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Proliferation with Variation and Motility: A First Principle in Biology

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Abstract

What properties have been bestowed by the Last Universal Common Ancestor (LUCA) on its descendants? We concluded that LUCA was a minimal autonomous agent, i.e., it was the organism that originated the notion of “common descent” and expressed the same default state of the diverse living organisms that biologists study today. Namely, LUCA proliferated constitutively, generating variation and movement. The organism’s ability to proliferate enabled natural selection to occur amid a constantly varying environment. All along, the historical record shows, however, that most biologists have implicitly interpreted data collected on the development of multicellular organisms under the opposite premise, namely, that quiescence was the default state of their cells. Based on both empirical evidence and theoretical considerations, we argue that adopting proliferation with variation and motility as the default state for all cells is consistent with evolutionary theory. In addition, adopting this fundamental first principle opens new productive vistas into normal and pathological developmental processes in multicellular organisms and in their interactions with the environment.

Keywords: evolution, theory of organisms, premises in biology, proliferation, quiescence, origins of Life, multicellularity, default state

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Introduction

Circumstances dealing with the Origins of Life are mired in controversy. For good reasons. Lack of evidence for how Life started prevents experts from accurately explaining how the original unit of Life, i.e., a cell, could have reproduced itself and whether all its descendants adopted the same strategy. As a result of this shortcoming, a variety of theories have been proposed to explain how that cell, LUCA (Last Universal Common Ancestor), that is, was “put together”, “created”, “emerged”, and other terms used by experts could have conveyed the complex

idea of Life. Regardless of these conceptual difficulties, it is widely acknowledged that the evolutionary process that followed the advent of LUCA triggered the complex interactions that generated the immense variety of living forms that, for approximately 3.8 billion years, have populated the Earth.

Despite the many unknowns surrounding the initial steps in cell generation, it has been implicitly accepted that cell proliferation has played a fundamental role throughout the evolutionary process of living organisms. For instance, the concept of “common

descent” introduced by Charles Darwin is supported by the above-mentioned axiomatic conclusion. Moreover, if, as suggested by Philip Ball in his well-argued, comprehensive book *How Life Works* (Ball, 2023) “living entities are generators of meaning”, the most meaningful property endowed by LUCA to all its descendants has been the absolute requirement that proliferation be maintained forever as a constitutive property (Soto and Sonnenschein, 1984). Originally, we described the default state as proliferation and motility [2]. The fact that each proliferation event produced two similar, but not identical cells was made explicit later on by describing the default state as “proliferation with variation and motility” [3,4]. Indeed, for evolution to have taken place, LUCA and its descendants had to proliferate constitutively. Remarkably, however, this specific relevant view has seldom been addressed in the specialized literature. This intriguing silence may explain why introductory biology textbooks at the high school, graduate, and postgraduate levels, aside from noting that such a cell must have existed, do not address its fundamental biological meaning: that proliferation with variation and motility is the default state of all cells. In this Essay, we explore this subject and, based on empirical data we and others have generated, speculate on the impact of defining the specific conditions that may have allowed evolution to start and continue unabated.

1. On the Biological Meaning of LUCA

As mentioned above, the circumstances surrounding the initial steps of the evolutionary process that involved controlling LUCA’s proliferation have not been adequately defined by researchers studying the origins of Life. Even the great Charles Darwin, who told us so much about the evolutionary process at large, explicitly refused to address this topic because, according to some commentators, it would have upset some of his friends and his beloved wife, all devoted believers in a powerful “creator” of Life. Indeed, discussing the process of “constructing” such a cell brings up several potentially awkward questions for anyone who would like to rigorously define how it, LUCA that is, was “put together from scratch”.

Several philosophers, physicists, chemists, and biologists speculated about how LUCA came to be. For brevity, we refer readers to comprehensive

conceptual and historical analyses of what is considered the living, including definitions of Life and the specific contributions of several experts in this field (Tirard *et al.*, 2010, Malaterre, 2024, Sutherland, 2017). Like many other commentators, Cornish-Boyden and Cárdenas focused their analysis on the physicochemical processes leading up to the emergence of LUCA (Cornish-Bowden and Cárdenas, 2020). Objectively, the empirical research conducted over the past century on “the origins of Life” has aimed to provide a “mechanistic understanding” of the molecular interactions allegedly involved in this process. Pragmatically, research on this topic has been answering somewhat unrelated, though still worthy, questions such as, *What are the essential ingredients of Life? How did those ingredients end up in the prebiotic soup? And whether those ingredients were generated on Earth, or did they come from outside the Earth’s atmosphere?*

More specifically, in this regard, living systems are thermodynamically open, far-from-equilibrium processes that maintain order by dissipating energy. From a chemical perspective, the survival of LUCA, like that of all contemporary life forms, critically depends on the continuous input and dissipation of energy. At the time of LUCA’s generation, energy was most likely derived from chemiosmotic processes driven by natural proton gradients. In this regard, recent data support the hypothesis that LUCA must have been an autotroph living in a geochemically active environment rich in H₂, CO₂, and iron (Weiss *et al.*, 2016, Martin, 2020, Moody *et al.*, 2024). These energy-harnessing processes were closely coupled to the synthesis of organic molecules, the building blocks of biological matter, and the need for organismal growth in number and size. From this viewpoint, the link between energy transformation and biosynthesis has been interpreted as if constitutive proliferation and motility were a natural and probably inevitable outcome of metabolism. The universality of metabolic pathways like glycolysis and segments of the Krebs cycle points not only to a common ancestry, but also to chemical and thermodynamic constraints that favored architectures capable of simultaneously transforming energy, producing biomass, and maintaining the capacity to evolve (Smith and Morowitz, 2004; Paldi, 2012). Only later, with the accumulation of organic substrates in the environment and the rise

of atmospheric oxygen, could Life evolve processes to decouple energy production from proliferation. However, this chemical perspective focuses on the necessary conditions for sustaining Life, which is not equivalent to what is sufficient for Life to happen with the robustness, resilience, and creativity required to overcome the multiple constraints present during the evolutionary process.

All along, the methodological rationale for addressing the origin of Life question has been based on the premise that, because living organisms are composed of physicochemical matter, an answer to the question “Why is there Life?” would be provided by detailing the interactions among the molecules in the prebiotic soup. This research strategy implicitly adopts a reductionist, bottom-up approach, grounded in the assumption that the original cell from which Life evolved on Earth was a machine-like entity capable of performing most, if not all, of the functions that living cells perform today (Sutherland, 2017, Walker *et al.*, 2017). The empirical evidence collected so far has failed to validate this expectation. In this regard, already in 1944, the physicist Erwin Schrödinger tried to make sense of living matter by stating,

From all we have learnt about the structure of living matter, we must be prepared to work 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 behaviour of the single atoms within a living organism, but because the construction is different from anything we have yet tested in the physical laboratory (Schrödinger, 1944).

Following Schrödinger’s cautionary comment, we consider that a biological system differs from an abiotic one in that the former is a goal-pursuing agent, capable of creating its own norms, able to change and thus to evolve (Moreno & Peretó, 2025). Instead, an abiotic system lacks this property and, therefore, does not create *biological* novelty. In our terrestrial world, this is illustrated by the built-in ability of cells to move and proliferate, thereby creating variation at each cell division (the default state). Thus, we conclude that i) the physico-chemical processes happening in the prebiotic soup at the time of the LUCAgenesis and ii) the biological meaning of those processes represent

two distinct epistemological subjects. On the one hand, researchers who have been studying the origins of Life have been doing so within the framework of physical theories where invariants take a fundamental role, and the phase space is predetermined (Longo & Soto, 2016). The process taking place in the prebiotic soup could then be equivalent to a physicochemical complexification. On the other hand, the fundamental theories of biology, those of the cell and evolutionary theories, deal with relentless change. From our analysis, we assume the pragmatic reality that once generated, LUCA inaugurates the study of evolutionary change.

For a variety of reasons, millions (billions?) of protocells or even genuine cells “did not make it” and, therefore, there is no way of knowing what evolutionary alternative qualities they could have possessed. Hence, theorizing about what might have happened to these unviable protocells serves no obvious explanatory purpose when interpreting whether the properties carried by LUCA are still carried by today’s cells and organisms. Regardless of whether the emergence of LUCA was the result of a “once-in-a-lifetime” event (a “unique/exceptional biological miracle”, “a lucky break”?), it is worth reflecting on the impact that the properties carried by LUCA and all its immediate descendants have had and still affect all the stages of ontogenesis and phylogenesis.

The specific questions addressing the biological implications of LUCA formation deserve a more refined analysis. This analysis can be formulated by asking: *What did LUCA do once it materialized?* And in hindsight, while applying its agential capability, it is also relevant to ask, *why did LUCA choose proliferation rather than quiescence as its default state?* For most cell and developmental biologists, epistemologically, the origin of Life remains as only a tangentially relevant quest to explain how, once cells became agents, they controlled their own proliferation. Within this context, we have been specifically asking... *What biological function(s) became inexorably built into the original cell (LUCA, that is) that initiated the evolutionary process?* Answers to this question may provide a fuller understanding of the yet-to-be-answered basic question: *Why is there Life on Earth?* Our research trajectory offers some hints on this narrative.

2. The Inauguration of Life Viewed from a Strict Biological Perspective

Why and how did our commitment to explain why cells proliferate begin? We extensively addressed this question over a quarter of a century ago in our book entitled *The Society of Cells*, as well as in theoretical and experimental peer-reviewed articles and commentaries (Sonnenschein & Soto, 1999, Soto & Sonnenschein, 1993, Sonnenschein & Soto, 2000, Soto *et al.*, 2016, Sonnenschein & Soto, 2017, Sonnenschein & Soto, 2021, Soto & Sonnenschein, 2018). Next, we provide a shorter version of our trajectory. Since the beginning of the 20th century, under a reductionist approach, canonical introductory and advanced biology textbooks, the vast community of biologists, and we implicitly and explicitly adopted the premise that the default state of cells in multicellular organisms was quiescence. This meant that those cells would not proliferate unless they were directly stimulated by “growth factors” and hormones. In our specific case, the alleged “stimulator” of their target cells was estrogens, that is, the female sex steroids whose molecular weight hovers around 272. From the beginning of our scientific journey, empirical evidence compelled us to conclude, to the contrary, that estrogen-target cells proliferated when estrogens neutralized a blood-borne specific inhibitory factor. This evidence-supported switching the default state of those cells to that of proliferation (Soto & Sonnenschein, 1984). The serum-borne inhibitory factor was albumin (Sonnenschein *et al.*, 1996) or coeluted with albumin (Laursen *et al.*, 1990). Later, using human recombinant albumin, we demonstrated that serum albumin was, indeed, the inhibitor (Sonnenschein *et al.*, 1996). After analyzing the conflicting data on the existence of alleged “growth factors” (GFs) for other target cells, we generalized the concept that the default state of all cells was proliferation with variation and motility (Soto & Sonnenschein, 1991). This principle, like the one of inertia in Classical Mechanics, determines what can be studied. More specifically, by adopting the default state of proliferation with variation and motility, the object of study should not be “what induces cells to proliferate and move”; instead, because these latter are constitutive properties, the quest becomes “what makes cells proliferatively quiescent and/or prevents them from moving”.

3. The Big Picture Linking Cell Proliferation and the Origin of Life

During the late 19th century, as microbiology entered laboratory practice and academic medicine, scientists developed methods to propagate microbes to study pathogenic bacteria. For example, microorganisms living on blades of grass were arbitrarily grown in a hay infusion. By analogy, it was believed that meat broth would provide adequate nutrients for human pathogens. Based on their nutritional needs, some prokaryotes were later shown to be autotrophs (i.e., they thrive solely on inorganic nutrients), while others were heterotrophs (i.e., they require complex organic nutrients). Still, even in a rich nutritive medium, some pathogens did not thrive in laboratory conditions. While studying the nutritional requirements of certain bacteria, scientists began referring to these nutrients operationally as GFs.

In the first two decades of the last century, technological attempts to grow and propagate cells in culture conditions were partially successful in the USA. The pioneers in this field were, separately, Ross G. Harrison (Yale University, New Haven, CT) whose primary aim was to use tissue explants to study neurogenesis, the Montrose Burrows-Alexis Carrel duo (Rockefeller Institute, New York, NY), and Margaret Reed Lewis and Warren H. Lewis (Johns Hopkins University, Baltimore MD). Followers of those pioneers mistakenly concluded that supplements such as plasma, serum, and embryo and tissue extracts, to the basic components of media (sugars, salts, amino acids, vitamins) used to propagate cells in culture conditions, contained discrete tissue-specific GFs. The putative tissue-specific purified GFs were polypeptides of different kinds. While using non-physiological in culture bioassays (such as nutrient starvation, inhibitory poisons of cell cycle steps, etc.), experimentalists mistakenly attributed the increase in cell numbers to the addition of a variety of so-called tissue-specific GFs supplemented to standard basic nutritional components. In the absence of serum or embryo extracts, metazoan cells were not proliferatively quiescent; in fact, *they were dying*. Years later, when the experimental protocols were carefully examined, it was shown that the so-called GFs lacked a physiological proliferative role in live animals. Objectively, those polypeptide GFs

were a non-specific source of nutrients that allowed starving cells to survive but not to proliferate. Instead of rejecting the principle of quiescence as the default state of cells in multicellular organisms, researchers rebranded those spurious GFs as “survival factors” (Durum & Muegge, 1998). Therefore, in the absence of specific inhibitors of cell proliferation, surviving cells were unconstrained to express their constitutive ability to proliferate.

To summarize, unicellular organisms and plant and animal cells in culture proliferate constitutively (Soto *et al.*, 2016, Soto & Sonnenschein, 2020). Moreover, Charles Darwin compellingly asserted in the text of his 1859 opus magnum *The Origins of Species*, that...

There is no exception to the rule that every organic being naturally increases at so high a rate, that, if not destroyed, the earth would soon be covered by the progeny of a single pair (Darwin, 1859).

Implicitly, this statement supports the inference that proliferation of LUCA did not require an active inductive process involving either a non-biological agent (a hypothetical “creator”) or a molecule whose specific function would have been to “stimulate” cells to enter the cell cycle. Also, the existence of autotrophs rules out the need for such a stimulator (Crockford *et al.*, 2023, Weiss *et al.*, 2018).

4. Implications of the Biological Meaning of LUCA in Biomedicine

Beginning in the mid-20th century, leading biologists abandoned theory construction when they mistakenly concluded that, after the discovery of DNA complementarity, biology could be reduced to physics and chemistry (Crick, 1966). This reductionist perspective and the metaphorical adoption of the novel mathematical theories of information introduced in the 1930s also led biologists to adopt vague concepts from which no useful theories could be generated (Longo *et al.*, 2012). Moreover, the adoption of a) the somatic mutation theory of carcinogenesis, during the 20th century, which claims that cancer is a cell-based disease, and b) that quiescence is the default state of cells in multicellular organisms, contributed to the misinterpretation of biological data, especially in the field of developmental biology, and in cancer

clinical data (Sonnenschein & Soto, 2020, Huang *et al.*, 2025).

Let’s return to the issue of the origins of Life. Despite being a hypothetical notion, LUCA represents an authentication of the cellular origin of Life on Earth, and of the concept of “common descent”. As its descendants do today, LUCA constitutively expressed organismal agency (Moreno, 2018). Acknowledging that *proliferation with variation* and *motility* is the default state of all cells implies that, since LUCA’s creation, during all stages of development of unicellular and multicellular organisms, control of cell proliferation could only be done by inhibiting it. Importantly, it is worth clarifying at this point that when we refer to control of cell proliferation, we aim to answer the question: *Why* do cells proliferate? Answering this question necessarily requires adopting one of the two available premises: i.e., quiescence or proliferation. This clarification is necessary because the notion of control of cell proliferation is often conflated with the question, “How do cells proliferate?” (Sonnenschein & Soto, 1999). Specific answers to this latter question have occupied cell biologists for decades by describing the numerous molecules and their interactions that participate in the phases of the cell cycle (Gap1, Synthesis, Gap2 and Mitosis) (Nurse, 2024).

Answers to the questions *Why* and *How* cells proliferate do not conflict with claims by Lynn Margulis, Carl Woese, and others that symbiosis (through horizontal transfer) played a significant role in the increasing complexity of the evolutionary process, as reflected in the immense variety of phenotypes across all biological kingdoms. Obviously, all these evolutionary novelties took place after LUCA emerged, and no evidence is available favoring the possibility that the default state of cells has been changed (Margulis, 2001, Gilbert, 2024).

The conclusion that proliferation with variation and motility should have remained unaltered during phylogenesis is also valid when explaining organization patterns during normal and pathological ontogenesis, as exemplified in cancers (Shyer & Rodrigues, 2025). Indeed, tissue-based pathological outcomes represent perturbations in the development of morphogenetic fields, as proposed by the tissue organization field theory of carcinogenesis (TOFT). This theory is

based on two premises: namely, i) the default state of proliferation with variation and motility, and ii) cancer is a tissue-based disease. Within this context, cancers occur when the reciprocal interactions between tissues (stroma/mesenchyme) that constrain the default state of the parenchymal cells are weakened (“development gone awry”). Moreover, these alterations of tissue organization are diagnosed by pathologists when they examine magnified images of tissue specimens using light microscopes (Sonnenschein & Soto, 2020).

The current crisis in biology has sparked criticism and few constructive alternative suggestions to address it (Noble, 2017, Gilbert & Sarkar, 2000, Soto & Sonnenschein, 2018, Rosslenbroich, 2023, Ball, 2023). Regretfully, as documented above, several generations of biologists and physicians have been educated under wrongly conceived premises (Soto & Sonnenschein, 2021, Noble & Noble, 2022).

Conclusion

LUCA and its descendants proliferated constitutively, producing variation and motility. This reinterpretation of data constitutes a significant epistemological change in the fields of normal and pathological developmental processes. When these empirically supported changes will be acknowledged and implemented, novel, rigorous lines of research will become open to being explored and applied based on an evolutionarily relevant and robust epistemology. Regarding specific pathological development, as exemplified in cancer, both basic and clinical research could be conducted, interpreted, and applied on the basis of reliable premises that should replace those that, for over a century, have been proven unproductive (Sonnenschein and Soto, 2020, Huang *et al.*, 2025, Prasad, 2020, Hasan, 2025, Letai and de The, 2025). Still to be addressed is the impact of adopting the above-referred principles in fields mistakenly considered outside the core disciplines of biology; among them, we include those in the social sciences, such as public health and economics.

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References

- Ball, P 2023 *How Life Works: A User's Guide to the New Biology*. Chicago: The University of Chicago Press.
- Cornish-Bowden, A & CÁRDENAS, ML 2020 “Contrasting theories of life: Historical context, current theories. In search of an ideal theory”, *Biosystems*, vol. 188, article 104063.
- Crick, FHC 1966 *Of Molecules and Man*. Seattle: University of Washington Press.
- Crockford, PW, Bar On, YM, Ward, LM, Milo, R, & Halevy, I 2023 “The geologic history of primary productivity”, *Current Biology*, vol. 33, article 4741-4750.e5 <https://doi.org/10.1016/j.cub.2023.09.040>
- Darwin, C 1859 *On the Origin of Species*. London: John Murray.
- Durum, SK & Muegge, K 1998 *Cytokine Knockouts*. Totowa: Humana Press.
- Gilbert, SF 2024 “Inter-kingdom communication and the sympoietic way of life”, *Frontiers in Cell and Developmental Biology*, vol. 12, article 1427798 doi: 10.3389/fcell.2024.1427798
- Gilbert, SF & Sarkar, S 2000 “Embracing complexity: Organicism for the 21st century”, *Developmental Dynamics*, vol. 219, pp. 1-9.
- Hasan, N 2025. *Metastasis: The Rise of the Cancer-Industrial Complex and the Horizons of Care*. Philadelphia: Common Notions.
- Huang, S, Soto, AM. & Sonnenschein, C 2025 “The end of the genetic paradigm of cancer”, *PLoS Biology*, vol. 23, article e3003052.
- Laursen, I, Briand, P, & Lykkesfeldt, AE 1990 “Serum albumin as a modulator on growth of the human breast cancer cell line, MCF-7”, *Anticancer Research*, vol. 10, pp. 343-351.
- Letai A & De The, H 2025 “Conventional chemotherapy: Millions of cures, unresolved therapeutic index”, *Nature Reviews Cancer*, vol. 25, pp. 209-218.
- Longo, G, Miquel, PA, Sonnenschein, C, & Soto, AM 2012 “Is information a proper observable for biological organization?”, *Progress in Biophysics and Molecular Biology*, vol. 109, pp. 108-14.
- Longo, G & Soto, AM 2016 “Why do we need theories?”, *Progress in Biophysics and Molecular Biology*, vol. 122, pp. 4-10.
- Malaterre, C 2024 “Is life binary or gradual?”, *Life (Basel)*, vol. 14, no. 5, article 564 <https://doi.org/10.3390/life14050564>.
- Margulis, L 2001 “The conscious cell”, *Annals of the New York Academy of Sciences*, vol. 929, pp. 55-70.
- Martin, WF 2020 “Older than genes: The acetyl CoA pathway and origins”, *Frontiers in Microbiology*, vol. 11, article 817 <https://doi.org/10.3389/fmicb.2020.00817>
- Moody, ERR *et al.* 2024 “The nature of the last universal common ancestor and its impact on the early Earth system”, *Nature Ecology & Evolution*, vol. 8, pp. 1654-1666.

- Moreno, A 2018 “On minimal autonomous agency: Natural and artificial”, *Complex Systems*, vol. 27, pp. 289-313.
- Moreno, A & Peretó, J 2025 *An Evolutionary Story of Agency: How Life Evolved to Act on its Own*. Cham: Springer
<https://doi.org/10.1007/978-3-032-05644-3>
- Noble, D 2017 *Dance to the Tune of Life: Biological Relativity*. Cambridge: Cambridge University Press.
- Noble, R & Noble, D 2022 “Physiology restores purpose to evolutionary biology”, *Biological Journal of the Linnean Society*, vol. 139, pp. 357-369.
- Nurse, P 2024 “The discovery of cyclin-dependent kinases”, *Nature Reviews Molecular Cell Biology*, vol. 25, article 763.
- Paldi, A 2012 “What makes the cell differentiate?”, *Progress in Biophysics and Molecular Biology*, vol. 110, pp. 41-43.
- Prasad, V 2020 *Malignant: How Bad Policy and Bad Evidence Harm People with Cancer*. Baltimore: Johns Hopkins University Press.
- Rosslenbroich, B 2023 *Properties of Life: Toward a Theory of Organismic Biology*. Boston: The MIT Press.
- Schrödinger, E 1944 *What is Life? The Physical Aspect of the Living Cell*. Cambridge: Cambridge University Press.
- Shyer, AE & Rodrigues, AR 2025 “Transcending the hegemony of the molecular machine through an organic renewal of biology and biomedicine”, *Cells & Development*, vol. 184, article 204018.
- Smith, E & Morowitz, HJ 2004 “Universality in intermediary metabolism”, *Proceedings of the National Academy of Sciences of the United States of America*, vol. 101, pp. 13168-73.
- Sonnenschein, C & Soto, AM 1999 *The Society of Cells: Cancer and Control of Cell Proliferation*. New York: Springer.
- Sonnenschein, C & Soto, AM 2000 “The somatic mutation theory of carcinogenesis: Why it should be dropped and replaced”, *Molecular Carcinogenesis*, vol. 29, pp. 1-7.
- Sonnenschein, C & Soto, AM 2017 “Misperceptions in cell and cancer biology. What pioneers and followers of cell culture bestowed on these fields”, *Organisms. Journal of Biological Sciences*, vol. 1, no. 2, pp. 83-92. DOI: 10.13133/2532-5876_2.12.
- Sonnenschein, C & Soto, AM 2020 “Over a century of cancer research: Inconvenient truths and promising leads”, *PLoS Biology*, vol. 18, article e3000670.
- Sonnenschein, C & Soto, AM 2021 “Control of cell proliferation: Is the default state of cells quiescence or proliferation?”, *Organisms: Journal of Biological Sciences*, vol. 5, no. 1, pp. 33-42. DOI: 10.13133/2532-5876/17338.
- Sonnenschein, C Soto, AM, & Michaelson, CL 1996 “Human serum albumin shares the properties of estrocolony-I, the inhibitor of the proliferation of estrogen-target cells”, *Journal of Steroid Biochemistry and Molecular Biology*, vol. 59, pp. 147-154.
- Soto AM, Longo, G, Montévil, M, & Sonnenschein, C 2016 “The biological default state of cell proliferation with variation and motility, a fundamental principle for a theory of organisms”, *Progress in Biophysics and Molecular Biology*, vol., 122, pp. 16-23.
- Soto AM & Sonnenschein, C 1984 “Mechanism of estrogen action on cellular proliferation: Evidence for indirect and negative control on cloned breast tumor cells”, *Biochemical and Biophysical Research Communications*, vol. 122, pp. 1097-1103.
- Soto AM & Sonnenschein, C 1991 “Regulation of cell proliferation: The negative control perspective”, *Annals of the New York Academy of Sciences*, vol. 628, pp. 412-418.
- Soto AM & Sonnenschein, C 1993 “Regulation of cell proliferation: Is the ultimate control positive or negative?” In: Iversen, OH (ed.) *New Frontiers in Cancer Causation*. Washington, D.C.: Taylor & Francis.
- Soto AM & Sonnenschein, C 2018 “Reductionism, organicism, and causality in the biomedical sciences: A critique”, *Perspectives in Biology and Medicine*, vol. 61, pp. 489-502.
- Soto AM & Sonnenschein, C 2020 “Information, programme, signal: Dead metaphors that negate the agency of organisms”, *Interdisciplinary Science Reviews*, vol. 45, pp. 331-343.
- Soto AM & Sonnenschein, C 2021 “The proletarianization of biological thought”. In: *Philosophy World Democracy*, London <https://www.philosophy-world-democracy.org/posts/article/the-proletarianization-of-biological-thought>.
- Sutherland, JD 2017 “Opinion: Studies on the origin of life — The end of the beginning”, *Nature Reviews Chemistry*, vol. 1, article 0012.
- Tirard, S, Morange, M, & Lazcano, A 2010 “The definition of life: A brief history of an elusive scientific endeavor”, *Astrobiology*, vol. 10, pp. 1003-9.
- Walker, SI, Packard, N, & Cody, GD 2017 “Re-conceptualizing the origins of life”, *Philosophical Transactions A*, vol. 375, article 20160337.
- Weiss, MC, Preiner, M, Xavier, JC, Zimorski, V, & Martin, WF 2018 “The last universal common ancestor between ancient Earth chemistry and the onset of genetics”, *PLoS Genetics*, vol. 14, article e1007518 <https://doi.org/10.1371/journal.pgen.1007518>
- Weiss, MC, Sousa, FL, Mrnjavac, N, Neukirchen, S, Roettger, M, Nelson-Sathi, S, & Martin, WF 2016 “The physiology and habitat of the last universal common ancestor”, *Nature Microbiology*, vol. 1, article 16116.