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Thoughts of a Senior Scientist

Chance and necessity revisited

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Thirty-five years have gone by since the first appearance, in Paris, of a book that was to become a worldwide bestseller [1]. The book's title, *"Le Hasard et la Nécessité" ("Chance and Necessity")*, was a gem, an inspiration for countless later expositions on the same topic. Its author, Jacques Monod, was one of France's most brilliant scientists, winner, with his mentor André Lwoff and his younger coworker François Jacob, of the 1965 Nobel prize in physiology or medicine. Monod died in 1976, merely 66 years of age. But the heated debates ignited by his book have still not come to an end. Scientists and philosophers looking at the place of life and mind in the universe continue to wrestle with the question: How much chance? How much necessity?

In his book, revealingly subtitled "Essay on the natural philosophy of modern biology", Monod surveyed the remarkable advances made in basic biology since the end of World War II and tried to assess their philosophical significance. His scientific position is summed up in a single sentence: "The universe was not pregnant with life, nor the biosphere with man." His philosophy concludes the book: "Man knows at last that he is alone in the universe's unfeeling immensity, out of which he emerged only by chance. His destiny is nowhere spelled out; nor is his duty."

When Monod's book came out, I was still immersed in the kind of biochemical and cell-biological research that has kept me busy during much of my life. I did, nevertheless, find the time to read the book and even reviewed it for a little-known Belgian monthly [2]. But my main interests were elsewhere. Since then, things have changed; I have closed my laboratories and now devote most of my time to the issues raised by Monod. I have followed the research that has been done in this field over the last decades and contributed a few ideas of my own [3–6]. It is from this perspective that I look back to Monod's book to ask what is left of it after 35 years.

Birth without pregnancy?

In stating that the universe was not pregnant with life, nor the biosphere with man, Monod obviously did not mean this literally. The universe *did* give birth to life, and so did the biosphere to man. Birth without pregnancy would imply a miracle, which is certainly not what Monod had in mind. What he meant was that life is the product of such an improbable combination of unlikely chance events that it is almost certainly unique in the entire universe and could very well, but for this fantastic stroke of luck, never have arisen at all. The fluke of life's birth having happened, a second highly improbable combination of unlikely chance events must have occurred, according to Monod, for life to give rise to intelligent, conscious beings. Hence the final conclusion: "Man knows at last that he is alone …."

The chemical origins of life

Monod's book was written at an awkward time in the history of origin-of-life research. Visionary precursors like the Soviet-Russian Alexander Oparin, the British geneticist J. B. S. Haldane, and the British physicalchemist John D. Bernal were no longer considered Marxist oddballs; but their theories attracted little interest from biochemists, more concerned with how life functions than with how it began. That was certainly my case. I remember hearing Oparin give a lecture on the topic in 1955 and my reaction was that trying to elucidate the origin of something that we hardly understood was futile. Even the startling results achieved by Stanley Miller [7] and those who joined with him in developing what has come to be known as "prebiotic" or "abiotic" chemistry had not yet greatly stirred the biochemical community at the time Monod wrote his book. The few biochemists who had given the question some thought tended to see life as an obligatory manifestation of matter, the physical-chemical conditions that surrounded its birth being what they were.

Witness the following statement, made in 1963 by George Wald, remembered for describing the chemistry of vision: "Life … is probably a universal phenomenon bound to occur wherever in the universe conditions permit and sufficient time has elapsed" [8]. Albert Lehninger, one of the leaders in the biochemistry of his time and the author of a highly successful textbook, wrote in 1970: "[The development of life] is the result of a long chain of single events, so that each stage in their evolution developed from the preceding one by only a very small change. Each single step in the evolution of the first cells must have had a reasonably high probability of happening in terms of the laws of physics and chemistry" [9].

One year later, Manfred Eigen, a world-known expert on the kinetics of ultra-fast chemical reactions who later pioneered the study of the early events in the appearance of RNA, went even further, writing: "The evolution of life, if it is based on a derivable physical principle, must be considered an *inevitable* process despite its indeterminate course … it is not only inevitable in principle but also sufficiently probable in a realistic span of time. It requires appropriate environmental conditions (which are not fulfilled everywhere) and their maintenance. These conditions have existed on earth and must still exist on many planets in the universe" [10].

Implicit in these statements are the two arguments that I have myself put forward in support of life as a "cosmic imperative" [4]: First, being essentially chemical in nature, the processes that gave rise to life were ruled by deterministic laws that made them obligatory under the conditions under which they occurred. Second, the fact that a very large number of steps was involved imposes the view that each step must, as Lehninger puts it, "have had a reasonably high probability of happening in terms of the laws of physics and chemistry". Make even a few steps highly improbable, and the probability of reaching the end, which is the product of the individual probabilities, approaches zero.

Monod thus disagreed with some of his eminent contemporaries. One issue remains, however, that could reconcile the two views. All those who take life to be obligatory are careful to specify that this is so "under the conditions that prevailed". It could still be that those conditions were themselves highly improbable, so that the universe indeed was "not pregnant with life", as Monod contended. Only Eigen ventured to state, but on the strength of no objective argument, that the necessary conditions "must still exist on many planets in the universe". Several findings relevant to this question have been made since Monod's time.

One important piece of information, which was unavailable to Monod, is that a number of organic substances, including amino acids and other chemical building blocks of life, arise spontaneously throughout the universe [11, 12]. This astonishing fact was first revealed by the spectral analysis of the faint microwave radiation that comes to us from outer space. It was further substantiated by chemical analyses performed on comets by spacecraft-borne instruments and, especially, on meteorites that have fallen on Earth. This astonishing cosmic chemistry is now beginning to be investigated in experiments that attempt to reproduce the physical conditions prevailing in outer space [13–16]. It thus appears that the chemical seeds of life are ubiquitously present in the cosmos, ready, so to speak, to give rise to living beings wherever conditions allow. The chemistry that the founders of chemistry called "organic" because they believed it to be an exclusive prerogative of living organisms turns out to be the most banal and abundant chemistry in the universe. It is simply the natural chemistry of carbon, which happens to be particularly rich because of the unique associative properties of the carbon atom. No mystery there, but it certainly came as a surprise.

These findings argue in favor of a universe "pregnant with life" but they say nothing about the chances of the pregnancy's successfully coming to term. It all hinges on what is implied by the phrase "wherever conditions allow". Unfortunately, the conditions needed for the chemical seeds of life to "germinate" are not known and will remain unknown as long as the reactions they favored are not identified and reproduced in the laboratory. The key issue lies in a single word: RNA.

The RNA watershed

It is now common knowledge that DNA (deoxyribonucleic acid) serves as the universal depository of biological information throughout the living world. What may be less well known is that DNA is, by itself, an essentially inert substance. It is no more than a set of coded instructions, which are copied (replication) whenever a cell about to divide makes duplicates of the instructions, one for each daughter cell. When it comes to implementing the instructions, DNA can do nothing by itself. It must act by way of another kind of nucleic acid, RNA (ribonucleic acid), which is closely similar to it chemically and derives its information from it by a replication-like mechanism called transcription. A few of the RNA molecules generated in this fashion are actively involved in the execution of the DNA instructions, as catalysts (ribozymes) or regulators. Most RNA transcripts serve as mere go-betweens, or messengers. They provide the information for the assembly of proteins, which are the main agents that carry out the instructions, either as catalysts (enzymes) or as structural or regulatory components. This step is called translation because it implies the passage from one language (nucleic acids) to another (proteins).

A fact, of immense significance with respect to the origin of life, is that RNA molecules may occasionally serve, like DNA and in much the same way, as replicable depository of biological information. This does not happen in living cells, which invariably have a DNA genome; but it is the case for certain viruses, such as the agents of polio or measles, which have an RNA genome. This fact has suggested the generally accepted hypothesis that RNA preceded DNA in the origin of life and, for a while, carried out the functions of both, acting simultaneously as bearer of replicable information and as vehicle of its expression until DNA came on the scene and took over the first function.

It is generally believed, in addition, that the first RNA molecules also served to carry out the instructions they were bearing, as occurs with today's ribozymes, and that proteins came later. The reason supporting this surmise is that the protein-synthesizing machinery includes several essential RNA parts – transfer RNAs, messenger RNAs, and catalytic ribosomal RNAs – and most likely consisted originally of RNA molecules. For obvious reasons, the protein components of the machinery must have come later, after the machinery had started functioning. These considerations have led the American molecular biologist Walter Gilbert, of DNA-sequencing fame, to formulate, in 1986, his celebrated model of an "RNA world", a hypothetical stage in the development of life in which DNA and proteins were still both absent and their functions were performed by RNA molecules [17]. Enthusiastically, sometimes uncritically hailed by the scientific community, the RNA-world model has had a tremendous influence on the thinking and research of many investigators, leading to a number of valuable discoveries and, especially, technological achievements. Although the model is open to some dissent in its literal formulation, the underlying contention that RNA preceded protein, as well as DNA, in the development of life is viewed by most investigators as highly likely. The appearance of the first RNA molecules thus represents a truly central problem posed by the origin of life.

This problem has, for more than thirty years, engaged the efforts of many outstanding chemists. Much has been found; but the problem continues to challenge the ingenuity of the investigators, to the extent that some have come to suspect that RNA may be too complex a substance to have arisen as the first information-bearing molecule and that it may have been preceded by a simpler organic compound [18] or, even, by clay crystals [19]. No vestige of such precursor molecules has, however, been detected so far in present-day organisms.

As long as the prebiotic synthesis of RNA remains unelucidated, the vexing "pregnancy" question will stay open, leaving the field free for even the wildest of speculations. It will be permissible, for example, to assume, as has occasionally been done, that the first RNA molecules arose through some extremely unlikely combination of circumstances, in line with Monod's contention, and were subsequently perpetuated thanks to their capacity for "self-replication". Alternatively and more radically, the natural assembly of RNA molecules could be viewed as spontaneously impossible and as having required the intervention of some supernatural, extraneous agency, as is claimed by creationists and, in a more subtle way, by the upholders of "intelligent design".

There are problems with the fantastic-luck/self-replication theory. In addition to the extreme unlikelihood of even a single RNA molecule's coming together by accident, the notion of self-replication is itself flawed. RNA molecules or, for that matter, DNA molecules do not replicate themselves; they merely serve as models for a complex chemical machinery that carries out the actual process of assembly. The molecules no more replicate themselves than do the texts introduced into a copying machine. Thus the hypothesized stroke of luck is even more improbable than first appears. Not only must it have given rise to an RNA molecule, but this molecule must, in addition, have been able to catalyze the synthesis of molecules of its own kind, a phenomenon that has never been observed in nature or, even, in the most ingenious laboratory condition. We are dangerously near the situation, postulated by the defenders of creationism or intelligent design, in which natural processes cannot account by themselves for the observed phenomena and the intervention of "something else" must be invoked.

In the opinion of most scientists, there is as yet no compelling need for such an attitude; it has been held on countless occasions in the past, when vitalism dominated much of biological thought, only to be demonstrated time and again as unnecessary by new discoveries. The only scientifically valid hypothesis is to assume that natural phenomena have natural explanations, which can be elucidated by research. Note that much of the research on prebiotic RNA synthesis has so far been carried out with the tools and approaches of organic chemistry. Perhaps a greater input from biochemistry may prove fruitful. It is particularly remarkable in this respect, and possibly revealing of some deep historical link, that the molecules that serve for the synthesis of RNA today – known in biochemical jargon under the acronyms ATP, GTP, CTP, and UTP – also play a central role in the biological transfer of energy. Perhaps, the key to the advent of RNA lies in the chemical roots of bioenergetics [6].

Also possibly relevant to the design of experiments are recent indications that life may have arisen in a volcanic environment, similar perhaps to present-day deep-sea hydrothermal vents. A Japanese group led by Koishiro Matsuno has, in recent years, obtained a number of interesting results with a hot-cold reactor designed to simulate the conditions in such a vent [20–24].

Another important new development not known to Monod is the active search for extrasolar planets. This has become a major quest for astronomers, with more than 150 planets already identified around nearby stars, and new ones regularly being added to the list. So far, technical limitations have allowed only large, Jupiter-like planets orbiting close to their sun to be recognized. But progress is constantly being made in this field, allowing the hope that the detection of Earth-like planets will soon become possible.

In the meantime, most experts in the field tend to be sanguine in their expectations. It is widely believed that, as surmised by Eigen, the conditions that gave rise to life "exist on many planets in the universe" and, hence, that life, viewed as an obligatory outcome of those conditions, is itself widespread in the universe. In the eyes of many scientists, this possibility is considered sufficiently likely to justify major efforts toward the detection of extraterrestrial life.

The dominant opinion among scientists today is that, contrary to Monod's assertion, the universe was and presumably still is "pregnant with life." There are a few dissenters. A prominent defender of the uniqueness of life is the British paleontologist Simon Conway Morris, who, in a recent book, has advocated the philosophically and theologically loaded view that life is probably unique in the universe but, once established, was bound to give rise to human beings [25].

The onset of selection

Natural selection, as first divined by Charles Darwin and his less known but equally perceptive fellow Britisher, Alfred Russell Wallace, is an obligatory consequence of replication, that is, the ability of molecules to induce the synthesis of copies of themselves (actually complementary versions, which, by the same mechanism, produce copies of the originals). Darwin and Wallace knew nothing of DNA, of course, or even of genes, but they knew of heredity, thanks to the successful efforts of animal and plant breeders. Today we know that it is because they are the owners of inherited, replicable DNA molecules that children resemble their parents, mice beget mice, acorns develop into oak trees, and so on. Replication, when perfect, endlessly creates identical copies, thereby ensuring informational continuity, the basis of heredity. Nothing ever being perfect, however, replication inevitably generates some imperfect copies, which, becoming themselves subject to error-free replication, start lineages that perpetuate the modified messages. Thus arises variation, itself the source of competition among variants for available resources, with as outcome the emergence of those best fit to survive and, especially, reproduce under the prevailing conditions, in other words natural selection.

By necessity, this process must have started to function at the molecular level from the moment the first replicable molecules, presumably of RNA, appeared. As soon as replication of these molecules began, variants were generated by imperfect replication, leading to the natural selection, among the variants, of those RNA molecules that were most able to resist damage and, especially, to serve as models for their own replication, under the prevailing conditions. First reproduced in the test tube in the 1960 s by the American molecular biologist Sol Spiegelman [26], this phenomenon has since been exploited under a wide variety of constraints, cleverly contrived to favor the selection of RNA (or DNA) molecules endowed with defined properties, a specific catalytic activity, for example. It is widely believed that, in the origin of life, the first functionally active RNA molecules, in particular those involved in the early development of protein synthesis, emerged through such a mechanism.

Molecular selection, though crucial at the start, was confined to properties that affected the stability and replicability of the RNA molecules involved. Soon, however, selection must have become indirect and no longer based on the intrinsic qualities of the RNA molecules themselves, but on their usefulness to some larger entity of which they were part. In order to benefit from such usefulness, the entities concerned must have been capable of growth, multiplication, and participation in Darwinian competition. Most likely, they were some kind of primitive "protocells", endowed each with their own set of replicating – and mutating – RNA molecules. Selective advantages would have been provided by those mutant RNA molecules that happened to favor the growth and multiplication of their protocellular owners. This could have been due at first to some functional property of the RNA molecules themselves, such as a new or improved catalytic activity. Once protein synthesis had been initiated, the main mechanism would have depended on the usefulness of the protein produced by translation of the mutant RNA. The first protein enzymes presumably arose in this manner. These facts imply that cellularization must have occurred very early in the development of life and that the protocells of that primitive stage must already have been sufficiently individualized to be subject to selection [27].

Once selection was launched, its influence was added to that of deterministic chemistry, which, however, remained at the core of events, just as hardware is the indispensable support of software. This point is sometimes neglected in discussions of biological information. In living organisms, chemistry continues until this day to provide the material support of information transfers, which invariably rely on the biosynthesis of some molecule, whether of DNA, RNA, or protein. Chemistry likewise continues to underlie the processes dictated by the information. Starting with the first appearance of RNA, which signaled the end of the chemistry-alone era and the onset of selection, the development and evolution of life have been entirely ruled by the continual interplay between these two forces – deterministic chemistry and selection, the hardware and the software – with chemistry defining the setting within which selection operates.

Contingency

Natural selection depends on the passive screening of variants arising by genetic modifications. A cardinal feature of this process is the strictly accidental, nonintentional nature of the modifications provided for selection to act on. This feature, already surmised by Darwin, though without proof, has been incontrovertibly borne out by all the findings of modern molecular biology. It is a cornerstone of Monod's thesis.

Except for the few proponents of intelligent design, all knowledgeable scientists agree on the accidental character of the mutations subjected to natural selection. Many evolutionists, perhaps a majority, go further and take as a corollary of this fact that evolution followed an unpredictable, nonreproducible course. In particular, it is widely believed, in agreement with Monod's second pronouncement – "the biosphere was not pregnant with man" – that the probability of evolution's giving rise to human beings was extremely low at the start, rendering repetition of the event close to impossible.

George Gaylord Simpson, one of the founders of American paleontology, wrote in 1963: "The assumption, so freely made by astronomers, physicists, and some biochemists, that once life gets started anywhere, humanoids will eventually and inevitably appear is plainly false" [28].

Ernst Mayr, the widely respected dean of American evolutionism, who died in 2004, aged 100, echoed this thought in 1988, writing: "An evolutionist is impressed by the incredible improbability of intelligent life ever to have evolved" [29].

The same notion was expressed by the American paleontologist and gifted popular writer Stephen Jay Gould, who wrote in 1989: "Wind back the tape of life to the early days … let it play again from an identical starting point, and the chance becomes vanishingly small that anything like human intelligence would grace the replay … Biology's most profound insight into human nature, status, and potential lies in the simple phrase, the embodiment of contingency" [30].

The authority and persuasiveness of these eminent personalities have proved so powerful that their opinions have gained the status of established truths. Today, the contingency notion dominates biological thought; it is widely taken by practitioners of other scientific disciplines (and by much of the general public) as the indisputable message of modern science, to be accepted however disturbing it may be. This is so despite the fact that the contingency notion is subjective. Chance is involved, the reasoning behind the notion seems to be, therefore events cannot be repeatable. But this is not necessarily so. Chance does not exclude inevitability.

Natural selection can act only on what is offered to it. A variant better adapted to the surrounding conditions could exist. If chance does not provide it, there is no possibility for it to be selected. What thus seems to be implicit in the contingency doctrine is the assumption that chance at any time only offers a small sampling of the possible variants; a different sampling, leading to the selection of a different variant, would obtain if the same situation were repeated. "Replay the tape", and another set of chance events will unfold a different story. This inference is intuitively appealing but logically flawed; it excludes without proof a possibility that may seem highly improbable to anybody acquainted with the complexity of genomes but should not be ruled out *a priori*, namely that evolving systems could have had the opportunity to explore all or most of the avenues open to them, so that they could have arrived, by selection, at reproducible, optimal or near-optimal outcomes. A key lesson of recent research is that such a phenomenon of optimizing selection may not be as uncommon as one might be inclined to believe.

Optimizing selection

Toss a coin once, and the chance of its falling on a given face is 50%. But toss the coin ten times, and, as a simple calculation shows [6], the chance that it will fall at least once on each face becomes 99.9%. The same calculation reveals that if you bet on a die, or play roulette, your number is guaranteed a 99.9% probability of coming out if the die is rolled some 40 times, or the roulette wheel spun about 250 times. Even a seven-digit lottery ticket has a 99.9% chance of winning if 69 million drawings are held. What these examples illustrate is that the likelihood that a chance event will happen depends on the number of opportunities chance is allowed to make it happen, relative to the event's probability. As a rule of thumb, an event is almost bound to occur (99.9% probability) if it benefits from a number of opportunities roughly equal to seven times the reciprocal of its probability (a little more for the coin).

Games of chance, of course, never offer such odds, which would be ruinous for the organizers. But the evolutionary game is different. It is often played with huge numbers of individuals, following each other, generation after generation, over very long times. With so many opportunities available for mutations to happen, the occurrence of a given, critical mutation could conceivably not be a long shot any more. In the case of point mutations (replacements of one base by another in a DNA message) due to replication errors, the answer to that question is readily calculated [6]. The result is no less than flabbergasting. In spite of the fantastically low error rate – one wrongly inserted base in about one billion, the equivalent of a single mistake in copying by hand the Concise Oxford Dictionary some fifty times! – the time needed for a given point mutation to occur with a 99.9% probability at a specific site of a genome is amazingly short: about 30 minutes in a bacterial culture containing 100 milligrams of cells; a mere two hours in the human bone marrow in the course of red-blood-cell renewal. But for a remarkable set of DNA repair mechanisms, none of us would have reached adulthood!

Admittedly, point mutations are not very important in evolution, which depends most frequently on more complex genetic changes – deletions, insertions, inversions, recombinations, transpositions, and other multi-base rearrangements – whose probability is impossible to predict. The fact remains that, even if very large, the number of significant mutations a given genome may undergo is finite and, perhaps, not always as large as one might be tempted to imagine, given the many inner and outer constraints that may restrict genetic modifications. The possibility that evolution may, in a number of cases, have had the opportunity to explore the range of possible genetic changes extensively, if not exhaustively, is realistic.

A possible instance of optimizing selection is the genetic code, the molecular dictionary according to which, in translation, the sequences of bases in messenger RNA molecules dictate the sequences of amino acids in the proteins that are being newly assembled. A property of the code that has long attracted attention is that it seems to be constructed in such a way that the harmful consequences of point mutations in protein-coding genes are minimized. If one base is replaced by another in a message, the code is such that, in many cases, the affected amino acid is either unchanged – the code contains many synonyms – or replaced by an amino acid with similar physical properties so that the modified protein remains functional. According to a recent modelling study using a physical property known as hydrophobicity as a measure of kinship among amino acids [31], the code appears to be a million times better than average and close to optimal in this respect. This feature could conceivably be the fortuitous – and fortunate – outcome of the manner in which protein synthesis originally developed; it is so outstanding, however, that one is inclined to suspect the intervention of some selective optimization process. This would imply a remarkable phenomenon in which cell populations using different codes – a challenging notion in itself – competed with each other on the strength of their ability to withstand the harmful effects of point mutations. Such a phenomenon could only have happened at a very early stage in the development of life, when genes, probably still of RNA, were both very short and very few in number.

Optimizing selection may have played a particularly important role in the appearance of proteins, a phenomenon often brandished by intelligent-design advocates in support of their doctrine. The problem, known as the sequence-space paradox, is familiar.

With twenty distinct kinds of amino acids as building blocks, the number of different possible protein molecules of 300 amino acids – roughly the average size of present-day proteins – is 20^{300}, or 10^{390}, one followed by 390 zeros. This number defies imagination. Next to it, the total number of protein molecules that have existed since life began vanishes into nothingness. Hence, so the argument goes, emerging life could not possibly have reached by chance the infinitesimally tiny speck it occupies in the immeasurably immense space of all possible sequences; it must have been "guided".

The argument would be compelling, except that life cannot possibly have developed its proteins full-blown. For reasons convincingly established by a number of theoretical and empirical investigations [32, 33], life must have started with very short protein molecules – actually very short molecules of RNA coding for the proteins – which subsequently joined by modular combination into chains of increasing length, with as main size-limiting factor the fidelity of replication. This mechanism allows for a stepwise process in which, at each stage, optimizing selection reduced the number of participating molecules to a value compatible with exhaustive or near-exhaustive exploration of all their combinations [6]. Protein development could thus have followed a largely obligatory course under the conditions that prevailed. Given the same conditions, the development of a roughly similar set of protein molecules does not appear impossible. Selection, rather than an unseen hand, would thus have guided life toward the "infinitesimally tiny speck it occupies in the immeasurably immense space of all possible sequences".

How about later evolution? Surely, there can be no better illustration of contingency than the amazing diversity of living forms that fill every nook and cranny of our planet. True enough, except that the diversity is a product most often of environmental vagaries, rather than of genetic fortuitousness. Each form of life appears snugly ensconced within its niche, clearly equipped to flourish in the local milieu, whatever it may be. Some (especially microbes) even manage to thrive in the most inhospitable environments – naked rocks, boiling water, drying brine, polar ice, mercury-loaded wastes, to mention only a few – in which any other organism would immediately succumb. To reach this state of adaptiveness by natural selection, the organisms must have gone through a long succession of improbable genetic changes that could not possibly have been achieved simply by isolated chance events. The kind of near-exhaustive exploration of the mutational field leading to optimizing selection almost mandatorily must have been involved.

Most impressive in this respect are the instances of mimicry, this remarkable phenomenon whereby certain organisms have become almost indistinguishable from their environment, an obviously valuable way of escaping predators. Just think of the pathway an insect had to follow to closely resemble the branch or leaf on which it sits, or of the evolutionary history that caused a fish to flatten, cover its back with scales that imitate the sandy bottom of the sea, and undergo all the anatomical and functional changes that allow it to swim on its belly. Unless you credit an unseen hand, only a long succession of optimizing selective steps can account for such remarkable happenings.

Totally unrelated organisms, when faced with the same environmental challenges, often have independently developed the same set of specializations. The extraordinary frequency of this phenomenon, which is known as evolutionary convergence, has recently been emphasized, with a wealth of illustrative examples, by two eminent British experts in the field.

Here, for example, is what the paleontologist Simon Conway Morris [25], already quoted above, wrote in 2003: "Convergence is ubiquitous and the constraints of life make the emergence of the various biological properties very probable, if not inevitable."

This view is echoed by the evolutionist and best-selling author Richard Dawkins [34] in his latest book, published in 2005: "I am impressed by how similarly evolution turns out when it is allowed to run twice." Although defending almost diametrically opposed philosophical positions – Conway Morris is a practicing Christian, Dawkins a militant atheist – the two scientists thus agree in pointing out how often, when nature has had the opportunity to actually "rerun the tape", the same story has unfolded, in direct opposition to Gould's affirmation. Conway Morris reinforces his view by underlining the important, additional, channelling effect of inner constraints, imposed by such factors as genome structure or body plan.

Even today, optimizing selection continues to take place all around us, in response to human-caused changes of the environment. In England, the ratio of black to white representatives of a certain variety of moths increased progressively after the industrial revolution filled the air with soot; it has been falling back since clean-air legislation was enacted after the last world war. Presumably, in both cases, the animals that blended with their background were better protected against predators.

In the last fifty years, pathogenic bacteria have become resistant to penicillin and other antibiotics; the plasmodial agents of malaria to chloroquine; mosquitoes to DDT; plants to herbicides; the examples are innumerable. Cancer cells even can become resistant to chemotherapeutic agents in a matter of months. Wherever humans have modified the environment, local life has responded adaptively. Often at a cost, to be sure – the damage we have caused is for everyone to see – but in a manner sufficiently impressive to illustrate the enormous power of optimizing selection.

The advent of humankind

The development of the human species represents the most astonishing and dramatic episode in the history of life on our planet. Consider the development of the animal brain in the course of evolution. Starting from zero, with the first sponges, some 600 million years ago, the size of the animal brain has increased slowly, at an average rate of some 0.6 mm^3 per millenium, to reach a volume of about 350 cm^3 in present-day chimpanzees, which, next to dolphins, have the largest brain, relative to body size, in the animal kingdom. This development was 99 % completed when, some 7 to 6 million years ago, a line detached from the chimpanzee line, tracing a slow, but exponentially increasing progression to reach, between two and one million years ago, the staggering rate of some 600 mm^3 per millenium – one thousand times the average rate of brain expansion in the course of animal evolution! – before slowing down and stabilizing, in *Homo sapiens*, at a volume of about 1350 cm^3, an almost four-fold increase over the chimpanzee (see references [35] for data and [6] for graphic representation).

The significance of this astonishing observation with respect to the problem under discussion – contingency versus inevitability – is difficult to fathom. There can be little doubt that the most striking feature of brain expansion, namely its exponential course, reveals the occurrence of an autocatalytic process in which each change increased the probability of the subsequent change. Whatever mechanism was operating, it clearly did not depend on a succession of improbable chance events. The short time spans and small number of individuals involved make such an explanation untenable. Once initiated, brain expansion seems to have been largely self-propelling. In fact, it could conceivably have continued further, leading to even bigger brains than ours, had the phenomenon not been braked by some opposing influence, making the shape of the curve sigmoid. Perhaps, the female birth canal did not evolve to accommodate bigger heads, whereas the fetal brain failed to enhance its capacity to pursue its development outside the womb (neoteny).

Two additional features attract attention. First, the autocatalytic phenomenon has apparently been initiated only once. At least, no evidence that more than a single line leading to brain expansion may have detached from the chimpanzee line – or from any other line – has been uncovered so far; which fact, incidentally, is not very significant, in view of the sparseness of the fossil record. Second, autocatalytic brain expansion was apparently arrested at several stages in some individuals, generating side branches that subsisted a long time, sometimes more than one million years, without increase in brain size. Most known hominoids, from Lucy to the different kinds of *Homo* whose remains have been unearthed by paleoanthropologists in various parts of the world, seem to have detached from the main line in this way. Thus, there may be some element of contingency in our past history, though not enough to obliterate the striking manner in which, once committed, the drive toward bigger brains proceeded at an ever increasing pace until it ran into an insurmountable obstacle.

Hominization is a very recent event, too close to us for its significance to be fully appreciated. A few million years from now, our descendants, if there are any left, may see it from a different perspective.

The environment in charge?

Less chance, more necessity. Such, in a nutshell, is the message emerging so far from the preceding overview. Squeezed between deterministic chemistry and optimizing selection, contingency has enjoyed less leeway than was believed by Monod. This conclusion would be overriding but for one major caveat, defined by the clause “given the prevailing conditions”. If the history of life has been largely molded by environmental conditions, these open the door wide for contingency to step in and play an infinity of nonreproducible variations. The tape will be repeated only if the innumerable factors that have affected the physical-chemical and, later, biological history of our planet are themselves repeated, obviously an impossibility, even at a cosmic level. This point represents a pivotal argument in favor of contingency.

The point is undoubtedly true for many details of the evolutionary tapestry. Without deserts, there would be no cactuses; without branches or green leaves, no insects imitating their appearance; without sand, no grey soles flattened against the sea bottom; and so forth. Even major happenings may have depended on chance environmental manifestations. Perhaps, a tropical lake had to go through exactly the right kind of alternating periods of wetness and dryness for a fish to venture out of water and return to it only to lay its eggs. Other often quoted examples are the fall of a large asteroid on the peninsula of Yucatan, 65 million years ago, which may have caused the extinction of the dinosaurs and allowed the rise of the mammals; or the geological split that carved the Great Rift Valley from North to South through the African continent and, according to a theory favored by a number of investigators, may thereby have cut off our ancestors from the forest and isolated them in the savannah, where conditions favored hominization.

All true. But were the events themselves critical, or merely their timing? If not this particular lake, another might, one million years later, have provided the conditions for a lungfish to complete the round of optimized changes that turned it into an amphibian. Perhaps the dinosaurs were fated to disappear in any case, together with the conditions that made such unwieldy creatures possible, and the asteroid only precipitated an event that was bound to take place. Similarly, some phenomenon other than the opening of the Great Rift Valley could have initiated the autocatalytic chain of events that produced the human brain, or would have done do so some time in the future.

Such conjectures must obviously remain unsettled. Coming back to the realm of the objective, one cannot fail to be impressed with the extraordinary versatility of life, its ability to invade almost any kind of environment and to adapt to an immense variety of conditions, its relentless drive toward complexity wherever and whenever conditions allow. Often attributed in the past to a special force, these qualities are now explained by the intrinsic properties of the life process and the combined power of chemical determinism and optimizing selection. They allow the hypothesis that a large number of environmental conditions could have produced a similar outcome, if not in detail, at least in its broad lines.

Conclusion

Much has happened since the appearance of *"Chance and Necessity"*, 35 years ago. On the whole, present knowledge argues against Monod's scientific position. To the objective, dispassionate observer, the universe does appear "pregnant with life", and the biosphere "pregnant with man". The universe to which we belong is such that life was virtually bound to arise and to evolve in the direction of increasing complexity, up to the appearance of human-like, conscious, intelligent beings. What significance is to be attached to this fact is the object of a wide array of speculations, ranging all the way from the view that our universe is only a meaningless part of an infinite "multiverse" to the notion that it is specially designed to give rise to the human species. As I have explained elsewhere [4, 5], my own position on this question is that, whatever cosmic view of our universe may eventually turn out to be correct, the very existence of such remarkable phenomena as life and mind remains a meaningful revelation of what I have called "Ultimate Reality". What now of Monod's philosophy, his conclusion that "man knows at last that he is alone in the universe's unfeeling immensity"? This statement is consistent with its scientific context, but goes beyond what may be scientifically affirmed, considering our physical inability to explore most of the universe's immensity for signs of life, whether intelligent or not. What the statement betrays is Jacques Monod's affinity for the philosophy of the absurd of the existentialists who strongly influenced French thinking in his time, especially Albert Camus, who shares with the Greek philosopher Democrites the distinction of being cited in the epigraph of Monod's book.

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