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THE QUALITY OF LIFE

"The man behind the microscope
Has this advice for you:
Never ask what something Is
Just ask, what does it Do?"
Hilaire Belloc

We picked our way gingerly down the boulder-strewn canyon, keeping an eye out for cactus spines and rattlesnakes. One walks warily in the Big Bend, and so it was some time before we spotted our first "living rock." The nickname is apt: flat, grey and crusty, half-covered with sand, they blend into their stony environment. But once noticed, their nature is not in doubt; they are unmistakably living plants masquerading as rocks. It is almost always so: though the definition of life is elusive, we seldom have difficulty distinguishing living creatures from lifeless objects by their special qualities.

As a subject for serious inquiry, the category "life" has all but vanished from the scientific literature; it is the particulars of life, not its nature, that fill the numberless pages of scientific journals. But any attempt to extract general principles from that tide of information must begin, if not with a definition of life, then at least with the criteria by which we recognize the phenomenon. With the advent of space travel, the question has ceased to be purely an academic one. When explorers from

Starship Enterprise boldly land upon some planet orbiting Betelgeuze, will they recognize life if they encounter it in an unfamiliar guise? Probably yes, for wherever the restless search for novelty takes us, we expect life to be a quality of the peculiar class of objects called "organisms." They are the devil to define, but it is not difficult to set forth general criteria that map out the process of living as we see it all about us, and that should apply as well to life as we can imagine it elsewhere in the universe. Here are the main ones.

(i) *The Flux of Matter and Energy.* Living organisms are the seat of incessant chemical activity. They absorb nutrients, produce biomass and eliminate waste products plus heat; most constituents undergo breakdown and resynthesis during the lifetime of an individual organism. Metabolism, a term derived from the Greek word for change, designates the totality of all the chemical transformations carried out by an organism. It is so practical a hallmark of life that evidence of metabolism is what the space probe sent to Mars in 1976 searched for, without success.

Much of this chemical business revolves around energy. The characteristic activities of living things—their growth, movements, the very maintenance of their structure and integrity—depend upon input of energy from the environment. That is one of the chief functions of the metabolic web, for chemical substances serve as carriers of energy as well as matter. Like a flame or an eddy, an organism is not an object so much as a process, sustained by the continuous passage through it of both matter and energy.

(ii) *Self-Reproduction.* Living things are generated autonomously, not by external forces, and what they generate is their own kind. Like begets like. Biological heredity is quite unlike the point-by-point transfer carried out by a copying machine. Instead, characteristics are transmitted from parent to offspring by a program or recipe that embodies instructions for producing the next generation. The process is extremely accurate, yet subject to occasional errors that account for the variation observed in every natural population.

(iii) *Organization.* Whenever we speak of organisms we acknowledge the fundamental connection between the living state and a special kind of order. Even the simplest unicellular creatures display levels of regularity and complexity that exceed by orders of magnitude anything found in the mineral realm. A bacterial cell consists of more than three hundred million molecules (not counting water), several thousand different kinds of molecules, and requires some 2,000 genes for its specification. There is nothing random about this assemblage, which reproduces itself with constant composition and form generation after generation. A cell constitutes a unitary whole, a unit of life, in another and deeper sense: like the legs and leaves of higher organisms, its molecular constituents have functions. Whether they function individually, as most enzymes do, or as components of a larger subassembly such as a ribosome, molecules are parts of an integrated system, and in that capacity can be said to serve the activities of the cell as a whole. As with any hierarchical system, each constituent is at once an entity in itself and a part of the larger design; to appreciate its nature, one must examine it from both perspectives. Organization, John von Neumann once said, has purpose; order does not (1). Living things clearly have at least one purpose, to perpetuate their own kind. Therefore, organization is the word that sums up the essence of biological order.

(iv) *Adaptation*. Any organism that is made up of distinct parts, and that reproduces by heredity with variation, must evolve parts that promote the organism's survival and multiplication. Their structure and function will alter over time, tracking changes in both the internal and the external environment. The reason is that an individual's reproductive success must be affected by environmental factors, and natural selection will favor the better adapted over the less well adapted. Adaptive evolution is seen throughout the living world, not only at the level of legs and leaves but also at that of enzyme proteins and cellular organelles. That adaptation stems from the interplay of random variation and natural selection was, of course, Darwin's central contention. By recognizing adaptation as a criterion of life we do justice to life's intrinsic diversity. And we assert that the chemical and physical features of organisms find their meaning, first in the context of organization and then of history. Physiology and evolution are both central to the grammar of life.

With the help of these criteria we can quickly dispose of some doubtful cases. Is a flame alive? No. True, one candle lights another, but the size and shape of the flame are wholly determined by the supply of fuel and air, not by whether it was started with another candle or with a match. Fire propagates, but not by heredity. Viruses make a more interesting issue. They do propagate their kind by means of heredity, and they evolve and adapt all too quickly to changing circumstances; those who regard reproduction and adaptation as the crucial features of life will consider viruses to be alive. But viruses are structurally far simpler than cells, even than many organelles, they lack metabolism of any kind and are obligatory intracellular parasites. Their capacities are so much more limited than those of any cell that I, for one, would disqualify viruses. Much the same argument applies to mitochondria, and intracellular organelles in general: since the genes required for their production are located chiefly in the cell nucleus, organelles do not reproduce autonomously and must therefore be excluded from the ranks of the living. And what about freeze-dried bacteria? They were alive once, and provided they are "viable," may be alive again, but they are not alive at present. Such borderline cases are instructive rather than alarming. If life originated from the mineral realm via natural processes, we should expect the line that divides the quick from the dead to be a little fuzzy. Sharp categories are generally something that we put into nature, not something we find there.

It was the ambiguous status of viruses, whose crystallization had just been accomplished, that led N. W. Pirie to conclude that the terms "life" and "living" are inherently meaningless. That has not deterred his successors from proposing definitions, the best of which slip a kernel of truth into the nutshell of epigram (2). To J. Perret, "Life is a [property of] potentially self-replicating open systems of interlinked organic reactions, catalyzed stepwise and almost isothermally by complex and specific organic catalysts which are themselves produced by the system." Gail Fleischaker and Lynn Margulis, following the original proposal of Francisco Varela, make the point more succinctly and with sharper emphasis on the deep organizational features, when they define living organisms as "autopoietic systems," i.e., self-generating. Freeman Dyson puts himself in the same camp with the assertion that "life resides in organization, not in substance." Others are content with contemporary fashion; for Dulbecco, "Life is the actuation of the instructions encoded in the genes." Maynard Smith, however, points in quite another direction when he suggests that life might simply be defined "by the possession of those properties which are needed to ensure evolution by natural selection. That is, entities with the properties of multiplication, variation and heredity are alive, and entities lacking one or more of these properties are not" (2).

I have come to suspect that the definition of life is a mirror in which the various biological specialties chiefly see themselves. Functional biologists—biochemists, molecular biologists and physiologists—tend to look upon organisms as complex, integrated, and self-reproducing systems maintained by the stream of matter and energy. They ask how these systems work, and search for the proximal causes of the phenomena they observe in terms of physical and chemical mechanisms. Evolutionary biologists, by contrast, take a longer view. They ask how these systems came about and how their parts became mutually adapted.

Their hope is to discover ultimate causes, such as selective advantage or historical contingency, that shaped the patterns of form and function which we observe in all organisms. The secret of life is that these are two aspects of a single reality which we must strive to see in the round. No biological phenomenon can be said to be understood until we have found both its functional and its evolutionary explanation—and each of these is sure to be multilayered. To thread the maze of arguments woven about the relationship between living and non-living states of matter we must walk on two legs, one functional and the other evolutionary.

Of all the inanimate objects in the universe, few have so captivated the imagination of biologists as our own machines and automata. Nowadays it is the computer that is held up as the most instructive analog of living organisms, with cellular architecture as hardware and the DNA tape as software. Automata have complexity, functional parts and purposeful behavior just as living organisms do, but since they are man-made they carry no metaphysical baggage. Ever since Descartes there have been mechanistic biologists who see it as their task to "reduce" biology to chemistry and physics, for instance, to demonstrate that all biological phenomena can be completely explained in terms of the motions of their constituent parts and the forces between them. Biochemists and molecular biologists, in particular, commonly believe that such reduction is their objective, though they will not all agree on the meaning of the term. Some are satisfied that reduction has effectively been accomplished, thanks to the near-universal consensus that all that living things do is based on their physical substance, and that no metaphysical agencies or vital forces need be invoked. Many more would agree with Francis Crick (3) that "the ultimate aim of the modern movement in biology is in fact to explain all of biology in terms of physics and chemistry." And a few reductionists go still farther, maintaining that the laws and theories formulated in biology should be rephrased as special cases of those propounded in the physical sciences. That the two latter goals are illusory has been amply documented by George Gaylord Simpson, Michael Polanyi, Ernst Mayr and Alexander Rosenberg (4). Indeed, even a machine is not explained by mechanical principles alone, for its construction is guided by the designer's purposes which constrain the blind operation of physical laws. In the case of living organisms, it is their hierarchical organization and their origin in the interplay of random variation and natural selection that should give pause to any radical reductionist. And it is noteworthy that our unquestioned success in unraveling the molecular mechanics of life have thus far yielded little insight into the genesis of coherent forms and functions on the scale of cells and organisms.

For that reason, a majority of organismic biologists would probably be found aligned with an alternative general position, commonly known as holism (some prefer the more precise but awkward term "organicism"). Adherents hold that living organisms make up a set of unique, hierarchically organized systems each of which functions as a whole. Whenever a system is assembled from its constituent parts, novel properties emerge that could not have been predicted from a knowledge of those parts alone. The airplane wing that we contemplated in Chapter 1 is a case in point, and the argument applies *a fortiori* to any organism. Morphology, behavior and development are examples of such emergent properties that would never be inferred from molecular mechanisms, even if these were known in every particular. It follows that biology is an autonomous science (5), governed by laws and theories that emerge successively at the level of a cell, a frog, a flock of birds and a prairie pond. We can set aside, for the present at least, the question whether biology is autonomous in principle or only in practice, but we must note that holists feel the pinch of a shrinking domain. Time was when heredity and energy conversion were thought to be strictly the prerogative of living systems. Is it not likely that, given a few more decades, development and morphogenesis too will have been successfully reduced to the play of mindless molecules obeying only local rules?

I do not think so, and am often reminded of the arid quarrels over the nature of the Trinity that kept Byzantium in turmoil for centuries. Why should we be compelled to swear fealty to either reductionism or holism? Like John Tyler Bonner (6), "What is utterly baffling to me is why one cannot be a reductionist and a holist at the same time." Reductionism is commonly the best strategy in research, and when successful, supplies satisfying (albeit partial) explanations. Holists remember the inherent complexity of living things, and keep the reductionists honest. I was pleased to see that Hunter (6), re-examining the question whether biology can be reduced to chemistry, likewise takes a conciliatory position. The two extremes are complementary, not antagonistic: those who seek to understand living organisms require both the holist's perspective from the top down and the reductionist's scrutiny from the bottom up. Neither is sufficient by itself.

Many years ago, in a delightful essay celebrating the origins of molecular biology, Gunther Stent (6) spoke of the paradoxical quality of living things, which obey all the laws of physics and chemistry yet are not fully explained in terms of those sciences. Niels Bohr, Max Delbrück and Stent himself hoped to discover new laws of physics, hitherto unknown, that would supply physical and chemical explanations for the functions peculiar to life. No such laws have turned up, but one wonders whether we have been looking in the wrong direction. Biological phenomena of any interest are almost always properties of a system, more or less hierarchically organized into multiple layers. Simplification ("reduction") is commonly useful, even essential, to make a problem tractable, but it carries the risk of changing the question rather than answering it. To my mind, the beginning of wisdom is to recognize that living things are wholly composed of molecules, and everything they do finds a mechanistic explanation in terms of the actions and interactions of their constituent molecules. But their organization into systems of mounting complexity guarantees the emergence of supramolecular structures and activities. The more advanced the level of organization, the less informative is it to seek understanding solely in terms of their molecular constituents. It makes little sense to seek the molecular basis of hibernation because that is inherently the function of an organism (though one may hope to find genes and proteins specifically involved in hibernation). By the same token, the chemistry of leather is of little use in describing a shoe. Common sense suggests that we steer cautiously between molecular machismo and a veiled vitalism, some insights can be usefully expressed in molecular terms, others call for physiological explanations or for ideas appropriate to still higher levels of organization. We should be especially on the lookout for organizational principles that link molecules into cells and organisms, and for the historical forces that shaped the outcome. Common sense concurs with Paul Weiss that, "There is no phenomenon in a living system that is not molecular; but there is none that is wholly molecular either." For all their ubiquity and familiarity, living organisms are truly strange objects.