Are There Recipes for How to Handle Complexity?

Biological Evolution Creates Complex Entities and Knows How to Master Them

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Present day societies are confronted with exceedingly complex problems in economy, in the exploitation of the planet Earth, in the development of sustainable technologies, and in many other areas as well as in everyday life. The causes of complexity are partly inherent in nature and, to a steadily increasing part, anthropogenic. The growing body of empirical experience and the theoretical concepts developed in science and technology provide increasing insights into the phenomena observed in nature and human society, but the problems waiting to be solved are growing at least with the same pace. The origin of most of the new problems is—directly or indirectly—the enormous growth of human population and urban culture in the recent past. In previous times—as archaeologists reconstruct correctly—mankind was also confronted with highly complex environments compared to the state of knowledge in those days. Weather provides an illustrative example.

Until the beginning of modern times, catastrophic weathering, storms, hail, lightning, tornados, hurricanes, floods, and droughts were either seen as punishment measures of outraged deities or they were attributed to the actions of daemons and witches. The Mayas of Chichen Itza saw the causes of weather phenomena in the moods of the rain and lightning god Chaac. In order to please him and to gain his favor, they sacrificed young humans who were thrown into the pond "Cenote sagrada." The detailed knowledge of the motions of celestial bodies and the highly elaborate calendar of the Mayas were completely useless in coping with environmental problems. The expectation that more human sacrifice would result in more rain was in vain. Some archaeologists suggest that the Maya culture of Chichen Itza collapsed around 1000 A.D. partly as a result of a long lasting drought. The physics of the late 17th and the 18th century, in particular, the discovery of various electric phenomena, provided a novel basis for the interpretation of weather. Benjamin Franklin made use of this new knowledge and invented the lightning rod in 1752 by sending a kite with a metal tip up to the clouds during a thunderstorm. It lasted about two centuries, before a comprehensive theory of cloud and thunderstorm development as well as lightning discharge became avail-

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DOI 10.1002/cplx.20243

able. Still the prediction where lightning is going to strike is rather limited, but thunderstorms have lost most of their threat because a successful protection became possible. Similarly, other insight-based protection measures were successful in dealing with nature. Examples are constructions against avalanches, hang slides, and floods.

In 1948, Weaver [1] published an article entitled "Science and Complexity" wherein he distinguishes disorganized and organized complexity. Disorganized complexity is irregular atomic motion called thermal motion. Brownian motion, for example, is the random walk of macroscopic particles that are exposed to irregular collisions by atoms. In their pioneering works on the fundamentals of statistical physics, Ludwig Boltzmann and Josiah Willard Gibbs showed how to deal with disorganized complexity by means of statistical techniques. Although thermal motion is highly irregular, ensembles of atoms in gaseous, liquid, or solid state have precise equilibrium properties, pressure, density, temperature, and others. Thermal motion transports heat and is taking care of heat exchange. In case of temperature differences, it therefore causes equalization of temperature. Under conditions sufficiently far off equilibrium, implying sufficiently large temperature differences, coordination of irregular motion occurs in a way to make heat exchange more effective. Coordinated motion leading to convection and turbulence is organized complexity in the sense of Weaver and covers phenomena on an enormously wide range of spatial dimension from the Raleigh-Bénard phenomenon occurring in layers of liquids heated from below, which shows coordinated motion at centimeter scale, to the Red Spot on Jupiter, which has a diameter as large as that of the Earth. Coordination of motion in the atmospheric air may have catastrophic consequences as it can develop into thunderstorms, tornados, hurricanes, or typhoons. The current state of knowledge in atmospheric physics provides well-developed theories for all these weathering phenomena and allows for predictions of the conditions under which they occur. What cannot be predicted—for principal reasons—are precise timings and locations when and where these events will happen. Local airflows depend on the—commonly very rough—structure of the Earth's surface and tend to become chaotic and turbulent. Chaotic dynamics as we understand well nowadays is highly sensitive to initial conditions.

Emergence of order or the onset of self-organization requires two conditions: (i) A flow of energy and/or matter has to sustain nonequilibrium conditions and (ii) the observed collective phenomena must be the result of some kind of self-enhancement or autocatalysis. Coordination of atomic motion in convection is only one out of numerous examples of self-organization describing spontaneous ordering. Highly instructive examples come from chemistry and biology. In 1952, the famous mathematician and computer scientist Turing [2] made use of a chemical model to predict the spontaneous formation of spatial patterns with the ultimate goal to explain pattern formation, in particular, in biology. Almost simultaneously with Turing's work oscillations and complicated spatiotemporal patterns were observed and reported by Boris Belousov. The reviewer of the paper, unfortunately, was completely lacking fantasy and did not recommend publication. Belousov was offended by the rejection of his paper and left science. Belousov's work on a complex chemical reaction involving—as we now know—more than 20 individual reaction steps was continued later by Anatol Zhabotinskii, and starting in the 1970s, investigations of complex chemical patterns became highly fashionable (for a review on self-organization phenomena in chemistry see [3]). Around 1990, a group of French chemists around Jacques Boissonade and Patrick De Kepper [4] succeeded to produce stationary Turing patterns in a chemical reaction-diffusion system. Self-organization in chemical systems far off equilibrium is well understood by now and the quantitative features of patterns like wavelengths, periods, or curvature of spirals can be computed with high precision. Similarly as in the case of Rayleigh-Bénard convection, precise locations where the waves or stripes appear require information on microscopic nucleation sites like microstructures of walls or dust particles in the solutions and hence remain a probabilistic element.

Pattern formation is a central topic in developmental biology. Biological patterns are most easily recognized when they occur on the leaves of flowers or on the skins or shells of animals. The Turing model has been frequently used to explain these patterns and was very successful: Murray [5] and Meinhardt [6, 7] performed mathematical analysis and extensive computer simulations on reaction-diffusion equations producing such patterns. They were able to reproduce the observed patches, dots, and stripes, and gave straightforward explanations for transitions between them. Every animal breeder is aware of the fact that the appearance of species is highly flexible and can be varied in a wide range. Mimicry [8] is one of nature's success strategies for mastering a complex world: It is cheaper to change appearance than to modify a whole organism. Illustrative examples of such special adaptations of cheating in nature are named after biologists who discovered them. In Bates' mimicry, harmless animals imitate the appearance of dangerous species in order to be mistaken and hence are avoided by predators. Müller's mimicry is found among unpleasant species that imitate each other in order to increase the numbers of individuals for encounters with predators. More encounters imply a

DOI 10.1002/cplx

higher chance that the predator had already experienced the disgust of eating an animal of the entire group of species in the past and therefore stays away from further predation. The biologists Emsley and Mertens discovered the trickiest kind of mimicry. The deadly poisonous coral snake performs mimicry of the moderately poisonous false coral snake. The explanation is based on the observation that predators kill the coral snake but die as a consequence of the snakebite before they can transmit or make use of their negative experience. Accordingly, it is advantageous for the deadly poisonous snake to imitate a less poisonous one.

In contrast to chemical patterns, stripes and dots on the skins or leaves of genetically identical organisms are highly reproducible in fine details. Examples from inbred strains of domestic animals are well known. The difference between chemical and biological patterns is genetic information, which is encoded in digital form in a molecule of deoxyribonucleic acid or DNA representing the genome of the organism. The molecular structure of this molecule—proposed first in 1952 by Jim Watson and Francis Crick and later confirmed by crystal structure determination—suggests already nature's principle of copying or replicating genetic information. In the cell, genetic information is copied prior to cell division. Replication of DNA and cell division require complex machinery consisting of several thousands of protein molecules and other constituents. These machinery drives a metabolism that provides the building blocks of biomolecules as well as the energy required for their synthesis. A genetic program regulates the development of multicellular organisms. The instructions for this program are laid down in encoded form in the DNA molecule: regulatory proteins activate or repress the genes for development. Unfolding of the genotype requires, in addition, proper epigenetic control and a specific environment that is provided directly or indirectly by the parent organisms. The outcome of development is the phenotype of the organism consisting of its appearance and all its—also the nonvisible—properties. The complexity of organisms is enormous and exceeds our imagination. The genetic information of a bacterium like *Escherichia coli* is stored in a DNA molecule with 4 million digits. This number of letters fills about three standard books of 450 pages. The spatial structure of the bacterium resolved by electron microscopy is very rich and revealed a variety of chemical factories in the nanometer range. Compared to a bacterium, the human genome is about 1000 times longer and represents a library of 3000 volumes in the book metaphor. The human body contains about 200 different cell types, and among them, 100 billion (10^{11}) neurons in the brain which are connected by about 7×10^{14} synapses. Nobody doubts that the complexity of organisms has increased tremendously from bacteria to man, but it turns out to be difficult to find a proper indicator for this complexity. Intuitively complexity scales well with genome size in prokaryotes, protists, and invertebrates but stays more or less constant in vertebrates from fish to man. Within multicellular organisms the number of cell types seems to be an appropriate measure for the complexity of organisms. Finally, with birds and mammals, in particular primates and man, a measure of complexity is the relative brain mass. The fact the song birds have a much higher capacity for learning skills from other individuals reflects well their higher relative brain mass. In summary, quantitative measures for complexity in biology can be found, but no single one is appropriate for all forms of life. Part of nature's molecular complexity in multicellular organisms is still weighting to be explored: The ENCODE (ENCylopedia Of DNA Elements) consortium [9] published last year the results of a pilot study on 1% of the human DNA and found that more than 90% of the DNA are transcribed, whereas only about 5% are translated into protein. The functions of the transcripts, which are not translated, are still to be discovered.

Nature's recipe to cope with the enormous complexity is the evolutionary mechanism that was first clearly formulated by Charles Darwin and Alfred Russel Wallace: Evolution giving rise to changes in the appearance of phenotypes and to formation of new species is based on three processes, (i) multiplication, (ii) variation, and (iii) selection. Multiplication is basic to all cells, for higher organisms at least to cells in germ lines. Variation, mutation, or recombination operates on the digitally encoded information, the genotype, whereas only the phenotype is the target of selection. Variations occur uncorrelated with their effects on the selection process. Selection is a straightforward consequence of finite population size. All three conditions are not only met by cellular organisms, but equally well fulfilled by nucleic acid molecules—DNA or RNA—in cell-free experimental assays. Biological evolution, in particular optimization by mutation and selection, can be formulated in the language of chemical reaction kinetics with the advantage of a straightforward interpretation in terms of molecular genetics. The underlying kinetic differential equations can be solved by approaches based on computer calculations [10]. These solutions provide the proper frame for in vitro evolution experiments. Application of nature's recipe to the synthesis of molecules with predefined properties gave birth to the new branch of evolutionary biotechnology [11, 12]. An unexpected and important result comes from the properties of biological macromolecules—proteins and nucleic acids: The mapping from sequences into structures is many to one in the sense that many sequences form the same structure. This property gives rise to neutrality not only in genotype–phenotype mappings but also in selection.

DOI 10.1002/cplx

Neutrality has been anticipated by the population geneticist Kimura [13], who concluded from sequence comparisons of proteins in different organisms that neutral drift is an important factor in evolution of higher organisms.

Complexity reaches a new and more involved dimension in situations where predictions influence the outcome of processes. Two well-studied examples from different disciplines are predictions of the stock market in economics and the placebo effect in medical therapy. If a reliable analyst makes the prediction that the stocks of a company will lose because of the expectation of an unsuccessful year, people will start to sell and the stocks will indeed fall no matter whether the assumption for the prediction was right or wrong. We are dealing with a case of self-fulfilling prophecy. I find the second example even more remarkable. Large-scale investigations provided strong evidence for the placebo effect, [14] in particular, with pain release and antidepression drugs. Instead of the usual medication, a harmless and ineffective compound is given to the patient, and the feelings of the candidate are recorded. A recent study reported that more than 70% of the placebo group felt the expected result of the effective drug. Even more impressive is the so-called nocebo effect: The candidates are informed about side effects of the drug that is not applied to them, but they nevertheless develop the negative symptoms. Complexity research in this area is a great challenge because it has to combine all our present knowledge from science, medicine, and psychology.

Decisions of individuals in extremely complex situations are often facilitated by simple empirical strategies [15, 16]. These intuitive strategies—often called fast and frugal decision-making—seem to be innate to human brains. The basic concept is to apply simple and inexpensive heuristics rather than sophisticated considerations, to decide fast but to be prepared to revise a decision if necessary. Such fast and frugal heuristics use simple rules for (i) guiding search for information, (ii) stopping search, and (iii) decision making. I illustrate by two examples. In case one does not know the answer to multiple-choice questions, it is the best strategy to take the most familiar alternative. The largest city should be chosen out of a collection: Choose one that you know and that you assume to be large. The other heuristic is important for sailors and pilots: if an object approaching you stays for some time in the center of your visual field, change direction as fast as possible and at an angle as large as possible in order to avoid collision. Interestingly, most of the recently developed guidelines for decision-making in emergency situations follow essentially unconscious intuitions. However, there are also cases where so-called gut feelings are entirely wrong, because we got no phylogenetic preparation. This is unfortunately true for many challenges of our modern, man-made world. Probability estimates are one example. Otherwise people would stay away from gambling.

Complexity research is one of the most important fields for the future, because it is essential for our societies and their decision makers to know, for example, what can be predicted and where begins the realm of the unpredictable. ''Fast and frugal'' strategies can represent an optimal tool for an individual, but they are doomed to fail when they are applied on a national or international level for two reasons: (i) the consequences of a wrong decision may be too large, and (ii) revisions after enormous investments may become impossible. Therefore, complexity research based on scientific and mathematical analysis of problems and model studies by computer simulation—becoming more and more reliable the more empirical data we have at hand—are indispensable and will—hopefully—be integrated as one source of information into political decisions.

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DOI 10.1002/cplx