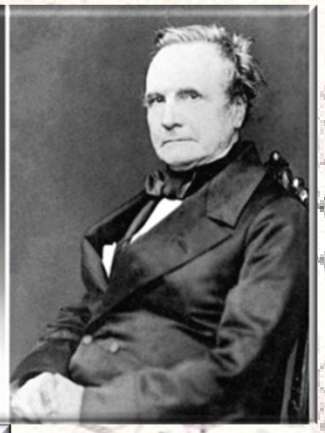
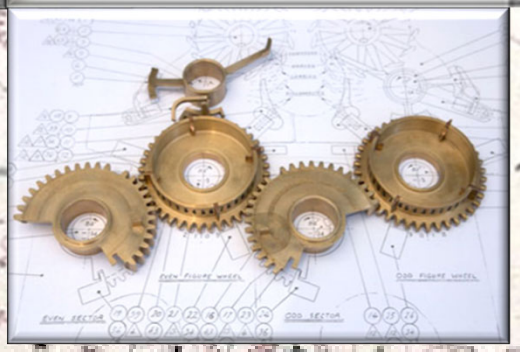
lecture 17

Self-Reproduction and Open-ended Evolution

Babbage/Lovelace first to try to build it (before Turing)

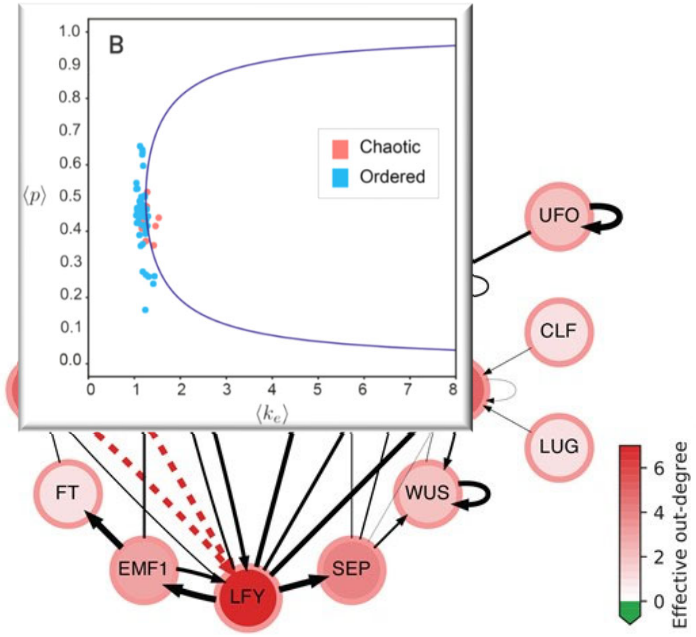


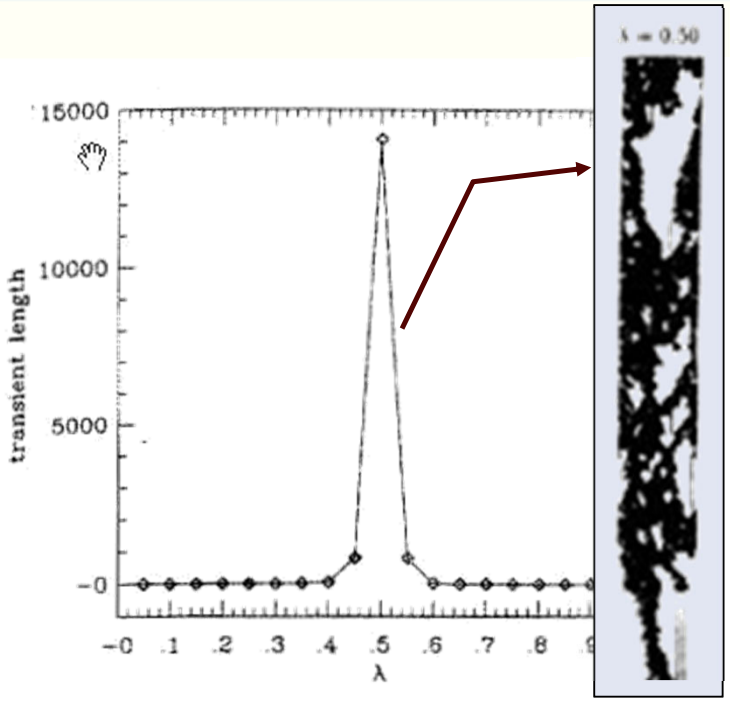



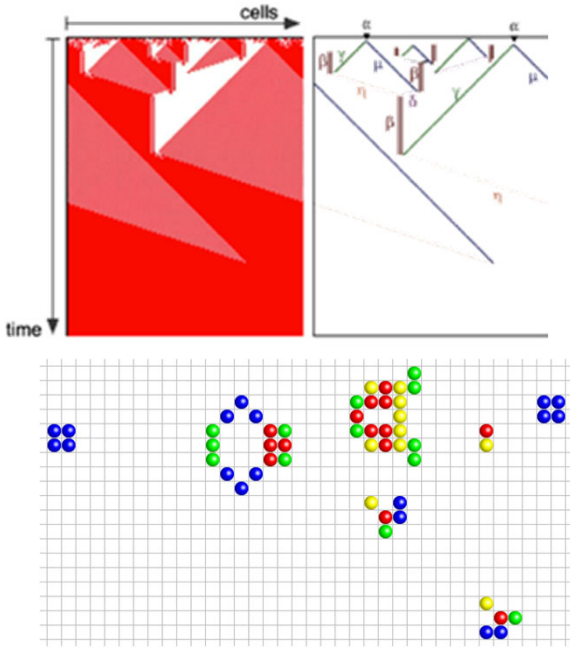

distinction between *numbers that mean things*
and *numbers that (do things) move matter*

computation and the edge of chaos

is self-organization enough?







- systems biology models operate in near critical regime, though many are ordered
- Dynamical systems capable of computation exist before the edge of chaos
  - A wider transition due to redundancy.
- Most important information transmission and computation in Biology an altogether different process than self-organization
  - Turing/Von Neumann memory

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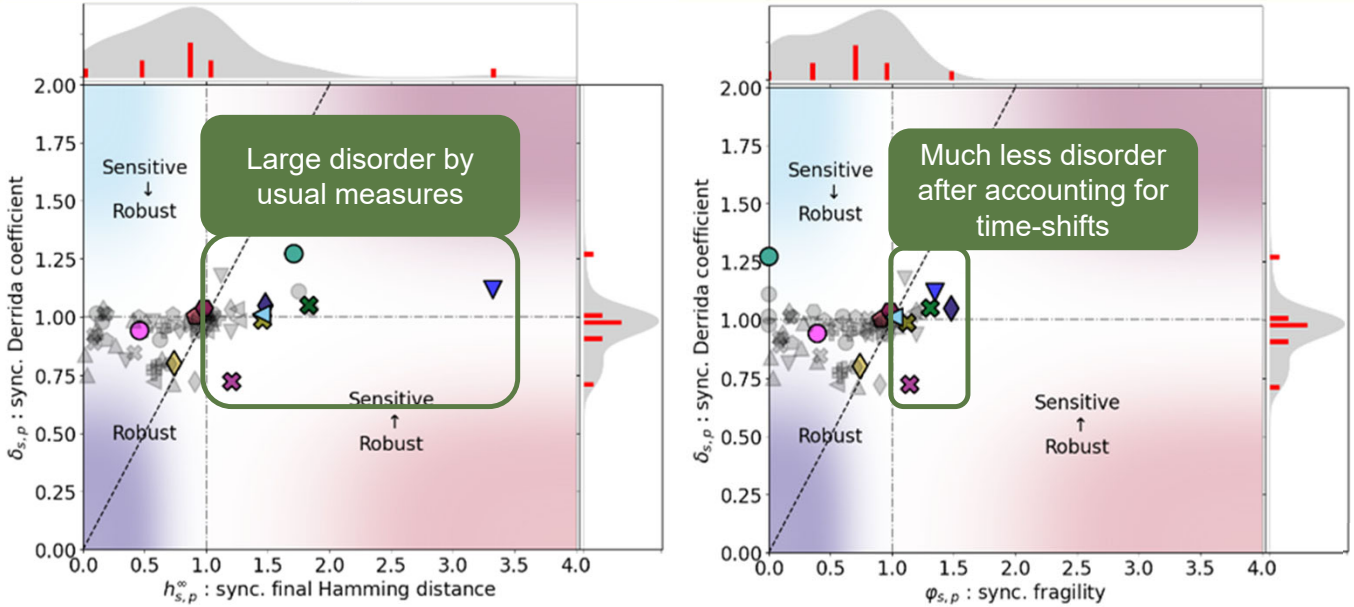
ubiquitous canalization in (experimentally-validated) systems biology models

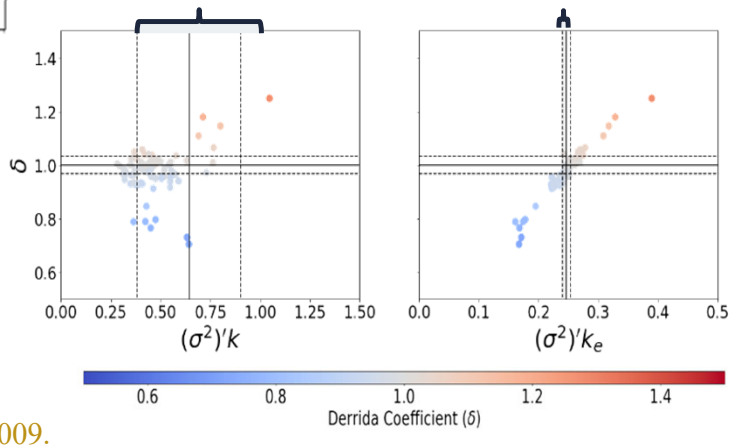
but is there an edge of chaos boundary?



Criticality might arise from interactions of amongst largely stable modules

Cell Collective

More accurate measures of dynamical regime show that experimentally-validated systems biology are far from the edge of chaos



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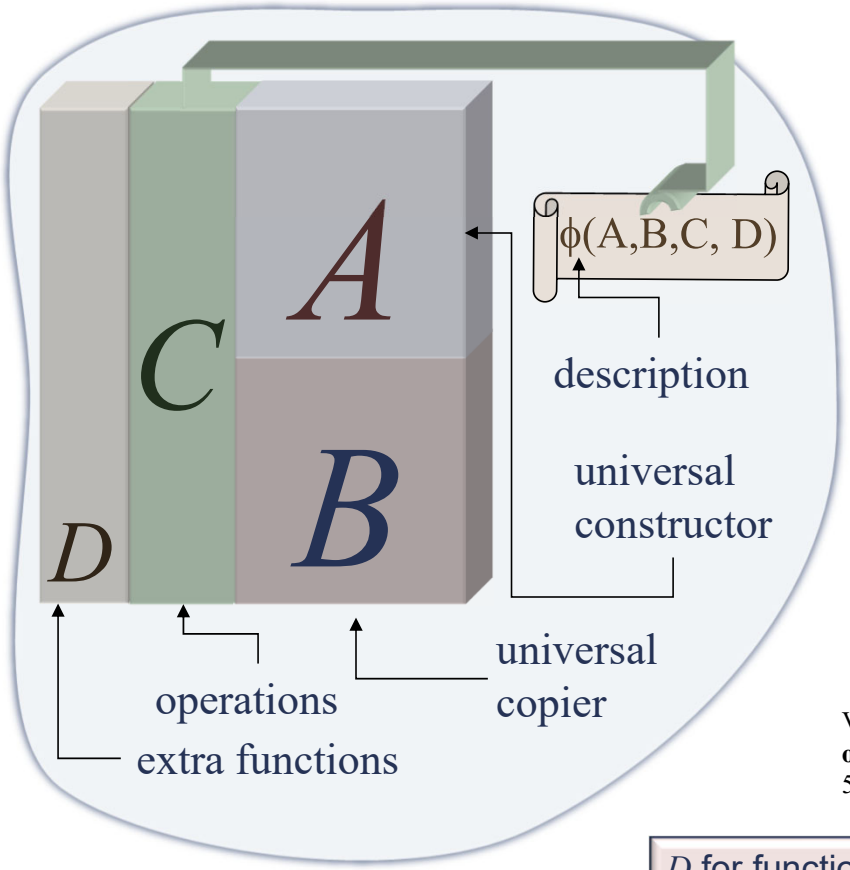
Park, Costa, Rocha, Albert, & Rozum [2023]. *PRX Life*. **1**, 023009.
Costa, Rozum, Marcus, & Rocha[2023]. *Entropy*. **25**(2):374.
Manicka, Marques-Pita, & Rocha, [2021]. *J. Royal Society Interface*. **19**(186):20210659.

Von Neumann's generalization of Turing's tape

as a general principle (system) of evolution or **open-ended complexity**

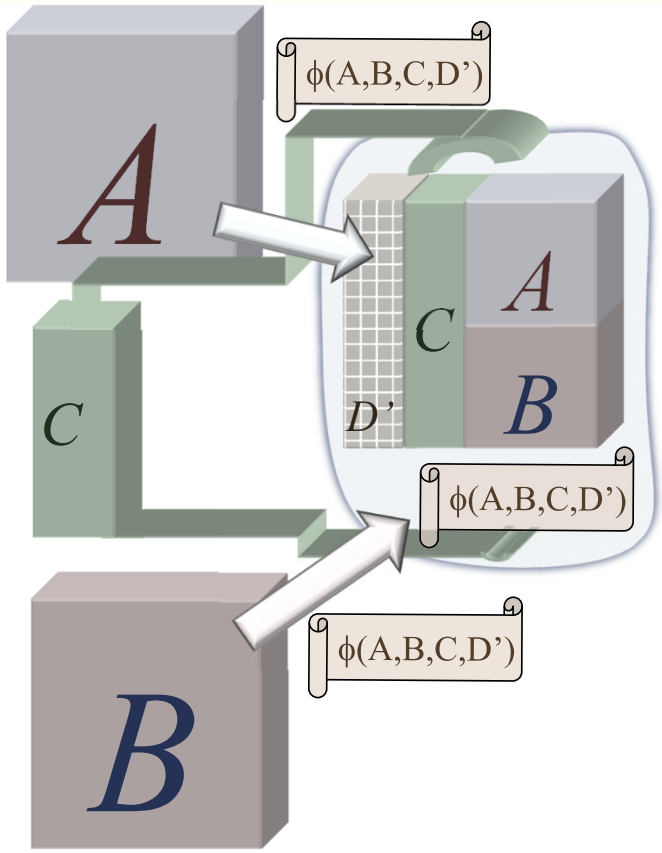


Description is copied **separately**

Construction: interpreted (horizontal transmission)

Copy: uninterpreted (vertical Transmission)

Von Neumann, J. [1949]. "**Theory and organization of complicated automata**." 5 lectures at University of Illinois



D for functions not involved in reproduction

Mutations in *D* can be propagated *vertically*

Leads to **open-ended evolution**

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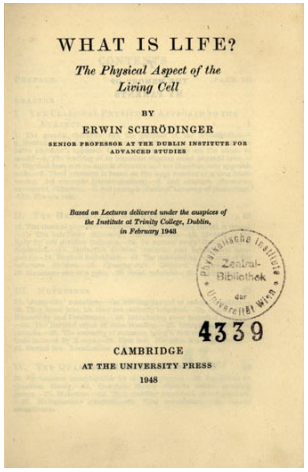
Erwin Schrödinger(1943-1944)


WHAT IS LIFE?

The Physical Aspect of the Living Cell

BY

ERWIN SCHRÖDINGER

SENIOR PROFESSOR AT THE DUBLIN INSTITUTE FOR ADVANCED STUDIES

Based on Lectures delivered under the auspices of the Institute at Trinity College, Dublin, in February 1943

CAMBRIDGE
AT THE UNIVERSITY PRESS
1948

- puzzled by the persistence of living structures
  - Call to understand how life stores and perpetuates order
  - "[…] **chromosomes**[…] contain in some kind of **code-script** the entire pattern of the individual's future development."
    - "complete (double) copy of the code-script."
- **aperiodic crystals as structures that can replicate themselves**
  - "We believe a gene—or perhaps the whole chromosome **fiber**—to be an aperiodic solid."
    - "structure without predictable repetition"
  - DNA is entirely regular
    - Instead of "aperiodicity" we have **encoded information**: separated description/construction

"Turing invented the stored-program computer, and von Neumann showed that the description is separate from the universal constructor. This is not trivial. Physicist Erwin Schrödinger confused the program and the constructor in his 1944 book *What is Life?,* in which he saw chromosomes as "*architect's plan and builder's craft in one*". This is wrong. The code script contains only a description of the executive function, not the function itself." (Sydney Brenner)

Brenner, Sydney. [2012]. "Life's code script." *Nature* **482** (7386): 461-461.

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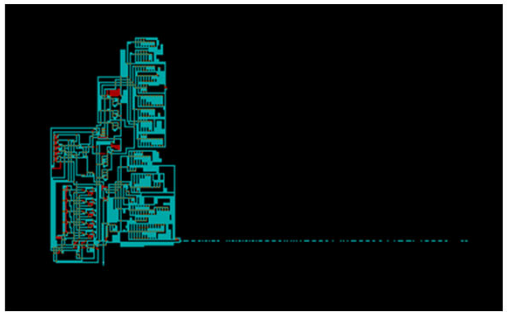
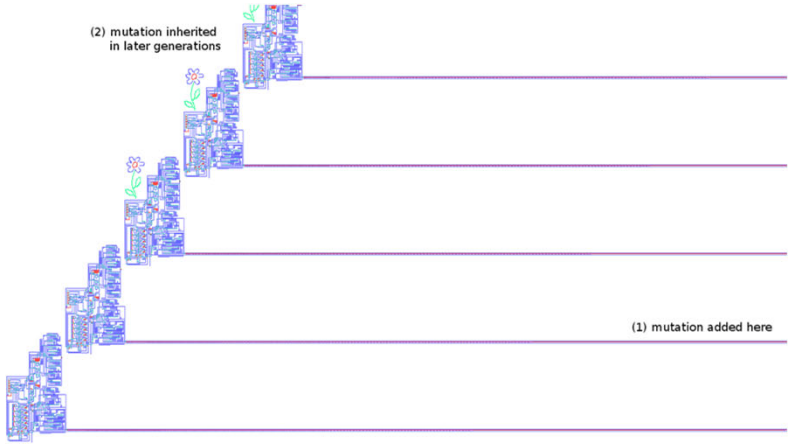
- von Neumann, J. (1966) The theory of self reproducing automata. A. W. Burks (Ed.), Univ. of Illinois Press.
  - From lectures delivered in 1949 at University of Illinois: "Theory and organization of complicated automata."
    - Defined an automaton with 29 states
- First Implementation
  - Pesavento, U. (1995) An implementation of von Neumann's self-reproducing machine. *Artificial Life* 2(4):337-354.





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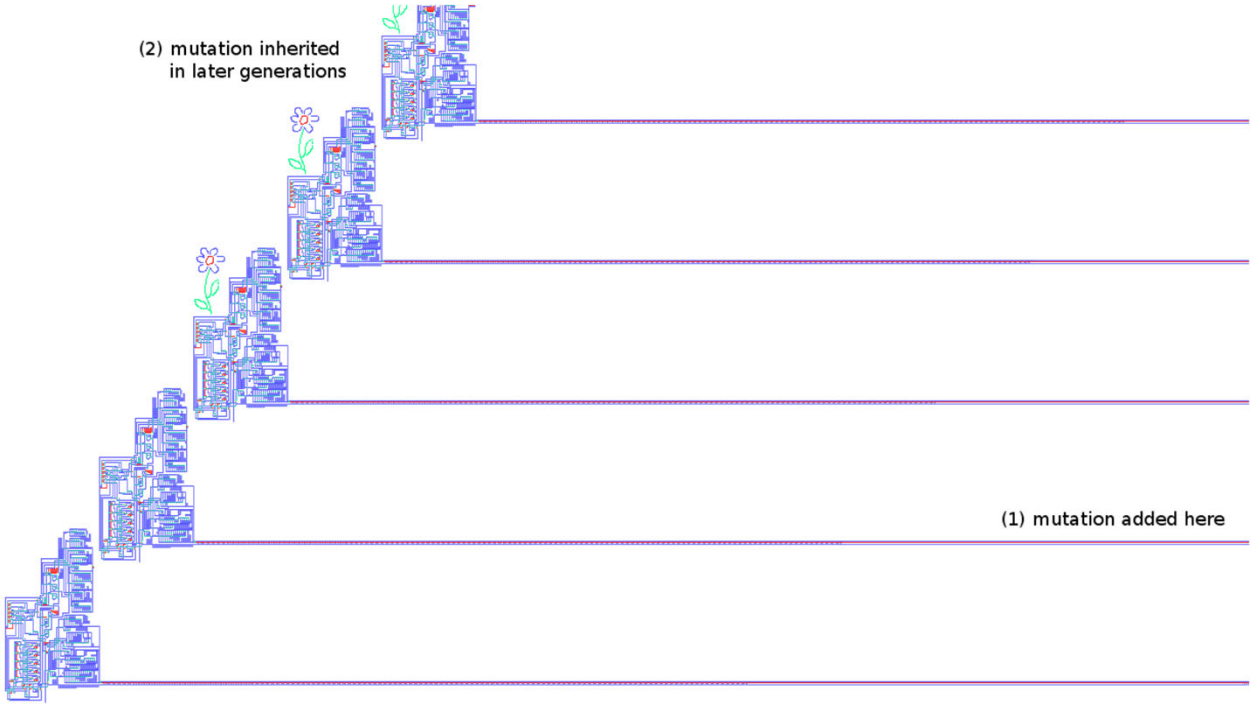
With mutations (by Tim Hutton)



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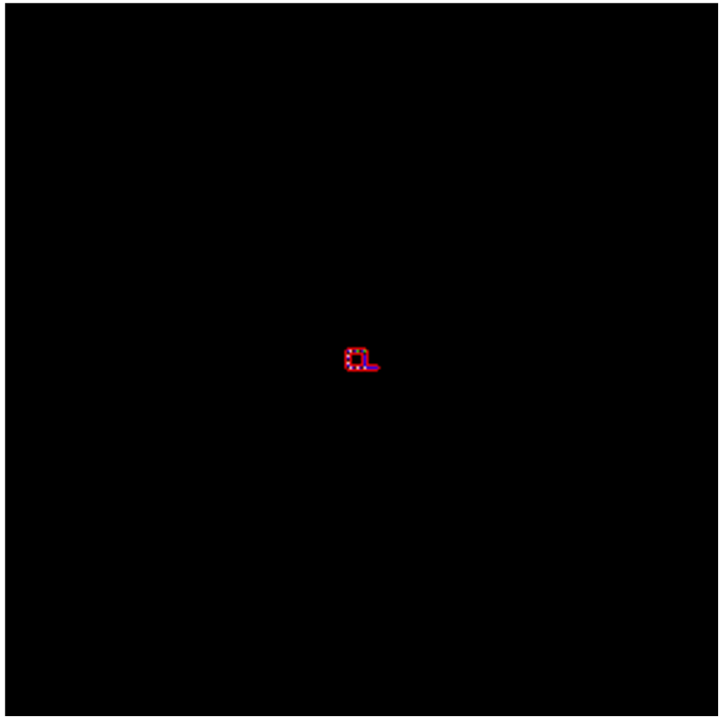
not enough for open-ended evolution



- Does this capture Von Neumann's threshold of complexity?
  - No mutations and evolution possible!
  - Reproduction without possibility of selection
    - Trivial Self-reproduction
  - No description-construction separation
    - genotype /phenotype
    - Tape without V.N. separation

Complex systems, artificial life, even synthetic biology often search for "crystal-like" replication

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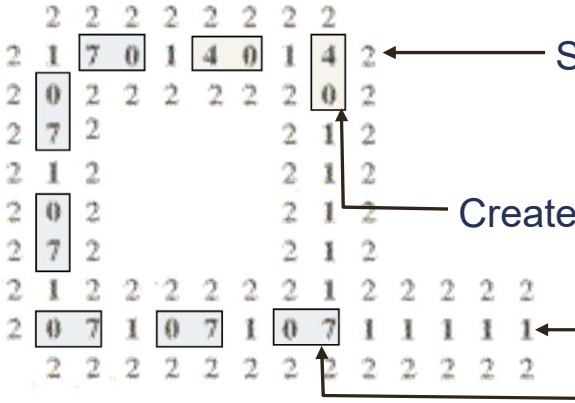
- Simpler self-reproduction
  - a structure whose components constitute the information necessary to its own reproduction
    - System is description and automaton simultaneously
      - Genotype and phenotype **simultaneously** (Schrodinger?)
- The Loop
  - CA with 8 states, 4 neighbors, and 219 neighborhood transition rules
    - a very small subset of the theoretically possible 8^5 = 262,144 transitions
    - Langton C.G., "Studying Artificial Life with cellular automata", *Physica D* 22, 1986.
  - A special initial condition
  - Further simplified and extended
    - Byl's loop, Reggia, Sayama



Sheath: state '2'

Creates left elbow

Inner cells: "genetic information"

Extends sheath

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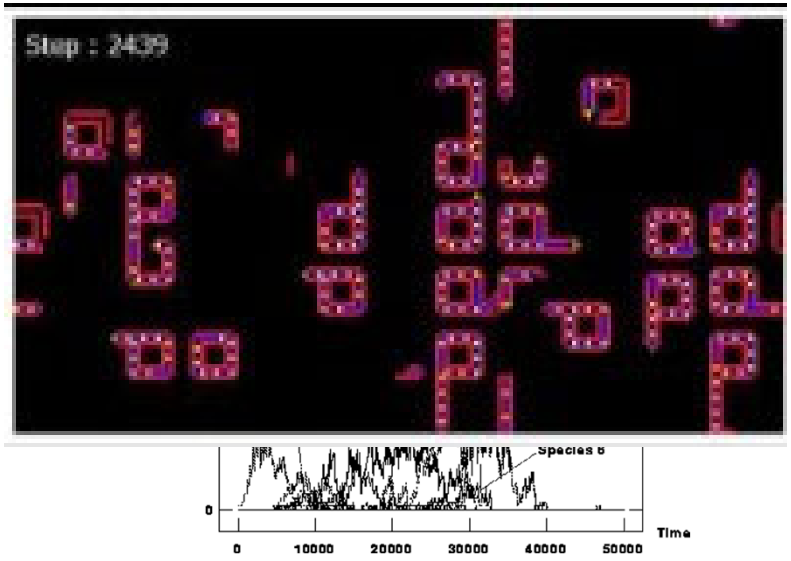
Hiroki Sayama

- Variation on Langton's loop
  - More robust to initial conditions and noise
  - CA leads to different "species" of loops
    - Competition, diversity
  - No real selection
    - Bias on rates of reproduction
  - No description-construction separation
    - genotype/phenotype



Hiroki Sayama [1999]: A New Structurally Dissolvable Self-Reproducing Loop Evolving in a Simple Cellular Automata Space, *Artificial Life* **5** (4): 343-365.

Sayama, Hiroki [2004]. "Self-protection and diversity in self-replicating cellular automata." *Artificial Life* **10** (1): 83-98.

Salzberg, Chris, and Hiroki Sayama [2004]. "Complex genetic evolution of artificial self-replicators in cellular automata." *Complexity* **10**(2): 33-39.

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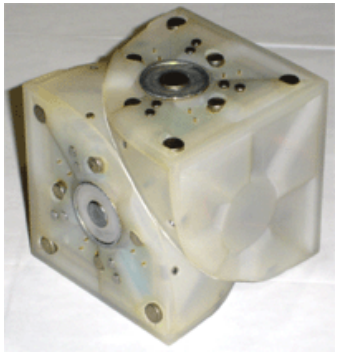
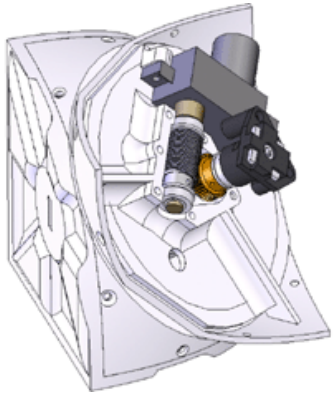
What about in physical self-reproduction?

- Lipson's group
  - Does it evolve?
  - No genotype /phenotype





Zykov V., Mytilinaios E., Adams B., Lipson H. (2005) "Self-reproducing machines", *Nature* **435** (7038): 163-164
Efstathios Mytilinaios, David Marcus, Mark Desnoyer and Hod Lipson, (2004) "Designed and Evolved Blueprints For Physical Self-Replicating Machines", *Ninth Int. Conference on Artificial Life* (ALIFE IX): 15-20

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Still looking for Schrodinger's self-replicating code-script?

RESEARCH ARTICLE | BIOPHYSICS AND COMPUTATIONAL BIOLOGY | OPEN ACCESS

Kinematic self-replication in reconfigurable organisms

Sam Kriegman, Douglas Blackiston, Michael Levin, and Josh Bongard Authors Info & Affiliations

PNAS
Vol. 118 | No. 49
November 29, 2021 | 118 (49) e2112672118 | https://doi.org/10.1073/pnas.2112672118

Significance

Almost all organisms replicate by growing and then shedding offspring. Some molecules also replicate, but by moving rather than growing: They find and combine building blocks into self-copies. Here we show that clusters of cells, if freed from a developing organism, can similarly find and combine loose cells into clusters that look and move like they do, and that this ability does not have to be specifically evolved or introduced by genetic manipulation. Finally, we show that artificial intelligence can design clusters that replicate better, and perform useful work as they do so. This suggests that future technologies may, with little outside guidance, become more useful as they spread, and that life harbors surprising behaviors just below the surface, waiting to be uncovered.

Abstract

All living systems perpetuate themselves via growth in or on the body, followed by splitting, budding, or birth. We find that synthetic multicellular assemblies can also replicate kinematically by moving and compressing dissociated cells in their environment into functional self-copies. This form of perpetuation, previously unseen in any organism, arises spontaneously over days rather than evolving over millennia. We also show how artificial intelligence methods can design assemblies that postpone loss of replicative ability and perform useful work as a side effect of replication. This suggests other unique and useful phenotypes can be rapidly reached from wild-type organisms without selection or genetic engineering, thereby broadening our understanding of the conditions under which replication arises, phenotypic plasticity, and how useful replicative machines may be realized.

Limits of autocatalytic network evolution

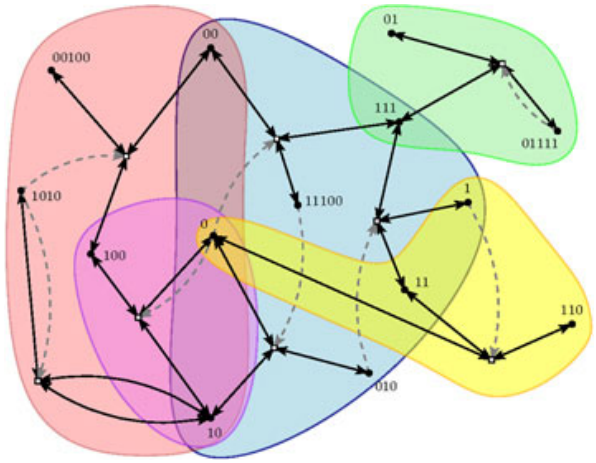
Vasas et al

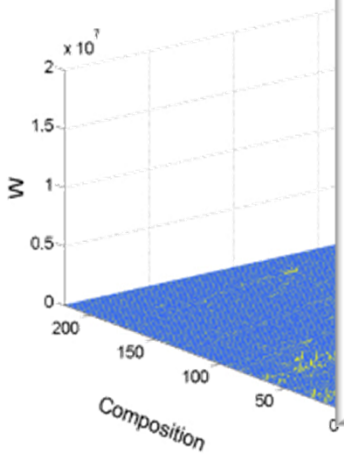
RESEARCH ARTICLE | BIOLOGICAL SCIENCES | FREE ACCESS

Lack of evolvability in self-sustaining autocatalytic networks constraints metabolism-first scenarios for the origin of life

Vera Vasas, Eörs Szathmáry, and Mauro Santos Authors Info & Affiliations

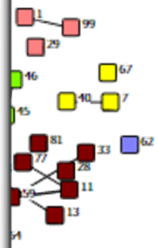
January 4, 2010 | 107 (4) 1470-1475 | https://doi.org/10.1073/pnas.0912628107





Abstract

A basic property of life is its capacity to experience Darwinian evolution. The replicator concept is at the core of genetics-first theories of the origin of life, which suggest that self-replicating oligonucleotides or their similar ancestors may have been the first "living" systems and may have led to the evolution of an RNA world. But problems with the nonenzymatic synthesis of biopolymers and the origin of template replication have spurred the alternative metabolism-first scenario, where self-reproducing and evolving proto-metabolic networks are assumed to have predated self-replicating genes. Recent theoretical work shows that "compositional genomes" (i.e., the counts of different molecular species in an assembly) are able to propagate compositional information and can provide a setup on which natural selection acts. Accordingly, if we stick to the notion of replicator as an entity that passes on its structure largely intact in successive replications, those macromolecular aggregates could be dubbed "ensemble replicators" (composomes) and quite different from the more familiar genes and memes. In sharp contrast with template-dependent replication dynamics, we demonstrate here that replication of compositional information is so inaccurate that fitter compositional genomes cannot be maintained by selection and, therefore, the system lacks evolvability (i.e., it cannot substantially depart from the asymptotic steady-state solution already built-in in the dynamical equations). We conclude that this fundamental limitation of ensemble replicators cautions against metabolism-first theories of the origin of life, although ancient metabolic systems could have provided a stable habitat within which polymer replicators later evolved.



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Hordijk, W. & M. Steel.[2017]"Chasing the tail: The emergence of autocatalytic networks." *Biosystems* 152 : 1-10.

Vasas et al

RESEARCH ARTICLE | BIOLOGICAL SCIENCES | FREE ACCESS

Lack of evolvability in self-sustaining autocatalytic networks constraints metabolism-first scenarios for the origin of life

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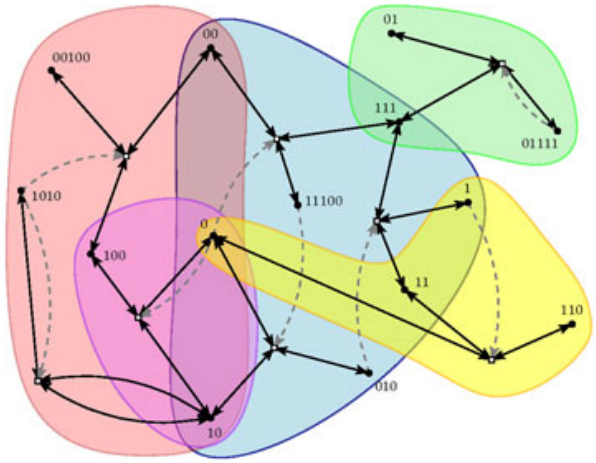

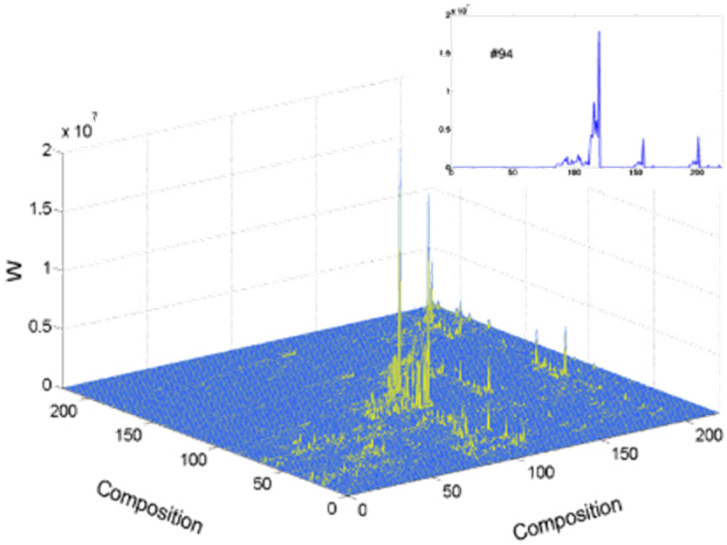

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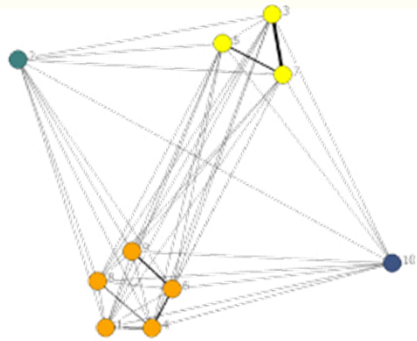

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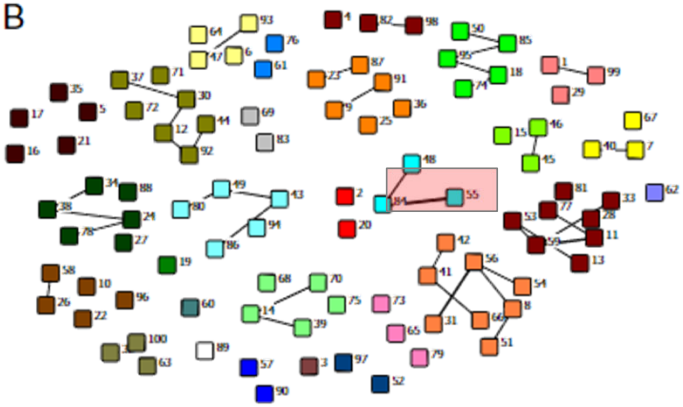

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Hordijk, W. & M. Steel.[2017]"Chasing the tail: The emergence of autocatalytic networks." *Biosystems* 152 : 1-10.

Ameta et al

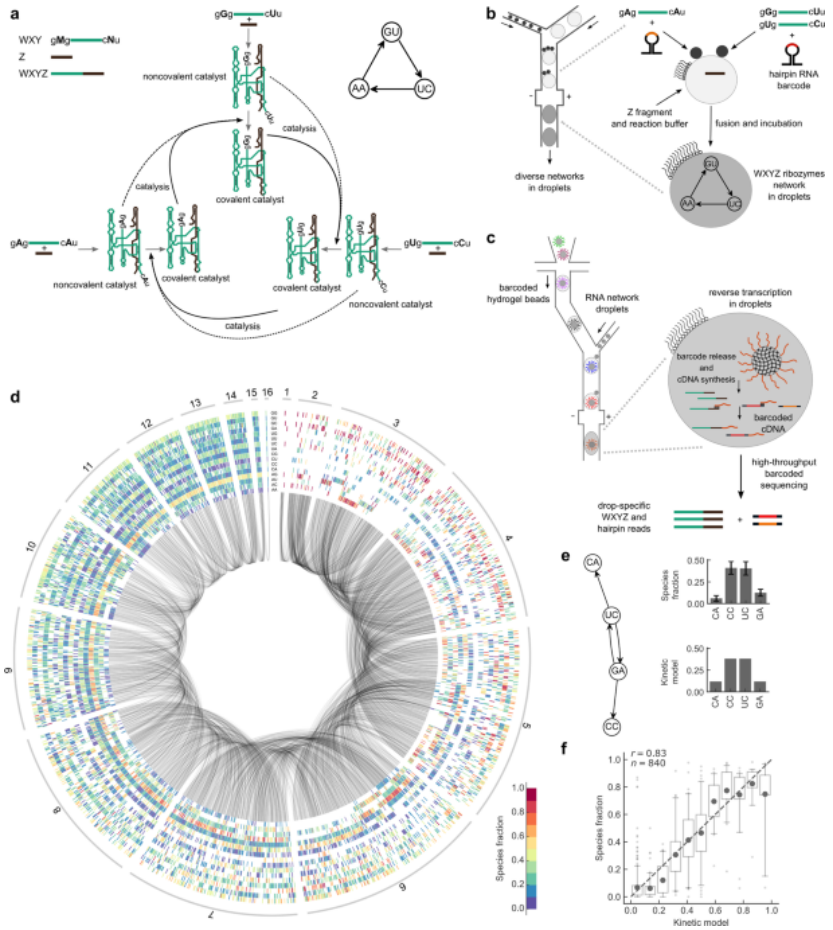
Abstract

Discovering autocatalytic chemistries that can evolve is a major goal in systems chemistry and a critical step towards understanding the origin of life. Autocatalytic networks have been discovered in various chemistries, but we lack a general understanding of how network topology controls the Darwinian properties of variation, differential reproduction, and heredity, which are mediated by the chemical composition. Using barcoded sequencing and droplet microfluidics, we establish a landscape of thousands of networks of RNAs that catalyze their own formation from fragments, and derive relationships between network topology and chemical composition. We find that strong variations arise from catalytic innovations perturbing weakly connected networks, and that growth increases with global connectivity. These rules imply trade-offs between reproduction and variation, and between compositional persistence and variation along trajectories of network complexification. Overall, connectivity in reaction networks provides a lever to balance variation (to explore chemical states) with reproduction and heredity (persistence being necessary for selection to act), as required for chemical evolution.

Darwinian properties and their trade-offs in autocatalytic RNA reaction networks

Sandeep Ameta, Simon Arsène, Sophie Foulon, Baptiste Saudemont, Bryce E. Clifton, Andrew D. Griffiths & Philippe Nghe

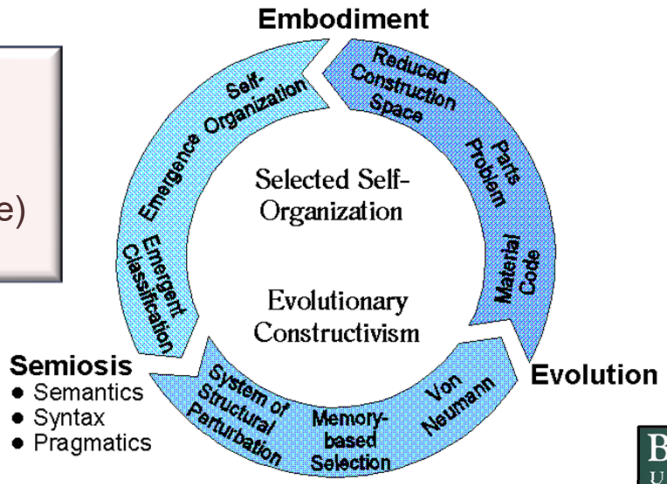
Nature Communications **12**, Article number: 842 (2021) | Cite this article



Material constraints

- Not the same as “universal” evolution
  - The ability to evolve any physical thing whatsoever
- Genotype/Phenotype self-reproduction is more powerful than self-inspection because the same material structure does not have to be simultaneously memory and (catalytic) machine
  - Selected self-organization
  - Needs only to reproduce initial conditions
- Open-endedness in reference to specific genotype/phenotype
  - Set of building blocks available to a symbol system for genetic memory
    - Anything possibly made of those building blocks, can be encoded in the symbol system and produced by development/self-organization
    - Can *evoloops* lead to all possible “attractor” structures in the same CA space?
    - What about self-reproducing robots?

two roles of information
data/program (Turing)
passive/active (Von Neumann)
description/construction-function (Pattee)
genotype/phenotype (Biology)



Rocha, L.M. & W. Hordijk [2005] *Artificial Life* **11**:189 - 214.
Rocha, L.M. [2001] *Biosystems* **60**: 95-121.
Rocha, L.M. [1996] *Systems Research* **13**: 371-384.

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why is a genotype/phenotype separation a good thing?

evolution is possible without codes via self-inspection (beyond autocatalytic networks)…

Phenotype

Dynamics, Rate-dependence, Catalytic, Construction, Function

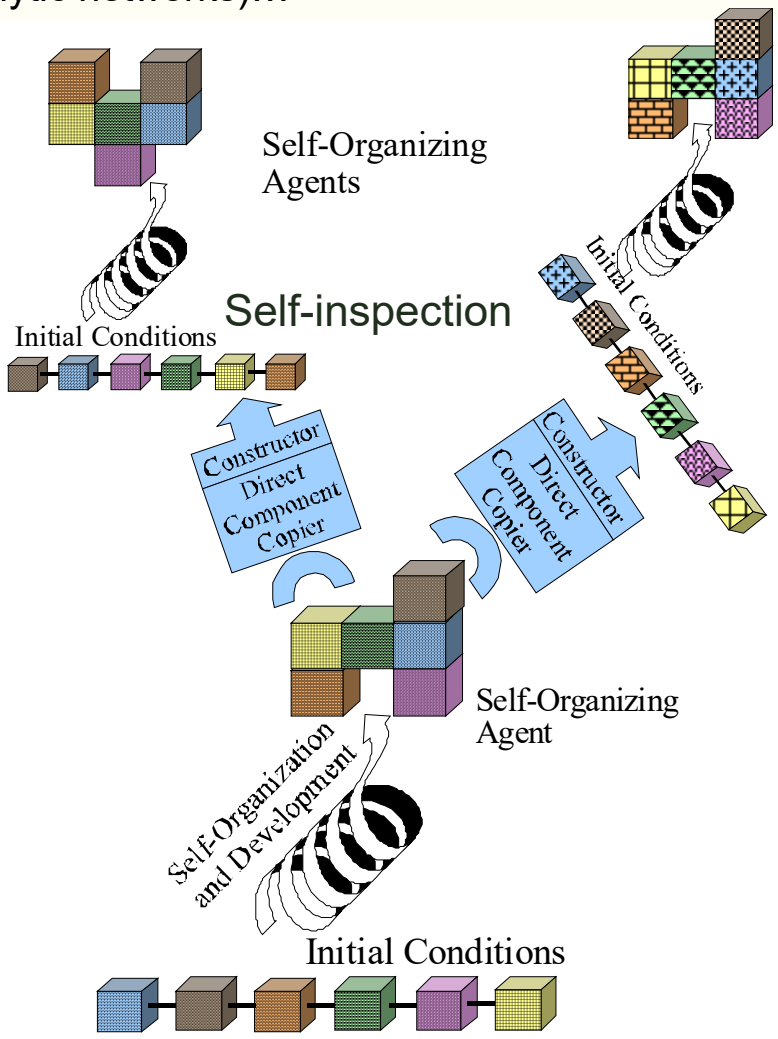
code

Genotype

Memory, rate-independence, Inert, inheritance, Description

Hypothetical reproduction of organisms based on aminoacid chains is possible

Instead of a ribosome another set of organic machinery would copy aminoacid chains



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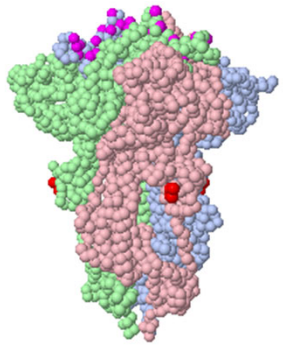
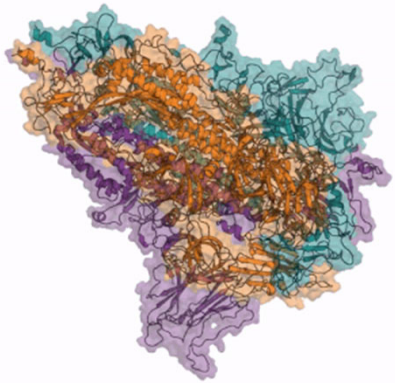
Rocha, L.M. [2001] *Biosystems* **60**: 95-121.

functional products that build up (self-organize) the phenotype



Jmol



Polypeptide chains of aminoacids

Primary Structure

Folding

3-dimensional structure

Secondary and tertiary bonds

- In proteins, it is the 3-dimensional structure that dictates function
  - The specificity of enzymes to recognize and react on substrates
- The functioning of the cell is mostly performed by proteins
  - Though there are also ribozymes

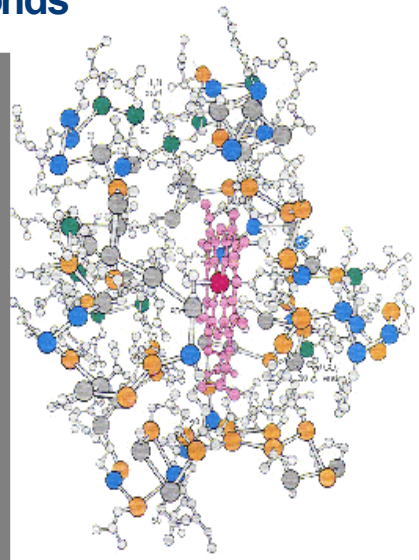


Table 1.4. Amino acid codes

Ala	A	Alanine
Arg	R	Arginine
Asn	N	Asparagine
Asp	D	Aspartic acid
Cys	C	Cysteine
Gln	Q	Glutamine
Glu	E	Glutamic acid
Gly	G	Glycine
His	H	Histidine
Ile	I	Isoleucine
Leu	L	Leucine
Lys	K	Lysine
Met	M	Methionine
Phe	F	Phenylalanine
Pro	P	Proline
Ser	S	Serine
Thr	T	Threonine
Trp	W	Tryptophan
Tyr	Y	Tyrosine
Val	V	Valine
Asx	B	Asn or Asp
Glx	Z	Gln or Glu
Sec	U	Selenocysteine
Unk	X	Unknown

Figures from Eigen [1992] . *Steps Towards Life*.

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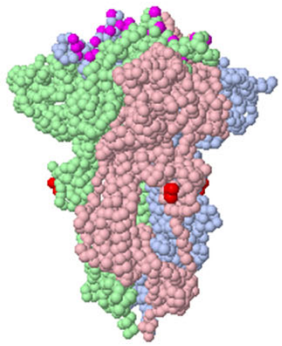
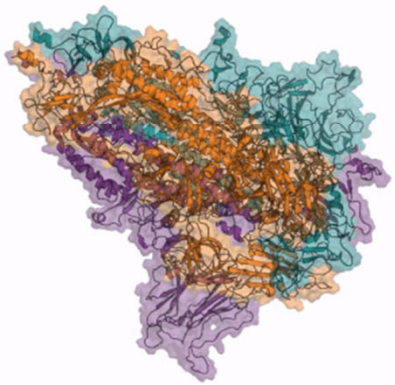
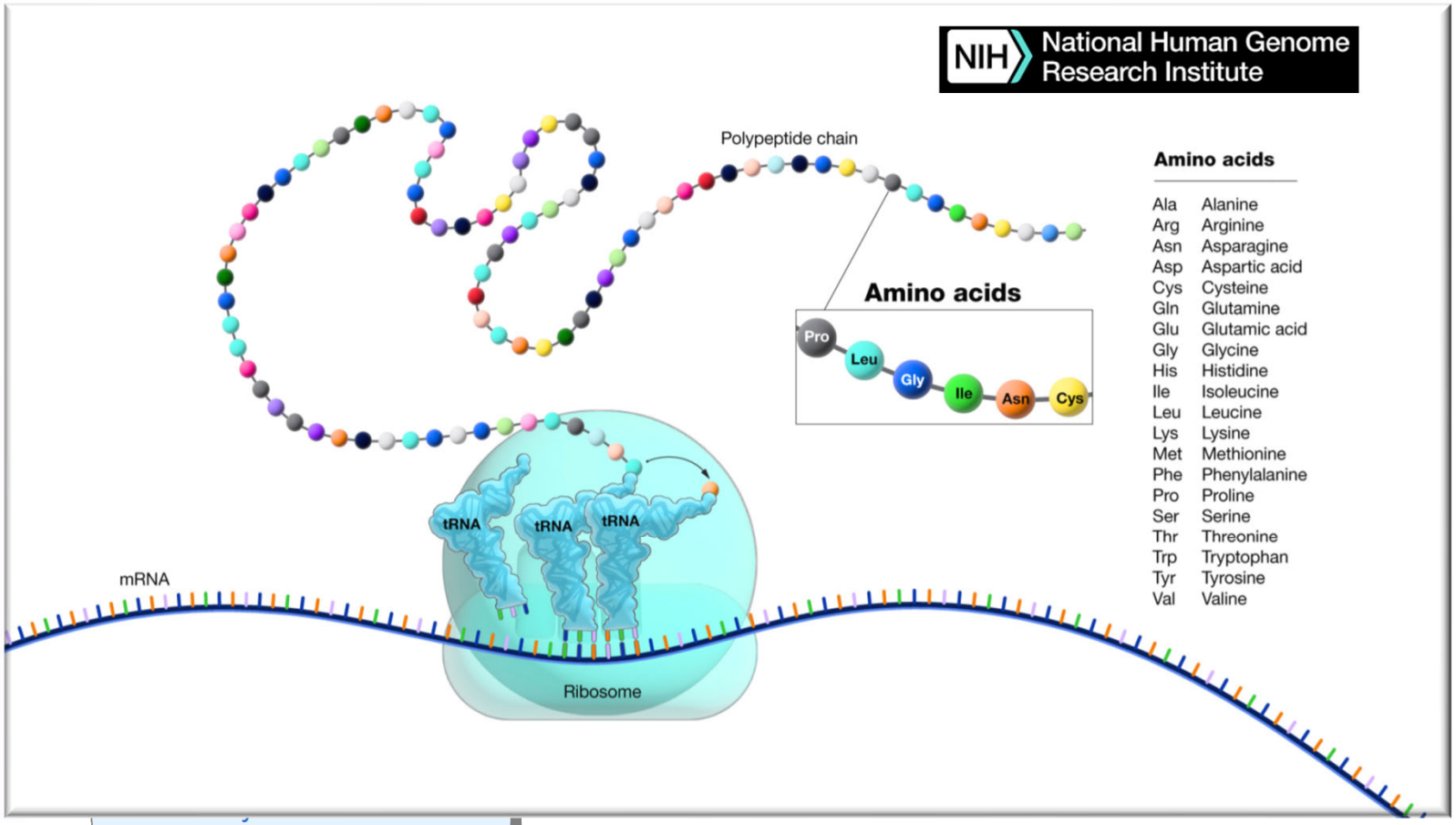
functional products that build up (self-organize) the phenotype



Jmol





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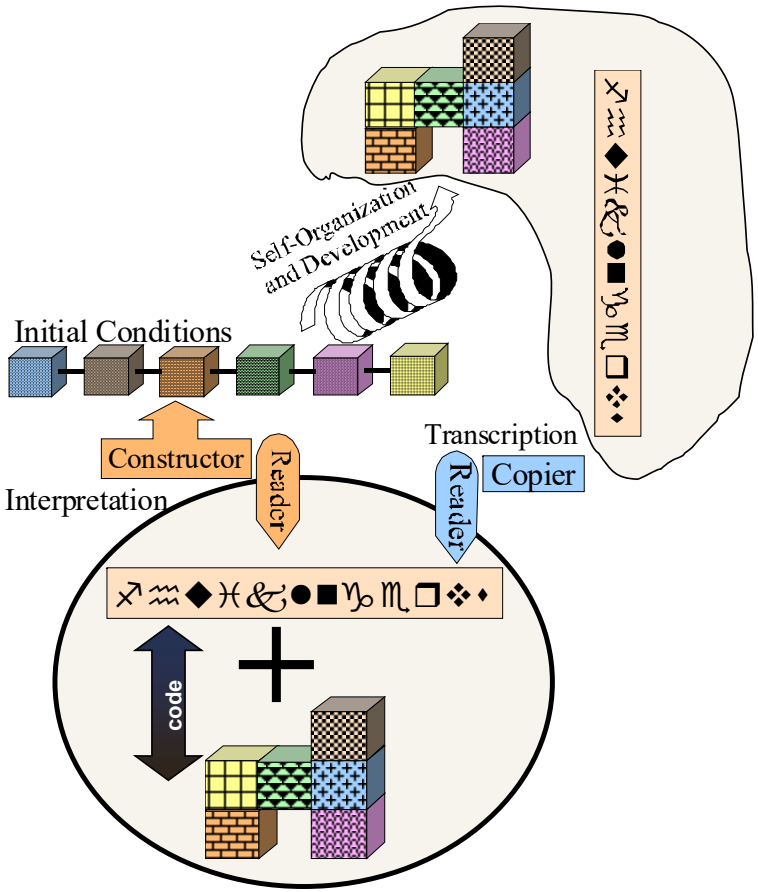
exploring material limits computationally



- Can consistently produce any configuration from a stable, inheritable description
  - Not Just those whose initial conditions are recoverable
- Variation on descriptions
  - Not on phenotypes
- Can reproduce complicated, developed phenotypes
  - Because it does not need to reduce the dynamics to recoverable components
- Uses memory of initial conditions
  - Open-Ended evolution

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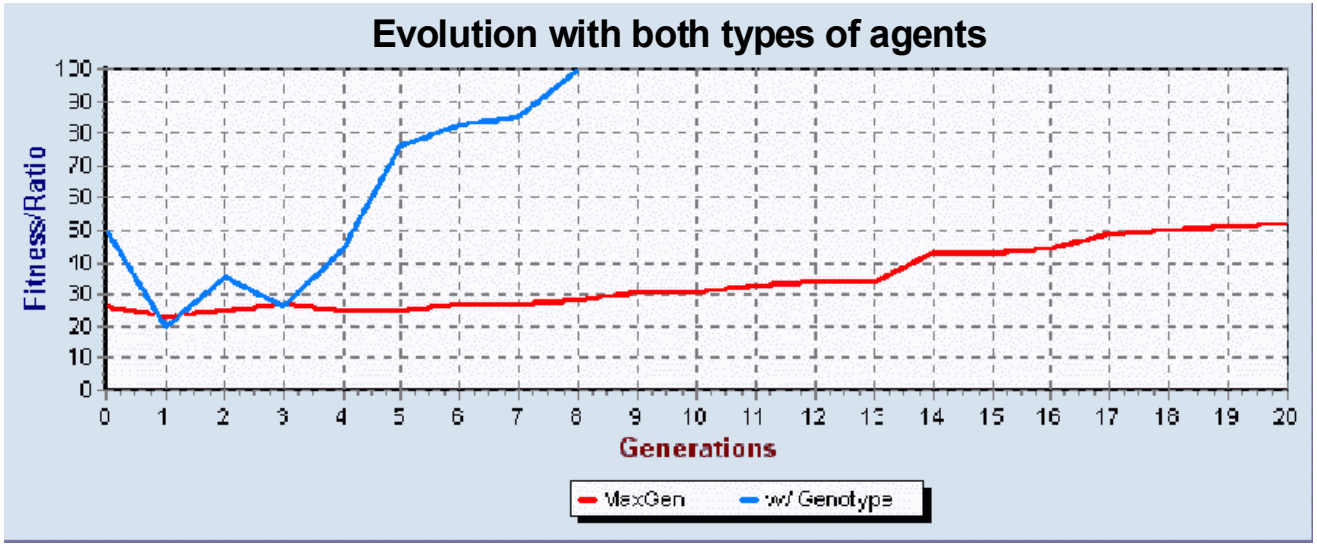
simulations of evolutionary potential



Under most conditions and types of evolutionary algorithms, coded agents overtake the population in a small number of generations. pattee/rocha.html

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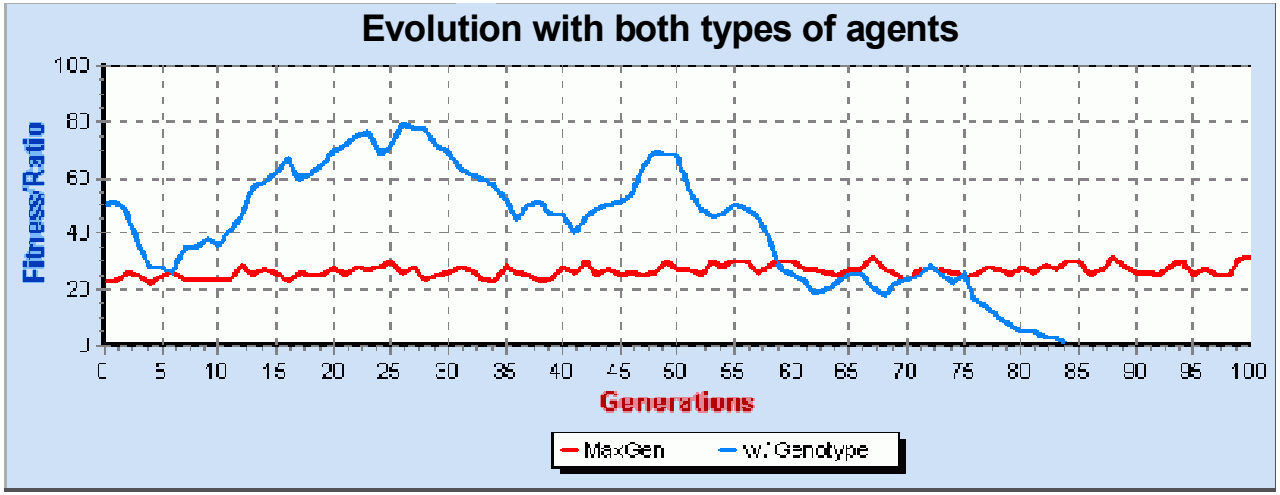
Rocha, L.M [2001]. *Biosystems.* **60**, 95-121

simulations of evolutionary potential



With too much genetic variation, the stability of descriptions is lost, resulting in occasional taking over of the population by noncoded agents. pattee/rocha.html

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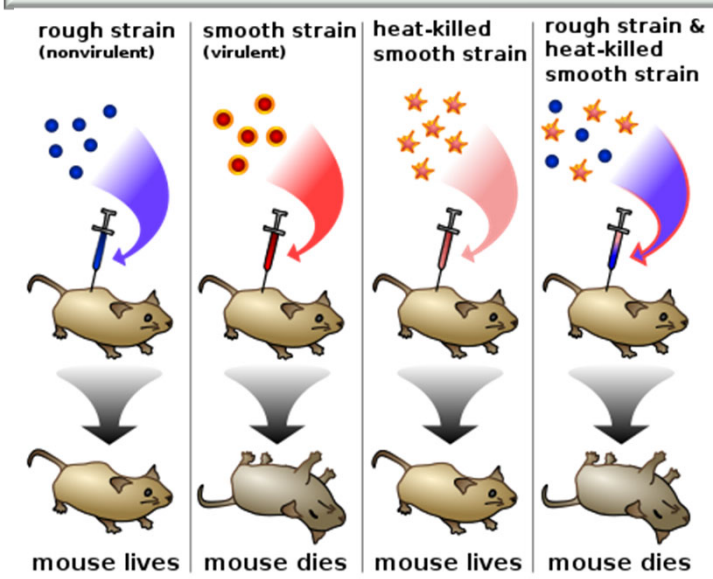
identifying the loci of genetic information

- Frederick Griffith's experiment
  - In 1928: Identified a "transforming principle"
- Avery's experiment
  - Oswald Avery, Colin MacLeod, and Maclyn McCarty
  - 1944: DNA as the loci of "transformation"
    - Chemically knocking off various cellular constituents until trying DNA
    - Considerable resistance in the community accepting this result until the early 1950's (Schrodinger, Delbruck, phage group)



initially not
well accepted
(No auto-catalysis with DNA)

2 different strains
of pneumococcus
bacteria

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Schrodinger vs. Von Neumann

self-replication vs. decoupled, encoded information

Von Neumann, J. [1949]. "**Theory and organization of complicated automata**." 5 lectures at University of Illinois

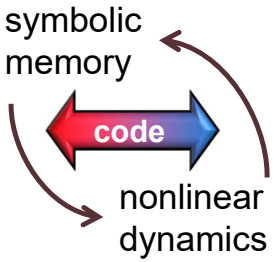
Brenner, Sydney. [2012]. "Life's code script." *Nature* **482** (7386): 461-461.

"Turing invented the stored-program computer, and von Neumann showed that the description is separate from the universal constructor. This is not trivial. Physicist Erwin Schrödinger confused the program and the constructor in his 1944 book *What is Life?,* in which he saw chromosomes as "*architect's plan and builder's craft in one*". This is wrong. The code script contains only a description of the executive function, not the function itself." (Sydney Brenner)

two roles of information
data/program (Turing)
passive/active (Von Neumann)
description/construction-function (Pattee)
genotype/phenotype (Biology)

semiotic closure (semiotic coupling)

fundamental principle of *organized complexity*
Leads to **open-ended evolution**
General principle that includes *Natural Selection*
Von Neumann described this scheme **before** structure of DNA molecule was identified in 1953 by Watson & Crick



Howard Pattee

Pattee, HH [2001] *Biosystems* **60** (1):5-21

Rocha, L.M. & W. Hordijk [2005] *Artificial Life* **11**:189 - 214.
Rocha, L.M. [2001] *Biosystems* **60**: 95-121.
Rocha, L.M. [1996] *Systems Research* **13**: 371-384.

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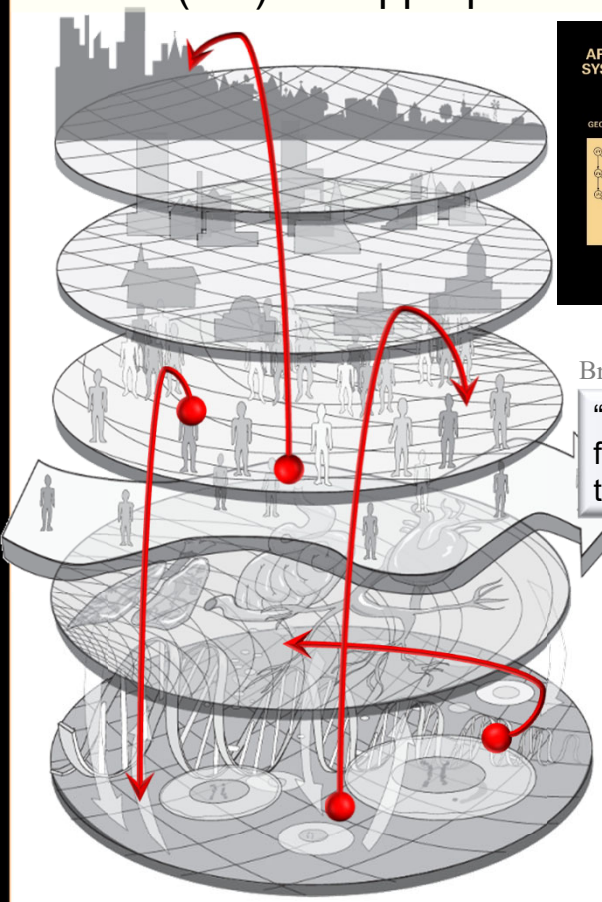
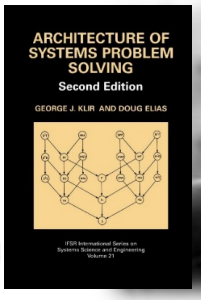
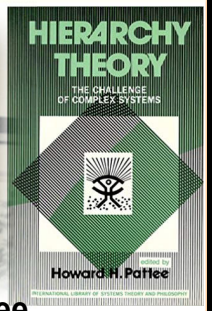
what is (are) the appropriate level(s)?





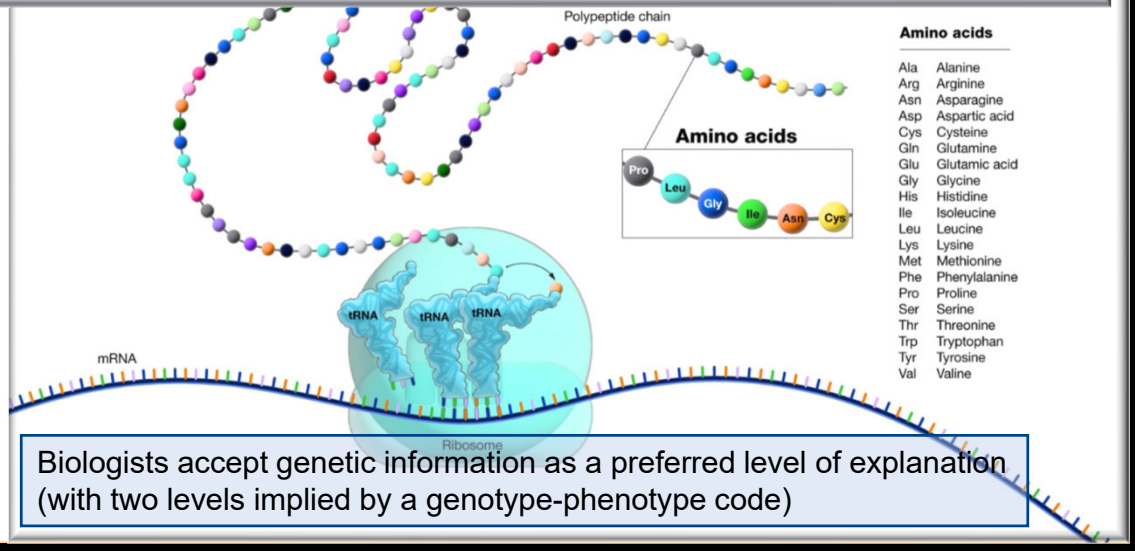
Key insight: complex systems not reducible to single level and deviate from past data eventually

Key insight: appropriate level of description of complex systems must be agnostically and pragmatically estimated



Brenner, Sydney. [2012]. "Life's code script." *Nature* **482** (7386): 461-461.

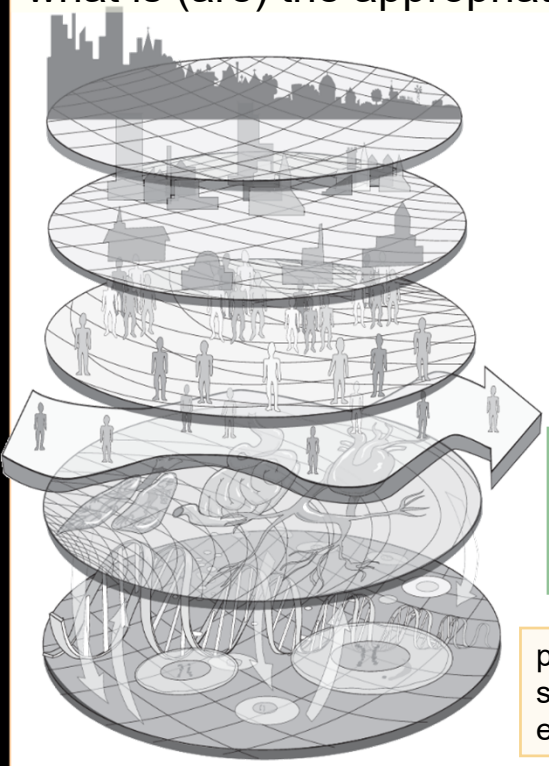
"The concept of the gene as a symbolic representation of the organism — a ***code script*** — is a fundamental feature of the living world and must form the kernel of biological theory. […] at the core of everything are the tapes containing the descriptions to build these special Turing machines." (Sydney Brenner)

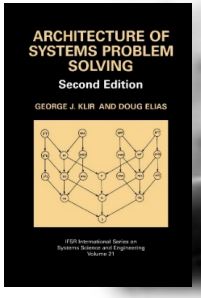


Biologists accept genetic information as a preferred level of explanation (with two levels implied by a genotype-phenotype code)

epistemic/pragmatic nature of mechanism?

what is (are) the appropriate level(s)?





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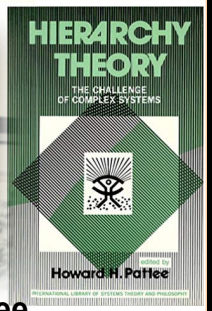


functional (control) hierarchies (especially symbolic codes) establish a “selective loss of detail”.

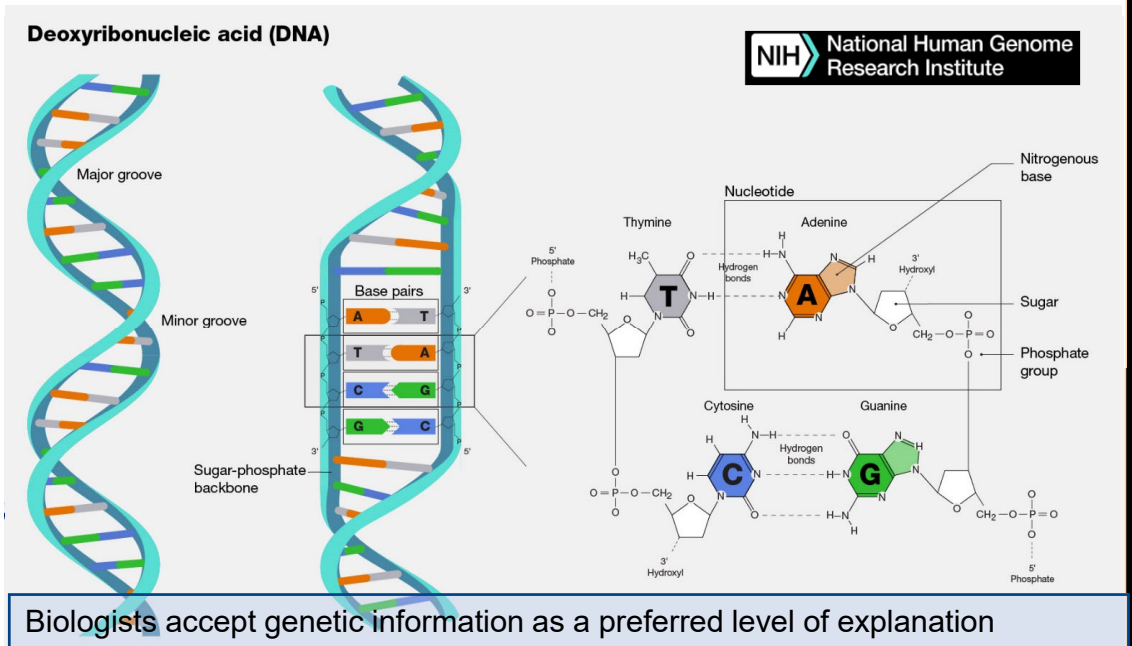
Not the same as near-decomposability because control hierarchies establish non-holonomic constraints.

preferred levels of explanation should not be assumed, but experimentally established

A theory of mechanism is valid if predicted interventions work better than other theories (suggesting ontological nature of theory)

micro-level details below genetic information can be ignored for most functional and evolutionary explanation

epistemic/pragmatic nature of mechanism?



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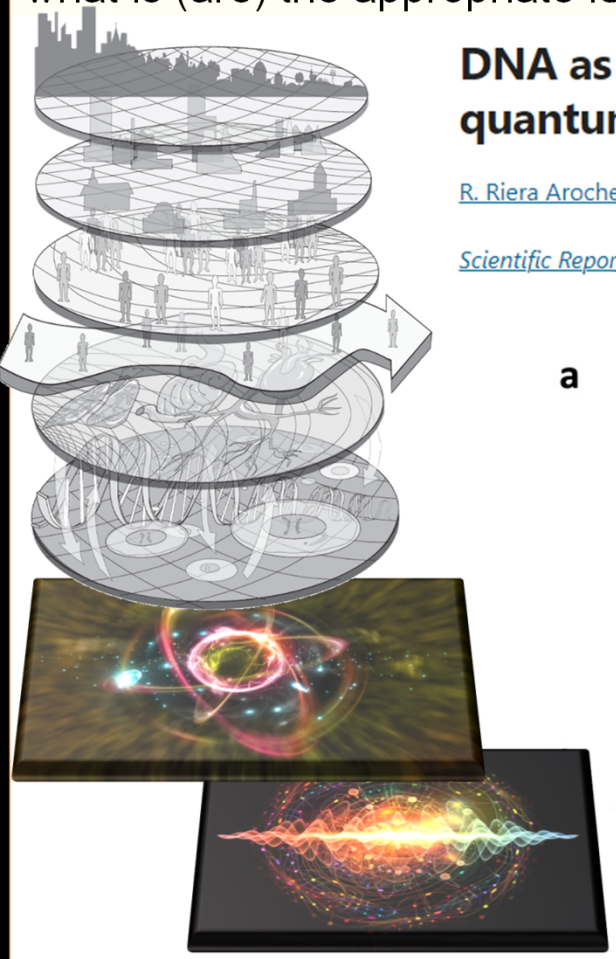


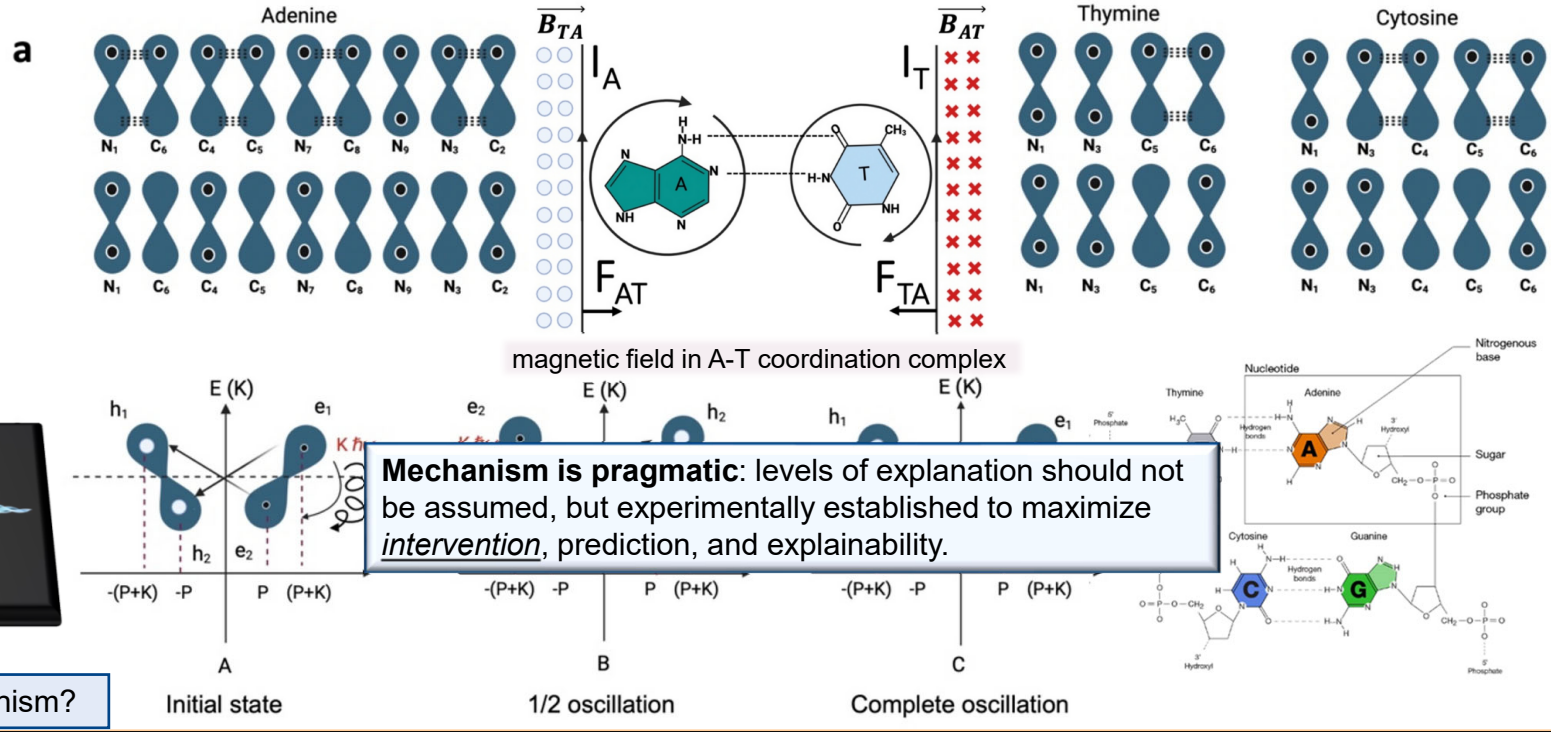
DNA as a perfect quantum computer based on the quantum physics principles

R. Riera Aroche, Y. M. Ortiz García, M. A. Martínez Arellano & A. Riera Leal

Scientific Reports **14**, Article number: 11636 (2024) | Cite this article

micro-level details below genetic information can be ignored for most functional and evolutionary explanation

but lower levels relevant if we are interested, e.g. in DNA as computational memory



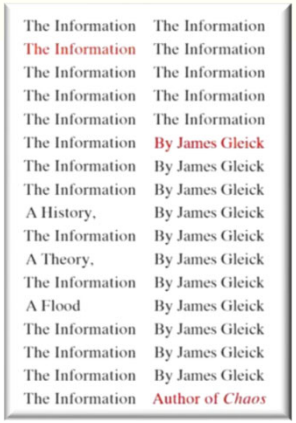
magnetic field in A-T coordination complex

Mechanism is pragmatic: levels of explanation should not be assumed, but experimentally established to maximize *intervention*, prediction, and explainability.

epistemic/pragmatic nature of mechanism?

importance of the “external tape”

In mind and culture



“The spoken symbol perishes instantly without material trace, and if it lives at all, does so only in the minds of those who heard it” (Samuel Butler)

- Written language as external symbols
  - Invention resulted in profound cognitive discontinuity
    - Eric A. Havelock: “The written word—the persistent word—was a prerequisite for conscious thought as we understand it. An irreversible change in human psyche”
  - Walter Ong: “[seeing oral literature as a variant of writing is] “rather like thinking of horses as automobiles without wheels.”
    - “an oxymoron laced with anacronism; (James Gleick)
    - Aleksander Luria studied illiterate people in Uzbekistan: oral people cannot think in oral syllogisms
  - Vocabulary size
    - oral language: a few thousand words
    - written language: well over a million words, grows by thousands of words a year

“Spoken words also transport information, but not with the self-consciousness that writing brings. Literate people take for granted their own awareness of words, along with the array of word-related machinery: classification, reference, definition.” (James Gleick)

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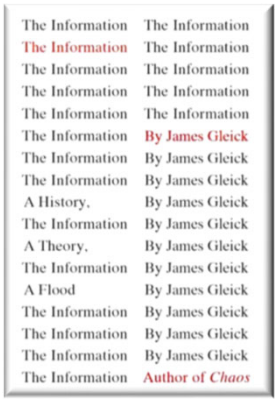
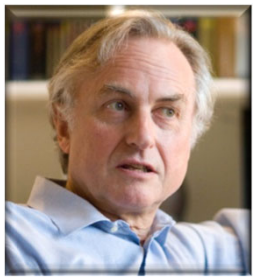
detached “external tape”?

selfish genes and memes as crystals, information in the wild

“Let the whole outside world consist of a long paper tape”. —John von Neumann, 1948



- the replicator (“crystal”) gene and meme
  - Information as its own replicator
    - “The gene has its cultural analog, too: the **meme**. In cultural evolution, a meme is a replicator and propagator (James Gleick)
    - What lies at the heart of every living thing [is] information, words, instructions. […] Think, instead, of a billion discrete, digital characters carved in tablets of *crystal*. — Richard Dawkins (1986)
- Disembodied information
  - Selfish genes and memes as autonomous crystals are a throwback to Schrödinger
    - Dawkins’ gene/meme is not the von Neumann/Turing code nor the molecular biology gene
- semiotic control networks
  - requires code, dynamics, embodiment, interaction, symbolic control of matter,



“The information has been detached from any person, detached from the speaker’s experience. Now it lives in the words, little life-support modules”. (James Gleick)

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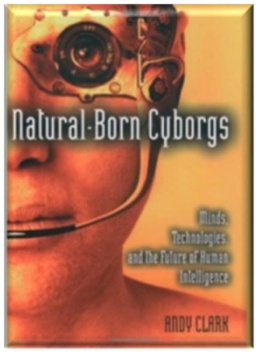
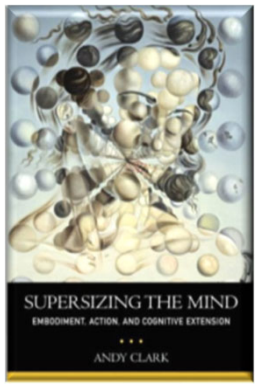
extended (embodied) information

"Let the whole outside world consist of a long paper tape". —John von Neumann, 1948

- Network Semiotic Control (cybernetics)
  - The power of Turing's tape in generating complexity is **coupling** with Von Neumann's constructor
    - With a universal code, ***semiotic control*** can be "plug-and-play"
    - separate but coupled
  - Chalmer's and Clark's extended mind
    - Cognitive science requires both neuroscience and understaning of semiotic coupling with external tape





two roles of information
data/program (Turing)
passive/active (Von Neumann)
description/construction-function (Pattee)
genotype/phenotype (Biology)
language/brain (Cognition)
symbol/society-mind-body (Social)

code

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collective behavior with an external tape

The human mental machinery led our species to have self-awareness but, at the same time, a sense of justice, willing to punish unfair actions even if the consequences of such outrages harm our own interests. Also, we appreciate searching for novelties, listening to music, viewing beautiful pictures, or living in well-designed houses.

However, why is this so? What is the meaning of our tendency, among other particularities, to defend and share values, to evaluate the rectitude of our actions and the beauty of our surroundings? **The human mental machinery obviously refers to the brain, so the answer to the preceding questions must come from neural considerations**. What brain mechanisms correlate with the human capacity to maintain inner speech, or to carry out judgments of value? To what extent are they different from other primates' comparable behaviors?

Cela-Conde, Gutiérrez Lombardo, Avise, & Ayala [2013]. "In the light of evolution VII: The human mental machinery". *PNAS* **110** (Supplement 2): 10339-10342

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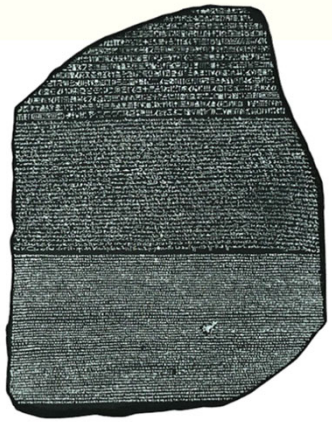
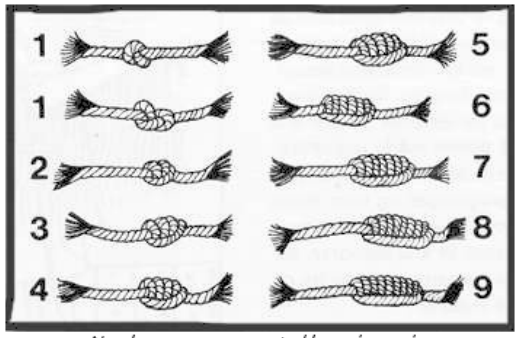
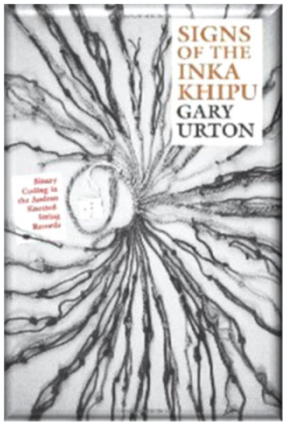


- Semiotic closure in culture is a general principle (system) of evolution of open-ended complexity
  - Are there societies without *writing systems* capable of ***constructing*** complex structures and technology?
    - Brains with symbols are very powerful, but writing systems do not *construct*.
- Brains with tapes
  - Same brains (same genes and biochemistry), different collective behavior via external tape.
  - Does it make sense to study cognition exclusively by looking at the brain's molecular level?



Numbers were represented by an increasing complexity of knots.



Inca Quipus

Urton & Brezine [2005] *Science.* **309** (5737):1065-1067.

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A 5th independent invention of writing?

At least **four independent inventions of writing** are generally recognized:

- Mesopotamia (c. 3400–3100 BCE)
- Egypt (c. 3250 BCE),
- China (c. 1200 BCE),
- Mesoamerica (before 500 BCE)

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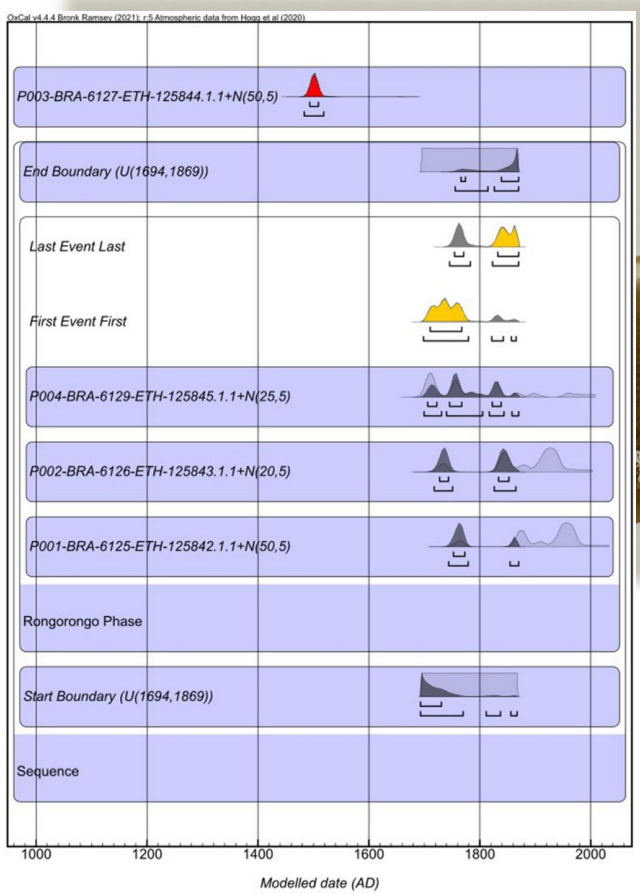
https://www.cabinetmagazine.org/issues/64/mikanowski.php

A 5th independent invention of writing?



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Ferrara et al. *Sci Rep* **14**, 2794 (2024).

https://www.cabinetmagazine.org/issues/64/mikanowski.php

Sam Van Aken

rocha@binghamton.edu
casci.binghamton.edu/academics/i-bic


THANK YOU!
OBRIGADO!