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The Complex and the Miraculous: A Closer Look at the Irreducible Complexity of Cell

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Abstract*:* It is the "irreducible complexity" of the cells which the Darwinian Theory of Evolution fails to fathom. As the basic unit of life, a cell exists in cooperation and harmonious conjunction with several other organelles, and if any one of these organelles become dysfunctional, the cell itself ceases to function. As more and more evidences are now accumulating, it is becoming increasingly clear that the collective assemblage and functioning of all these organelles in a cell seems quite unlikely to arise from a simple, random, mutation-driven section mechanism which is at the core of the Darwinian Theory of Evolution. The first cell from which all life on Earth later arose had to be a complete cell with all its organelles and functionalities full developed. This seems miraculous since even the smallest polypeptide with a size as small as the smallest of the proteins could not have arisen spontaneously by random chance. Now, it becomes billions of times more improbable for more than a million of these proteins to come together and give rise to the first, fully functioning cell. Along with the assemblage of proteins, a cell also contains carbohydrates, proteins, nucleic acids, lipids, and other chemicals arranged in highly specific order and all attuned to fulfilling the one single purpose, which is to keep is alive.Through pure abiogenetic processes, even the formation of a single, fully functioning protein appears to be utterly unlikely, let alone a complete living cell. However, processes such as chemical evolution and self-organization can give rise to the complex macromolecules which are essential for life.
Keywords: irreducible complexity; cells; evolution; DNA; RNA; proteins; amino acids

Introduction: Cells are among the most co-ordinated and complex entities that we come across in our world which is made of several other complex entities like DNA, RNA, membrane and proteins and act as one tangled system which is nonetheless highly organized and directed. Without the existence of cells, there will be no story to tell, no narrative to record, no information to relay, and no existence would have been ever possible: "Neurons, information, thought, and awareness are essential for the story of mind—and with that the narratives proliferate: myth to religion, literature to philosophy, art to music, telling of humankind's struggle for survival, will to understand, urge for expression, and search for meaning" (Greene, *Until the End of Time* 5). Within the cells we see a dance of several clouds of signal molecules around the untangled loops of DNA which aims to bind to certain sites near genes and these genes have many binding sites around them. Now, when the binding process begins, we see how in a very co-ordinated and planned way, binding proteins send signals before settling onto DNA and also attracts several other proteins to form a cluster which in turn invites the RNA polymerase to join the party and begin transcribing DNA into mRNA at a pace of almost 50 nucleotides per second. "Chain elongation continues (at a speed of approximately 50 nucleotides/sec for bacterial RNA polymerases) until the

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enzyme encounters a second signal in the DNA, the terminator, where the polymerase halts and releases both the DNA template and the newly made RNA chain…" (*Molecular Biology of the Cell*, 337*).*The polymerase does not do one single task al the time, rather switches between two functions- sometimes, it forms an RNA from two chromosomal strands, while on other occasions, it helps DNA to duplicate through replication forks: "The proteins that initiate DNA replication bind to DNA sequences at a replication origin to catalyze the formation ofa replication bubble with two outward-moving replication forks. The process begins when an initiator protein–DNA complex is formed that subsequently loads a DNA helicase onto the DNA template. Other proteins are then added to form the multienzyme "replication machine" that catalyzes DNA synthesis at each replication fork" (Alberts, et al. "The Initiation and Completion of DNA Replication in Chromosomes"). Now, proteins act as the building blocks in the cell and the proteins are formed from the processed parts of RNA within cytoplasm where proteins like polymerase are formed. Now, a paradox arises in that DNA is copied to make RNA while RNA is transcribed to make proteins but DNA itself cannot exist without the proteins since proteins are the fundamental building blocks of the cell. Now, while replicating the DNA, proteins first disentangle the DNA by creating forked strands where one strand is created toward the right side while another towards the left before stitching the left-handed stand back together. Now, in this regard, fork rotation and DNA precatenation also need to mentioned since it is with the restriction of two processes that chromosomal instabilities are also kept under check: "Precatenation thus appears to have important biological roles involving the timing of DNA segregation and cell division, and is not merely a side effect of DNA replication that causes topological problems to the cell. Precatenanes may also prevent closely-spaced recombination events (so-called "crossover interference"), an important process in meiosis. Finally, by converting left-handed positive supercoils ahead of the fork to right-handed precatenanes behind the fork, precatenation might alleviate positive supercoiling, which would otherwise slow fork progression and spur potentially toxic and mutagenic double-strand breaks at stalled replisomes" (Bates, et al. "Importance of Disentanglement and Entanglement during DNA Replication and Segregation"). Now, proteins also play a major role in the process of proofreading the errors that might creep up during the entire process of replication of DNA and help to keep the errors under 1 mistake per billion nucleotides. Also, within the cells, another mysterious entity called the ribosome operates which are tremendously efficient protein making factories. Ribosomes receive the message from messenger RNA and translates it to for amino acids after matching it to tRNAS. A 2014 article in *Nature* explains it lucidly: "Three general classes of RNA molecules are involved in expressing the genes encoded within a cell's DNA. Messenger RNA (mRNA) molecules carry the coding sequences for protein synthesis and are called transcripts; ribosomal RNA (rRNA) molecules form the core of a cell's ribosomes (the structures in which protein synthesis takes place); and transfer RNA (tRNA) molecules carry amino acids to the ribosomes during protein synthesis" ("Ribosomes, Transcription, Translation"). Now, the biological processes of replication, transcription and translation are three processes which govern all the life-forms life on Earth. Not only these, but also mitochondria in the cell generate power by constantly breaking down glucose into ATPs and besides being incredibly efficient. it also recycles the

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by-products of each cycle to use them in the next cycle. “Now, inside the cell, we see how a complex interplay takes place between microfilaments and microtubules. Microtubules act as supporting structures which enable the proliferation of various other substructures and novel pathways, while microfilaments are the superfine threads of protein that stay beneath each cell to give it shape. This in many ways, also parallel the cosmic processes of evolution of galaxies through channelling of gas via filaments that form and follow the web-like stringy structures made of dark matter.A 2019 study proposes that the points of intersection between these galactic filaments can host extremely energetic active galactic nuclei like Quasars which are rapidly accreting and frantically feeding supermassive black holes (“Gas filaments of the cosmic web”) and also ultraluminous and hyperluminous starburst galaxies, as can be seen in the case of the most luminous known galaxy, W2246−0526 (“The multiple merger assembly of a hyperluminous obscured quasar at redshift 4.6”). Now, returning to our discussion of cells, we shall find that the complex network of endoplasmic reticulum emerges from the nucleus many of which have ribosomes included in them. Now, while ribosomes continue to churn out more and more proteins and, in the process, consume more and more ATPs, certain tubules stick out from the surface of the cell which connect the nucleus to the Golgi apparatus where proteins are stored and sorted for delivery at a later period. Even the cytoplasm itself is covered with several thousands of ribosomes and mitochondria and networks of signal molecules transmit information back and forth from the cell surface to the nucleus and back again. Enzymes also destroy, rebuild and repair worm put structures for the purpose of creating even more durable portions within the cell and all that by using more and more ATPs. Messenger RNAs search for ribosomes and properly processed and folded proteins as incomplete or incorrectly folded proteins and damaged RNAs can contribute to diseases like Alzheimer’s.

Mystery of Life: Life, overall acts a synchrony of several microscopic forces and processes whose true nature scientists are yet to fully figure out. The big question that lies at the heart of our quest to understand the emergence of life is how individual constituents give rise to this emergent, collective phenomenon we call life. Even a single cell is full of immense complexity as it is made of as many as trillions of atoms. Cells are among nature’s most sophisticated and multifunctional factories where various complex tasks like intake of nutrients, disposal and expulsion of waste, fusion of nutrients and substances for the proper functioning – all take place at a dizzying pace and almost unmatched accuracy, and yet, cells are over 70% water. Albert Szent-Györgyi comments on the role of water bas the bedrock of life: “Water is life’s matter and matrix, mother and medium. There is no life without water. Life could leave the ocean when it learned to grow a skin, a bag in which to take the water with it. We are still living in water, having the water now inside” (“Biology and Pathology of Water”). Cells are incredible entities for their abilities to encode and utilize information to sustain all sorts of lifeforms ranging for simple, unicellular to the highly complex, multicellular ones. Now, cells require proteins to perform and proteins arise out whenspecific sequences of amino acids combine together. If we look closely, we shall find that mere randomness should fail to give rise to a particular protein from a random assortment of twenty distinct amino acids in a specific chain. Even a simple protein that is as little as one hundred and fifty amino acids have 10^195 distinct possibilities of arrangements. Creation or

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synthesis of specific proteins that can participate and facilitate in life's functioning requires some kind of highly sophisticated cellular programming and cells have those sets of specific instructions embedded in them which are encoded by DNA. Now, it is the genes which carry the protein encoding information in them and they are thus ca be classified as instructional blueprints for manufacturing of proteins in cells. Now, it is through the redox reaction that cells generate, transport and transmit energy. When we ingest food, the electrons do not get transferred directly to oxygen but undergo a series of small redox reactions before ultimately ending with oxygen. Electrons rollick their way from one energy receptor to another before finally ending with oxygen which grabbing them tightly and extracting all the energy these can provide. Now, it is through the clustering of protons on one side that biological redox reactions operate. Now, the membrane that divides the collected protons on one side is extremely thin measuring up to no more than five or six atoms' width, and the electric field can have up to a voltage of some few megavolts per meter.These tightly clustered protons can flow only along certain direction across the fine membrane and this generates power for the cellular batteries to function. As the protons move, input molecules called the ADP, or adenosine diphosphate synthesize the ATP, or adenosine triphosphate. Now, it is through the disassociation of these ATP bonds which have potential energy stored in them like some compressed spring, that the energy can be derived and extracted thereby allowing the ATPs to relax into lower energy states. Each second, the human body consumes the energy equivalent of some 10^20 ATPs (10^7 ATPs consumed by the 10^13 cells) and this is enormous. Also, the recycling process continuesin its own pace as for each ATP consumed,it dissociates intoan ADP and a phosphate, which can then power the which the proton-powered microscopic power plants of the cell, or mitochondria can gather together to again manufacture new ATP molecules. These ATP molecules then hit the road again, delivering energy throughout the cell. For keeping with the body's normal energy demand even for as trivial a task as watching TV or reading a book, in every second as many as 10^20 ATPs need to be synthesized at an unimaginably fast pace. The singular and universal mechanism for synthesis of molecules and coding of cellular instructions points towards the origin of life from a common ancestor. Weiss et al. writes, "All known life forms trace back to a last universal common ancestor (LUCA) that witnessed the onset of Darwinian evolution…Because the genetic code and amino acid chirality are universal, all modern life forms ultimately trace back to that phase of evolution. That was the time during which the last universal common ancestor (LUCA) of all cells lived" ("The Last Universal Common Ancestor between Ancient Earth Chemistry and the Onset of Genetics"). Watson and Crick explored the process through which the DNA's double helix ladder transmits copies of instructions. When the cell undergoes division, the ladder splits into two rails, where on each of those rails, an A from one rail seeks to attach to its partner base T on the second rail; while a C from one side seeks to attach to a T on the second side. Now, it is during the division that a daughter cell receives duplicate copies thus transferring information from one generation to the next. Also, during these copying processes errors can creep up naturally or artificially thereby introducing differences in the inherited DNA sequence of the daughter cell. Even though most of the mutations are neutral, the positive mutations can help the cell to become fitter and thus more likely to spread these changes through reproduction. Sexual reproduction is one such mechanism where duplication of the genetic materials always produces a concomitant rise in complexity. During the process of copying, modifications wrought upon DNA can have errors at the rate of 1 per 10^8 or so base pairs, and the cells error-correcting mechanism ensures that the rate goes down to some 1 error per billion base pairs.

Mysteries of Origin: Now, we should consider the problem of the abiotic origin of the first living cell on the primitive Earth. There is a hug gap between the artificially concocted protocell in the laboratories and the simplest of living cells that can be found in nature. As Jowett et al. observes, "Attention has focussed upon four critical processes: the formation of organic molecules such as amino and nucleic acids, the polymerization of these molecules, the formation of membranes, and the development of metabolic networks for power" ("Myth and Fact in the Origins of Cellular Life on Earth"). The deeper we look into the microcosm of the amazingly organized cells the more we become convinced that mere simple chemicals though their random interaction could not have given birth to the mind-bending complexity of the cell. Before the actual cells arrived on the scene, we had protocellswhich after existing for a certain period of time became complex and certain polypeptides with specificity also evolved into enzymes. Then hereditary molecules like nucleic acids began to develop and became the chief regulator of biological processes. Now, we have to keep it in mind, that during those formative periods of life on Earth, various dilution processes were also operating which would have easily prevented the concentration of life's precursor molecules in any significant amount. Now, it is the organization of atoms and molecules which even though individually obey physical laws like laws of thermodynamics when organized into a whole obeys the laws of a macroscopic, collective system. Living systems are similar to but far more complex in their organized behavior than computers, and have far greater organization than any non-living object. Prigogine et al. notes:"All these features bring the scientist a wealth of new problems. In the first place, one has systems that have evolved spontaneously to extremely organized and complex forms. Coherent behavior is really the characteristic feature of biological systems" ("Thermodynamics of Evolution," 23). Now, the problem of synthesizing DNA and RNA from simple biomonomers requires an extremely precise way of channeling energy and this itself is a great challenge. Living beings are obviously much more than just simple DNAs and enzymes but they are the first steps for replication to occur.

In this chapter we will consider only the problem of the origin of living systems. Specifically, we will discuss the How can we specify in a more precise way the work to be done by energy flow through the system to synthesize DNA and protein from simple biomonomers? While the origin of living systems involves more than the genesis of enzymes and DNA, these components are essential to any system if replication is to occur. It is generally agreed that natural selection can act only on systems capable of replication. This being the case, the formation of a DNA/enzyme system by processes other than natural selection is a necessary. Now, various recent studies such as the one done by Patrick W. Kudella, Alexei V. Tkachenko, AnnalenaSalditt, Sergei Maslov, and Dieter Braun (2021), have pointed out that the subunit composition of polymeric molecules can initiate Darwinian selection processes even in a prebiotic setting. In the prebiotic setting, several chaotic physiochemical processes occurred where nucleotide bases such as those found in DNA and

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RNA were also present in certain combination. The study conducted by Dieter Braun and his team has shown that in a prebiotic environment, certain polymers could act in such a way as to reduce the level of chaoticity. The study shows that in the presence of temperature differences and Soret effect, base sequences if longer molecules tend to become chaotic, and "the emergence of longer information-carrying and functional nucleotide polymers from random short strands was a major stepping stone at the dawn of life" ("Ligation of random oligomers leads to emergence of autocatalytic sequence network"). Now, RNA-based enzymes called evolved ribozymes helped molecules to fold into specific shapes while most of the oligomers formed in the primitive Earth were mostly random. Since the sequence space or the total number of possible base sequences is inconceivably large, assemblage of complex structures through purely random processes become next to impossible. So, the study suspects that there was definitely some preselection mechanism at play during those early phases where molecules began assembling into larger oligomers. Also, during the very early periods of emergence of life, those simple physio-chemical processes that helped in the selection of sequences, should have relied primarily on the environment. It is also necessary that the processes should give rise to the double stranded helical structures like that found in DNA for executing catalytic functions and for ensuring stability of the oligomers.Through the process ofpolymerization, single-based strands form double strands, and through ligation, longer oligomers unite together. When both double-stranded and single-stranded parts are formed, oligomer begins to grow further. Now, in the experiment conducted by Dieter Braun and his team they used two complementary bases, adenine and thymine and found that the formation of longer strands had the degree of randomness or disorder reduced. They also discovered some kind of emergent self-generate order where the sequences generated fell into either the class of 70% adenine and the class of 30% thymine.So, in a prebiotic environment, certain features of oligomers and environment can provide the ingredients for triggering a pre-selection mechanism. "According to Braun, these selection mechanisms were a prerequisite for the formation of catalytically active complexes such as ribozymes, and therefore played an important role in the emergence of life from chaos" ("Origin of Life -- Did Darwinian Evolution Begin before Life Itself?" *Newswise.com*).

The Irreducible Complexity : Erica Hayden states in the journal Nature that with the advancements in sequencing and other related technologies, scientists have begun to uncover the incredible complexity of this simple unit of life, "Delving into it has been like zooming into a Mandelbrot set… that reveals ever more intricate patterns as one peers closer at its boundary" ("Human Genome at Ten: Life is Complicated"). Commenting on the incredible complexity of such a minuscule bacterium called *E. coli*, H.C. Berg notes, "*E. coli* is a cylindrical organism less than 1 μm in diameter by 2 μm long—20 would fit end-to-end in a single rod cell of the human retina or some 3000 in that of a frog. Yet, it is adept at counting molecules of specific sugars, amino acids, or dipeptides; at integration of similar or dissimilar sensory inputs over space and time; at comparing counts taken over the recent and the not so recent past; at triggering an all-or-nothing response; at swimming in a viscous medium; and as we shall see, even at pattern formation" ("Bacterial Microprocessing"). Cells possess a number of amazing characteristics: Certain cells can measure the passage of time (*Physical Biology of the Cell*, Chapter 3), some can sense and respond to magnetic and electric fields,

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some possess very thick, armor-like protective encasing, some possess a lens to project an image from one region of the cytoplasm to another and some can repair and regenerate themselves even when they are cut (Tartar, “Regeneration”). An average human body contains as many as 10^14 cells and during gestation, it constructs the brain by creating few millions of connections each minute for nine months. Cells also participated in the process of terraforming of the planet and photosynthesis for over 3 billion years through which it generated oxygen. Cells can even engage in various socially valued actions and thus display traits that mimic animal social behavioral intelligence (Clark, “Origins of learned reciprocity in solitary ciliates searching grouped 'courting' assurances at quantum efficiencies”). Herbert Jennings in his book *Behavior of the Lower Organisms* states, “If Amoeba were a large animal, so as to come within the everyday experience of human beings, its behavior would at once call forth the attribution to it of states of pleasure and pain, of hunger, desire, and the like, on precisely the same basis as we attribute these things to the dog” (337). Brian Ford also finds parallels between our own world and the microscopic world of the single-celled organisms: “The
microscopic world of the single, living cell mirrors our own in so many ways: cells are essentially autonomous, sentient and ingenious. In the lives of single cells we can perceive the roots of our own intelligence” (“The Secret Power of the Single Cell,” 26). Ford further comments, “We regard amoebas as simple and crude. Yet many types of amoeba construct glassy shells by picking up sand grains from the mud in which they live. The typical Difflugia shell, for example, is shaped like a vase, and has a remarkable symmetry… We just don’t know how this single-celled organism builds its shell” (26). Cells are not sentient or conscious in any traditional sense of the term, but through their organized structuring, functioning and various accomplishments, they strike us as incredibly sophisticated entities.

Various technologies such as X-ray crystallography and electron microscopy have revealed that the atomic ingredients of complex macromolecules in the cell can help them to get arranged in 3-D shapes which are at once extremely unique and able to execute various specific biochemical and genetic purposes. This high degree of specificity is a remarkable feature of the cells. Whether they be genes or proteins like enzymes or antibodies, al these entities are surcharged with an extreme degree of biological specificity. The cells help construct a number of complex biomolecular machines that can execute so many of the highly specialized tasks. For example, enzymes bind to specific substrates to carry out functions which are essential for the maintenance of life, and unless the atoms are arranged in highly specialized 3-D shapes these enzymes could not be directed to bind to specific sites.These two features of directionality and spatial constraining go to great lengths in creating the molecular building blocks. Now, nomcomplex macromolecules ca be made to serve specific biological functions unless the bonds from which they are made are themselves directional and spatially oriented. Ionic bond demands energy many times higher than what carbon makes with hydrogen, oxygen and nitrogen. Atkins in his *Periodic Kingdom* makes this insightful observation, “In general,molecular compounds [made up of covalently bonded atoms] arethe soft face of nature, and ionic compounds [inorganic] are the hard. Few distinctions make this clearer than those between the soft face of the Earth —its rivers, its air, its grass, its forests, all of which aremolecular—and the harsh substructures of the landscape, which are largely ionic. This is why theupper triangle of the Eastern Rectangle [in the periodic table] is soimportant to the existence of life, and why all the rest of the kingdom is soimportant in the formation of a stable, solid platform" (178). Elements such as carbon (C), nitrogen (N), oxygen (O), and hydrogen (H), phosphorus (P) and sulfur (S), which perform a crucial life in the creation and maintenance of carbon-based life all depend on the properties of directionality and spatial constraining to function properly, and there the role of covalent bond becomes apparent. It is though the weak bonds such as the highly directional covalent bonds, the electrostatic forces and van der Waals forces that molecules and atoms interact with varying amounts of specificity, help them come together in any physically meaningful sense. DNA's double helical structure points to the need of such alternating plays between strong and weak bonds as the spatial position of atoms in each of these nucleotides is determined by the highly directional bonds, while the weak bonds join the two strands of DNA in double helical, 3-D helical structure. DNA's double helical structure also points to the hassle-free reversibility of the weak bonds and this trait becomes extremely important in separating the two strands of the helix during the process of DNA replication and transcription. Any strong bond between two strands would make the processes of transcription and replication not only difficult but also quite impossible. It is only through a series of selective, reversible, weak bondings that various molecular surfaces such as the two strands of DNA, a protein's two strands of polypeptide chains, and attachment between an enzyme and a substrate can grow.

Conclusion: Michael Denton remarks: "To grasp the reality of life as it has been revealed by molecular biology, we must magnify a cell a thousand million times until it is twenty kilometers in diameter and resembles a giant airship large enough to cover a great city like London or New York. What we would then see would be an object of unparalleled complexity and adaptive design. On the surface of the cell we would see millions of openings, like the port holes of a vast space ship, opening and closing to allow a continual stream of materials to flow in and out. If we were to enter one of these openings we would find ourselves in a world of supreme technology and bewildering complexity."(*Evolution: A Theory In Crisis).* This article endeavored to throw some light on the so-called irreducible complexity of the cell which makes the Darwinian theory of evolution through 'Natural Selection' insufficient in explaining the emergence of sophisticated functionalities of cells. Evolutionist W.H, Thorpe writes, "The most elementary type of cell constitutes a 'mechanism' unimaginably more complex than any machine yet thought up, let alone constructed, by man" (quoted in Groff, *"*The Language of Life*,")*. As we have peered deep into the microcosm of cellular world, we have uncovered an incredible amount of diversity of mechanism and purpose in every living cell which range from power stations generating power for the maintenance of the rest of the body, specific sites for manufacturing of enzymes and hormones, a storage-house where all the necessary data about the process is kept and maintained, laboratories for tinkering with the data and refineries for decomposing the raw materials into finished ones, specialized membrane which separates the incoming and outgoing material etc. to name a few. Overall, the incredible complexity of the cells makes it a thing of pure wonder and deserve lots of research. Even for an average sized protein molecule consisting of as few as 288 amino acids, and containing some 12 amino acids can be arranged in as many as 10^300 different possible sequences and only 1 out of all these 10^300 sequences form the one, fully functioning protein molecule. Even the accidental and random formation of as few as 2000 types of proteins in a simple bacterium has a probability of 1 in 10^40,000, and a single huma cell has over 200,000 different proteins. Also, the spontaneous emergence of complex life through totally random processes appears to be thermodynamically impossible too, as more complex a system becomes the more prone it gets towards disintegration and destabilization. So, the task of overcoming the barrier of the 2nd Law of Thermodynamics through the adoption of various efficient energy conversion mechanism like photosynthesis itself poses a great challenge towards the emergence of complex lifeforms. Even the highly favored RNA World theory requires some miraculous ways through which it can replicate the entire process of protein synthesis without the presence of any protein.

<u>References/Bibliography</u>:

1. Greene, Brian. *Until the End of Time: Mind, Matter, and Our Search for Meaning in an Evolving Universe*.Allen Lane Publishing, 2020.
2. Atkins, Peter. *The Periodic Kingdom***:** *A Journey Into the Land of the Chemical Elements*.Hachette UK, 2013.
3. Denton, Michael. *Evolution: A Theory in Crisis*. Adler & Adler Publishers Inc., U.S. 1996.
4. Groff, Jim. *"*The Language of Life*." Rootsministries.com, 27 Apr. 2018,* rootsministries.com/2018/04/27/the-language-of-life/. Accessed 25 Feb. 2021.
5. *Molecular biology of the cell*, **5th** edition by B. Alberts, A. Johnson, J. Lewis, M. Raff, K. Roberts, and P. Walter. Taylor and Francis.
6. Boyle, John. "Molecular Biology of the Cell, 5th Edition by B. Alberts, A. Johnson, J. Lewis, M. Raff, K. Roberts, and P. Walter." *Biochemistry and Molecular Biology Education*, vol. 36, no. 4, July 2008, pp. 317–318, iubmb.onlinelibrary.wiley.com/doi/full/10.1002/bmb.20192, 10.1002/bmb.20192. Accessed 23 Feb. 2021.
7. Umehata, H. et al. "Gas Filaments Of The Cosmic Web Located Around Active Galaxies In A Protocluster". *Science*, vol 366, no. 6461, 2019, pp. 97-100. *American Association For The Advancement Of Science (AAAS)*, doi:10.1126/science.aaw5949. Accessed 23 Feb 2021.
8. Díaz-Santos, T. et al. "The Multiple Merger Assembly Of A Hyperluminous Obscured Quasar At Redshift 4.6". *Science*, vol 362, no. 6418, 2018, pp. 1034-1036. *American Association For The Advancement Of Science (AAAS)*, doi:10.1126/science.aap7605. Accessed 23 Feb 2021.
9. Albert Szent-Györgyi, "Biology and Pathology of Water," Perspectives in Biology and Medicine 14, no. 2 (1971): 239.
10. Bates, David, et al. "Importance of Disentanglement and Entanglement during DNA Replication and Segregation." *Physics of Life Reviews*, vol. 18, Sept. 2016, pp. 160–164, www.ncbi.nlm.nih.gov/pmc/articles/PMC5320565/, 10.1016/j.plrev.2016.09.004. Accessed 23 Feb. 2021.
11. "Ribosomes, Transcription, Translation | Learn Science at Scitable." *Nature.com*, 2014, www.nature.com/scitable/topicpage/ribosomes-transcription-and-translation-14120660/. Accessed 23 Feb. 2021.
12. Alberts, Bruce, et al. "The Initiation and Completion of DNA Replication in Chromosomes." *Nih.gov*, Garland Science, 2021,

www.ncbi.nlm.nih.gov/books/NBK26826/#:~:text=The%20proteins%20that%20initiate%20DNA%20replication%20bind%20to%20DNA%20sequences,helicase%20onto%20the%20DNA%20template.. Accessed 23 Feb. 2021.

13. Weiss, Madeline C., et al. "The Last Universal Common Ancestor between Ancient Earth Chemistry and the Onset of Genetics." *PLOS Genetics*, vol. 14, no. 8, 16 Aug. 2018, p. e1007518, www.ncbi.nlm.nih.gov/pmc/articles/PMC6095482/, 10.1371/journal.pgen.1007518. Accessed 24 Feb. 2021.
14. Ilya Prigogine, Gregoire Nicolis, and Agnes Babloyantz, "Thermodynamics of Evolution," Physics Today 25, no. 11 (1972): 23, doi: 10.1063/1.3071090.
15. Patrick W. Kudella, Alexei V. Tkachenko, AnnalenaSalditt, Sergei Maslov, Dieter Braun. "Structured sequences emerge from random pool when replicated by templated ligation." *Proceedings of the National Academy of Sciences*, 2021; 118 (8): e2018830118 DOI: 10.1073/pnas.2018830118
16. Kudella, Patrick W., et al. *Ligation of Random Oligomers Leads to Emergence of Autocatalytic Sequence Network.* 18 Aug. 2020, www.biorxiv.org/content/10.1101/2020.08.18.253963v1, 10.1101/2020.08.18.253963. Accessed 24 Feb. 2021.
17. "Origin of Life -- Did Darwinian Evolution Begin before Life Itself?" *Newswise.com*, 2021, www.newswise.com/articles/origin-of-life-did-darwinian-evolution-begin-before-life-itself. Accessed 24 Feb. 2021.
18. Jowett, Paul, et al. "Myth and Fact in the Origins of Cellular Life on Earth." *Bioscience Horizons: The International Journal of Student Research*, vol. 10, 2017, academic.oup.com/biohorizons/article/doi/10.1093/biohorizons/hzx017/4693744, 10.1093/biohorizons/hzx017. Accessed 24 Feb. 2021.
19. Erika Check Hayden, "Human Genome at Ten: Life is Complicated," Nature 464 (2010): 664–667.
20. Berg, H.C. "Bacterial Microprocessing." *Cold Spring Harbor Symposia on Quantitative Biology*, vol. 55, no. 0, 1 Jan. 1990, pp. 539–545, symposium.cshlp.org/content/55/539.short, 10.1101/sqb.1990.055.01.052. Accessed 24 Feb. 2021.
21. Vance Tartar, "Regeneration," in 檱e Biology of Stentor (London: Pergamon Press, 1961), 105–13
22. Rob Phillips, Physical Biology of the Cell, 2nd ed. (New York: Garland Science, 2013), chap. 3.
23. Clark, Kevin B. "Origins of Learned Reciprocity in Solitary Ciliates Searching Grouped 'Courting' Assurances at Quantum Efficiencies." *Biosystems*, vol. 99, no. 1, Jan. 2010, pp. 27–41, www.sciencedirect.com/science/article/abs/pii/S030326470900135X?via%3Dihub, 10.1016/j.biosystems.2009.08.005. Accessed 24 Feb. 2021.
24. Brian J. Ford, "The Secret Power of the Single Cell," New Scientist 2757 (2010)