Available online at www.sciencedirect.com

BioSystems 88 (2007) 178–184

www.elsevier.com/locate/biosystems

The mathematical biophysics of Nicolas Rashevsky

Paul Cull

Computer Science Department, Oregon State University, Corvallis, OR 97331, USA

Abstract

N. Rashevsky (1899–1972) was one of the pioneers in the application of mathematics to biology. With the slogan:

mathematical biophysics : biology :: mathematical physics : physics,

he proposed the creation of a quantitative theoretical biology. Here, we will give a brief biography, and consider Rashevsky's contributions to mathematical biology including neural nets and relational biology. We conclude that Rashevsky was an important figure in the introduction of quantitative models and methods into biology.

Keywords: Rashevsky; Mathematical biophysics; Mathematical biology; History; Neural nets; Relational biology

1. Introduction

Who was Nicolas Rashevsky? When I recently asked a few people if they knew Rashevsky, I got some funny replies:

> "Oh, you mean Nikolai Lobachevsky (1792–1856), the Russian who invented non-Euclidean geometry and the one Tom Lehrer wrote the song about?"

> "Do you mean Samuel Reshevsky (1911–1992), the chess prodigy and grandmaster?"

The answer is, of course, "No, I mean Nicolas Rashevsky who created mathematical biophysics" (see Fig. 1). Fifty years ago, Rashevsky was quite well known, but he is less known today. I did a quick Google search to see current interest in Rashevsky. I found a number of references to his work on neural nets and on relational biology. In this short note, I will briefly outline Rashevsky's life and work, and hopefully explain why he is still an important but controversial figure.

E-mail address: PC@CS.ORST.EDU.

2. Brief biography

Nicolas Rashevsky was born in Chernigov, Russia on September 1899. He studied at the University of Kiev, completing his graduate work in physics in 1919. He taught physics at the University of Kiev and at Robert College in Constantinople. In 1921, he became Professor of Physics at the Russian University at Prague. In 1924, he came to the United States and joined the Westinghouse Research Laboratories. In 1934, he came to the University of Chicago as a Rockfeller Fellow in Mathematical Biophysics. From 1935 to 1940, he worked in the departments of Psychology and Physiology. In 1939, he started and was the first editor of the Bulletin of Mathematical Biophysics. In 1940, he founded the Section of Mathematical Biophysics within the Department of Physiology. In 1947, he founded and became Professor and Chairman of the Committee on Mathematical Biology. He continued in this position through 1964. In 1965, he became Professor of Mathematical Biology in the Mental Health Research Institute at the University of Michigan in Ann Arbor. He died in Holland, Michigan in 1972.

0303-2647/$ – see front matter © 2006 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.biosystems.2006.11.003

Fig. 1. Rashevsky and the participants in the course on Physicomathematical Aspects of Biology held at Varenna, Italy in 1960. Rashevsky is, of course, the bearded gentleman in the center (Rashevsky(ed.), 1962).

During his career, Rashevsky published a large number of books: Rashevsky (1938, 1940, 1947/1949, 1948, 1951/1959, 1960, 1961, 1964b, 1968, 1972). He also edited a few volumes: Rashevsky (ed.) (1962), Richardson (1960).

This brief biography is based on the biographical sketch in a special issue of the Bulletin of Mathematical Biophysics (BMB, 1965).

3. Mathematical biophysics

In the 1920's, Rashevsky conceived of the idea of a systematic development of a mathematical biology that would cover the whole field of biology. Such a mathematical biology would stand in the same relation to experimental biology as mathematical physics stands to experimental physics. To express this comparison and to acknowledge his use of physics based models, Rashevsky called his new field Mathematical Biophysics. There were two hallmarks of his approach:

the theory had to be quantitative, and
the theorist had to be in contact with experiments.

He could thus distinguish his new field from previous attempts at a purely verbal non-quantitative theoretical biology. Further, by keeping in contact with experiments and making quantitative predictions, he could demonstrate that his efforts were relevant to real biologists.

Some idea of Rashevsky's techniques can be gleaned from his treatment of diffusion (Rashevsky, 1960, vol. 1, p. 7). He starts by acknowledging that a full treatment of diffusion in a biological system is complicated both by the mathematics and by the lack of sufficient biological data to specify all of the parameters in an exact mathematical treatment. He proceeds by suggesting that some quantities can be assummed to be constant. For the nonconstant quantities, he approximates them with a linear function or when necessary a linear differential equation. Continuing in this manner, he derives a set of algebraic equations, which will roughly describe a diffusing process over time. While in detail these formulas may be inaccurate, they indicate trends correctly. This sort of analysis is standard practice in physics and applied mathematics. That is, models are simplified and approximations are used to predict trends rather than exact values.

The usefulness of Rashevsky's methods and their relevance to experiments was demonstrated in the second edition of Mathematical Biophysics (Rashevsky, 1948). In particular, such physiological topics as cell respiration, and cell dynamics, and such psychological topics as descrimination of intensities, reaction times, and learning, were all covered. By the third edition (Rashevsky, 1960) even more topics were covered. These included neural nets and relational biology, which we'll discuss next. But, here, we'll just mention that Rashevsky maintained an interest in the social as well as the biological sciences, and wrote or edited several books in this area: Rashevsky (1947/1949, 1951/1959, 1968), Richardson (1960).

4. Neural models

Rashevsky invented one of the first models of the neuron and started the idea of artificial neural networks. The basic idea was to use a pair of linear differential equations and a nonlinear threshold operator: (Rashevsky, 1933; Cull, 1967)

$$\text{Input}{:=}I(t)$$
$$\frac{\mathrm{d}e}{\mathrm{d}t} = AI(t) - ae$$
$$\frac{\mathrm{d}j}{\mathrm{d}t} = BI(t) - bj$$
$$\text{Output}{:=}H(e - j - \theta)$$

θ is the threshold and $H(x)$ is the Heaviside operator. Here e and j could represent excitation and inhibition or the amount or concentration of two substances within a neuron. After the work of Hodgkin and Huxley in the 1950's, it might be possible to identify these as sodium and potassium concentrations. The Heaviside operator, $H(x)$ takes positive values to 1, and non-positive values to 0. This gives an easy way to model the all-or-none firing of a neuron.

Rashevsky showed that this simple model was able to model many of the known experimental results for the behavior of single neurons. He also made the point that networks of these model neurons could be connected to give quite complicated behavior and even serve as a model for a brain.

Nowadays when people speak of neural nets, they usually mean the discrete time, Boolean or almost Boolean models. While such models were not invented by Rashevsky, they were invented at Chicago. Warren McCulloch, a professor at the University of Illinois at Chicago, and Walter Pitts, a student in Mathematical Biology at the University of Chicago, together created the idea of a logic based neural net that could serve as a model for a brain. Their work was published in the Bulletin of Mathematical Biophysics (McCulloch and Pitts, 1943). In the hands of John von Neumann, the McCulloch–Pitts model became the basis for the logical design of digital computers.

Which model is better, the continuous model or the discrete model? For some purposes, one model is better, but for other purposes, the other model is better. Rashevsky and Landahl were quick to notice, that in physics, one often averaged over a large set of discrete events to obtain a continuous model which represented the large scale behavior of a system, and so they posited that the continuous neuron model might be suitable for modeling whole masses of neurons even if each individual neuron obeyed a discrete model. In the hands of Householder and Landahl (1945), this observation led to the idea of modeling psychological phenomena by neural nets with a small number of continuous model neurons. In particular, they found that the cross-couple connection (see Fig. 2) was extremely useful. For such problems as reaction time, enhancement effects, flicker phenomena, apparent motion, discrimination and recognition, they were able to fit these models to experimental data and to use their models to predict phenomena that could be measured and verified.

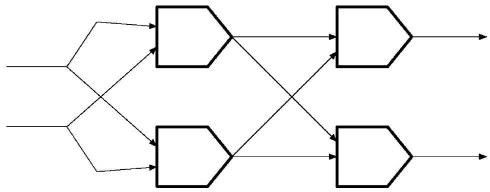

Fig. 2. This cross-couple connection of four neurons is capable of modeling a large number of phenomena.

5. Relational biology

In the 1950's, Rashevsky took up a new research direction. Perhaps he was responding to criticism that his mathematical biophysics was old-hat in the sense that everyone (or at least many biologists) were now using quantitative methods and physics based models for their experiments. In any case, Rashevsky turned from methods tied closely to experiments to a search for *general principles* in biology.

His first attempt at a general principle is the principle of Optimal Design:

> For a set of prescribed biological functions an organism has the optimal possible design with respect to economy of material used, and energy expenditure, needed for the performance of the prescribed function. [Rashevsky, 1960, vol. 2, p. 292].

He was able to show that various properties of the vascular system obeyed optimality laws. For example, the optimal angle of branching for veins could be calculated and actual veins seem to show this optimal branching angle. Robert Rosen took up this work and wrote a whole book devoted to a study of biological optimality (Rosen, 1967).

At first glance, this optimality principle seems to fly in the face of the received opinion that all biological optimization is done by natural selection and evolution by natural selection is strictly *ad hoc*. For instance, as Gould has pointed out, the panda needs a thumb for stripping bamboo, but it can't easily grow a thumb, so instead a wrist bone is modified to serve in place of the impossible thumb (Gould, 1981). But, Rashevsky's principle uses the word "possible" to indicate that the predicted optimization is *local* rather than *global*. The panda's thumb is an example of this local optimization. A structure that is present is optimally modified for a function, but a completely new structure is unlikely to appear.

In his search for general biological principles, Rashevsky also annunciated his Generalized Postulate of Relation Forces:

> The development of an organismic set proceeds in such a manner as to maximize the total number of relations and the number of different kinds of relations during the total course of development. [Rashevsky, 1972, p. 93].

What does this mean? I'm not sure. From statements like this, Rashevsky attempted to draw some conclusions about biology. For example, he tried to show why there should be only two sexes. This part of his work has remained controversial. Is there any mathematics here? Is there any biology? Robert Rosen (Rosen, 1991, 1985) has gone on from Rashevsky's start and produced a theory of metabolizing-reproducing systems using category theory from mathematics. This work has also remained controversial.

6. Administration

Two of Rashevsky's major accomplishments were the establishment of the first journal devoted to mathematical biology, and the first Ph.D. granting program in mathematical biology.

6.1. The Committee on Mathematical Biology

Establishing a new academic program in a recognized area is difficult, but it is much more difficult to build the first program in a new area. By its very nature, mathematical biology is an interdisciplinary field. Successful practice in this area requires the collaboration of researchers skilled in the various biological fields from anatomy to zoology, and researchers knowledgeable in both physical and chemical modeling, and researchers adept in mathematical techniques from algebra to Z-transforms.

The University of Chicago is unique in many ways. According to the joke: it is a Baptist institution in which atheistic professors teach Catholic philosophy to Jewish students. More seriously, Chicago is unique in having an administrative mechanism for promoting interdisciplinary studies. This structure is the Committee. A Committee is usually formed from professors who have appointments in other departments, but may also have faculty with appointments only in the Committee. A Committee is usually much smaller than a Department. Some Committees may exist only to offer interdisciplinary courses, but some Committees are also degree granting organizations. A student's program will generally consist of some Committee courses and a selection from the regular course offerings in the cooperating departments. (For example, in my time at the University of Chicago, there was a Committee on Information Science (the forerunner of Computer Science), and the members of this Committee had appointments in the Physics Department, the Mathematics Department, The Library School, the School of Business, and the Committee on Mathematical Biology. Chicago's world famous Committee on Social Thought has members from a wide variety of departments in the humanities, the social sciences, and even law and religion.) This special structure, allowed Rashevsky to form the Committee on Mathematical Biology, the first Ph.D. granting program in mathematical biology. From 1949 to 1963, the Committee awarded 14 Ph.D. degrees (The first Ph.D. in mathematical biology was awarded to Herb Landahl in 1941 before the Committee was formed (Rashevsky, 1963).

6.2. The Bulletin of Mathematical Biology

The most important theme of the Bulletin of Mathematical Biophysics was inclusiveness. The bulletin started out as a "house journal" in which all of the papers were produced by people at Chicago working in mathematical biophysics, but Rashevsky opened the journal to other workers. He encouraged those doing various kinds of biological research to write and formalize mathematical models of their experiments and submit reports on these models to the Bulletin. Since the Bulletin is a refereed journal, it would be easy to imagine that most of these "first step" papers would be rejected. But instead, Rashevsky encouraged. He and Landahl and others would spend many hours going over a manuscript, correcting and extending the mathematics and the models. Then they would send the manuscript with their notes back to authors with an encouragement to re-submit the paper after it had been re-written in line with the comments. Encouragement was not the only service they provided. In those days publication quality graphics were not just a computer away. Herb Landahl with his pen and India ink carefully prepared the many graphs and drawings that eventually appeared in the Bulletin.

The Bulletin has undergone a number of changes over the years. The title was changed to "The Bulletin of Mathematical Biology" around 1970. Rashevsky was the original editor, and was succeeded by Landahl. There have been a number of editors since then. The present editor is Philip Maini of Oxford University. The Bulletin was originally published by the University of Chicago Press. It has gone through a number of publishers and is now being published by Springer.

6.3. The Society for Mathematical Biology

As well as having a journal, a recognized science usually has a professional organization. Although Rashevsky did establish a degree granting group and a journal, he did not establish a professional society. He took some steps in the direction of a society when he created Mathematical Biology, Inc. It was left to Herb Landahl with his many contacts and administrative skill to establish the Society for Mathematical Biology in 1973. This society is still quite active. They hold a yearly meeting usually in association with either a biological society or a mathematical society. The current president is Mark Chaplain of the University of Dundee.

7. Three battles

Rashevsky's career was not one of "peaches and cream" with always upward progress (Rashevsky, 1963, 1964a). He was involved in several important battles and he was not always the victor.

Being a tenured Professor and heading one's own group at the University of Chicago would seem to be a safe position. But, the *RED SCARE* of the early 1950's changed that. At that period, which was called the Cold War, many people were convinced that the United States was going to be overthrown by Communists. It was widely claimed that secret Communists had weaseled their way into positions of power in the government and national institutions, and that they were only awaiting the word from Moscow to start the revolution. Because of their positions, these secret Communists would be able to take over our country without firing a shot. For some reason, the University of Chicago had a reputation as having a very leftist faculty, and the school was a target of a Congressional investigation. To forestall this investigation and to demonstrate that the university was 100% American, the University President required all faculty members to sign a loyalty oath and swear that they were not and had never been Communists. Although he was Russian, Rashevsky was known to be unsympathetic to the communist cause. He had served in the Russian Navy under the Czar and he had taken no part in the Red Revolution. But, one of the faculty members in Mathematical Biology had been a communist. As I understand it, he and his wife were active in various communist organizations in the 1930's (before WW II). Obviously, it was going to be difficult for him to swear that he had never been a Communist. To protect this person and to uphold American ideals of liberty, Rashevsky and the other members of the Committee on Mathematical Biology refused to sign the oath. They seemed to hope that the rest of the faculty would also resist the oath. Unfortunately many signed, and the University President announced that he would fire all the suspected Communists. In one of the rare instances that tenure worked, Rashevsky and Landahl, the two tenured members of the Committee, were not fired, but everyone else was. The Committee was reduced to a single office (without a telephone) that had to be shared by Rashevsky and Landahl. While this was a major set-back, the *Red Scare* died out and the Committee was eventually able to grow back to its old size and even to re-hire some of the fired faculty.

Perhaps the biggest battle of Rashevsky's career was his campaign to establish Mathematical Biology as a recognized science. In the 1950's, the United States built up the National Institutes of Health (NIH) to be the premiere health sciences research facility in the world. As well as the intra-mural research at the institutes, the NIH was also to fund through grants the "best" research in the biological sciences. These grants were handled in an interesting way. For each research area, a Study Group was established and these groups decided on grant funding in their areas. So when one applied for a grant, the proposal would be sent to several reviewers, and their reports would be sent to the Study Group which then ranked the proposals on scientific merit. Some of these proposals would then be funded depending on the budget available. As Rashevsky immediately noticed, there was no study group for mathematical biology. Any mathematical biology grant proposal would have to be sent to a Study Group in an area of application. Of course, there were almost no mathematically trained biologists at that time, and so there was no representation of mathematical biology on the Study Groups. As may be expected, the Study Groups preferred to fund purely experimental research because they were not familiar with the uses of mathematics. Rashevsky campaigned both within and outside NIH for the formation of a Mathematical Biology Study Group. In this matter, he was unsuccessful, but he did eventually convince people that more mathematical training for biologists was necessary. This led to the NIH Training Grant that supported graduate and post-graduate students in Mathematical Biology at the University of Chicago for about 15 years.

Training in biomathematics was the subject of a conference held in North Carolina in 1962. Rashevsky gave a paper on the development of mathematical biology at this conference (Lucas(ed.), 1962).

Rashevsky's last major battle was over the chairmanship of the Committee. The University of Chicago had a strict out-at-65 policy. Although one could continue as a professor, one had to leave all administrative posts, like chairman, at age 65. There were more restrictions as one grew older. For example, after age 70, one could not have new graduate students. These restrictions usually also brought with them a loss of lab and office space. For this reason, many senior professors, including, for example, the well-known geneticist Sewell Wright, left Chicago in their late 60's. As Rashevsky neared 65, he assumed that Landahl would replace him as chairman. But, when he talked to the dean, he was informed that time was ripe for a change, and so an outsider would be appointed as the new chairman. With various tactics, Rashevsky tried to fight this decision, but to no avail. Finally, he resigned from Chicago and took up a position at the University of Michigan.

So in Rashevsky's battles, he often lost but was often vindicated later. No one would seriously propose a loyalty oath these days. Mathematical biology is now a recognized field. It even has its own AMS code number. Whether a new chairman was the right thing for the Committee is open to question, because the program disappeared under the weight of budget cuts.

8. Conclusion

Mathematical biophysics has been criticized as being neither good mathematics nor good biology nor good physics. I hope that I have shown that this should be regarded as a quip, meaning only that mathematical biophysics (and mathematical biology) is a interdisciplinary field. Was new biology created? Yes, the introduction of quantitative methods and the creation of new models certainly add up to new biology.

Was new physics created? No, certainly not in the sense that Newton, or Einstein, or the quantum theorists created new physics. But, the adaptation of physical models to biological (and psychological) phenomena created new applications for physics and encouraged a new way of thinking about biology.

Was new mathematics created? At least to some extent, the answer is: YES. While Rashevsky in his early work used mathematics and models that had been extensively used in physical sciences, Rashevsky's later work on relational biology may be seen as considering new applications of the theory of sets and relations and at least the start on some new mathematics. Rashevsky's collaborators did create new mathematics. McCulloch and Pitts (McCulloch and Pitts, 1943) invented logic based neural nets, which became the mathematics underlying digital computers. Rapoport and Chammah (1965) introduced nonzero sum games and demonstrated the applications in the social sciences. Rosen (1991) took the new mathematics of category theory and showed how it could be used to create a general theory of metabolizing-reproducing systems.

In summary, Rashevsky was successful in incorporating quantitative models and methods in biology (Rashevsky, 1963). This work has become so “main stream” that Rashevsky's work is undervalued because many people think that quantitative methods were always used. Rashevsky's attempt at general theories for biology was less successful. His optimality principle is often misunderstood to be a claim for perfection in biological entities. His work on relational biology is derided as being meaningless or not leading to any testable consequences. So, those who know some of his work, consider Rashevsky to be a controversial figure, while those who follow in the quantitative tradition have forgotten Rashevsky's importance as a trailblazer.

I will end with one note of caution. Many of the things I have said here are based on personal recollection or stories I have heard from others. Stories and facts may or may not agree.

References

BMB, 1965. A biographical sketch of Nicolas Rashevsky. Bull. Math. Biophys. 27 (3/4), Special issue.

Cull, P., 1967. General two factor models. Bull. Math. Biophys. 29, 405.

Gould, S.J., 1981. The Panda's Thumb. W.W. Norton, New York.

Householder, A.S., Landahl, H.D., 1945. Mathematical Biophysics of the Central Nervous System. Principia Press, Bloomington, IN.

Lucas, H.L. (Ed.), 1962. The Cullowhee Conference on Training in Biomathematics. The Institute of Statistics of North Carolina State University, Raleigh, North Carolina.

McCulloch, W.S., Pitts, W.H., 1943. A logical calculus of the ideas immanent in nervous activity. Bull. Math. Biophys. 5, 115–133.

Rapoport, A., Chammah, A., 1965. Prisoner's Dilemma. University of Michigan Press, Ann Arbor, MI.

Rashevsky, N., 1933. Outline of a physico-mathematical theory of excitation and inhibition. Protoplasma 20, 42.

Rashevsky, N., 1938. Mathematical Biophysics: Physico-Mathematical Foundations of Biology. University of Chicago Press, Chicago.

Rashevsky, N., 1940. Advances and Applications of Mathematical Biology. University of Chicago Press, Chicago.

Rashevsky, N., 1947/1949. Mathematical Theory of Human Relations: An Approach to Mathematical Biology of Social Phenomena (second ed., 1949). Principia Press, Bloomington, IN.

Rashevsky, N., 1948. Mathematical Biophysics: Physico-Mathematical Foundations of Biology (second ed.). University of Chicago Press, Chicago.

Rashevsky, N., 1951/1959. Mathematical Biology of Social Behavior, (revised ed., 1959). University of Chicago Press, Chicago.

Rashevsky, N., 1960. Mathematical Biophysics: Physico-Mathematical Foundations of Biology, vol. 1–2. Dover, New York.

Rashevsky, N., 1961. Mathematical Principles in Biology and Their Application. Charles C. Thomas, Springfield, IL.

Rashevsky, N. (Ed.), 1962. Physicomathematical Aspects of Biology: Proceedings of the International School of Physics "Enrico Fermi" XVI Course. Academic Press, New York.

Rashevsky, N., 1963. The History of The Committee on Mathematical Biology of the University of Chicago. The Committee on Mathematical Biology, Chicago.

Rashevsky, N., 1964a. Address by N. Rashevsky. The Committee on Mathematical Biology, Chicago.

Rashevsky, N., 1964b. Some Medical Aspects of Mathematical Biology. Charles C. Thomas, Springfield, IL.

Rashevsky, N., 1968. Looking at History Through Mathematics. MIT Press, Cambridge, MA.

Rashevsky, N., 1972. Organismic Sets: Some Reflections on the Nature of Life and Society. Mathematical Biology, Inc., Holland, Michigan.

Richardson, L.F., 1960. In: Rashevsky, N., Trucco, E. (Eds.), Arms and Insecurity: A Mathematical Study of the Causes and Origins of War. The Boxwood Press and Quandrangle Books, Chicago.

Rosen, R., 1967. Optimality Principles in Biology. Butterworth Publishers, Stoneham, MA.

Rosen, R., 1985. Anticipatory Systems. Pergamon Press, New York.

Rosen, R., 1991. Life Itself. Columbia University Press, New York.