Miguel M. Garcia *Editor*

Tales of Discovery

Delving into the World of Biology and Medicine

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Foreword

The Oxford English dictionary gives six meanings for the definition of *story*:

1. A description of events and people that the writer or speaker has invented in order to entertain people;
2. The series of events in a book, film, play, etc.;
3. An account of past events or of how something has developed;
4. An account, often spoken, of what happened to somebody or of how something happened;
5. A report in a newspaper, magazine, or news broadcast;
6. Something that somebody says which is not true.

This same dictionary gives four meanings for the definition of *science*:

1. Knowledge about the structure and behavior of the natural and physical world, based on facts that you can prove, for example by experiments;
2. The study of science;
3. A particular branch of science;
4. A system for organizing the knowledge about a particular subject, especially one that deals with aspects of human behavior or society.

In the work presented here, these two terms (*stories* and *science*), apparently distant but nevertheless very close, merge.

Science is exciting, so is reading a story. Discovering and explaining the origin of things, phenomena, or events that occur around us is not a simple task. There are many observations that have to be made. The complicated interrelationships between the observations have to be explained. Sometimes, methodologies have to be established to be able to verify that everything observed and deduced is true. One of the primary characteristics of the long road in the scientific method is this: it is exciting! The same thing happens with a good story—a compelling tale. We enjoy it—and sometimes we can get lost in it.

These short stories of science are structured into sixteen short scientific tales which show us, in a simple way, theories about the origin of life, our relationship with bacteria, the ecological footprint of some ruminants, the secret life of fungi, the consequences of current lifestyle trends, the theory of aging, food addiction, or the treatment of pain, the fifth vital sign.

The work is written by 20 researchers from different academic fields (biology, pharmacy, medicine, and food science and technology), whose professional work includes teaching, research, and scientific dissemination. These varied aspects add value to the work and make it easy to understand and enjoyable reading, while maintaining the rigor of the information presented. The illustrations, created by professors of Fine Arts, deserve special mention. They are completely original works and reflect their scientific theories with total accuracy. Science and Art. Art and Science. Another exciting fusion!

This book reveals the exciting world of science through entertaining short stories, without losing scientific rigor. They demonstrate the contribution research makes to our understanding of the world around us, but also the significance of research to improving such world.

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Preface

This book is intended primarily for use by anyone with science interest but also by students with a background in science. In addition to the text, all figures are original and have been conceived after thoroughly studying and discussing each topic with the corresponding authors. Each chapter (emplaced in the fields of genomic, endocrinology and metabolism, pain, food and environmental industry, cell aging, addiction and therapeutics or evolutionary biology) begins with a short introduction, followed by separate subtitles that introduce projecting issues from the main topic.

As science is becoming more and more specialized, academic and research institutions are demanding professional growth on teaching, research, and transference. At the same time, the European common framework advocates for multidisciplinary and multicentric works, which deepen in that specialized profile, but adopting a holistic focus. Under this frame, divulgation of research is although accessible, yet too specialized and incomprehensible for many. Besides, evenly mastering all three skills is an enormous task. For some people, science has made an impression on their consciousness, but it has yet not provided a good reason to the taxpayer to accept an increase of the budget set aside for research aims.

In addition to this, through the past years we have noticed that many of our students lack the practical application for the knowledge base they amass. Our research is often far from what we teach, and at the same time, our laboratories are made up of people specialized on a particular purpose or area of knowledge but with different backgrounds: physicians, dentists, physical therapists, biologists, biochemists, pharmaceutics or food and science technologists, just to mention a few. All in all, this favors the presence of education inequities and gaps in a milieu that is eminently biological. No one is devoid of areas of ignorance and confusion. The university entourage and research career provide however a magnificent and diversified contact portfolio. After having taken part in multiple science festivals and events to discuss our latest research with local average citizens, we decided to capture our talks in a book series to reach more people. It is with this aim that *Tales of Discovery: Delving into the World of Biology and Medicine* has been created.

The book aims to present current topics on varied disciplines approaching them to the ordinary reader in a language that they can understand, avoiding the technicality of an academic journal but also the personal tone of a speech or blog and produced in a media that insures rigor and reliability. Made up mainly of postdoctoral researchers and assistant professors with current or past positions in different locations worldwide, the group of scientists herein aims to let the reader take a glance at some of the research we perform and the concepts and the questions we deal with in our daily routine. Furthermore, I strongly believe that effective communication is key to succeed. Pursuing this goal, we have turned the tables and illustrations, normally performed by biologists with artistic flair, have been carried out by two colleagues from Fine Arts, experts in digital illustration, drawing, and design. The illustrations herein have the advantage that they have been designed by strangers to the biological field, in equal conditions with the ordinary citizen. In this sense, particular stress has been laid upon the artistic and conceptual meaning of the illustrations. It is my wish that the book presents a balance between scientific correctness and reading comprehension for the largest audience possible.

During the writing and compilation of this book, I have received the help and advice of my masters, professors Carlos Goicoechea and Visitación López-Miranda, who transmitted me their conviction on the richness of this enterprise. Together with the authors themselves, they were first to believe in this project. Life is way easier with comforting words and encouragement messages. Special recognition deserve professors Raquel Sardá and María Martínez de Ubago, responsible for the art concept, idea, drawing, and digital illustration, whom I started this project hand in hand with. They have been repeatedly meeting every author to study the fundamentals of the chapters and to understand what to capture on the different illustrations, spending endless hours also at night and during their holidays. I would also like to express my most sincere thanks to Gonzalo Córdova, Scientific, Publishing, and Commissioning Editor at Springer Nature. Sometimes you just need someone with a shared view who can understand and envisage the same outlook as you do. Gonzalo has been that bit of an oracle to me. He took a stance for us from the first moment, notwithstanding the role of Springer Nature as a world leader publisher on specialized titles. He had the patience and presence of mind to await the finalization of the project, no matter what. Last but not least, I would like to extend my special thanks to Chris Clarke, who not only did translate the chapters from a preliminary broken English, but interpreted our words gracefully and conferred a homogeneous narration to the work. It must certainly have been an arduous work striving with the language in addition to the intricacy of the topics.

Madrid, Spain Miguel M. Garcia

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Editor, Illustrators and Contributors

About the Editor

Miguel M. Garcia holds a degree in Biochemistry from Universidad Autónoma de Madrid (UAM), a master's degree in the Study and Treatment of Pain, and a Ph.D. in Pain Research from Universidad Rey Juan Carlos (URJC). He is currently Assistant Professor and Researcher in the Area of Pharmacology, Nutrition and Bromatology of the Department of Basic Health Sciences at Universidad Rey Juan Carlos. He belongs to the High Performance Research Group in Experimental Pharmacology (PHARMAKOM) and coordinates the Teaching Innovation Group in Diseases and their Treatment (EducaPath) of Universidad Rey Juan Carlos. He is a member of the International Association for the Study of Pain (IASP), the Spanish Pain Society (SED), and the Spanish Society of Pharmacology (SEF). His research work focuses on basic pharmacology in the field of pain, particularly on the role of glial cells and cannabinoid and TLR4 receptors in nociception. As a disseminator, he has experience as a speaker at different science festivals and activities.

About the Illustrators

Raquel Sardá Sánchez holds a degree in Fine Arts from Universidad Complutense de Madrid (UCM) and a Ph.D. in Communication Sciences from Universidad Rey Juan Carlos (URJC), where she has been working since 2004, and is currently Associate Professor. She coordinates the degree in Fine Arts, the Teaching Innovation Group in Art and Technology: Methodologies, Strategies and Means (ArTec), and is Director of the University Master's Degree in Contemporary Artistic Practices. She also makes part of the Consolidated Research Group in Visual Culture and Contemporary Artistic Practices: Languages, Technologies and Means (CUVPAC) of Universidad Rey Juan Carlos. Between 1997 and 2008, she worked for the company *Telefónica* as Designer and Director of Multimedia Projects and Technological Innovation applied to art and heritage conservation. She has participated in more than forty national and international teaching innovation conferences and has taught at universities in Turkey, Germany, Italy, Belgium, France, Finland, Canada and China. Her artistic projects have been exhibited at the *Robert Capa* *was here festival* (MNCARS, Madrid), Cibart Festival 2017 (Seravezza, Italy), *The First Dream of Sunbird* (Yiwu, China), *Hans Kock Symposio* (Seekamp, Germany), *Fundación Montenmedio de Arte Contemporáneo* (Cádiz, Spain), the International Exhibition of Contemporary Medal (Ottawa, Canada; Sofia, Bulgaria), and at the *Real Jardín Botánico de Madrid*.

María Martínez de Ubago Campos holds a degree in Fine Arts, specializing in Sculpture, and obtained her master's degree in Art, Creation and Research and her Ph.D. in Fine Arts from Universidad Complutense de Madrid (UCM). She currently works as Researcher and Assistant Professor in Fine Arts and Fashion Design and Management at Universidad Rey Juan Carlos (URJC) and makes part of the Teaching Innovation Group in Design, Innovation, Art and Fashion (DINAMO). Her lines of research are focused on educational innovation with the use of art as a learning tool and scientific illustration. She has directed and developed the educational program *Art and Culture* with the use of art as Mediator of learning for twelve years, and she has been part of the project *The scientific drawing in the travelogue* in collaboration with the Society of Natural History of the Sea and the Center for Marine University Studies (CEMU) for three years. While maintaining her artistic activity in the field of drawing and sculpture, she participates or attends symposiums, conferences, and congresses in universities and museums, taking an active part with papers, communications, or book chapters.

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Gaia: A Planet Dominated by Bacteria

Cristina González Fernández

Life appeared on earth approximately 3.5 billion years ago, and since then, the Earth and its living beings have been part of a structure that is capable of self-regulating as a single integrated physiological system. Gaia,[1] Mother Earth, the Goddess of classical mythology who was born out of chaos and is the mother of all, gave her name to the *Gaia Hypothesis*, formulated by the English chemist James Lovelock[2] in 1969. According to this hypothesis, the Earth behaves like a living organism that has managed to maintain the right conditions for life but, in turn, the system feeds back: the temperature of the Earth's surface, the composition of reactive gases in its inner core, the state of oxidation, acidity and alkalinity

[1] *Gaia* from Greek or *Gaia* from Latin is the goddess who personifies *Mother Earth.* According to Greek mythology, she emerged from nothing and, on her own, conceived *Uranus* (the Titan who personified the sky) and his brother *Pontus* (god of the sea). Later she turned her sons into husbands, and with them she became the mother of a multitude of mythological Titans and Titanides. Her Roman equivalent is *Terra.*

[2] James Lovelock is an English scientist famous for formulating the "Gaia Hypothesis": *the living matter of the Earth and its air, oceans, and surface form a complex system that can be regarded as an individual organism capable of maintaining the conditions that make life on our planet possible.* He also invented the electron capture detector, which is a very sensitive method of chemical analysis especially useful for the detection of polluting chemicals. He also experimented with freezing rodents to revive them later (cryopreservation).

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in the Earth, are maintained by the activity of life on the planet. That is, life produces and maintains its immediate environment, appearing on Earth as a planetary phenomenon. Sociologists have been able to explain this very well in the field of economics with Simmel's "The Philosophy of Money," and this could well be transferred to a biological context. Money, like life, is more than a value; it is a means of exchange that influences relations between humans (and living beings) in such a way that money begets money and life begets life.

A World of Daisies

To deal with the criticism and try to explain how Gaia works, in 1983, Lovelock and his colleague Andrew Watson created a computer simulator they called *Daisy World*. In the first phase of the simulation, a hypothetical barren planet, with a simple atmosphere, orbits around a sun that increases its temperature in a linear mode, and causes the planet's temperature to increase as solar radiation hits it. In a second phase, the planet is planted with two different varieties of daisies: black and white. The dark color of the black daisies allows them to absorb solar radiation more easily, while the white daisies reflect it. Since the temperature of the planet is gradually increasing in line with that of the sun, in the beginning of time the planet would be cold, but over the years it would reach a temperature sufficient to be habitable. At the beginning, only the black daisies would be able to proliferate because they retain more heat than the white ones, thus dyeing the planet black. Eventually, this would lead to an increase in the temperature of the planet, regardless of the radiation received from the star. As the temperature increased, not only would black daisies be more likely to proliferate, but white daisies would also proliferate until an ideal temperature of 22.5 °C was reached, where there would be an equal number of black and white daisies. The white daisies would start growing mainly around the equator, where there is more sunlight and the temperature is higher. As solar radiation increases, the temperature on the planet rises, and the black daisies begin to absorb too much radiation, overheat, and die; they becoming restricted to the poles, which receives less sunlight, and where the temperature is lower. White daisies would then begin to predominate, keeping the temperature at habitable conditions, until finally only white daisies would remain. In the third phase of the simulation, an extreme situation would be created in which the gradual but incessant increase in temperature would make it impossible for even white daisies to take on the solar radiation, and their population would crash. Eventually, the sun's rays are programmed to decrease in power to a more comfortable level, allowing white daisies to grow which would, in turn, begin to cool the planet again. The simulation shows that from the moment life appears on the planet the temperature does not increase linearly but remains stable at approximately 22.5 °C (optimum temperature for a balanced proliferation of black and white daisies). In other words, life on the planet modifies the temperature of the environment to create more favorable conditions for itself. In new simulations, the program has been reconstructed to include other forms of life (rabbits, foxes, etc.) to see if the same effect on the temperature of the planet is produced. What Lovelock advocates always happens: life on Earth, or rather, the interactions between living beings and the environment, produce optimum conditions for their own development. Moreover, the greater the number of introduced species, the better the regulation of global temperature, proving the value of biodiversity for the planet. The Earth and all its living beings are cogs in a machine that works with precision to keep itself in balance and thus ensure its survival. If just one cog fails, it will affect the whole system, which will have to readjust and adapt to the new conditions in order to continue functioning.

The Origin of Life: Much More Than a Single Theory

On our hypothetical planet, we can introduce new species at will, but how does it work on Earth? Imagine Earth 3.5 billion years ago: an inhospitable planet, volcanoes, an atmosphere totally incompatible with life as we know it today, ammonia, methane, carbon dioxide, lots of radiation… In these conditions it is not difficult to imagine that life originated under the Earth, protected from such conditions. In fact, apart from other religious theories such as *Genesis*, or social movements such as the *Flying Spaghetti Monster*,[3] efforts to locate life on nearby planets lacking an atmosphere compatible with life (such as Mars) are focused precisely on the study of the subsoil. If there is life on Mars, it must be there protected from the cold, from an inhospitable environment, or from extreme radiation. Understanding the past (how life originated on Earth) to understand the future (how to colonize other planets). Following this line, the theory of *Panspermia* argues that life is not a phenomenon exclusive to Earth, but is also found on other planets in the universe,

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[3] *Genesis* is the first book of the Bible. "And God said, Let the earth bring forth grass, the herb yielding seed, and the fruit tree yielding fruit after his kind, whose seed is in itself, upon the earth: and it was so. And the earth brought forth grass, and herb yielding seed after his kind, and the tree yielding fruit, whose seed was in itself, after his kind: and God saw that it was good." (Genesis 1:11–12). "And God said, Let the waters bring forth abundantly the moving creature that hath life, and fowl that may fly above the earth in the open firmament of heaven. And God created great whales, and every living creature that moveth, which the waters brought forth abundantly, after their kind, and every winged fowl after his kind: and God saw that it was good. And God blessed them, saying, Be fruitful, and multiply, and fill the waters in the seas, and let fowl multiply in the earth." (Genesis 1:20–22). "And God said, Let the earth bring forth the living creature after his kind, cattle, and creeping thing, and beast of the earth after his kind: and it was so. And God made the beast of the earth after his kind, and cattle after their kind, and every thing that creepeth upon the earth after his kind: and God saw that it was good." (Genesis 1:24–25). For its part, the religion of the *Flying Spaghetti Monster* or *Pastafarianism* is a social movement that emerged in the United States as a social protest to denounce and oppose the teaching, in public schools, of Christian creationism and intelligent design as an alternative to the theory of evolution. Bobby Henderson (a physics graduate from Oregon State University) sent a letter to the Kansas State Board of Education in which he expressed his faith in a god resembling a huge spaghetti ball with flying meatballs (*Flying Spaghetti Monster*) who created the universe after drinking too much and, because of the monster's drunkenness, the world is imperfect.

and is *seeded* by travelling through space on board meteorites which, when they fall on the right planet, cause life to germinate on that new planet. In fact, there are microorganisms capable of withstanding the conditions of life in space, such as large temperature contrasts or high levels of radiation. Hypothetically, if there had been life on another planet before Earth, a meteorite that had hit its surface could have launched organic material towards our planet. In reality, this hypothesis does not solve the problem of the origin of life, it only changes its location. There are many different theories about the origin of life on Earth's surface. Some examples are as follows:

- The *hydrothermal source theory*, which proposes that life originated in hydrothermal vents under the sea from inorganic materials (carbon monoxide, sulfides, etc.) at high temperatures and pressure. The first proteins could have formed under these conditions.
- *Glacial theory* postulates that 3700 million years ago, the Earth was covered with ice and that this ice acted as a protective layer for organic compounds.
- The *RNA world hypothesis* argues that RNA is responsible for the emergence of life on the planet. Experiments have been done with some clays that suggest that they could have helped the formation of RNA and fatty vesicles and that, together, they would have been able to form primitive cells.
- The *theory of simple principles*, which argues that the first organic molecules must have been simple—not molecules as complex as RNA.

However, these are all theories—3500 million years ago there was no one on Earth who could document what truly happened. Any of these theories could be valid since no theory is absolutely true, but at best, not disproved. How life appeared on Earth is an unresolved question. It may have arisen spontaneously, or it may have been "seeded" on the planet. Whatever the case, we know that the first forms of life that inhabited the planet were very simple and primitive unicellular microorganisms, bacteria and archaea, which even today continue to share the planet with us. How then did life reach the level of complexity that we know today?

The *endosymbiont* or *serial endosymbiosis theory* is quite well known and accepted. Proposed by Lynn Margulis as the origin of the eukaryotic cell, this theory describes how primitive microorganisms form symbiotic associations among themselves in a specific order, giving rise to more complex eukaryotic cells. The eukaryotic cell would be the result of those primitive microorganisms engulfing each other without digesting each other. Certain ingested bacteria would have been trapped inside the cell bodies of other cells, becoming organelles and resulting in more complex eukaryotic cells. Let us go back to Earth 3.5 billion years ago, that cruel and inhospitable planet, where the first forms of life appeared: prokaryotes (bacteria and archaea). This theory postulates that, first, a fermenting archaeobacterium (a type of bacterium that lives in warm, sulfur-rich water) fused with a swimming bacterium, giving rise to the last eukaryotic common ancestor LECA (Last Eukaryotic Common Ancestor). This one would be anaerobic, so it would live in muds and sludges, puddles, ponds, rock crevices, etc.—places where oxygen is scarce. Over time, the archaeobacteria would form the current cell cytoplasm, while the swimming bacteria would give rise to cell appendages such as cilia, flagella, or sensory protrusions. Later, in a second fusion, aerobic bacteria would be incorporated, which would be the origin of mitochondria. Finally, in a third fusion, green photosynthetic bacteria would be incorporated, thus generating the chloroplasts present in plant cells (Fig. 1).

However, Margulis did not stop there; she also developed the theory of *symbiogenesis*. Contrary to Darwin's theory, which argues that evolution occurs thanks to the appearance of modifications in the offspring (random mutations) followed by natural selection by competition, the theory of symbiogenesis argues that collaboration between species has been more decisive in biological evolution than competition. That is, it is symbiotic associations and not random mutations that drove evolution. In this regard, the term *symbiosis* refers to an association between two organisms in which both receive a mutual benefit; an example of this is lichens, which are organisms that arise from the association between a fungus and an alga. Within lichens, there are some that form a very simple association and others that form more complex structures. Corals, for example, are colonial animals that live in symbiosis with photosynthetic algae from which they obtain a large part of their energy. The Portuguese Caravel is a colonial organism in which each individual in the colony performs a specialized function (some are in charge of floating, others of hunting, others of digestion, others of reproduction, etc.). Without the resident symbiotic bacteria in their digestive tracts, herbivores would not be able to obtain energy by feeding on plants. Where is the limit? When does a colony cease to be a colony and become an individual with different specialized tissues? At what point do we consider that an organism and its symbiont, essential for its survival, become a single individual? The limit is usually at the level of communication between its cells. We humans like to classify things, put each one in a well-differentiated drawer, and give each drawer a name, but sometimes nature is not so organized. It does not classify or set the limits, rather it evolves and optimizes. When, in these associations, an organism lives inside another we speak of *endosymbiosis*, an example of which is bacteria that live inside some species of insects. These associations can become so close that the insect cannot survive without these bacteria. However, when we talk about *symbiogenesis,* we are taking it a step further. The association between host and symbiont becomes so close that the symbiont transfers part or all of its genome to the host, resulting in the appearance of new morphologies, tissues, metabolic pathways, behaviors, organs, organ systems, or other evolutionary novelties that make it better adapted to the environment than its individual components.

We could say that eukaryotic organisms present communities of prokaryotes that have coevolved and are closely integrated. We humans would be the result of a set of millions of highly specialized and intercommunicated bacteria collaborating in order to survive; bacteria are the forms of life that dominate the planet. Wherever there are plants there will be their chloroplasts obtaining energy from the sun and wherever there is an animal there will be their mitochondria providing energy. No individual (be it protist, fungus, animal, or plant) can survive without

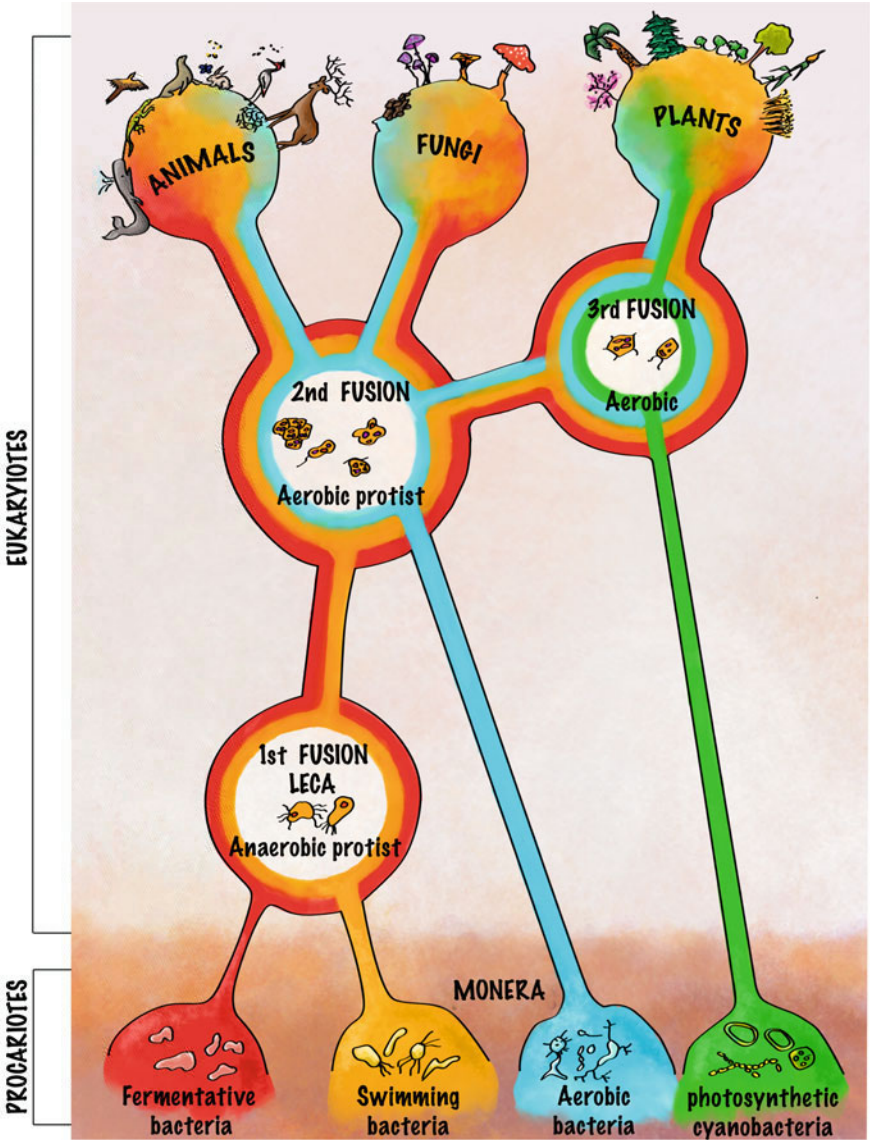

Fig. 1 Serial endosymbiosis theory. The most accepted theory postulates that the organisms that populate the Earth today are the result of fusions and associations of more elementary organisms. Through comparative studies, vestiges of these more primordial organisms can still be observed by analyzing the cells that compose us