Preprint. Final version to appear in *Oren Harman and Michael R. Dietrich (eds.), Biology Outside the Box: Boundary Crossers and Innovation in Biology.*

.

Theoreticians as Professional Outsiders: The Modeling Strategies of John von Neumann and Norbert Wiener

Ehud Lamm

Introduction

Somewhat ironically for a discipline known for its austerity, the folklore of mathematics has more than its fair share of anecdotes and myths about heroes, mavericks, and eccentrics. Typically, one is introduced to these characters in the course of becoming a mathematician, via anecdotes and tall tales that are, so to speak, passed from father to son. Two 20th century mathematicians that are the subject of often repeated anecdotes are John von Neumann and Norbert Wiener. Both are well known as significant mathematicians, and both worked at influential centers of learning (von Neumann eventually residing at the Institute for Advanced Study at Princeton, Wiener at MIT). However, the two are typically portrayed in very different terms. Anecdotes portray von Neumann as a "mathematician's mathematician" – the one who is able to outsmart other mathematicians. Wiener is typically portrayed as the absent minded professor. The role von Neumann played in the history of computing is well known, as are his contributions to systems biology. Wiener's contribution is often downplayed, and the cybernetic research program he is best known for is portrayed as being ultimately a failure.

Both von Neumann and Wiener were outsiders to biology. Both were inspired by biology and both proposed models and generalizations that proved inspirational for biologists. Around the same time in the 1940s von Neumann developed the notion of *self reproducing automata* and Wiener suggested an explication of teleology using the notion of *negative feedback*. These efforts were similar in spirit. Both von Neumann and Wiener used mathematical ideas to attack foundational issues in biology, and the concepts they articulated had lasting effect. But there were significant differences as well. Von Neumann presented a how-possibly model, which sparked interest by mathematicians and computer scientists, while Wiener collaborated more directly with biologists, and his proposal influenced the philosophy of biology. The two cases illustrate different strategies by which mathematicians, the "professional outsiders" of science, can choose to guide their engagement with biological questions and with the biological community, and illustrate different kinds of generalizations that mathematization can contribute to biology. The different strategies employed by von Neumann and Wiener and the types of models they constructed may have affected the fate of von Neumann's and Wiener's ideas – as well as the reputation, in biology, of von Neumann and Wiener themselves.

Our two distinguished suitors, overbearing and brash as mathematicians are wont to be when discussing mathematical ideas, were pursuing in this case a rather reluctant, bashful, bride to be. Nine years before Wiener and his co-authors John Bigelow and Arturu Rosenblueth published their paper about teleology, E.B Wilson articulated the reserved attitude of biologists towards uninvited theoreticians.[1] Wilson's remarks at the Cold Spring Harbor Symposia on Quantitative Biology in 1934 were ostensibly about the "Mathematics of Growth" but it is impossible to fail to notice their tone and true scope. Wilson suggested orienting the discussion around five axioms or

[1] For a discussion of this paper and its significance see Evelyn Fox Keller, *Making Sense of Life: Explaining Biological Development with Models, Metaphors, and Machines* (Harvard University Press, 2003), 84-87.

“platitudes” as he called them. The first two are probably enough to get his point across. Axiom 1 states that “science need not be mathematical,” and if that’s not bad enough, axiom 2 solidifies the reserved attitude towards mathematization by stating that “simply because a subject is mathematical it need not therefore be scientific.” Our two protagonists, renowned and accomplished mathematicians however they clearly were, had a lot of courting to do. Still, Wilson seemed to leave an opening for the two prospective suitors. Despite his otherwise disparaging remarks, he concluded by noting that “One must not fail to mention, as contrasted with empirical curve plotting analyses, the attempts at fundamental rational analysis.” Mathematics, it turns out, is not all of a piece. Fundamental rational analysis was precisely what Wiener and von Neumann purported to do, but entering the world of biology, as we shall see, each suitor would adopt his unique approach to courtship.

Behavior, Purpose and Teleology

Wiener (1894-1964) and von Neumann (1903-1957) are probably the most well known American mathematicians of the mid-twentieth century. In the mid 1940s to mid 1950s, they were driving forces behind the Macy Conferences, one of the most celebrated multi-disciplinary series in recent scientific history. The first meeting was held in 1946. The annual meetings, entitled “Conference on Circular, Causal and Feedback Mechanisms in Biological and Social Systems,” were by-invitation-only events, and were chaired by the neurophysiologist Warren McCulloch. Among the participants were William Ross Ashby, Gregory Bateson, Margaret Mead, Paul Lazarsfeld, and G.E. Hutchinson. Partly as a result of their shared interest in computing machines, both Wiener and von Neumann pursued related questions about the organization and functioning of the brain and the analysis of behavior and social behavior. Their perspective was that of the then cutting-edge science of computing automata and information theory. Wiener's work on target-tracking machines for the Air Force led him to think about feedback mechanisms, specifically negative feedback. This became a central organizing notion in his conception of *cybernetics*. Experience with the behavior of actual target-tracking mechanisms led to a conjecture about intentionality and purpose-driven behavior, which Wiener then tried to generalize by arguing that negative-feedback is the defining characteristic of purposeful behavior. Von Neumann, in turn, grew increasingly frustrated with attempts to understand the brain. Trying to understand the brain using the techniques of neurology was like trying to understand the ENIAC computer "with no instrument… smaller than about 2 feet across its critical organs, with no methods of intervention more delicate than playing with a fire hose…".[2] He argued that this hopeless task be replaced by the attempt to arrive at a complete and full understanding of less-than-cellular organisms, namely viruses and bacteriophages. Their fundamental property is that they self-reproduce, and von Neumann devoted a lot of energy to a formal analysis of the question of self-reproduction. Von Neumann and Weiner worked in the same milieu, had similar interests, and even corresponded. And yet they arrived at two very different questions – the nature of purpose, and the necessary conditions for self-reproduction – and would approach the two questions in remarkably different ways.

Both Wiener and von Neumann were early starters, and began their intellectual journey being home-schooled. Wiener started his academic studies at the tender age

[2] Letter to Wiener, Nov. 29, 1946. McCulloch Papers, American Philosophical Society.

of eleven, and referred to himself in later life as an ex-prodigy. He studied philosophy, the field in which he obtained his PhD, and biology, where he preferred theorizing to anatomical work, before becoming a mathematician. Around the time Wilson expressed the skeptical view about the role of mathematics in biology, Wiener began attending an inter-disciplinary seminar group at Harvard Medical School and developed an interest in physiology. What better background for the kind of work we are discussing? Von Neumann was and remained a true outsider – a mathematician, first and last, who contributed to many scientific fields from quantum physics to economics.

Wiener and his junior colleague, the electrical engineer Julian Bigelow, developed their ideas about negative feedback and purpose while working on the problem of predicting the location of enemy aircraft during WWII.[3] While working on this problem they noticed that systems governed by negative feedback may fall prey to ever more powerful oscillations, finally loosing track of the target. They wondered if similar phenomena are found in human pathology, since this would suggest that it too was governed by negative feedback. They approached Wiener's long time friend Arturo Rosenblueth, a physiologist then at Walter Cannon's lab at Harvard, who told them that exactly this phenomenon is found in patients suffering from *intention tremors*. These patients exhibit oscillatory behavior with ever wider oscillations around the target they aim for. The chain connecting intentionality and feedback was being closed. The idea emerged from the interaction of Wiener (a mathematician by self-determination and institutional affiliation), Bigelow (an engineer), and

[3] Norbert Wiener, *I am a Mathematician* (New York: Doubleday, 1956), 252-4.

Rosenblueth (a physiologist). This was an interdisciplinary group through and through.

The programmatic paper that resulted from this work, *"Behavior, Purpose and Teleology"*, authored by Rosenblueth, Wiener and Bigelow (referred to henceforth as RWB), was published in January 1943 in *Philosophy of Science*. Several things about RWB's article are worth noting. The authors stress that their interest lies in the "behavioristic study of natural events," which is concerned with a black-box analysis of the behavior of systems. This they contrast with functional analysis which is concerned with the internal organization of systems. The tension between these two approaches is endemic in biology in general, and was particularly painful in the context of studying animal learning and behavior in the hey-day of Behaviorism. RWB used the first paragraphs to make sure their commitments are known to the reader, and are unwavering about the idea that behavioristic analysis is applicable to machines and to living organisms alike, though organisms and machines may be radically different when it comes to functional analysis. The paper then delves into a series of distinctions that are summarized in the single, and not visually stimulating, figure in the paper (fig. 1).

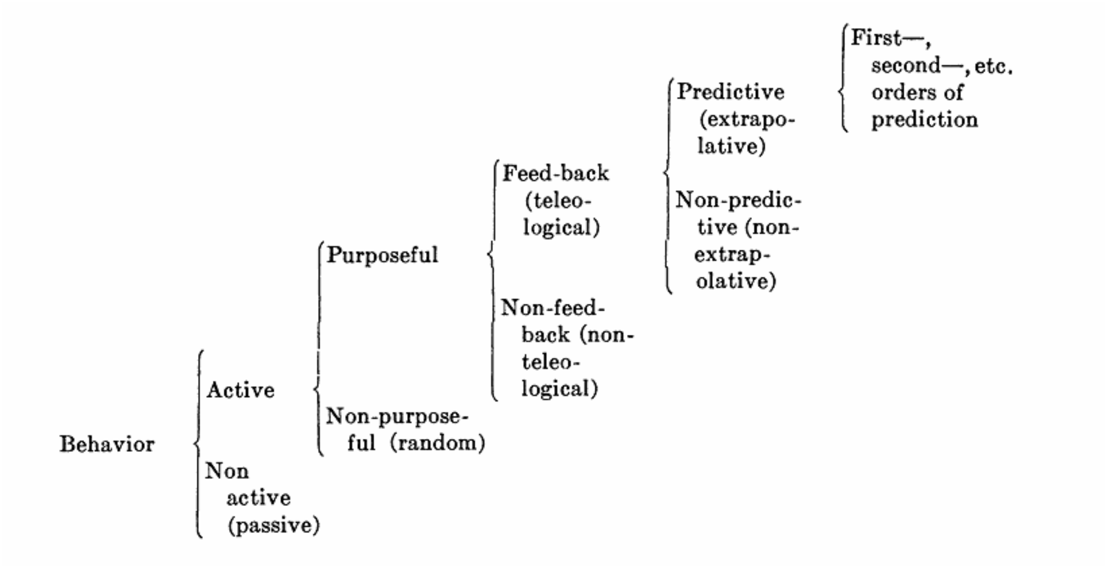

Figure 1. (From: *Behavior, Purpose and Teleology*, Rosenblueth, Wiener, Bigelow, 1943)

According to RWB, purposeful behavior is behavior aimed at fulfilling a particular goal, such as picking up a glass of water from the table. Attaining the goal, or failing irrevocably, may be an immediate result of the action taken by the organism, as happens when a frog strikes at a fly. Alternatively, the behavior of the system may be continuously guided by input from the environment, leading the system to correct its behavior, a mechanism referred to as *negative feedback*. Negative feedback was used by the target-tracking systems Wiener and his colleagues studied as part of the war effort. There they observed that un-damped negative feedback quickly leads to oscillatory behavior, which results from over-correction. This observation, which is immediately apparent to anyone who tries to build a system which relies on negative-feedback, led Wiener and his colleagues to raise a startling suggestion:

> This picture of the consequences of undamped feed-back is strikingly similar to that seen during the performance of a voluntary act by a cerebellar patient.

> At rest the subject exhibits no obvious motor disturbance. If he is asked to carry a glass of water from a table to his mouth, however, the hand carrying the glass will execute a series of oscillatory motions of increasing amplitude…. The analogy with the behavior of a machine with undamped feed-back is so vivid that we venture to suggest that *the main function of the cerebellum is the control of the feed-back nervous mechanisms involved in purposeful motor activity* (p. 20, my italics).

In a sense, Wiener and Bigelow used the target-tracking system, and its formal analysis, as a model, albeit one that was found serendipitously, and appealed to it in asking concrete questions about the human nervous system. The model in this case is not a representation of the target system, the human brain, but rather an example system that exhibits properties that are of interest. If similar behavior were found in patients, the model could then provide a tentative hypothesis about mechanisms that can bring it about. The model provides a *how-possibly* account of the behavior in question.

How does the promise for black-box modeling sit with the article's focus on feedback? Wiener and his colleagues defined negative feedback as referring to behavior that is controlled by the margin of error of the system relative to some specific goal. The term feedback is also commonly used to refer to the way components of a system interact with one another, thereby creating "feedback loops." RWB were not interested in this kind of functional analysis. Their black-box model of intention tremors referred to properties of behavior, not directly to neuronal mechanisms.[4]

The discussion of intention tremors is scientifically interesting, but the bulk of the article is devoted to establishing the set of distinctions that appear in figure 1. The authors acknowledged that this is merely one way to classify behaviors. Their main justification for their particular conceptual scheme was that it highlights the importance of the notions of purpose and teleology, which they defined as "purpose controlled by feed-back":

> Teleology has been interpreted in the past to imply purpose and the vague concept of a "final cause" has been often added. This concept of final causes has led to the opposition of teleology to determinism… purposefulness as defined here, is quite independent of causality, initial or final. Teleology has been discredited chiefly because it was defined to imply a cause subsequent in time to a given effect. When this aspect of teleology was dismissed, however, the associated recognition of the importance of purpose was also unfortunately discarded. Since we consider purposefulness a concept necessary for the understanding of certain modes of behavior we suggest that a teleological study is useful if it avoids problems of causality and concerns itself merely with an investigation of purpose… causality implies a one-way, relatively irreversible functional relationship, whereas teleology is concerned with behavior, not with functional relationships.

Self-Reproducing Automata

[4] For a discussion of whether feedback can be defined solely by reference to external behavior see William C. Wimsatt, "Some Problems with the Concept of 'Feedback'", *Proceedings of the Biennial Meeting of the Philosophy of Science Association* 1970 (1970): 241-256.

In 1947, a year after the first Macy Conference, Wiener published in the *Atlantic Monthly* a letter written in December 1946 in which he advocated against cooperating scientifically with the military. After Hiroshima and Nagasaki, Wiener wrote, the scientist knows that if he works with the military he will end up putting unlimited powers in the hands of those "he is least inclined to trust." At the same time Wiener was taking this stand, von Neumann was getting more and more involved with the workings of the recently formed Atomic Energy Commission (AEC). Already deeply involved in strategic thinking in the Navy and Air Force, and sitting on numerous governmental committees, von Neumann was eventually appointed member of the AEC in 1955. Throughout this time, von Neumann's and Wiener's scientific interests continued to overlap.[5]

At around the time Wiener published his thoughts on teleology, John von Neumann became actively interested in the brain in the wake of the work of Warren McCulloch and Walter Pitts; his ground breaking book on social behavior, *The Theory of Games and Economic Behavior*, coauthored with Oskar Morgenstern, was published in 1944.[6] After several years thinking about the problem of self-reproduction, von Neumann discussed his thoughts on the subject in September, 1948 at the Hixon Symposium on Cerebral Mechanisms and Behavior.[7] Von Neumann began his talk by asking his audience for forbearance, emphasizing that he was an outsider to the fields to which the conference was dedicated. His goal was to give the audience of

[5] See Steve J. Heims, *John Von Neumann and Norbert Wiener: From Mathematics to the Technologies of Life and Death* (Cambridge, MA: MIT Press, 1980).
[6] Steve J. Heims, "Gregory Bateson And The Mathematicians: From Interdisciplinary Interaction to Societal Functions," *Journal of the History of the Behavioral Sciences* 13 (1977):141-159.
[7] *The General and Logical Theory of Automata,* Read at the Hixon Symposium in September, 1948; published in 1951. John von Neumann, *Collected Works* edited by A. H. Taub (New York:Macmillan, 1961-1963). Vol. V, 288-328. Von Neumann's publications on self-reproduction are surveyed by Burks in the preface to John von Neumann, *Theory of Self-Reproducing Automata* edited and completed by Arthur W. Burks (Urbana: University of Illinois Press, 1966).

psychologists and biologists a picture of the mathematical approach to their problems, and to “prepare you for the experiences that you will encounter when you come into closer contact with mathematicians.”

Living organisms are more complicated and subtle than automata, von Neumann argued, but each can provide lessons applicable to the other. He distinguished between the study of the elementary units from which organisms are composed, and the study of how the organization of these components leads to the functioning of the whole. Those with the background of the mathematician or logician, von Neumann explained to his audience, will be attracted to questions of the second kind. Like RWB who distinguished between behavioristic and functional analysis, von Neumann was interested in high-level behavior, namely self-reproduction. In contrast to them he was concerned with functional organization. Instead of black-boxing the system as a whole, his approach was to black-box the components by axiomatizing their behavior. Essentially, his goal was to consider the functional organization of systems composed of idealized components. Starting with the work of McCulloch and Pitts to which von Neumann referred, this type of idealization has been typical in the study of artificial neural networks by computer scientists. Analysis of the kind von Neumann proposed can support generalizations that are not otherwise easy to make, as McCulloch’s work demonstrated. It is not, as he himself noted, a very effective way to determine if the idealization provides a good representation of reality, of the sort presumably sought by biologists. It is also not obvious that when models of this sort exhibit behavior that is similar to that of the modeled system they in fact help explain it. This may depend on whether the model provides necessary or sufficient conditions, and on the extent of idealization involved in defining the components. It may also depend on whether the behavior of the model is simple enough for us to understand. If the model is capable of self-organization and learning, abilities that were later introduced to artificial neural network models, the problem is exacerbated. In the discussion of the applicability of von Neumann's model to the real world following the talk, McCulloch observed that while his own results proved that neural networks can compute any computable number, in Turing's sense, they did not explain how the nervous system achieved any particular result. Other participants of the Macy conferences had similar reservations.

While the idea of self-reproduction seems incredible, and some might even have thought it to involve a self-contradiction, with objects creating something as complex as they are themselves, von Neumann's solution to the problem of self-reproduction was remarkably simple. It is based on two operations: (1) constructing an object according to a list of instructions, and (2) copying a list of instructions as is:

> The general constructive automaton *A* produces only *X* when a complete description of *X* is furnished it, and on any reasonable view of what constitutes complexity, this description of *X* is as complex as *X* itself. The general copying automaton *B* produces two copies of $\phi(X)$ [the instructions which represents *X*], but the juxtaposition of two copies of the same thing is in no sense of higher order than the thing itself… Now we can do the following thing. We can add a certain amount of control equipment *C* to the automaton *A* + *B*. The automaton *C* dominates both *A* and *B*, actuating them alternately according to the following pattern. The control *C* will first cause *B* to make two copies of $\phi(X)$. The control *C* will next cause *A* to construct *X* at the price

> of destroying one copy of *ϕ(X)*. Finally, the control *C* will tie *X* and the remaining copy of *ϕ(X)* together and cut them loose from the complex *(A + B + C)*. At the end the entity *X + ϕ(X)* has been produced. Now choose the aggregate *(A + B + C)* for *X*. The automaton *(A + B + C) + ϕ(A + B +C)* will produce *(A + B + C) + ϕ(A + B +C)*. Hence auto-reproduction has taken place.[8]

This procedure is trivial for anyone computer-literate to understand; it was a remarkable theoretical result in 1948. What, however, does it tell us about biology? It is often observed that von Neumann's explanation, which involves treating the genetic material both as instructions and as data that is copied as-is, is analogous to the reproduction of cells, since DNA, the analogue of the instruction list, is passively replicated. Von Neumann compared the construction instructions that direct the automaton to genes, noting that genes probably do not constitute instructions fully specifying the construction of the objects their presence stimulates. He warned that genes are probably only general pointers or cues that affect development, a warning that alas did not curtail the "genetic program" metaphor that became dominant in years to come.

Von Neumann noted that his model explained how mutations that do not affect self-replication are possible. If the instruction list specifies not only the self-replicating automaton but also an additional structure, this structure will also be replicated.

[8] John von Neumann, "Theory and Organization of Complicated Automata," in von Neumann, *Theory of Self-Reproducing Automata*, 85. Originally lecture delivered at the University of Illinois in December 1949. Note that automaton A is assumed to be a *universal constructor*, able to construct any machine described in its input.

“Mutations” in the additional structure will be copied indefinitely, since they do not affect self-replication. This could be thought of as an explanation of non-lethal mutations. Back in 1922 the geneticist H. J. Muller observed that the genetic material retains the ability to reproduce even after an unlimited number of mutations occurred. He considered this special property to be a crucial difficulty for theories that ground the origin of life in auto-catalysis. Muller initially considered the possibility that genetic replication involves the help of external machinery (in the protoplasm) that acts as a general purpose copier or “mimeograph”, akin to automaton B in von Neumann’s model. Eventually he came to dismiss this solution as far as the origin of life was concerned, because an early division of labor did not make evolutionary sense.[9] Von Neumann’s highly abstract existence proof does not help answer Muller’s evolutionary conundrum.

Unsatisfied with a purely formal proof, von Neumann developed a series of models that tried to put flesh on the abstract notion of construction. He eventually came up with five models, the most famous of which is the cellular automaton model.[10] In this model, construction activities are modeled explicitly, yet the model abstracts away unessential properties of motion in space, energetic considerations, and so on. Cellular automata are comprised of a homogenous grid of cells, each of which is in one of a finite number of states. Time proceeds in discrete steps; the state of a cell at any given step is a function of the states of its immediate neighbors in the previous time step. Von Neumann sketched a cellular automaton consisting of cells with twenty-nine states in which self-reproducing ensembles of cells could be embedded (see figure 2).

[9] Muller recounts the trajectory of his thoughts in Hermann J. Muller, “The Gene Material as the Initiator and the Organizing Basis of Life,” *The American Naturalist* 100 no. 915 (1966):493-517.
[10] See von Neumann, *Self-Reproducing Automata* .

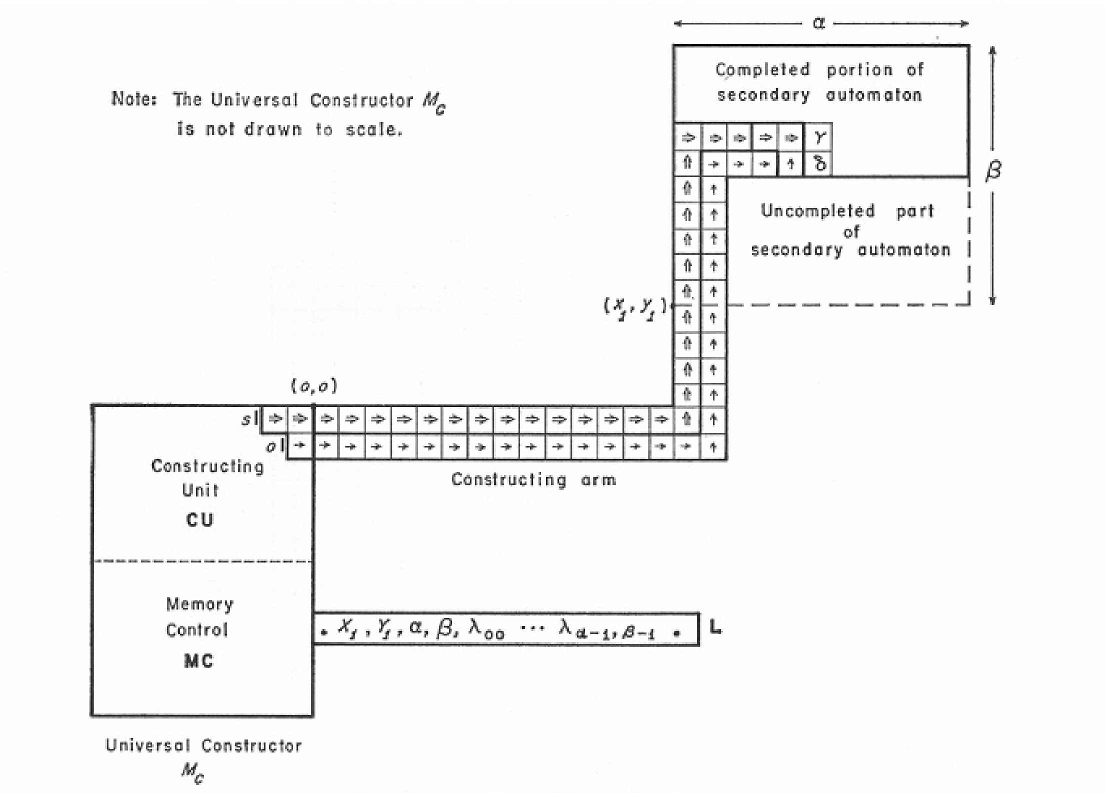

Figure 2. Self-Reproducing Cellular Automaton (From: Theory of Self-Reproducing Automata, Burks A. (ed.), 1966)

Although more concrete than the formal proof quoted above, the cellular automaton is no truer to biological detail. However, it is this model that is most closely associated with von Neumann's work on self-reproducing automata, and figure 2 has become iconic. Von Neumann's work on self-reproducing automata is often given as an example of the essence of Artificial Life research.[11] Since von Neumann's work, cellular automata have become a standard modeling approach, used heavily in theoretical biology and physics.[12] In addition to these uses, there has been continual

[11] Christoper G. Langton, "Artificial Life,". in *The Philosophy of Artificial Life*, ed. Margaret A. Boden (New York: Oxford University Press, 1996).
[12] See Palash. Sarkar, "A brief history of cellular automata", *ACM Computing Surveys* 32, no. 1 (2000): 80-107; G. Bard Ermentrout and Leah Edelstein-Keshet, "Cellular Automata Approaches to Biological Modeling", *Journal of Theoretical Biology* 160, no. 1 (1993):97-133.

research on formal models of self-replication.[13] This theoretical work is however largely divorced from the empirical study of self-reproduction by mainstream biologists.

In 1955 the soon to be Nobel Laureate geneticist Joshua Lederberg exchanged several letters with von Neumann. Lederberg began this remarkable correspondence by asking von Neumann what his work indicated concerning "the minimal information required for 'self-reproduction'".[14] Lederberg was concerned with the notion of self-reproduction as applied to intracellular particles such as genes, noting that their reproduction depended on an appropriate surrounding cell. He was thus enthusiastic about von Neumann's black-boxing of the components of the system, allowing him to focus on the functional organization of the system, only the whole of which is self-reproducing. In this way, the issue with self-reproducing genes is seemingly avoided, and the mathematical model could provide insight.[15] But Lederberg was searching for a model that would help identify the minimal biological structures that underlie reproduction. He hoped for criteria indicating how intracellular components correspond to the elements of von Neumann's model, but noted that he would be surprised if von Neumann's conceptual model was intended as a structural representation of the biological system.[16] Like Muller, Lederberg was concerned with the evolution of self-reproducing systems from simple autocatlytic processes, and envisaged *chemical models* of self-reproducing systems.

[13] Moshe Sipper, "Fifty years of research on self-replication: An overview", *Artificial Life* 4, no. 3 (1998): 237-257.
[14] Lederberg to von Neumann, March 10, 1955. Joshua Lederberg Papers, National Library of Medicine. For more on this correspondence and how the notion of information invaded biology see Lily E. Kay, *Who Wrote the Book of Life?* (Stanford: Stanford University Press, 2000).
[15] Lederberg to von Neumann. April 3, 1955. Joshua Lederberg Papers, National Library of Medicine.
[16] Lederberg to von Neumann. April 3, 1955, September 3, 1955. Joshua Lederberg Papers, National Library of Medicine.

On the notion of information, the original topic raised by Lederberg, the illustrious mathematician and the illustrious geneticist had difficulty finding common ground even after exchanging long and detailed letters. Von Neumann emphasized the independence of a self-reproducing organism embedded in the cellular automaton grid from the definition of the cellular automaton itself. The former is simply an arbitrary collection of cells in specific states, while the latter is essentially the definition of the function determining the transition between states. Von Neumann stressed that the information content of the organism is not contained in the definition of the transition function. Lederberg, in turn, could not regard the cellular automaton definition, independent of any particular self-reproducing organism embedded in it, or the universal constructor, as mere material resources that do not contain information.[17] Noting that they were talking at cross purposes, Lederberg highlighted the two issues that concerned him most: how can autocatalytic molecules be combined so that they can store an arbitrary amount of information, and how does organismal complexity come about. Both questions were not answered by von Neumann's model.

Inspired by von Neumann's formal proof, the British geneticist Lionel Penrose built a series of mechanical models of self-reproduction, which he published in 1958 in, of all places, the *Annals of Human Genetics*.[18] Penrose designed wooden tiles which could hook together, in either of two configurations. Shaking a series of unhooked tiles arranged on a horizontal track did not cause the tiles to hook up – unless one

[17] Von Neumann to Lederberg August 8, 1955. Lederberg to von Neumann August 8, 1955. Von Neumann to Lederberg August 15, 1955. Joshua Lederberg Papers, National Library of Medicine.
[18] Lionel. S. Penrose, "Mechanics Of Self-Reproduction", *Annals of Human Genetics* 23, no. 1 (1958):59-72. The idea was first proposed in Lionel S. Penrose and Roger Penrose"A Self-reproducing analogue". *Nature*, 179 (1957):1183.

hooked-up pair, that he called a "seed", was introduced to the chain, in which case the shaking caused other tiles to hook up in pairs having the same configuration as the seed (see fig. 3). This model showed that reproduction could be achieved by very simple mechanisms – if the notion of reproduction is indeed an appropriate description for what happens in the model.

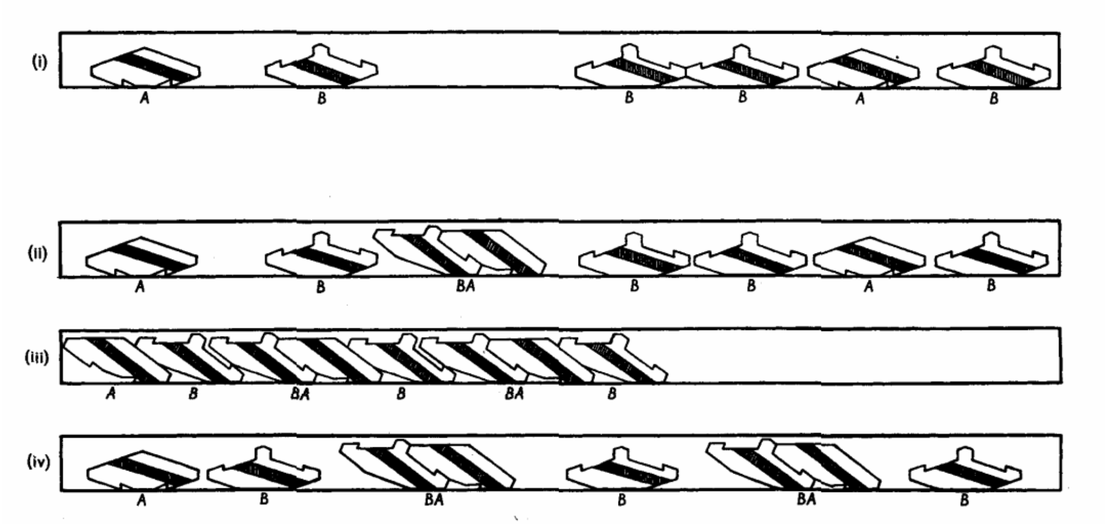

Figure 3. Self replicating chain with units of two kinds (From: Mechanics of Self-Reproduction, L. S. Penrose,1958)

Penrose elaborated this simple model, designing tiles that could propagate increasingly complicated seeds, in a way addressing one of the two issues that concerned Lederberg. The final Rube Goldbergesque tile he called the S-unit (fig. 4). Each component of the S-unit provides the model with a specific capability. For example, pendulums are used to count the number of units that together make up one replicating organism and the wedges are used to control the order in which units are assembled.

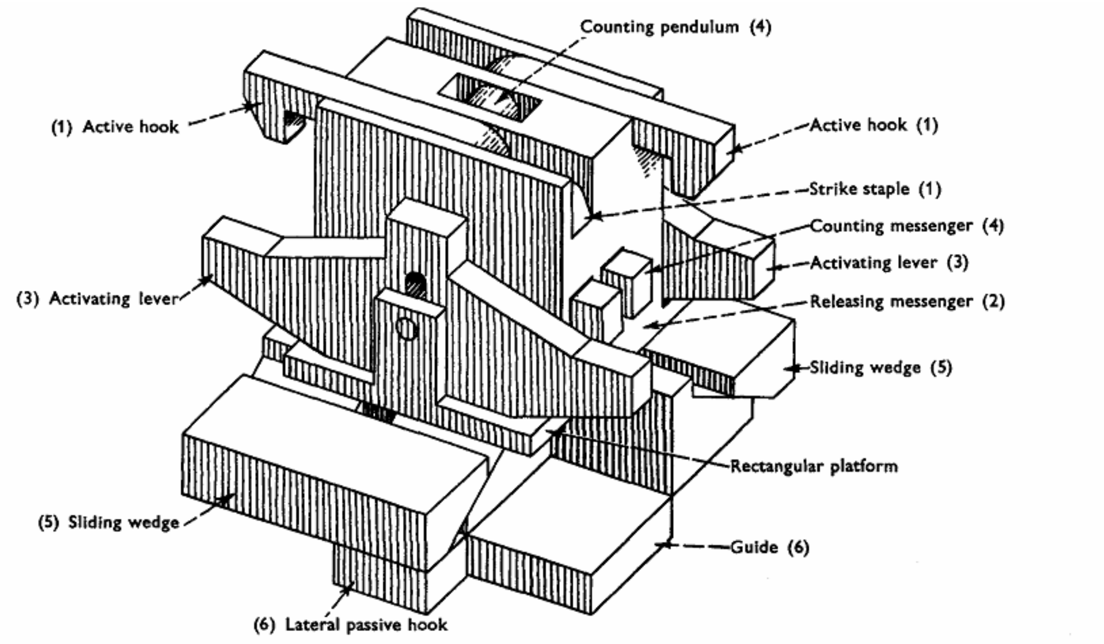

Figure 4. Complete S-unit (From: Mechanics of Self-Reproduction, L. S. Penrose,1958)

Watching Penrose's ingenious tiles on film is mesmerizing. But as Penrose acknowledged, while there were some similarities to DNA they were not conclusive. He made some preliminary suggestions about the function of various chemical components of the DNA molecule by comparing them to the elements of the S-unit, but thought the further speculation was not worthwhile.

Von Neumann's model interested and inspired biologists. It was not able to answer the kinds of questions they had, significantly those that dealt with the physical and chemical aspects of self-reproduction and questions about the evolution of the machinery involved in self-reproduction. Penrose's physical models, which are closer in some respects to the phenomena, also fell short. Like the RWB article, what these models could do was to help clarify and pin-point the phenomenon in question. Von

Neumann demonstrated that the notion of self-reproduction does not involve a logical contradiction, he mitigated the implications of arguments based on considerations of complexity, and he opened the way to a discussion about the minimal requirements for self-reproduction. His models did not represent phenomena; they carved out of the biological mélange one question amenable to formal study. Whether it was appropriate to study this question independently from thinking about the development of the organism as a whole or of the evolution of genetic systems remained open questions.

Teleology

Wiener's article about teleology led to a flurry of responses. Many valid, supposedly fatal, criticisms were raised. For example, groping in the dark for matches that are not there cannot be considered purposeful behavior, if purpose is understood as behavior aimed at achieving a desired relation with an existing aspect of the environment.[19] More fundamentally, it was argued that attributing purpose purely by observing behavior, while ignoring intention, simply misses the point. The simplistic identification of purpose with negative feedback was rejected.[20] Further philosophical reflections clarified tremendously that aspect of teleology that RWB tried to capture, and influenced thinking on *biological function*, on the notion of a *genetic program*, and on teleology in evolution. Often described as flawed, the article remains a classic treatment of the notion of teleology. A fundamental goal of the article was to

[19] Richard Taylor, "Purposeful and non-purposeful behavior: A rejoinder", *Philosophy of Science* 17, no. 4 (1950): 327–332.
[20] See Kay *Book of Life*, chap. 3; Israel Scheffler, "Thoughts on teleology," *British Journal for the Philosophy of Science* 9 no. 36 (1959): 265–284; Larry Wright, "The case against teleological reductionism", *British Journal for the Philosophy of Science* 19, no. 3 (1968): 211–223; Larry Wright, "Explanation and Teleology," *Philosophy of Science* 39 no. 2 (1972): 204-218

encourage conceptualizing both living and artificial systems as goal-directed systems, controlled by feedback. These notions are now commonplace.

In a 1954 Princeton lecture devoted to the role of mathematics in science and society, von Neumann also reflected on the question of teleology and the opposition between causal determinism and teleological laws, which apply to a whole process "viewed as a unity".[21] He used the example of mechanics to argue that mathematical transformations can show that the two supposedly contradictory explanations are in certain cases formally equivalent. Two formulations of mechanical laws, the Newtonian or causal formulation, and the teleological principle of least action, were shown to be mathematically equivalent. According to the first formulation, motion is determined by causal laws applied to the state of the object at each time-point. According to the second, the trajectory of objects is such that a certain formally defined quantity is minimized, when the trajectory is considered as a whole. Teleology, von Neumann acknowledged, may be important when thinking about biology, but only mathematical reasoning can tell us when the distinction is in fact meaningful.

Both Wiener and von Neumann suggested ways to diffuse the problem of teleology that besets biology. Wiener, seemingly more modestly, restricted his "solution" to the behavioral level, leaving aside the question of causality and determinism. Von Neumann, who playing the role of the mathematician emphasized that only by doing math can the question be sensibly addressed, seems more hubristic. On the other hand, Wiener redefined words and concepts to suit his perspective. While RWB

[21] John von Neumann, "The Role of Mathematics in the Sciences and in Society". Address at the 4th Conference of the Association of Princeton Graduate Alumni. June 1954. (Collected Works, vol. VI).

acknowledged that their conceptual scheme is one among many, the article did not endorse pluralism, and suggested that conceptual house-cleaning was in order. Seemingly very different, Wiener and von Neumann's reflections on teleology are not mutually exclusive. Indeed a teleological description of behavior, of the sort suggested by Wiener and his colleagues, can be deterministic and causal, in the sense used by von Neumann, and the formal equivalence highlighted by von Neumann in no way prohibits teleological behavioral descriptions – in fact it legitimizes them. What remains however is a striking difference in rhetoric and emphasis between the two men.[22]

Conclusions

So how did the two suitors fare? Writing in 1951 the geneticist Theodosius Dobzhansky reflected widely held sentiments about the role of theory in biology when he wrote,

> …experience has shown that, at least in biology, generalisation and integration can best be made by scientists who are also fact-gatherers, rather than by specialists in biological speculation.[23]

Quoting this negative sentiment, the cyberneticist Michael Apter offered a rebuttal culminating in a quote from von Neumann's 1948 lecture on self-reproduction, in which he elaborated on the distinction between studying the elements of a system and attempts to study how elements, defined by stipulation, constitute an integrated

---

[22] Arturo Rosenblueth and Norbert Wiener, "Purposeful and non-purposeful behavior", *Philosophy of Science* 17, no. 4 (1950): 318–326 makes stronger metaphysical claims.
[23] Theodosius Dobzhansky, "Mendelian Populations and Their Evolution", *The American Naturalist* 84, no. 819 (1950): 401-418.

system.[24] Von Neumann argued that in spite of the limitations of this approach, it is "important and difficult".[25] The goals of this «systems biology», given its obvious limitations, are to study the larger "organisms" that "can be built up from these elements, their structure, their functioning, the connections between the elements, and the general theoretical regularities that may be detectable in the complex syntheses of the organisms in question."

As Claude Shannon put it in a 1958 review of von Neumann's contributions to automata theory, and specifically self-reproducing automata:

> If reality is copied too closely in the model we have to deal with all of the complexity of nature, much of which is not particularly relevant to the self-reproducing question. However, by simplifying too much, the structure becomes so abstract and simplified that the problem is almost trivial and the solution is un-impressive with regard to solving the philosophical point that is involved. In one place, after a lengthy discussion of the difficulties of formulating the problem satisfactorily, von Neumann remarks: "I do not want to be seriously bothered with the objection that (a) everybody knows that automata can reproduce themselves (b) everybody knows that they cannot."[26]

The empirically-minded biological retort to this view was articulated bluntly by the neurophysiologist John Eccles in his review of the published record of the Hixon

---

[24] Michael J Apter, *Cybernetics and development* (Pergamon, 1966), 23.
[25] Von Neumann, *The General and Logical Theory of Automata*.
[26]Claude E. Shannon, "Von Neumann's contributions to automata theory", *Bulletin of the American Mathematical Society* 64, no. 3 (1958): 123-9.

Symposium. Wiener and Von Neumann sought to bring mathematical abstraction to biological questions. Eccles objections apply to both:

> It seems to the reviewer that the development of neurophysiology is likely to be impeded rather than aided by superficial analogies with automata. Despite all its grandiose claims cybernetics has contributed nothing to neurophysiology except the confusion of some neurophysiologists… One further criticism concerns the section on the reproduction of automata. One may doubt if von Neumann expects us seriously to accept this logical game which is but a mere caricature of reproduction, for it involves the tacit assumption of a supervising genius who not only designs automata and has blue-prints of them, but also initially inserts instructions into them so that in principle they would go through the motions of a reproductive cycle![27]

In contrast, Warren McCulloch, who presided over the Macy cybernetics conferences, looked to mathematics for a theory "so general that the creations of God and men must exemplify it," acknowledging that these necessary conditions could not determine what neural mechanisms are to be found in humans. Robots, the quintessential how-possibly models, then suggest specific hypothesis about the human brain which can be tested experimentally. The very generality of math, McCulloch told a reserved psychologist, meant that the influence of mathematicians should be welcomed rather than feared.[28]

---

[27] John C. Eccles, untitled review, *The British Journal for the Philosophy of Science* 4, no. 16 (1954): 345-47.

[28] Warren McCulloch to Hans-Lukas Teuber. December 10 1947. McCulloch Papers, American Philosophical Society.

But even he sounded downtrodden in the concluding comments he prepared for the tenth and final conference in 1953. After noting the diversity of the research fields of the participants he wrote,

> Our most notable agreement is that we have learned to know one another a bit better, and to fight fair in our shirt sleeves… our consensus has never been unanimous… In our own eyes we stand convicted of gross ignorance and worse, theoretical incompetence.[29]

What role did the theoreticians play in all of this? Wiener took a specific biological phenomenon, intention tremors, and generalized. Von Neumann did the opposite: He took a general biological category, "reproduction", and developed a concrete, though formal, and hence general, model. While in some respects these look to be exactly the same type of work: a model of teleology (as negative feedback), and a model of reproduction (as self-reproducing automata), the endeavors are in some respects mirror images. Von Neumann, the ultimate outsider, worked by himself and developed a formal but concrete model, seemingly unconcerned in this work with being faithful to biological knowledge. Most of this work was sketched out in talks and presentations. Wiener, who had biological training himself, speculated about neuroanatomy, worked closely with collaborators, thinking with and "like" engineers, as well as physiologists, and published in a philosophy of science journal. Von Neumann developed a series of models that illustrated how self-reproduction is possible. Wiener argued for a particular and stringent definition of a central notion in biology. It also seems at first as if von Neumann inspired a significant body of work that explicitly traces itself back to his work on self reproducing automata, and is

[29] Warren S. McCulloch, *Summary of Points of Agreement Reached in the Previous Nine Conferences on Cybernetics,* in Transactions of the Tenth Conference on Cybernetics, Heinz Foerester ed., 1953.

portrayed as a father figure of Artificial Life research, while Wiener's analysis of purposeful behavior that was influential for a short period can safely be categorized as flawed and not having a lasting effect.

On reflection the differences in the ways our two suitors went about trying to woo their coy muse are rather less clear cut. Wiener and Von Neumann were corresponding and collaborating about these issues since 1944. Together they pushed forward what became the Macy Conferences that brought together many people interested in these ideas. They both were evangelizing, and evangelizing together – even if the two had their differences and a level of mutual dislike. Each employed various infiltration tactics, and invested time engaging with biologists. I discussed only two infiltration attempts, Wiener’s conceptual analysis and von Neumann’s models, works in which mathematics clearly played very different roles. The influence of both can be found in contemporary systems biology. Rather than finding a winner and a loser, we end up with two tales about reputation, contingencies, and the variety of strategies mathematicians employ when engaging with biology.

Further Reading

Steve J. Heims, *John Von Neumann and Norbert Wiener: From Mathematics to the Technologies of Life and Death* (Cambridge, MA: MIT Press, 1980).

Giorgio Israel and Ana Millán Gasca. *The World as a Mathematical Game: John von Neumann and Twentieth Century Science*, trans. Ian McGilvay. (Basel/Boston: Birkhäuser Verlag, 2009).

Evelyn Fox Keller, *Making sense of life: Explaining biological development with models, metaphors, and machines* (Cambridge, MA: Harvard University Press, 2003).

Lily E. Kay, *Who Wrote the Book of Life?* (Stanford: Stanford University Press, 2000).

Norbert Wiener, *I Am a Mathematician: The Later Life of a Prodigy* (Cambridge, MA: MIT Press, 1964).