poor financial situation and pointing out that there were people in Europe who were "interested in his work" and he felt it important to visit these groups.[102] Rashevsky had told Hanson that he could not go to Copenhagen without funding to cover all expenses. Rashevsky also had asked Dean William H. Taliaferro for larger quarters and more research assistants. Taliaferro, as reported by Hanson, was "entirely sympathetic" with Rashevsky, and would send to the RF a formal request for Rashevsky to get money for Copenhagen.[103] Taliaferro promised to talk to University of Chicago President Robert M. Hutchins to get funds to cover part of Rashevsky's trip. Hanson reported that the RF would provide a grant-in-aid to cover the rest of the expenses.[104] Rashevsky departed during the first week of June 1936.[105]

The Copenhagen meeting, held from June 21 to 26, 1936, was on the "Problem of Causality with Special Consideration of Physics and Biology."[106] Participants at the meeting included Niels Bohr, Philipp Frank, Karl Popper, J.B.S. Haldane, and Otto Neurath. Although the theme of the conference was "causality," few of the papers dealt directly with this topic. The first session, on the 22nd of June, included Bohr and Frank, who were to speak on the "causal problem" in physics and

[102] Rashevsky was to visit London, Cambridge, Edinburgh, Berlin, Prague, Vienna, Innsbruck, Frankfurt, and Paris. (Taliaferro to Hanson, February 29, 1936, Record Group 1.1, Series 216D, Box 12, Folder 160, RAC.)

[103] Frank Blair Hanson Diary, January 13, 1936, Record Group 1.1, Series 216D, Box 12, Folder 160, RAC.

[104] Frank Blair Hanson Diary, February 7, 1936, Record Group 1.1, Series 216D, Box 12, Folder 160, RAC.

[105] Rashevsky to Bitter, June 9, 1936, Francis O. Bitter Papers, Box 1, Correspondence Q-R, 1931–38. MC 77, MITSC.

[106] Carnap and Reichenbach, 1937. This meeting was one in a series of conferences organized by the logical positivists, the first in Prague in 1929, the year in which the name "Vienna Circle" was coined. The 1929 meeting was followed by a congress in Königsberg (1930) and another in Prague (1934). The "First Congress on Scientific Philosophy" was held in Paris in September 1935.

biology; however, their papers dealt more with the relationship between physics and biology and the validity of the ''physicalist'' thesis.[107]

Rashevsky's paper, which essentially reviewed much of his previously published material, raised two methodological questions: the relation of physico-mathematical and biological sciences, and the usefulness or impossibility of applying mathematics to biology. Rashevsky argued that the answers to such questions *must* be found in the ''*actual* development of a [research program in] mathematical biology.'' In the past, he noted, the application of mathematical methods in biology often involved attempts to find ''empirical formulae to fit certain experimental data.''[108] Rashevsky described his approach as distinct from this: his goal was to develop ''mathematical biology as a *rational* theoretical science, according to patterns suggested by theoretical physics.'' Rashevsky then outlined his work so far, on idealized cells, cell dynamics, and the central nervous system. He began by reviewing some of his ideas on the theoretical treatment of an idealized cell. For Rashevsky, the most general aspect of all cells is that a cell is ''essentially a small metabolizing unit or system.'' Rashevsky proceeded to examine three cases in terms of the physico-chemical configurations of the cell, the first, simplest case involving a spherical homogenous cell, in a liquid medium, producing or consuming at a constant rate. In this case, only one substance is involved, whose concentration in the external medium is maintained constant. Diffusion equations will determine the distribution of concentrations, and these, noted Rashevsky, are easily solved. The next case Rashevsky discussed was that of a distorted sphere, which is very nearly spherical. If certain conditions (A) between physical constants within the cell are satisfied, that is, between the rate of reaction, the diffusion co-efficients, permeability, and distribution of forces, the spherical shape of the cell is restored. However, if other conditions (B), the opposite of (A), are satisfied, the cell will tend to deform even further and eventually divide in two, provided that the size of the cell reaches a critical value. The next two cases considered by Rashevsky were when several different substances are metabolized, using the example of respiration, and when inter-molecular forces are taken into account. Rashevsky continued with a discussion of the interactions of cells on the basis of concentration gradients, leading to interpretations of the typical shapes of early stages of embryonic development, as well as an extension of his theory to the social sciences, for example, in

[107] Bohr rejected the physicalist thesis in his paper, arguing that laws in biology are fundamentally different from those in physics (Bohr, 1937), while Frank advocated the physicalist position (Frank, 1937).

[108] Rashevsky, 1937, p. 358.

understanding relations between individuals and other social phenomena. At the end of his paper, he argued that mathematical biophysics opens up a "fertile and useful field, which may equally attract the physicist, the biologist, the pure mathematician, and even the social scientist." His last remark reflected the most fundamental belief of the unity of science movement: "there is only one Science, infinitely ramified, and if Science is not to resolve itself into mere verbalistic disputes, it *must* be mathematical."[109]

The commentators for Rashevsky's paper were the French biophysicist Pierre Lecomte du Noüy, and John M. Somerville, a philosopher from Columbia University in New York. Lecomte du Noüy had made extensive contributions to the study of surface equilibria in colloids, and had performed countless experiments on the surface tension of blood serum with a measuring device he had invented – the tensiometer – and had discovered, among other things, that the surface tension decreased with time.[110] Lecomte du Noüy would use differential equations to relate the quantities in his observations, and through this, he drew conclusions about the relationship between diffusion, osmotic pressure, surface tension, and time. Lecomte de Noüy said that he found Rashevsky's paper interesting, but pointed out that in 1926 he himself had published a "physico-chemical hypothesis" based on experiments and measures of superficial tension that could account for the same facts outlined by Rashevsky, and even more phenomena, such as mitosis. He told Rashevsky that he felt that his own hypothesis went further than Rashevsky's.[111] Somerville was not in disagreement with what Rashevsky had to say, but wanted to point out certain "methodological principles" that in his view could shed light on the "*philosophic* significance (orig. emphasis)" of the ideas Rashevsky presented. Essentially he warned Rashevsky that merely stating a biological problem in terms of a mathematical axiom does not lead to a solution of the problem, only, perhaps, a hypothesis that then must be validated or invalidated by experiment. Further, applying mathematical techniques to biological "problems" only reformulates the problems, it does not lead to solutions. For a biomathematical statement to be of value, it must facilitate the formulation of "new problems."[112] In essence, Somerville was questioning the relevance of what Rashevsky had presented: that merely using mathematics did not necessarily lead to testable hypotheses or to ultimate solutions of biological problems. In his reply to these

[109] Rashevsky, 1937, p. 365.
[110] E.g. Lecomte du Noüy, 1926.
[111] Lecomte du Noüy in Carnap and Reichenbach, 1937; pp. 375–376.
[112] Somerville in Carnap and Reichenbach, 1937, pp. 376–377.

comments, Rashevsky apologized for not having mentioned Lecomte du Noüy's work, and acknowledged the validity of his critique. Replying to Somerville, Rashevsky stressed that in the material he had presented, he has been able to "unify a number of disconnected fragments of empirical knowledge." Rashevsky was to face more significant criticism later that year, in the form of official assessments of his work procured by Warren Weaver.

Weaver's First Retreat

On September 19, 1936, Weaver wrote to Rashevsky that during the last month or so he had a chance to read Rashevsky's papers a little more carefully than he had originally, and that he felt that they could be "somewhat improved as to clarity by minor and infrequent changes."[113] Weaver felt that in certain places in his work, Rashevsky had given an impression that he was claiming more for his work than he should, and that such claims would have probably "irritated" some of the biological readers. Rashevsky responded 5 days later, and politely admitted to Weaver that some of his more recent publications he had made remarks that "might irritate *some* biologists" [original emphasis].[114] He insisted though, that he had never meant for his statements to be construed as exaggerated, and asked Weaver to point out specific areas in his papers where he might have given the wrong impression.[115] In accordance with the Foundation's policy of submitting work of their grantees to "assessors," in the fall of 1936, Weaver passed on some of Rashevsky's work to the Danish biochemist Kaj Linderstrøm-Lang.[116] In his letter to Linderstrøm-Lang, Weaver confessed that he was "somewhat irritated, at places, by [Rashevsky's] terminology; but I think it is entirely possible that the phrases which bother me result from the fact that Rashevsky is, after all, writing in a language foreign to him…Even if this excuse is pushed to the utmost, there still remains a certain flambuoyancy and pretentiousness of phraseology which I think is distinctly unfortunate,

[113] Weaver to Rashevsky, September 19, 1936, Record Group 1.1, Series 216D, Box 11, Folder 147, RAC.

[114] Rashevsky to Weaver, September 24, 1936, Record Group 1.1, Series 216D, Box 11, Folder 147, RAC.

[115] Rashevsky to Weaver, September 24, 1936, Record Group 1.1, Series 216D, Box 11, Folder 147, RAC.

[116] For biographical information on Linderstrøm-Lang, see Tiselius, 1960. Weaver had discussed Rashevsky's case with Linderstrøm-Lang in Copenhagen in the summer of 1936, at the Carlsberg Laboratory. The papers that Weaver sent to Linderstrøm-Lang were: Rashevsky, 1932c, 1934b, 1935b, c, 1936a.

especially because I really believe that this does not accurately reflect Rashevsky's personal position. I am not at all sure that this is not another instance of the well-known phenomenon of an apparent superiority complex which is only a superficial mask to cover up an attitude which is in reality somewhat shy and modest."[117]

Linderstrøm-Lang replied that his first quick reading of Rashevsky's papers gave him a feeling of confusion. He noted that during the development of his mathematical model, Rashevsky often arrived at a stage where "several possibilities" presented themselves. "He then," Linderstrøm-Lang wrote to Weaver, "chooses one of these ways either because experimental facts from biology seem to lead him in this direction or because this way is mathematically the simplest one. During the progress of the calculations those occasions where he has to make a choice become more and more frequent and my impression is that the regard for mathematical simplicity becomes more dominant."[118] Linderstrøm-Lang expressed uneasiness at this, because as a reader he was left with the impression that Rashevsky's choice of solution, while occasionally based on experimental results, was based on those found for much more complicated systems than those Rashevsky was dealing with. Essentially, Linderstrøm-Lang felt Rashevsky's use of mathematics was misguided: "A mathematics I am able to understand is no very refined mathematics possessing any beauty in itself. It is a tool very commonly used in physico-chemistry and a good tool. Only it must be used with very skilful hands in the present case."[119] Linderstrøm-Lang did not seem to have qualms with the use of mathematics in biology *per se*, but took issue with Rashevsky's particular *use* of mathematics.

Linderstrøm-Lang's comments focused on three of Rashevsky's papers – all of which were on the "mathematical physics" of metabolizing systems, namely, living cells.[120] He noted that Rashevsky had postulated that in addition to osmotic forces being active in a small liquid droplet, other "forces" are at play, however, Linderstrøm-Lang criticized Rashevsky's vagueness with respect to this force and of his derivation of a mathematical expression for this force. Furthermore, besides Rashevsky's mathematical treatment being "not very elegant,"

[117] Weaver to Linderstrøm-Lang, September 18, 1936, Record Group 1.1, Series 216D, Box 11, Folder 147, RAC.

[118] Linderstrøm-Lang to Weaver, November 9, 1936, Record Group 1.1, Series 216D, Box 11, Folder 147, RAC.

[119] Linderstrøm-Lang to Weaver, November 9, 1936, Record Group 1.1, Series 216D, Box 11, Folder 147, RAC. Linderstrøm-Lang was referring to Rashevsky, 1934a.

[120] Rashevsky, 1934b, 1935b, c.

Linderstrøm-Lang also wrote that Rashevsky did not account for certain empirical considerations in his treatment, and introduced undefined quantities.[121] After reading Linderstrøm-Lang's comments, Weaver replied to him, saying that his comments would certainly help Rashevsky, and that they should have a "salutary" influence on his work. Weaver said that Rashevsky was open-minded and thus would likely profit from the comments.[122]

Weaver sent these comments to Rashevsky, who replied that although admittedly there were weaknesses in some of his work, he "could not entirely agree" with Linderstrøm-Lang's criticisms.[123] He did plan to send a written answer to Linderstrøm-Lang, as per Weaver's request.[124] Rashevsky did reply, and Weaver sent both the reply and Linderstrøm-Lang's original letter to John Warren Williams, a physical chemist at the University of Wisconsin – Madison. Williams had read the letters with "much interest," but had a similar feeling of confusion as Linderstrøm-Lang had. He saw Linderstrøm-Lang's criticisms as entirely valid, and almost conservative. Despite this, Williams did feel that Rashevsky's articles had interesting suggestions, and might lead to significant results. And he did agree that the construction of physical and mathematical models to aid "physico-chemical study" was worthwhile.

Forging a Discipline

By late summer 1936, Rashevsky began putting together a proposal for a book on mathematical biophysics. He sent a proposed table of contents to Weaver, in hopes of receiving some Rockefeller funding for the publication of the book. In September 1936, Weaver wrote to Rashevsky with his comments on the proposal: "…as I read over the titles of the various chapters I could not help wondering whether or not, relative to the standard and classical theories and techniques of physical chemistry, physics, etc., which you use, you propose to include a sufficient treatment so that the book will be reasonably self-contained. That

[121] Linderstrøm-Lang went so far as to say that "R. has made a *relatively* simple problem complicated [original emphasis]."

[122] Weaver to Linderstrøm-Lang, November 30, 1936, Record Group 1.1, Series 216D, Box 11, Folder 147, RAC.

[123] Rashevsky to Weaver, December 9, 1936, Record Group 1.1, Series 216D, Box 11, Folder 147, RAC.

[124] Williams to Weaver, April 29, 1937, Record Group 1.1, Series 216D, Box 11, Folder 147, RAC.

is to say, I should think that the book would be more useful and appeal to a much wider audience if an intelligent physiologist with only a reasonably good background of mathematics, physics, etc. could get from this book a reasonably complete introduction to your type of work."[125] Rashevsky replied that he "had considered the possibility of making a physico-chemical introduction to the whole book." However, after thinking it over, he decided it would not be the best thing to do, and would rather take up these sort of issues in individual chapters. He told Weaver that this approach had been successful in his lectures to students, who had comprised a very mixed audience. Rashevsky felt that only a very general knowledge of physics and chemistry were required, but of course familiarity with mathematics would be "unavoidable."[126]

Despite Weaver's misgivings, by October 1936, the University of Chicago Press, in agreement with the RF, agreed to publish Rashevsky's book, with the Press and the foundation sharing the cost of publication.[127] The book, *Mathematical Biophysics: Physicomathematical Foundations of Biology*, was eventually published in 1938. It dealt with three broad topics: the mathematical biophysics of the vegetative cell, the mathematical biophysics of excitation and conduction in nerves, and the mathematical biophysics of the central nervous system. Reviews of *Mathematical Biophysics* were mixed. University of Illinois (Chicago) neuroanatomist Gerhardt von Bonin reviewed the book and expressed that it was "not easy reading" – pointing to Rashevsky's use of differential equations and vector analysis.[128] Although von Bonin felt that mathematical theory "constitutes the clearest and most powerful logical instrument we possess" it was "unfortunately an instrument that can be handled only by experts."[129] Other reviewers wondered about the practical utility of Rashevsky's mathematical treatments of biological problems, since, as one reviewer observed, they seemed to depend "much on postulates that for the present cannot be verified experimentally."[130]

[125] Weaver to Rashevsky, September 19, 1936, Record Group 1.1, Series 216D, Box 11, Folder 147, RAC.

[126] Rashevsky to Weaver, September 24, 1936, Record Group 1.1, Series 216D, Box 11, Folder 147, RAC.

[127] Rashevsky received a Grant-in-Aid of $2000 from the foundation for the publication of the book. (Grant-in-Aid Agreement, October 1936, Recored Group 1.1, Series 216D, Box 11, Folder 147, RAC).

[128] Von Bonin, 1939.

[129] Von Bonin, 1939, p. 72.

[130] 1939. Review of Mathematical Biophysics: Physico-Mathematical Foundations of Biology, by Nicolas Rashevsky. *Quarterly Review of Biology* 14(1): 106.

By April 1937, Rashevsky had two research assistants and four graduate students, had quarters in the Department of Psychology at Chicago, and soon began an independent group within the department, for "mathematical biophysics." His first students included Herbert D. Landahl, Alston Householder, and Alvin M. Weinberg. Householder was actually supported by the RF, and in Rashevsky's view, was doing exceptional work. As he described to Weaver in March 1938, "Dr. Householder also has not only fulfiled all my expectations but actually exceeded them. He not only is working on the mathematical aspects of various biophysical problems, but he actually went very seriously into the biological aspects of those problems and spent considerable time on the study of biological literature. Such a proper balance of interests in the two aspects is, as I have found, very rarely to be found."[131]

In this letter, Rashevsky asked Weaver if Householder's fellowship could be renewed for at least 1 year, as he wished to have him as a permanent member of his group. Weaver was clearly impressed by Householder, and a few days later he wrote to Hanson: "In view of our proposed general support to Chicago Biology…I would oppose any special direct help to Rashevsky outside of the general help. On the other hand, I think we have every right to be interested in the training of Householder. He has been thoroughly well trained in pure mathematics. To supplement this with a thorough training in biophysics is a matter which comes directly within our interests…I think we would wish to view this as a desirable thing, quite apart from any special relationship it may bear to Rashevsky's plans…"[132] Householder garnered a positive response from Weaver precisely because of Rashevsky's own observation about him: that he was making efforts to become well versed in biological literature, something which Rashevsky apparently failed to do.

By the late 1930s, Rashevsky's group had acquired several students who began producing papers, and they needed a place to publish them. Although Rashevsky had managed to find a forum for some of his earlier

[131] Rashevsky to Weaver, March 26, 1938, Record Group 1.1, Series 216D, Box 11, Folder 148, RAC. Later Rashevsky reported to Weaver that Householder had been taking courses in histology and neurology, and eventually both Householder and Landahl had been taking courses in anatomy, physiology, neurology, and genetics (Weaver Interviews, January 19, 1939 and June 18, 1940, Record Group 1.1, Series 216D, Box 11, Folder 148, RAC). In 1944, Householder collaborated with Landahl in the publication of a monograph, *Mathematical Biophysics of the Central Nervous System*. In 1946, Householder joined the mathematics division at the Oak Ridge National Laboratory and eventually made important contributions to numerical analysis.

[132] Weaver to Hanson, March 28, 1938, Record Group 1.1, Series 216D, Box 11, Folder 148, RAC.

work in mathematical biophysics, he saw a need for a journal totally devoted to this new field.[133] He proposed a new journal of "biophysics" to Weaver, with little success. In October 1938, Rashevsky sent a letter to John Berrill, the editor of the journal *Growth*, asking if the papers could be published in his journal. Berrill replied, noting that although the papers showed "excellence" he felt that the "number of subscribers [to the journal] who appreciate them is probably very small indeed."[134] By January 1939, Rashevsky approached the editor of the journal *Psychometrika*, L.L. Thurstone, who was one of his earliest supporters at Chicago. Rashevsky formed an agreement with them that a new journal, the *Bulletin of Mathematical Biophysics*, would be published as a supplement to their quarterly issues.[135] This journal was to become Rashevsky's main publication outlet. He published extensively in the journal, sometimes having several of his own papers appear in the same issue. As Alvin Weinberg noted, since Rashevsky was also the editor of the *Bulletin*, his "publication there did not receive the peer review required by the established journals. But Rashvesky had little choice: since his models were poorly understood by the biological community, it was often a case of publishing in the *Bulletin*, or not at all."[136]

In 1940, Rashevsky published *Advances and Applications of Mathematical Biology*. In the preface to this book, Rashevsky noted that although in his 1938 book he had attempted "to establish contact between mathematical conclusions and experimental facts, still the theoretical foundations occupied a much more prominent place than their actual applications. During the 2 years which have elapsed since the completion of the manuscript of that book, considerable progress has been made in this field especially in the direction of applications of the mathematical theory to various observations..."[137] The mathematical treatments here were more elementary than in Rashevsky's previous work. More data were presented, a move one sympathetic reviewer

[133] In July 1938, weaver reported that Rashevsky had "moved from one journal to another as difficulties...developed." After a conflict with a referee of the journal *Protoplasma*, which, in Weaver's view, was through no fault of Rashvsky's, Rashevsky began to seek other outlets for publication. Weaver Interviews, July 3, 1938, Record Group 1.1, Series 216D, Box 11, Folder 148, RAC.

[134] Berrill to Rashevsky, October 19, 1938, Record Group 1.1, Series 216D, Box 11, Folder 148, RAC.

[135] Weaver Interviews, January 19, 1939, Record Group 1.1, Series 216D, Box 11, Folder 148, RAC. Beginning in the summer of 1940, the *Bulletin* was published by the University of Chicago Press.

[136] Weinberg, 1994, p. 7. Weinberg nevertheless speaks fondly of Rashevsky as an important mentor.

[137] Rashevsky, 1940, p. ix.

noted seemed to be an "implicit reply to those biologists who tend to say: 'This is a very pretty mathematical exercise, but what has it to do with me?'"[138] On the whole, any positive evaluations of Rashevsky's 1940 book were muted: the book was not seen as presenting a "clear and irrefutable case" for using mathematics in biology, but rather a good beginning.

By 1946, Rashevsky was full professor at the University of Chicago and had a fairly large group of students, which existed from 1940 to 1947 as the "Section on Mathematical Biophysics" in the Department of Physiology. By 1947, it had become a separate, independent unit, the Committee on Mathematical Biology, with Rashevsky as its chairman. They were producing a considerable amount of work, most of which was published in the *Bulletin for Mathematical Biophysics*. In 1948, Rashevsky's monograph, *Mathematical Biophysics*, went into a second and enlarged edition.[139] Over 20 new chapters appeared, mostly taken from his 1940 book. In a review of the 1948 edition, Robert G. Grenell, a biological psychiatrist at Johns Hopkins University, felt dissatisfied: "A satisfactory mathematical biology, from the point of view of the biologist, would either help to fill the hole created by lack of quantification in this field, or would set itself the task of pointing out paths for the experimentalist to follow..."[140] Although Grenell was ultimately somewhat positive in his review, he noted that while mathematicians might be impressed with the "elegance" of a mathematical expression of a biological problem, for biologists, "...the power of mathematical analysis lies in its ability to go beyond experiment and available empirical data, to the formulation of a hypothetical principle, which may or may not then be validated in the laboratory."[141] Another reviewer had a similar reaction: "The utility of any theoretical science depends entirely upon its ability not only to correlate existing facts into theories, but also to predict new relationships which may be sought through experimentation..."[142] On the whole, much of the negativity

[138] Reiner, 1941, p. 134.

[139] Rashevsky, 1948. In 1951, the University of Chicago Press published *Mathematical Biology of Social Behavior* (revised 1960). In his review of *Social Behavior*, Herbert A. Simon stated that "the ratio of theory to empirical verification is excessive," and that he thought it unlikely that "any single one of the models Rashevsky employs will survive in recognizable form as part of a developed theory of mathematical sociology." Nevertheless, Simon felt the text did have worth simply as a mathematical text, and that it served as a good starting-point (Simon, 1951).

[140] Grenell, 1950.

[141] Ibid.

[142] Juni, 1949.

directed toward Rashevsky was aimed at the specific use he saw for his theories, that it was acceptable and even desirable to produce mathematical theories that served only as possibilities and that promised to lead to fundamental biological principles. Following the Second World War, the United States, the disciplinary landscape of the life sciences had changed: molecular biology was on the rise, and biology was seen to have more pragmatic dimensions.[143] Ultimately, within the utilitarian climate of the life sciences, Rashevsky's stance would lead to more significant obstacles.

The Demise

In December 1948, after meeting with Rashevsky, Weaver reported that the "University of Chicago has found it necessary to be much more careful in permitting Rashevsky to take on young people" and that although Rashevsky had "several important inquiries before him" there was no chance of him securing any further funding from Chicago.[144] Although Weaver wrote that he had "reservations" concerning Rashevsky's work, he did believe that Rashvesky's department remained the "most important and active center in the US for mathematical biology. Furthermore," reported Weaver, "they have trained some excellent people." Weaver suggested that the RF would be willing to contribute $7500 over a 3-year period, "provided that Rashevsky is able to raise a similar amount from other sources." In February 1949, Weaver reported that he had just spent "two hours listening to Rashevsky."[145] By this time Rashevsky had made no progress in his attempts to secure funds from other sources, but by March, Weaver was able to report that Rashevsky and the "Chicago authorities" were now trying to raise $60,000 for "mathematical biology:" "As a result of an hour of frenzied conversation (any South Russian can out-talk anybody else in the world, and in South Russia [Rashevsky] was rated as

[143] Benson, Maienschein and Rainger, 1991.

[144] Weaver Interviews, December 20, 1948, Record Group 1.1, Series 216D, Box 11, Folder 149, RAC. Weaver made visits to the University of Chicago on a regular basis, to interview and receive reports from the many RF-funded scientists at the university.

[145] Part of this was a "long lecture" by Rashevsky on his desirability of establishing a friendship with Russia, with Weaver commenting in his report that this was "perfectly genuine – [Rashevsky] is a very loyal American." Weaver Interviews, February 7, 1949, Record Group 1.1, Series 216D, Box 11, Folder 149, RAC.

an orator) it is agreed that the University of Chicago will make a definite request for a grant in aid of $7500 payment to be conditional upon their raising at least that amount for some new outside sources."[146] In the end, Rashevsky and the University of Chicago were able to secure $7500 of funding from the Lucius N. Littauer Foundations.[147]

In September 1950, Robert Hutchins, then chancellor of the University of Chicago, came to Weaver to discuss Rashevsky.[148] Hutchins reported that Rashevsky had been "importuning him very vigorously and strenuously" in attempts to get him to raise funds for the development of mathematical biophysics at Chicago. Hutchins had replied to Rashevsky that he was unable to get any "critical estimate" of the value of the work that Rashevsky was doing. Weaver gave his assessment of Rashevsky in the following way:

> If one went about the country and asked 20 well-informed scientists who would have a presumptive interest in Rashevsky's work, [Weaver] guesses that their reports would be as follows. Probably five of them would say that they had no use for it whatsoever, and that they simply could not understand what Rashevsky is about. Of the other 15, all would agree that this is an interesting and very possibly an important development. They would say that they thought that some adventure of this sort ought to be supported, and that the University of Chicago is probably a very good place to try such an adventure. About five of this 15 would be greatly confident that the adventure was going to be successful. About five of them would probably consider the adventure a good one, but would not rank it as really excellent nor would they be very overly optimistic about the outcome. The final five would give a still lower rating, but would still say that they thought it ought to be supported and continued.[149]

[146] Weaver Interviews, March 24, 1949, Record Group 1.1, Series 216D, Box 11, Folder 149, RAC. The grant in aid was given to the University of Chicago "as a contribution toward research and development in mathematical biology..." Grant in Aid Agreement, April 13, 1949, Record Group 1.1, Series 216D, Box 11, Folder 149, RAC.

[147] Harry Starr to Brinton H. Stone, August 26, 1949, Record Group 1.1, Series 216D, Box 11, Folder 149, RAC.

[148] Warren Weaver Diary, September 8, 1950, Record Group 1.1, Series 216D, Box 11, Folder 150, RAC.

[149] Weaver Diary, September 8, 1950, Record Group 1.1, Series 216D, Box 11, Folder 150, RAC.

When asked by Hutchins about the students that Rashevsky had had, Weaver reported that they had been a "very queer lot on the whole," although there were one or two exceptions, such as Householder.

Weaver was critical of Rashevsky's "habit" of producing "a large number of very short papers, each of which is chuck full of numerous references to other very short papers by himself." In addition, Rashevsky's papers continued to be full of self-referencing and focused on a remarkably broad range of topics. Between 1939 and 1945, his papers dealt with the mathematical biophysics of amoeboid movements, organic asymmetry, the plasticity of the central nervous system, growth, human relations, organic form, cancer, chromosome movement, interaction of social classes, structure of social groups, auditory perception, visual esthetics, sizes of cities, origin of life, locomotion of snakes, shape of quadrupeds, bird and insect flight, blood circulation, mental phenomena, and molecular biophysics.[150] As Weinberg noted, "his canvas was so broad that he could hardly carry any of his models to a crucial test."[151] Despite the eclectic and somewhat esoteric nature of Rashevsky's work, Weaver believed that "it must be admitted that they have made some important progress." He predicted that if progress continued to be made over the next 5–10 years, "there is a really good chance that biologists will begin to pay serious attention to this line of work…[I] do not think that it either needs or deserves to have a large inflation of staff or of support, but [I] hope that the University of Chicago will not run out on an experiment which is, after all, going along pretty well." However, when asked by Hutchins if Weaver thought it likely that the RF will contribute to this development in any substantial way, Weaver said that it was "very unlikely."

By November 1951, Rashevsky asked Weaver about the possibility of further funding after the $7500 grant that was to expire in July 1952. Weaver thought it "only fair" to warn Rashevsky that he was "very

[150] By the 1960s, this list had expanded to include altruism, automobile driving, molecular biology, imitative behavior, schizophrenia, the lung, energy expenditure in walking on level ground and uphill, reward and punishment, memory, organismic sets, and epilepsy. Rashevsky's lack of contact with experiment continued during this period: one reviewer of an edited volume resulting from a summer school Rashvesky conducted in July 1960 (Rashevsky, 1962), stated that Rashevsky's approach was like a game, since the models that resulted from the excessive over-simplifying bore no relation to reality (Wolbarsht, 1963).

[151] Weinberg, 1994, p. 7.

pessimistic" about the possibility of further funding from the RF for Rashevsky's group: "As you yourself said, you are now receiving substantial recognition and support from other quarters, and I think that this is almost without question the natural moment for us to retire from the scene…our important function is to assist in the earlier and more adventuresome stages."[152] In his response Rashevsky seemed to concede defeat: "Though, as you know, I am a rather persistent, not to say stubborn, individual, nevertheless I can assure you that I know when it is time to stop. From your letter it is perfectly clear to me that that time has come in regard to any further requests for help from the Rockefeller Foundation."[153] Rashevsky went on, however, to suggest that since mathematical biology was being applied to phenomena of social behavior only recently, these applications may in effect be creating a new field of study. In a sense, the new, unexplored possibilities in this area warrant characterizing the mathematical biology of social behavior as in an "adventuresome" stage, and thus, on Weaver's criteria, eligible for Rockefeller funding. Although he said that he proposed this question "merely for my [Rashevsky's] information," it seemed that he was making a last desperate attempt for more funding from the RF. In his reply, Weaver noted that any activity had passed out of an "adventuresome" or "early pioneering" stage when it was generally considered eligible for financial support.[154] Since the other agencies that had begun to support Rashevsky's work operate under the policy that they ought to deal with "scientific activities which have already substantially proven their worth," Weaver argued, his activities had, although still "adventuresome," passed out of the pioneering stage.[155]

By 1953, Chicago's administration had changed: Lawrence A. Kimpton became chancellor in 1951. Hutchins had left the university with a considerable deficit, and Kimpton proposed many reforms to remedy the situation, and with drastic budget cuts came lower salaries and a smaller staff.[156] According to Anatol Rapoport, the new chan-

[152] Weaver to Rashevsky, November 17, 1951, Record Group 1.1, Series 216D, Box 11, Folder 150, RAC.
[153] Rashevsky to Weaver, November 26, 1951, Record Group 1.1, Series 216D, Box 11, Folder 150, RAC.
[154] Weaver to Rashevsky, November 29, 1952, Record Group 1.1, Series 216D, Box 11, Folder 150, RAC.
[155] By this time, Rashevsky had been receiving funding from the National Institutes of Health.
[156] McNeill, 1991, pp. 166–169.

cellor had "little use for work that in those days was regarded as esoteric."[157] Several of Rashevsky's former students have recalled a "setback" Rashevsky and his Committee suffered by the end of 1954, one that, according to Bartholomay, Karremann, and Landahl, was "never justified."[158] According to Robert Rosen, several members of his Committee were targeted by the House Un-American Activities Committee, apparently accused of pro-Communist leanings.[159] Rashevsky was asked to "rid" the University of these individuals, which he flatly refused to do. His punishment was monetary: the University cut his budget drastically, and two National Institutes of Health grants he had obtained in the early 1950s were not renewed.[160] Rashevsky's health was said to have suffered as a result, and after this, the work continued but the committee was reduced to two members.

In February 1955, Gerhardt von Bonin, a former colleague of Warren McCulloch's, wrote to McCulloch at MIT: "It appears that Dr. Rashevsky of the University of Chicago has run into difficulties (I think he has been accused – of all things – of being a Red, in spite of the fact that he fled Russia in 1917 or 1918 and has ever since been a stout defender of the old regime). These difficulties threaten to dissolve his department and leave him more or less high and dry."[161] Von Bonin went on to say that Karl Menger, a mathematician at the Illinois Institute of Technology, was trying to organize a group of people who would be willing to speak in defense of Rashevsky and to sign a letter that would be sent to the Chancellor or President of the University of Chicago. Von Bonin asked McCulloch if he would be interested in

[157] Rapoport, 2000, p. 5. Keller has suggested that Rashevsky's collapse in 1953–54 was most likely due to the discoveries of Watson and Crick on the structure of DNA (Keller, 2002, p. 83). It is also possible that Rashevsky's work in "relational biology" might have marginalized him even further. By 1950, according to Rosen, Rashevsky began to ask the question "What is life?" and found that he couldn't answer it using the "reductionistic" approach he had been using (Rosen, 1991, p. 111). In 1954, in his first published work on what he later called "relational biology," Rashevsky noted that up until that point, mathematical biology had focused on the quantitative aspects of life – dealing with the phenomena occurring in the organism as separate phenomena. Now, Rashevsky urged, there was a need to treat the organism's activities in an integrative way. Rashevsky's relational biology was anti-mechanistic, placed emphasis on the functional rather than the material aspects of organisms, and was completely against the current of mainstream biology (Rashevsky, 1954).

[158] Bartholomay, Karremann, and Landahl, 1972.

[159] For an account of McCarthyism and its effect on academics during this period, see Schrecker, 1986.

[160] Rosen, n.d. p. 71.

[161] Gerhardt von Bonin to Warren S. McCulloch, February 4, 1955, Warren S. McCulloch Papers, APS.

participating. McCulloch replied 6 days later, opening his letter assertively: "That Rashevsky is in trouble for being a red is as old as it is false. The rumor did discredit him with many who would otherwise have befriended his department. Openly he was accused of harboring communists when two of his men invoked the fifth amendment."[162] At issue was the reduction of Rashevsky's staff from 20 to 3 and the drastic cuts to his funding, and if the suspicion of Rashevsky as a communist is invoked as the reason for this, his supporters will be shut down with the officials simply pointing to "budgetary difficulties." McCulloch thought that any letters on Rashevsky's behalf would be most effective if they emphasized the quality and importance of Rashevsky's *work*, his contributions to mathematical biophysics, his committee, his teaching, and his journal. McCulloch closed his letter with strong sentiment: "As it is, men who know Rashevsky's history are outraged, which means that there are scientists in a dozen universities who are needlessly infuriated. I am one of them."[163]

By the summer of 1955, a letter was submitted to and accepted by the journal *Science*. However, by December of that year, Dael Wolfle, the administrative secretary of the AAAS, expressed some hesitancy about publishing the letter. He saw the situation as simply one of budgetary problems on the part of the University. He proposed that an official reply from the Chicago's Dean of Medicine, Lowell T. Coggeshall, be published along with the letter, and that perhaps it might be best for the signers of the letter to simply write directly to the university administrators.[164] Apparently, Coggeshall "flatly denied" excessive cuts in Rashevsky's budget. In January 1956, von Bonin wrote to Wolfle, saying that the Dean's answer was "…at variance with the facts" and implied that "we are publishing incorrect information obtained in some underhanded way…"[165] The group of supporters protested that Rashevsky's group, which in June 1953 had consisted of seven full time members and one part time member, had been reduced to three full time members, a matter, they argued, of public record. By April 1956, concrete evidence of these reductions was presented to Wolfle. Later that month, the editor of *Science* wrote to McCulloch to say that Wolfle had relented and that the original letter would be published. *Science* finally published the letter in its issue of April 27, 1956. It expressed dismay at the recent restrictions in Rashevsky's funding, pointing out that "the

[162] McCulloch to von Bonin, February 10, 1955, Warren S. McCulloch Papers, APS.
[163] McCulloch to von Bonin, February 10, 1955, Warren S. McCulloch Papers, APS.
[164] Dael Wolfle to McCulloch, December 13, 1955, Warren S. McCulloch Papers, APS.
[165] Von Bonin to Wolfle, January 12, 1956, Warren S. McCulloch Papers, APS.

work of this department, the only one of its kind in the world, is of great interest and importance in our diverse fields of research, that is, biology, clinical medicine, mathematics, psychology, philosophy, and sociology. We feel that it would be a loss if that work were seriously reduced."[166]

The letter was signed by eight scholars; notably, McCulloch, Rudolf Carnap, von Bonin, Menger, and the Nobel Prize-winning biochemist Albert Szent-Gyorgyi. McCulloch and the other signers of the letter clearly believed that the reduction in Rashevsky's budget happened for scientific reasons. It was written in support of academic freedom, however, at the root of their concern, it seems, was the sentiment that Rashevsky's work was valuable and that he had blazed important trails. The rise of the cybernetics movement in the middle part of the 20th century brought about increasingly theoretical, mathematical, and idealized accounts of biological phenomena.[167] McCulloch, in particular, was a strong advocate of this modeling approach, and while his actual method differed somewhat from Rashevsky's, he strongly believed the power and relevance of using theory in neurobiology.[168]

Rashevsky's committee was eventually rebuilt to a larger group, however, on July 21, 1964, Rashevsky tendered his resignation.[169] A letter from Rashevsky to H. Stanley Bennett, the Dean of the Division of Biological Sciences at Chicago, dated August 7, 1964, indicates that Rashevsky's resignation was over his proposed successor, who was to take over after Rashevsky's scheduled retirement date, July 1965. Rashevsky expressed anger at the Dean's refusal to hire his own chosen successor, and felt it wrong that the decision of who was to be the new successor was made entirely over his head and without any consultation with the Committee on Mathematical Biology.[170] It seems his resignation was a matter of principle for Rashevsky – he repeatedly stated that it was wrong to keep him and his Committee completely out of the

[166] McCulloch et al., 1956.

[167] See, e.g. Kay, 2000.

[168] A letter McCulloch later wrote to Rashevsky indicates his position: "You have put the scientific world in your debt by giving it a place to publish the mathematics necessary for biology…You have, with simple nobility, defended new ideas on their young hind legs…The solution of any problem is always less important than the proper challenge. We, who still remember these things, salute you as their beginner." (McCulloch to Rashevsky, December 16, 1964, Warren S. McCulloch Papers, APS).

[169] For months after this, according to Rashevsky's account of things in a farewell address, there was a "flurry of letters of protest" (Address by N. Rashevsky to the Staff and Students of the Committee on Mathematical Biology, December 15, 1964, Warren S. McCulloch Papers, APS).

[170] Richard Lewontin, who was Associate Dean of Biological Sciences at the time, appointed Jack Cowan as Rashevsky's successor.

picture when it came to deciding about a successor and the fate of mathematical biology at Chicago. In late October 1964, President George Beadle wrote to Rashevsky requesting that he withdraw his resignation. Rashevsky wouldn't yield, and in December 1964, he officially resigned as professor and chairman of the Committee on Mathematical Biology at the University of Chicago, 7 months before he was scheduled to retire.[171] He became Professor of Mathematical Biology at the Mental Health Research Institute of the University of Michigan at Ann Arbor, and retired in 1970. Judging from several tributes and obituaries for Rashevsky that appeared upon his retirement in 1970 and his death in 1972, his supporters believed him to be a pioneer, despite having his share of detractors.[172] His advocates described him as a man of integrity and humility, and in possession of high principles and ideals. These high principles, it was argued, were applied "to the defense of his acquaintances whose cause he was first to take up when he sensed the existence of an injustice or adversity in their own professional affairs. In this sense he was the most loyal of friends and the toughest of opponents when he sensed an injustice..."[173] These strong principles, it seems, prevented Rashevsky from budging from his vision of mathematical biophysics and the particular role he saw for mathematics and theory in biology.

Conclusions

The resistance of experimental biologists to mathematical biology during Rashevsky's time is captured by biophysicist Harold Morowitz's 1965 remarks about the fate of Rashevsky's approach: "The biologist who has devoted great effort in examining some aspect of nature in all its richness and fullness often feels uncomfortable with the idealized system which fails to embody the details to which he has devoted so much effort."[174] In the end, Rashevsky had little contact with empirical biological research, and this lack of first-hand knowledge brought about some skepticism and hostility from biologists and physiologists trained in the experimental tradition. As J. Arthur Harris, a botanist and biometrician at the University of Minnesota, observed, "Mathematics

[171] Herbert Landahl, who had been professor and secretary of the Committee on Mathematical Biology since 1948, became the acting chair of the committee until 1968, when he moved to the University of California at San Francisco.

[172] See, e.g. Bartholomay, Karremann, and Landahl, 1972.

[173] Bartholomay, Karreman, and Landahl, 1972.

[174] Morowitz, 1965, p. 31.

might quite properly be an end in itself, but in biology it is strictly a means to an end…Mathematicians have often asserted the need for mathematics in the biological sciences, but the claim has too often made in an *ex cathedra* manner by those who, while perhaps being qualified to speak of things mathematical, have been relatively little fitted to discuss the needs of biology."[175]

It is not clear whether the character of Rashevsky's work might have changed drastically had he devoted more time to familiarizing himself with empirical research in biology. As it was, Rashevsky repeatedly faced criticisms from experimental biologists, physiologists, and others that his theories lacked a proper connection to empirical work, and that as a result, it was difficult to see how his theories might be relevant for their own work or even how Rashevsky's work might advance biological knowledge. Although mathematics was not entirely foreign to physiologists, Rashevsky was using mathematics in a distinct way. He was not arranging experimental data in quantitative terms, but rather representing the problem at hand as a set of variables, drawing connections between phenomena using mathematical functions, and then studying the relations between the variables. To do so, he needed to make idealizations and abstractions, and rather than introduce idealizations informed by empirical research, Rashevsky often made apparently "*ad hoc*" simplifying assumptions.

From the outset, Rashevsky defended his approach using rhetoric that extolled the virtues of using the "physico-mathematical" method in biology. At the time, one might have done so to bring legitimacy to a discipline that was still struggling to establish itself as a field on par with physics. It is more likely that Rashevsky's rhetoric stemmed from his arguably extreme belief in the power of mathematical, formal, deductive reasoning in science. As a result, the relationship Rashevsky perceived between theory and experiment was distinct from the role that physiologists saw for theory. The experimental ideal was highly valued in physiology: results and conclusions must be testable, verifiable, and refutable. For most physiologists, mathematics, theories, and models could be used for the explanation of observed phenomena or for prediction – that is, to inform future research. Rashevsky, in contrast, had the goals of simplifying complex processes and developing general, fundamental principles. Rashevsky presented his theories for their own sake, as possibilities. As one contemporary observed, while the mathematician – or mathematical physicist – may be interested in consistency, validity, and mathematical beauty, the biologist wants to be convinced

[175] Harris, 1928, p. 144.

of its usefulness to the solution of biological problems.[176] For biologists, mathematics was seen as a tool, and a model or theory needed to somehow relate to "real" observable phenomena or have some utilitarian or predictive use. This, in fact, was one of the aspects of theoretical physics that, despite all of his rhetoric about using "the method" of theoretical physics, Rashevsky appeared to disregard. Although he defended his approach by pointing to the success of this method in the physical sciences, he seemed to ignore a key element of mathematical theories in physics: predictive power.

Today, a spectrum of positions exists regarding the relationship and relevance of theoretical and mathematical biology for experimental work, however, theoretical and mathematical biology are thriving. Academic programs are becoming more ubiquitous – over 30 centers devoted to mathematical biology exist in the US, the UK, Australia, and Canada. Rashevsky's *Bulletin of Mathematical Biophysics* now exists as the *Bulletin of Mathematical Biology*, and the Society for Mathematical Biology was founded in Rashevsky's memory. There are several journals today that are totally devoted to mathematical and theoretical treatments of biological phenomena in addition to the *Bulletin*, such as the *Journal for Theoretical Biology*, the *Journal of Mathematical Biology*, *Acta Biotheoretica*, *Rivista di Biologia*, *Mathematical Biosciences*, and *Theoretical Population Biology*. Although there still exists a "cultural divide" between mathematicians and biologists, and arguably between mathematical biologists and biologists, efforts are being made to forge stronger links between these fields.[177] Much of the current research in mathematical biology is used for more practical reasons, for e.g. community ecology of disease, population dynamics, ecosystems, genomics, predicting the effects of global climate change, and bioinformatics. This stress on the more pragmatic applications of research in the life sciences arguably began following the Second World War. The character of postwar life sciences proved to have two effects on Rashevsky and his work. The rise of molecular biology made it difficult for him to find a niche for "mathematical biophysics," which in this context appeared esoteric. At the same time, the cybernetics

[176] Harris, 1928, p. 141.

[177] For example, two recent NSF-sponsored workshops on "Quantitative Environmental and Integrative Biology" focused on the ways in which mathematics could and should be used biology. A more recent joint NSF-NIH workshop, on "Accelerating Mathematical-Biological Linkages," dealt with the problems of conservation ecology, cell structure and function, computational biology, and bioinformatics (see Hastings and Palmer, 2003).

movement and the use of mathematical methods and theory by a specific group of researchers, mainly in neurology, neurobiology, and the emerging field of artificial intelligence most likely motivated Weaver's eventual opinion that the Committee for Mathematical Biology should exist even if only for training scientists in the field of mathematical biology. Additionally, those who eventually supported Rashevsky did so, it appears, because to them he had created a space for those interested in bringing together mathematics and biology, that he blazed important trails, that he had given a voice to those interested in using mathematics and logic in the study of the nervous system. So in the end, for Rashevsky's sympathizers, it was not about his own body of work, or about a specific theory he introduced that was influential, but what he had created – a center for training and a higher profile for mathematical work in the life sciences. For his detractors, both in his own time and today, it was his lack of contact with biology, his idealistic belief in theory for its own sake, and the eclecticism of his later work. Rashevsky's passion and high ideals, praised by his supporters, ultimately doomed him as an outsider in the life sciences.

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