PHYSICS FOR UNDERSTANDING LIFE

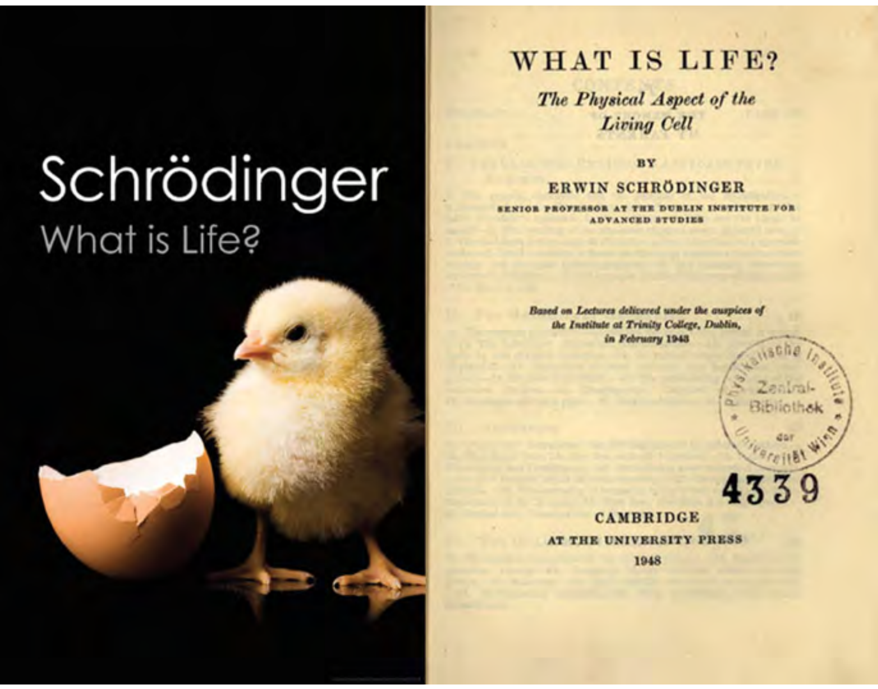
Felix Ritort[1] and Bart van Tiggelen[2] DOI: https://doi.org/10.1051/epn/2022508
[1] Small Biosystems Laboratory, Condensed Matter Physics Department – Facultat de Física – Universitat de Barcelona, Spain
[2] University Grenoble Alpes, CNRS, LPMMC, Grenoble, France

"Living" matter distinguishes itself from "ordinary" matter by its capacity to grow, to reproduce or to multiply, and most of all by its autonomous functional activity, baptised "intelligence", to sense its environment to adapt or to survive. This last feature truly is one of the miracles of life. Find out more in Chapter 3 of the EPS Grand Challenges.

Our current knowledge of life is relatively recent. The "molecule of life", Deoxyribose Nucleic Acid or DNA, was first discovered by Miescher in 1860. The discovery of the double helix structure by Watson and Crick in 1951, and the determination of its sequence of nucleic acids by Sanger and Coulson in 1975 have been major breakthroughs of the last century. Can science discover what conditions have facilitated the origin of life on Earth? Does some kind of "life" exist on extra-terrestrial planets? Can we create "artificial life" that self-replicates or has intelligence? Can we design and implement "artificial intelligence"? These challenges are hopefully within reach on the Horizon 2050. Is life nothing but "vital dust", *i.e.* a natural consequence of non-equilibrium physics and chemistry, or was it rather a "magnificent accident"? Famous physicists like Erwin Schrödinger and Freeman Dyson struggled with the role of physics in the origin of life. Schrödinger wondered how life manages to stay out of equilibrium while respecting the Second Law. Dyson argued that metabolism and replication could have originated separately and that "life actually began twice". Physics is not enough for understanding life, but life may reveal new physics. To understand life, we need interdisciplinary collaborations between biologists, computer-scientists, chemists, physicists, astrophysicists and engineers. Chapter 3 of the EPS Grand Challenges is devoted to the field of physics for understanding life.

J.D. Watson and F.H.C. Crick, A structure for deoxyribose nucleic acid. Nature ***171****, 737 (1953).*
F. Sanger and A.R. Coulson, A rapid method for determining sequences in DNA by primed synthesis with DNA polymerase, J. Mol. Biol. ***94*** *(3): 441 (1975).*
C. De Duve, Vital Dust (Basic Books, 1995).
E. Schrödinger, What is life?, Cambridge University Press (1944).
F. Dyson, Origins of Life, Cambridge University Press (1992).

▼**FIG. 1:** What is life? by Erwin Schrödinger (source: Wikipedia)



Where do we come from? How life on Earth began remains an unsolved, complex scientific problem. After the brilliant experiments by Pasteur and Tyndall in the nineteenth century, the concept of "spontaneous generation" of life from non-living matter was rejected for once and for all. Life may have emerged only 400 million years after the "Hadean" Earth was created (Hades was the king of the ancient Greek underworld), only 200 million years after liquid water had first appeared. The absence of a well-preserved crust older than 3.3 billion years makes it difficult to get a precise information about the chemical composition of the Hadean Earth. The time variations on all scales of the Earth-Sun connection must have played a major role in the chemistry that created life. Stellar evolution models tell us that the young Sun was 70 % fainter than today. The "faint young Sun paradox" states that this low flux implies water on Earth to be frozen until well beyond the Hadean age, which we know is not true. Greenhouse gases such as CO_2 must have been present, heating up the atmosphere much like they do today. The rapid rotation of the young Sun in only a few days led to strong magnetic activity and intensive space weather, so that energetic X-ray fluxes must have been up to 100 times larger than today.

The presence of liquid water is a major condition for life to form, but other habitability conditions exist, such as the presence of organic molecules and energy sources – providing at least 150 kJ/mol - to initiate prebiotic chemistry. Energetic solar photons must have provided a lot of this energy. Organic molecules such as HCN and CH_2O could also have been created by the lightning-triggered dissociation of carbon-dioxide and abiotic methane. A mostly reducing (oxygen-poor) early atmosphere with energetic sparks could have been a play-ground for prebiotic chemistry and a world-famous "Miller-Urey" experiment supporting this vision was done in 1952. Carbonaceous meteorites impacted the Earth and brought also many organic compounds, including amino acids. Where exactly prebiotic chemistry took place is still subject to a large debate. Energetic radiation does not penetrate more than 1 cm in water.

H.J. Cleaves, Prebiotic Chemistry: What We Know, What We Don't, Evolution: Education and Outreach ***5****, 342 (2012).*

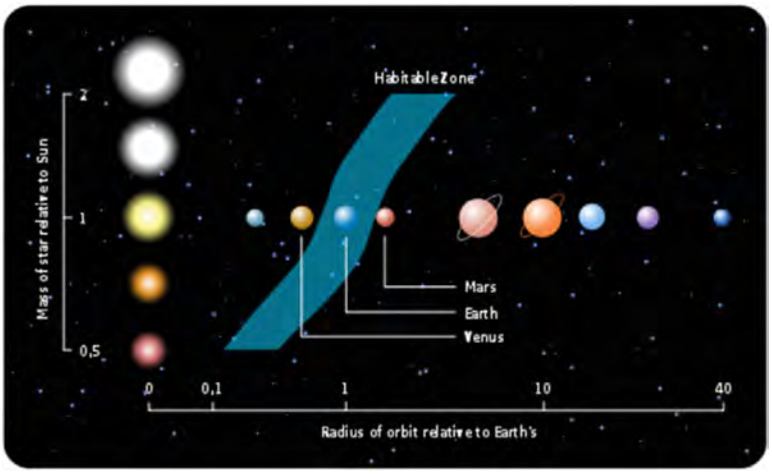
C. Sagan and G. Mullen, Earth and Mars: Evolution of Atmospheres and Surface Temperatures,Science. ***177*** *(4043): 52 (1972).*

H.C. Urey, On the early chemical history of the Earth and the origin of life, P.N.A.S. ***38****, 351 (1952).*

S.L. Miller, Production of Amino Acids Under Possible Primitive Earth Conditions, Science ***117****, 528 (1953).*

Life for understanding new physics. In his 1944' beautiful essay Erwin Schrödinger wrote: "*The large and important and very much discussed question is: how can the events in space and time which take place within the spatial boundary of a living organism be accounted for by physics and chemistry?*". The marvellous complexity of living matter raises the question of whether biology hides new, emerging physical laws awaiting discovery. From the Brownian motion of pollen grains to cell motility, animal motion, the many behaviours of active matter, and the evolution of bacterial populations, the interface between biology and physics offers an unprecedented wealth of new phenomena that can be investigated at an exquisite level of detail. For example, single-molecule techniques permit us to monitor how a protein folds and measurements of energies with 1 kT ($\approx 10^{-21}$J) accuracy reveal how a molecular motor moves one step at a time. By increasing the bar of spatial, temporal, and energy measurement accuracy, we hope to uncover vital discrepancies between our current theoretical knowledge and experiments on biological systems. Teleonomy is the continuous "purposefulness" of living beings to sleep, feed, trade, play, laugh, *etc.* They are not found in non-living matter where just the laws of physics and chemistry prevail. Does it escape our comprehension? What is the role of physical information in biology? Does information set a new paradigm for emerging complexity that connects biology to quantum physics? All these are relevant questions waiting for an answer.

F. Ritort, The Noisy and Marvellous Molecular World of Biology, Inventions ***4.2****, 24 (2019).*



▲ **FIG. 2:** The habitable zone predicted on the basis of liquid water present at the surface of the planet. (source: Wikipedia)

What is the nature of the human mind? Artificial intelligence (AI) covers all techniques that enable machines to solve tasks like humans do. AI applications are immense, from medicine to robotics and basic science. AI has seen fast growth since the fifties when cybernetics and feedback, the branch of science introduced by Wiener in 1948, took off as an effort to understand information processes in machines and living beings. The Greek term "cybernetics" (*kybernetiké*), the art of guiding, was introduced by Ampère in his classification of sciences published in 1834, subsequently taken up by Maxwell. Subsequent work by Bertalanffy on the general theory of biological systems, Maturana and Varela on *autopoiesis* (the idea of self-sustaining cycles), Von Neumann, Shannon, and Gabor on automatic systems have set the basis of modern AI. Good old-fashioned AI (GOFAI), as it is called nowadays, embraces the power of using basic symbols (words, pictures, actions, *etc.*.) to represent physical patterns to build up high-order symbolic structures to be manipulated with programs and algorithms. A key limitation of GOFAI is that programs can neither adapt themselves nor acquire new knowledge on their own, which led to the "AI winter" in the eighties without significant progress. The subsequent development of connectionism in artificial neural networks and statistics-based inference methods (machine learning) that allow data internal structure to evolve, has led to new functionalities. In the current view, intelligence stands for the ability to avert the ever-present threat of the exponential explosion of search options. What about consciousness? If brains can be considered as probabilistic prediction machines they must somehow deal with uncertainty. Is this related to consciousness? Are we going to understand consciousness one day?

N. Wiener, Cybernetics or Control and Communication in the Animal and the Machine, MIT press (2019)

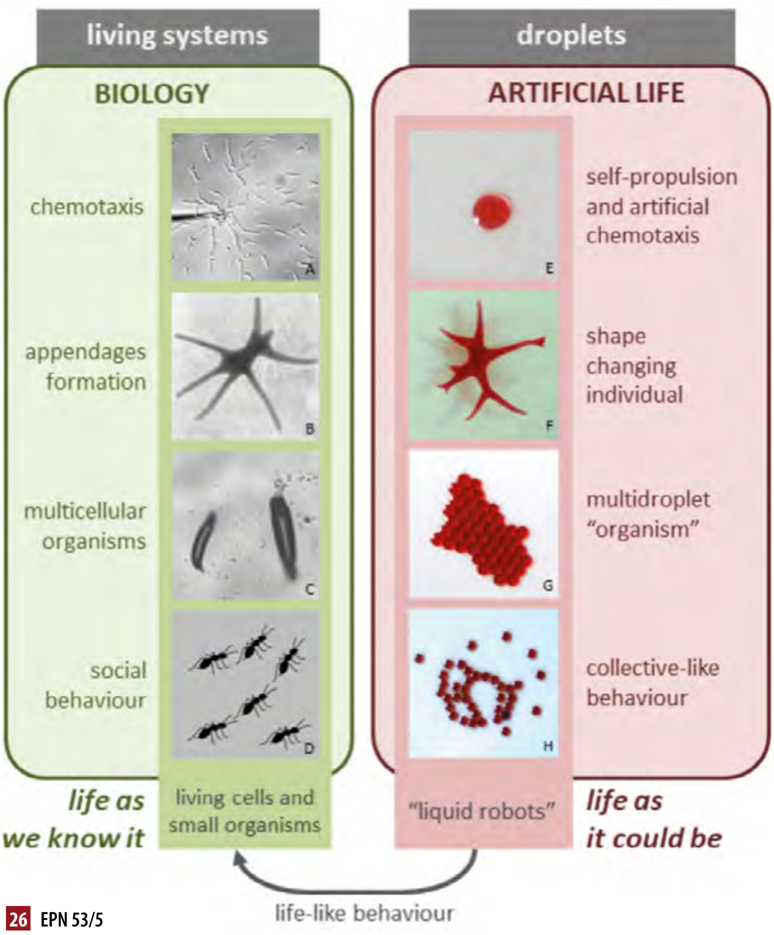
J.C. Maxwell, On Governors. Proceedings of the Royal Society of London ***16****, 270 (1868)*

O.A. Newell and A.S. Herbert, Computer science as empirical inquiry: Symbols and search, ACM Turing award lectures, 2007 (1975).

Can we build artificial life? Artificial life (ALIFE) aims at building sustainable self-replicating systems resembling living beings. ALIFE comes in three forms: computer-designed AI programs and algorithms (soft ALIFE), hardware-based robots (hard ALIFE), and chemical and biochemical systems with life-like behaviour (wet ALIFE). The basic tenet of ALIFE is that if Nature has found one way of organizing living matter, other (unknown) ways should exist. Can we build synthetic cells endowed with homeostasis, self-reproduction, and evolution? Man-designed cell-like droplets exhibit limited properties and functionalities, such as self-propulsion, artificial chemotaxis, organism-like multi-droplets, collective-like behaviours, *etc.* Building synthetic ALIFE systems represents a daunting task ahead. Besides possessing basic properties such as robustness, autonomy, efficiency, recycling, intelligence, self-repair, adaptation, self-replication, *etc.*, they must show open-ended evolution and teleonomy. Are we ever going to leap this gap?

A. Pross, What is life?: How chemistry becomes biology. Oxford University Press, 2016.

▾ **FIG. 3:** Life-like behaviour, comparison between living systems in biology and droplets in artificial life.



Is there anybody out there? The question whether extra-terrestrial life exists is as old as mankind. No matter how small the probability is for life to emerge, its existence "somewhere, sometime" in the huge Universe is largely accepted by scientists. The Drake equation, actually proposed as an agenda item for a meeting on alien communications in 1961 but today argued to be one of the most important equations in science, gives estimates of up to many millions of detectable alien civilisations in our own Galaxy. The famous paradox raised by Enrico Fermi during an after-dinner talk in 1950 states that if there are really so many, then "where are they?". One possible answer is that intelligent civilisations tend to self-destruct.

With the recent observation of exoplanets, the first proof of extra-terrestrial life may be within reach. Will it have the same biochemistry that created life on Earth? The establishment of a list of "biosignatures" - molecules whose origin we believe requires a biological agent - has top-priority. Molecular oxygen is a clear biosignature, and is hardly found elsewhere in our solar system. A molecular biosignature must be stable with respect to the local planetary environment, though its detection may be false alarm due to abiotic reactions. Within our solar system several bodies such as Mars, Jupiter's moon Europe and Saturn's moon Titan have been identified as possible candidates to host or to have hosted life. Sample-return missions and in-situ search for "biosignatures" started with the Viking lander missions to Mars in 1976 and continue today with the rover Perseverance. Indications exist that Mars might host methane-producing micro-organisms at its subsurface. The complication on Mars is that many identified biosignatures were possibly destroyed by (per)chlolates.

Our knowledge about exoplanets outside the solar system entirely depends on remote sensing. Today, more than 4000 exoplanets have been identified. The recently launched James Webb telescope will facilitate the study of infrared absorption lines in the spectra of exoplanet atmospheres, observed while transiting in front of the star, and possibly due to biosignatures. The perfect exoplanet to observe "Earthian" life would be an Earth-sized planet in an Earth-like orbit around a Sun-like star. Unfortunately, due to observational selections effects, few such perfect exoplanets are currently known. A recently observed candidate is one of the