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Mary Shelley, 1818

We are going to die. And that makes us the lucky ones.

—RICHARD DAWKINS, *UNWEAVING THE RAINBOW: SCIENCE, DELUSION AND THE APPETITE FOR WONDER*

Have we the right to counteract, irreversibly, the evolutionary wisdom of millions of years, in order to satisfy the ambition and the curiosity of a few scientists?

—ERWIN CHARGAFF

"MARY SHELLEY'S grave is many graves at once. Someone opening it would not find a regular human body but rather a different kind of creature, something akin to a monster." This is how Argentine writer Esther Cross describes the uniqueness of the English novelist's resting place; at eighteen years old, Shelley created what many consider the first science fiction novel. In her book *La mujer que escribió "Frankenstein"* (*The Woman Who Wrote "Frankenstein"*), Cross explores the writer's human side. Although very young when she completed that extraordinary narrative, Shelley had already experienced firsthand the elements that would shape the course of her novel.[1] The teenager

who gradually assembled the pieces of her story in early nineteenth-century London—a city filled with chimneys and shrouded in fog—grew up in an environment where both death and the possibility of defying it were omnipresent. In 1818, when *Frankenstein* was published (anonymously and with a preface by Percy Shelley, Mary's poet husband),[2] the trafficking of corpses in collusion with medical schools was a common and highly controversial practice in London's streets. It was well known that a fresh corpse could be stolen (on moonless nights) by gangs who would then deliver the bodies to doctors uninterested in asking too many questions. During that time, when Mary spent part of her days reading in Saint Pancras Cemetery while seated on her mother's grave, people could be seen standing guard for days over fresh graves. These were men paid by families to deter grave robbers until the body was no longer useful to medical professionals. But Mary Shelley was also aware that, in the same streets of London, there were those who claimed that they could bring executed criminals back to life. The law turned the bodies of the hanged into material for experimentation, and using electric batteries (the famous Voltaic piles), Giovanni Aldini briefly gained fame for his public demonstrations in which bodies—or their severed heads—seemed to regain the spark of life, whether by opening their eyes, breathing, or lifting an arm. These displays inspired not only immense fascination but also strong opposition, eventually leading to their prohibition.[3]

Thus is the writer usually portrayed alongside her horror story. But within that story, where the challenge is not just to defeat death but also to understand it, there is an often-overlooked element that speaks to us of Mary Shelley herself. Once the monster escapes from the laboratory and is rejected

by his creator, he must start from scratch, hiding from humans while trying to stay close to them so he can learn how to speak and write. The Hollywood films of the 1930s featuring Boris Karloff as the monster—with his characteristic neck bolts and clumsy movements, incapable of communicating with words—have left a lasting cultural imprint that does a disservice to the original work.[4] In the novel, the monster is also covered in scars and deformities, but he develops an intellect that allows him to grasp the abandonment he has suffered. The loss he has endured transforms into the desire for a companion like himself, also created from parts of other bodies. From the moment his mind awakens to life, what the creature seeks is an escape from solitude. Feelings of pain and loss—emotions Mary Shelley had experienced time and again—recur throughout the book. Her mother, the brilliant writer and essayist Mary Wollstonecraft, died from an infection just days after giving birth to her. Years later, Mary Shelley would also lose her daughter from her relationship with Percy, whom she had known since she was fourteen. The baby, born prematurely, died shortly after birth. The couple had to overcome many hardships and had three more children, only one of whom survived. Each time, Mary kept a lock of hair or a piece of clothing from her deceased child—a common practice at the time. When her husband drowned, his body was cremated (figure 1.1), but a mutual friend delivered the poet's heart to his widow, as it had apparently survived the flames. Mary wrapped it in the first page of one of his poetry books and kept it. A year after her death, these relics were found on her desk and were ultimately placed in her grave. As Cross notes, they were "her partial and anatomical ghosts," something akin to a diminished, inanimate family finally together in a tomb bearing one name and holding two hearts.[5]

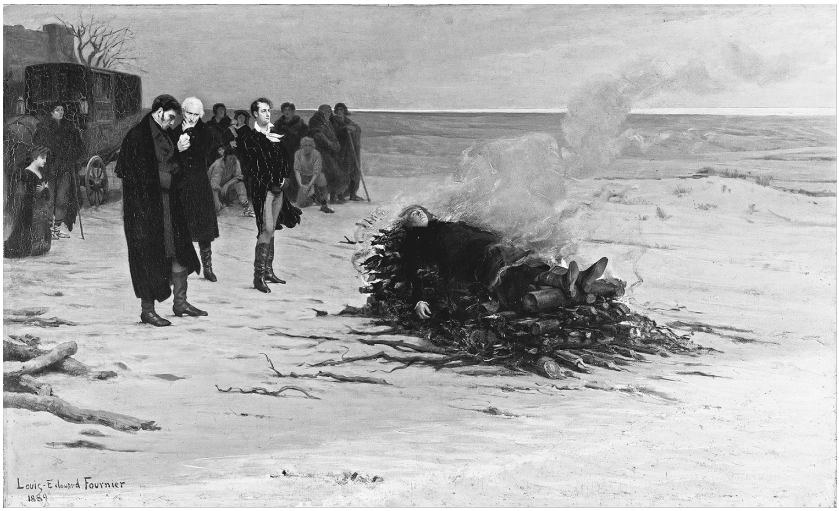

FIGURE 1.1 .*The Funeral of Shelley*. Painted by artist Louis Édouard Fournier in 1889, it depicts the premature death and subsequent cremation of the English poet, who drowned in 1822 off the coast of Spezia, Italy. The painting shows three of the poet's close friends, including Lord Byron (on the right).
© Album / Alamy Stock Photo.

What has been *Frankenstein*'s impact? The story of a scientist seeking the key to immortality, creating a human being from corpse parts and bringing it to life using electricity, has reached far beyond what its young author could have ever imagined. Within the pages of that Victorian tale, Doctor Frankenstein experiences an epiphany: "It was with these feelings that I began the creation of a human being." The dream of reviving inert matter found in morgues or hanging from the gallows does not lead to a happy ending. In this sense, the novel does not propose a triumph over death but rather serves as a warning about the dangers of reckless science. However, *Frankenstein* is

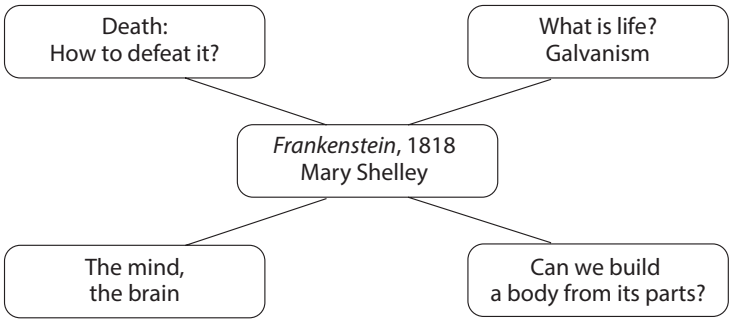

FIGURE 1.2. Four of the major questions that arise from or influence Mary Shelley's novel. These include the possibility of avoiding death, the understanding of life (in relation to electricity), the persistence of the mind and its relationship to the organ that generates it, and the possibility of "constructing" a living being from assembled parts.

much more than that; it has sparked debates and controversies that persist to this day, keeping alive the vision of a world where we might not have to face death. More than two hundred years later, we continue researching ways to better understand life and the nature of its end. Can we say that the ideas and implications arising from *Frankenstein* are still relevant? Without a doubt. One example of this influence can be found in *Jurassic Park*. In Spielberg's classic, based on the original novel by Michael Crichton, extinct creatures are also resurrected from remnants—this time, however, the fragments are of fossilized genomes trapped in their amber tombs.[6]

Philosophical and scientific speculations abound in the novel. Its four major themes raise fundamental questions (figure 1.2). The attempt to escape death raises the age-old question of immortality. The use of electricity to bring inert matter back to life prompts us to question the nature of life and the mind. Finally, the idea of creating a human being from stitched-together parts

serves as a primitive outline of what, in a sense, marks the early engineering of human material.

We can assess the relevance of the novel's themes by analyzing their impact. For this we will use a database containing millions of books, allowing us to measure the relative abundance of different keywords. Figure 1.3 shows the results obtained when searching for the terms *Frankenstein* and *Artificial Life*. In most cases, the frequency of a word tends to decline over time, indicating a loss of relevance.[7]

Here, however, Mary Shelley's work exhibits growth, reflecting its enormous impact and undeniable relevance. Far from fading, its influence has been extraordinary, and its use as a metaphor in various fields has steadily increased. Looking at the second timeline in the figure, the concept of artificial life gains significant traction after the book's publication, and its importance never wanes. Much later, in the second half of the twentieth century, with the advent of genetic engineering in the early 1970s, *Frankenstein* surfaces once again. During the intense debates of that period, the novel's underlying message of humility before nature is revisited. Erwin Chargaff, for instance, one of the pioneers of molecular biology, warns us:

> This world is given to us on loan. We come and we go; and after a time, we leave earth and air and water to others who come after us. My generation, or perhaps the one preceding mine, has been the first to engage, under the leadership of the exact sciences, in a destructive colonial warfare against nature. The future will curse us for it.[8]

During the 1950s, with the development of the first computers, the myth of the monster is retold—this time in terms of inanimate matter. Can we create an intelligent being from the components we use to design a machine? So far, nothing of the

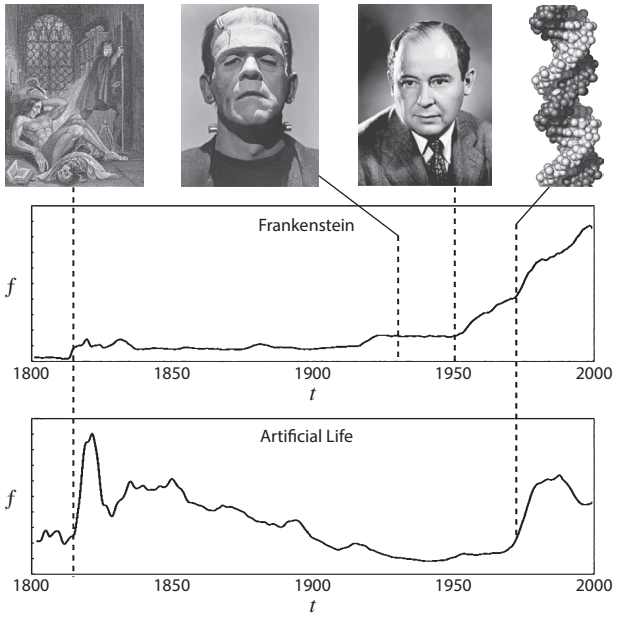

FIGURE 1.3. The growing impact of Mary Shelley's novel *Frankenstein* can be measured using the Google Books Ngram Viewer, which allows us to determine the relative frequency of a word or phrase within a database containing millions of books. The frequency of the term *Frankenstein* has shown a continuous upward trend, as illustrated here alongside key milestones. From left to right: the publication of Shelley's book in 1818, its film adaptation starring Boris Karloff (1931), the emergence of ideas about self-replicating machines (suggested by Von Neumann around 1950), and the development of genetic engineering. For comparison, the same analysis is shown for the term *Artificial Life*. Images, left to right: © Album / Alamy; © Bridgeman Images / Album; Los Alamos National Laboratory / Science Source; Created using Pymol Software.

sort has happened. But the idea has also emerged of creating a machine capable of doing something only living systems can do: reproduce. The great mathematician John von Neumann wanted to know what it would take for a machine to make a

copy of itself.[9] During the same era, cybernetics and information theory were born and developed, laying the groundwork for artificial intelligence. As computers became more powerful, they began to mimic some brain functions. In 1971, with the publication of the first scientific paper presenting the possibility of manipulating genetic material—adding to or removing an organism's genes—a new domain of knowledge was created: genetic engineering. This field revisited many of the earlier questions and proved that living matter could indeed be modified. With the emergence of synthetic biology in the early twenty-first century, Shelley's narrative became a reality on a molecular scale.[10] Now the assembled parts are genes, and the final product is a cell with properties and behaviors that do not exist in nature. Thus, before considering the death of the individual, we must examine the death of life's fundamental unit: the cell.

The French biologist and Nobel Prize laureate in medicine François Jacob once said that "the dream of every cell is to become two cells." In most cases this is true. Cell division is one of the essential mechanisms required to regenerate our organs and tissues. Unlike machines, we require not only maintenance but also constant renewal, which entails a continuous consumption of energy and matter. Metabolism converts these into stable structures capable of growing and multiplying. The second part of this process, equally necessary, determines the ultimate fate of all our cells: their death. What is the scale of this process for us humans? The answer is that cellular mortality is constant, massive, and inevitable. Estimates are that every second, a million cells die in our bodies. If we sum up their weight over just one day, we are talking about approximately a kilogram of dead cells that must be processed and eliminated. This balance between cell birth and death is a key and unavoidable

property of complex life. Maintaining the proper equilibrium is crucial to preventing disease. In a way, we could say that our body is a special kind of machine whose architecture remains consistent over time while nearly all its components change. An enviable property that keeps many bioengineers awake at night: Could we create custom-made machines whose components could self-regenerate when necessary? It is also one of the greatest nightmares faced by biomedicine. In order to regenerate and repair tissues, the processes of proliferation (cell growth), along with control mechanisms, must always remain active. As life progresses, however, the chances of control failure increase. When the balance is broken, illness arises.

Although this book explores the problem of death within the context of systems—whether cells, organisms, machines, or languages—we can begin our journey by examining the simplest systems, those formed by a single autonomous cell. Anyone with a microscope and a drop of pond water has the opportunity to observe different species of single-celled organisms, such as paramecia or amoebas, actively moving in search of food. At times, one of these organisms may appear to have completely stopped, and we can observe drastic changes in its structure and shape. The before- and after-death images in figure 1.4 are taken from a video by photographer James Weiss, which shows an organism in motion with clearly visible internal organelles (figure 1.4a). At some point in the video, however, we see it stop. We might assume that it has entered a dormant state to conserve energy—a common phenomenon in nature—but after a few seconds, we realize that life has ceased. In an instant, the separation between the inside and the outside of the organism seems to disappear (figure 1.4b). Although we can still clearly see all the internal structures that once coordinated its actions, something has gone terribly wrong. All

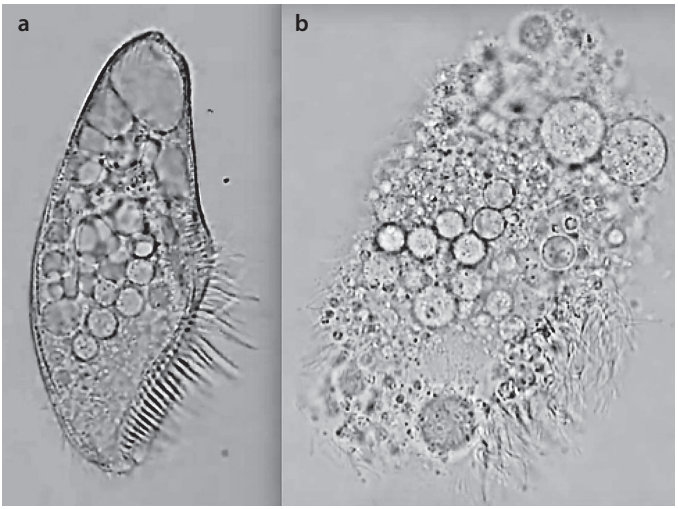

FIGURE 1.4. Death of a single-celled organism. The living state of any organism requires the convergence of multiple mechanisms in order to remain stable. Here we see a single-celled organism before (a) and after (b) its death. The images are separated by only a few seconds. While the integrity of many structures is still visible after death, the separation between inside and outside has disappeared.
© James Weis.

indications suggest that death has occurred. If this is the case, how can we be sure? In this realm of simplicity, cells have provided us with essential clues to address the very problem that Shelley posed.

The first answer to the question of what it means to die comes from our modern understanding of life, which tells us that the complexity of living matter depends on maintaining highly dynamic structures—life is a process. How can we prove this? The idea proposed by American biophysicist Harold Morowitz in 1955 was based on the following experiment: A living cell can be frozen at extremely low temperatures until its entire structure becomes solid once the water has been

removed.[11] In every imaginable sense, the cell would be "dead"—it does not respond to its environment, process information, or reproduce. However, when water is added and the temperature is raised to ambient levels, the bacterium returns to its normal dynamic state. Or, as we like to say, it "comes back to life." Freezing has been a constant process on our planet, and in fact, global warming is now awakening countless microbial species from their dormant state—species that have remained trapped in polar ice for millennia. This simple experiment teaches us that for a living system to function, interactions among its components must be set in motion and maintained. It is these interactions that ultimately define death at a microbial scale. In particular, there is a crucial molecular process whose failure leads to lethal consequences. It is one of the key mechanisms that enabled the emergence of the first cells and is essential for their evolution as autonomous systems. This process involves active transport mechanisms occurring in the membranes of all cells—from those that move through a pond in search of food to the neurons transmitting impulses across the brain. Using proteins anchored to the cell surface, which defines the boundary between external and internal, these transporters create differences in ion concentration (figure 1.5). Much like a waterfall, where the height difference allows water to flow in one direction (generating energy), these mechanisms influence the movement of required molecules either into or out of the cell. These inflows and outflows drive many processes that keep the cell away from equilibrium. They allow cells to capture the molecules necessary for metabolism or, in the case of neurons, generate electrical impulses. When these flows cease, equilibrium is restored, and the distinction between inside and outside vanishes.[12] Once the equilibrium is achieved, the processes that sustain the living state come to an

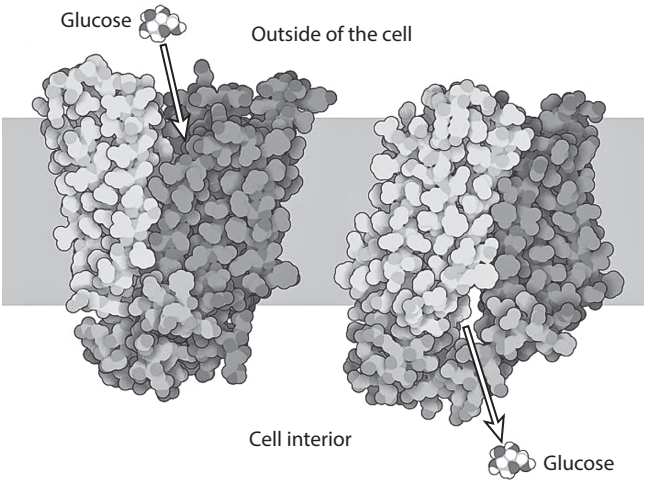

FIGURE 1.5. What causes cellular death? Although various mechanisms—such as viral infections or genetic defects—may play a role, the inability to maintain different concentration levels in the interior and exterior of the cell ultimately leads to the cessation of cellular activity and, eventually, to the death of the cell. The image is a diagram of a protein that spans the membrane (gray horizontal band) and facilitates the transport of glucose from the outside to the inside of the cell. To accomplish this, the protein requires an energy input, enabling it to change shape and transfer glucose into the cell.
© David S. Goodsell, RCSB Protein Data Ban.

end. However, as we will see, the situation remains reversible for a certain time.

This is merely the first link in the hierarchy of organization within a complex organism. Can we extrapolate from the cellular level to understand complex organisms? Many years after Morowitz's proposal, a real-life accident involving human beings reproduced the conditions of his experiment: People who had been submerged for hours in near-freezing waters were successfully revived. Furthermore, individuals who had

experienced severe hypothermia and showed no vital signs—neither pulse nor brain activity—were able to recover without suffering long-term complications. Ongoing research on using deep hypothermia, combined with appropriate organ preservation fluids, confirms that such reversible states can be induced under experimental conditions. The method has been tested on pigs, in which massive hemorrhages leading to clinical brain death were induced. Under controlled conditions, the pigs underwent a state of hypothermia for an hour, after which their bodies were gradually warmed and cardiopulmonary bypass was performed, restoring normal physiological conditions. Remarkably, none of the animals exhibited detectable neurological deficits or cognitive impairments once revived. The brain, whose activity had completely ceased, regained its full function—cognitive abilities returned intact. Much like the frozen cell whose molecular machinery restarts, an entire organism in a frozen state retains the necessary elements to recover its normal state as soon as its processes—this time across multiple scales—resume.[13]

It is no surprise that these clinical cases have caused a renewed interest in the possibility of reviving frozen bodies after subjecting them to procedures that adequately preserve tissues. Some researchers have attempted to develop technologies to make this idea a reality. The company ALCOR, based in the United States, has been a pioneer in this field, although the reliability of its methods and their potential outcomes remain controversial. With more than 150 bodies stored (which the company prefers to call "patients"), it offers the hope that, in the future, it may be possible to thaw individuals without harm through a process known as "vitrification." The process requires the convergence of several highly complex conditions. The subject must undergo the necessary procedures as quickly

as possible—because the brain can suffer damage—making it particularly important to replace a large portion of intracellular water with glycerol, a compound that prevents the formation of ice crystals.[14] This concept has been a trope of science fiction books and movies. One of the best examples is Woody Allen's satirical comedy *Sleeper*,[15] in which the protagonist is mistakenly frozen (after what was supposed to be a routine tonsillectomy) and wakes up two hundred years later in a world where cloning and domestic robots are commonplace (and where a Volkswagen abandoned in a cave for two centuries starts up on the first try). This, of course, is a work of fiction, but hibernation occurs naturally in many organisms, which profoundly alter their physiology to withstand the hardships of winter. Surviving periods of scarcity has been a driving force in the evolution of many species, which must always adapt their way of life to the environmental conditions available to them. In temperate climates where periods of warmth and cold alternate, temperatures approaching freezing point, accompanied by a reduction in available resources, demand drastic changes in energy consumption. The bodies of animals that cannot regulate their body temperature, such as amphibians, reptiles, and insects, can become solid structures when temperatures drop below freezing. In such cases, evolution has led to the development of special molecules that prevent the formation of ice crystals, which would otherwise irreparably destroy cell structures. For organisms that can regulate their temperature, the strategy is clear: To prevent cardiac arrest, when resources are scarce and heat must be produced to compensate for its loss, body temperatures must be allowed to drop closer to ambient levels, thus significantly reducing the energy expenditure required to maintain ion gradients and the integrity of cellular membranes (which would rupture if

frozen). This process results in a near-death state that appears to have significant advantages. But why has this strategy not been adopted more broadly? Why don't humans, in particular, undergo this form of temporary death? The answer to these questions lies in the study of metabolism in relation to body mass: As body mass increases, the metabolic needs per unit of biomass decrease rapidly.[16] In other words, once a certain body size is reached, complete hibernation may become less advantageous, which is why it is rare in animals larger than five kilograms.[17]

Although the apparent state of some politicians during legislative sessions might suggest otherwise, attaining a sustained and reversible condition of minimal metabolism is no easy feat. Edgar Allan Poe speculated on the possibility of inducing such a state through hypnosis. In his short story *The Facts in the Case of M. Valdemar*, a patient on the verge of death is hypnotized so that he may linger in a kind of limbo between life and non-life—a state closely resembling hibernation, in which everything is suspended.[18] Similar scenarios are depicted in films about long interplanetary voyages: in *Alien*, the crew of the *Nostromo* awakens from a long-induced slumber, and the same happens to the astronauts in *Planet of the Apes*. In *Passengers*, the crew must wait a hundred years in their enclosed pods before they can become settlers on a distant planet. Hibernation offers an opportunity to travel not only through space but, above all, through time. In *Passengers*, the protagonist—a journalist played by Jennifer Lawrence—plans a temporary journey: after reaching the planet set to be colonized, she intends to return to Earth. Upon waking from her adventure, she will witness our future world, as two hundred years will have passed. For some advocates of cryopreservation, this possibility is one of the main incentives for undergoing the process.[19] So, will the dream

of being frozen and returning to consciousness in a future world ever come true? Yes and no.

Assuming the necessary technology can be developed, the dream of "waking up again" after all activity has ceased is, in truth, an illusion. In fact, hibernation entails a subtle—yet real—form of death. To understand this, let us consider a thought experiment we'll call "the replica problem." Imagine someone could make an exact (and instantaneous) copy of your body. The replica is identical to the original and therefore possesses exactly the same memories and the same personality—generated by the exact same brain. The creator of the replica then proposes that, because the copy is perfect and indistinguishable, the original can be sacrificed without consequence. Would we accept such a deal? Obviously not. Each of us—replica or not—experiences a subjective and irreplaceable consciousness. Our elimination is not harmless, even if a copy exists that is indistinguishable from the human originally used to create it. The reason is simple: every copy of the hardware—the physical brain—gives rise to a subjective conscious experience. Although it may not seem so, the situation is equivalent for individuals who have been frozen and later reanimated in a distant future. Their brain activity has ceased completely. Suppose we were to replace that solidified lump of gray matter with an exact replica. What difference would there be from the original? Absolutely none. If we were now to awaken the body carrying this identical brain, we would witness the return to life of the original mind that once inhabited it. Yet, from a subjective standpoint, it would not be the same: the consciousness that emerges is necessarily different. In reality, there is no possible awakening.[20]

In Shelley's work—and in that of many other authors—the ultimate goal is immortality. Death must not happen. But defying it requires solving other problems that may have no solution

at all. The passage of time brings with it the aging of tissues and organs. And there is no way that *The Curious Case of Benjamin Button* could come true—unless the rules were to be broken, as happens with cancer.[21] For physicists, the issue must be reframed in terms of entropy and the second law of thermodynamics. All systems in the universe inevitably move toward a state of disorder over time. This idea is often illustrated by watching a film in reverse: We smile when watching someone rise out of a swimming pool, the water's surface flattening as the diver returns to the diving board. None of this can happen in the real world. By the same logic, we will not see our faces grow younger in the mirror as the years go by. Within this overarching framework in which everything (including the universe) must die, there seems to be little room left for immortality.

Is it possible to bring a dead body back to life? The case of cryopreservation is somewhat exceptional, as no damage prevents normal function from being restored once the proper conditions are reestablished. Later, we will examine the concept of life's end in the context of the mind, but some opportunists—driven by the obsession for profit or fame—have not required such reflection. One particularly egregious case occurred in 2017 in the United States, involving the Philadelphia-based company Bioquark.[22] This corporation promised true resurrection for patients who had entered a state of irreversible clinical death following massive brain damage, often caused by a stroke. The unfortunate fate of these individuals is to be kept alive by artificial respiration—in a state of living death—until the decision is made to withdraw life support. Irreversibility is the result of damage to tissues, as well as to the communication between various brain centers, making any form of recovery impossible. The sharp-minded members of Bioquark, however, saw a business opportunity under the

pretense of using "advanced stem cell–based techniques" or by resorting to "electrical brain stimulation" and "laser therapies." To all this the company added a protein cocktail—because, of course, proteins and their magical effects couldn't be left out—and thus put forth a proposal as absurd as it was effective. Who wouldn't invest their money to try the impossible? Bioquark promoted its idea and quickly garnered media attention with the promise of a revolutionary treatment that could "bring the dead back to life." Despite the company's efforts to embellish its language with a thin veneer of science and frame the endeavor as an experiment, its plans to conduct clinical trials on patients were ultimately banned: the proposal rested on no scientific foundation (one obvious problem was the complete absence of prior animal testing) and merely served to foster false hope among grieving families.[23]

Setting aside these charlatans—hovering somewhere between fiction and reality—our understanding of the nature of death continues to evolve, and there is still room for surprise. A striking example comes from so-called zombie genes, something that surely would have intrigued Mary Shelley and fits perfectly with the idea of understanding death to understand life. During a study on cellular responses following the death of an organism, researchers discovered that, contrary to all logic, certain genes became active and remained so for days. One particular study, which used brain tissue extracted during neurosurgery,[24] showed that this tissue—technically speaking, dead—contained cells whose genetic activity increased over the course of an entire day. This occurred in a type of cell essential to maintaining neuronal function: neuroglial cells (or glial cells). Unlike neurons, these cells—far more numerous—can reproduce under normal conditions and play a vital role in the brain by supplying nutrients and structural

support. Why do they activate? Their function under normal conditions offers a partial explanation. Among other tasks, glial cells must respond to potential cellular damage that may occur over a lifetime, whether from drops in oxygen supply or from a stroke. The response to tissue death—an extreme stress condition—involves the activation of these cells, although this activation is limited to the expression of their genes. The response is transient (lasting no more than twelve hours) and coincides with the progressive degeneration of neurons, as the genes essential for brain function begin to shut down. A curious combination of hope and defeat.

Two centuries after *Frankenstein,* our approach to the mysteries of life and death rests on a view of biological complexity in which systems—rather than parts—play a central role. In figure 1.6, we see the modern counterparts to the Victorian science outlined earlier in figure 1.2. Death is part of a broad spectrum of phenomena tied to an organism's homeostasis and its response to the passage of time and to stress. In this area, we have learned a great deal about how such systems normally function and especially about pathological states, such as cancer. Tumor cells represent everything that our tissues and organs must avoid—particularly from an evolutionary perspective. For the body to function properly, there must be stable cooperation of all its parts, beginning with the cells. Some cells, owing to mutations, cease to follow regulatory rules and begin to reproduce too rapidly. Some discover (once again, Darwinian evolution) mechanisms to escape control. One of these mechanisms (as we'll see in the next chapter) is none other than immortality. At the same time, advances in the science of complex networks have enabled the development of a new perspective on processes that occur across vastly different scales—from cells to brains.[25] Far from viewing these systems as

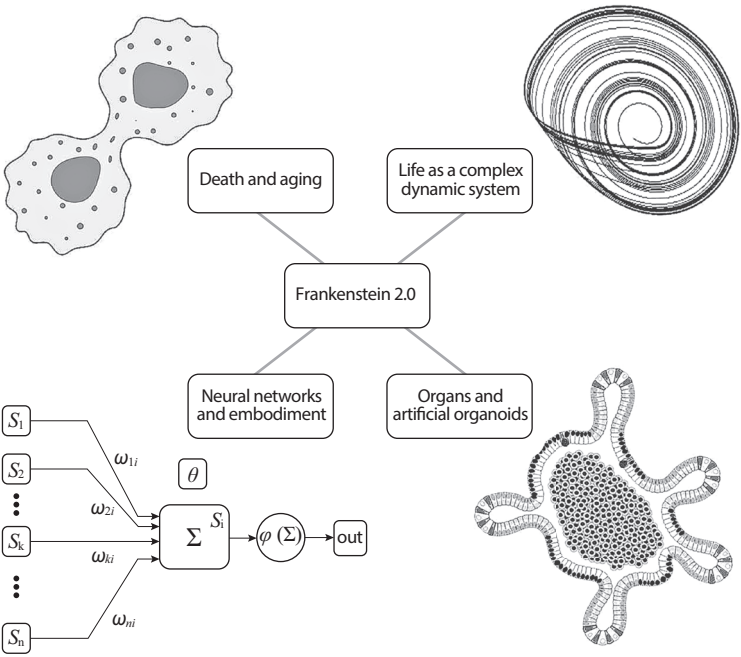

FIGURE 1.6. A current view of figure 1.2, representing a version 2.0 of the problems raised in *Frankenstein*. In the modern scientific view, death is deeply connected to the biology of aging, life is understood in terms of nonlinear networks and systems, the mind and the brain are examined through the lens of neural networks, and the possibility of creating a human being from assembled parts is reinterpreted as the creation and interconnection of artificial organs.
All images © Author Archive.

separable into disconnected parts, the emerging perspective connects us to the complexity of the world and of life, in particular.

Finally, returning to Victor Frankenstein and his attempt to reconstruct a body from parts obtained from corpses, a new discipline within bioengineering points to the potential of

designing what are known as "organoids." These are derived from individual cells and are miniature models of various organs, which can remain alive for extended periods. Without going into detail, this technology relies on the ability to *reprogram* cells to convert them into pluripotent stem cells—cells capable of giving rise to any specialized cell type.[26] Each organoid is created under specific conditions and remains very small (hundreds or even thousands of times smaller than the actual organ), but under a microscope, organoids exhibit the fundamental features of livers, kidneys, lungs, pancreases, or brains. In addition to having the right cell types for each tissue, they also display spatial structures that replicate key aspects of the target organ. In the case of the brain, we can observe layers of neurons organized within a "mini brain," where researchers can study various properties of the full brain, although these mini brains are far from having the cognitive capacities that define the organ of thought. Much research is still needed before organoids can reach the size and functional complexity of the organs they aim to mimic, but they are already extraordinary tools for studying physiology and disease development, and testing potential treatments. Among current developments, one stands out that allows us to close this chapter by returning to its opening question: Can we recreate an entire organism through the combination of organoids? To do so, we would once again need to assemble the different parts to generate the equivalent of an individual. The technology of so-called microfluidic chips provides the foundation to make this possible. These chips, only a few centimeters in size and commonly used in bioengineering, allow for the separation of various cell populations, which are then connected through channels that carry nutrients, growth factors, and other molecules required to

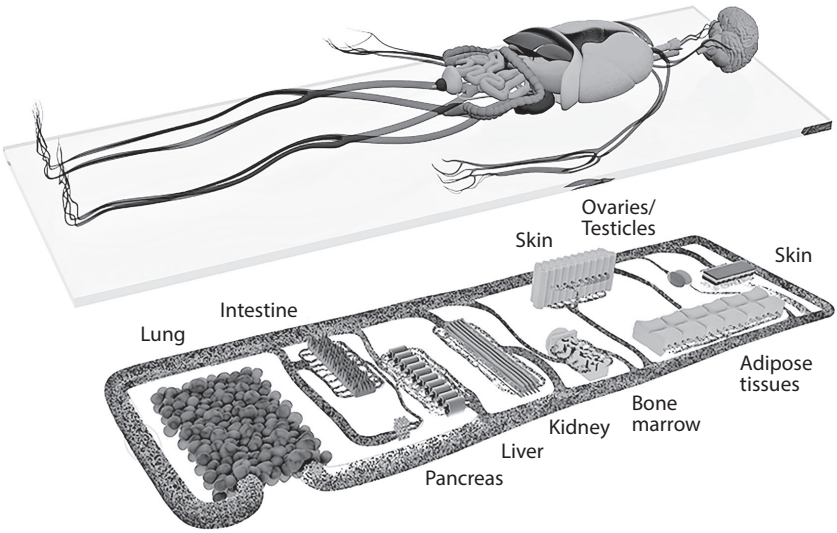

FIGURE 1.7. A modern analogy to a human being assembled from body parts is offered by the "human-on-a-chip." In this system, based on microfluidic chip technology, the body is replaced by a set of organoids that emulate each of the real organs and are interconnected by a fluid, which can be artificial blood. The fluid is pumped through the chip by a computer-controlled system. Although the two images are shown at the same scale, the chip is actually a hundred times smaller.

sustain the function of the different tissues. By placing different organoids in separate chambers within one of these devices—each chamber providing the necessary conditions—we can design what has already been called a "human-on-a-chip," as illustrated in figure 1.7.[27] While these artificial systems are far removed from the drama of grave robbers, lack the capacities and perceptions of a real human being, and exist on a minuscule scale, they will very likely shed some light on what enables a

complex living organism to coordinate its many functions with a reliability that surpasses that of any machine.

On this long journey—from the notebooks of a teenage girl seated in Saint Pancras Cemetery to the engineering of tissues and stem cells, two things have remained unchanged. The first is the enduring question of whether the end of life can be avoided. The second is the spirit of inquiry that drove young Victor Frankenstein to attempt the impossible—and that has never ceased.[28]

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