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Historical paradigm shifts in defining life: from *spontaneous generation* and *vitalism* to the *Pasteurian Wall* and the quest for artificial creation

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For much of recorded history, the question “Where does life come from?” was answered with certainty: Aristotle’s doctrine of *spontaneous generation* and staged “*ensoulment*” defined both natural philosophy and Christian scholasticism. Life, in this view, could spring from nonliving matter, and human personhood emerged only after a gradual developmental process. The Scientific Revolution began to unravel this consensus. Lavoisier’s chemistry embedded life within universal physical laws, while the invention of the microscope exposed previously invisible worlds. Science often advances through profound epistemic ruptures, not gradual accumulation. Individual discoveries acted as paradigm shifts that, together, constituted a non-Kuhnian revolution, redefining humanity’s understanding of nature. This study explores how successive revolutions in methods and technologies transformed both scientific and societal understandings of life’s origins. We distinguish four dimensions of their impact: technological (new instruments and techniques), ideological (emergent political and social philosophies), cultural (changes in art, literature, and everyday thought), and epistemological (shifts in what counts as knowable or real). Our analysis focuses primarily on the last, how each technological advance reconfigured the boundaries of knowledge itself. The chemical revolution, from Lavoisier’s demolition of phlogiston to Wöhler’s synthesis of urea, progressively undermined vitalism by showing that “organic” substances obey the same principles as inorganic matter. *Pasteur’s* swan-neck flask experiments overthrew the millennia-old assumption of *spontaneous generation* and enshrined *omne vivum ex ovo* (“all life comes from an egg”) as biological dogma. Yet these advances built new intellectual boundaries, culminating in what we term the *Pasteurian Wall*, a barrier that has constrained experimental abiogenesis and remains unbreached today. By tracing these historical transformations, we show how revolutions in methods and technologies both expand and restrict the scope of inquiry, reshaping not only what we can investigate, but how we imagine life, its origins, and its possible artificial creation.

KEYWORDS

abiogenesis, *omne vivum ex ovo*, origins of life, paradigm shifts, *Pasteurian Wall*, *spontaneous generation*, synthetic biology, xenobiology

1 Paradigm shifts in science

1.1 On the distinctiveness of biology and the pre-scientific status of Aristotelian views

While modern biology emerged as a distinct empirical science only in the 19th century, its intellectual and observational roots reach much further back. To call pre-modern conceptions of life “non-empirical” would be misleading. “Empirical,” in its broad sense, denotes knowledge grounded in observation and experience, and by that definition the study of life had long relied on direct engagement with nature. Anatomists such as *William Harvey* (1578–1657), who demonstrated the circulation of blood in the 17th century, conducted rigorously experimental work. At the same time, natural historians, including *John Ray* (1627–1705), *Carl Linnaeus* (1707–1778), and *Georges-Louis Leclerc Comte de Buffon* (1707–1778), built vast taxonomic and descriptive systems through painstaking observation, specimen collection, and comparison. These endeavours were profoundly data-driven even if they lacked the theoretical integration and experimental instrumentation of later centuries.

The limitation of this early empiricism lay not in its observational quality but in the absence of unifying explanatory frameworks. Concepts such as *vitalism*, the *spontaneous generation* of life, and Aristotle’s teleological embryology persisted because the physical and chemical bases of living systems were unknown. The 19th century supplied the missing scaffolds, *cell theory*, *evolution by natural selection*, and the rise of *experimental physiology*, thereby transforming dispersed empirical practices into a coherent discipline (Wolpert, 1996). In this sense, the emergence of biology itself constituted a paradigm-forming event, while earlier empirical traditions represent the indispensable groundwork upon which that paradigm was built.

The consolidation of biology as an experimental science thus did more than unify diverse empirical practices: it also established new epistemological boundaries. By defining life in physico-chemical terms and excluding metaphysical explanations, 19th century biology both expanded the domain of inquiry and delimited what could count as legitimate knowledge. The same methodological rigor that liberated biology from *vitalism* also gradually constructed a barrier between the living and the non-living, a conceptual threshold later crystallized in what we term the *Pasteurian Wall*. In the present study, we trace and dissect the historical, empirical, and epistemological developments that led to the formation of this boundary, revealing how the very progress of empirical science generated intrinsic limits to its own explanatory framework – much as *Einstein’s revolution* later defined the ultimate limit of velocity in physics (Gutfreund and Renn, 2025).

1.2 The Pasteurian Wall and beyond

Scientific progress is often portrayed as linear, yet history is marked by radical transformations that redefine entire fields. Following Kuhn and Hacking (Kuhn and Hacking, 1970), these are *paradigm shifts* within emerging communities. This study, however, emphasizes that micro-revolutions like the microscope and urea synthesis were constitutive of the broader, non-Kuhnian

Scientific Revolution, a foundational transition that reshaped modern thought across philosophy, theology, and social imagination (McMullin, 1993).

We aim to explore the profound connections between technology, philosophy, and experimental science. A pivotal example is the microscope. Its invention and use not only overturned the long-held tenets of Aristotelian embryology, but also exerted a profound influence on Catholic doctrine, serving as a powerful case study of how scientific discovery can redefine society’s deepest beliefs. The social impacts of scientific and technological revolutions lie not in their direct applications, but how they reshape our cultural metaphors, ideologies and fundamental conceptions of human condition. The taxonomy of these impacts includes: (i) technological (new inventions); (ii) ideological (new political and social philosophies); (iii) cultural (changes in art, literature, daily life); and (iv) epistemological (shifts in what is “knowable”).

We center our analysis on the epistemological repercussions of major techno-scientific shifts. A foundational example is the telescope, whose use by Galileo dismantled the Aristotelian-Euclidean worldview by providing empirical evidence against heavenly perfection and geocentrism. In a parallel vein, the microscope (Wilson, 2020) catalyzed a transformation that extended far beyond the laboratory, triggering a fundamental reconfiguration of scientific, philosophical, and societal conceptions of life itself. By enabling direct observation of spermatozoa, ova, and embryonic development (Lane, 2015), the microscope facilitated the dismantling of Aristotle’s ancient embryological framework, which had postulated sequential *ensoulment* (*vegetative* → *sensitive* → *rational*), and replaced it with empirical evidence of life’s continuum from conception (Horowitz, 1987). This technological leap not only gave rise to *Cell Theory*, establishing cells as life’s universal units (Wolpert, 1996) and the chromosomal basis of inheritance (Morgan, 1910), but also redefined humanity’s perception of life’s origins, displacing scholastic dogma with biological mechanism (Kuhn, 1963). Yet this very progress has been weaponized in modern ideological battles: certain groups now cite microscopic embryology as ‘proof that life begins at conception, a claim that, while scientifically coherent for developmental biology, remains ethically and legally contested, fueling societal polarization (Kurjak and Spalldi Barišić, 2021). While these debates endure (Ford, 1991), the microscope’s most enduring legacy lies in its irreversible fusion of observation with empirical truth.

Aristotle (384–322 BC) believed in *entelechy* (an internal principle of development and purpose) (Chapouthier, 2018). His biology was *teleological*: living beings had intrinsic purposes and forms (*eidos*) guiding their growth and behavior (Toepfer, 2012). He explained life through the soul (*psyche*) as the form of a living body. Although Aristotle was not the originator of the idea of *spontaneous generation*, which was widespread in antiquity (*vide infra*), but he was the first to give it a systematic scientific and philosophical formalization within his *teleological biology* (Mossio and Bich, 2017). Before the 19th century, theories of *spontaneous generation*, the idea that life could arise from non-living matter, were widely accepted (Lillie, 1942). *Vitalism* as we know it, the idea that life depends on a special, non-physical force beyond chemistry and physics, came much later (17th–19th centuries) from the work of thinkers like *Georg Stahl*, *Xavier Bichat*, and later even *Louis Pasteur’s* early

opponents (Haigh, 1975). However, neither *spontaneous generation*, nor *vitalism* survived the formalization of the scientific method from Alchemy, which was an eclectic mix of mystical and proto-scientific doctrines (Harding, 2019).

The transition from alchemy's eclectic blend of mystical and proto-scientific doctrines to the empirical discipline of chemistry was not a simple evolution, but a fundamental reorientation. Chemistry inherited alchemy's experimental techniques and transformed them through standardization, quantification, and a materialist framework, turning the art of transmutation into a science of matter (Greenberg, 2007). A landmark moment in this transition was Friedrich Wöhler's 1828 synthesis of urea from inorganic precursors, which dismantled the doctrine of *vitalism*, the belief that organic compounds could only be produced by living organisms through a "life force" (*vis vitalis*) (Kinne-Saffran and Kinne, 1999). This paradigm shift demonstrated that the same laws govern both organic and inorganic matter. Pasteur (1822–1895) further solidified this empirical approach by using controlled chemical experimentation to disprove *spontaneous generation* once and for all. His work entrenched the principle *omne vivum ex ovo* ("all life comes from an egg"), a paradigm that remains unchallenged to this day (Monti and Redi, 2013). Together, these shifts exemplify how scientific revolutions are not merely accumulations of knowledge, but radical redefinitions of what is considered possible.

While Pasteur's principle cemented the understanding that life arises from pre-existing life under observable conditions, it has occasionally been co-opted by creationist narratives to argue against natural abiogenesis or synthetic life (Javor, 1998; Bergman, 2000). This misrepresents both Pasteur's work, which never addressed life's ultimate origins, and modern science, which distinguishes between *spontaneous generation* (refuted by Pasteur) and abiogenesis (a testable hypothesis) (Luisi, 2016). The synthesis of artificial cells and advances in prebiotic chemistry demonstrate that life's emergence and engineering indeed remain within the domain of natural inquiry, not supernatural exclusion (Oderberg, 2013).

Yet, it must be acknowledged that to this day Pasteur's principle has not been experimentally overturned: no laboratory has created a self-sustaining, evolving living system entirely from non-living components (Benner, 2010). This enduring limitation can be described as the *Pasteurian Wall*, a currently insurmountable boundary in our operational capabilities. To advance, science must either find a way to cross this wall by demonstrating life's genesis under controlled conditions or rigorously explain why such a feat may be impossible. Such an explanation might involve recognizing that life's emergence was not a single, Miller-Urey-style event, (Bada and Lazcano, 2003), but a planetary-scale transition (Smith and Morowitz, 2016) in which a portion of geochemistry progressively became geo-biochemistry, culminating in a *Biosphere* (Vernadsky, 1998). Grappling with this possibility requires intellectual courage: the willingness to accept that the origin of life may be far more complex, distributed, and contingent than our current textbook narratives suggest.

A theological and philosophical distinction, articulated by Soriano and Herce (Soriano and Herce, 2024), differentiates between the *creatio ex nihilo* ("creation out of nothing") of the universe, a direct act of divine origination, and the subsequent emergence of life and humanity as part of the universe's natural

unfolding. From this view, divine action resides not in episodic intervention but in the *law-bound structure of a cosmos* inherently capable of self-organization and complexity. Incorporating this perspective refines our argument: exploring the natural emergence of life through synthetic biology can coexist with broader theological concepts of creation. While theology addresses the metaphysical question of *why* there is something rather than nothing, synthetic biology examines *how* life might arise within that created order. Recognizing this complementarity adds depth to the science–religion dialogue without conflating their distinct explanatory domains.

Finally, it must be acknowledged that no strict, empirically based definition of life has yet achieved consensus. Some argue that such a definition is unnecessary for understanding the origins of life (Szostak, 2012), while others maintain that it is essential for engineering life (Budisa et al., 2020), much as the standardization of biological parts and devices is central to synthetic biology (Canton et al., 2008). Since this study is primarily concerned with the historical evolution of our basic understanding of life's origins and defining features, these issues will be addressed in greater detail in a separate work, together with the relevant literature.

2 When life begins? - vegetative, sensitive, and rational soul under the microscope

Scientific advancements rarely settle ancient debates: they more often forge new orthodoxies, redefine ethical boundaries, and reshape societal convictions in unforeseen ways. The microscope exemplifies this phenomenon with striking clarity. By revealing previously "invisible worlds," microscopy (Lane, 2015) did not merely expand human knowledge, it fundamentally altered humanity's understanding of life's origins, hierarchy, and essence. These shifts did not necessarily unfold in ways that align with contemporary ideals of "progress" or "progressivism" (Eisenach, 1994). Instead, the microscope radically transformed belief systems and redefined humanity's understanding of life's complexity, and in the process created new orthodoxies, reframed old debates, and, in some cases, reinforced boundaries rather than dissolving them. The microscope did not simply uncover life's complexity: it redefined the very terms by which life was debated and governed (Hagmann, 2023).

2.1 Microscopy and the hidden world of human life

The invention and refinement of the microscope by Robert Hooke (1636–1703) and Antonie van Leeuwenhoek (1632–1723) revealed an invisible universe of microorganisms. When Hooke [1660s] and van Leeuwenhoek [1670s] developed their microscopes, they demonstrated that life exists in forms unimaginably small and complex (Gest, 2004). This challenged established theological and philosophical categories, expanding public awareness of life's diversity and sparking curiosity about its fundamental building blocks and whether they could be manipulated. Crucially, microscopy enabled scientists to directly

TABLE 1 Milestones in scientific thought on the beginning of human life, highlighting paradigm shifts that inspired doctrinal change with profound societal impacts, initially driven by the invention of the microscope and its transformative role in studying embryonic morphology and development.

Period	View on ensoulment	Status of abortion before ensoulment
Aristotle (4th C. BCE)	40 days (male)/90 days (female)	Not homicide
Medieval Catholicism (13th–19th c.)	Adopted Aristotle via Aquinas	Sinful, but lesser penalty
Post-1869 Catholicism	Soul at conception	Abortion = homicide from conception

observe early embryonic development, demonstrating that from fertilization onward, growth follows a continuous, organized process, not the separate “*plant–animal–human*” stages proposed by Aristotle (Zagris, 2022). This evidence undermined the notion of delayed *ensoulment* and supported the view that a new, distinct organism, and thus potential human life, exists from conception.

2.2 Aristotle’s concept

Aristotle discussed the beginning of human life in several works, most notably *Historia Animalium* (Balme and Gotthelf, 2002) and *De Generatione Animalium* (*On the Generation of Animals*) (Aristoteles and Gotthelf, 1972). He proposed the theory of “*delayed ensoulment*”, the idea that the embryo passes through successive stages before becoming fully human. In his observational embryology, development began with a *nutritive* (*vegetative*) soul, comparable to that of plants. This was followed by the acquisition of a *sensitive* (animal) soul, capable of sensation and movement, and finally the *rational* soul, unique to humans. Based on what he considered empirical evidence, Aristotle estimated that *ensoulment* occurred 40 days after conception for a male fetus and 90 days for a female fetus, the latter reflecting his (now discredited) belief that female development was slower (Khitamy, 2013). For Aristotle, “*human life*” in the full sense began only with the infusion of the *rational* soul. Before that, the developing organism held a moral status closer to that of animals (Miller, 1999).

2.3 Aristotle’s concept reception in the middle ages

In the 13th century, Aristotle’s natural philosophy entered Western Europe through Latin translations from Arabic and Greek sources. Thomas Aquinas (1225–1274) incorporated Aristotle’s theory of delayed *ensoulment* into Catholic theology (Owens, 1993). He maintained that the rational soul was created directly by God and infused only after the earlier vegetative and sensitive stages (Skrzypek, 2021). Consequently, early abortion (before *ensoulment*), while considered sinful was not considered homicide, whereas abortion after *ensoulment* was classified as homicide (Table 1). In canon law, this distinction was formalized: the *Decretals* of Pope Gregory IX (1234) differentiated between abortion before and after the “*formation*” or “*animation*” of the fetus, and penalties were more severe for abortion after *ensoulment* (Coriden, 1973). Scientifically, the Aristotelian model aligned with prevailing medieval medical theories, such as Galenic embryology and humoral physiology, and it was widely taught in universities and ecclesiastical schools (French, 1979).

2.4 When and why the Aristotelian view was abandoned

From the 17th to the 19th century, advances in anatomical dissection and, later, the use of the microscope began to challenge Aristotle’s developmental model. Researchers such as William Harvey (1578–1657) and subsequent embryologists observed early development in unprecedented detail, and the idea that a complete human organism is present from conception steadily gained ground (Harvey and Willis, 1847). The discovery of sperm and egg cells in the 17th century, combined with improved understanding of fertilization, revealed an unbroken developmental continuum from the moment of conception, undermining the notion of distinct *vegetative*, *sensitive*, and *rational* stages. In 1869, Pope Pius IX removed from canon law the long-standing distinction between “*animated*” and “*unanimated*” fetuses (Rankin, 2013). From that point onward, the Catholic Church treated abortion at any stage as equivalent to homicide (Table 1). This doctrinal shift was influenced by new embryological evidence demonstrating continuous development from conception, as well as a theological move toward safeguarding potential human life from its earliest point.

The abandonment of the Aristotelian model (Schmitt, 1973) was driven by three converging factors. Scientifically, microscopy revealed that fertilization marks the beginning of a single, organized life process. Theologically, many came to believe that the rational soul could be infused at conception, removing uncertainty over the moment of *ensoulment*. Morally and pastorally, the Church adopted a “safer” position, treating all stages of pregnancy as fully human to avoid the possibility of permitting the destruction of an ensouled being. The collapse of Aristotelian embryology (Jones, 2004) marked not just a scientific revolution, but a paradigm-shift in how humanity defines itself, a testament to how tools like the microscope can reshape metaphysics as decisively as they reveal the physical world.

3 Spontaneous generation of life and omne vivum ex ovo: from self-evidence to the Pasteurian barrier

3.1 The enduring legacy: Aristotle’s spontaneous generation and its long influence

For much of human history, the belief that simple life forms could arise spontaneously from nonliving matter was considered self-evident. Everyday experience seemed to confirm it: mold on bread, maggots in meat, or worms in mud after rain, appeared to

demonstrate that life emerged naturally under the right conditions. Sacred texts also reinforced this view (Moritz, 2013). In *Genesis*, creeping animals were said to arise from earth and water by divine command, while the plagues of *Exodus* described frogs and gnats emerged from dust and water (Lehoux, 2017). Similar notions appear across world traditions: in India, the *Laws of Manu* (ca. 500 BCE) classified life into womb-born, egg-born, seed-born, and moisture-born categories, while Greek natural philosophers linked life's origin to elemental forces: earth, water, air, or fire (McCartney, 1920).

Aristotle (384–322 BC) advanced the idea of *spontaneous generation*, the belief that certain forms of life arise directly from nonliving matter under the right conditions. In *History of Animals*, *On the Generation of Animals*, and *Meteorology* (Balme and Gotthelf, 2002; Aristoteles and Gotthelf, 1972), he described how animals such as insects, shellfish, and even small vertebrates could emerge from decaying organic matter, mud, or slime, guided by a *pneuma* (“vital spirit” or life force) inherent in nature. Human reproduction, in his view, was distinct and required male seed and female menstrual blood, but many lower organisms, he claimed, emerged without parents (Zagris, 2022). This concept was absorbed into *Hellenistic natural philosophy* and later became deeply interwoven with *Alchemy*, which sought to transform matter and saw *spontaneous generation* as a natural parallel to the “transmutation” of metals (Dufault, 2015). Through the translation movement in late antiquity and the early Middle Ages, Aristotle's biological works entered Islamic scholarship (via thinkers like *Avicenna* and *Averroes*) and Jewish philosophy (e.g., *Maimonides*), where they were harmonized with theological doctrines about divine creation acting through natural processes (Zonta, 2000). In Christian Europe, scholastics such as *Thomas Aquinas* (1225–1274) integrated Aristotle into medieval theology, interpreting *spontaneous generation* as compatible with *Genesis* (Owens, 1993): God had endowed nature with the powers to bring forth life from inert matter under certain conditions (Sheldrake, 1994).

This synthesis gave Aristotle's ideas near-canonical status in the universities, shaping natural history, medicine, and proto-scientific thought for over a millennium. By the late Middle Ages and Renaissance, *spontaneous generation* was accepted as settled fact in both popular culture and learned discourse. It provided explanations for common phenomena, such as lice or flies, appearing from filth and was deeply entwined with theological and alchemical traditions. Only in the 17th and 18th centuries did controlled experiments by *Francesco Redi* and *Lazzaro Spallanzani* begin to dismantle it (Schummer, 2009).

3.2 Religious cosmologies of spontaneous life: *biomorphic*, *technomorphic* and *logomorphic* traditions

The concept of life arising spontaneously from nonliving matter is deeply embedded in religious traditions, though rarely as a central tenet. The Judeo-Christian creation myth in *Genesis* 2:4 (Benner, 2010) describes *Yahweh* forming humans from soil and breathing life into them, an artisanal act, while plants and lower animals emerge spontaneously from the earth, seemingly without direct

divine intervention. This duality reflects a hybrid view: complex life requires craftsmanship, but simpler organisms arise autonomously. The *Qur'an* diverges by stating all life was made from water (Sura 21:30), making artisanal creation less explicit.

These narratives share roots with older myths, like the Babylonian *Enūma Eliš*, where gods fashion humans from clay. Such parallels suggest the *technomorphic* (craftsman-like) creation motif was culturally transmitted rather than universal. Even *Plato's Timaeus*, where a *Demiurge* shapes the world geometrically, devalues material creation, later inspiring *Gnostic* reinterpretations of the *demiurge* as malevolent. Similarly, the *Prometheus myth*, though originally devoid of human creation, was later Christianized to underscore the exclusivity of divine power. Yet *technomorphic* myths are exceptions. More common are *logomorphic* (word-based) creation stories, as in *Genesis* 1:1–2:4a, where God commands life into being. This tradition culminates in the *Gospel of John's* opening (“*In the beginning was the Word*”), which reframes creation as a divine utterance, merging Jewish and Hellenistic thought. Such ideas, echoed in ancient Egyptian myths (e.g., *Ptah's* self-creation through speech), avoid the paradoxes of craftsmanship by positing thought as the origin of matter (Johnston, 2008). These narratives influenced *Christian idealism*, as in Berkeley's belief that God's mind sustains reality (Spiegel, 2017).

The *biomorphic tradition*, however, dominates globally. In the *Enūma Eliš*, the world is fashioned from the corpse of the goddess *Tiamat*, blending violence and biology (Lambert, 2013). Hindu, Jain, and Mesoamerican *cyclical cosmologies* reject a single origin entirely, framing creation as perpetual renewal, a worldview deeply rooted in Indo-European cultures shaped by predictable seasonal cycles. In contrast, the “*desert religions*” (Judaism, early Christianity, Islam) developed linear cosmologies, reflecting the austere, non-repeating landscapes of their origins. The *Gospel of John's Logos* theology (Culpepper, 1988) represents a deliberate synthesis of these traditions: it preserves the Hebrew emphasis on a divine beginning while incorporating the Hellenistic cyclical notion of eternal Word, thus laying the intellectual foundation for Judeo-Christian civilization. Even in the *Old Testament*, *biomorphic* elements persist: *Job* 38:4–40:2 frames creation as a display of divine authority, yet plants and animals emerge from the earth autonomously.

These myths reflect cultural priorities: agrarian societies favor *biomorphism*; craft-based cultures, *technomorphism*; and literate traditions, *logomorphism* (Bremmer, 2005). The Egyptian *Khepri myth*, for instance, merges all three (Pinch, 2004). But the *technomorphic* motif's true significance lies in its utility for monotheism, asserting a singular creator's absolute power, evident in *Yahweh's* rebuke to *Job* or Islam's emphasis on divine will. Notably, many traditions reject the question of origins altogether. Greek skeptics and Buddhists deemed it futile (Vassiliades, 2004), while Aristotle and Kant saw it as fundamentally unanswerable (Wächtershäuser, 1997). This diversity undermines the notion that life's origin must involve divine craftsmanship.

Spontaneous generation, whether in myth or modern abiogenesis, finds precedent in *biomorphic* and *logomorphic* traditions, where life emerges from earth, water, or speech without direct intervention. The religious and philosophical underpinnings of spontaneous life formation are neither uniform

nor strictly divine, but rather a complex tapestry of competing ideas that continue to influence scientific and ethical debates. As explored in depth by Joachim Schummer, the historical evolution of artificial life concepts reveals how cultural taboos, creation myths, and public fascination have shaped, and often constrained, modern perceptions of synthetic biology. His work highlights the enduring interplay between scientific ambition and societal imagination (Schummer, 2009).

3.3 Animating matter: Alchemy's pursuit of synthetic life

The idea of “creating life from elements” or primordial matter was indeed a central aspiration of Alchemy, deeply embedded in its philosophical and practical traditions (Tramer et al., 2007). Alchemists sought not only to transmute base metals into gold, but also to uncover the secrets of life itself, often through the synthesis of artificial life forms or the revival of inanimate matter. This ambition manifested in several key concepts such as one of the most iconic examples was the *homunculus* (Latin for “little human”), a miniature, fully formed human believed to be creatable through alchemical procedures. The 16th-century alchemist Paracelsus (1493–1541) famously described a method to generate one by fermenting human sperm in a sealed vessel, claiming it would develop into a living, albeit tiny, being (Murase, 2020). This reflected the alchemical belief that life could be engineered from its elemental components. The *Philosopher's Stone*, alchemy's legendary substance, was thought to grant not just metallic transmutation, but also eternal life and the power to “animate” matter (Buchanan et al., 2006). Some alchemists (e.g., Johann Conrad Dippel) experimented with reviving dead tissue or creating life-like compounds, blurring the line between chemistry and vitalism (Aynsley and Campbell, 1962). Symbolic rituals like the “chemical marriage” (e.g., of sulfur and mercury) framed creation as a generative act, mirroring biological reproduction (Greenberg, 2002). This metaphorical language often crossed into literal attempts to “give birth” to new forms of life. Alchemy inherited Aristotelian ideas about *spontaneous generation* (life arising from non-living matter, like maggots appearing on rotting meat). Many alchemists sought to replicate this process artificially, attempting to synthesize life from “*primordial matter*” (*prima materia*) or “*chaos*” (an undifferentiated primal substance) (Jung and Hull, 2023).

3.4 Spontaneous generation and life-creation in Renaissance thought

During the Renaissance, belief in *spontaneous generation* persisted across a wide spectrum of intellectual traditions as excellently covered by Schummer (Schummer, 2011). In the hermetic-humanistic circles of Paracelsus, Giambattista della Porta, and van Helmont, in the mechanical philosophy of Johannes Kepler, Galileo Galilei, René Descartes, and Issac Newton, and in the atomistic natural philosophy of Kircher, there was broad agreement that life could arise spontaneously, and might even be deliberately produced by humans (Dobbs, 1983). Whereas antiquity had attributed such creative powers to the gods, early

modern culture increasingly ascribed them to human ingenuity. Medicine and natural history reinforced this outlook. The writings of Hippocrates (460–370 BC) suggested intestinal parasites arose spontaneously, a view carried forward by Greco-Roman and later physicians who developed diets and herbal remedies to prevent such “generations” (Shugaar et al., 1998). Even into the 18th century, physicians such as Johann Gottfried Bremser (1767–1827) reported worms in the human eye as spontaneous formations (Sattmann et al., 2014). Practical recipes abounded: van Helmont (1580–1644) famously claimed that mice could be generated from soiled linen and wheat, while Johann Franz Grienl von Ach (1631–1687) described producing a miniature frog under a microscope (Partington, 1936). Some creatures were valued: silkworms, cochineal insects, snails, and especially honeybees, were seen as divine gifts. Vergil's *Georgics* (written between 37 and 29 BC) codified the belief that bees could be generated from ox carcasses, a technique repeated in farmer's manuals across Europe until the 18th century (Schummer, 2011).

Renaissance naturalists elevated these traditions into systematic programs. Giambattista della Porta's *Magiae Naturalis* (1589/1598) compiled the era's most comprehensive set of instructions for life creation, including animal breeding and speculative ideas for human improvement (Kodera, 2015). Francis Bacon's *New Atlantis* (1623) presented the most ambitious vision: a three-stage program involving selective breeding, trait modification, and artificial production of new species from basic matter. His utopian plan, encompassing animal training, human optimization, and even life extension, effectively sketched an early form of synthetic biology, transforming folk belief into programmatic science (Bacon, 2016).

3.5 From scriptural authority to empirical inquiry

These Renaissance traditions fed directly into the transformations of the Scientific Revolution (mid-16th to late 18th century), which fundamentally reshaped how Western societies understood life and its origins. Prior to this shift, explanations were dominated by theology, particularly Judeo-Christian creation narratives, and reinforced by classical authorities such as Aristotle (384–322 BC) and Galen (129–216 AD). Life was viewed as a divine gift, fixed and immutable. The *Scientific Revolution* gradually loosened this framework. Francis Bacon (1561–1626) championed inductive reasoning, arguing that natural phenomena should be studied through observation and experiment rather than deference to scripture or ancient texts.

New instruments like the microscope and telescope, along with the circulation of printed works, expanded what could be observed, shared, and tested. At the same time, broader philosophical shifts de-centered humanity. The *Copernican revolution* displaced Earth from the center of the cosmos, while mechanistic thinkers like Galileo, Descartes, and Newton showed that natural phenomena obeyed universal laws. Once Earth was no longer the cosmic center and life itself was reframed as subject to discoverable physical and chemical principles, it became plausible to imagine both extraterrestrial life and the artificial creation of organisms. By systematically decoupling life from divine mystery and embedding it within universal natural laws, the *Scientific*

Revolution laid the intellectual groundwork for modern biology and biotechnology.

3.6 Mechanistic worldview and life as a system

The *Scientific Revolution* reframed the cosmos, and by extension life, as a realm governed by universal, discoverable laws. *Descartes* (1596–1650) advanced a radical form of this view, describing animals and many human bodily functions as *automata*: complex mechanical arrangements explainable entirely through matter sensing and motion (Morris, 1969). *Descartes*'s division between *res extensa* (mechanical body) and *res cogitans* (immaterial mind) reinforced the idea that living bodies, especially those of animals, could be studied as complex machines (Descartes, 1996). This mechanistic outlook encouraged early modern anatomists and natural philosophers to investigate physiology, reproduction, and development through physical principles rather than vitalistic or mystical explanations. In the microscopy era, this framework helped shift embryology toward viewing life's formation as an observable, material process governed by natural laws.

Newton (1643–1727) extended this law-bound view to the entire physical universe, showing that even celestial motion followed precise mathematical principles (Newton et al., 1999). Together, they helped detach explanations of living phenomena from purely mystical or vitalist causes. Into this mechanistic turn stepped *Gottfried Wilhelm Leibniz* (1646–1716), who both embraced and refined the machine metaphor. Rejecting *Descartes*'s reductionism (Noble, 2023), *Leibniz* argued that living beings are “natural machines” or “divine automata”: organized systems whose parts are themselves machines, down to the smallest scale (Leibniz, 1989a). Unlike man-made automata (such as clocks), which cease to be machines when disassembled into inert parts, natural machines are machines within machines, exhibiting organization at every level of magnification. *Leibniz*'s model preserved a theological dimension: these nested *automata* were the product of divine design, each animated by *monads*, defined as ‘indivisible metaphysical units’ that endowed living beings with unity and purpose (Leibniz, 1989b). This synthesis made mechanistic biology more palatable to a religiously minded society, easing its cultural integration.

By combining *Descartes*'s mechanistic rigor, *Newton*'s universal laws, and *Leibniz*'s hierarchical organization, 17th- and 18th-century thought laid crucial conceptual foundations for later science. Life could be imagined as a system analyzable into discrete components, whose functions could, in principle, be reconstructed. This shift planted the earliest seeds of the modern vision in synthetic biology: that living systems are both analyzable and engineerable, their complexity residing in organized hierarchies rather than in an ineffable life force.

3.7 From divine automata to the enlightenment's “man machine”

By the mid-18th century, the mechanistic worldview had shed much of its theological framing. In France, *Julien Offray de La*

Mettrie (1709–1751) took the metaphor to its most provocative conclusion in *L'Homme Machine* (1747), arguing that humans are not merely like machines, they are machines (Vartanian, 2015). *La Mettrie* rejected any immaterial soul, claiming that thought, emotion, and morality emerge from the organization and function of physical matter (de La Mettrie, 2016). In doing so, he fused Cartesian mechanics with a radical materialism that scandalized religious and political authorities. *The Encyclopédistes*, led by *Denis Diderot* (1713–1784) and *Jean le Rond d'Alembert* (1717–1783), expanded this secular mechanistic vision in the *Encyclopédie* (1751–1772). This monumental work sought to catalogue all human knowledge, with natural history, anatomy, and chemistry presented as fully accessible to human reason and empirical inquiry (d'Alembert, 1995). Their project not only disseminated mechanistic biology to a wider public but also framed life as part of a rational, knowable order, implicitly supporting the idea that life processes could be replicated or engineered.

3.8 Philosophical refinements: Kant and Hume

While materialists such as *La Mettrie* embraced strict reductionism, *Immanuel Kant* (1724–1804) sought to preserve a special status for living beings within a law-governed universe. In the *Critique of Judgment* (1790), *Kant* described organisms as “natural purposes” (*Naturzwecke*): their parts exist for and through each other, forming self-organizing wholes that cannot be fully explained by mechanical causation alone (Menting, 2020). *Kant* accepted mechanistic explanations for many natural phenomena but argued that the internal purposiveness of life demanded a distinct mode of understanding, what today might be called systems thinking (Steigerwald, 2006). *David Hume* (1711–1776), by contrast, used his empiricism to dismantle teleological arguments for life's design. In his *Dialogues Concerning Natural Religion* (1779), he questioned the analogy between organisms and human-made machines, underscoring the limits of inference from such comparisons and leaving open the possibility of multiple, natural origins for life-like order (Hume, 2004). *Hume*'s skepticism helped normalize the view that life could be explained entirely through natural causes, without recourse to a divine artificer.

3.9 Natural scientists of the enlightenment and their enduring legacy

The mid-to late- 18th century witnessed advances in the life sciences that gave concrete form to philosophical speculation. Here, we highlight only a few prominent examples, while referring interested readers to the numerous excellent books and articles that explore this vibrant era in depth. This period immediately preceded the *Industrial Revolution*, which in turn triggered the long-wave *Kondratiev cycles* of technological innovation: a process that continues to shape our world today (Alexander, 2002). For example, *Albrecht von Haller* (1708–1777) explored physiology as an integrated system, identifying nerve irritability and muscle

contractility as fundamental properties of life (Siegrist, 2017). Carl Linnaeus (1707–1778) developed a comprehensive classification system (*Systema Naturae* (Linnaeus, 2024)), that organized plants, animals, and minerals into hierarchical categories, reflecting the Enlightenment belief in a rational and orderly natural world. Georges-Louis Leclerc Comte de Buffon (1707–1788), challenged fixed species concepts, hinting at transformism (a precursor to evolutionary theory) and emphasizing the role of environmental factors in shaping life (Browne, 1988). Georges Cuvier (1769–1832), by contrast, argued for the fixity of species and the *finite number of anatomical “plans” or body types in nature*, laying the foundations of comparative anatomy and paleontology (Cuvier, 1798). Johann Wolfgang von Goethe (1749–1832) coined the term “*morphology*” around 1796 to describe the study of biological form and transformation, first applied in his *Metamorphosis of Plants* (Steigerwald, 2002). He also proposed the idea of a universal “*Urform*” or archetypal structure as the primal blueprint from which all living forms could be derived through modification (Pivar, 2009).

3.10 From enlightenment materialism to the chemistry of life

By the late 18th century, the mechanistic and materialist views advanced during the Enlightenment had prepared the ground for a decisive shift: the transformation of chemistry from an alchemical art into a quantitative science. Antoine-Laurent Lavoisier (1743–1794), in his 1789 *Traité Élémentaire de Chimie*, famously declared that “*life is a slow combustion*” (*la vie est une combustion lente* (Lavoisier, 1864)). In making this claim, he demonstrated how the precision of chemical experimentation, with its unambiguous identification and quantification of substances, could be applied to biological processes, thereby further embedding life within the framework of universal physical laws. Often called the father of modern chemistry (Eagle and Sloan, 1998), Lavoisier systematically abandoned the speculative language of *Alchemy* in favor of precise measurement, elemental analysis, and conservation laws (Poirier, 1998). His demonstration that respiration was a form of slow combustion closed the gap between physiology and chemistry, reinforcing the idea that life processes could be explained by the same physical laws governing inanimate matter. This chemical framework opened the way to a more audacious question: could a living substance, or even life itself, be created from purely inorganic materials?

3.11 Experiment that ended an idea: urea and the fall of *vitalism*

Emerging in the 17th and 18th centuries as a reaction to mechanistic views of life, *vitalism* argued that living organisms were governed by a unique, immaterial force distinct from the laws of physics and chemistry (Kinne-Saffran and Kinne, 1999). This doctrine posited that a “*vital spark*” or *anima* was responsible for the processes of life, asserting an unbridgeable gap between organic and inorganic matter. However, the foundational principle of *vitalism* faced a devastating challenge from the burgeoning field of organic chemistry. In 1828, chemist Friedrich Wöhler (1800–1882) inadvertently catalyzed its

decline by synthesizing urea, a biological waste product found in urine, from the inorganic salt ammonium cyanate (Kauffman and Chooljian, 2001). This landmark experiment demonstrated for the first time that an organic compound could be created from plainly inorganic starting materials without the need for a living organism or a *vital force* (Figure 1). Wöhler’s discovery, followed by further organic syntheses, fundamentally dismantled the core tenet of *vitalism*. It proved that the molecules of life obeyed the same chemical principles as all other matter, allowing biology and medicine to gradually shift from a philosophical to a physico-chemical foundation.

3.12 From Wöhler to Pasteur: life-synthesis ambitions and the emergence of the *Pasteurian Wall*

In 1828, Wöhler’s synthesis of urea from inorganic salts shattered the barrier between organic and inorganic chemistry. For many, it ignited the hope that a living organism might one day be assembled in a single experimental setup using purely chemical means. This optimism built on a longer arc of challenges to the ancient doctrine of *spontaneous generation*, the belief rooted in Aristotle, that life could arise fully formed from nonliving matter. Alchemy’s quest to create life from elements, exemplified by the *Homunculus* or the animating powers ascribed to the *Philosopher’s Stone*, reveals an enduring fascination with life’s artificial synthesis. Though these efforts were mystical, they anticipated chemistry’s later overthrow of *vitalism*, as seen in Wöhler’s urea experiment (Kinne-Saffran and Kinne, 1999). Together with microscopy’s redefinition of life’s origins, this underscores how scientific paradigm shifts often fulfill, or subvert, humanity’s oldest dreams.

Francesco Redi (1626–1697) had shown that maggots on meat came from fly eggs, not the meat itself (Gottdenker, 1979). A century later, in 1768, Lazzaro Spallanzani (1729–1799) demonstrated that boiled broth remained sterile unless exposed to air, though critics argued he had destroyed a mysterious “*vital force*” by sealing his containers (Capanna, 1999). In the 1860s, Louis Pasteur’s swan-neck flask experiments resolved the debate (Bordenave, 2003). By allowing air into sterilized nutrient broths while preventing dust and microbes from entering, he showed that no microbial growth occurred unless contamination was introduced. Pasteur’s elegant design eliminated the “*vital force*” objection and established ‘all life from pre-existing life’ (*omne vivum ex ovo*: “*all life comes from an egg*”) as an irrefutable biological fact (Monti and Redi, 2013). While a triumph for microbiology and germ theory, it also closed, for decades, the intellectual space for serious experimental exploration of life’s emergence from nonliving matter. What had seemed, after Wöhler, like a reachable chemical frontier was now fenced off by what we may call the *Pasteurian Wall*, a reminder of our continued incapacity to create life *de novo* from inorganic matter.

4 Life as problem and project: intellectual lineages and the *Pasteurian Wall*

Kant, in his *Critique of Judgment* (1790) (Kant, 1987), sought to explain why living beings seem to resist purely mechanistic

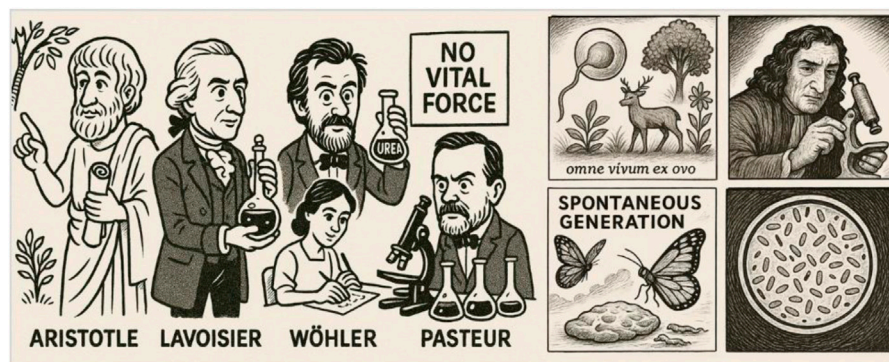


FIGURE 1

Some protagonists of the major scientific revolutions and the related paradigm shift in the history of *Life synthesis* from Aristotle to Lavoisier, Wöhler and Pasteur. It was establishment of rigorous empirical method of chemistry that dispute vitalistic theory with its 'vital force' (*vis vitals*) and yielded decisive experiments that established the principle *omne vivum ex ovo* ('all life comes from an egg', giving rise to the 'Pasteurian Wall'). The theory and related science of *spontaneous generation* which dominated scholarly thoughts for more than thousand years was virtually terminated also by the invention of microscope by Hooke and van Leeuwenhoek with the profound impact on human society (see Table 1). Seated at the table is Marie-Anne Pierrette Paulze Lavoisier (1758–1836), an essential collaborator and secretary to Antoine Lavoisier (typical of women's roles in 18th-century science). Although cross-era analogies are imperfect, a cautious parallel with Rosalind Franklin remains apt: crucial, historically under-credited contributions. (AI [ChatGPT ver. 5] generated graphics).

explanation. Unlike machines assembled from parts, an organism is *self-organizing*: its parts exist for and by means of the whole, continually generating and maintaining one another. Kant described such beings as "*natural purposes*," entities that appear to possess an internal principle of design. For him, this principle was not a mechanical cause but a *regulative idea*, a necessary way of thinking about life, even if its ultimate cause remained unknowable. The modern theory of *autopoiesis*, introduced by Maturana and Varela (Ma et al., 2012) and elaborated by Weber and Varela (Weber and Varela, 2002), gives this philosophical insight a concrete biological form. An *autopoietic system*, exemplified by the living cell, is a network of molecular processes that continuously produces and regenerates its own components. It thereby achieves what Kant could only posit: a *physically realized self-organization* that defines life as a self-producing, operationally closed system.

Before the *Scientific Revolution*, life's origin was seen as a fixed historical event, controlled by divine will and beyond human influence. Afterward, life became an open question: both its origin and its possible synthesis entered the domain of empirical inquiry. Enlightenment thought deepened this transformation. In France, *l'homme machine* stripped life of metaphysical protections; in Germany, Kant framed organisms as self-organizing systems, anticipating holistic biology (Roqué, 1985); in Britain, Hume's skepticism eroded the authority of design arguments. These philosophical currents translated into new experimental programs in physiology, chemistry, and eventually microbiology. The result was a double legacy for modern synthetic biology: (i) *Life as a fully material, law-governed phenomenon*, a precondition for attempting to construct it; (ii) *Life as organized complexity*, a reminder that synthesis must address the synergistic integration of parts into a coherent whole, not just the assembly of components.

This Kantian analogy finds a profound biological instantiation in the genetic code (here it is important to distinguish the *genetic code* - the universal rules translating nucleotide triplets into amino acids - from *genomics*, which studies the specific organization and expression of those sequences in living systems). Natural scientists

and philosophers such as Konrad Lorenz (1903–1989) have interpreted Kant's *a priori* categories in evolutionary terms, viewing them as phylogenetically acquired cognitive frameworks (Lorenz, 1982). Extending this reasoning to the molecular level, the genome constitutes the most fundamental *a priori* information of the organism - a transcendental biological framework that precedes any individual experience. Just as Kant's forms of intuition (space and time) and categories of understanding (such as causality) structure all possible perception, the genetic code provides the pre-experiential rules that make biological existence possible. It is the innate "*synthetic program*" that determines developmental potential, physiological responsiveness, and adaptive boundaries; the environment supplies a *posteriori* stimuli, but the genome defines the conditions of possibility for responding to them. In this sense, the genetic code does not merely instruct - it constitutes the operational logic of life, shaping a biologically meaningful world before any individual interaction occurs.

If the genome is life's *a priori* informational framework, the fundamental challenge of synthetic biology becomes its *a posteriori* reconstruction. Today, synthetic biology - encompassing genetic code expansion, xenobiology, synthetic metabolism, AI-aided bioengineering, and artificial cells - directly inherits this intellectual lineage (Schmidt et al., 2017). Lavoisier's scientific process in chemistry and Wöhler's urea synthesis demonstrated that life's building blocks could be produced from inorganic matter. Yet, Pasteur's proof that all life comes from life established *omne vivum ex vivo* as a contrasting, empirically grounded principle (Figure 1). Building on Fry's (Fry, 2000) historiography of origins-of-life research, we introduce the concept of the *Pasteurian Wall*: a barrier that has long constrained experimental abiogenesis and remains a central challenge in synthesizing life from nonliving matter. This framework, we argue, could eventually inform broader scientific consensus on the feasibility of life synthesis.

The successes of 19th century organic chemistry fueled hopes that artificial life might eventually be created. Emil Fischer

(1852–1919) and *Jacques Loeb* (1859–1924) were among the first to suggest that the laboratory synthesis of substances identical to those produced by living organisms could, in principle, be extended to life itself (Schummer, 2011). For decades, from the early coacervate droplets of *Oparin* and *Fox* (Novak, 1984) to the synthetic protocells (Venter et al., 2022) and minimal genomes (Mushegian, 1999) and synthetic nucleic acids (Chaput et al., 2020) of today, origins-of-life research has proceeded within a *Pasteurian paradigm*. It approached abiogenesis primarily as a historical inference problem, not as a target for direct, reproducible synthesis.

In its most radical forms, especially top-down xenobiological approaches (Budisa, 2014), synthetic biology now confronts the *Pasteurian Wall* directly, seeking to blur the line between living and nonliving systems. This endeavor revives premodern ambitions: alchemy's mysticism, for instance, anticipated modern synthetic biology's drive to construct life *de novo*. Yet despite centuries of progress, the core challenge remains unchanged: biology must either create life from nonliving matter or explain why it cannot.

The concept of *panspermia*, that life's seeds are widespread throughout the cosmos, originates not with modern scientists but with the Greek philosopher *Anaxagoras* in the fifth century BCE (Mitton, 2022). While 19th century thinkers like *Lord Kelvin* revived the idea, it was *Svante Arrhenius* (1859–1927) who provided its first major scientific mechanism with his theory of “*radiopanspermia*” (Raulin-Cerceau et al., 1998). The hypothesis took a more provocative turn when *Francis Crick* (1916–2004), co-discoverer of DNA, alongside *Leslie Orgel* (1927–2007), proposed “*directed panspermia*”, the deliberate seeding of Earth by an advanced civilization (Crick and Orgel, 1973). Critically, however, *panspermia* in all its forms does not overcome the fundamental challenge of the *Pasteurian Wall*, our continued incapacity to create life *de novo* from non-living matter. It merely displaces this profound problem elsewhere in the cosmos, leaving the ultimate origin of life unexplained.

Contemporary efforts must navigate not only technical hurdles (e.g., metabolic closure in protocells) but also epistemic legacies of past revolutions (Marliere, 2009). By directly challenging 19th century developmental dogmas like *Haeckel's* ‘Biogenetic law’ (Levit et al., 2022), synthetic biology tests a core Enlightenment ideal: the commitment to relentless inquiry. It compels us to consider whether foundational discoveries can be honored without ossifying into intellectual constraints. As we now live amid overlapping paradigm shifts, from artificial intelligence to climate science, the analytical framework developed here offers a critical lens for examining the wider interplay between scientific innovation, societal turbulence, and the enduring epistemological crises that define our age.

Within this broader landscape, synthetic biology provides a paradigmatic case of how new sciences both inherit and transcend older frameworks of knowledge. *Ernst Mayr's* distinction between historical (evolutionary, “*why*”) and functional (mechanistic, “*how*”) biology (Mayr, 2004) offers a useful framework for positioning synthetic biology. The field effectively dissolves this dichotomy by transforming evolutionary “*why*” questions into experimentally tractable “*how*” problems. Through the deconstruction and reassembly of biological systems, synthetic biology employs mechanistic tools to reconstruct historical processes, thus merging explanation with

creation. Its ultimate expression lies in confronting the *Pasteurian Wall*, where the origin of life, a quintessential historical question, becomes accessible only through functional experimentation. In this sense, synthetic biology represents not merely a synthesis of *Mayr's* two domains but a new epistemological mode: a science that rewrites biological history through design.

5 Beyond the *Pasteurian Wall*: reopening life's oldest questions

As *Thomas Kuhn* (1922–1996) observed (Kuhn and Hacking, 1970), scientific revolutions simultaneously expand and delimit the intellectual horizon, a dual legacy that is often obscured by triumphalist narratives of “progress” (Eisenach, 1994). While *Kuhn* referred primarily to transformations within established scientific frameworks, the broader Scientific Revolution operated on a different scale, inaugurating a modern epistemology in which empirical inquiry replaced metaphysical speculation as the organizing principle of knowledge. In *Kuhn's* terms, both the *Pasteurian Wall* and the redefinition of life's beginning revealed by microscopy, represent decisive *paradigm shifts*: moments when old explanatory frameworks collapse and new ones take hold (Kuhn and Vetter, 1976). The concept of the *Pasteurian Wall* has replaced the long-standing belief in *spontaneous generation* through decisive experimental refutation, advancing microbiology and public health, and in the process, erecting a boundary that discouraged inquiry into life's emergence from nonliving matter for nearly a century. The *Pasteurian Wall* paradigm, that life can only arise from life, has not only redefined what can be empirically proven but also limited what can be imagined. In doing so, it has supplanted old explanatory models and restricted certain research approaches.

Likewise, microscopy's revelation that fertilization marks the start of a continuous, organized developmental process displaced *Aristotle's* staged *ensoulment* model, reshaping both scientific and theological discourse (Bergman, 2000). A parallel can be drawn to *Einstein's* revolution of 1905 (Gutfreund and Renn, 2025), which established the speed of light as an absolute and universal limit. In contrast with earlier times, when faster signals seemed possible in principle, the special theory of relativity made *c* the fundamental speed that cannot be exceeded by anything, including mass or information.

Contemporary synthetic biology, particularly in its bottom-up and xenobiological forms, reopens both frontiers, probing life's origin from nonliving matter and challenging developmental definitions rooted in 19th century biology. In doing so, it must navigate not only formidable technical challenges, but also the cultural and ethical entrenchments left by earlier scientific revolutions (Schummer, 2018). Such work now navigates the *Nagoya Protocol* restrictions on ‘artificial’ biodiversity (Bagley, 2016), revealing how past policy frameworks struggle to accommodate new ontologies of life. Here, the progressivist ideal of continual questioning meets its test: whether past breakthroughs can be celebrated without allowing their conceptual boundaries to become the unexamined limits of the future.

It is not our intention here to enter the politically and ideologically charged debate over when life begins. Nor will we

detail 20th century “life synthesis” efforts (which are treated in a separate manuscript). Our central hypothesis is that scientific progress is not always accompanied by societal progress in understanding, or accepting, implications of scientific breakthroughs. In other words, paradigm shifts in science do not necessarily lead to social emancipation or the broadening of intellectual horizons. The moral of this history is twofold. First, technological innovations can radically shift belief systems, yet the direction of change does not always align with contemporary ideals of “progress.” Second, once scientific conclusions are canonized, they can harden into dogma, only to be re-opened by new technologies or experimental methods. In this sense, synthetic biology is not merely advancing biotechnology, it is reopening philosophical questions last debated in Aristotle’s Lyceum.

The synthesis of life *de novo*, whether through *top-down* (radically reengineering existing life) or *bottom-up* (assembling life from inorganic matter) approaches, will likely require rewriting genetic instructions within synthetic cells, potentially culminating in artificial life itself (Budisa et al., 2020). This remains one of the last great, still-unachieved challenges in the life sciences and bioengineering and also demands effective communication across disciplinary boundaries (Schummer, 2008). At the same time, it is a technology with enormous, potentially revolutionary potential to transform both conventional industries and the fabric of human society. For this reason, we cannot be indifferent to its consequences (Schummer, 2018). Instead, we must actively engage in critical discussions about the social, ethical, artistic, educational, and philosophical implications of creating artificial life with radically altered chemistry, metabolism, and genetic codes (Schmitt et al., 2021; Berger et al., 2020).

For us, this is not an abstract debate. It is central to our own research on genetic code expansion, metabolic engineering, and plastic degradation, the deliberate rewriting of life’s molecular grammar and the use of novel building blocks, preferably “synthetic” ones derived from human-made plastics, is part of this unfolding story (Levin and Budisa, 2023). Each codon reassigned, each noncanonical amino acid integrated, each synthetic metabolism pathway established, and each engineered degradation process that converts synthetic polymers into biomass of “synthetic cells” is both an experiment in molecular design and a step into philosophical territory once reserved for metaphysics. It is a reminder that in exploring the boundaries between the living and the nonliving, we are not only engineers of genes, their proteins and codes as well as pathways, but also participants in a millennia-old conversation about what it means to be alive.

6 The new genesis: reinventing life as a collective human endeavor

Scientific and technological advances do not automatically coincide with prevailing cultural ideas of “Progress” or “Progressiveness.” The historical fate of Aristotle’s doctrines of *spontaneous generation* and *staged ensoulment* illustrates that new knowledge often dismantles, rather than affirms, the moral and philosophical certainties of its time. Scientific change proceeds not

by linear accumulation but through discontinuities that redefine what can be known and imagined. Each such transformation, from the microscope’s overturning of scholastic embryology to the chemical refutation of *vitalism* and the enshrinement of *omne vivum ex ovo*, expanded understanding while erecting new conceptual boundaries, culminating in the *Pasteurian Wall*.

Today, synthetic and xenobiological research confronts this wall directly. A living system with a rewritten genetic code is not merely a new biological object but a challenge to biology’s own definition. Synthetic biology transforms discipline from one that discovers the laws of life as we know it into one that explores the *space of possible life*. Reopening Pasteur’s closed door is therefore not only an experimental enterprise but a societal and philosophical one, demanding reflection by scientists, activists, theologians, ethicists, artists, and legislators alike. Changing the nature of life, and of ourselves, must remain a collective human endeavor, pursued with both intellectual daring and moral responsibility.

Author contributions

NB: Methodology, Supervision, Data curation, Conceptualization, Investigation, Visualization, Formal Analysis, Validation, Writing – original draft, Project administration, Funding acquisition. DL: Writing – review and editing, Funding acquisition, Investigation, Formal Analysis, Validation.

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