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A Computational Approach

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To,
Sri Aurobindo and the Mother

Preface

"The human brain is the most complex organ in the body" "The brain is the most complex thing in the universe," and therefore, "We won't be able to understand the brain." This is just a tiny bite of unqualified, unreasonable adulation that the brain receives in popular literature. There is a rather unhealthy tendency in popular media to portray the brain as some sort of a god-organ. It creates around the brain an agnostic mystique, an impenetrable aura that is only meant to be admired but never understood.

The vague and confusing explanations of brain function that are often offered by textbooks, and therefore by experts alike, do not help to dispel the mystique. For example, planning and coordination are said to be the functions of the prefrontal cortex, but cerebellum, the textbooks tell us, shares the same functions. Similarly, memory is said to be the function of both the prefrontal cortex and hippocampus. But why does the brain engage multiple systems to perform the same duty? Consider another example of an explanation that does not explain much. The thalamus, a massive portal to sensory information streaming into the brain, is called a "relay system" which means that the thalamus merely passes on the influx of signals beyond. But why does the brain need a whole complex organ to pass on incoming signals intact; a bundle of fibers would do the job. In such situations, as in a thousand others, the eager student of neuroscience is quickly told answers to a large number of questions of "what" category, but rarely "how" and almost never "why." Such a fundamental restriction makes the brain, despite all goodwill and intent to understand on the part of an earnest student, unfathomable.

The reason behind this mysteriousness of the brain is not merely its complexity, as popular media again would like us to believe. The A380 and the International Space Station are no doubt some of the most complex systems that humans have ever created. But we are able to handle and master that complexity because we know the underlying physical principles. The complexity in the details can be effectively handled by organizing manpower or by the use of computational power. Complexity can be mastered by comprehending the principles. When we separate principles from the details, the complexity does not disappear but merely ceases to be intimidating. The sense of jaw-dropping wonder gives way to satisfaction that comes from perfect understanding.

But when it comes to brain science, the distinction between principles and details varies from being weak to nonexistent. One wonders whether it is not just brain science, but a good part of biology that suffers from this tendency. The strongly descriptive and information-rich traditions of biology—particularly classical biology—stand in stark contrast to modern physics and engineering where the principles are primary, and the details are handled effectively and effortlessly thereof.

This near lack of discrimination between principles and details in biology has been brought to fore by molecular biologist Yuri Lazebnik in a regaling article titled: “Can a biologist fix a radio?—Or, what I learned while studying apoptosis.” Lazebnik considers a quaint thought experiment of how a biologist would proceed to understand the operation of a radio. Since biologists do not believe that physics can be of much use in their pursuit, they launch their own, unique biology-style attack on the problem of the radio. First, they would get enough funds and procure a large number of radios. They would then embark on a bold study of the radios and their constituents in gruesome detail. The vast universe of radio components—yellow and blue, spherical and cylindrical, striped and otherwise—is painstakingly mapped and embedded in an impressive taxonomy. That consummates a valorous course of structural research on the subject.

Next follows a functional study. Our biologists with their unflagging energy would now begin to pluck out components of the radio one at a time and study the effect of the missing component on the radio’s key function—to produce intelligible sounds. This new line of effort may reveal that certain components are not crucial, since when these are plucked out, the radio sputters and hisses but does not fail to make itself heard. But there are other components—perhaps a wire that connects the circuit board to the battery—in whose absence the radio is practically dead. The discovery marks a tremendous breakthrough in our biologically inspired study of the radio. It is doubtful if this line of research would consummate in a humanly meaningful time frame.

By contrast, the study of radio that is armed with a prior understanding of physical principles of the radio would proceed very differently. Basically, a radio picks up electromagnetic signals from the ambience, amplifies them, converts them into audible sounds, and plays them. Each of these steps requires a certain device, a mechanism, which can take a variety of possible physical implementations. But once we know the framework, the overall pattern, we would look for the substrates for that pattern in the physical system and quickly identify them. While a biology-style investigation may take decades to unravel a radio, an approach based on an understanding of the underlying principles, assuming they are readily available, might take a week or two, even in case of a radio of an extremely novel design.

What then is the situation in neuroscience? Do we deal today in terms of principles of brain function, or are we willingly stuck in the quicksand of details? A revolution has begun in brain science about three decades ago, though the first seeds have been sown more than half a century ago. The goal of this revolution is to answer every possible "why" about the brain, by unearthing the principles of brain function. It has given us the right metaphor, a precise and appropriate mathematical language which can describe brain's operations. By the application of these principles, it is now possible to make sense of the huge sea of experimental data, resolve long-standing points of confusion, and truly begin to admire the architecture of the brain. To borrow an analogy from astronomy, the new mathematics is drawing us away from the era of "epicycles," ushering in the era of "inverse square law and Lagrangian dynamics."

Researchers of the new computational and mathematical neuroscience have unearthed a small set of principles of *Neural Information Processing* as they are often called. As it happens in physics, researchers succeeded in explaining a wide range of neural phenomena with the same compact set of principles. That set may not be complete. There might be other principles yet to be discovered. But what has already been discovered is enough to create confidence in the existence of such a complete set. The first of these principles is the idea that information is stored in the form of strengths of connections among neurons in the brain, and learning entails appropriate modification of these connections. There are precise rules that describe such modification. Then, there is the idea that memories are stored as persistent states, the "attractors," of brain's dynamics or the idea that synchronized activity of neurons in distant parts of the brain has a great significance, not only to sensory-motor function, but also to more intriguing phenomena like conscious awareness. There are some more.

This book is about the neural information processing principles, since the aim of this book is to demystify and deconstruct the brain. Chapter 1 in the book, as it presents a brief history of ideas about the brain, also introduces some of the key ideas and concepts. Chapter 2 sets out to understand the logic of brain's anatomy. It takes the reader on a quick journey through the evolutionary stages in the brain and seeks to explain some of the broad stages in that development using the minimum wire principle. Chapter 3 is an introduction to the neuron and mechanisms of a neuron's electrical and chemical signaling. Chapter 4 takes up the neuron model just introduced and presents a simple mathematical model of the same. Using this neuronal model, Chap. 4 shows how to construct complex networks that can explain a variety of phenomena from psychology. Chapters 5 and 6, on memory and brain maps, respectively, use mathematical models to explain how memories are represented in the brain and how the formation of brain maps can be explained. Chapters 7 and 8 describe the architectures of the brain systems that process vision and touch senses, respectively. Chapter 9 is about motor function, about the brain makes life go. Chapter 10 presents a history of theories of emotions and introduces some of the key neurobiological substrates of emotion processing. Chapter 11 on language deals with the essential language circuits in the brain and describes how words are represented and produced. It does not discuss more advanced aspects of sentence-level processing. Chapter 12 takes up the conundrum of consciousness from a neuroscience perspective. After briefly touching upon several philosophical approaches to the problem, it presents some elegant experimental approaches to this intriguing question, concluding with an outline of some of the contemporary neuroscientific theories of consciousness.

Chennai, India V. Srinivasa Chakravarthy

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Contents

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V. Srinivasa Chakravarthy obtained his Ph.D. from The University of Texas at Austin and completed his postdoctoral training at Baylor College of Medicine, Houston. He is currently a professor of biology at the Indian Institute of Technology Madras, India. His research interests are in the areas of computational neuroscience and machine learning. In computational neuroscience, his research focuses on the modeling of basal ganglia to understand Parkinson's disease, modeling of neuron-astrocyte-vascular networks, and modeling of spatial cells of the hippocampus. Further, his work on character recognition in Indic scripts led him to develop the Bharati Script—a simple and unified script that can be used to express all major Indian languages.

Chapter 1
Brain Ideas Through the Centuries

> *My hand moves because certain forces—electric, magnetic, or whatever 'nerve-force' may prove to be—are impressed on it by my brain. This nerve-force, stored in the brain, would probably be traceable, if Science were complete, to chemical forces supplied to the brain by the blood, and ultimately derived from the food I eat and the air I breathe.*
>
> —Lewis Carroll (1832–1898), from *Sylvie and Bruno*, 1890.

The Beginnings

The story of what the human brain thought of itself over the millennia would be a very interesting read. From the days when men were not even certain about the status of the brain as the seat of mind and intelligence, to the present times of gene therapies and deep brain stimulation, brain science has come a long way. Like any other science history, history of the brain is a history of errors in our ideas about the brain. A study of historical questions in this science, followed by an account of some of the questions answered (or remain unanswered, like the vexing question of "consciousness") in contemporary thinking, helps us arrive at a balanced and realistic perspective of contemporary knowledge in neuroscience.

The father of Western medicine, Greek physician, Hippocrates (460–379 B.C.), believed, as we do now, that brain is responsible for sensation and is the seat of intelligence. Plato, who is known to us for his ideas of the republic, for his imaginings of an ideal society, for his memorable dialogues in philosophy, also thought of brain on similar lines. But his famous disciple, Aristotle, who held views (many of them dead wrong) on a wide variety of physical phenomena, believed that the *heart* is the seat of consciousness. Perhaps, he was guided by a common medical fact that a body can survive a dead brain but not a heart that had stopped beating.

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Fig. 1.1 Greek physician Galen

Among the ancient Greek scientists, substantial progress in understanding of the brain, particularly its structure, was achieved by Galen, one of the first Greek physicians (Fig. 1.1).

At Galen's time, the clinical medical practice was in a sort of a disarray. There was no sound scientific framework to guide clinical practice. While many blindly followed the Hippocratic tradition, others (like some present-day "holistic" clinics) used "healing music" and magical chants. A religious injunction of those times, that forbade the use of human cadavers for anatomical studies, seriously constrained progress. This forced Galen to study animal cadavers and extrapolate those observations to human anatomy. He mastered the art of dissection, wrote extensively and laid foundations to anatomical tradition. For example, in his book "On the brain" he gave precise instructions regarding how an ox' brain has to prepared and dissected:

> When a [brain] part is suitably prepared, you will see the dura mater… Slice straight cuts on both sides of the midline down to the ventricles. … Try immediately to examine the membrane that divides right from left ventricles [septum]. … When you have exposed all the parts under discussion, you will have observed a third ventricle between the two anterior ventricles with a fourth beneath it. …

Guided by prodigious anatomical studies, which earned him the title "restorer of anatomy," Galen learnt a lot about the structure of the brain. As the above excerpt indicates, he knew about the ventricles, the pia mater, and the hemispheres. He knew about the autonomous nerves that control internal organs like the heart and the lungs. He knew of the somatic nerves that control, for example, the vocal cords. (By snapping these so-called “nerves of voice,” he demonstrated how he could silence bleating goats and barking dogs.) But when it comes to brain function, he erred deeply. A microscopic study of brain function needs a technology that would come one and a half millennia later. Thus he only speculated on brain function. He believed, just like his predecessors like Erasistrasus and others, that there exist certain “winds”—the *pneumata*—or animal spirits that surge through the hollows of the nerves and produce movement. When there are no bodily movements, these unemployed “spirits” lodge themselves in the ventricles of the brain. Thus Galen considered the ventricles to be the seat of the “rational soul.”

Galen’s case is quite representative of a line of thinking, of a puzzling dichotomy, that prevailed for nearly one and a half millennia (if not longer) in the world of neuroscience. There was a longstanding dichotomy between knowledge of structure versus knowledge of function of the brain. Those that came later in Galen’s tradition, da Vinci, Vesalius, and other great anatomists, constantly reconfirmed and expanded anatomical knowledge. But when it came to brain function, the archaic ideas of animal spirits and pneumata lived on perhaps too long. In a sense, this dichotomy in our knowledge of brain structure as opposed to that of brain function, survives even to this date. (We now have extremely detailed 3D anatomical maps of the brain, but we do not know, for example, why the Subthalamic Nucleus is the preferred target of electrical stimulation therapy for Parkinson’s disease.) The right insights and breakthroughs in our understanding of brain function, the right language and metaphor and conceptual framework, emerged all within the last half a century. These new ideas have hardly yet impacted clinical practice. We will visit these ideas, which are the essence of this book, again and again.

Leonardo da Vinci: This great artist, the creator of the immortal Monalisa, had other important sides to his personality, one of them being that of a scientist. The human cadavers that he used in his artistic study of the human figure, also formed part of his anatomical studies. His studies earned him a deep knowledge of brain’s anatomy. He likened the process of dissection of brain to the peeling of layers of an onion: to get to the brain, you must first remove the layer of hair, then remove the scalp, then the fleshy layer underneath, then the cranial vault, the dura mater… In the artist’s view, these are the brain’s onion rings. Leonardo too, like his predecessors, had knowledge of the ventricles. And like his predecessors, he erred by attributing a deep cognitive function to ventricles. He believed that the third ventricle is the place where the different forms of sensory information—sight, touch, hearing, etc.—come together. He too imagined animal spirits in the body activating limbs and producing movements. Thus, the dichotomy between knowledge of structure and function continues in Leonardo and survives him (Fig. 1.2).

Descartes: Those from the “hard” sciences know of Rene Descartes as the creator of analytic geometry, a result of the marriage of algebra and geometry. In the history of neuroscience, Descartes marks an interesting turning point. Descartes gave a new twist to the mind–body problem that has vexed all his predecessors. While knowledge of structure was founded on concrete observations, understanding of function was fantastic and often baseless. Descartes cut this Gordian knot by simply suggesting

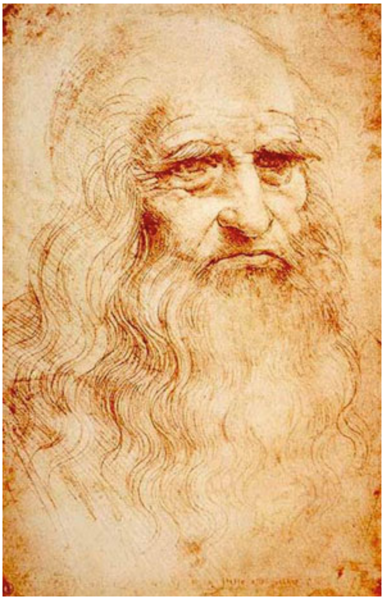
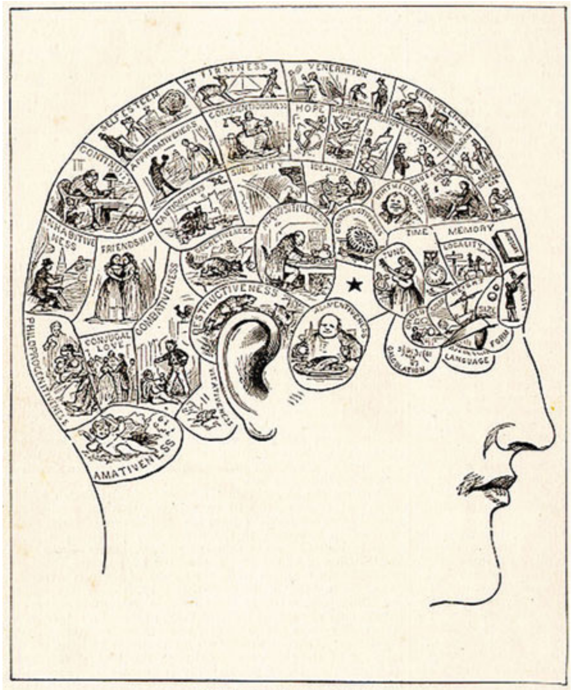


Fig. 1.2 Leonardo da Vinci

that mind and body follow entirely different laws. Body is a machine that follows the familiar laws of physics, while mind is an independent, nonmaterial entity lacking in extension and motion. However, he allowed a bidirectional influence between the two: mind on body and vice versa. Though such pure dualism did not solve the real problem of mind versus body, it seems to have unshackled neuroscience research. It allowed researchers to ignore the "soul" for the moment, and apply known laws of physics to brain and study the "machine." It is ironical—and perhaps has no parallel in the history of any other branch of science, that an immense progress in a field was accomplished by bypassing the most fundamental question ("What is consciousness?") of the field and focusing on more tractable problems (e.g., "How do neurons of the visual cortex respond to color?").

Once Descartes exorcized the "soul" from the body, it was left to the scientists to explain how the cerebral machine, or the "computational brain" in modern language, worked. Since all the cognitive abilities cannot be attributed to an undetectable soul anymore, it became necessary to find out how or which parts of the brain support various aspects of our mental life. A step in this direction was taken by a German physician named Franz Joseph Gall in 1796. Gall believed that various human qualities are localized to specific areas of the brain. This modular view of brain function is a refreshing change from the lumped model of the soul. But that's where the virtues of the new theory end. Gall thought that the size of a specific brain region corresponding to a psychological quality is commensurate to the strength of that quality in that individual. A generous person, for example, would have a highly enlarged "generosity" area in the brain. As these brain areas, large and small, push against the constraining walls of the skull, they form bumps on the head, which can be seen

Fig. 1.3 A map of the brain used by phrenologists



Phrenological Chart of the Faculties.

or felt by a keen observer, as the theory claimed. A person's biodata is graphically written all over the skull! This quaint science was known as Phrenology (its haters called it "bumpology"). Even in its early days, phrenology was criticized by some as a pseudoscience. Nevertheless, its followers grew and its popularity and practice survived to recent times (In 2007, the American state of Michigan began to tax phrenology services) (Fig. 1.3).

Phrenology was an interesting, though awkward, first step toward understanding localization of functions in the brain. Its strengths over the "soul theory" lie in this localization approach. But it failed to go very far since its hypotheses were not based on any sound physical theory. An ideal explanation of brain function must emerge, not out of unbridled imagination, but out of the rigorous application of physical principles to the nervous system. Thus, progress in our understanding of the brain occurred in parallel to progress in various branches of science.

Anatomy

Knowledge of large-scale anatomy of the brain existed for at least two millennia. However, insight into the microscopic structure of the brain came with the develop-

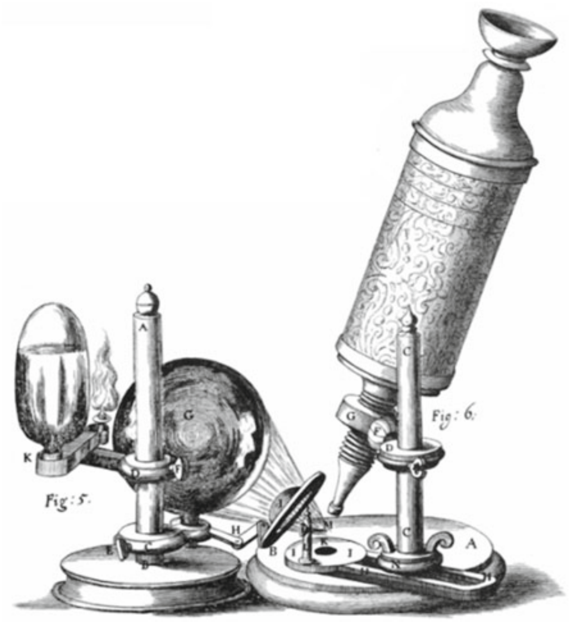


Fig. 1.4 The microscope used by Anton van Leeuwenhoek

ment of tools to peer into the smallest recesses of the brain. The compound microscope with illumination created by Robert Hooke gave us the first glimpses of the microstructure of the biological world. Hooke observed organisms as diverse as insects, sponges, bryozoans, or bird feathers with this new device. He made delicate drawings of what he observed and published them in the famous "Micrographia" in 1665 (Fig. 1.4).

Anton van Leeuwenhoek, who had a passion for constructing microscopes, took this tradition further, by making observations at a much smaller scale. In 1683, one day, as he was observing his own sputum in the microscope, he noted that "in the said matter, there were many very little animalcules, very prettily a-moving." These "animalcules," these minuscule "animals," that Leeuwenhoek saw were the first biological cells ever observed. Subsequently, he also observed a nerve fiber in cross section.

Microscopic observations of nerve cells posed a new problem that did not exist in other tissues of the body. Nervous tissue everywhere had these long fibers connected to cell bodies. These did not resemble the blob-like cells of other tissues. It was not clear if neural tissue had discrete cells with clear boundaries separating cells. Thus, early microscopic observations led people to believe that cells in the nervous tissue are all connected to form a continuous, unbroken network—not unlike a mass of noodles—known as the "syncitium." The limitations of early microscopy, compounded with the transparent appearance of cells, were at the root of this difficulty. It was not too long, before Camillo Golgi developed a way of "coloring" the cell, so that they stood out stark against a featureless background. Putting this Golgi staining

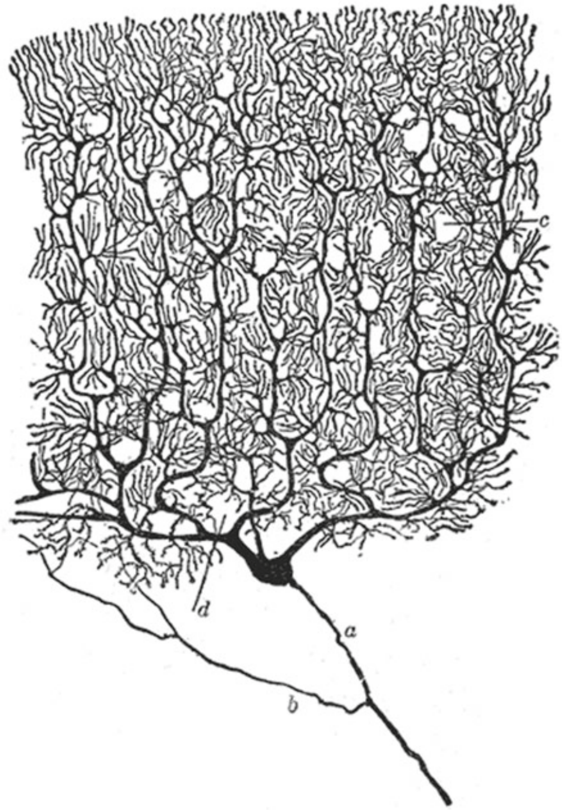


Fig. 1.5 A drawing by Ramon y Cajal of a Purkinje cell, a neuron located in the cerebellum

technique to brilliant use, Ramon y Cajal observed neural tissue from various parts of the brain. Figure 1.5 shows an intricate drawing made by Cajal of Purkinje cell, a type of cell found in cerebellum, a large prominent structure located at the back of the brain.

From his observations, Cajal decided that neural tissue is not a featureless neural goo, and that it is constituted by discrete cells—the neurons. What distinguishes these brain cells from cells of other tissues are the hairy structures that extend in all directions. Cajal taught that these discrete, individualized cells contact each other using these "wire" structures. Thus, the interior of one cell is not connected to the interior of another by some sort of a direct corridor. At the point where one cell contacts another, there must be a gap. (Interestingly, the gap between two contacting neurons was too small to be observable in microscopes of Cajal's day. But Cajal guessed right.) Thus he viewed the brain as a complex, delicate network of neurons, a view known as the "neuron doctrine." In honor of the breakthroughs they achieved in micro-neuroanatomy, Golgi and Cajal shared a Nobel prize in 1906. Subsequently, Ross Harrison performed microscopic observations on the developing brain in an embryo. Neuron-to-neuron contacts would not have matured in the embryonic brain.

In this stage, neurons send out their projections, like tentacles, to make contact with their ultimate targets. Harrison caught them in the act and found that there exists indeed a gap, as Cajal predicted, between neurons that are yet to make contact with each other, like a pair of hands extended for a handshake.

These early microanatomical studies of the brain revealed that the brain consists of cells called neurons with complex hairy extensions with which they make contact with each other. Thus brain emerged as a massive network, a feature that distinguishes itself from nearly every other form of tissue, a feature that perhaps is responsible to its unparalleled information processing functions.

Learning about brain's microanatomical structure is the first step in learning what makes brain so special. But in order to understand brain's information processing function, one must study what the neurons *do*. What is the nature of the "information" that they process? How do they produce and exchange that information? A beginning of an answer to these questions came with the realization that neurons are electrically active, like tiny electronic circuits. Progress in this line of the study came with the development of a branch of biology known as electrophysiology, which deals with the electrical nature of biological matter.

Electrophysiology

Though classical biology teaches that all life is chemical, and solely chemical, it is equally valid to say that all life is electrical. The field of bioelectricity sprang to life on one fine day in 1771, when Italian physician Luigi Galvani observed that muscles of a dead frog suddenly contracted when brought into contact with an electric spark. When Galvani's assistant touched the sciatic nerve of the frog with a metal scalpel which had some residual electric charge, they saw sparks fly and the leg of the dead frog kick. At about that time, Galvani's associate Alexandro Volta developed the so-called Voltaic pile, which is the earliest battery or an electrochemical cell. While Galvani believed that the form of electricity found in the muscle is different from what is found in an electrochemical cell, Volta believed the opposite. Volta was right. Thus began the realization that what activates the muscle is not some mysterious "animal electricity," but the very same electricity found in a nonliving entity like the electrochemical cell (Fig. 1.6).

In the early nineteenth century, German physiologist Johannes Muller worked on the mechanism of sensation. He found that the sensation that results on stimulation of a sensory nerve depends, not on the nature of the stimulus (light, sound, etc.), but merely on the choice of the nerve. Thus when the retina, which contains a layer of photoreceptors in the eye, or the optic nerve, which carries visual information to the brain, are activated by light or pressure or other mechanical stimulation, a visual sensation follows. (This fact can be verified by simply rubbing on your closed eyes with your palms.) Muller termed this the *law of specific energies* of sensation. Muller began a tradition in which physical principles are applied without hesitation

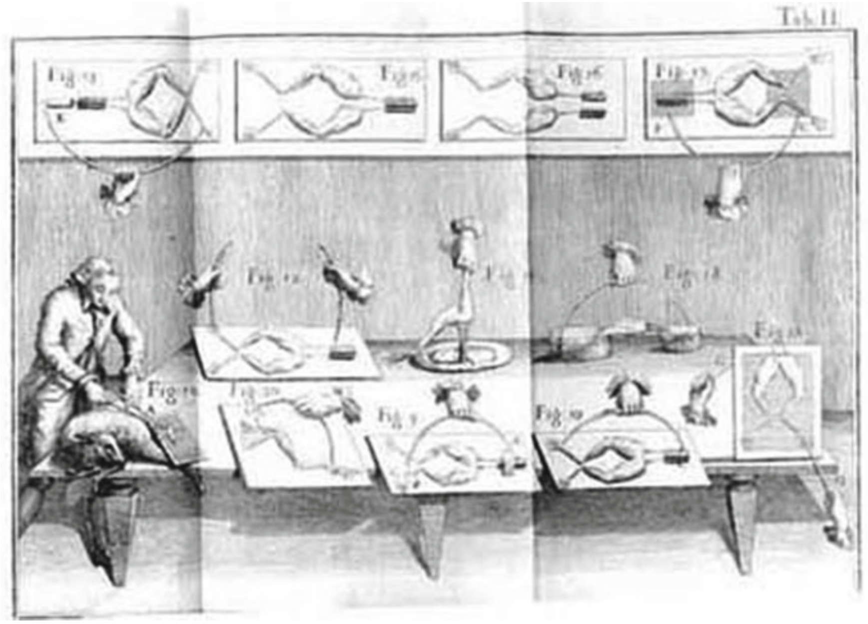


Fig. 1.6 Drawings by Galvani depicting his experiments with electrical activation of frog legs

to understand the electrical nature of the nervous system. In a volume titled *Elements of Physiology*, he states this perspective, though with some caution, as follows:

> Though there appears to be something in the phenomena of living beings which cannot be explained by ordinary mechanical, physical or chemical laws, much may be so explained, and we may without fear push these explanations as far as we can, so long as we keep to the solid ground of observation and experiment.

Two of Muller's illustrious disciples—Emil du bois-Reymond and Hermann von Helmholtz—developed Muller's vision. Du-bois Reymond, who proceeded along experimental lines, began his career with the study of "electric fishes," creatures like the electric eel, catfish, and others that are capable of producing electric fields. He worked extensively on electrical phenomena related to animal nervous systems and described his findings in the work *Researches on Animal Electricity*. His important contribution to electrophysiology was the discovery of the action potential, a characteristic, well-formed voltage wave that is seen to propagate along nerve fibers. But he did not possess the requisite theoretical prowess to understand the physics of the action potential.

Another event that greatly helped our understanding of the electrical nature of the brain, is a revolutionary development in our understanding of electricity itself. It took the genius of James Clerk Maxwell, the theoretical physicist who integrated electricity and magnetism in a single mathematical framework. Out of this framework emerged the idea that light is an electromagnetic wave propagating through vacuum.