‘A TRULY GOLDEN HANDBOOK’

THE SCHOLARLY QUEST FOR UTOPIA

Veerle Achten, Geert Bouckaert
and Erik Schokkaert (eds)

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'A Truly Golden Handbook,
No Less Instructive than Delightful,
by the Most Learned and Distinguished Professors
of the Renowned University of Leuven.'

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Will Life Go Live One Day?

Bart De Moor, Mathematical Engineering

During the last century, both physics and biology were characterized by tremendous progress and breakthroughs. In physics, we witnessed the birth of the theories of general relativity, quantum mechanics and the first attempts to design a Grand Unifying Theory, each of them deeply rooted in an almost platonic belief in the consistency of mathematics. A turning point in the phase of intensive scientific search was the invention of the transistor. The exponential proliferation of science, engineering and technology that followed, has been tremendously beneficial for society.

The same sequence of analysis and design will occur in biology. Impressive scientific breakthroughs over more than 50 years have led to a deep understanding of the basic mechanisms of life and its Darwinian evolution. Through mathematics and technology, biology has become an information driven discipline facing a tsunami of data. These provide us with a better understanding of life, health and disease. Based on these insights, we have now started designing life and living organisms. Nevertheless, important issues remain. Among others, we lack a basic understanding of the phenomenon of 'emergence', which is ubiquitous in life and nature and which seems to offer a plausible explanation for consciousness.

In this chapter, I would like to explore three utopian visions. First, I believe that one day, we will truly understand the unreasonable effectiveness of mathematics in physics. Second, one day, we will design and build life from scratch. And third, one day, we will build artificial brains with emerging consciousness.

The Unreasonable Effectiveness of Mathematics

All of science is archeology. Take physics, for instance. The current reality of the universe is the result of 13 billion years of cosmological evolution. It has left many traces: the cosmic background radiation as a leftover of the Big Bang; gravitational waves that squeeze and stretch space-time as they propagate, and which were generated by a collision of two black holes as 'recent' as 1.5 billion years ago. Or take biology. Nature has been executing millions of genetic experiments every single day since millions of years. We call it Darwinian evolution. It has left many traces in the genomes of all living organisms. Today, we are only beginning to understand the basics of life itself. We can now imagine how it originated billions of years ago and how it has evolved ever since. Both in physics and biology, we dig up observations from a remote evolution in the past. The more we unearth, the better we understand.

The fundamental insights from physics in the search for a Theory of Everything appear to form the bedrock of the rest of science, engineering and life itself. And most remarkably, all of this is captured in the language of mathematics with an 'unreasonable' effectiveness.[1]

Mathematics is about geometry and algebra. The classic Greeks were basically geometers, think of Euclides (mid 4th century BC - mid 3rd century BC), Archimedes of Syracuse (ca. 287 BC - ca. 212 BC) or Apollonius of Perga (ca. 262 BC - ca. 190 BC). Centuries later, René Descartes (1596-1650) discovered the notion of coordinates. Geometrical forms could now be 'quantified' and represented by real (and later also complex) numbers. Their spatial properties, like surfaces, volumes and intersections, could be computed numerically. As a result, the classic Euclidean geometry could be extended in many ways, leading to a new mathematical discipline called 'algebraic geometry', considered to be the queen of mathematics. One of these extensions is towards thinking in higher dimensions, leading to 'higher algebra' since the work of 19th-century mathematicians. We can leave behind our intuitive, visual notion of geometry in three dimensions, pictures of which can often be misleading when 'working' in higher dimensions.

Descartes quantified space and time. Then Isaac Newton (1643-1727) entered the stage. It took his genius to introduce the notion of 'dynamics'. He discovered how to mathematically describe 'fluxions', properties that 'flow' as a function of time. We use 'differential equations' ever since: they describe mathematically how the coordinates of an object evolve as a function of time. Using differential equations, Newton formulated three fundamental laws of motion and a law of universal gravitation. Today, it would certainly earn him a Nobel Prize.

Since Newton, we realize that mathematics as a universal language describes nature, while reversely physics brings a lot of mathematics to life. Newton showed us how the very idea of a precise physical law and the mathematics to describe it, are born together. And then came Albert Einstein (1879-1955). For his general theory of relativity he had to fine-tune the language of Riemannian differential geometry to describe new physics. A little later, quantum physics once more impacted many branches of mathematics, from geometry and topology to representation theory and analysis, extending the pattern of beautiful and deep interactions between physics and mathematics.

At around the same time, we started realizing that our geometric intuitive notions of space and time are inadequate. The general theory of relativity taught us that there is a non-Euclidean Riemannian space-time continuum, the one indeed that is stretched by gravity waves. From quantum mechanics we learned that quantities that we intuitively think of as continuous, are actually discrete. Planck showed us that energy comes in discrete packets, called quanta. A quantum, like a photon, can simultaneously be wave and particle. The wave-particle duality was born.

And with the development of string theory,[2] for the sake of mathematical consistency we have to accept that the reality of our universe unfolds in 11 dimensions. String theory forces us to give up the notion of point-like zero-dimensional particles. They are replaced by one-dimensional objects called strings. A string is a mathematical construct. It is 'vibrating energy', and we do not really understand it. Nobody has ever observed a string, and probably we never will. But the mathematics is fine and exciting. It describes how strings propagate through space-time, and how they interact with each other. It describes how from a distance a string looks like an ordinary particle with mass, charge and other properties, determined by the vibrational state of the string. String theory is a theory of quantum gravity, i.e. an attempt to reconcile Einstein's general relativity with quantum mechanics, an attempt to unify the four fundamental forces of nature and all forms of matter and energy into one Grand Unified Theory of Everything.

For sure, there is something unreasonably effective about mathematics. As Edward Witten, one of the founding fathers of string theory, said: "There must be skeptics out there who will tell you that these beautiful equations might have nothing to do with nature. That's possible, but it is uncanny that they are so graceful and that they capture so much of what we already know about physics while shedding so much light on theories that we already have."[3]

Most scientists consider mathematics as a symbolic language in which we can describe reality. We use mathematics to 'explain' and 'understand' observations and to make predictions: why and how is Newton's apple falling to the earth? Obviously, as we increasingly unravel more details of the physical reality, we increasingly need to develop more mathematics. Johannes Kepler (1571-1630) adopted the conic sections of Apollonius to describe the elliptic orbits of the planets. Newton discovered differential equations to describe the proportionality between force and acceleration. Einstein mapped general relativity into the non-Euclidean differential geometry of Bernhard Riemann (1826-1866).

And in string theory, mathematical physicists use Calabi-Yau surfaces – wildly curved complicated surfaces in 11 dimensions, with many 'holes' in them.

The real strength of mathematics lies in its predictive power. Just by logical deduction, we can postulate events that have not been observed yet. The existence of the Higgs boson was postulated long before it was actually experimentally observed in CERN. From the mathematics of the Englert-Brout paper, we knew exactly 'where' to look. We have observed gravitational waves exactly as they were predicted by Einstein's theory of general relativity. His theory hinted at where to find them. We know that in the universe, there must exist unobserved 'dark matter', and quite a bit of it, because without it our mathematical theories cannot explain the increasing accelerations of certain galaxies as they move away from us.

So, mathematics 'explains' reality. But what if it were the other way around? What if physical reality is just a manifestation of a deeper, underlying mathematical 'truth'? Because, actually, what 'is' reality? Why is the speed of light in vacuum exactly 299 792 458 meter per second? Why is the mass of a proton exactly 938.3 mega-electron-volt? Is anti-matter gravitationally attracted or repulsed by matter (actually, we don't know)?

In their deepest dreams, mathematicians and physicists would like to come up with a theory that eliminates the need to experimentally determine the value of the 'universal' physical constants we use (there are about 20 of them). These physical constants, such as the speed of light in vacuum c, the gravitational constant G, Planck's constant h, are believed to be 'fundamental', i.e. universal and constant in space and time. Such a constant-free theory would be based on first principles, in which the value of all these 'experimental' constants derives from pure mathematics, for instance as a discrete eigenvalue of some operator, just like the energy levels of a quantum derive as eigenvalues from Schrödinger's wave equation. This for sure is an almost platonic view of reality and mathematics, cultivated by many, including Penrose and Tegmark.[4] Mathematics is not developed, nor constructed, we do not invent it, but we discover what has always been around as a hidden mathematical truth to be unraveled. Maybe there is an ideal world of perfect forms after all. And maybe all our theories rest on the prior supposition of the existence of an absolute mathematical truth.

And this platonic view on mathematics captures the first of my three utopian dreams: I firmly believe that one day, we will really 'understand', and ruthlessly exploit, the unreasonable effectiveness of mathematics. We will no longer wonder about the seemingly coincidental explanatory power of mathematics, but on the contrary, take its logical consistency for granted, and exploit its predictive power to discover 'new' physical reality. Like the Nobel Prize winning physicist Steven Weinberg once remarked: "Our mistake is not that we take our theories too seriously, but that we do not take them seriously enough". Maybe, after all, reality is just another model …

Engineering Technology: Design Follows Analysis

In our archeological endeavors to unravel and understand physics, there is another important catalyst besides mathematics, namely technology. Mathematics and technology allow us to understand the origins of space and time. Think of the Big Bang, the cosmological background radiation, black matter and energy, etc.

The word 'technology' derives from the Greek '*techne logos*', loosely translated as the know-how to do something. Technology comprises systems, processes and artefacts that are man-made and realize a specific functionality to achieve certain objectives or implement certain challenges. Without doubt, our modern society has evolved from a biotope into a so-called 'technotope',[5] where the presence and deployment of technology is ubiquitous. Technological systems become more sophisticated, they start interacting socially, they get higher precisions and resolutions, grow smaller and more compact yet stronger, become more robust yet sustainable, and more complex yet increasingly user-friendly. In terms of 'big evolutionary history', one could therefore characterize technology as the trans-biological evolution building on the natural biological evolution. We no longer undergo evolution, we have started to accelerate it. We will shape our evolution.

This acceleration is catalyzed by mathematics and technology. They allow us to design the future and turn it into 'our' future. That's where engineering comes in, the systematic design of objects and systems, to develop new technology that integrates insights from science, craftsmanship, expertise, social experiences and earlier technology. Engineering is not only about hardware (buildings, bridges, cars, airplanes, computers, etc.). Increasingly, it is also about software, optimization methodologies, algorithms, machine learning and artificial intelligence, all of which belong to the domain of mathematical engineering. Engineering technological systems is fundamentally driven by imagination, inspiration, design and creativity. In the technotope, we engineer our own future. We apply the knowledge acquired from the basic sciences and deploy it in the development and enhancement of new technology. The famous physicist Theodore Von Karman once said that "Scientists study the world as it is, engineers create the world that has never been".

Let's look at physics once again. In the second half of the 19th century, James Maxwell (1831-1879) wrote down his four fundamental equations that describe electromagnetic fields, a gigantic achievement from which we have developed all the technology that generates and uses electricity and magnetism, light and radiation, with thousands of applications in power and communication systems, in health, in transportation and entertainment.

Another example is quantum mechanics, which nobody really 'understands'. How on earth can one particle be in two different positions with a certain probability? How can two particles be entangled and show 'spooky actions at a distance'? Richard Feynman, one of the world's leading physicists, once said in a lecture: "If you think you understand quantum mechanics, you don't." So admittedly we do not understand quantum mechanics, but then, we use it every day. Seventy years ago, William Shockley, Walter Brattain and John Bardeen successfully tested the point-contact transistor, based on the laws of quantum mechanics. The rest is history: computers, internet, smartphones, social media, global communication and interaction.

Today, we design and build incredibly complex integrated circuits, with billions of transistors on a square millimeter of silicon.[6] The complexity of this design and construction process is orders of magnitude larger than building a completely new city from scratch. When designing such a micro-electronics chip, we normally do not think about the individual transistors. We adopt a modular way of thinking. Take your typical smartphone. Before designing and building it from scratch, there is a whole process of formulating specifications at several levels. How large should the memory capacity of the device be? At what speed should it communicate with the external world? With which protocols (Bluetooth, Wi-Fi, mobile network)? What type of antenna is required? What is the maximum allowed power consumption? What type of functionalities (applets) should it have? What type of computations and how many should be going on simultaneously? How many transistors per module?

Once the specifications are clear, a design and production process starts up that itself contains chronologically ordered logical steps, like architectural design, functional and logic design, circuit and physical design, physical verification, fabrication, packaging and testing and ultimately chip delivery. Simultaneously, there is also a tremendous ongoing technological evolution in the design and production of the functionalities of each of the submodules. Think of the spectacular evolution of storage-memory capacity over the years, or of computational complexity (e.g. the number of floating points operations per second), both of which are driven by Moore's law (the observation that the number of transistors in a dense integrated circuit doubles approximately every 2 years).[7]

The basic observation I want to make here is that it took the first half of the 20th century to develop and mathematical understand quantum mechanics, but around 1950 the phase of analysis was followed by an incredibly fruitful explosion of design activities, leading to the information-based society we live in today. The second utopian dream I would now like to explore, is the insight that something similar will happen with biology. We are now still analyzing and trying to understand its incredible complexity, but one day, we will design forms of life that do not exist in nature.

Understanding Life, Designing Life

All of science is archeology. So is biology. Nature has been designing life for billions of years. As Eric Lander, who played a prominent role in the Human Genome project, describes it: "For the last three and a half billion years, evolution has been taking notes. It tries experiments. It wakes up each morning, does a little mutagenesis, changes a nucleotide here and there, and sees how it works. If it's a success, it keeps the notes. In this notebook, we have all the information of the greatest experimental tinkerer ever." Indeed, whenever we look into the genome of men, animals or bacteria, we basically look at the encyclopedia of life. Every single experiment, based on mutations and crossovers, of the past 3.5 billion years has been stored carefully in our DNA and the phylogenetic trees we construct to keep track of the evolution of species.

The fact that in nature, every day, millions of genetic experiments are performed, and variations on existing templates are being tested on their survival skills, certainly helps to explain biodiversity. For some, however, it is hard to believe that biodiversity is the result of evolution only, and not of some sort of intelligent design. The dilemma is the following: "If the universe began with a quantum particle blipping into existence, inflating godlessly into space-time and a whole zoo of materials, then why is it so well suited for life? [In the past,] the purported perfection of the universe was the key to proving the existence of God. The universe is so fit for intelligent life that it must be a product of a powerful, benevolent external deity. Or, as popular theology might put it today: all this can't be an accident."[8]

It is estimated that life began more than 3.5 billion years ago, and that more than 99% of all species, amounting to over five billion species that ever lived on Earth, have gone extinct. Estimates on the number of current species range from 10 to 14 million, of which about 1.2 million have been documented, which means that over 86% still have to be documented. From Charles Darwin's insights in the mechanisms of evolution (1859), over Gregor Mendel's 'statistical' laws (1865), the insight of Oswald Avery, Colin MacLeod and Maclyn McCarty that DNA contains the hereditary material (1944), the double helix description of Francis Crick and James Watson (1953), the discovery of restriction enzymes (genetic 'scissors')(1965), the discovery of the 'genetic code' by Marshall Nirenberg, Har Khorana and Robert Holley (1966), the description of recombinant DNA by Stanley Cohen and Herbert Boyer (1972), DNA sequencing by Frederick

Sanger, Allan Maxam and Walter Gilbert (1977), the Polymerase Chain Reaction (1985), Herman the bull, the first transgenic animal (1991), the appearance of genetically modified tomatoes on the market (1994), the sheep Dolly as the first cloned animal (1997) and in 2001, the unraveling of the full human genome: we have come a long and exciting way. And the road continues.

Step by step we are unraveling the archeology of biology: we are starting to grasp how evolution did its job, how it made us into the complex living beings we are today, how species come and go, how we survive and die. In a famous abiogenesis experiment in 1952, Stanley Miller and Harold Urey demonstrated how putative conditions on the primitive Earth could have favored chemical reactions that synthesized more complex organic compounds from simpler inorganic precursors. Miller showed how amino acids can be formed by continuously firing electrical sparks (simulating the effect of lightning) through a gaseous mixture of water, methane, ammonia and hydrogen. Simply turning on the sparks in that prebiotic experiment yielded several amino acids in every case. These experiments and later more refined ones convincingly show how organic compounds of building blocks of proteins and other macromolecules can be formed from gases with the addition of energy.

Nevertheless, the whole story turns out to be much more complicated than we ever envisaged. Four billion years have created an enormous complexity. Take genes. At the beginning of the 1970s, we thought that every gene specified one protein. The basic idea was a one-to-one mapping between a gene and a protein. The genome was like a linear program, like a tape being read from beginning to end. The genes in the genome were like subroutines in a computer program, a list of parts that together would produce an organism. And the 'junk DNA' in between the coding regions of the genome was thought to contain the deactivated leftovers of millions of years of biological evolution, preserved like a useless archive.

Today, almost 50 years later, we know that the genome is not a linear script, but rather, it is a dynamic, three-dimensional structure, heavily interacting with its environment.[9] Genes are no longer considered to be static unchangeable subroutines. They may be fragmentary and act combinatorially because there is a complete jungle of badly understood regulatory and modulatory elements hidden in the 'junk DNA'. These elements can switch on and off genetic networks like we do on the World Wide Web, where we can connect with or disconnect from any other person in the world. In other words, genes can cooperate in genetic networks, the composition of which can be modulated by the environment in which specific cells are active. Epigenetics is the study of external or environmental factors that turn genes on and off. These alterations may or may not be heritable.

And there are many, many new and exciting technological developments. Take for instance genetic editing. Researchers have long sought better ways to edit the genetic code in cultured cells or laboratory organisms, to silence, activate or change targeted genes, to gain a better understanding of their role. Recently, a new groundbreaking genome editing technology was developed, known as 'clustered regularly interspaced short palindromic repeats' – or CRISPR.[10] The discovery grew out of the surprising observation that bacteria could remember viruses.[11] This mechanism was then adapted by researchers to edit DNA in higher organisms. CRISPR provides a relatively easy and effective technique for modifying a cell's DNA in precise and targeted ways. Some researchers claim it has brought about 'the democratization of gene targetting'.[12]

Many experiments with the CRISPR technology are going on these days, e.g. in some embryos researchers try to unpick the genes that control early development in humans, they disable three to four genes in the first embryonic cells and then observe what happens. Similar work in animals has taught us a lot about how mammals in general develop. One of the objectives is to try to understand why IVF success rates are so low, with only half of the embryos implanted in the womb developing sufficiently, and also to identify mutations that might lead to miscarriages. Other applications are: modifying plants, enhancing pest resistance in wheat, fine-tuning rat models of human disease, reproducing the carcinogenic effects of specific chromosome translocations in mouse lungs, or correcting a mutation in adult mice that in humans causes the disease of hereditary Tyrosinemia, a serious metabolic condition. Clinical researchers are already applying CRISPR to create tissue-based treatments of cancer and other diseases.

CRISPR is but one fine example of many fascinating technological breakthroughs. Because of technology, our basic understanding of biological systems is exploding. Multidisciplinary teams of biologists, medical doctors, statisticians and engineers deliver and digest the tsunami of data. As a result, biology has turned into an information science, in which mathematics becomes an indispensable tool. Just like in physics, there is now a 'mathematization' of biology, with the same unreasonable effectiveness. There is for instance systems biology, in which we try to understand the system theoretic interaction of all the modules in a living organism, intercellular and extracellular, and their interaction with the environment. This description of biological systems as a networked connection of interacting modules on several hierarchical levels is very reminiscent of the modular way in which we describe microelectronics circuits of billions of transistors. Actually, the methodology is identical, but the language and toolbox differ.

And these observations lead to the second utopian dream I would like to launch here: one day we will design life, in forms that do not exist in nature. Inspired by the design of electronic systems, we start thinking about designing and building biological systems, in a brand new discipline that is called 'synthetic biology'.[13] It combines biological research with engineering principles, so as to design and assemble biological systems that process information, manipulate and produce chemicals, fabricate materials and structures, produce energy or food, or maintain and enhance human health. In synthetic biology, genetic code is abstracted into modular chunks, known primarily as 'bio-parts', which allow us to build increasingly complex systems. Putting parts together creates devices such as biological 'clocks', on-off switches, cell-death mechanisms, color-changing mechanisms, etc., with a design methodology based on modular thinking that is identical to designing very large scale integrated circuits (VLSI chips) from scratch.

By combining the profound new insights in biological mechanisms with the principles of engineering complex systems, scientists can now use computers and wet lab environments to design new living organisms – 'new' in the sense that they do not exist in nature. This utopian dream, when fulfilled, would heavily impact our daily life in particular and society in general.[14]

Think of cancer cell detecting bacteria that eliminate themselves after a week if no cancer cell is found. If one is detected, however, the bacteria will destroy it, long before the cancer can be detected by any macroscopic scanner in a hospital environment. Think also of bacteria that turn purple when they detect heavy metals in polluted water.

Of course, before we can start to deploy genetic editing and synthetic biology in real world applications or commercial products, there are many important legal, ethical and democratic concerns and deficits that have to be resolved.[15] CRISPR and related technologies have the potential to revolutionize the treatment of disease, but when abused they are not beneficial to society at all. The CRISPR-Cas9 nucleases are widely used in gene editing and can be readily customized. But they can also induce substantial, genome-wide off-target mutations at sequences that resemble the on-target site. For instance, in the human embryo experiments that have been performed so far, CRISPR also cut many non-targeted genes. If one copy of a disease gene is repaired, sometimes a healthy copy is mutated as well by CRISPR. If editing is attempted in an early stage of a human embryo, sometimes CRISPR only reaches some cells and not all of the targeted ones, resulting in a mosaic embryo with some mutant tissues. Another sensitive question is whether genome editing techniques could be used for non-medical enhancement. Governments, regulators and other stakeholders are largely unaware of the breathtaking pace of genome-editing research.[16] Should the global scientific community not refrain from using any genome-editing tools to modify human embryos for clinical applications until we have sorted out all the medical and ethical ramifications?

Emergence

In all the aforementioned scientific endeavors, the aim is to get down to the basic 'atomic' levels. We start top-down, and dig our way down to lower hierarchical levels to understand how physics and biology really work. We deconstruct reality to find its basic building blocks and laws. Often this is to be interpreted literally. Think of the Large Hadron Collider at CERN, where all the elementary particles of the standard model, including the Higgs boson, are 'created' through collisions at velocities close to the speed of light. Think of full human genome sequencing, in which we reconstruct the precise sequence of 3 billion nucleotides that are linearly arranged in every double helix of every cell in our body. Here mathematics and technology help us in going from the macroscopic to the microscopic level.

Yet, the reverse is much more difficult, if not (still) impossible. How can we explain, let alone predict, the properties and behavior of a system from the properties of its individual constituents and their interaction? How to predict the characteristics of a material (e.g. a plastic) from its individual atoms and molecules? How to understand the turbulent flow of water around the rocks in a river from our knowledge of the chemical structure of water molecules and their interaction? How to understand the functioning of a human liver from the properties of its cells? How do large numbers of cells organize in processes such as tissue growth, wound healing or the spread of tumors? What is life? How can the present conditions here on Earth even exist in an otherwise cold universe? How to understand consciousness from our knowledge of neural networks? What is free will?

The fact that often the whole has macroscopic properties that are not effectively 'computable' from the knowledge of the properties of its constituents and their basic interaction laws is called 'emergence'. Emergence is a phenomenon whereby larger entities, patterns, regularities, properties, behaviors and characteristics arise through interactions among smaller or simpler entities that themselves do not exhibit such properties.

Most physical variables that we can measure are emergent. The temperature of a body or a gas is an emergent characteristic: it is basically a measure of the average kinetic energy of constituting atoms or molecules. Forces like gravitation are emergent, the emergence in this case being explained by the Englert-Brout-Higgs theory. And even the basic notions of space and time may be emergent from a different, more fundamental picture. Indeed, there is a fundamental problem with time. In physics, at an elementary particle level, almost all of the basic equations are time-symmetric: whether time ticks forward or backward does not make any difference. Yet, at the macroscopic level, we age, we build up memories and we forget, all of which are irreversible processes. There is an obvious arrow of time here. We know and experience causality in our physical reality, in which cause and effect are not interchangeable. According to the Russian-born Belgian physical chemist and 1977 Nobel Prize winner Ilya Prigogine, the arrow of time is dictated by the dissipation of energy, and is quantified by the thermodynamic notion of entropy. Entropy is a fundamental measure of the messiness, the lack of order in a physical system. As entropy grows, time ticks forward. Where entropy is involved, there is no time-reversibility. But currently we do not really understand how time-irreversibility in real life processes emerges from the lower, smaller scale layers where interactions are time-reversible.

Not only basic physical variables are emergent. Most of the laws of physics that we use every day, and that describe relations between physical variables, are emergent laws. Think of Ohm's law of electricity (the proportionality of voltage over and current through a resistor, involving billions of charged electrons and atoms of the conductor 'resisting' the flow of electrons). Think of Newton's law of the proportionality of force and acceleration. These are all physical laws that emerge from deeper, more fundamental physical laws.

Actually, emergences occur at all possible levels of reality, in physics as well as in biology, whenever one jumps from one level of description to the level immediately higher. In physics, already in 1928 the physicist Werner Heisenberg, of quantum mechanics fame, came up with a model in which he imagined every atom to be a freely rotating bar magnet and then found that large scale magnetism emerges from interactions between these atomic magnets causing the majority of them to align. Emergence in the realm of physics is called 'active matter'.[17] It is increasingly being made in the laboratory. Synthetic components on a micrometer scale that consist of light-sensitive plastic 'swimmers' form structures when a lamp is turned on.

Researchers hope that more mathematical insight in 'active matter' will coincide with more insight in the way biological systems really work. Because in biology emergence is ubiquitous. On a macroscopic scale, think of social insects, e.g. ant colonies.[18] They work without a central control, yet collectively, they achieve specific goals. Termites for instance build impressive 'cathedrals', in such a clever way that even heating and ventilation is taken care of. Yet, we assume that an individual termite has no comprehension of what they are doing collectively. Understanding how ant colonies work, might help us to understand other manifestations of emergence in which there is no apparent leader or control, ranging from our brains to the internet. Another example can be found in the collective behavior of flocks of birds or schools of fish. These are swarms of thousands of self-propelled entities that communicate and interact locally, short-range, but from a certain critical density on demonstrate a collective and synchronized behavior.

The challenge regarding emergence is clear when it comes to creating artificial human organs, like the liver or the kidneys. It is not because we understand how one liver or kidney cell works, that we can artificially grow a new liver or kidney. We not only need to 'understand' an individual liver cell, but we need to understand how these cells locally interact and organize themselves so as to collectively execute the tasks of detoxification of various metabolites, protein synthesis and the production of biochemicals for digestion. Yet, today, our understanding of systems biology has evolved to such an extent that we can grow a human kidney in a living sheep. In a first step, genetic information is taken out of animal embryos of two days old. Then these embryos are injected with human stem cells, which grow into a human organ within the animal embryo. But we cannot yet grow organs *in vitro,* in a wet lab environment, from scratch.

All known life forms are based on self-propelled entities uniting to create large-scale structures and movements. Biologists have been speculating for centuries about the general principles of living matter. Yet today, most of the research is concentrating on identifying the dizzying array of molecules involved in cellular processes, rather than on working out the principles by which they self-organize. Life in itself is an excellent example of emergence at several hierarchical levels. Life is perceived as an emergent property of several different interacting modules, which themselves are built from millions of interacting molecules. Those interactions are studied in chemistry, which in itself does not predict whether molecules, when put together, will live. In their turn, chemical reactions reflect interactions among elementary particles, studied in physics. So we distinguish several hierarchical layers, yet none of the properties of a layer higher up in the hierarchy can be predicted in a straightforward way from properties in a lower layer.

In general, emergence can only occur when certain necessary conditions are present. It occurs in layered, hierarchical systems, where there are two or more levels of complexity (e.g. the individual atoms of a certain element on the basic level, attracting each other via forces, and arranging themselves in a regular grid, creating a material with a certain hardness and melting temperature on a second level superseding the first one). There is modularity, in which modules are described by their interaction (inputs and outputs) with other modules on the same level, higher or lower, but in which the precise internal details of the specific module do not matter.

Often there are 'control' loops of positive and negative feedback. Negative feedback introduces regularity, structure and stability. Positive feedback promotes switching behavior and the growth of local patterns into global patterns. Often reaction-diffusion equations are involved. These describe how the concentration of one or more substances distributed in space changes under the influence of two processes: local chemical reactions in which the substances are transformed into each other, and diffusion that causes the substance to spread out over space. A wide range of dynamical behaviors is the result: wave-like phenomena like travelling waves or the formation of self-organizing patterns. Simultaneous positive and negative feedback occurs in a special class, namely activator-inhibitor systems: close to the ground state, one component stimulates the production of both components, while the other one inhibits their growth. Reaction-diffusion processes are key in understanding morphogenesis in biology, tumor growth and wound healing.

For emergence to occur, there are also necessary conditions of energy transfer involved that lead to certain forms of self-organization, which decrease the local entropy. In other words, streams of energy 'through' the system create ordered structures that we call emergent. Seemingly, there is a 'propensity' towards increasing complexity, diversity and modularity as long as there is enough delivery of energy. In that sense, emergence is very close to creativity: by consuming energy, some ordered, self-organizing structures are being created, that, as a whole, do something more than would be apparent from the properties of the constituents. Emergence definitely represents a constructive and evolutionary aspect of reality, where new properties and characteristics pop up as one jumps from one hierarchical layer to another one 'higher up'.

It was Ilya Prigogine who explained how life could continue indefinitely in apparent defiance of the classical laws of physics, based on his insights in non-equilibrium thermodynamics. He attempted to reconcile a tendency in nature for disorder to increase (as described by the Second Law of Thermodynamics, e.g. the irreversible melting of ice, the irreversible mixing of coffee and milk, etc.) with so-called self-organization, a countervailing tendency to create order from disorder (e.g. the formation of complex proteins from a mixture of simple molecules as in the Miller-Urey experiment). Indeed, systems with emergent properties or structure seem to defy the Second Law of Thermodynamics, namely that the entropy of a (closed) system always increases. But for open systems that interact with their environment, this is not necessarily the case: they can form and increase order and structure, provided they can dissipate energy (and typically, they are far from the thermodynamic equilibrium).

Prigogine's framework could perhaps be used to explain why in our earthly biotope, due to the gigantic flow of energy from the sun, nature could develop life as we experience it, surrounded by a cold and hostile galactic cosmos.

And what about our own (self)consciousness as an emergent behavior?[19] Does it emerge as the collective behavior of billions of neurons that interact? Do we lose it as soon as our brains no longer dissipate energy, or a certain critical density of interactions is locally destroyed? We don't know. In his book *Shadows of the Mind*,[20] Penrose speculates that Gödel's Incompleteness Theorem implies that conscious awareness cannot be simulated. Yet, billions of years of evolution have shown us that building an intelligent brain from scratch is possible, since every day about 350 000 babies are born worldwide, who later develop into intelligent beings. Maybe our brain uses algorithms and methods of reasoning that do not comply with the formal axiomatic systems in which Gödel thought. There seem to be several levels at work, in which "the unconscious system pieces together fragments of our perceptions, anticipating patterns and filling gaps when necessary, to devise a single meaningful interpretation. It tells a story. The conscious system experiences that story but can also reflect on it and question it."[21]

Will we one day build living organisms that reproduce and procreate? Will we one day build true artificial intelligence that can convincingly withstand the Turing test?[22] Will we one day build artificial brains in which self-consciousness emerges? There is the 1931 quote of Max Plank: "I regard consciousness as fundamental. I regard matter as derivative from consciousness. We cannot get behind consciousness. Everything that we talk about, everything that we regard as existing, postulates consciousness."

Therefore, the third utopian dream I would like to put forward here is my deep belief that one day, we will indeed build a conscious 'non-human' brain from scratch; that, in order to do that, we will understand in one way or another the phenomenon of emergence, and that we will have learned how to design it. This capacity to build artificial brains that will reason and interact emotionally and empathically, will be deeply rooted in an understanding of fundamental physics and biology, based on and inspired by sophisticated mathematics.

Physics, biology and emergent consciousness: they are deeply rooted in mathematics. Maybe, one day, in Utopia, we will bring them all together in a thorough understanding of our world.

Notes

1 Wigner, E., 'The Unreasonable Effectiveness of Mathematics in the Natural Sciences', *Communications in Pure and Applied Mathematics* 13:1, 1960.

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3 Gamwell, L., *Mathematics + art, a cultural history*, Princeton: Princeton University Press, 2016.
4 Tegmark, M., *Our mathematical universe*, New York: Penguin Random House, 2014.
5 De Moor, B., 'World views, Science and Technology', in Aerts, D., Apostel, L., De Moor, B., Hellemans, S., Maex, E., Van Belle, H., and Van der Veken, J., *Perspectives on the World: an interdisciplinary reflection*, Brussels: VUB University Press, 1995, 103-125.
6 See also Rudy Lauwereins, 'Preventive Maintenance for a Future without Disease', in this book (p. 36).
7 See also Philip Dutré, 'Thinking and Conscious Machines?', in this book (p. 454).
8 Rubenstein, M.J., 'God versus the multiverse', *New Scientist* 19/26, 64-66, 2015.
9 See also Koen Devriendt & Hilde Van Esch, 'Healthy Genes for Everyone', in this book (p. 93).
10 Doudna, J.A., and Charpentier, E., 'The new frontier of genome engineering with CRISPR-Cas9', *Science* 346, 1258096, 2014; Travis, J., 'Making the cut. CRISPR genome-editing technology shows its power', *Science* 350:6267, 1456-1457, 2016; See also Koen Devriendt & Hilde Van Esch, 'Healthy Genes for Everyone', in this book (p. 93).
11 Looking for that mechanism, researchers found remnants of genes from past infections, sandwiched between odd, repeated bacterial DNA sequences – the 'clustered regularly interspaced short palindromic repeats'. The viral scraps serve as an infection memory bank: from them, bacteria create guide-RNAs that can seek out the DNA of returning viruses to chop up the viral genes with a nuclease, a genetic scissor.
12 In essence, the method consists of a DNA-cutting enzyme called a nuclease (usually Cas9) and a piece of 'guide-RNA' that homes in on a DNA sequence, enabling researchers to create precisely targeted mutations, corrections to mutations or other alterations. Along with two other earlier genome editors, zinc finger nucleases and TALENS (Transcription Activator-Like Effector Nucleases), CRISPR is transforming basic biology in a spectacular way. In a variation, by making 'dead versions' of Cas9, scientists have eliminated CRISPR's DNA cutting ability but preserved its talent for finding sequences. In this way CRISPR can be turned into a versatile, precise genetic delivery vehicle. For instance, one can 'ship' various regulatory factors, hence enabling them to turn on or off any gene, or adjust its level of activity. In this way, CRISPR is turned into a control device (in control theory this is called an 'actuator').
13 *Design ontmoet biologie. Synthetische biologie in Vlaanderen* [Design meets biology. Synthetic biology in Flanders], IST Dossier 27, Instituut Samenleving en Technologie, Flemish Parliament, 2012.
14 For a glimpse of the near future, and the thousands of synthetic biology applications in health, energy, environment, etc., that await us, have a look at the website of the international Genetically Engineered Machine competition (iGEM), organized by MIT. Every year selected student teams convene in a large scientific 'jamboree', to present their synthetic biology designs. The iGEM *Registry of Standard Biological Parts* is a growing collection of genetic parts that can be mixed and matched to build synthetic biology devices and systems, and is in open access mode available to academic labs.
15 Travis, J., 'Germline editing dominates DNA summit. Prospect of heritable changes sparks questions about safety, ethics and rationale', *Science* 350:6266, 1299-1300, 2015.
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17 Popkin, G., 'The physics of life', *Nature* 529, 16-18, 2016.
18 Gordon, D.M., 'Collective wisdom of ants', *Scientific American* 314:2, 44-47, 2016.
19 See also Rudi D'Hooge, 'The Replaceable Brain', in this book (p. 61).
20 Penrose, R., *Shadows of the mind. A search for the missing science of consciousness*, Oxford: Oxford University Press, 1994.
21 Sternberg, E., *NeuroLogic: The brain's hidden rationale behind our irrational behavior*, New York: Pantheon, 2016.
22 See also Philip Dutré, 'Thinking and Conscious Machines?', in this book (p. 454).