being applied to real problems, albeit on an extremely limited scale.

A key role for unconventional computing researchers is to recognise and understand the failings of quantum computers, rather than just their advantages. This article offers no specific mathematical or experimental method by which we can propose to exert control over a number of error-corrected qubits greater than the number of subatomic particles in the observable universe and hence enable the creation of 'useful' quantum computers, but we have seen how a bioinspired unconventional computing tool (machine learning) has already been applied to clean the output of true quantum computers, which goes at least some way to bridging this gap.

Quantum computers are noisy, don't achieve true parallelism and will demand comparatively strenuous engineering, but this doesn't detract from the magnificent vision with which they are being developed.

Regardless of whether the future is quantum, unconventional computing research fill both seek to improve its sister field and look for alternatives. We will still find enormous use in parameterising biological mechanisms that afford us control over biomedical systems, designing chemical systems which realise true massive parallelism and developing naturally-inspired algorithms for use on conventional systems that solve open problems on computability, to name but a few, limited examples. In an ideal world, we would have a different specialised computing substrate for each task: a biological CPU (Central Processing Unit) for neural networks, a quantum computer for database searches and a conventional computer to compose text documents with, and so on. Until then, unconventional computing research will continue to find new methods, materials and applications for novel computing materials.

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[2] A. Tero, S. Takagaki, T. Saigusa, *et al.*, "Rules for biologically inspired adaptive network design," *Science 327(5964)*, 2010, 439-442.

[3] Y.-P. Gunji, Y. Nishiyama, A. Adamatzky, "Robust soldier crab ball gate," *AIP Conference Proceedings 1389(995)*, 2011, 10.1063/1.3637777.

[4] R. Mayne, T. Draper, N. Phillips, *et al.*, "Neuromorphic liquid marbles with aqueous carbon nanotube cores," *Langmuir 34(40)*, 2019, 13182-13188.

[5] A. Chiolerio, T. Draper, R. Mayne, *et al.*, "On resistance switching and oscillations in tubulin microtubule droplets," *Journal of Colloid and Interface Science 560*, 2020, 589-595.

[6] A. Adamatzky, *The Silence of Slime Mould*, Bristol, Luniver, 2019.

[7] A. Adamatzky (ed.), *Slime Mould in Arts and Architecture*, Gistrup, River, 2020.

[8] P. Shor, "Polynomial-time algorithms for prime factorization and discrete logarithms on a quantum computer," *SIAM Journal on Scientific Computing 26(5)*, 1997, 10.1137/S0097539795293172.

[9] IBM, *Newsroom image gallery*, available at *https://newsroom.ibm.com/image-gallery-research.*

[10] L. Grover, "A fast quantum mechanical algorithm for database search," *STOC '96: Proceedings of the 28th Annual ACM symposium on Theory of Computing*, 1996, 212-219.

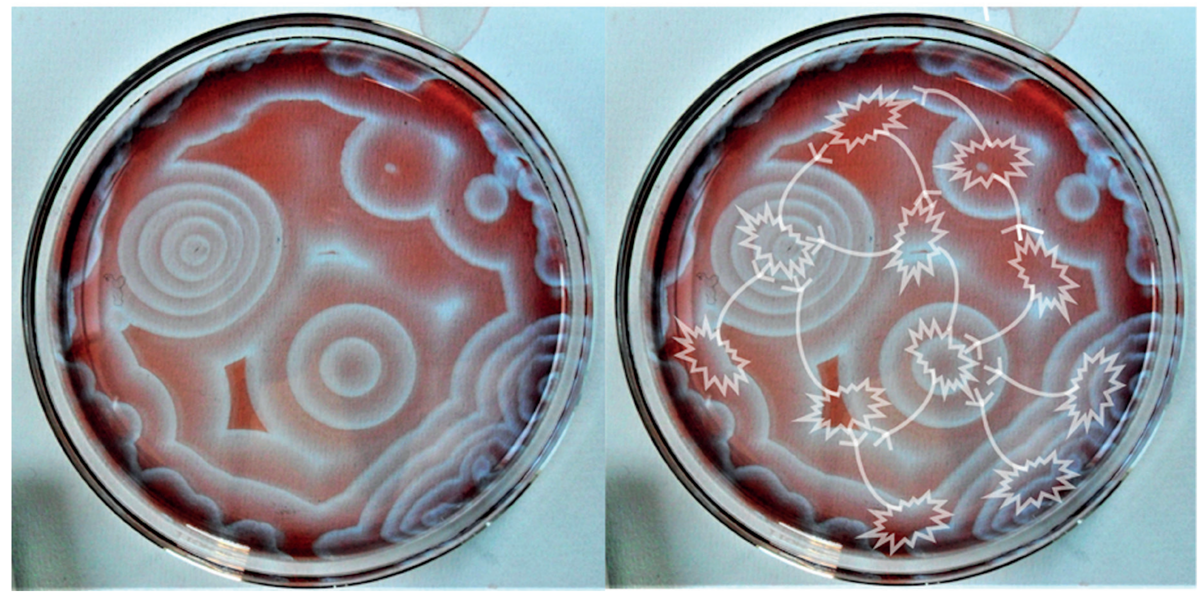
[11] W. Pfaff, B. Hensen, H. Bernien, *et al.*, "Unconditional quantum teleportation between distant solid-state quantum bits," *Science 345(6196)*, 2014, 532-535.

[12] J. Rice, T. Gujarati, T. Takeshita, *et al.*, "Quantum chemistry simulations of dominant products in lithium-sulfur batteries [preprint]," *ArXiv*, 2020, available at http://arxiv.org/abs/2001.01120.

How to face the Complexity of the 21st Century Challenges? The contribution of Natural Computing

Pier Luigi Gentili[1]

The 21st Century Challenges are Complexity Challenges because they regard Complex Systems, and hence other types of Complexities, such as Bio-ethical, Computational, and Descriptive Complexities. This article proposes some strategies to tackle the compelling challenges of this century. A promising strategy is the interdisciplinary research line of Natural Computing that includes Artificial Intelligence.



The phenomenon of chemical waves generated by the Belousov-Zhabotinsky reaction (on the left) and its interpretation according to the theory of Natural Computing that describes the thin film of the solution as a collection of artificial neuron models communicating chemically (on the right).

A fundamental role of science is that of solving practical problems and improve the psychophysical well-being of humans. Science succeeds in playing this role when it promotes technological development. Mutual positive feedback action exists between science and technology: science sparks technological development. At the same time, new technologies allow an always more-in-depth analysis of natural phenomena. Cutting-edge technologies let us manipulate materials at the molecular and atomic scale, send robots to other planets of our solar system, and engineer living beings. Despite many efforts, there are still compelling challenges that must be won. They are the so-called 21st Century Challenges included in the 2030 Agenda composed by the United Nations. Examples of these challenges are all those diseases that are still incurable. There are challenges that concern about human activities. Our manufacturing processes must become circular, minimizing waste. They should not perturb the fragile stability of natural ecosystems and contribute to climate change.

Poverty should be eradicated from the Earth, and justice should be assured in our societies. Whenever we tackle one of these challenges, we need to deal with Complex Systems, such as living beings, ecosystems, climate, and human societies. When we focus on human health, the immune and the nervous systems are other examples. Complex Systems appear so diverse. Currently, they are investigated by distinct disciplines. The burgeoning Complexity Science is trying to point out the features shared by all Complex Systems, *i.e.*, the characteristics of Natural Complexity (NaC).[2] All Complex Systems can be described as networks with nodes and links. Different Complex Systems usually have distinct architectures; the nodes and links are often diverse and evolve in time. Complex Systems are constantly out-of-equilibrium in the thermodynamic sense. The behaviour of inanimate matter is driven by force fields, whereas that of living beings is information-based. Furthermore, Complex Systems exhibit emergent properties. The integration of the features of nodes and links gives rise to properties that belong to the entire network. The whole is more than the sum of its parts. Finally, there is another universal attribute: Complex Systems cannot be described exhaustively. In other words, science finds many difficulties in predicting the behaviour of Complex Systems, especially in the long term. These difficulties are due to three principal reasons.

The first reason has a computational character. Most of the computational problems regarding Complex Systems and their simulation, such as scheduling, machine learning, financial forecasting, solving the Schrödinger equation, and the Traveling Salesman problem are solvable but intractable. According to the theory of Computational Complexity (CoC),[3] all the solvable problems can be grouped into two sets: the set of Polynomial Problems and that of Exponential Problems. A problem is polynomial when the number of computational steps grows in a polynomial way with respect to the dimension of the problem. The Polynomial Problems (P) are problems of recognition. They are tractable because it is possible to achieve the exact solution in a reasonable lapse of time with the available computing machines. On the other hand, an Exponential Problem, whose number of computational steps is an exponential function of the problem's dimension, is tractable only if it has a small dimension. Exponential Problems with large dimensions are intractable. In these cases, they are transformed into Non-deterministic Polynomial Problems (NP). After fixing an arbitrary criterion of acceptability, solutions are generated through heuristic algorithms, and they are checked if acceptable or not. Meanwhile, some scientists, allured by the amount of money promised by the Clay Mathematics Institute in Cambridge, are trying to rigorously verify if the NP problems are reducible to P problems or this reduction is impossible.
The second reason why we find unsurmountable difficulties in describing Complex Systems is that they show variable patterns. Variable patterns are objects or events whose recognition is hindered by their multiple features, which vary and are extremely sensitive to the context. Examples of variable patterns are: the human faces, voices, and fingerprints; handwritten cursive words and numbers; patterns and symptoms in medical diagnosis; patterns in apparently uncorrelated scientific data; aperiodic time series; political and social events. It is necessary to formulate algorithms for recognizing every type of pattern. The steps of pattern recognition are: acquisition of instrumental data; selection of the features that are considered as representative of the pattern; application of an algorithm for the classification step. Despite many attempts, it is still necessary to propose universally valid and effective algorithms for recognizing variable patterns. This difficulty generates a third type of Complexity that it might be named "Descriptive Complexity" (DeC).
The third reason why we find difficulties in predicting the behaviour of Complex Systems derives from the intrinsically limited predictive power of science. In the description of the microscopic world, it is necessary to deal with the Heisenberg Uncertainty Principle. Such a principle asserts the impossibility of determining position and momentum of every microscopic particle, simultaneously and accurately.

Therefore, the Uncertainty Principle places concrete limits to the deterministic dream of describing the dynamics of the universe, starting from the description of its microscopic constituents. We might think of describing Complex Systems only from the macroscopic point of view, neglecting their microscopic "bricks." However, Complex Systems can exhibit chaotic dynamics. Chaotic dynamics are aperiodic and extremely sensitive to the initial conditions. Since the determination of the initial conditions is always affected by unavoidable experimental errors, the chaotic dynamics are unpredictable in the long term by definition.

The limited predictive power of science makes many ethical issues related to technological development fiercely arguable. The unstoppable technological development induces humanity to continuously raise a fundamental question: "*Is it always fair to do what technology makes doable?*" It is a tormenting question that has accompanied humankind since the beginning. Suffice to think about the Greek myth of Prometheus or the most recent novel *Frankenstein* written by Mary Shelley in the 19th century. Cutting-edge technologies allow for manipulating and re-engineering life. Therefore, bioethical issues arise. There are bioethical issues that concern about the beginning of a new life. Examples are: "*Is it fair to manipulate human embryonic stem cells?*" or "*Is it safe to originate genetically modified organisms?*" Other bioethical issues regard suffering and the end of human life. Examples are: "*Is euthanasia fair?*" or "*What can we state about the therapeutic obstinacy?*" Finally, there are forefront technologies that enhance human intellect and physiology. "*Is it fair to exploit such enhancement's techniques?*" It is tough to find shared solutions to all these queries. They are intrinsically linked to the meaning we give to our lives. Furthermore, from both a biological and a physiological point of view, every living being is a Complex System, and we have already declared the limitations we encounter in predicting the behaviour of Complex Systems. The bioethical issues mentioned above generate another type of Complexity, which can be named as Bio-Ethical Complexity (BEC).
From this discussion, it is spontaneous to name the challenges of the 21st century as Complexity Challenges. They involve Natural Complexity (NaC) and Bio-Ethical Complexity (BEC), which are interlinked with Computational Complexity (CoC) and Descriptive Complexity (DeC). How can we think of winning these Complexity Challenges?
First of all, we need an interdisciplinary approach. Natural Complexity must be faced by all the scientific disciplines, including the social and economic ones. Philosophers can help to formulate new epistemological models and new methodologies. When we tackle the Bio-Ethical Complexity, the involvement of scientists and philosophers and jurists, artists, and theologians is appropriate. The artists, guided by their intuitions, could spark new ideas and unconventional ways for interpreting Complexity. The theologians offer an extra dimension for giving meaning to our lives. The Universities worldwide should offer Interdisciplinary courses on Complex Systems,[4] and the formation of genuinely interdisciplinary research groups should be favoured by public and private funding.
The investigation of Complex Systems cannot be performed by relying only on the reductionist approach, because Complex Systems exhibit emergent phenomena. A systemic approach is also needed. Furthermore, when we study the behaviour of Complex Systems, we cannot trust anymore in one of the cornerstones of the scientific method, which is the reproducibility of the experiments. Experiments on Complex Systems are usually historical events. The philosopher Karl Popper has effectively described this state of affairs by declaring[5] that, in the past, science had been occupied with clocks, *i.e.*, simple, deterministic systems having reproducible behaviours. Currently, instead, science has to deal with clouds, *i.e.*, Complex Systems having unique and hardly replicable behaviours.
The investigation of Complex Systems requires to monitor them continuously because their behaviour is hardly static, but rather highly dynamic. Therefore, it is necessary to collect,

process, and store massive data sets, *i.e.*, the so-called Big Data. Furthermore, it is becoming evident that an alternative way of doing experiments on Complex Systems is to perform simulations with computers. To deal with the huge volume and the fast stream of data, their variety, and variability, and to extract insights from them, it is necessary to speed up our computational machines, extend their memory space, and always contrive more effective algorithms.

There are two relevant strategies to succeed.
The first strategy consists of improving current electronic computers. Electronic computers are based on the Von Neumann's architecture, wherein the memory, storing both data and instructions, is physically separated from the central processing unit. The pace of computers' improvement has been described by Moore's law, stating that the number of transistors (*i.e.*, the ultimate computing elements that are binary switches) per chip doubles every two years. There is a worldwide competition in devising always faster supercomputers. It is the TOP500 project. According to the last list compiled in June 2020, globally, the fastest supercomputer is the Japanese Fugaku that reaches the astonishing computational rate of 415.5 PFlops/s. Meanwhile, Chips' producers are investing billions of dollars in contriving computing technologies that can go beyond Moore's law.
The second strategy is the interdisciplinary research line of Natural Computing. Researchers working on Natural Computing draw inspirations from nature to propose:

- new algorithms,
- new materials and architectures to compute and store information,
- new methodologies, new models, and a new theory to interpret Natural Complexity.

It is based on the rationale that any distinguishable physicochemical state of matter and energy can be used to encode information. Every natural transformation is a kind of computation. Within Natural Computing, there are two important research programs. The first one exploits the physicochemical laws to make computations. Every physicochemical law describes a causal event, and any causal event can be conceived as a computation. In fact, the causes are the inputs, the effects are the outputs, and the law governing the transformation is the computation algorithm. The second research program of Natural Computing mimics the features and performances of the natural information systems that belong to living beings. We might mimic living cells (called Biomolecular Information Systems), nervous systems (called Neural Information Systems), immune systems (called Immune Information Systems), and societies (Social Information Systems). All these systems have the peculiarity of exploiting matter and energy to encode, collect, store, process, and send information.

With human intelligence as its emergent property, the human nervous system is particularly attractive when we want to face Complexity. It allows us

- to handle both accurate and vague information, computing with numbers and words.
- To reason, speak, and make rational decisions in an environment of uncertainty, partiality, and relativity of truth when the Incompatibility Principle holds: "*As the* complexity *of a system increases, accuracy and significance become almost mutually exclusive characteristics of our statements.*"
- To recognize quite easily variable patterns.

Therefore, it is worthwhile studying human intelligence and trying to reproduce it by developing Artificial Intelligence. Artificial Intelligence is revolutionizing our lives and societies. It is used in basic and applied science, medicine, well-being, economy, and security. There are two strategies to develop AI.[6] One strategy consists in writing human-like intelligent programs running in computers or special-purpose hardware. The other is through neuromorphic engineering. In neuromorphic engineering, surrogates of neurons are implemented through non-biological systems either for neuro-prosthesis or to design "brain-like" computing machines. Surrogates of neurons can be implemented through specific solid materials, in hardware. Such hardware can be

rigid if made of solid inorganic compounds or flexible if based on organic films. Alternatively, surrogates of neurons can be implemented through solutions of specific non-linear chemical systems, in wetware (see the Figure on p. 77). Finally, specific hybrid electrochemical systems can play as surrogates of neurons. In our research group, we are exploiting molecular, supramolecular, and systems chemistry to mimic some performances of human intelligence and develop Chemical Artificial Intelligence.[7]
Specifically, we are devising modules for futuristic chemical robots. A "chemical robot" is thought as a molecular assembly that reacts autonomously to its environment through molecular sensors; it makes decisions by its intrinsic Artificial Neural Networks, and performs actions upon its environment through molecular effectors. The intelligent activities of a chemical robot should be sustained energetically by a metabolic unit. Chemical Robots should be easily miniaturized and implanted in living beings to interplay with cells or organelles for biomedical applications. They should become auxiliary elements of the human immune system and help us to defeat the still incurable diseases.
Finally, this research line of Chemical Artificial Intelligence hopefully will give clues about the origin of life on Earth. The appearance of life on Earth was a phase transition or sudden change in how chemical systems could process and use information. In the beginning, the world was abiotic, and any chemical matter was unable to process information. About 4 billion years ago, the phase transition from a purely abiotic to the biotic world occurred. What happened at that time? The answer to this question might favor a new general theory on Natural Complexity.

[1] Physical Chemistry Professor focused on Complex Systems, Department of Chemistry, Biology, and Biotechnology, Università degli Studi di Perugia, Italy.
[2] M. Mitchell, *Complexity: A Guided Tour*, New York, Oxford University Press, 2009; P. Charbonneau, *Natural Complexity: A Modeling Handbook*, Princeton, Princeton University Press, 2017; P. L. Gentili, *Untangling Complex Systems: A Grand Challenge for Science*, Boca Raton, CRC Press, Taylor & Francis Group, 2018.
[3] O. Goldreich, *Computational Complexity: A Conceptual Perspective*, Cambridge, Cambridge University Press, 2008.
[4] P. G. Mahaffy, A. Krief, H. Hopf, G. Mehta, S. A. Matlin, "Reorienting chemistry education through systems thinking," *Nature Reviews Chemistry 2(4)*, 2018, 0126; S. A. Matlin, G. Mehta, H. Hopf, A. Krief, "One-World Chemistry and Systems Thinking," *Nature Chemistry 8(5)*, 2016, 393-396; P. L. Gentili, "Designing and Teaching a Novel Interdisciplinary Course on Complex Systems To Prepare New Generations To Address 21st-Century Challenges," *Journal of Chemical Education 96(12)*, 2019, 2704-2709.
[5] K. Popper, "Of clouds and clocks", in *Objective Knowledge: An Evolutionary Approach* Oxford, Oxford University Press, revisited edition, 1972, 206-255.
[6] S. J. Russell, P. Norvig, *Artificial Intelligence: A Modern Approach*, Englewood Cliffs, Prentice-Hall. 2009; C. Mead, *Analog VLSI and Neural Systems*, Boston, Addison-Wesley, 1989.
[7] P. L. Gentili, "The Fuzziness of the Molecular World and Its Perspectives," *Molecules 23(8)*, 2018, 2074; P. L. Gentili, "Small Steps towards the Development of Chemical Artificial Intelligent Systems," *RSC Advances 3*, 2013, 25523-25549.