Mathematics in Life, lecture 1 In the process of rewriting and editing

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...combinaisons, d'arrangements, de causes, d'effets, de principes, qui tous concourent au même but, et que nous ne connaissons que par des résultats si difficiles à comprendre. Georges-Louis Buffon, Histoire générale des animaux, 1749.[1]

The principle of continuity renders it probable that the principle of Life will hereafter be shown to be a part, or consequence of some general law.
Charles Darwin, Letter to George Wallich, 1882.

Today, living organisms are seen as the site of a triple flow of matter, energy and information.
Francoise Jacob, The Logic of life 1970. [2]

$$\frac{1}{\pi} = \frac{2\sqrt{2}}{9801}\sum_{k=0}^{\infty}\frac{(4k)!(1103+26390k)}{(k!)^4 396^{4k}}$$

$$= \frac{2\cdot 1103\sqrt{2}}{9801} + \frac{48\cdot 27493\sqrt{2}}{9801\cdot 396^4} + \dots$$

Numbers ↦ Geometry

Probability-by-Numbers

Narrative ↦ Information

Contents

[1] https://www.azquotes.com/author/19916-Georges_Louis_Leclerc_Comte_de_Buffon
[2] Quotes are not to canonise the ideas of their authors but to stimulate our brains.

Abstract

Our objective: *Develop a mathematical language for description of matter-energy-information triple flows and their formal generalisations, which would include, for instance, human languages along with processes of their learning;*

illustrate the "triple flow idea" by biological phenomena potentially describable in such a formal language.

1 Introduction: Numbers, Probabilities, Information, Multiplicity and Complexity of Life

No matter where you look, Life strikes you as mathematically impossible.

For instance, 200 bones in the skeleton of the human body[3] *fit one another* at 350 joints[4] with better than 10% precision. (Shoes fit your feet with 5% accuracy.)

The probability of finding a 10% coherent skeletal arrangement of 200 pieces on a planet anywhere in trillion observable galaxies is below 10^{-100} – virtually zero, while finding a couple of thousand of *almost identical copies* of such a "skeleton" in anyone of 10^{1000} universes predicted by the string theory is *incomparably less probable*. Yet, there are several billion of such skeletons on the single planet Earth. How could it be?[5]

However improbable, human skeleton is a geometrically simple structure, which can be described with a good precision on a few hundred pages. But the *apparent informational complexity* of the cellular/molecular architecture of the human body is beyond the range of any imaginable "library".

One can't describe in details the arrangements of all capillary ($\approx 10^{10}$) in your muscles[6], synaptic connections ($\approx 10^{14}$) in the brain[7] or positions (even less so the functions) of all protein molecules ($> 10^{15}$) in the cells in your body.[8]

Encrypting and transfer of this amount of information from a parent to child seems a hopeless task.

But what makes Life more realistic from the mathematical perspective is an encoding of the *essential part* of this huge ($> 10^{??}$ bits) information on a moderate $\approx 10^9$ bits long molecular string, called DNA. (This "encoding" could

[3] You are born with 270 bones with about 206 remaining in the adulthood. `https://en.wikipedia.org/wiki/List_of_bones_of_the_human_skeleton`.

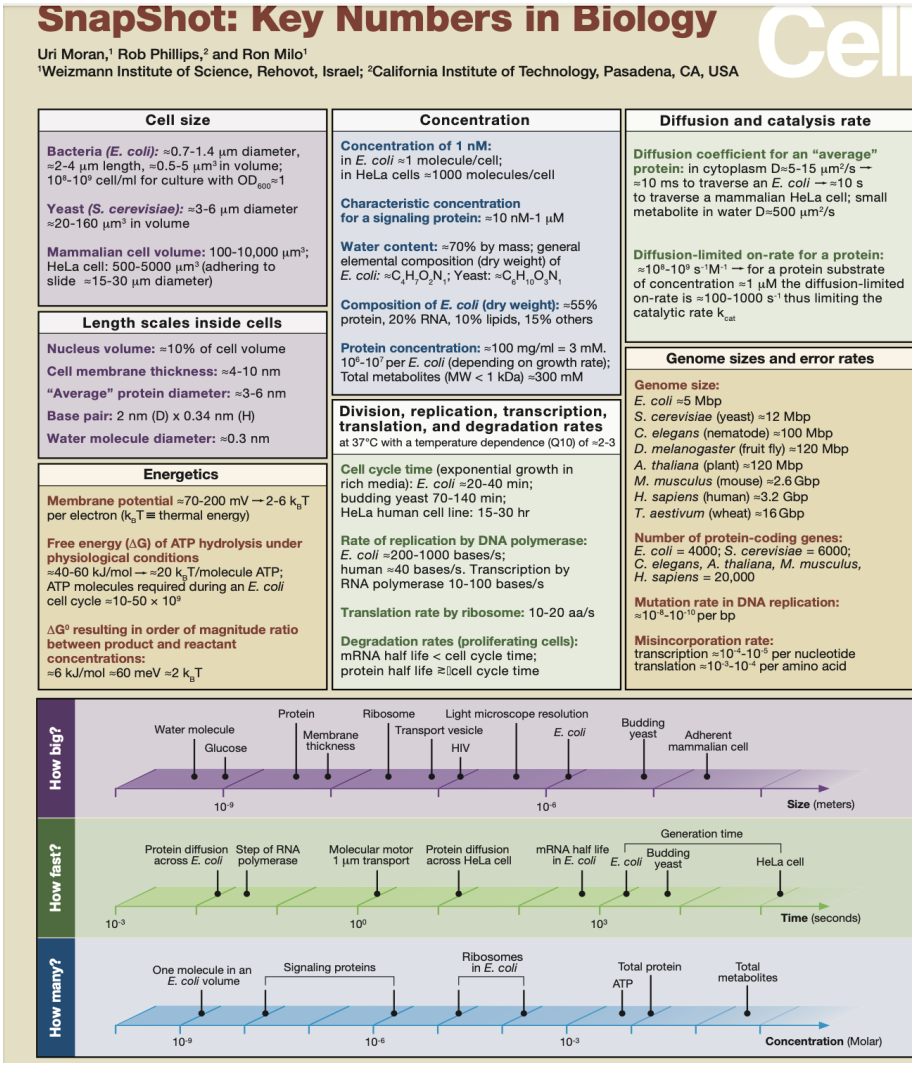
[4] Morphogenesis of joints is beautifully complicated `https://www.sciencedirect.com/science/article/pii/S0945053X14001590`.

[5] Besides, the bones at the joints, all parts of an animal body must be in harmony; this, according to Georges Cuvier (1769-1832), is incompatible with the idea of evolution.

[6] https://www.nature.com/articles/eye199128.pdf

[7] https://www.jneurosci.org/content/27/12/3069

[8] There are more, about $10^{26} \sim 10^{24} = (10^8)^3 10^{26} \sim 10^{24} = (10^8)^3$, of basic small molecules in your body – glucose, amino acids, nucleotides, proteins in the range of 0.5-5 nm ($1nm = 10^{-9}m$).



be not 100% complete even modulo normal stochasticity and the logic of this "encoding" is still insufficiently understood.)

What makes Life actually possible is materialization of the information encoded on DNA, a kind of collection of "programs", by physical/chemical processes run in living systems in (mainly stochastic) environments, which implement these "programs".

Outcomes of these processes are what we see as the positional and functional cellular and intercellular features of cells and organisms, where a (the?) basic transition $information \rightsquigarrow structure$ is implemented by the *protein folding* along with other *programmed self-assembly processes,* which rely on week ($\backsim kT$) molecular interactions and which are reinforced by covalent bonding ($\gtrsim 10kT$) between molecules. and where the logic of some (many? most?) of these "programs" remains unknown.[9]

[9]Description of the basic functions of of these "programs" takes volumes, e.g. see *Alberts*

Bio-specific Terminology. There is no precise mathematical notions, which correspond to the main biological concepts such as

- biological (non-Shannon) information,
- descriptional (non-Kolmogorov) complexity,
- biological structure,
- biological function (performed by a particular strutcture),
- biological purpose (of a function).

To ascribe the meaning to these and similar words one has to incorporate these in a "bio-mathematical" language, which would allow one to speak of the matter-energy-infomation networks, which include:

- $\bullet_1$ information/program *encoded* and *stored by* a material structure,
- $\bullet_2$ information/program, which controls such a "flow",
- $\bullet_3$ biological structures build by (*networks of*) matter/energy flows,
- $\bullet_4$ information/signals *transmitted* by a *matter/energy process/flow*,

where these four are entangled in many selfreferential loops and cycles.

Higher Level Information Structures and Processes. A simple matter-energy-information language may be suitable for mathematically speaking about Life on the basic cellular level, but the logic of the material and informational implementation of the *embryogenesis programs of multicellular organisms* depends on the second level of "information", where the basic level plays the role of the energy/matter on the cellular level.

When we turn to the nervous system and to the *animal muscle-brain signalling processes*, we need to add the third level to the informational hierarchy and then we have to go yet another step higher when approaching information processes, which make the *animal cognition, the human mind,* and *the human language.*

Hopefully, there are resources in mathematic needed for this purpose.

(*Mathematics is the art of giving the same name to different things.* Henri Poincaré)

In what follows, I try to present what little I know of biology in terms suggested by matematical thinking about Life, where, the true bio-mathematical language is yet to be developed.

What is meaning of Life? Phillip Ball in his book *How Life Works* rejects the matter-energy-information description of (multicellular) organisms, especially of animals - *"living entities are generators of meaning"* he says.

Indeed, it is hard to think of a living animal as of a meaningless contraption of matter, energy and information. But what is meaning?

For us, this stands for *mathematical meaning*, where

the meaning of a concept, including "meaning" itself, is defined by (the combinatorial structure of) the class of contexts where (and how) this concept ever comes up.[10]

Accordingly, to get the meaning of a concept/idea in biology, we need to express this idea in a maximally *simple and general* language and then try it

Molecular Biology Of The Cell and Developmental Biology by Barresi- Barresi-Gilbert. I am not qualified to seriously describe and/or classify these "programs".

[10] *The meaning of a word is its use in the language.* Wittgenstein.

out outside biology per se, e.g. when speaking about human cognition, human languages and mathematics itself.

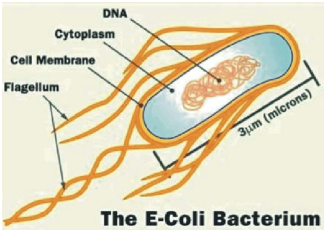
(We shall later explain that this "meaning" is not so far from your intuitive idea of *meaning*, e.g. of *meaning of Life on Earth*, as you may think.)

1.1 Units of Life: Individuality, Multiplicity and Interconnectivity

The Life as we know it (this must apply to any chemically based life in the Universe) is represented by *structurally, functionally and informationally indivisible* individual units, where each unit is present in (improbably) many nearly identical copies, as, for instance, humans on Earth and cells in organs of human bodies.

The basic units of Life on Earth, (the only Life we know of) are cells and organisms, where organisms are composed of cells and where the principle constituents of cells are macromolecules and macromolecular complexes.

The major macromolecules in the cells are heteropolymers: DNA, RNA and proteins (polypeptides).



The basic biological functions of *bacterial cells* are:

• *reproduction by binary fission*;

• *chemical metabolism*, which sustains the reproduction;

• *communication, signalling* and exchange of genetic material as well as fighting with other bacteria;

• *warfare with viruses and other hostile entities, e.g. immune systems agents of bacterial hosts* .

⋆ *Chemical metabolism* includes in particular:

cellular respiration by oxidation of nutrients,
synthesis of macromolecules, such as DNA, RNA and mainly of proteins,
degradation of macromolecules (including *foreign* DNA),
repair of the native (chromosomal) DNA.

These processes, especially the macromolecular synthesis, which is assisted by *molecular motors*, are more than a mere chemistry and they are accompanied on the next level by:

⋆⋆ *Assembly of sub-cellular molecular structures* and production of *new copies* of cells.

There also several types of non-cellular units with specific informational individualities (encoded by DNA or RNA), which are able to replicate inside host cells.

Some of these permanently live in cells:

◦ *Mitochondria and plastids*, inhabitants of *eukaryotic*[11] cells.

[11] All organisms are divided into *prokaryotes* and *eukaryotes*; (most) prokaryotes are unicellular and are classified into *bacteria* and *archaea* (superficially, these looks like bacteria), while eukaryotes can be both, unicellular, e.g. amoebas, paramecia and yeasts (unicellular fungi) and multicellular: plants, animals and (some) fungi. Eukaryotic cells are structurally more

∘ *Plasmids*: small (~ 10^3- ~ 10^5 base pairs) circular DNA found in bacteria and other unicellular organisms.[12]

∘ *Transposons:* segments of the cellular DNA able to produce their own copies at new locations in DNA.[13]

Also there are non-cellular entities – *viruses, satellits, viroids, obelisks*, which invade and often destroy cells in order to reproduce.

• *Viruses* are nucleic acid molecules surrounded by protective coats of protein. They come in different kinds, structures and overall complexities, where their volumes may range from ~*thousand* to *hundred million* cubic nanometers.

Examples *Tobacco mosaic virus*: single-stranded RNA 6400 nucleotides, 30×300nm rode shaped.

Pandora virus: double stranded DNA, 2 8000 000 base pairs, 500×1000nm.

• *Satellits* are small viruses which depend on other viruses to infect cells.

• *Viroids*, which infect plants and *Obelisks* (discovered in 2024 in human stool and saliva samples) are very small circular RNA molecules (~200 - ~1000 nucleotides) able (this is hard to believe!)) to penetrate and replicate in cells.

On the other side of the spectrum, there are larger than organisms functionally and/or informationally but not geometrically connected units:

⊛ *colonies*, e.g. ants in an ant hill,

⊛ *communities*, such as a coral reef community or the microbial community in your guts,

⊛ (interbreeding) populations of given *species*[14] e.g. rabbits in Australia.

Basic (but not the only) directed binary relations between individual (specifically space-time positioned) organisms (as well as other units and/or classes of units) are

▶ *parent* → *progeny*. The (suitably modified/factorized clusters, e.g. components of the) graphs of these define species as well as evolution trees of species.

▶ *trophic* relation: *who eats whom* (including pollination and parasitism)[15]. These define the ecological food-chains.

1.2 From DNA to Proteins in the Cell

A typical bacterial cell, a couple of microns ($1\mu = 10^{-6}$m) in diameter, contains a *distinguished* long (double stranded) chain molecule –DNA – "aperiodic crystal" envisioned by Schrödinger in 1945[16].

This is a randomly looking. (circular) string of *a few million* (pairs of) "molecular letters" A,T,C,G "written on" the (periodic) *sugar-phosphate backbone.*[17]

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elaborate and usually larger than bacterial cells. All eukaryotic cells contain mitochondria; plastids, which are responsible for *photosynthesis*, are present in plant cells.

[12] `https://en.wikipedia.org/wiki/Plasmid`

[13] There are also non-nuclear acid molecules with a similar property, called *Prions* that are particular (abnormal?) conformations of certain proteins that can "imprint" their conformations on normally folded proteins of the same kind.

[14] "Species" is usually understood as a *class* of such populations,

[15] https://academic.oup.com/biolinnean/article-abstract/141/2/214/7256006

[16] The idea can be traced to the Three-Man Paper (1935) by Timoféef-Ressovsky Zimmer and Delbrück and earlier experiments by Timoféef-Ressovsky and Müller. `https://link.springer.com/content/pdf/10.1007/1-4020-4956-0_1`

[17] DNA – *deoxyribonucleic acid* in the cell is a double stranded heteropolymer composed of

DNA is a "master-molecule",[18] a 1-*dimensional* keeper of digitally stored *inheritable genetic information*, – a set of instructions/programs/laws[19] for the cell to fulfil it's functions:

Proteins. A protein chain, also called called *polypeptide*, is a molecular string of several hundred[20] *amino acids* of 20 types.[21]

Such a chain P is synthesised in the bacterial cell following blueprints of P "written" on a segment[22] $S = S(P)$ of DNA, where each amino acid is represented by several *triplets* of nucleotides, called *codons.* [23]

This representation, that is a particular (partially defined) map

$$code_{\mathbf{E}} : \mathcal{B} \times \mathcal{B} \times \mathcal{B} \to \mathcal{A},$$

where $\mathcal{B} = \{A, T, C, G\}$ is the set of 4 base letters in DNA and $\mathcal{A}$ is set of 20 amino acid letters,[24] is called **the genetic code**. This code is the trademark of the Life on Earth – all organisms use the same code. [25]

Newly synthesised polypeptide chains turn in *functional proteins* by (more or less) spontaneously *folding* to closely packed three-dimensional shapes.[26]

There is a fundamental logical difference between the *translation* (via mRNA) of the "text" encoded in DNA in $\mathcal{B}$ letters to the $\mathcal{A}$-alphabet of a polypeptide string and the *transition* from the latter to a particular geometric shape.

The former is formally simple – all what is in there amounts to the "dictionary" $\mathcal{B} \times \mathcal{B} \times \mathcal{B} \to \mathcal{A}$. (Never mind the reliance of this implementation on sophisticated programs encoded in DNA and on elaborated physical/chemical processes – *transcription DNA* $\rightsquigarrow$ *mRNA, aminoacyl-tRNA synthesis, ribosome assembly, translation,* which "materialise" these programs.)

On the contrary, the folding of a polypeptide chain requires no particular effort on the part of the cell: the dynamics of the folding process is taken care of by purely physical forces – the weak interactions between *amino acid residues*[27]

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pairs of four *nucleotides*, made of one of the four *bases* **A**denine, **T**hymine **C**ytosine, **G**uanine, a *phosphate group* and a a five-carbon sugar molecule *Deoxyribose*, 50-60 atoms in a nucleotide.

[18] Some people disagree, e.g. Peter R. Wills who says that *DNA is being deposed from its role as the Master Molecule to that of an information-carrying servant of quasi-autonomous molecular biological processes* `https://royalsocietypublishing.org/doi/10.1098/rsta.2015.0066`

[19] DNA-sequence, similarly to a "physical law" is shared by (almost) all cells of a given type and it is conserved under all cellular process including the binary fission of cells.

[20] *Insulin* is composed of 51 amino acids and *titin*, of ≈ 30 000 amino acids.

[21] Alanine, Arginine, Asparagine, Aspartic acid, Cysteine, Glutamic acid, Glutamine, Glycine, Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Proline, Serine, Threonine, Tryptophan, Tyrosine, and Valine.

Besides, some (human) proteins include *Selenocysteine* and some (non-human ones) need *l-Pyrrolysine.*

[22] It may be several disjoint segments in a *eukaryotic* cells.

[23] For instance, the codons for *alanine* C3H7NO2 are GCT, GCC, GCA, GCG, the codons for *cysteine* C3H7NO2S are TGT, TGC, and the codon for *tryptophan* C11H12N2O2 is TGG. `https://en.wikipedia.org/wiki/DNA_and_RNA_codon_tables`.

[24] Three out 64 codons in $\mathcal{B} \times \mathcal{B} \times \mathcal{B}$ are used by cells for other purposes.

[25] There are exceptions, e.g. in DNA of *mitochondria* and *plastids*, `https://medicine.jrank.org/pages/2292/Genetic-Code-Exceptions-Universal-Genetic-Code.html`.

[26] Folding may be partial or none at all: `https://en.wikipedia.org/wiki/Intrinsically_disordered_proteins`, `https://pmc.ncbi.nlm.nih.gov/articles/PMC9693201/`.

[27] Joining amino acids in a polypeptide chain is accompanied by removing a water molecule borrowing from an amino group (–NH2) of one amino acid and a carboxyl group (–COOH) of the adjacent amino acid. What remains are called amino acid *residues*.

in the chain. But the actual production of the map [sequence] $\mapsto$ [form] remains a black box magic.

Roughly, the original randomly spread configuration of the polypeptide molecule moves to a folded shape driven by the gradient of the total energy of these interactions, where all this happens in the medium of the *cytoplasm in the stochastic state of Brownian motion.*[28].

Physicists, who unlike the cell itself are limited in their understanding of intracellular environment, can evaluate the inter-residue interactions *only approximately* and they have a limited picture of the physical properties of cytoplasm on the molecular level.[29]

But even granted the full knowledge of the inter-residue and residue-cytoplasm interactions a computational modelling of zillions of steps of the folding process remains beyond the range of modern computers.

The cell, however, folds most of it's proteins in several millisecond time; this is possible due to special features of the $\mathcal{A}$-sequences of the extant proteins, which were evolutionary selected to folds fast, properly and, moreover, to serve the *functions they were meant to perform.*

This biological specificity brings the folding problem further away from the province of physical (and practical mathematical) science: there is no means in physics to determine how a protein performs it's function in molecular details and even less so to figure out what this function could be.[30]

RNA. These are molecular chains composed of four *ribonucleotides*, where the bases are similar to A,T,C,G. These chains, which serve several different functions in the cell, are assembled by templating segments of DNA.

For instance, (**m***essenger*) mRNA molecules, serve as "scripts" for assembly of proteins. [31] The assembly is performed by large (20-30 nm) macromolecular complexes- *ribosomes*, (composed of proteins and RNA), which cooperates with other proteins and RNA, by a chemically/physically elaborated process, called *translation*.

The information encoded by triples of letters in mRNA (with inevitable loss of Shannon information for $20 < 64$) from the set $\{A, T, C, G\}^3$ to the set of twenty "amino-acid-letters" augmented by signs of "start" and "stop" instructions for translation.

Each amino acid according to this map is coded by several *codons* that are *triplets of the base-letters*. For instance the codons for *valine* C5H11NO2 are GTA, GTG, GCT.

(The genetic code is unusual in that it codes for its own translating machinery[32]. Besides, unlike how it is in the macroscopic world, the protein made by the "script" written in the A,T,C,G-letters is ten times lighter than the weight of the letters in this "script", since nucleotides are about 3 times heavier than

[28] We mean here the jelly-like substance filling the cell. `https://www.sciencing.com/cytoplasm-definition-structure-function-with-diagram-13717294/`.

[29] `https://www.sciencedirect.com/book/9780128096765/protein-physics`.

[30] However, the biological specificity of folded proteins made the problem approachable by the bioinformatic methods combined with the machine learning techniques, https://en.wikipedia.org/wiki/AlphaFold.

[31] Bacterisl mRNA are on the average ~1 000 nucleotides long, they are short-lived (not only in bacteria) and their numbers in cells are thousand time smaller than that of proteins. `https://book.bionumbers.org/how-many-proteins-are-made-per-mrna-molecule/`

[32] John Maynard Smith,*The Concept of Information in Biology* 2000

amino acids.)

Cell Membranes. The *metabolic autonomy* (and individuality) of all cells are sustained by the outer *plasma membranes* that limit diffusion of certain molecules in and out of the cell,[33], while the physiologies of eukaryotic cells depend on a dense networks of internal membranes.

Comparison with Languages. *Functional purpose* of linguistic units – words, phrases, sentences – in texts in natural languages is as significant for formal analysis of texts as it is for the study of cells and macromolecules in living entities.

In both cases, we want to visualise the colored network (graph or hypergraph) defined, besides *positional and compositional similarities*, by the "spectra" of binary (possibly, non-binar) relations of *cofunctionalities* and of corresponding *functional similarities.*

1.3 Cell Metabolism of Matter, Energy and Information

The main participants of cell metabolism are

water molecules,

several kinds of metal ions, mainly Na+, K+, Ca2+, Mn2+, Mg2+, Fe2+.[34],

hundreds of different kinds of small molecules (amino acids, lipids, sugars, ATP, H2O2,...)[35],

a few macromolecules: DNA, RNA, proteins, polysaccharides as well as macromolecular complexes of these, such as ribosomes, microtubule and other parts of the cytoskeletons in eukaryotic cells, membranes etc.

the main "matter-energy flows"

⋆ *chemical metabolism* within cells,

⋆⋆ *production* of new cells, sub-cellular molecular structures and multicellular organisms.

The main observable transfer of information is inheritance of traits by offsprings: phenotypic features pass from parents to children. This depends on what happens on the molecular level.

Central Dogma. *I shall... argue that the main function of the genetic material is to control (not necessarily directly) the synthesis of proteins.* Francis Crick, 19 September 1957 [36]

The central dogma of molecular biology deals with the detailed residue-by-residue transfer of sequential information. It states that such information cannot be transferred back from protein to either protein or nucleic acid. Crick 1970[37]

In multicellular organisms (but not in bacteria) this is manifested by the presence of *Weismann barrier*: germ cells are separate from somatic cells.

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[33]For instance H_20, O_2, CO_2 and small *hydrophobic* molecules easily diffuse across phospholipid bilayer but the transport of ions and large molecules, such as sugars and amino acids relies on specific proteins embedded in the membrane `https://www.ncbi.nlm.nih.gov/books/NBK9847/`

[34]`https://book.bionumbers.org/what-are-the-concentrations-of-different-ions-in-cells/`.

[35]`https://nerd.wwnorton.com/ebooks/epub/ecb6/EPUB/content/2.2-chapter02.xhtml#`

[36]`https://journals.plos.org/plosbiology/article?id=10.1371%2Fjournal.pbio.2003243`

[37]`https://en.wikipedia.org/wiki/Central_dogma_of_molecular_biology`.

The template could consist of perhaps a single chain of RNA. . . . Each adaptor molecule [tRNA]... ... would each be joined to its own amino acid by a special enzyme. ... then ... attach to the proper place on the basis of the RNA by base-pairing.

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... before long we shall have ... 'protein taxonomy'—the study of the amino acid sequences .... vast amounts of evolutionary information may be hidden away within them.[38]

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[38] https://pmc.ncbi.nlm.nih.gov/articles/PMC5602739/.

1.4 Order from Disorder– Chick from an Egg.

Do you see this egg? ...How is this mass to make a transition to a different structure, to sentience, to life? Through heat. And what will produce that heat in it? Motion. Conversation Between D'Alembert and Diderot[39]

When kept mildly warm for three weeks, an eggs "spontaneously transforms" to a chick. Since the chemical reactions in the embryogenesis are exothermic – the egg loses heat, the entropy does increase. Yet, if you judge the probability of such a transformation by a few random samples of the *fully amorphous* material inside the egg, this will strike you as magic – as likely to happen as *a tornado sweeping through a junkyard might assemble a Boeing 747 from the materials therein.*[40]

Discussion. If the structure of an egg were truly amorphous – stochastically (quasi)-*homogeneous* on all scales, then an emergence of anything like a chick would be virtually impossible (probability $<< 10^{-100}$) for two related reasons.

1. *Break of Symmetry.* To make sense of this, one has to mathematically describe/define admissible (quasi)symmetry transformations of the egg material – yolk[41]and white [42] and of symmetries preserving mathematically formalized physical/chemical dynamics of the (short term) temporal evolution of this material. (Beware of symmetry breaking in Turing's diffusion reaction and similar equations.[43])

2. *Increase in Complexity.* The descriptional complexity of the *probability law*, which describes the egg material, is much less than what is, conceivably, needed to describe a live entity, such as a chick, for example.

(This complexity is related to symmetry. For instance, periodic structures, such as crystals, and maximally random ones, such as sequences of *independent* random 0-1 numbers, have minimal descriptional complexities.)

Remark on Abiogenesis and Selection. It may seem that 1 and/or 2 are incompatible with abiogenesis and evolution by natural selection on Earth.

But the appearance of a contradiction, besides a difficulty of intuitive assessment of the scale of the space-time-complexity difference between an egg and the Earth, is due to confusion between "random law", which is a purely mathematical concept and "random sample" which manifests such a "law" in the real world.

Back to the egg. What makes the egg → chick transition possible is a presence of *something* inside the egg comparable in the *information complexity* to that of a chick.

This something is located inside a large 0.1 millimetre in diameter cell – *the chicken zygote*,[44] which contains 156 heteropolymeric DNA molecules in the 78

[39] https://en.wikiquote.org/wiki/Denis_Diderot

[40] This is how Fred Hoyle's characterized the probability of emergence of life from the primordial soup on early Earth.https://en.wikipedia.org/wiki/Junkyard_tornado

[41] https://scijournals.onlinelibrary.wiley.com/doi/10.1002/jsfa.6247
https://www.sciencedirect.com/science/article/abs/pii/S0308814621005756

[42] https://en.wikipedia.org/wiki/Egg_white
https://www.sau.edu.bd/uploads/pdf/dept/class_lecture/24_2020-08-11_5f32f9c652b9a.pdf

[43] https://en.wikipedia.org/wiki/Turing$_-$pattern

[44] https://pmc.ncbi.nlm.nih.gov/articles/PMC11104987/

chromosomes within the *nucleus*[45] of the zygote. (This is tiny on the egg scale and it will be missed by random sampling.)

The information-to-structure transform DNA $\overset{\text{egg}}{\rightsquigarrow}$ chick is *guided by the information encoded in this very DNA* (complemented by that in the mitochondrial DNA and by a few additional bits of epigenetic information), and *driven by physical/chemical forces* in accordance with (statistical) rules of the molecular physics.

The properties of this forces *faithfully abide by* the (statistical) *rules* of the molecular physics; yet, the processes run by these "forces" c̀an't be faithfully described in terms of physics. What we hope for, however, is that. there is a sufficient level of universality in the properties of such transforms that would make a mathematical parlance about them possible.

Non-chromosomal Information in the Egg. In addition to the chromosomal DNA, an essential information is contained in the (maternal) mitochondrial DNA (about 15 000 bp in size;[46]) in the zygote.

Besides, the zygote contains maternal and paternal RNA and protein molecules, but the information carried by these can be, "in principle", reconstructed from what is encoded on DNA.

Also there are *epigenetic markers* on *chromatin* (I am not certain if there are some on the DNA of fertilized zygote per se) but (???) the amount of the *independent* information remained in the markers after *epigenetic reprogramming*[47] seems *minuscular*. (Many biologists think otherwise and I am ready to admit my ignorance on this subject matter.)

On Soft and Rigid Information.....

1.5 Mathematics of Darwin: Return to Common Sense

I have taken some pains to estimate its probable minimum rate *of natural increase; it will be safest to assume that it* [elephant] *begins breeding when thirty years old, and goes on breeding till ninety years old, bringing forth six young in the interval, and surviving till one hundred years old; if this be so, after a period of from 740 to 750 years there would be nearly* nineteen million *elephants alive descended from the first pair.*

This is written by Darwin in section Geometrical Ratio Of Increase in *"On the Origin of Species"*[48] first published in 1859 (following the 1858 Darwin-Wallace paper[49]) to exemplify the *mathematical* idea *that every organic being naturally increases at so high a rate, that, if not destroyed, the earth would soon be covered by the progeny of a single pair.*

The kind of errors made in this computation[50] (which don't undermine the idea behind it) illustrate (this is also seen in other Darwin's writings) Darwin's conceptual style of thinking – not lost in details, but focused on the general principles. The conceptual/mathematical/philosophical mode of thinking and

[45] This is ~O,01 mm in size.

[46] I couldn't find the exact number on the web.

[47] `https://pmc.ncbi.nlm.nih.gov/articles/PMC5097126/`

[48] p.72 `https://ecologia.ib.usp.br/ffa/arquivos/abril/darwin.pdf`

[49] `https://www.zoology.ubc.ca/~bio336/Bio336/Readings/DarwinWallace.pdf`

[50] The Fibonacci formula for Elephants is written in `https://link.springer.com/article/10.1007/s10739-017-9488-5`

expressing his ideas made Darwin the main 19th century figure in shaping *the mechanical view of nature* [of Life] in the words of Boltzmann:[51]

If you ask me about my innermost conviction whether our century will be called the century of iron or the century of steam or electricity, I answer without hesitation: it will be called the century of the mechanical view of nature, the century of Darwin.

(I wonder, what Boltzmann would say if he had read Mendel's 1866 paper.)

It is nearly impossible for a 21st century mathematician to understand why the description of evolution in terms of selection (as outlined below) is hailed as "a revolutionary groundbreaking theory"...

In fact, Patrick Matthew (fruit farmer and forester rather than a professional mathematician), who articulated this idea in 1831[52], writes:

To me the conception of this law of Nature came intuitively as a self-evident fact, almost without an effort of concentrated thought.[53]

But Buffon, who was no less a mathematician than Darwin, couldn't understand the meaning of the cruel cut-off of most branches of the *imaginary mathematical trees* of exponentially reproducing populations.

What purposes then are served by this immense train of generations, this profusion of germs, many thousands of which are abortive for the one that is brought to life?

Buffon would answer himself IF he had replaced "purposes ... served" by "evolutionary roles played", but... he knew better than to speak openly in the face of the French church: *It is better to be humble than hanged.* [54] We can only guess what his true ideas on evolution and the origin of Life were.

The fear of being hanged had kept the evolution ideas dormant until 19th century.,[55] But these ideas, along with the idea of atoms, were common among educated people two thousand years ago.

.....And in the ages after monsters died,
Perforce there perished many a stock, unable
By propagation to forge a progeny. ...
Titus Lucretius, 50 BCE.[56]

Evolution by Selection: Biased Random Walk in the "Cube of Life and Death".

[51] https://www.smithsonianmag.com/science-nature/hidden-connections-between-darwin-and-physicist-who-champione
See more on the relations of the ideas of Darwin and Boltzmann in https://www.sciencedirect.com/science/article/pii/S0370157313001191
file:///Users/mgromov/Downloads/344-Boltzmann_and_Darwin.pdf

[52] There is a controversy, often politically coloured, on authorship attribution of this idea.

[53] https://victorianweb.org/science/matthew/evolution.html https://academic.oup.com/biolinnean/article/115/4/785/2530994

[54] https://www.strangescience.net/buffon.htm

[55] A evolutonary picture of the natural world was proposed by Lamarck in 1801 and published in his 1809 book "Philosophie zoologique" (see
https://www.encyclopedie-environnement.org/vivant/lamarck-darwin-deux-visions-divergentes-monde-vivant/).
But even at the early 19th century, an argument for spontaneous generation of parasitic worms, was that carrying representatives of all species of parasitic worms on Adam's body wouldn't be in harmony with life Eden. (see J. Frley, *The Spontaneous Generation Controversy (1700-1860) : The Origin of Parasitic Worms*, https://link.springer.com/content/pdf/10.1007/BF02113487.pdf

[56] http://infomotions.com/etexts/philosophy/100BC-1BC/lucretius-on-395.htm

Imagine an organism P (the phenotype of which is) characterised by N (observable) numerical features[57] $0 \le f_i \le 1$, $i = 1, 2, ..., N$, and represent P by a point in the unit N-cube $[0,1]^N$. [58]

For instance, if f_i represent certain parameters of *all cells* in an animal P, this N is huge, more than 10^{11} times *kg-weight* of P, while the realistic number N of *evolutionary essential* features, say of a human organism, is much smaller: judging by the number of the protein coding genes, the number $N = N_{essen}(human)$ must be between 10^4 and 10^6.

Evolution in these terms is a *biased random walk.* where the bias is defined by the *fitness function* $R(P)$, $P \in [0,1]^N$, which represent the *reproductive success* of P.

Problems

1. Find what the features f_i are, or, at least, evaluate their number N.

2. Evaluate the function $R(P) = R(f_1, ..., f_n)$ and/or describe, at least approximately, the subset $\mathcal{L} \subset P$ of reproducing (potentially living) organisms L, i.e. where $R(L) > 0$. For instance estimate the dimension $dim(\mathcal{L})$ in the form $d(\mathcal{L}) = \lambda N$ for some positive constant "Life exponent" $\lambda > 0$.

The main information about $\mathcal{L}$ comes from what we know of the actual organisms composing the (full) *evolutionary tree of Life* embedded to $\mathcal{L}$. Also there are theoretical constrains on $\mathcal{L}$ based on physical and chemical considerations.

3. Find probabilities of transitions $P_1 = P_{parent} \to P_2 = P_{child}$ for all (many) $P_1 \in \mathcal{L}$.

4. Granted 1, 2, 3 evaluate the expected number of generations leading from one subset in $\mathcal{L}$ to another one, that is an evolution of species $\mathcal{L}_1 \rightsquigarrow \mathcal{L}_2$.

1, 2, 3 are difficult biological problems; one is satisfied by making reasonable conjectures.

The problem 4 is a mathematical one; one tries to solve it conditionally modulo possible solutions to 1,2,3.

For instance, if you take $N = 10^5$-10^6, you would expect, as Darwin did, that the evolutionary time must be counted in millions, tens or even hundreds of millions of generations; this agreed with what Darwin knew from his friend Leyll: geology of Earth suggested the age of several hundred of millions, even billions years.

Physicist Kelvin Thomson, who relied on an Earth's heat loss model, estimated the age of Earth by 20-100 million years.[59] and a similar estimate of ~20 million years was obtained by Newcomb and by Helmholtz by evaluating the amount of heat of the Sun derived from its gravitational contraction.[60]

Exceptionally in the history of science, an insight by a natural philosopher (based on the idea of evolution-by-selection and partly supported by geological

[57] Real numbers do not always adequately represent biological features, but they are, I think, what Darwin's an Wallace's had in mind speaking of evolution by *smal* modifications of organisms.

[58] We freely switch from trees to cubes despite arXiv:math/9902116.

[59] This model din't take into account convection in the Earth mantle, `https://www.americanscientist.org/article/kelvin-perry-and-the-age-of-the-earth`. Earlier, Buffon evaluated the age of Earth by *linearly* (rather than correctly quadratically) extrapolating the time of cooling of cannon balls, `https://comptes-rendus.academie-sciences.fr/geoscience/item/10.1016/j.crte.2017.08.002.pdf`.

[60] The nuclear fusion was discovered half century later`https://en.wikipedia.org/wiki/Nuclear_fusion`

data) has led to an essentially correct result unlike two independent mathematically rigorous arguments by great physicists. (The current estimate of the age of Earth is 4.6 billion years, `https://en.wikipedia.org/wiki/Age_of_Earth`.)

Philosophical Remarks. The concept of natural selection (as it was understood in the 19th century) is a logically convincing starting point of thinking about evolution in rational terms, [61] but not what is commonly called "theory" in science , e.g. in physics or in genetics.

Taken per se, idea of "natural selection" doesn't explain evolution. This can be compared to what Democritus' idea of atoms[62] could do with the *stability of matter* problem [63] or with how the idea of differential equations serves for explanation of motion without correctly(!) guessing (discovering) a particular equation adequate to a given situation.

Evolutionary Metaphors

Climbing Mount Improbable,
branching rivers flowing uphill,
forces of selection and forces of banks which keep/direct flows (pre Aristotle idea of force),
selfish gene.

Metaphoric "force of natural selection" has nothig to do with the mathematical concept of force in physics and "the fittest survives" can't be compared to the second law of motion $x'' = const \cdot force/mass$ as some people do.

To see this, assume the layman knowledge about the Sun the Earth plus the distance to the Sun – ~150 000 000km, (measuring it is non-trivial). Use the second and the third ($force = const \cdot mass_1 \cdot mass_2/dist^2$) laws of motion and thus estimate the temperature at the centre of the Sun: $\sim 2 \cdot 10^7$ °C. Then try something of the kind with what "the fittest survives" adds to the common knowledge about Life.

Do this exercise and you'll see by how far in the sky $x'' = const \cdot force/mass$ is positioned relative to "the fittest survives".

Evolution by selection idea is easily accepted and absorbed by an unprejudiced mind of a six year old child. But the Newtonian laws of motion contradict our innate mechanical intuition. I think a simple experiment : *"blink"* exactly *when it hits the ground* (behind the screen) would show that majority of (21st century) people expect heavy object to fall faster than light ones.(This not for fear of being hanged, but for fear of being hurt by something heavy falling on your head.)

1.6 Mathematics of Mendel: Atoms of Inheritance

The striking regularity with which the same hybrid forms always reappeared whenever fertilization took place between the same species... Gregor Mendel 1865.[64]

[61] Thomas Huxley: "...*how extremely stupid not to have thought of that*".

[62] `https://flexbooks.ck12.org/cbook/ck-12-middle-school-physical-science-flexbook-2.0/section/3.11/primary/lesson/democrituss-idea-of-the-atom-ms-ps/`

[63] `https://en.wikipedia.org/wiki/Stability_of_matter`. Daniel Kastler told me about 30 years s ago that this problem was brought up by Napoléon Bonoparte in his conversation with members of the French Academy, but I couldn't find a reference to this on the web.

[64] `http://www.esp.org/foundations/genetics/classical/gm-65.pdf`

This was the second main step toward understanding Life after the discovery of infusoria by Antonie van Leeuwenhoek in 1674.[65] (The third step is yet to come.)

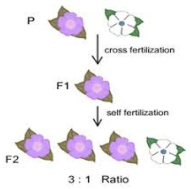
Both Leeuwenhoek and Mendel were hard experimental workers. Mendel cultivated and tested ~30,000 plants and the main Mendel's tool was his mathematical mind eye; his vision penetrated a deeper level of the substance of Life then the spherical lens ×300 microscope of Leeuwenhoek.[66]

Applied on the average, Mendel's laws lead to the following prediction (undoubtedly known to Mendel).

Plant a thousand flowers of the same species in you garden, 500 red and 500 white ones. The flowers pollinate each other on random, you seed them the next year and nowthe proportion of red:white flowers is (approximately) 750:250=3:1

The exponential nature of the common sense "fittest survives" law makes you think that the proportion on the third year will be about $9:1$, and in 10 years no white flower will remain.

But the counter intuitive(!) Mendel law tells you that the proportion $\sim 3:1$ will remain generation after generation (essentially) unchanged.



At the turn of the 20th century when Mendel's ideas were (re)discovered, Darwinian biologists felt uncomfortable with the mathematics behind these ideas. Then an English mathematician G. H. Hardy and a German physician Wilhelm Weinberg had rewritten the above as an identity equivalent to the following.[67]

$$\frac{\big((p+q)^2+(p+q)(q+r)\big)^2}{((p+q)^2+(p+q)(q+r))\cdot((p+q)(q+r)+(q+r)^2)}=\frac{(p+q)^2}{(p+q)(q+r)}$$

https://en.wikipedia.org/wiki/Peppered_moth_evolution

This *mathematics of the multiplication table type* (Hardy's words) was algebraized by S. Bernstein in 1942,[68] where the class of (non-associative) Bernstein algebras includes those introducd by the German physisist Pascual Jordan in 1933.[69]

[65] https://royalsocietypublishing.org/doi/10.1098/rstb.2014.0344

[66] https://pmc.ncbi.nlm.nih.gov/articles/PMC9295954/.

[67] https://www.science.org/doi/pdf/10.1126/science.28.706.49?casa_token=Tf8FdWJrsCsAAAAA:EzZBiU0ikRRjFqxXahpd3doga8BbunWVu95YIwlFwLxpVFbetBEc_rAvmQLooBdjVmnQlFGtgt-yFVw

https://pmc.ncbi.nlm.nih.gov/articles/PMC2475721/.

[68] https://projecteuclid.org/journals/annals-of-mathematical-statistics/volume-13/issue-1/Solution-of-a-Mathematical-Problem-Connected-with-the-Theory-of/10.1214/aoms/1177731642.full

https://encyclopediaofmath.org/wiki/Bernstein_algebra

https://arxiv.org/pdf/2203.13627v3

[69] https://en.wikipedia.org/wiki/Jordan_algebra

The simplest (linear algebraic form of the) Mendel *next generation map*, that is the transformations of n-allele distributions under *random matings* applies to matrices $P = (p_{ij})$, $i, j = 1, ..., n$, where each (i, j)-entry p_{ij}[70] is substituted by the product of the sums of the entries in the i-row and the j-column in P,

$$M(P = \{p_{ij}\}) = P' = \{p'_{ij}\} \text{ for } p'_{ij} = \left(\sum_j p_{ij}\right) \times \left(\sum_i p_{ij}\right).$$

The (counter intuitive ☺) Hardy-Weinberg theorem says in these terms that

$$P'' = const \cdot P', \text{ that is } M(M(P)) = const \cdot M(P), \text{ for } const = \textstyle\sum_{ij} p_{ij},$$

which corresponds to the above (p, q, r)-formula for symmetric 2×2 matrices in Hardy's notation.)

`https://encyclopediaofmath.org/wiki/Bernstein_problem_in_mathematical_genetics` bernstein problem `https://encyclopediaofmath.org/wiki/Bernstein_algebra`

Nothing in science is as dissimilar as the two pictures of evolutionary dynamics drawn in "On the Origin of Species" and in "Versuche über Plflanzenhybriden":

the former, fuelled by the clear mathematical intuition,

sheds a *powerful conceptual* light on the *familiar* panorama of Life,

while the letter presents *a new phenomenon*, which allowed one a glimpse of the *deep hidden fundamental structure of Life,*

where this was obtained by a (seemingly self-contradictory) *statistical analysis* of results of *multiple experiments*,[71]

The distinction between the two pictures can be already seen in the difference between their mathematical (both probabilistic) models: Darwinian "cube of life and death" and the Mendelian "next generation map".

These divergent ideas were put together at the beginning of 20th century by J.B.S. Haldane – mathematically minded scientist, and R. A. Fisher – scientifically oriented mathematician and also by Sewall Wright[72] by shifting the focus of selection from individual organisms to distributions of gene alleles in populations of species.

Haldane writes in his 2024 *"A Mathematical Theory of Natural and Artificial Selection–*I"[73] the following:

... we must show not only that it [natural selection] *can cause a species to change, but that it can cause it to change at a rate which will account for present and past transmutations....*

...we can only obtain rigorous solutions when selection is very rapid or very slow. At intermediate rates we should require to use functions of a hitherto

`https://www.math.uci.edu/~brusso/worzbusekrosArchMath87.pdf`.

[70] These numbers represent probabilities relative densities) of (ij)-pairs of alleles in the population. Thus, $p_{ij} \geq 0$ and $\sum_{ij} p_{ij} = 1$, but this is not essential in the present mathematical discussion.

[71] Compare with `https://www.nature.com/articles/s41437-019-0289-9`, `https://pmc.ncbi.nlm.nih.gov/articles/PMC9335343/` `https://www.cambridge.org/core/journals/development-and-psychopathology/article/nature-of-nurture-darwinian-and-mendelian-perspectives/6205622C26716CA78A068025DD2FD40C`

[72] `https://en.wikipedia.org/wiki/Modern_synthesis_(20th_century)`

[73] `https://link.springer.com/article/10.1007/BF02459574`.

unexplored type. Indeed the mathematical problems raised in the more complicated cases to be dealt with in subsequent papers seem to be as formidable as any in mathematical physics.

Haldane's evaluation of the selective advantage necessary for the fast evolution of *peppered moth*: in 1848 the frequency of dark-coloured moths was 2%, and by 1895 it was 95% rules out the stochastic process of genetic drift.

(Albeit applied to biological systems, the mathematics involved in the (neo)-Darwinism as well as in the classical genetics is the familiar mathematics based on numbers – elaboration on "mathematics of the multiplication table type", same as you find in the classical physics. [74])

Mathematical Digression: Algebraic Dynamics, Veronese Maps and Bernstein Algebras. The dynamics of alleles distributions with in populations can be expressed in terms of multiplicative endomorphisms of (truncated) polynomial algebras

Let us represent p_{ij}, $i,j = 1,...n$, as coefficients of quadratic polynomials $P(x,y) = \sum_{ij} p_{ij}x_iy_j$ and write the Mendel next generation map as

$$P(x,y) \overset{\mathcal{M}}{\mapsto} P'(x,y) = P(x,(1,...,1)) \cdot P((1,...,1),y)$$

The so defined map $\mathcal{M}$ applies to all polynomials in two (vector) variables, where $P(x,y) \mapsto P(x,(1,...,1))$ and $P(x,y) \mapsto P((1,...,1),y)$ define endomorphisms of the polynomial algebra $\mathcal{P}$ in $2n$ variables.

The products of such maps, e.g. the Mendel map, are *multiplicative endomorphisms* of this algebra, where the idempotency of $\mathcal{M}$, i.e. the (Hardy-Weinberg in the present case) relation $\mathcal{M}^2 = \mathcal{M}$ follows from idempotency of $P(x,y) \mapsto P(x,(1,...,1)), P((1,...,1),y)$, where $P(x,(1,...,1))$ and $P((1,...,1),y)$ are regarded as polynomials in two (rather than one) variables, which are constant in y and in x respectively.

[74] See more about it:
population genetics https://www.mabs.at/fileadmin/user_upload/p_mabs/2024-lecturenotes.pdf math https://services.math.duke.edu/~rtd/CPSS2006/cornelllect.pdf https://homepage.univie.ac.at/Reinhard.Buerger/PopGenVO2020_LN.pdf https://link.springer.com/book/10.1007/978-0-387-21822-9
is useful https://pmc.ncbi.nlm.nih.gov/articles/PMC4512530/
limitations https://pmc.ncbi.nlm.nih.gov/articles/PMC1448894/
https://www.researchgate.net/publication/341976946_Demon_of_Darwin_Idea_of_optimality_and_natural_selection

There are other *probabilistic fixed point theorems* e.g. the *central limit theorem* and the (Robbins)-*Geiringer convergence property* of the Mendelian multilocus transformations,[75] which admit a similar algebra-geometric interpretation.[76]

Veronese Maps. The projectivized Mendel map M_{pro} (which is idempotent, that is a *retraction*in topological terms,), when applied to symmetric matrices which are regarded as quadratic forms in n-variables, *rationally retracts* the space of these form onto the *Veronese variety* V^{n-1} of the squares of linear forms. In Euclidean geometric terms, this $V^{n-1} = S^{n-1}/\mp 1$ is the real projective space, which is $O(n)$-equivalently imbedded to the unit sphere $S^{\frac{n(n-1)}{2}-1}$, where the normal Riemannian projection of $S^{\frac{n(n-1)}{2}-1}$ to $V \subset S^{\frac{n(n-1)}{2}-1}$, which a homotopy retraction of the complement of the normal *cut locus* [77]

Bernstein Problem and Bernstein Algebras. [78]

Problem. Classify *idempotent quadratic* polynomial selfmaps of the Euclidean N-space.

$$B : \mathbb{R}^N \to \mathbb{R}^N,\ B \circ B = B,$$

which send a simplex $\Delta^n \subset \mathbb{R}^N$ into itself.

Equivalently, classify algebraic subvarieties $A \subset \mathbb{R}^N$, which admit quadratic retraction $B : \mathbb{R}^N \to A$ and which send some simplex into itself.

Example. The Mendel map $p_{ij} \mapsto \left(\sum_j p_{ij}\right) \times \left(\sum_i p_{ij}\right)$, of the $(N = n_1 n_2 - 1)$-dimensional hyperplane in the space of $n_1 \times n_2$ matrices p_{ij}, $\sum_{ij} = 1$, is idempotent by the Hardy-Weinberg theorem and it sends the simplex of positive such matrices into itself.

Algebras. A commutative non-associative algebra $\mathcal{A}$ over real numbers is *Bernstein* if

$$(a^2)^2 = w(a)^2 a^2$$

for all $a \in \mathcal{A}$ and some algebra homomorphism $w : \mathcal{A} \to \mathbb{R}$ independent of a.

In the Mendel case, $A = P = \{p_i j\}$, where the bilinear map $P \otimes P \to P$, which defines the algebra structure in P, is derived from the quadratic(!) next generation map $\mathcal{M} : P \to P$ by the usual formula,

$$p \circ q = \frac{1}{2}\mathcal{M}(p+q) - \mathcal{M}(p) - \mathcal{M}(q),$$

such that $p^2 = p \circ p = \mathcal{M}(p)$.

1.7 Lotka–Volterra Equations, Stability, Persistence, Permanency and Rebirth of Yellowstone's Wolves

Mathematically simplest Predator-Prey Equations.[79]

[75] see `https://homepage.univie.ac.at/Reinhard.Buerger/PopGenVO2020_LN.pdf`.

[76] I thought this must have been be known, but I couldn't find a reference and summarized this in `https://www.ihes.fr/~gromov/wp-content/uploads/2018/08/mendel-may31.pdf` along with mathematical interpretation of Alfred Sturtevant's idea of construction of genetic maps on the basis of statistics of observable mutations.

[77] It is probably not difficult to equivariantly describe the topology of this cut locus and to check the Alexander duality between V and $^\circ V$.(Compare with `https://arxiv.org/pdf/2307.04224v3` and `https://arxiv.org/abs/2408.05909`.)

[78] `https://www.math.uci.edu/~brusso/worzbusekrosArchMath87.pdf`.

[79] Introduced by Lotka in 1910 as a model of an autocatalytic chemical reaction and ecologically interpreted by Volterra in 1926. `https://en.wikipedia.org/wiki/Lotka%E2%80%93Volterra_equations`.

$\frac{dp_1}{dt} = a_1 p_1 - b_1 p_1 p_2 = p_1(a_1 - b_1 p_2)$
$\frac{dp_2}{dt} = -a_2 p_2 + b_2 p_1 p_2 = p_2(-a_2 + b_2 p_1)$
where

p_1 and p_2 represent amounts (population densities) of prey and predators,

a_1 is the reproduction rate of prey in the absence of predators,[80]

a_2 is the death rate of predators by starvation with no pray

b_1 and b_2 are the effect of pray consumption on the two populations.

It is known [81] that (the orbits of) positive solutions are periodic around the equilibrium point $(p_1 = a_2/b_2,\ p_2 = a_1/b_1)$.

Despite a nonrealistic simplifying assumption, this system correctly predicts oscillation of predator-pray populations and, for instance , *paradox of the pesticides*[82] where worsening the environment mostly damages the preadator.

For example, applying pesticides to phytophagous mites - pests in apple orchards, also effects predatory mites, which prey upon phytophagous mites. The total result is an *increase* of phytophagous mites.

Kolmogorov Equations

These equations, which maximally generalize Lotka–Volterra, can be written as

$$\frac{dp}{dt} = Ap + Bpp, \text{ where } p = (p_1, ..., p_m).$$

where $A = \{a_{i,j}(p)_{i,j=1,...,m}\}$ is an $(m \times m)$-matrix valued function and $B = \{b_{ijk}(p)\}$ represent coefficients of quadratic forms in the p_i variables and where one wants loos for certain conditions on A and on B that, on one hand, would correspond to ecologically realistic sitations, and on the other hand, would be sufficiently simple from the mathematical perspective, e.g. allowing evaluation of ecological stability[83] and, more importantly, *permanense* of positive solutions.[84]

If $p = (p_1, p_2)$, these equations are often written as
$\frac{dp_1}{dt} = p_1 S(p_1, p_2)$
$\frac{dp_2}{dt} = p_2 W(p_1, p_2)$,
where the essential conditions on S and W include, for instance, their monotone decrease in p_2[85]

---

[80] This is highly unrealistic: the population growth $\frac{dp}{dt}$ tends to decrease with increase of p, which can be modelled by *logistic equation* $\frac{dp}{dt} = ap - \varepsilon p^2$, see `https://www.jstor.org/stable/2529810?seq=1`.

And for small p, there may appear the reverse *Allee effect,* e.g, animals that act in groups may suffer if the population density become too low."`https://en.wikipedia.org/wiki/Allee_effect`.

[81] See `https://link.springer.com/article/10.1023/A:1019172114300` and references therein

[82] `https://en.wikipedia.org/wiki/Paradox_of_the_pesticides`.

[83] `https://en.wikipedia.org/wiki/Ecological_stability`.

[84] `https://www.sciencedirect.com/science/article/pii/002555649290078B`
`https://ielab.recherche.usherbrooke.ca/assets/pdf/Gravel,%20Massol,%20Leibold%20-%202016%20-%20Stability%20and%20complexity%20in%20model%20meta-ecosystems.pdf`.

[85] See `https://homepage.univie.ac.at/karl.sigmund/Kolmogorov.pdf` for an overview of these equations.

1.8 Multiple Sequence Alignment, Mitochondrial Eve, LUCA and Beyond

2013 genome sequencing of 69 people from 9 different populations: the age of "Mitochondrial Eve" 100 000~150 000 and of "Y-chromosomal Adam" 120 000~150 000 yars.

https://en.wikipedia.org/wiki/Lucy_(Australopithecus)
https://www.sciencedirect.com/science/article/pii/S2666498423000650
https://www.nature.com/articles/s41598-019-50373-z
https://esajournals.onlinelibrary.wiley.com/doi/10.1002/fee.2253

LUCA – the last universal common ancestor. with a lipid bilayer membrane, ribosomes and the current genetic code, $3.6 \sim 4.210^9$ years old, is the estimated common ancestral cell for the Bacteria, the Archaea, and, hence, the Eukarya.

Analysis of 6.1 million protein-coding genes and of 286,514 protein clusters identified 355 protein clusters that were probably common to the LUCA and suggested that LUCA was an anaerobic thermophile with ~ 2 000 genes and that it had an CAS-based anti-viral immune system.

A 2024 study estimated the order in which amino acids were added into the genetic code from early protein sequences, found that amino acids that bind metals, and those that contain sulphur, came early in the sequence. https://www.pnas.org/doi/pdf/10.1073/pnas.2410311121.

1.9 History of Ideas by Quotes

[86]

1. QUOTES FROM WEISMANN'S THE EVOLUTION THEORY VOLUME II :

...Darwin adhered to Lamarck's assumption of the transmission of functional adaptations...

Darwin was the first to think out a theory of heredity which was worthy of the name of theory, for it was not merely an idea hastily suggested, but an attempt, though only in outline, at elaborating a definite hypothesis.[87]

His theory of 'Pangenesis' assumes that cells give rise to special gemmules which are infinitesimally minute, and of which each cell brings forth countless hosts in the course of its existence. Each of these gemmules can give rise to a cell similar to the one in which it was itself produced, but it cannot do this at all times, but only under definite circumstances, namely, when it reaches 'those cells which precede in order of development' those that it has to give rise to.

Darwin calls this the 'elective affinity' of each gemmule for this particular kind of cell. Thus, from the beginning of development there arises in every cell a host of gemmules, each of which virtually represents a specific cell. These gemmules, however, do not remain where they originated, but migrate from their place of origin into the blood-stream, and are carried by it in myriads to all parts of the body.

Thus they reach also the ovaries and testes and the germ-cells lying within these, penetrate into them, and there accumulate, so that the germ-cells, in the

[86]

[87] Maupertuis anticipated these ideas a century before Darwin. https://www.jstor.org/stable/2811480?seq=1 https://pmc.ncbi.nlm.nih.gov/articles/PMC1080035/pdf/jmedgene00070-0057.pdf.

course of life, come to contain gemmules from all the kinds of cells which have appeared in the organism, and, at the same time, all the variations which any part may have undergone, whether due to external or internal influences, or through use and disuse.

In this manner Darwin sought to attribute to the germ-cells the power of giving rise, in the course of their development, to the same variations as the individual had acquired during its lifetime in consequence of external conditions or functional influences. ... .

If we were now to try to think out a theoretical justification we should require to assume that the conditions of all the parts of the body at every moment, or at least at every period of life, were reflected in the corresponding primary constituents of the germ-plasm and thus in the germ-cells.

But, as these primary constituents are quite different from the parts themselves, they would require to vary in quite a different way from that in which the finished parts had varied; which is very like supposing that an English telegram to China is there received in the Chinese language.

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QUOTES FROM JOHN MAYNARD SMITH: *The Concept of Information in Biology*[88]

The use of information...in biology dates back to Weismann.

In both protein synthesis and in later development, genes are symbols, in that there is no necessary connection between their form (sequence)and their effects.

The sequence of a gene has been determined, by past natural selection, because of the effects it produces.

In biology, the use of informational terms implies intentionality, in that both the form of the signal, and the response to it, have evolved by selection. Where an engineer sees design, a biologist sees [assumes?] natural selection.

"Natural", as opposed to artificial, may be *neutral* rather than, as it is often assumed, "Darwinian" that is biased (as random walk) by the reproduction rate potential.

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... the same information can be transmitted by different physical carriers. So far, engineers have not used chemical carriers, essentially because of the difficulty of getting information into and out of a chemical medium. The living world has solved this problem.

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Transcription, translation, code, redundancy, synonymous, messenger, editing, proofreading, library.

These can't be expressed in the language of physics and/or chemistry

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Developmental biology ... information in the genome is translated into adult structure,

evolutionary biology ... the information came to be there in the first place.

[88] https://link.springer.com/content/pdf/10.1007/978-94-017-0475-5_18.pdf.

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... the statement that A carries information about B implies that A has the form it does because it carries that information. A DNA molecule has a particular sequence *because* it specifies a particular protein, but a cloud is not black *because* it predicts rain. This element of intentionality comes from natural selection.

Not always intentional: genetic linkage, epistasis, genetic drift. (prions)

... justifies biologists in saying that:

DNA contains information that has been programmed by natural selection;

this information codes for the amino acid sequence of proteins;

in a much less well understood sense, the DNA and proteins carry instructions, or a program, for the development of the organism;

natural selection of organisms alters the information in the genome;

genomic information is 'meaningful' in that it generates an organism able to survive in the environment in which selection has acted.

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What is inherited is not the dark pigment itself, but the genetic mechanism causing it to appear in response to sunlight.

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.... The image of development ... is ... hierarchy of regulatory genes, and ... a signalling system that is essentially symbolic.

Such a system depends on genetic information, but the way in which that information is ... different from the way in which a computer program works, although it is a lot nearer the truth than the idea that complex dynamic systems will generate biological forms "for free".

... Monod's notion of "gratuity", which I think is most clearly expressed by saying that molecular signals in biology are *symbolic*.

Mathematically these "signal" and "symbolic" mean that ???

A gene can be said to carry information, but what of a protein coded for by that gene?What about prions?

I think one must distinguish between two cases. A protein may have a function directly determined by its structure for example, it may be a specific enzyme, or a contractile fiber. Alternatively, it may have a regulatory function, switching on or off other genes. Such regulatory functions are arbitrary, or symbolic. They depend on specific receptor DNA sequences, which have themselves evolved by natural selection. The activity of an enzyme depends on the laws of chemistry and on the chemical environment (e.g., the presence of a suitable substrate), but there is no structure which can be thought of as an evolved "receiver"of a "message" from the enzyme. In contrast, the effect of a regulatory protein does depend on an evolved receiver of the information it carries:

the eyeless gene signals "make an eye here," but only because the genes concerned with making an eye have an appropriate receptor sequence. In the same way, the effect of a gene depends on the cell's translating machinery ribosomes, tRNAs, and assignment enzymes. For these reasons, I want to say that genes and regulatory proteins carry information, but enzymes do not.

Is, the only mathematically, difference between "specific" (for an enzyme) and "symbolic" for regulatory protein that the both partners in signalling/interactions

are evolutionary selected? But if you think about the pair sender-receiver as a signe unity then...???

itself.]

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Quotes on the question *What is Life* by Schrödinger1944, Gánti 2003 Koonin 2012, Jaime Gómez-Márquezhttps 2023 with Comments

Schrödinger:[89] WHY ARE THE ATOMS SO SMALL? Why must our bodies be so large compared with the atom? [bacteria are small compared to their numbers]

THE WORKING OF AN ORGANISM REQUIRES EXACT PHYSICAL LAWS

PHYSICAL LAWS REST ON ATOMIC STATISTICS AND ARE THEREFORE ONLY APPROXIMATE

THEIR PRECISION IS BASED ON THE LARGE OF NUMBER OF ATOMS INTERVENING

THE $\sqrt{n}$ RULE

(BROWNIAN MOVEMENT, DIFFUSION)

(LIMITS OF ACCURACY OF MEASURING)

... the physical and chemical laws ... in the life of organisms are of this statistical kind.

... biologically relevant processes ... must have an extremely 'many-atomic' structure and must be safeguarded against haphazard, 'single-atomic' events attaining too great importance.

[unless specifically designed for this purpose]

The laws of physics and physical chemistry are inaccurate within a probable relative error of the order of $1/\sqrt{n}$.

[The $1/\sqrt{n}$-fluctuations are instrumental for the function of the subcellular biological processes.]

[Macroscopic observables are averages of microscopical ones. where principle physical observables abide by the *main rule of statistic*, also called *concentration of measure property*:

"average" agrees with "typical", which makes "observables" *actually* observable.

But this rarely work in the living wold: winners in the survival game are *atypical* (Solutions of physical equations are also atypical but in a different way.)]

THE HEREDITARY CODE-SCRIPT (CHROMOSOMES)

... incredibly small groups of atoms, much too small to display exact statistical laws, do play a dominating role in the very orderly and lawful events within a living organism.

... the whole of its [organism's] ontogenetic development from the fertilized egg the cell to the stage of maturity... is known to be determined by the structure of that one cell, the fertilized egg.

... the all-penetrating mind, once conceived by Laplace, to which every causal connection lay immediately open, could tell from their structure whether the egg would develop, under suitable conditions, into a black cock or into a speckled hen,...or... .

[89] https://www.arvindguptatoys.com/arvindgupta/whatislife-schrodinger.pdf

...The chromosome structures are at the same time instrumental in bringing about the development they foreshadow. They are law-code and executive power -or, to use another simile, they are architect's plan and builder's craft -in one.

The information encoded in a DNA molecule is an *instruction for action*, which is read, interpreted as an initial condition and executed by the stochastic physical/chemical molecular environment of this molecule.

Delbruck, N.W. Timofeeff and K.G. Zimmer experiment.

THE GENERAL PICTURE OF THE HEREDITARY SUBSTANCE

Are these structures, composed of comparatively few atoms, capable of withstanding for long periods the disturbing influence of heat motion to which the hereditary substance is continually exposed?

The energy thresholds, separating the actual configuration from any possible isomeric ones, have to be high enough (compared with the average heat energy of an atom) to make the change-over a rare event. These rare events we shall identify with spontaneous mutations.

[What is stable is the information encoded in DNA, not the molecule itself, where this stability is sustained by an energy consuming process of DNA repair.]

... complicated organic molecule in which every atom, and every group of atoms, plays an individual role... . We ... call that an aperiodic crystal or solid and express our hypothesis by saying: a gene -or perhaps the whole chromosome fibre -to be an aperiodic solid.

STABILITY OF NATURALLY SELECTED GENES

From Delbruck's general picture of the hereditary substance it emerges that living matter, while not eluding the 'laws of physics' as established up to date, is likely to involve 'other laws of physics' hitherto unknown, which, however, once they have been revealed, will form just as integral a part of this science as the former.

ORDER BASED ON ORDER

... to reconcile the high durability of the hereditary substance with its minute size, we had to evade the tendency to disorder by 'inventing the molecule', in fact, an unusually large molecule which has to be a masterpiece of highly differentiated order, safeguarded by the conjuring rod of quantum theory. The laws of chance are not invalidated by this 'invention', but their outcome is modified.

The living organism seems to be a macroscopic system which in part of its behaviour approaches to that purely mechanical (as contrasted with thermodynamical) conduct to which all systems tend, as the temperature approaches absolute zero and the molecular disorder is removed.

LIVING MATTER EVADES THE DECAY TO EQUILIBRIUM

IT FEEDS ON 'NEGATIVE ENTROPY'

How does the living organism avoid decay?

the essential thing in metabolism is that the organism succeeds in freeing itself from all the entropy it cannot help producing while alive.

[Living systems go against the entropic flow (to equilibrium) by feeding on free energy from environment].

A dead thing can go with the stream, but only a living thing can go against it. A dead dog can be lifted on the leaping water with all the swiftness of a leaping

hound; but only a live dog can swim backwards. [90].

WHAT IS ENTROPY?

THE STATISTICAL MEANING OF ENTROPY

[relative entropy, relative information, relativisation in math.]

ORGANIZATION MAINTAINED BY EXTRACTING 'ORDER' FROM THE ENVIRONMENT

... simple thermodynamical considerations cannot account for our having to feed on matter 'in the extremely well ordered state of more or less complicated organic compounds' rather than on charcoal or diamond pulp.

Energy is needed to replace not only the mechanical energy of our bodily exertions, but also the heat we continually give off to the environment. And that we give off heat is not accidental, but essential. For this is precisely the manner in which we dispose of the surplus entropy we continually produce in our physical life process.[Unclear; the laptop also dispose of the surplus entropy by giving off heat but. how essential is this?...].

So the parallelism between body temperature and 'intensity of life', which I believe to exist, may have to be accounted for more directly by van't Hoff's law, ...: the higher temperature itself speeds up the chemical reactions involved in living.

[Stomach temperatures of white sharks, ... recorded by acoustic telemetry ... were elevated over ambient water temperatures by 14°C.] [91]

NEW LAWS TO BE EXPECTED IN THE ORGANISM

An organism's astonishing gift of concentrating a 'stream of order' on itself and thus escaping that the decay into atomic chaos -of 'drinking orderliness' from a suitable environment -seems to be connected with the presence of the 'aperiodic solids', the chromosome molecules, which doubtless represent the highest degree of well-ordered atomic association we know...

.... something like a vicious circle is implied.

SUMMARIZING THE PHYSICAL SITUATION

... to the physicist the state of affairs is not only not plausible but most exciting, because it is unprecedented. ...

...the regular course of events, governed by the laws of physics, is never the consequence one well-ordered configuration of atoms

... when the chemist handles a very complicated molecule in vitro he is always faced with an enormous number of like molecules. To them his laws apply.

In biology ... single group of atoms existing only in one copy produces orderly events, marvellously tuned in with each other and us number of with the environment according to most subtle laws.

...events whose regular and lawful unfolding is guided by a 'mechanism' entirely different from the 'probability mechanism' of physics.

physicists were so proud to have fallen in with the other one, the 'order-from-disorder' principle, which is actually followed in Nature and which alone conveys an understanding of the great line of natural events, in the first place of their irreversibility.

We must be prepared to find a new type of physical law prevailing in it. Or are we to term it a non-physical, not to say a super-physical, law?

[90] G.K. Chesterton 2025https://www.worldinvisible.com/library/chesterton/everlasting/part2c6.htm

[91] `https://link.springer.com/article/10.1007/s003600050092`.

...living matter, whose most striking features are visibly based to a large extent on the 'order-from- order' principle.

we have to go to some length, including a refinement, not to say an amendment, of the assertion previously made, namely, that all physical laws are based on statistics.

Tibor Gánti[92] Everything can be classified as :

living,

potentially living but not dead. For example: resting seeds, dried-out or frozen micro-organisms (66)

dead (irreversible change from a living to a non-living state)

non-living (physical and chemical systems)

A living system must inherently be an individual unit.

A living system has to perform metabolism.

[**Gert Korthof**: Possible exceptions: Bacteria can be in a temporary dormant state called microbial cyst. An endospore is a stripped-down, dormant, tough, and non-reproductive structure produced by some bacteria; endospores can survive without nutrients. Dry Baker's yeast maybe an example of an organism without metabolism. Cryptobiosis is is a metabolic state of life entered by an organism in response to adverse environmental conditions such as desiccation, freezing, and oxygen deficiency]

A living system must be inherently [stochastically] *stable:*

(Remains itself despite changes in the external environment... homeostasis and excitability)

A living system must have a subsystem carrying information necessary for its origin, development and function.

Processes in living systems must be regulated and controlled.

A living system must be capable of growth and reproduction.

(But: Sterile animals and plants cannot reproduce,

[**Gert Korthof**: for a multicellular organism growth means multiplication of its cells. Because growth and reproduction need not be present in a living system, this criterion is not an absolute criterion . Most of our brain cells do not divide, but they are not dead. Some cells in a multicellular organism are in an inactive state, termed senescence, in which they are alive but have permanently stopped dividing.]

A living system must have the capacity for hereditary change and, furthermore, for evolution, i.e. the property of producing increasingly complex and differentiated forms over a very long series of successive generations.

[**Eörs Szathmáry**: evolution is not a property of an individual but of a population.]

Living systems must be mortal.

Non-living systems cannot die, so death is characteristic of life. Without death organisms would be immortal. Cell division produces two new individuals, the original cell ceases to exist, but does not die.

[**Gert Korthof**: animal germline cells, embryonic stem cells, tumor cells and immortalised cell lines are potentially immortal, while body cells are mortal.

[92] *The Principles of Life* reviewed by Gert Korthof, `https://wasdarwinwrong.com/korthof66.htm`.

Bacteria are potentially immortal. Therefore, being mortal is not an absolute life criterion]

(Non-living systems cannot die, so death is characteristic of life. Without death organisms would be immortal. Cell division produces two new individuals, the original cell ceases to exist, but does not die.)

[Gert Korthof: Bacteria, animal germ line cells, embryonic stem cells, tumor cells and immortalised cell lines are potentially immortal

Cells are the building blocks of life. ... But single cell organisms are still too complex. They can be simplified still further and still be called living.

The above "inherently" and "must" (these maybe artifacts of translation from Hungarian) are direction for making a chemical life model, where Ganti suggests a minimal such model, which he calls *chematon*. (What is chemistry for a mathematician?)

Eugene V. Koonin: Defining Life: An Exercise in Semantics or A Route to Biological Insights? [93]

... in itself the question 'What is Life?' hardly can be considered scientific. Falsification is impossible: .... [and]... ... to count a case as supportive, an independent criterion is required, but this can only be intuitive.

So we seem to 'know it when we see it' but defining life is an elusive goal and apparently an inherently meta-scientific (metaphysical) task.

Trifonov's approach[94] ... consists in compiling as many (supposedly) independent definitions as possible and then comparing vocabularies [see the tables below] of these definitions to derive a consensus, the "essential core"...

...the phrase *self-reproduction with variation* is actually redundant because any replication process will be characterized by some intrinsic error rate.

The problem is exactly the opposite:

... a necessary condition for life to evolve is replication with *an error rate below the sustainability threshold*

[Also] ...differential fitness effect of mutations is a necessary condition of selection, both in its purifying and positive (Darwinian) incarnations.

[What are minimal evolutional phenotype (block) modifications on the molecular level and what are corresponding genome modifications?]

Hence replication with an error rate below the sustainability threshold, with non-uniformly distributed fitness effects of errors could be a candidate for a necessary and sufficient definition of life, or probably more precisely, a criterion for identification of life forms.

missing components: i) chemistry (metabolism),

ii) energy conversion,

iii) structure (various forms of compartmentalization): ... *operational components* of life forms, in contrast to *informational components.*

[Hierarchical (tree-like) modularity of operational components.]

Even more damning for the informational definitions of life, it may appear that these definitions are easily falsified by computer viruses and all forms of 'artificial life' that replicate, mutate and evolve but arguably are not actual life forms.

[93] https://link.springer.com/article/10.1007/s00114-023-01882-5.

[94] *Vocabulary of Definitions of Life Suggests a Definition* https://web.iitd.ac.in/~amittal/2011_2012_JBSD_Def_Life.pdf

However, such falsification is illusory for the simple reason that these evolving entities themselves are produced by highly evolved life forms. ...

The operational components seem to be pre-requisite for the evolution of replicators fitting the above criteria, hence the informational definition of life presupposes the existence of some forms of metabolism, energy transformation and compartmentalization.

However, all life forms on earth, with the exception of viruses which are obligate intracellular parasites, encompass a much stronger connection between replication, chemistry, energy and structure: the replicating moiety (genome) encodes key information on the operational components (primarily in the form of proteins).

Is encoding operational components in the genome a necessary attribute of life?

This does not appear certain at all, and here we come to the potential heuristic value of life definitions. Let us formulate a hypothesis:

there are purely informational life forms in which genomes carry only the minimal information required for replication whereas all operational components are supplied by the (conducive) environment.

Actually, hypothetical 'information-only' replicators are among the essential features of several origin of life scenarios because emergence of complex genomes encoding operational components prior to the advent of an efficient replication mechanism appears effectively impossible.

This hypothesis may be hard to falsify but it certainly can be corroborated under two types of settings: in the laboratory and in extraterrestrial biospheres if and when such are discovered. Exploration of putative life outside earth belongs in the future but vigorous attempts to create in the laboratory an evolving system of replicators employing exogenous supplies chemicals and energy are underway, and certain progress has been achieved with ribozyme polymerases.

However, these experimental systems remain a far cry from the efficient replicators required to start the evolution of life. Thus, the jury is still out on the 'information only life' hypothesis.

A remarkable feature of all known biological replicators is their *digital character*: these replicators are polymers consisting of multiple types of monomers. Such polymers appear uniquely suited for information encoding, so a plausible hypothesis seems to be that digital properties are necessary for life.

This hypothesis certainly would be falsified by the (remarkable) discovery of analog life forms.

[Probably, there is a mathematical proof of this with a minimal input from physics and chemistry.]

To summarize, I believe that the 'democratic' approach applied by Trifonov to the definition of life problem did not lead him far astray and converged on a natural and sensible, if not quite precise, informational definition. In my view, although life definitions are metaphysical rather than strictly scientific propositions, they are far from being pointless and have potential to yield genuine biological insights.

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Reflections upon a new definition of life (2023) Jaime Gómez-

Márquezhttps[95]

Why should life be considered a process and not a system?

Can life be defined?

[Definitions of an object needs a preliminary definition/description of a category of similar objects, e.g in the definitionz of "probability" by Kolmogorov and of "algebraic variety" by Groethendieck]

Traits common to all living systems, The cornerstones of life

(i) carbon chemistry. Whether life can exist based on a different chemistry we do not know.

(ii) Living beings are open thermodynamic systems, highly ordered entities, that constantly exchange matter, energy, and information with the external environment, ... preserve their internal order by importing energy from the outside in the form of food, sunlight, oxygen, etc. and exporting entropy as heat, and end products of metabolism.

disorganized structures do not support the vital process,

[Are there. consistent and functional definitions of "(higly) organized/disorganized" and of self/nonself-organized?]

iii. Self-organizing: pattern at the global level emerges solely from interactions among lower-level components. Cells represent the perfect playground for self-organization, and we can find spontaneous formation of patterns, metabolic networks, self-assembly processes, etc.

the reconstitution of Escherichia coli ribosomes from purified native components can be achieved in the test tube. Likewise is the assembly of infectious bacteriophage λ particles in cell-free extracts where λ heads and tails spontaneously assemble and join in vitro.

[these follow the "free energy gradient lines" prescribed by information from DNA] similar to the protein folding

Embryonic development is another example of a controlled process of self-organization to gives rise to a complex multicellular organism from a single cell. [does this also follow *visible* "free energy gradient lines" prescribed by information from DNA?]

At the macroscopic level, we can see many examples of selforganization such as the coordinated movements of a school of fish or a flock of birds, the behavior of social insects, or the functioning of an ecosystem.

(iii) pre-programming: the genome contains all the instructions necessary to create a new living system and its ability to be modified (mutations, recombination, epigenetic changes) is the key to the evolutionary process;

(iv) Capacity to interact and adapt:

Any living system develops its vital functions through multiple interactions at different levels of complexity, from molecular to ecological.

Metabolism, gene expression, physiological dynamics, signal transduction, or trophic chains are some examples of the multiple interactions that occur in nature. We can see life as a complex process that is the result of the sum of all the interactions at different levels that take place in the living system.

(vi) reproduction...

(vii) evolution, both essential for the perpetuation of the species, as well as for its evolution through the transmission of changes in the genetic program to offspring. ...

[95] `https://link.springer.com/article/10.1007/s00114-023-01882-5`.

[but] life [can be] defined as an interactive process occurring in entropy-producing, adaptive, and informative (organic) systems ... taking into account that reproduction and evolution are not essential for life.

The inseparable system-process duality

...duality between the system (living being) and the process (life)... **[**is like that between an object in a *mathematical category* and the category itself.**]**

Lifeless living things..., viruses,... Dormant seeds and deep-frozen cells.

Artificial-life and Extraterrestrial-life

The principle of inexorability says that "things are like this because they have to be like this."

[Formulate this mathematically and try to prove in some cases.]

It means that many structures and mechanisms that we find in living systems are so because the laws of physics and chemistry would not allow them to be otherwise and neither would the requirements of biology. Let me give two examples of this principle: the need for wings to fly and enzymefree metabolic pathways.

Wings are analogue structures (similar structures present in organisms without a common ancestor) that evolved independently for the same purpose: to fly. All flying organisms (birds, bats, insects, dinosaurs) have wings: there is no flying organism without wings! If you want to fly, you must have wings.

What would happen with a hypothetical flying ET organism? It is highly probable that it would have to have wing-like anatomical structures and would therefore be like the flying organisms of this planet. In the history of life, there was no evolutionary predetermination that dictated the existence of winged animals.

On the other hand, the paradigm that a metabolic pathway could only occur in the presence of enzymes changed when it was shown that glycolysis and pentose phosphate pathway-like reactions could take place under plausibly archaic conditions in the absence of enzymes (Keller et al. 2016). Subsequently, it was reported that Krebs cycle and glyoxylate cycle inter- mediates were also produced in the absence of enzymes (Muchowska et al. 2019). These results demonstrate the existence of a certain metabolic determinism (the inexorability principle) and provide strong evidence for the prebiotic genesis of metabolism. In a hypothetical metabolism in an ET organism, what the principle of inexorability tells us is that glucose (or other monosaccharides), for example, would eventually generate pyruvate as an intermediate product in the energy generation pathways.

Life between the chaos and the tyranny of time

Life, like all processes, has a beginning and an end. It arises when the living system is assembled, and all its components function in coordination and ends when it succumbs to the tyranny of time because there is a submission of life to time. We are born, we grow, we age, and we die and there is noth- ing we can do about it and that is why I speak of the tyranny of time.

Chemistry and Life ... Life is a selfsustaining kinetically stable dynamic reaction network derived from the replication reaction.

Biology is just an elaborate extension of replicative chemistry.

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Robert Pascal & Addy Pross: *... nature is able to achieve greater persistence by either of two mathematically governed processes, one that governs change in the 'regular' world, the other that is effectively operational in the replicative world. ...*

Within the physicochemical world, change takes place toward the equilibrium state, the state of maximum entropy, while in the replicative world, change (toward increasing DK stability) involves a process of complexification, though the term is notoriously difficult to define or quantify [97]

1.10 Suggestions to Read and References to Chapter 1

Selected Articles

fundamental numbers in molecular biology `https://kirschner.med.harvard.edu/files/bionumbers/fundamentalBioNumbersHandout.pdf`

Haldane writes in his 2024 *"A Mathematical Theory of Natural and Artificial Selection*

Kolmogorov and population dynamics - Karl Sigmund

The Concept of Information in Biology John Maynard Smith

Books

Unraveling DNA: The Most Important Molecule Of Life, Revised And Updated Edition by Frank-Kamenetskii.

Demon of Darwin: Idea of optimality and natural selection by Alexander N. Gorban and Rem Grigorevich Khlebopros.

Biological Physics: Energy, Information, Life by Philip Nelson, with the assistance of Marko Radosavljevié, `https://www.esalq.usp.br/lepse/imgs/conteudo_thumb/Biological-Physics-Energy--Information--Life.pdf` .

The Major Transitions in Evolution by John Maynard Smith and Eörs Szathmáry.

Protein Physics 2nd Edition A Course of Lectures by Alexei Finkelstein Oleg Ptitsyn.

The Science and TechnologyBehind the Human Genome Project, by Charles R. Cantor and Cassandra L.

The Logic of Chance: The Nature and Origin of Biological Evolution by Eugene V. Koonin.

[96] How biology becomes chemistry review by Gert Korthof `https://wasdarwinwrong.com/korthof99.htm` of Addy Pross 'What is Life?'`https://books.google.fr/books?id=M_6YSuKCzVsC&printsec=copyright&redir_esc`

[97] *The Logic of Life* `https://link.springer.com/article/10.1007/s11084-016-9494-1`.

The Plausibility of Life Resolving Darwin's Dilemma Marc W. Kirschner and John C. Gerhart.

Cell Biology by the Numbers by Ron Milo, Rob Phillips.

Lateral DNA Transfer: Mechanisms and Consequences by Frederic Bushman..

Landmark Experiments in Molecular Biology by Michael Fry.

RNA, the Epicenter of Genetic Information A new understanding of molecular biology by John Mattick and Paulo Amaral.