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Biology transcends the limits of computation

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ABSTRACT

Cognition—sensing and responding to the environment—is the unifying principle behind the genetic code, origin of life, evolution, consciousness, artificial intelligence, and cancer. However, the conventional model of biology seems to mistake cause and effect. According to the reductionist view, the causal chain in biology is chemicals → code → cognition. Despite this prevailing view, there are no examples in the literature to show that the laws of physics and chemistry can produce codes, or that codes produce cognition. Chemicals are just the physical layer of any information system. In contrast, although examples of cognition generating codes and codes controlling chemicals are ubiquitous in biology and technology, cognition remains a mystery. Thus, the central question in biology is: What is the nature and origin of cognition? In order to elucidate this pivotal question, we must cultivate a deeper understanding of information flows. Through this lens, we see that biological cognition is volitional (i.e., deliberate, intentional, or knowing), and while technology is constrained by deductive logic, living things make choices and generate novel information using inductive logic. Information has been called "the hard problem of life' and cannot be fully explained by known physical principles (Walker et al., 2017). The present paper uses information theory (the mathematical foundation of our digital age) and Turing machines (computers) to highlight inaccuracies in prevailing reductionist models of biology, and proposes that the correct causation sequence is cognition → code → chemicals.

It is a stunning fact that the universe has given rise to entities that do, daily, modify the universe to their own ends. We shall call this capacity 'agency' (Stuart Kauffman and Philip Clayton, 2006)

1. Introduction

1.1. What is the role of cognition in evolution?

The Modern Synthesis—a term coined in 1942 by the evolutionary biologist and eugenicist Julian Huxley—integrates the theory of Darwinian evolution and Gregor Mendel's work on heredity. Nearly 80 years later, The Modern Synthesis (MS) is still the prevailing evolutionary model, despite multiple landmark discoveries of modes of inheritance and genetic exchange it did not account for (i.e., epigenetics, horizontal gene transfer, transposons, symbiogenesis, and the role of viruses, all of which contradict the MS to a degree) (Margulis, 1971; McClintock, 1953; Noble, 2013; Shapiro, 2011). Evolutionary reductionists such as Richard Dawkins seek to reduce explanations of evolution to the lowest or most simple level or parts. Consequently, the prevailing and conventional model of reductionist biology has assumed an order of cause and effect: chemicals → code → cognition. However, it has so far been impossible to reduce evolution to mere biochemistry; there are to this day no examples in the literature to show that chemicals produce codes ("Origin Of Life: $10 Million Prize at the Royal Society," 2019; Yockey, 2005).

While chemical processes can generate a DNA or RNA strand, no communication system in existence has code without encoding and decoding machinery (Shannon 1948). This stands in agreement with theoretical biologist Howard Pattee (1969), who stated, "A molecule does not become a message because of any particular shape or structure or behavior of the molecule. A molecule becomes a message only in the context of a larger system of physical constraints …" In addition, there are no examples in technology that demonstrate that codes produce cognition (Floridi, 2005a). The Oxford English Dictionary defines "cognition" as i) the action or faculty of knowing; knowledge, consciousness; acquaintance with a subject, and ii) apprehension, perception. Cognition—a purposeful process by which knowledge is acquired via sensing and experiencing—is ubiquitous in living systems, and is the unifying principle behind the

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genetic code, the origin of life, evolution, consciousness, artificial intelligence, and cancer. We now know that cognition takes place not only at the level of the organism, but has also been robustly demonstrated at the cellular level in all three domains of life (see Shapiro 2020 for a review).

Cognition is necessary to create information because a choice (exercising volition) between two alternatives (1 or 0) is a single unit of negentropy. Negentropy (short for negative entropy) was introduced by Schrödinger to represent the resource upon which an organism feeds to avoid rapid decay into equilibrium, creating order from disorder (Schrödinger 1944). Today negentropy is also used in broader contexts, as a measure of distance to normality. By creating order and increasing negentropy, cognition stands in sharp contrast to the destruction of information, which is information entropy, where entropy is the universal tendency from order to disorder (Davies 2019). This means that cognition is not merely an aspect of biology that deserves more attention than it has received; rather it ranks among the most fundamental questions in all of science.

1.2. Shannon, Turing and information in biology

> "The thing that separates life from non-life is information" (Davies, 2019).

Information theory was established in 1948 by Claude Shannon's landmark paper "A Mathematical Theory of Communication" (Shannon, 1948), which has been termed "The Magna Carta of the information age" (Verdú, 1998). Shannon's seminal work laid the foundations for the modern era of digital communication and bioinformatics. The basic tenet of information theory is that digital communication consists of three main components: an encoder, a message passing through a communication channel, and a decoder (Fig. 1). Claude Shannon's model has been standard in bioinformatics since the 1960's (Yockey 2005). Yet, while humans suppose we invented digital communication systems in modern times, cells have been employing and depending on them for over three billion years.

Communication uses symbols, which are defined as physical patterns, that are designated to represent an entity other than the object itself (DeLoache et al., 1999). A referent is anything to which a symbol refers. Anything can be designated as a symbol, provided that what it represents is clearly defined and recognizable by the decoder. For example, in Morse code, 'A' is encoded by 'dot dash'; in ASCII, 'A' is encoded by '1000001'; in IUPAC one-letter coding for amino acids, 'A' means Alanine, which in the genetic code can be coded for by 'GCT', 'GCC', 'GCA', or 'GCG' (in which A is short for Adenine, G for Guanine, C for Cytosine and T for Thymine). In digital communication, both the encoder and decoder are defined by tables that relate each symbol to a referent (Fig. 1). Information in the message is measured in bits N, and the number of states a message is capable of representing is 2^N.

One of the most vexing problems in digital communication (i.e., DNA replication, Wi-Fi, radio and TV signals) is that noise in any communication channel introduces uncertainty, in other words, noise destroys information. Noise can be defined as anything that interferes with accurate transmission of the message, including random genetic mutations. One of Shannon's signature victories was identifying noise as *information entropy*. Shannon (1948) showed that noise is mathematically identical to Boltzmann's entropy in thermodynamics. This implies that information lost from noise is lost forever (Fig. 2). Information entropy is as irreversible as exhaust going back into a car engine and becoming useable energy again, by turning back into gasoline (thermodynamic entropy). Even natural selection cannot remedy this; it can only slow the pace of degradation, as selection can only subtract information (Dupré, 2017; Marshall 2015 Appendix 1 "All about randomness").

Shannon (1948) also showed that adding sufficient redundancy to a given communication system via i) error detection and ii) correction could compensate for noise. Digital communication systems check transmission for accuracy through checksums and cyclic redundancy checks (Marshall and Rinaldi, 2017). A calculation is done on message contents, added at the end of the message and sent. The receiver performs an identical calculation and compares its own answer to the one sent. If the two don't match, an error has occurred; the transmitter is asked to re-send the packet. This requires extra bandwidth to be built into the system, but it makes it possible to use a cellular phone on a busy expressway in the presence of interference from spark plugs, radio and TV signals, solar radiation, etc. In Biology, i) and ii) are essential tasks for all cells, in the form of DNA and RNA multi-stage proofreading, and DNA repair, respectively (Noble, 2013; Shapiro, 2011). Living organisms also employ the same principle of avoiding the deleterious effects of noise in the well-known redundancy of the genetic code (Yockey, 2005).

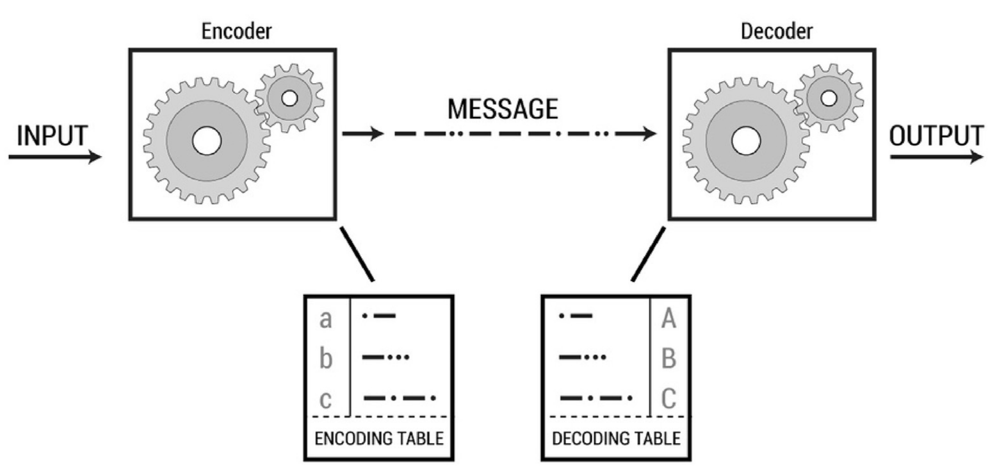

Fig. 1. Anatomy of a digital communication system. Information is encoded into a message in a communication channel according to the rules of an encoding table, then decoded by a decoder using a corresponding set of rules (which may not be an exact inverse). In biology, DNA transcription is encoding, while translation is decoding (Yockey, 2005). Figure adapted from Marshall (2015).

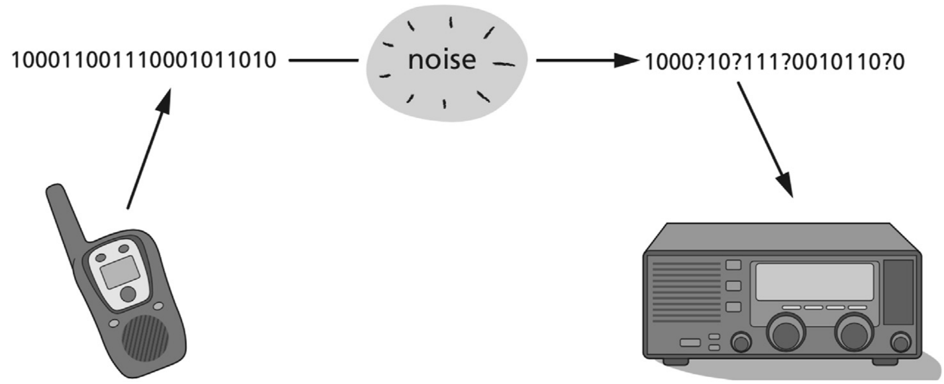

Fig. 2. Communication in the presence of noise. A digital radio sends a signal, picked up by another radio. Noise from sunlight, outer space, and other radio signals alters some of the bits, represented as question marks in the received signal. The actual received signal is 1000**0**10**1**111**1**001011**0**0, *but the receiver doesn't know the question marks are question marks or that the bolded digits are wrong*. While we can tell by comparing the two signals, the receiver does not have the original signal. This loss of information is irreversible for nearly identical reasons that heat energy moves from useable to unusable in the second law of thermodynamics. Without error correction and detection to solve this, life would not have survived and thrived for more than 3 billion years.

The process of DNA transcription-translation conforms to the principles of digital communication, defining the field of bioinformatics. Mathematically, DNA transcription-translation is equivalent to a Turing machine, (Yockey, 2005), an idealized mathematical model of a computer by Alan Turing (1936) the man who cracked the WWII German communication code. Turing drew precise parallels between mathematics and computers, by showing that any arithmetic, in theory, can be calculated by a computer, and therefore computers have the same fundamental limitations as arithmetic itself.

Turing's model stored information on a tape and allowed for infinite memory capacity. While the Turing machine is an abstract model of computation, a real-world computer is fully equivalent to a Turing machine with finite memory. Doctors and biologists do not typically speak in such terms, but all modern people are intimately familiar with Turing machines and their limitations and carry them in their pockets every day. Smart phones, computers and algorithms are Turing machines. The terms "Turing machine", "computer", and "algorithm" are all synonymous in this paper.

Turing machines are a key concept in mathematics, because a Turing machine can solve any computable function, and Galileo said, "the laws of nature are written in the language of mathematics" (Wigner 1990). An extreme view states that "all is computation" (Wolfram and Gad-el-Hak, 2003). Yanofsky says, "For the past three millennia a major goal of science has been to give deterministic rules for all phenomena" (Yanofsky, 2013). If this goal is achievable, it means all of reality can in principle be modeled my mathematics and computers, including biology and human minds. It would mean the iPhone of the far future might not merely provide access to all the world's information, but house a working model of the universe. On the other hand, if it can be proven that information or mathematics itself cannot be reduced to computation, then such a proof would shake the very foundations of science itself. It would mean that science's goal of defining rules for everything is impossible. This paper provides such a proof.

Even if we set aside cellular processes and focus merely on the genetic code, we are faced with what Walker and Davies (2016) termed "the hard problem of life", which is "the identification of the actual physical mechanism that permits information to gain causal purchase over matter" (Walker and Davies, 2016; also discussed in Pattee, 2012). Although mainstream evolutionary biology has held that the direction of causality is from chemicals to code to cognition for many decades (Dyson, 1982; Koch, 2012; Orgel, 1968; Watson and Crick, 1953), there is no empirical evidence for either of these steps (Floridi, 2004; Marshall, 2015; "Origin Of Life: $10 Million Prize at the Royal Society," 2019).

Information theory, as presently understood, indicates that traditional chemical "chance and necessity" (Monod, 1974) approaches to the origin of life are not likely to succeed. This is because necessity—governed by the laws of physics and chemistry—is not known to generate codes (Yockey, 2005), while randomness ("chance") is equivalent to entropy (Machta, 1999). Therefore, the objectives of the present paper are to: i) use information theory and Turing machines (i.e., computers) to counter conventional reductionist evolutionary models, and ii) highlight the preeminence of cognition in shaping the physics and chemistry of life. In doing so, I propose that the correct causation sequence is cognition → code → chemicals. The cognition-first model presented here, which is based on what we know of technology and information theory, hints that the "hard problem of life" may indeed be solvable.

2. All living cells are cognitive

Cognition manifests agency, which is exclusive to biology (Cronin and Walker, 2016). Agents are cognitive entities with the capacity to choose (volition). Cognition refers to the total set of mechanisms and processes that underlie information acquisition, storage, processing, and use, at any level of organization (Baluška and Levin, 2016). Once thought to be a trait unique to only higher order mammals, it is now well understood that all living cells exhibit what can only be described as cognition (Lyon, 2015; Shapiro, 2020). According to Shapiro (2020), "Cognition is a basic feature of life because all living organisms have to adapt their physiology and behavior to novel circumstances. Biological cognition means that cells are able to perceive changing features of their internal and external environment and undertake responses directed to survival, growth, and reproduction of themselves or their clonal relatives." Shettleworth (2009) defined biological cognition as "the mechanisms by which animals acquire, process, store, and act on information from the environment. These include perception, learning, memory, and decision making." The reason that agency and cognition do not exist in the physico-chemical world is because neither physical laws nor random interactions make choices (Walker et al., 2017). According to Margulis (1996), "to go from a bacterium to people is less of a step than to go from a mixture of amino acids to that bacterium."

The deep question of the role of cognition in evolution was brought into focus by the Nobel prize winning work of Barbara McClintock. When McClintock's corn plants were presented with unique and unforeseeable chromosome damage events, precisely what was it that made the plants successful? The outcome can't simply be attributed to natural selection, since such a small population of plants were involved, and furthermore the experiments were not lethal to many of the plants. We should ask whether the innovations generated by McClintock's plants are best categorized as i) random, ii) algorithmic, or iii) cognitive. Was it simply chance events that caused transposons to move from one chromosome to another and effectively repair the genome? This option can be immediately ruled out, because the behavior of transposons by definition cannot be categorized as "random mutations." Transposons are semiotic elements (Witzany 2020a) that originate and move to specific locations, not unlike adjectives and adverbs belonging in strategic parts of a sentence. This might lead us to hypothesize that the behavior of transposons is "algorithmic"—following a predetermined set of rules. While this is surely true to a degree, it cannot be the complete picture because neither the damage nor the plant's response to the damage was deterministic, it was contextual. Since algorithms are deterministic (Turing 1936), McClintock's "jumping genes" cannot have been the result of an algorithm. The hard limits of algorithms are delineated in section 4.1 and 4.3, based on Turing machines and information theory.

One might attempt to solve the above problem by acknowledging that the mutations were not random, but perhaps the placement of the transposable elements was random. This is analogous to saying, 'the word spellings weren't random, but arrangements of sentences were.' When that explanation fails, one then suggests, 'The sentences aren't random but the paragraphs are.' Such modes of explanation may go on indefinitely, but this evades the central question because "randomness" has only retreated to higher and higher levels of the system. One could as well say, 'Cells in our bodies aren't random but arrangements of organs and limbs are.' At every level of biological systems we do understand, "randomness" has been replaced by testable predictions and systematic explanations. This is the task of every scientist. Section 4.3 proves that adding randomness to algorithms doesn't solve this problem because randomness increases information entropy. Cognition remains the only viable explanation, because no known algorithm adapts to an unbounded range of situations and succeeds some percentage of the time.

McClintock herself believed the plants she studied possessed cognition:

> "The responses of genomes to unanticipated challenges are not so precisely programmed. Nevertheless, these are sensed, and the genome responds in a discernible but initially unforeseen manner."
>
> "The ability of a cell to sense these broken ends, to direct them toward each other, and then to unite them so that the union of the two DNA strands is correctly oriented, is a particularly revealing example of the sensitivity of cells to all that is going on within them. They make wise decisions and act upon them."
>
> "A goal for the future would be to determine the extent of knowledge the cell has of itself, and how it utilizes this knowledge in a "thoughtful" manner when challenged." (McClintock 1984)

In evolutionary biology, such questions are rarely given the attention they deserve. It is taken for granted that organisms can and will make these adaptations, but the question is seldom asked: "What *does* a cell know about itself? How does it utilize knowledge in a 'thoughtful' way when challenged?" Shapiro (2020) explores these issues in further detail, concluding that all such activity in evolution is at least in part the result of processes most properly labeled as "cognitive." He says:

> For those who believe that cognition only operates in animals, it is helpful to point out that there are extensive literatures on cognitive behaviors in both single-celled eukaryotes, starting at the beginning of the 20th Century [Jennings, 1906 (republished 1962); Jennings, 1902] and also in plants. Recall that Darwin referred to the roots as the "brains" of a plant [Darwin, 1880; Baluska, 2009].

Based on all we know about randomness and algorithms in computer science, the data rules out both and favors cognition as playing a necessary role in biology. Miller and Torday show that cognitive faculties of cells include individual perception and sensing, collective sensing and cooperation, complex communication, autoduction and indirect sensing through proxies, memory and information storage, learning and behavioral adaptation, anticipation and prediction, computation, directional motility, combinatorial decision-making and problem-solving, trading of resources, and sociality (Miller and Torday, 2017). An impressive body of literature demonstrates that cognition is invested in living things at all levels. Self-awareness of status is a necessary attribute of life and innate property of all cells (Miller and Torday, 2017).

A striking example of scalable cognition is quorum sensing, a mechanism by which bacteria count signals from neighboring bacteria to assess group size and act as a unit. Colonies assess the environment and influence their neighbors based on population levels and species identity; this "enables bacteria to act as multicellular organisms." Bacterial chemical communication networks integrate, process and transduce to control gene expression and accomplish intra- and inter-species cell-cell communication (Waters and Bassler, 2005). The fact that quorum sensing adapts contextually at vast levels of scale and across species and even kingdom boundaries (Williams et al., 2007) indicates that quorum sensing is neither random nor algorithmic but cognitive.

Michael Levin says, "I propose a fundamental definition of an Individual based on the ability to pursue goals at an appropriate level of scale and organization and suggest a formalism for defining and comparing the cognitive capacities of highly diverse types of agents … Many examples of memory, anticipation, context-dependent decision-making, and learning are exhibited by organisms from yeast and bacteria to plants and somatic cells … This is even true of subcellular-level components, e.g., gene-regulatory networks can execute similar learning and computational properties as neural networks, as can cytoskeletal networks, cell signaling pathways, reaction-diffusion chemistry, and metabolic networks." (Levin 2019) He says, "The next level of advances in this field will be based on recognizing that the scale and definition of the biological agent, and the boundary between its own Self and its environment, are actually much more complex and malleable than has been appreciated." (Levin 2020a).

Table 1 concludes this chapter by highlighting examples of living systems that alter their own genetics and that actively participate in their own evolution, via cognition. Many definitions of cognition can be found in the literature. They consistently apply to one or all of the following: sensing the environment (e.g. epigenetics and initiation of hypermutation), interpreting the meaning of signals (e.g. DNA linguistics, repair and checkpoints), making decisions (e.g. transposition events), taking action based on self-interest (e.g. self/non-self identification; resistance to cancer therapies), and modifying themselves (e.g. genome chaos and hypermutation).

Table 1
Examples of cellular cognition that result in heritable evolutionary changes.

Instance	Description
Transposable elements in Barbara McClintock's corn plants	Mobile genetic elements were shown to insert themselves into new areas of the genome in response to chromosomal damage and then disappear over the course of development, indicating that cells can sense damage and restructure the genome in the face of adversity (n.b., maize genomes evolved without invoking natural selection) (Jones, 2005; McClintock, 1953, 1984).
Plant galls	Insect burrowing in a plant leaf causes a gall to form, and genetic reconstruction in response to each species is unique (McClintock 1984).
Acquired inheritance via epigenetics	Licking/grooming of rat pups by both biological or foster mothers results not only in phenotypic changes, but also in epigenetic changes that are passed through the germline to future generations (see Zhang and Meaney, 2010 for review).
Genome chaos	Most cancer genomes contain evidence of gross chromosomal rearrangements (i.e., karyotypic changes) that drive oncogenesis, Chromothripsis ('chromosome shattering') and chromoplexy (complex genome restructuring) challenge the paradigm that cancer is caused by incremental changes over time, and result in the rapid speciation of hundreds of novel cell types. Genome chaos is an active response of the cancer cell to threats from the immune system, radiation and chemotherapy (Heng, 2019; Heng et al., 2011; Jones and Jallepalli, 2012; Liu et al., 2014).
DNA repair and checkpoints	Tomas Lindahl, Paul Modrich, and Aziz Sancar were awarded the Nobel Prize in Chemistry (2015) for their work on "mechanistic studies of DNA repair" (Lindahl et al., 2015). Cells also use 'checkpoints' to maintain order, dependency, and timing in the cell cycle, so that late events do not occur until earlier (dependent) events are completed (Hartwell and Weinert, 1989). Checkpoints arrest the cell cycle in response to damage by upregulating suppressors (e.g., the p53 tumor suppressor) in response to damage and upregulate genes involved in repair (Elledge, 1996). The dysregulation of this process promotes the evolution of normal cells into cancer cells (Engeland, 2018).
Linguistics of DNA	Language involves the transmission of information "between communicating partners". Out of 13 design features of human language, the language of the cell shares 10. (Ji, 1997). Languages are non-random and ergodic (Shannon 1948), and the widespread "multiplicity of coincident messages" and structures encoded within a given stretch of sequence underscores the sheer complexity of the genetic code (Shapiro, 2012).
Bacterial hypermutation under stress	Bacteria under extreme stress increase mutation rates by 100,000X to search for a survival solution (Shapiro, 1984)
Ciliated protozoan hypermutation	Starvation induces male and female protozoans to mate and subsequently completely restructure the genome to make a new nucleus, processing DNA into 100,000s of pieces, then splicing to rearrange the code (Prescott, 2000; Vogt and Mochizuki, 2013).
Epigenetic Asthma inheritance	Ninety-eight percent of human diseases cannot be accounted for via Mendelian genetics (Torday and Rehan, 2013). Torday and Rehan (2013) observed that maternal exposure to nicotine resulted in the transmission of asthma for two subsequent generations. Exposure to nicotine during pregnancy results in multigenerational epigenetic fingerprints in lungs and gonads, as well as and changes in lung function, which are passed down from grandmother to grandchild via the germline, even if the mother herself was not exposed (Rehan et al., 2012). This is the first experimental evidence for true epigenetic transgenerational inheritance. These findings indicate that the effects of environmental stress on cell-cell signaling may be the primary driving force in evolution (Torday, 2015).
Self/non-self identification of dsDNA in bacteria	Bacteria have at least three different systems for recognizing incoming DNA and discriminating between it and their own genomic molecules: 1) DNA restriction-modification (R-M) systems (Ershova et al., 2015; Vasu and Nagaraja, 2013), 2) self/non-self discrimination in DNA uptake via the recognition of DNA-uptake sequences that have multiple 'dialects' (Mell and Redfield, 2014; Redfield et al., 2006), and 3) detecting and disabling invading nucleic acid sequences via CRISPR/Cas-based adaptive immunity systems. (Wright et al., 2016; Salsman and Graham, 2016)
Self/non-self identification in cancer	One view of cancer is that it is a dysregulation of the algorithms that normally direct the activities of individual cells to specific anatomical structures and functions, which reduces "the boundary of their computational selves" to the level of a single-celled, unicellular lifestyle (Moore et al., 2017).
Capacity of cancer to thwart all therapies	In all incurable cancer patients, cancer cells evolve both the capacities for metastasis and resistance independently (i.e., *de novo*) in each patient. The evolutionary path of all metastatic cancers is the same, arising from a speciation event in which some of the cells "evolve the capacity to evolve", migrate throughout the body, and "evolve into new tissues and habitats". Over the course of disease, evolvability (i.e., the ability to evolve, or heritable phenotypic variation) allows cancer cells to evolve responses to and swiftly evade therapies. Cancer cells that are not resistant to therapies or that are too slow to evolve resistance can be therapeutically cured (Pienta et al., 2020).

2.1. Code, goals, and evolution require choices

Codes are not generated by chance or by necessity; they are generated by choice (Davies and Gregersen, 2014). Choice, defined here as a decision made by a cognitive agent, could perhaps be an emergent property of chance and necessity, but at present this is speculation. Thus, mechanisms that relate choice to chance and necessity are missing, and should be expected to be a major future scientific discovery. Such mechanisms, also called "other laws of physics" (Schrödinger, 1944) are the source of biology's ability to solve *undecidable propositions*, problems which in principle cannot be solved by computation (Gödel, 1931; from Davis, 1965)). In other words, while cellular behavior is normally algorithmic, it also responds uniquely to novel situations, and this is what makes processes such as evolution and cancer possible. Hence, the origin of biological information is likely an unsolved cognition problem, as cognition is what gives any code its meaning.

A goal is a choice—a decision about the unknown, because the future is an undecidable proposition. This is because there is in principle no guarantee that any future goal can be reached. There is no guarantee the sun will come up tomorrow morning. Scientific laws are fallible approximations of reality, and specific formulations of these laws are not only represented in codes (because they are symbolic) they are also choices consensually made by scientists, and subject to constant revision.

Real time evolutionary adaptations are active responses to unforeseeable circumstances (Shapiro, 2011). Torday and Rehan (2013) determined that the most harmful factor of secondhand smoke is epigenetic changes triggering asthma, passed from a smoking woman to daughter to granddaughter. This and other examples in Table 1 demonstrate that observable evolutionary events are products of cognition and not merely chance and selection, while Table 2 shows that choices are similarly required for axioms in mathematics, formulations of scientific laws, inductive reasoning, negative entropy, and evolution.

2.2. The three levels of cause and effect in biology

As previously stated, there is no known pathway from chemicals to code, and there is no known way to produce code without

Table 2
Phenomena that exceed the limits of computation.

Computational Choices	Information is measured in bits, not kilograms, meters, seconds, joules, or other physical quantities. A bit is a record of a choice. All codes and communication systems reflect choices (Pattee, 1969). A 64-Gb USB stick holds 549,755,813,888 bits, which yield $2^{549,755,813,888}$ choices or degrees of freedom. An unattended computer can fill the USB stick with data (e.g., a running log of temperature data with date stamps), but the data format still had to be chosen at some point in the past. All codes for which we know the origin are the result of choices by agents (Witzany, 2020b).
Inductive Reasoning	Algorithms, by definition, cannot make choices because algorithms are deductive. A choice is an undecidable proposition because an opportunity to choose is only available if there is no logical proof, or deterministic or stochastic law to inform the outcome. A random variable in a program is not a choice, but a deferment to an outside input.
Evolution	Under extreme threat, real-time evolution is a strategic adaptation to a novel situation for which pre-programmed responses do not exist. This situation was the focus of McClintock's 1984 Nobel Prize paper: rapid evolutionary events are an active response by the organism to stress with uncertain outcome (McClintock, 1984; Torday and Rehan, 2013).
Assigning meaning to symbols	Assigning meaning to a symbol (e.g., in ASCII, 01000001 represents the letter "A") is a choice because the symbol for "A" could just as easily have been 10111110 or any other sequence. Symbol assignments are based on desired goals not physical laws (Pattee, 2012). It has been asserted that the genetic code is a frozen accident (Stegmann, 2004; Watson and Crick, 1953) but no evidence has been produced that randomness can generate code.
Harnessing Stochasticity	A cell harnessing stochasticity (Noble and Noble 2018) is performing inductive reasoning by exercising choice in search of a goal. This is because the goal itself is a choice (Kauffman and Clayton, 2006; Kull, 1998). This defines Schrödinger's negentropy (Schrödinger, 1944), which is converting disorder → order.
Axioms in Mathematics	Any axiom in mathematics is a choice because: 1) Axioms are chosen, not deduced (Weyl 2013). 2) by choosing a different axiom, one can construct a new system of logic. In geometry, you can omit Euclid's parallel postulate, retain the other four, and have hyperbolic geometry instead.
Representation of Scientific Laws	Formulations of scientific laws are similar to axioms in mathematics, except that they are based on measurements in addition to pure logic. Measurements are based on units which are arbitrary. Scientific laws are chosen from numerous options by scientists and are subject to constant revision.
Measurement and perception	Measurements and sense perceptions are symbolic representations of the outside world. At all levels of scale, appraisals of distance, weight, sound, smell, temperature, etc. also assign meaning to symbols (Lyon, 2013; Miller et al., 2020; Pattee, 2012; Witzany, 2020b).
Negative Information Entropy or Negentropy	In "*What is Life*?" Erwin Schrödinger introduced the term 'negentropy' or 'negative entropy' (Schrödinger, 1944). He states, "It is by avoiding the rapid decay into the inert state of 'equilibrium' that an organism appears so enigmatic ….What an organism feeds upon is negative entropy." Negative entropy is necessary to create information (Schrödinger, 1944) Negentropy is extensively discussed in the literature, and after 75 years, the consensus has barely changed (Davies, 2019) from Schrödinger's views. Choice is negative information entropy (i.e., the opposite of noise) because it converts uncertainty to certainty, order out of chaos. Randomness is defined by the absence of a pattern (Chaitin, 1990). While randomness cannot be proven absolutely (Chaitin, 1975), it is easy enough to tell if a signal does not conform to the ergodic patterns of a specific language or communication system (Shannon, 1948). In other words, judging entropy vs. negentropy can only be done with reference to teleology, which is choice. Negative information entropy is measured in bits, just as in information transmission. Coin toss = 1 bit of entropy Choice between two sides of a coin = 1 bit of negentropy A system that can make choices via cognition can, in theory, generate any Turing machine. Since axioms are the starting points for deductive logic, deductive logic cannot construct them. This has been known since Euclid's time. A choice must be made. Thus the link between induction and cognition is established. Induction is a choice based on what is anticipated to be most reasonable.

cognition. In all technology as well as information theory, causation is always cognition → code → chemicals. This suggests that biology obeys similar principles. Therefore:

i) Cognition is inductive reasoning which allows novel predictions to be made. Choices are made in uncertain circumstances with insufficient existing knowledge. Here, causation is disorder → order (Schrödinger, 1944). Cognitive systems consume energy so thermodynamic entropy increases (Collell and Fauquet, 2015; Landauer, 1961), but information entropy still decreases.
ii) Code pertains to symbols, communication, and computation i.e. languages, machines, algorithms, and genetics. The rules of codes are freely chosen and local to any system (Pattee, 1969). In biology, codes control chemicals and can use any physical medium for transmission (DNA and RNA; humans also transmit genetic and other information via copper, fiber, paper and ink) (Pierce, 1980). The computation of codes is deductive, making logical statements about what is inside a system based on its axioms, moving from the general to the specific. Computation is also deterministic: one output for given input (Turing, 1936).
iii) Lastly, there is the physico-chemical layer of cause and effect, which refers to laws of physics and chemistry which apply to matter and energy in various complex systems such as star and planet formation, magnetic fields, weather, geological activity, etc. The laws that govern this layer are universal (Halliday et al., 2013). In contrast to cognition, change over time in the physico-chemical layer is generally order → disorder (entropy) (De Groot and Mazur, 2013), and chemicals constitute the physical layer, not the information (i.e., code) itself (Shannon, 1948; Spurgeon, 2000).

3. The six open questions

Six open questions concerning the role of cognition in biology resist reductionist scientific models. These questions are not solvable using the conventional bottom-up approach, which places cognition at the end of the causal chain. These questions become unified under a cognition framework with prospects of a single elegant solution. They are as follows and will each be addressed in detail below:

i. What is the origin of life?
ii. How is information created?
iii. How do organisms generate evolutionary novelty in real time?
iv. How do agency and consciousness arise?
v. Can artificial intelligence exhibit cognition?
vi. What drives cancer's ability to thwart nearly every therapy?

3.1. What is the origin of life?

The origin of life—the process by which life originated from non-living matter—eludes us. This matter is further complicated by the lack of a universally accepted definition of "life" (Gayon et al., 2010). Chemically and structurally, we are far from explaining how the most minimal cell could form (Pross, 2016; Xavier et al., 2014), and numerous thermodynamic and kinetic problems also remain unsolved (Preiner et al., 2020). Despite much consideration, we do not yet have an account for the origin of life based on laws of physics and chemistry alone (Peacocke, 1983; Walker and Davies, 2016; Yockey, 2005).

Pattee stated that "the essence of the matter-symbol problem and hence the measurement or recording problem must appear at the origin of life where the separation of genotype and phenotype through language structures took place in the most elementary form" (Pattee, 2012). Merely understanding how molecules work does not explain how hierarchical organization originated (Pattee, 1969), and thus this question remains unanswered. This is entangled with a particular problem within the broader question of the origin of life that is looked at in depth in the section below. That is, in spite of monumental advances in the fields of genetics, biochemistry, and physics, we have not yet managed to develop an explanation for the origin and evolution of the genetic code.

3.2. How is information created?

In information theory, one bit of information is a decision or choice (Shannon, 1948). Examples of choice include assigning the arbitrary relationship between symbol and referent. For example, there is no physical law that states that we must use a binary system in computers. We could use a ternary or quaternary system; there is no law that states '0 = off' and '1 = on'. There is no law of physics that says in ASCII, '01000001' must represent the letter "A". Likewise, there is no law that says "apple" is the English word for a fruit as well as the name of a famous computer manufacturer—these are choices. Accordingly, there is no known physical law that states that, in the standard genetic code, 'GGG' must represent instructions to make Glycine. Alternative genetic codes are also known (Santos et al., 2004). The presence of choice is intrinsic to many aspects of information systems that have no known origin in physico-chemical laws (Pattee, 2012).

The genetic code, which is a study in computational elegance, is a universal set of rules that governs how gene sequences are translated into protein sequences (Barbieri, 2003). Genes and the proteins for which they code differ from all other molecules in the inorganic world because of the way that they are produced by living systems (i.e., built by external 'molecular machines' that assemble them based on a template) (Barbieri, 2003). While there are several prevailing theories and hypotheses regarding the paradox of the genetic code, its origin remains obscure (Jee et al., 2013; Wolf and Koonin, 2007; "Origin Of Life: $10 Million Prize at the Royal Society," 2019). According to Hubert Yockey, a pioneer in bioinformatics, "There is nothing in the physico-chemical world that remotely resembles reactions being determined by sequence and codes between sequences … There is no trace of messages determining the results of chemical reactions in inanimate matter … The origin of a genetic code is a bridge that must be crossed to pass over the abyss that separates chemistry and physics from biology … The existence of a genome and the genetic code divides living organisms from inanimate matter" (Yockey, 2005).

3.3. How do organisms generate evolutionary novelty in real time?

The majority of the literature in the biological sciences takes the capacity of life to evolve for granted. Despite detailed investigation of many evolutionary mechanisms (section 2; Table 1), our understanding of evolution is very superficial and incomplete. Furthermore, the mystery of what drives adaptation is deepened by the phenomenon of evolving evolvability (Payne and Wagner, 2019). Since we don't know the origin of information (section 3.2), not only are we baffled by a given cell's manifest capacity to evolve, its ability to evolve its own evolvability could very well be described as "the hard problem of life squared." Nothing in the technological sphere possesses anything like the evolutionary capabilities of a single bacterium.

The Modern Synthesis proposed that random copying errors combined with natural selection and population genetics would provide a gradual increase in speciation. But there are several problems with this view, five problems of which are highlighted below:

i) Evolution is not steady and gradual, it instead consists of long periods of stasis followed by rapid stages of punctuated equilibrium, contrary to Darwin's predictions (Gould and Eldredge, 1993).
ii) Mechanisms such as horizontal gene transfer, transposition, symbiogenesis, and hybridization are applied in a non-random way by natural genetic engineering systems (J.A. Shapiro 1993), which tailor responses to hundreds of sensory inputs in a cognitive manner (Shapiro, 2011).
iii) Random mutations are noise, and noise destroys information (section 1.2 and Fig. 2; Shannon, 1948; Witzany, 2020b).
iv) Transposons can jump around the genome, repairing damage in real time (McClintock, 1953). Under the Modern Synthesis framework this should be impossible, and her findings were initially rejected. This is because the MS insisted organisms are passive recipients of accidental mutations which are selected for fitness. However, McClintock's plants engineered novel solutions to unforeseeable problems in real time by activating DNA editing systems and copying coding sequences from other chromosomes. Cancer cells similarly reprogram their own genomes in real time, especially when subjected to chemotherapy. One species of cancer cell can generate hundreds of species in weeks (Heng et al., 2011).
v) Epigenetic inheritance has vindicated Lamarck, who for decades was derided for suggesting that acquired learnings can be passed to progeny (Baverstock, 2013; Noble, 2020; Torday and Rehan, 2013).

3.4. What is the role of agency in evolution?

Biological systems are the only known source of agency in the universe (Cronin and Walker 2016). In this paper, choice and agency are attributes of cognition, while consciousness is a particular type of cognition. While the essence of consciousness is far beyond the scope of this paper, the question is nonetheless central to evolution, as it is linked to the role of agency—the capacity to act in one's own self-interest—and choice in evolution. Consciousness continues to resist quantification or classification. Presently, we have no clear idea what consciousness is or where it comes from (Ginsburg and Jablonka, 2019; Hands, 2017; Koch, 2012; Nagel, 2012).

Because future events are undecidable propositions, in principle no algorithm can exist that will guarantee any future goal can be reached. Goals are central to evolution, particularly when sexual selection is a dominant force. Mate choice in sentient animals is agency. It is a major factor in evolutionary history (Noble and Noble, 2020). Furthermore, there are extensive examples in the literature of cellular cognition in single-celled eukaryotes, prokaryotes, and plants that date back to the early 20th century (Shapiro, 2020). Specific examples of cellular cognition that lead to heritable changes (i.e., have the potential to drive evolution) can be found in Table 1. Even the most rudimentary functioning model of consciousness, if developed, promises revolutionary implications for most branches of physics and every aspect of biology and the social sciences.

3.5. Can artificial intelligence exhibit cognition?

Artificial Intelligence has been heavily explored since the 1950s, has gone through multiple cycles of optimistic "summers" and pessimistic "winters," and is the subject of much unreasonable hype (Floridi, 2020). However, general intelligence does not exist in machines (Floridi, 2005b, 2013), and the model presented in the present paper suggests that "strong AI" will not exist until the problem of cognition is solved. Even the most sophisticated machine learning requires monitoring by humans (Floridi, 2013, 2020; Floridi and Taddeo, 2018; Nield, 2019). Advertising platforms such as Google and Facebook have invested billions of dollars on machine learning and Artificial Intelligence; a famous example was when Google bought AI firm DeepMind (whose AlphaGo program beat a human Go player) for $500 million. In the advertising industry, bidding, audience targeting and message combinatorics are all controlled by very sophisticated algorithms, and these ad platforms work on very "Darwinian" principles. The author has written bestselling books on both these platforms (Marshall et al., 2020a; Marshall et al., 2020b) and educated hundreds of thousands of advertisers in the use of these technologies. These platforms do not exhibit any form of cognition. If the capabilities of Google or Facebook rivaled even that of a tiny colony of bacteria, the market caps of these companies would skyrocket overnight. There are no computers or machines that can evolve the way a bacterium can, or that are capable of universal adaptive learning, as higher animals are (Ginsburg and Jablonka, 2019).

Genetic Algorithms—which allegedly mimic Darwinian evolution—are practical implementations of AI. They require programmers to determine and specify parameters and fitness functions, and are hardly a panacea in the software industry (Skiena, 2020). Beyond a certain size, computer optimized solutions become impossible to compute owing to a phenomenon called combinatorial explosion (Daintith and Wright, 2008). This places a severe limitation on the power of natural selection to determine outcomes (Dupré, 1992).

Once we truly understand evolution, we may be able to build self-evolving machines. Short of identifying the undiscovered laws of physics that make cognition possible, Siri is not going to "wake up" any time soon. This suggests that cognition is a dimension of behavior that will never be solved by Moore's law alone, the 50-year trend that computers double in speed every two years. If machines become capable of cognition (i.e., by being capable of negentropy or order from disorder), technology will possess exponentially greater capabilities. This is also a sobering realization, as cancer provides an analogy for how strong AI might become if accompanied by certain inevitable tendencies.

3.6. What drives cancer's ability to thwart nearly every therapy?

It is clear enough that the conventional approach to cancer: surgery, chemotherapy, and radiation—the "slash and burn" strategy—is not working (Raza, 2019). We are currently confronted with the tremendous power of cancer cells to out-evolve radiation and chemotherapy (Heng, 2019; Heng et al., 2011). Late-stage cancers remain elusive to the world's top laboratories, despite the many purported advances in the field. Even though we have spent a total of $250 billion on cancer research, the percentage of unsolved Stage 4 cases has decreased little since 1930 (Raza, 2019). What causes such lack of progress? A major cause, as argued here, is that chemicals are only the physical layer of the cognitive, information-based system that is cancer. The cognition-first model suggests that the signature moment in cancer development is when cells start making evolutionary decisions of their own volition, instead of 'following the algorithm' based on their cell type and role. Many, perhaps all kinds of cells appear capable of autonomous behavior in certain situations (Levin, 2020a). The identity of cancer cells (Moore et al., 2017) switches from regular Turing machine to *volitional* Turing machine, where the term "volitional" indicates it is an agent which can choose rather than just obeying its program. Parts of a larger organism defect and start optimizing for their own immortality. A Turing machine with agency is no longer a Turing machine; it is something new.

Cancer informatics is a decryption problem far more ambitious than Alan Turing's cracking of the German code in World War II. It is an interdisciplinary project that calls for the finest minds in the world in cryptography, oncology, evolutionary biology, semiotics and engineering … and perhaps music and psychology as well. The endless novelty of cancer is not algorithmic, it's volitional. What if we tried to solve cancer at the level of cognition, and not at the level of chemicals? Cancer is a struggle of information and intent (Levin, 2020b). If the cognition model is correct, then cancer is not strictly a genetic disease as is normally assumed. It would suggest genetics is merely a trailing indicator of the agency of cancerous cells. Preventing or arresting cancer may be a matter of persuading cancer cells to pursue different goals. Similar implications may apply to the antibiotic arms race and infectious diseases. If this is true, chemotherapy alone can never provide a complete solution.

4. Biology transcends the limits of computation: proof

I have argued above that six major open questions in biology pose deep challenges to the prevailing reductionist model of science. As defined by many, starting with Descartes, the aim of this model is to reduce all behaviors of the physical world to logic and mathematics. This, if accomplished, was believed to make all the behaviors of the universe predictable and computable. The reductionist model has been challenged by post-Newtonian physics (Mazzocchi, 2008), yet it persists in the expectation that someday supercomputers will model all aspects of the cosmos. In biology—which has been said to be sophisticated physics and chemistry—and even in the social sciences, the reductionist or materialistic view is still widely held.

A series of syllogisms which follows in the next section proves that the reductionist view violates the laws of logic itself. Statements come in two types: the first two are deductive syllogisms which provide rigorous mathematical proof; the rest are statistical syllogisms which are true based on the laws of information entropy and the 2nd law of thermodynamics. However, an exception could be found for the latter. Statistical proof is less rigorous than mathematical proof, but all scientific laws exist in this latter form.

4.1. Mathematical functions and computer programs are equivalent and deterministic

The deductive syllogism in support of the above statement is as follows:

1. General recursive logic is by definition deductive and deterministic ("General recursive function - Encyclopedia of Mathematics," n.d.)

2. Turing machines (computers) are equivalent to general recursive logic (Turing 1936)
3. Therefore, computers are deductive and deterministic

In other words, computers and arithmetic always generate the same output for the same input. Math functions by definition generate one and only one output for one input (determinism). Deductive logic is when one is able to mathematically prove "A is true, therefore B is true", where B logically follows from A ("Deduction theorem - Encyclopedia of Mathematics," n.d.). For example, "All men are mortal, therefore Socrates is mortal." In this paper, inductive reasoning is defined as inferring facts about A given knowledge about B, when deduction is not possible. For example, "Socrates is mortal, therefore all men are mortal." All inference statements take one of these two forms. Inductive reasoning is often based on Bayesian methods or statistical syllogisms.

It is often not possible to ascertain that a complex problem can be solved deductively until it is tested. This is equivalent to Turing's halting problem (Turing 1936), which states that no general method exists that can know whether a program will find a solution (halt) or continue searching forever. This means all unsolved problems are induction problems by default until a deductive solution is found and proven. Since deductive proofs have been proven impossible for large classes of problems (Davis, 1965) the goal of science's reducing everything to mathematics is also impossible.

4.2. Deterministic Turing machines are deductive

The deductive syllogism in support of the above statement is as follows:

1. Induction and deduction processes as defined above are mutually exclusive
2. Processes in classical Turing machines are equivalent to deductive processes
3. Therefore Turing machines cannot perform inductive reasoning

In other words, a line of computer code cannot write itself (even though it may write or rewrite other lines of code). Thus, a program is only as good as the axioms it has been given.

4.3. Adding randomness to Turing machines generates information entropy, not negentropy

The statistical syllogism in support of the above statement is as follows:

1. Turing machines become non-deterministic by adding randomness (noise) to a communication channel (Bohan Broderick, 2004; Hopcroft et al., 2001).
2. Randomness in a communication channel is positive information entropy (Shannon, 1948).
3. Therefore, non-deterministic Turing machines do not generate negative information entropy.

In other words, adding random variables to computer logic is not an escape from the limitations of computing. Randomness must not be confused with choice, because randomness is the opposite of choice (Shannon, 1948).

4.4. There is a severe limit on the size of useful statements that can be generated by randomness

The statistical syllogism in support of the above statement is as follows:

1. For a computer to generate specific statements consisting of more than 332 bits of information (42 bytes, or 42 letters) through a random "brute force" process requires 10^{100} trials to test all combinations
2. 10^{100} trials could not be made by any real-world computer in the history of the universe.
3. Therefore, specific statements longer than 332 bits are not realizable through randomness.

The reason this is an empirical observation rather than a mathematical proof is that, for example, there is a nonzero chance you can guess a password correctly the first time. But everyone who relies on bank accounts and computer passwords votes against exceptions with their behavior. In other words, if the computer uses random numbers to test passwords, it reaches "combinatorial explosion" with less than 50 characters of data. An alphanumeric password including upper and lower case and special characters >50 letters long requires 10^{100} iterations to guarantee one right answer. There are only 10^{80} particles in the universe, and thus it would take unimaginably long to guess the answer. Password lengths of 8–12 characters are ostensibly sufficient to protect valuable data and generating passwords with random numbers is far easier than generating mathematical axioms or scientific theories with random numbers. This applies to genetics as well, because 166 base pairs of DNA also represent 10^{100} possibilities; yet the smallest bacteria have over 400,000 base pairs. Therefore, even natural selection cannot overcome the combinatorial explosion problem. This is why chance and selection alone do not account for life's origin or evolution.

Experimental biologists know that random mutagenesis can trigger useful mutations, especially in bacteria. However, recall that organisms have extensive error detection and correction machinery, which is activated by DNA damage (Shapiro, 2011). McClintock (1984) triggered highly ordered transpositions, restructured by maize plants, via random mutations. The organism plays an active, not passive, role in the mutation process, so the generation of successful coding sequences is often not truly random.

4.5. Negentropy (inductive reasoning, choice) requires agency

The statistical syllogism in support of the above statement is as follows:

1. Negentropy is choice
2. Only agents make choices
3. Therefore, negentropy requires agency

Since generating codes is equivalent to generating negentropy (Shannon, 1948), the above is a re-statement of the inductive logic behind the Evolution 2.0 prize: 1) The pattern in DNA is code, 2) All codes whose origin we know are designed, and 3) Therefore the genetic code is designed ("Origin Of Life: $10 Million Prize at the Royal Society," 2019).

The above is a statistical, not deductive proof, because there are five possible solutions to the origin of the genetic code:

I. Time travel is possible and humans designed the genetic code
II. Extraterrestrials designed the genetic code
III. The genetic code emerged randomly and accidently
IV. There are unknown laws or emergent properties of physics and chemistry
V. Divine intervention.

I do not consider (I) to be possible. (II) only kicks the can down the road. (V) is possible but the author wishes to avoid making god-of-gaps arguments (Marshall, 2015, Ch. 24), and furthermore (V) implies that code precedes cognition, which this paper has already argued to be incorrect. (III) is not a testable hypothesis, and thus does not qualify as science. Furthermore, (III) violates information entropy. Thus, given that nearly all organisms can redesign their own genomes, (IV) merits further investigation, and is the subject of this paper: cognition and agency. The fact that codes and the other phenomena in Table 2 are only known to come from biology places great weight on the origin of life problem.

4.6. Generating mathematical axioms is, by definition, inductive reasoning, which invokes choice

The statistical syllogism in support of the above statement is as follows:

1. Computation requires axioms.
2. Axioms in mathematics are not computed but must be chosen inductively. The celebrated mathematician Hermann Weyl said, “Without inventing new constructive processes, no mathematician will get very far. It is perhaps proper to say that the strength of modern mathematics lies in the interaction between axiomatics and construction” (Weyl, 2013). This was also supported by Enderton: “Of course our selection of axioms will be guided by the desire to reflect as accurately as possible our informal (preaxiomatic) ideas regarding sets and classes” (Enderton, 1977).
3. Therefore, computing is a derivative of agency.

Since physics and chemistry compose the physical layer in all information systems, causation in computing is cognition → chemicals → code. Given that biology is the only known source of agency in the universe (Cronin and Walker, 2016; Kauffman and Clayton, 2006) we conclude section 4. with the following syllogism.

4.7. The agency exhibited by life is not matched by computers

The statistical syllogism in support of the above statement is as follows:

1. Neither classical nor nondeterministic Turing machines can produce negentropy
2. Biology produces negentropy.
3. Therefore, biological systems are not Turing machines, and biology transcends the limits of computation.

This last statement is statistical and not deductive because entropy and negentropy are empirical and statistical entities, not pure mathematics. That said, this conclusion is as reliable as the scientific principle of entropy. Evolution is not a product of chance, but relies on principles of cognition that we do not yet understand.

Some will challenge the statement “biology produces negentropy” and assert that organisms are not making choices, but only running very sophisticated algorithms. Walker and Davies (2016) counter this flavor of determinism by saying, “To explain a world as complex as ours—which includes things like bacteria and at least one technological civilization with knowledge of things like the laws of gravitation—requires that the universe have a very special initial state indeed. The degree of ‘fine-tuning’ necessary to specify this initial state is unsatisfactory, and becomes ever more so the more complex the world becomes. One should hope for a better explanation than simply resorting to special initial conditions (or for that matter stochastic fluctuations, which in many regards are even less explanatory).”

Perhaps the most poignant example of negentropy is the persistent failure of drugs and gene therapies to stop late-stage cancer. The fact that tumors initiate rapid, chromosome restructuring (Heng, 2019) in response to therapies and often evade them, *should* lay to rest the notion that evolutionary mutations are random or guided only by selection. At the other end of the spectrum of examples, mathematics itself is a manifestation of the ability of agents to not merely be confined to systems of logic but to create new ones. This is why all great achievements in mathematics (and other fields like technology and business) are triumphs of creativity and not mere analysis.

Thus, we have two directions of causation: 1) Bottom-up, where noise, accidental mutations, and information entropy destroy information and order; 2) Top-down, where agents make choices (increasing negentropy) using cognition, which enables inductive reasoning and symbolic communication so they can exercise control over their environments.

5. Discussion

5.1. Choices by definition are not computable

Choice is intrinsic to information theory (Shannon, 1948), where one bit of information is a choice. This paper takes as axiomatic that choice is not an illusion. This axiom is ubiquitous and essential in society, from consequences for committing crimes to the ability to propose and debate mathematics and scientific laws.

I have not arbitrarily defined codes, goals, inductive reasoning, and evolution as choices, and presumed them to be non-computable. The very definition of choice and the observed behaviors of agents dictate that they are *necessarily* non-computable. Thus, there is a vast chasm between life and non-life, and things as “ordinary” as language and abstract mathematics do not exist, and in principle cannot exist, without cognition (Pattee, 2012). This chasm is an inevitable consequence of Gödel, Turing, and Shannon. It is interesting to compare this with proposals by Chalmers (1995) and others that consciousness is an “irreducible fundamental property of mind with its own laws and principles” (Walker et al., 2017).

5.2. Cognition is the most fundamental question in biology

Shapiro (2020) says, “We have long grown accustomed to thinking of cognition as the result of highly evolved sensory organs, transmission systems and signal evaluation capacities. But prokaryotes show us that even the smallest and simplest cells have the molecular tools to respond cognitively to a broad range of environmental opportunities and threats.” Mechanistic biology treats life as though it were dead, and assumes purposeful actions are accidental or formulaic. Information theory and technology practice suggest that the origin of information, the origin of life, evolution, cancer, AI, and cognition are not six problems but one problem: the problem of cognition. This is evident in that many breakthroughs that Silicon Valley is seeking are already solved in the cell. A worthy pursuit for 21st-century biology is to comprehend the systems that enable all living things to express, with seeming ease, the decision-making abilities that thus far have eluded computer scientists. Perhaps the secret of "The First Cell," the title of Azra Raza's book—which refers to the first cancer cell in an oncology case—is also the secret of the very first cell 3.8 billion years ago (Raza, 2019).

5.3. Falsification

Any experiment that demonstrates chemicals can give rise to code without inserting biological cognition will show the model proposed in this paper to be wrong ("Origin Of Life: $10 Million Prize at the Royal Society," 2019), as will any experiment that demonstrates code can give rise to cognition. One instance of any of the phenomena listed in Table 2, if produced by a computational process having emerged with no assistance from biology, would be sufficient to disprove this model.

5.4. Implication: biology and evolution are neither reductionistic nor deterministic

Biology has been saddled with "physics envy" when in fact it is a far more sophisticated discipline than physics, with numerous unique principles (Kaufmann, 2005; "The social sciences' 'physics envy," 2012). Biology obeys the rules of mathematics, physics and chemistry, but cannot be reduced to those things (Schrödinger, 1944; Walker and Davies, 2016). Biology possesses properties unknown to physics, chemistry, and computing. Evolution is not computation.

The foundations of biology were laid incorrectly when August Weismann asserted that information only flows one way (Noble, 2020; Noble and Noble, 2020). The attempt to purge agency from biology has not only crippled basic biological theory, but also treatments of diseases and cancer. Life is impressive and mysterious, yet many reductionist scientists seem ashamed of its mystery. The eminent biologist Carl Woese lamented at how reductionist thinking caused biology to "become a science of lesser importance, for it had nothing fundamental to tell us about the world." He described how biology has been shackled by the confines of physics, and hoped that it would "press forward once more as a fundamental science" (Woese, 2004).

The proposition that cognition cannot be modeled does not mean it cannot be built. Many problems in mathematics cannot be solved analytically but can still be solved numerically. Many physical systems are far too complex to simulate on computers, but are still built and used. In other words, just because cognition cannot be reduced to our current mathematical formulations does not mean it cannot be engineered. Perhaps it can be. Perhaps alternate systems of mathematics that model cognition are also possible. Einstein said "Imagination is more important than knowledge."; our capacity to create is more powerful than our analysis. This also means that biology and medicine ought to be considered as soft sciences, not hard sciences. Please bear in mind that the word "soft" is not derogatory, it simply refers to the fact that humanity's most complex disciplines defy reductionist analysis. Biology has non-deterministic phenomena and behaviors (Table 1) that can only be analyzed in the aggregate. Thus, biology is less close to physics and closer to sociology, psychology, marketing, and economics. A superior understanding of biology and evolution will, in turn, powerfully inform these fields (Lee et al., 2019; Shapiro, 2011).

Every book, movie, poem, legal mandate, hero, heroine and epic story is a study in action and choice. Choice and agency are the most fundamental questions of all. Molecular biology, information theory, and technology affirm these questions at cellular and even sub-cellular levels—even viruses are not exempt. Denying the centrality of choice does not merely deny our humanity, it diminishes the sciences of biology, physiology, and medicine, as well as their potential for solving our most pressing problems. By acknowledging choice as the central actor in the life sciences, one can fulfill Woese's vision of biology's rich possibilities and restore the unity of science with the humanities (Hoffmeyer and Emmeche, 1991; Kull, 1998). We have barely begun to understand what cognition is, let alone how it works. A breakthrough in this area will be as revolutionary as the discovery of gravity, relativity, the transistor or the genetic code.

6. Conclusions

This paper has used Turing mathematics and the laws of information entropy to prove that cognition is the driving force in biology, which cannot be reduced to known laws of physics. The reductionist model is incorrect; the direction of causation in biology is cognition → code → chemicals and not the reverse. This is consistent with the fact that there are no known examples in the literature of chemicals producing codes, or codes producing cognition. The central question in biology is agency: the origin and nature of choice. A cognition-based model has the potential to solve and unify Origin of Life, Origin of Information, evolution, consciousness, AI and cancer.

Nearly 80 years ago, Schrödinger (1944) said "From all we have learnt about the structure of living matter, we must be prepared to find it working in a manner that cannot be reduced to the ordinary laws of physics. And that not on the ground that there is any "new force" or what not, directing the behavior of the single atoms within a living organism, but because the construction is different from anything we have yet tested in the physical laboratory." The situation is essentially no different in the 21st century than it was in 1944.

Evolutionary theory is now in a sea change (Baverstock, 2013). In 2013 Denis Noble said, "all the central assumptions of the Modern Synthesis (often also called Neo-Darwinism) have been disproved. Moreover, they have been disproved in ways that raise the tantalizing prospect of a totally new synthesis" (Noble, 2013). Despite detailed investigation of many evolutionary mechanisms, from niche construction to epigenetics to the hyper-speciation of cancer cells termed "The Cancer Cambrian" (Pienta 2020), our understanding of evolution is very incomplete. We only have a surface level comprehension of it. Thus, a solution to the origin of life might someday be found in the cell itself. Surely it should be possible to observe closely enough to discern what is happening. No one understands the mechanism in the cell that performs cognitive tasks, but it tirelessly does its work and awaits our discovery.

Origin of information prize

I have organized a $10 million USD prize for the origin of information. Prize judges include George Church (Harvard Genetics) and Denis Noble (Oxford Physiology). Winners must produce an encoder, message, and decoder without biological agents defining the code in advance. The system needs to transmit at least five bits of information (32 states; the genetic code supports 64), and one must be able to draw an encoding and decoding table and determine whether or not the data has been transmitted. Thus far it remains unsolved.

A non-reductionist model of biology is still needed that does not violate the laws of physics or mathematics. Most submissions for the Evolution 2.0 Prize thus far—and nearly all origin of life models—have presumed the traditional model of chemicals → code ("Entries for the 'Chemicals to Code' Technology Prize," n.d.). Such an approach appears contrary to known principles of information theory and practice. No example of such a transition has ever been observed (Yockey, 2005). As Wolf and Koonin state in Table 1 (2007), no one knows how to make this work. A much less explored but plausible route is cognition → code, by taking a homeostatic view of the cell.

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