

Turing and von Neumann's Brains and their Computers

Dedicated to Alan Turing's 100th birthday and John von Neumann's 110th birthday

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In this paper we discuss the lives and works of Alan Turing and John von Neumann that intertwined and inspired each other, focusing on their work on the brain. Our aim is to comment and to situate historically and conceptually an unfinished research program of John von Neumann, namely, towards the unification of discrete and continuous mathematics via a concept of thermodynamic error; he wanted a new information and computation theory for biological systems, especially the brain. Turing's work contains parallels to this program as well. We try to take into account the level of knowledge at the time these works were conceived while also taking into account developments after von Neumann's death. Our paper is a call for the continuation of von Neumann's research program, to metaphorically put meat, or more decisively, muscle, on the skeleton of biological systems theory of today.

In the historical context, an evolutionary trajectory of theories from Leibniz, Boole, Bohr and Turing to Shannon, McCulloch-Pitts, Wiener and von Neumann powered the emergence of the new Information Paradigm. As both Turing and von Neumann were interested in automata, and with their herculean zest for the hardest problems there are, they were mesmerized by one in particular: the brain. Von Neumann confessed: "In trying to understand the function of the automata and the general principles governing them, we selected for prompt action the most complicated object under the sun – literally."

Turing's research was done in the context of the important achievements in logic: formalism, logicism, intuitionism, constructivism, Hilbert's formal systems, S.C. Kleene's recursive functions and Kurt Gödel's incompleteness theorem. Turing's machine, exclusively built on the paper, as an abstract computing device, has been the preliminary theoretical step towards the programmable electronic computer. Turing's 1937 seminal paper, one of the most important papers in computer science, prepared the way for von Neumann's 1948 programmable computer.

Von Neumann's unfinished research program was outlined in his seminal articles "The general and logical theory of automata" (1951) and "Probabilistic logics and the synthesis of reliable organisms from unreliable components" (1956), his posthumous book *The Computer and the Brain* (1958) and the unfinished book *The Theory of Self-Reproducing Automata*, completed and published by A. Burks (1966). He proved in 1948, inspired by Turing's universal machine, part of his theory of self-reproduction of automata, five years before Watson and Crick, the structure of the DNA copying mechanism for biological self-reproduction. Biologist and Nobel Laureate Sydney Brenner, in his memoirs, acknowledges von Neumann's prophetic theorem: "You would certainly say that Watson and Crick depended on von Neumann, because von Neumann essentially tells you how it's done."

1. The Duo

Were it not for two decades of the intertwined intellectual lives of Alan Turing and John von Neumann the disciplines of mathematics and computer science would not be what they are today.

Their shared intellectual path began in 1933, when college student Turing wrote to his mother, Sarah, that his prize book was von Neumann's *Mathematical Foundations of Quantum Mechanics*, which he described as being "very interesting, and not at all difficult reading, although the applied mathematicians seem to find it rather strong."

Shortly after, in 1935, von Neumann finds his way into the first line of the first sentence in Turing's first published paper: "In his [1934] paper 'Almost periodic functions in a group,' J. v. Neumann has used independently the ideas of left and right periodicity. I shall now show that these are equivalent." Such a demonstration of Turing's power of proof must have caught von Neumann's attention, for in 1937 he wrote a letter in support of a Princeton fellowship for Turing, and in 1938 offered Turing a position as his assistant which, although it paid \$1,500 a year, Turing declined as the shadows of war lengthened in Europe.

(The admiration was mutual. In a letter written home from Princeton, von Neumann's is the first name on a list of Princeton luminaries that included "Weyl, Courant, Hardy, Einstein, Lefschetz, as well as hosts of smaller fry.")

Though Turing returned to his native England, the two continued to correspond and collaborate for the rest of their all-too-short lives. In 1939, after hearing of a continuous group problem from von Neumann, Turing proved the general negative solution and sent it to von Neumann for *Annals of Mathematics*. A 1949 letter from von Neumann to Turing acknowledged receipt of Turing's submission of a paper for *Annals of Mathematics* for which von Neumann served as an editor: "exceedingly glad to get your paper" and "agree with your assessment of the paper character ... our machine-project is moving along quite satisfactory but we are not at the point you are." (It may be interesting to note that by 1946, von Neumann would be assigning Turing's famous paper on computable numbers as required reading for his collaborators in the EDVAC project of constructing his computer.)

Even in critical discourse, Turing and von Neumann are intertwined. "The fathers of the field had been pretty confusing," E. W. Dijkstra wrote. "John von Neumann speculated about computers and the human brain in analogies sufficiently wild to be worthy of a medieval thinker and Alan M. Turing thought about criteria to settle the question of whether Machines Can Think, which we now know is about as relevant as the question of whether Submarines Can Swim." (EWD898, "The Threats to Computing Science")

Although Turing was 11 years younger than von Neumann, they acknowledged one another's intellectual seniority, with von Neumann serving as an elder in mathematics to Turing and Turing the elder in computer science to von Neumann. Turing papers on almost periodicity, Lie groups, numerical matrix analysis and word problem for compact groups build on von Neumann's work; as an example, in "World problems ..." Turing acknowledges that his results follow from two relatively deep theorems – one due to Tarski and the other to von Neumann. In a letter to Max Newman, Turing talks about Godel and von Neumann: "Godel's paper has reached me at last. I am very suspicious of it now but will have to swot up the Zermelo-v. Neumann system a bit before I can put objections down in black and white." In his ACE paper describing his electronic computer he acknowledges von Neumann's paper on his electronic computer: "The present report gives a fairly complete account of the proposed calculator. It is recommended however that it be read in conjunction with J. von Neumann's 'Report on the EDVAC' ... Most of the most hopeful scheme, for economy combined with speed, seems to be the 'storage tube' or 'iconoscope' (in J. v. Neumann's terminology)."

Their age difference is irrelevant in another respect: We could consider Turing the grandfather of computer science and von Neumann its father, because the Turing machine was invented in the 1930s, while von Neumann's basic work in the field belongs to the 1940s and 1950s.

We find similarities on many fronts: Turing and von Neumann were essentially involved in the creative intellectual effort required by their governments during the Second World War against Nazism and fascism, and each was considered a war hero by his country, with von Neumann receiving the Presidential Medal of Freedom and Turing the OBE; both showed interest for biology (although von Neumann's interest in this respect was much longer and deeper); they both were struck by Gödel's incompleteness theorem and both contributed to a better understanding of its meaning and significance; they both were strongly related in some periods of their lives to Princeton University; they both were attracted by game aspects of computing and of life; and they both left some important unpublished manuscripts. Both lived lives that were too short: Just 41 when he died, Turing lived two years longer than Bernard Riemann; von Neumann died at 53, four years younger than Henri Poincaré was at the time of his death.

Von Neumann was a high achiever from a young age. At 15, he began to study advanced calculus. At 19, he published two major mathematical papers, the second of which gave the modern definition of ordinal numbers. He was 21 when he published "An axiomatization of set theory," 22 when he began his work on *Mathematical Foundations of Quantum Mechanics* (finished when he was 25) and 24 when he published his *minimax* theorem. By 26, he was one of the first four people (among them Einstein) Princeton University selected for the faculty of its Institute for Advanced Study. He was the first to capture the meaning and significance of Gödel's incompleteness theorem, realizing that "if a system of mathematics does not lead into contradiction, then this fact cannot be demonstrated with the procedures of that system." ¹

In examining the totality of von Neumann's work, it is difficult to find names equal in class. If we refer to those historically near to him, maybe Poincaré and David Hilbert before him and A.N. Kolmogorov after him. But even with respect to these great names, it is important to observe that von Neumann's impact spans the whole landscape of sciences, be they more or less exact, natural sciences or social sciences, science or engineering (like in his work related to nuclear weapons). From axiomatic foundations of set theory to the foundation of continuous geometry, from measure theory to ergodic theory, from operator theory to its use to build the foundations of quantum mechanics, from probability theory to lattice theory, from quantum logic to game theory, from mathematical economics to linear programming, mathematical statistics and nuclear weapons, computer science, fluid dynamics, weather systems, politics and social affairs, everywhere he shined new light upon the very essential roots of the respective problems.

Turing's achievements as a young man are no less remarkable than von Neumann's. On the strength of his fellowship dissertation, "On the Gaussian Error Function," completed and submitted in November 1934, the 22-year-old Turing was elected a Fellow of King's College

¹ von Neumann, "The Mathematician," *The Works of the Mind* (ed. R.R. Heywood), University of Chicago Press, 1947, 180-196

four months later, on March 16, 1935. The most influential economist of the 20th century, John Maynard Keynes, was among the committee members electing him. The paper contained a proof of the Central Limit Theorem, one of the most fundamental theorems in probability theory. In 1937 at age 25 he published his seminal paper "On Computable Numbers, with an Application to the *Entscheidungsproblem*," solving one of the famous problems in mathematics proposed by Hilbert. This paper, with negative and positive results of greatest depth, defining the Turing machine and inspiring the designers of electronic computers in England and United States -- von Neumann, in particular, in such a decisive way -- is without question the most important and influential paper in computer science, one offering proof positive that the new field had emerged.

2. From Leibniz, Boole, Bohr and Turing to Shannon, McCulloch-Pitts, Wiener and von Neumann and the emergence of the Information Paradigm

The middle of the past century has been very hot, characterized by the appearance of the new fields defining the move from the domination of the energy paradigm, characterizing the second half of the 19th century and the first half of the 20th century, to the domination of the information-communication-computation paradigms, appearing at the crossroad of the first and the second halves of the 20th century. Von Neumann's reflection, by which he became a pioneer of the new era, developed in the context of concomitant emergence in the fifth and the sixth decades of the 20th century of theory of algorithms (A.A. Markov), lambda calculus (Alonzo Church), game theory (von Neumann and Oskar Morgenstern), computer science (Turing and von Neumann), cybernetics (Norbert Wiener), information theory (Claude Shannon), molecular genetics (Francis Crick, James Watson, Maurice Wilkins, among others), coding theory (R. W. Hamming), system theory (L. van Bertalanfy), control theory, complexity theory, and generative grammars (Noam Chomsky). Many of these lines of development were no longer available to von Neumann and we are in the situation to question the consequences of this fact.

Von Neumann was impressed by results of Warren McCulloch and Walter Pitts connecting logic, language and neural networks. ² In von Neumann's formulation, this result shows "that anything that can be exhaustively and unambiguously described, anything that can be completely and unambiguously put into words, is *ipso facto* realizable by a suitable finite neural network. Three things deserve to be brought into attention in this respect: a) In the 19th century, George Boole's project to unify logic, language, thought and algebra (continuing Leibniz's dream in this respect) was only partially realized ('An investigation in the laws of thought, on which are founded the mathematical theories of logic and probabilities,' 1854) and it prepared the way for similar projects in the 20th century; b) Claude Shannon, in his master's thesis ('A symbolic analysis of relay and switching circuits') submitted in 1937, the same year Turing published his famous 'On computable numbers...', proved the isomorphism between logic and electrical circuits; c) Niels Bohr, in his philosophical writings, developed the idea according to which the sphere of competence of the human language is limited to the macroscopic universe; see, in this respect, David Favrholt's 'Niels Bohr's views concerning language' in *Semiotica* 94, 1993, 1/2. Putting together all these facts, we get an image of the strong limitations that our sensations, our intuitions, our logic and our language have to obey. We can put all these things in a more complete statement: The following restrictions are mutually equivalent: to be macroscopic;

² "A logical calculus of the ideas imminent in nervous activity," Bull. Math. Biophysics 5, 1943, 115-133

to be Euclidean (i.e. to adopt the parallel axiom in the way we represent space and spatial relations); to be Galileo-Newtonian in the way we represent motion, time and energy; to capture the surrounding and to act according to our sensorial-intuitive perception of reality; to use and to represent language, in both its natural and artificial variants (moreover, to use human semiosis in all its manifestations)."

So a natural sequence emerges, having Leibniz, Boole, Bohr, Turing, Shannon, McCulloch-Pitts, Wiener and von Neumann as successive steps. It tells us the idea of the unity of human knowledge, the unifying trend bringing in the same framework logic, language, thought and algebra. But we have here only the discrete aspects, while von Neumann wanted much more.

3. John von Neumann's Brain

It was only too fitting for von Neumann to study the most inspiring automaton of all: the brain. Hans Bethe, physicist and Nobel Laureate, said, "I have sometimes wondered whether a brain like von Neumann's does not indicate a species superior to that of man."

"Our thoughts ... mostly focused on the subject of neurology, and more specifically on the human nervous system, and there primarily on the central nervous system. Thus in trying to understand the function of the automata and the general principles governing them, we selected for prompt action the most complicated object under the sun – literally."

3.1 Von Neumann's unification research project: formal logic + mathematical analysis + thermodynamic error

"There exists today a very elaborate system of formal logic, and specifically, of logic as applied to mathematics. This is a discipline with many good sides, but also with certain serious weaknesses. ... Everybody who has worked in formal logic will confirm that it is one of the technically most refractory parts of mathematics. The reason for this is that it deals with rigid, all-or-none concepts, and has very little contact with the continuous concept of the real or of complex number, that is, with mathematical analysis. Yet analysis is the technically most successful and best-elaborated part of mathematics. Thus formal logic is, by the nature of its approach, cut off from the best cultivated portions of mathematics, and forced onto the most difficult part of mathematical terrain, into combinatorics." -- John von Neumann 1947

His theory of the synthesis of reliable organisms from unreliable components and the associated probabilistic logics was focused on modeling system errors in biological cells, central nervous systems cells in particular. His research program aimed boldly at the unification of the "most refractory" and "rigid" formal logic (discrete math) with the "best cultivated" mathematical analysis (continuous math) via a concept of thermodynamic error.

"It is the author's conviction, voiced over many years, that error should be treated by thermodynamical methods, and be the subject of a thermodynamical theory, as information has been, by the work of L. Szilard and C.E. Shannon."

Turing also uses thermodynamics arguments in dealing with errors, calculating reliability of computing memory, using thermodynamics probability. For von Neumann this unification program was at the core of a theory of information processing for the nervous system and the brain. The error model was conceived as an approximation of "the more complicated

aspects of neuron functioning: threshold, temporal summation, relative inhibition, changes of the threshold by aftereffects of stimulation beyond synaptic delay, etc.” He proposed two models of error. One, concrete – like Weiner’s and Shannon’s, “error is noise,” where in every operation the organ will fail to function correctly in a statistically independent way with respect with the state of the network, i.e. with “the (precise) probability epsilon” and another one, more realistic, but assuming an unspecified [to be defined] dependence of the errors on the network and among them. For concrete error models of the dependence to the general state of the network, more needed to be known. Von Neumann was growing increasingly frustrated about the unavailability of technology, at that time, to find a way to glance into the biological “microscopic” mechanism. Indeed, it is here where molecular biology developments since von Neumann’s time could bring the next concrete concepts of errors that would satisfy his axioms. His “Probabilistic logics ...” provided in the context of his neural system-inspired synthesized organisms, however, a constructive version of the deep concept of information channel “capacity” that Shannon could only prove non-constructively. It provided the first major step towards the new information theory envisioned by von Neumann.

In a 1946 letter to Norbert Wiener, von Neumann expresses his unhappiness with the results of “Turing-cum-Pitts-and-McCulloch:” “What seems worth emphasizing to me is, however, that after the great positive contribution of Turing-cum-Pitts-and-McCullough is assimilated, the situation is rather worse than before. Indeed, these authors have demonstrated in absolute and hopeless generality that anything and everything Brouwerian can be done by an appropriate mechanism, and specifically by a neural mechanism – and that even one, definite mechanism can be ‘universal.’ Inverting the argument: Nothing that we may know or learn about the functioning of the organism can give, without ‘microscopic,’ cytological work any clues regarding the further details of neural mechanism ... I think you will feel with me the type of frustration that I am trying to express.”

He expresses skepticism that neurological methods would help in understanding the brain; he compared that futility as experimenting with a fire hose with water (or nitroglycerine) on an electronic computer. “Besides the system is not even purely digital (i.e. neural): It is intimately connected to a very complex analogy (i.e. humoral or hormonal) system, and almost every feedback loop goes through both sectors, if not through the ‘outside’ world (i.e. the world outside the epidermis or within the digestive system) as well. And it contains, even in its digital part, a million times more units than the ENIAC.”

3.2 “You would certainly say that Watson and Crick depended on von Neumann”

Nobel Laureate Sydney Brenner talks about von Neumann as one of his heroes in his memoir, *My Life in Science* (2001). Brenner was a close collaborator with Francis Crick. These reflections and the story are possibly the greatest mathematical insight of all time for biology. That qualifies von Neumann as a prophet.

Freeman Dyson noted that what today’s high school students learn about DNA is what von Neumann discovered purely by mathematics five years before Watson and Crick. In von Neumann’s words in 1948: “performs the fundamental act of reproduction, the duplication of the genetic material, which is clearly the fundamental operation in the multiplication of living cells ... small variations of the foregoing scheme also permit us to construct automata

which can reproduce themselves, and in addition, construct others. ... This is the typical nonlethal mutant.”

Brenner recalls a symposium titled “The Hixton Symposium on Cerebral Mechanism in Behaviour,” held in Pasadena, California, in 1948. “The symposium was published in 1951, and in this book was a very famous paper by John von Neumann, which few people have read. The brilliant part of his paper in the Hixton Symposium is his description of what it takes to make a self-reproducing machine. Von Neumann shows that you have to have a mechanism for not only copying the *machine*, but copying the information that specifies the machine. So he divided – the *automaton* as he called it – into three components: the functional part of the automaton; a decoding section which actually takes a tape, reads the instructions and builds the automaton; and a device that takes a copy of this tape and inserts it into the new automaton.

“Now this was published in 1951, and I read it a year later in 1952. But we know from later work that these ideas were first put forward by him in the late 1940s. ... It is one of the ironies of the entire field that were you to write a history of ideas of the whole DNA, simply from the documented information as it exists in the literature – that is, a kind of Hegelian history of ideas – you would certainly say that Watson and Crick depended on von Neumann, because von Neumann essentially tells you how it’s done. But of course no one knew anything about the other. It’s a great paradox to me that in fact this connection was not seen.”

He claims that von Neumann made him see “what I have come to call this ‘Schrodinger’s fundamental error’ in his famous book *What is Life?* When asked who are his scientific heroes he lists three names. “There are many people whom I admire, both people I’ve known and whom I’ve read about. Von Neumann is a great hero to me, because he seemed to have something special. Of course it may be envy rather than admiration, but it’s good to envy someone like von Neumann.” The other two names: Francis Crick and Leo Szilard.

4. Turing’s Brain and the Most Important Paper in Computer Science

For both von Neumann and Turing, mathematical proof was their ideal way on how truth is won. In discovering it, they possessed a power almost unequalled by mathematicians of any era. This modus operandi is well articulated by Freeman Dyson in 2009:

“The subject of chaos is characterized by an abundance of quantitative data, an unending supply of beautiful pictures, and a shortage of rigorous theorems. Rigorous theorems are the best way to give a subject intellectual depth and precision. Until you can prove rigorous theorems, you do not fully understand the meaning of your concepts.”

For Turing the power of mathematical proof was a subject of admiration: “... one will not be able to prove any result of the required kind which gives any intellectual satisfaction.”

Turing’s seminal paper solved Hilbert’s *Entscheidungsproblem* (decision problem) in the negative. After Godel’s first hit to Hilbert’s program to find a mechanical process for deciding whether a theorem is true or false in a given axiomatic system, Turing provided the second hit, effectively terminating Hilbert’s program.

“The exactness of mathematics is well illustrated by proofs of impossibility. When asserting that doubling the cube ... is impossible, the statement does not merely refer to a temporary

limitation of human ability to perform this feat. It goes far beyond this, for it proclaims that never, no matter what, will anybody ever be able to [double the cube]. No other science, or for that matter no other discipline of human endeavor, can even contemplate anything of such finality." -- Mark Kac and Stan Ulam, 1968

Papers proving negative results as such Turing's are the most impressive and deep in mathematics. To understand the magnitude of Turing's challenge to prove mathematically "such finality," one has to rule out "everything," and this needed a definition of what a most general "mechanical process" is, i.e., a machine that could compute "everything" that is computable. In turn, the construction of the Turing machine – although logically equivalent with several other constructions -- was one of the most positive and powerful results in mathematics. The computer era, with Turing and von Neumann as founding fathers, had this paper, with negative-and-positive results of greatest depth possible, as its foundation.

5. Not the Language of Mathematics but the Language of the Brain

Universality is an important concept in mathematics, in computer science, in linguistics, in philosophy. There are universal sets in set theory and topology, universal functions in mathematical analysis, universal recursive functions in logic, universal grammars in linguistics.

According to a long tradition that originated with Roger Bacon and endures still, awareness of an idea of a universal grammar came from multiple directions -- Joseph Greenberg and Noam Chomsky sought universals of natural languages; Richard Montague for universals of all human languages, be they natural or artificial. In the theory of formal languages and grammars, results outline in what conditions universality are possible in the field of context-free languages, of context-sensitive languages, of recursively enumerable languages.³

Each of these types of universal grammars can be used to obtain a specific cognitive model of the brain activity; it concerns not only language, but any learning process. The potential connection between universal Turing machines and the nervous system is approached just towards the end of *The Computer and the Brain*, at the moment when von Neumann had to stop his work, defeated by his cancer. We are pushed to imagine possible continuations, but we cannot help but consider ideas, results, theories that did not yet exist at the moment of his death. A joint paper with Cristian Calude and Gheorghe Paun adopted the assumption according to which any type of human or social competence is based on our linguistic generative competence. This assumption was motivated in a previous paper (S. Marcus, 1974). The generative linguistic nature of most human competences may be interpreted as a hypothesis about the way our brain works. But it is more than this, because nature and society seem to be based on similar generative devices.

It seems to be more realistic to look for a metaphorical brain (Arbib 1975), giving an *a posteriori* explanation of various creative processes. But for Arbib, the metaphorical brain is just the computer.

Our aim is to explain how so many human competences, i.e. so many grammars, find a place in our brain, how we successfully identify the grammar we need and, after this, how we

³ Solomon Marcus, "Linguistics as a pilot science". *Current Trends in Linguistics* (ed. Th. A. Sebeok), vol. XII, 1974, The Hague-Paris: Mouton, 1974, 2871-2887

return it to its previous place for use again when necessary. An adequate alternation of actualizations and potentialisations needs a hyper-grammar. For instance, if we know several languages, at each moment only one of them *does*, it is actualized, all the other *are* only, they remain only in a potential stage. We are looking for a hyper-competence, i.e. a universal competence, a competence of the second order, whose role is just to manage, to activate at each moment the right individual competence. This is *the universal grammar as a hypothetical brain*, appearing in the title of our joint paper.

Behind this strategy is the philosophy according to which any human action is the result of the activity of a generative machine, defining a specific human competence, while the particular result of this process is the corresponding performance. Chomsky used the slogan "linguistics is a branch of cognitive psychology." Learning processes are the result of the interaction among the innate and the acquired factors, in contrast with the traditional view, seeing these processes only as the interaction among stimuli and responses to them. The historical debate organized in 1979 between Chomsky and Piaget aimed just to make the point in this respect. With respect to the claim formulated by von Neumann on page 82 in his final book – "The logics and mathematics in the central nervous system, when viewed as languages, must structurally be essentially different from those languages to which our common experience refers" -- it seems that the prevalent view today, at least in the field of linguistics, is to replace the strong requirement asking for the grammar of the brain by the weak requirement asking for a grammar whose result is similar to that of the brain. In the first case, the form of the generative rules should be iconic images of the operations taking place in the brain; in the second case, this strong requirement, for which there is little evidence in the existing experiments, is replaced with the less demanding requirement that the result of the grammar is similar to the result of the brain activity. Chomsky never claimed that the regular, the context-free and the context-sensitive rules have their correspondent in the brain's activity, despite the fact that he imagined the architecture of his grammars having as term of reference the grammatical needs of natural languages. No such claims were formulated with respect to other generative devices used in logic or in computer science.

An idea emerging frequently in von Neumann's writings is clearly expressed in his general theory of automata (*p. 526-527*): "Natural organisms are, as a rule, much more complicated and subtle, and therefore much less understood in detail, than artificial automata." The highest complexity is realized by the human central nervous system. We can approach it by decomposing it in various parts and by analyzing each part (component) on its own. Physics, chemistry and, in a near future, quantum mechanics are involved here, believed von Neumann. But for the mathematician and the logician, the data of the first step can be organized in a system of axioms, adopting for each component the representation as a black-box metaphor used in Norbert Wiener's cybernetics. Then, in a second step, we try to understand how these different components interact as a whole and how the functioning of the whole is obtained by the right interaction of the components. While the first step is just here, logic and mathematics are at home.

6. Continuing von Neumann's Unification Research Program: His Firehouse with Nitroglycerine, the Regulatory Genome and the Computer

Von Neumann would have liked very much to see cellular molecular biology data. "Nothing that we may know or learn about the functioning of the organism can give, without 'microscopic' cytological work any clues regarding the further details of neural mechanism."

In fact, he put together an interdisciplinary team of scientists and wrote a proposal to develop a facility to obtain molecular protein structures by X-ray crystallography, a proposal very similar to the large efforts done today in the U.S. and Europe for large-scale protein structure determination. His proposal, unfortunately, was not funded.

The Regulatory Genome. Knowledge of the molecular biology mechanisms of cell regulation, especially genomic cis-regulatory systems and gene regulatory networks, governing all cells, is now available, revealing the cell regulatory mechanism – and for those cells of the nervous system they are key part of the “neural mechanism.” Our paper, “The regulatory genome and the computer,” with Eric Davidson of California Institute of Technology,⁴ the foremost experiment biologist in gene regulatory networks and the regulatory genome, is written in the same compare-and-contrast format as “The Computer and the Brain,” as a homage to von Neumann’s last book written in large measure on his deathbed. In it, we present a first comprehensive view of the information processing capability of the genomic regulatory system of the cell. Davidson’s experimental work is focused exclusively on *causality*, as the exquisite genomic regulatory mechanisms, locked down by evolution, can only be revealed through experimental DNA perturbations. In this respect, for the biological cell, Davidson’s work stands out as the flagship work on causality-based systems, as articulated by Einstein in 1953. “Development of Western science is based on two great achievements: the invention of the formal logical system (in Euclidean geometry) by the Greek philosophers, and the discovery of the possibility to find out causal relationships by systematic experiment (during Renaissance).” Our paper brought together the full information processing system view, building on our decade-long collaboration focused on genomics, logic functions of the genomic cis-regulatory code, and transcriptomics.

In short, there are many thousand of cis-regulatory modules -- DNA regions upstream of genes a few thousand bases long -- in animal genomes that are “wired” together into very large networks that control biological processes of such development. Each cis-regulatory module is an “information processor” and each gene is controlled by several cis-modules; then the genes and their cis-modules are assembled in gene regulatory networks. Each cis-module has “inputs” which are transcription factor proteins that bind to short DNA subsequences of the cis-module. The communication of information is done by means of diffusion of transcription factors as opposed to pre-organized wires in the electronic computer. The design principles are dramatically different in respect to time, speed, synchrony-asynchrony, memory, hardware and software, parallel computing processors, as well as fascinating new concepts of fault-tolerance. Building on the exciting work of Pippenger, Gacs, Reif and others, investigating error models based in the present day gene regulatory networks and cis-regulatory systems, with their kinetics based structure and their fault tolerant mechanism that are started to be unveiled by the cis-regulatory analysis would make concrete von Neumann’s more general framework for system error, his “dependence on the network” parameter. This is a promising avenue for the exquisite embrace of von Neumann’s biological systems vision with the today causality inferred biological systems networks. Further insight one could get from glances of von Neumann’s information theory in his biological channel capacity constructive proofs compared to the non-constructive proof of Shannon.

7. The Axioms

⁴ S. Istrail, S. De-Leon, E. Davidson “The regulatory genome and the computer” *Developmental Biology*, 310 (2007) 187-195

Here are the Turing and von Neumann axioms:

Axiom 0. Be an automata theorist

Axiom 1. Work on most theoretical and most practical at the same time

Axiom 2. Be a mathematician of the discrete and continuous

Axiom 3. Be intra-math, inter-sciences, cross-cultures scientist

Axiom 4. Work on the hardest problems

Axiom 5. And in the end, the love you take is equal to the love you make.

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