

Chapter 1

Introduction

What is first goes first, what is last goes last, and often there is something in between.

1.1. Ancestor's Light: The Seven Lamps

A statement reaches its maximum clarity and beauty when it can be expressed in mathematical terms. Saint Mathesis, patron of mathematics, used to be surrounded by seven lamps: *lampas utilitatis*, *lampas imaginationis*, *lampas poesis*, *lampas infinitatis*, *lampas mysterii* and *lampas religionis*. Bioengineering, strongly supported by mathematics, searches the quantification of the biomedical sciences and thus, no doubt, these lamps also illuminate its course because this discipline is certainly useful (*utilitatis*) for it applies directly or indirectly to the human being, it requires tremendous imagination (*imaginationis*) and creativity (*poesis*), it extends unlimited in all directions (*infinitatis*) branching off here and there, while it shines with some degree of mystery (*mysterii*) when penetrating the darkness of the unknown, so spurring curiosity, and shows also even mystical and mythical edges when human, ethical and religious aspects are touched on (*religionis*). Thus, as an intellectual rainbow, the *Seven Lamps* spread their light over us. I hope and wish, you, **my young motivated student**, will find the proper and best path with it.

1.2. Definitions: Are They Really Necessary?

The *métier* of this book refers to the use and application of principles, laws, techniques and general knowledge, taken from the physical and engineering sciences, to the better understanding and solution of biological and medical problems at large. No one will argue this. No specific

name is given yet. We just realize how wide and ambitious the intent is. But we need names to identify our field and activity, and here is where discrepancies may begin.

Several terms dance around and seem to have relatively settled down in the last ten years or so, while other words have tried to find a place (such as bioelectronics or biocybernetics or electromedicine). However, a closer look immediately indicates that many of the latter really belong to the wider set given below:

Bioengineering, considered as the most general and scientific, refers to biology as a whole, tries to discover new phenomena in the biological processes and intends to clarify others already known. One difficulty: It is also associated with biotechnology, as for example production of combustible gas or hormones (say, insulin) from bacteria or with genetics, so broadening perhaps excessively the field. An alternative name sometimes used is **Biological Engineering**, however, an advantage of the former is to be brief and powerful.

Biomedical Engineering, contained in the previous one, more pragmatic, oriented toward human health, but still with a good dose of scientific curiosity where the basic biological or physiological process is present. **Medical Engineering** would walk a step away from biology dealing just with man.

Clinical Engineering, the newest of the three divisions, contained in **Medical Engineering**, directed to problems found in health care systems, hospitals and emergency services, and working side by side with medicine. It shows a well-defined personality with publications of its own.

Boundaries are not well delimited, nor they need be, and information and activities must flow freely from one division to another in a constant exchange if results are to be fruitful. In daily language, the names given above are frequently interchanged. Even the two biggest international organizations do not use them officially, preferring longer combinations of words: The *IEEE/Engineering in Medicine and Biology Society* and the *International Federation for Medical and Biological Engineering*.

Definitions are always controversial and, in this particular case, perhaps more for there is still a state of development and evolution of concepts,

making terms obsolete in a relatively short time. Recall that this discipline officially celebrated its first 50 years in 2002 (see *IEEE/EMB Magazine*, May–June 2002). Thus, **a flexible and open mind becomes mandatory** (quite an attractive characteristic of our discipline!). To answer the question by the subtitle: **Not quite, because definitions are not absolute, they are secondary; they can and should be changed as required. They are simply convenient.** Look with a serious frown at those people who stick stubbornly to definitions (and even worse, to standards!). Imagine what it would be like had we fastened ourselves to the definitions (and the concepts supporting them) of the Middle Age or, without going as far back, of just 100 years ago!

1.3. Quantification Process

I know about something when I can describe it with a number.

Lord Kelvin

Scientific fields and disciplines constantly evolve, usually starting at a *qualitative stage* (by being mostly *descriptive*, as the early anatomical or zoological knowledge), to enter later into more *quantitative stages* (like counting the number of lobes of an organ, weighing it and/or searching for a known geometrical shape to approximate it). It is obvious that some disciplines are more *quantifiable* and *quantified* than others. The cardiovascular and respiratory systems, for example, are easier in this respect because their variables have precise mathematical definitions. Psychophysiology, instead, does not have yet clear-cut variables to work with and, as a consequence, its quantification process is slower. Variables like anxiety, fear or anguish are rather elusive.

One of the objectives of Bioengineering is to bring quantification to the biological and biomedical sciences. A first step consists of breaking up a given system into several interconnected functional units, i.e., the *block diagram*, usually based on previous qualitative information. This is similar to studying, say, a super-heterodyne radio receptor (formed by well defined blocks: antenna, radio frequency unit, oscillator/mixer-converter, intermediate frequency unit, detector, audio stage, and loudspeaker). The second step is *the measurement of physiological events*,

which, in turn, requires an *exact, precise, mathematical definition of the variables* to be measured (as mentioned above) and, simultaneously, *the availability of an adequate technology* to develop the sensors or transducers to apply.

During the French Revolution, two astronomers, Pierre Méchain and Jean Baptiste Delambre, were commissioned by the National Assembly to determine a standard unit of length — **the meter** — *pour tous les hommes, pour tous les temps* (for all men, for all times), based on the measurement of the terrestrial meridian passing through the cities of Barcelona, Paris and Dunkerke [$1 \text{ m} = 10^{-7} \times \text{quarter of meridian} = 25 \times 10^{-9} \times \text{full } 360^\circ \text{ meridian}$]. It took them from June 1792 until June 1799, seven full years of exhausting fieldwork plus innumerable experiences and personal sacrifices, including a serious accident and even political and military threatening, to accomplish it, but in the end they supplied the basis of the present and universal Decimal System (Guedj, 1997). A transcendental highly significant step ahead had been taken in the quantification process of knowledge at large. In more recent times and under the light of new findings, that definition of meter was changed to $1/299,792,458$ of the distance light travels in vacuum in 1 s.

Interpretation of the signals, by means of from simple visual inspection to sophisticated techniques, is essential for the understanding of normal phenomena and diagnosis of pathologies. In other words, signals must be perused. In the end, the development of mathematical models leads to *prediction*, which is the highest level of quantification. As such, astrophysics or atomic physics are well ahead of any other discipline. Recall, for example, how accurately the movements and positions of astronomical phenomena can be anticipated. And, after all, what is a physician trying to do when he/she examines a patient? He/she tries to determine what the disease is and, above all, to **predict its most probable course**. A veterinarian, an ecologist and other biologically related activities take a similar stand.

In short: Scientific disciplines show a slow, sometimes faster, but steady process of quantification. Biology, physiology and medicine are no exceptions. A still distant and well-yearned objective is to anticipate disease, as much in advance and as much quantifiably as possible, based on the current known condition of a given individual. For the time being,

even with the tools nowadays at hand of the medical profession, that prediction is still far from being exact and precise. Genetics and the sequencing of the Human Genome in 2000 certainly brought us closer to that possible prediction.

1.4. Witchery, Charlatanism, Frankenstein, Science Fiction

*From the witch doctor to the biomedical engineer
When suffering hits, people seek relief wherever and from any hand:
From the real and the illusion, from the truth and from lies,
in spells and in magic, in praying and faith.
They're hopes and beliefs of so many
that few, just barely, are able to grasp.*

Ever since the appearance of man on the surface of the Earth, diseases along with natural phenomena and catastrophes have interfered with his life. Sorcerers, witch doctors and their witchery were the only way to fight them off. As knowledge slowly and painfully advanced (discovering, for example, the effects of water, heat, cold and herbs or foods), the former practice freely interlaced with charlatanism or quackery (people who take actual scientific facts, perhaps distorting them, claiming to cure this or that illness). In between, we find the “old mothers”, “barefoot doctors”, medicine men and healers of all sorts — many times applying surprisingly good and efficient concoctions or procedures, so indicating keen observational abilities — and still acting all over the world, mainly in the country or in mountainous areas. Man is always attracted by the supernatural mysterious action.

Old Mother Hutton, in Shropshire, England, used to cure the dropsy, which highly qualified doctors did not know how to handle, with a decoction of herbs. William Withering (1741–1799) took the recipe from her, even when he did not explicitly recognize it, and experimented extensively with it in his medical practice publishing, later on in 1785, the famous book entitled *An Account of the Foxglove*. So was digitalis introduced (*Digitalis purpurea*, of Linnaeus, who taxonomically classified it), first cardiac drug already well beyond its bicentennial anniversary and still widely used. He never understood its action but he consistently

found a dramatic slowing of the heart rate clearly stating “... *it has a power over the motion of the heart, to a degree yet unobserved in any other medicine*” (Willius and Keys, 1941).

In China, the barefoot doctors are peasants who have gained some prestige and respect as healers among his village co-citizens. They are recommended by the communal brigades to spend a training period in the city, between three and six months, on elements of modern medicine **but without abandoning the traditional methods** (people would not accept it, either). They must return to their original places. China has in the order of more than one million barefoot doctors that significantly and efficiently reinforce the health care system. The use of herbs and the millenary acupuncture are nowadays academically recognized.

The advent of electricity (a good threatening unknown phenomenon!), with Luigi Galvani, Alessandro Volta, and their famous controversy in the middle, brought along the sweet story of Mary Godwin Wollaston (Shelley’s very young and beautiful lover), Percy Shelley (the English poet), George Gordon (Lord Byron, a superb impetuous writer and unfillable drunkard) and their friends in one of those 1816 summer *soirees*, giving birth to the *Frankenstein* novel and, thus, inaugurating the now widely popular science fiction style. Apparently, that evening the young girl came up with the idea of a scientist and his monstrous creation, but the two literary geniuses turned it down for themselves and told her to go ahead and write it as her own ... what she did, and with extraordinary success, for the *Frankenstein* tale projected far ahead into the years with a thousand and one modifications and updatings! During that romantic period, Aldini (who was Galvani's nephew) proclaimed the use of electrical discharges to “resuscitate the dead or the quasi-dead”, as some kind of quack anticipation of the present and daily defibrillation shocks in emergency rooms, operating theaters, industrial and street heart episodes.

Suggested study subject: What was the Galvani–Volta controversy? Search in the Web for The Bakken Library and Museum, in Minneapolis, MN, to find out more about the Frankenstein story and the medical uses of electricity during the XIXth Century.

S. Furman and Wilson Gretchbach, with the cardiac pacemaker (Furness, 1975) and William Kouwenhoven and Michael Mirowski, with the external and the implantable defibrillators (Tacker and Geddes, 1980), respectively, are quite recent names associated with the develop-

ment of these devices which have saved and prolonged the life of millions of patients all over the world. It even sounds as magic or supernatural or science-fictional: To order the heart when to contract! To revive it, when it stops! Does it not sound as *Frankensteinian*? After all, Frankenstein, a scientist, gave life to his monster by electric discharges!

All this is bioengineering ancestry: Galvani rocketing off electrophysiology with his concept of animal electricity, Volta starting up electrical engineering with his pile, Mary Wollaston launching a new literary style, hints of revolutionary medical electrotherapy by a charlatan ... no ordinary light from the Seven Lamps, indeed, and just a mere 200 hundred years or less back!

1.5. Koestler's Creative Collisions

Two women meet at the supermarket. One looks cheerful, the other depressed. The following quick dialogue is started by the former: "What's eating you? Nothing's eating me. Death in the family? No, God forbid! Worried about money? No ... nothing like that. Trouble with the kids? Well, sort of, it's my little Jimmy. What's wrong with him? Nothing is wrong, just his teacher says he must see a psychiatrist. PAUSE. Well ... what's wrong with seeing a psychiatrist? Nothing ... just the psychiatrist says he's got an Oedipus complex. ANOTHER PAUSE. Well ... Oedipus, Shmoedipus, what the heck, I wouldn't worry so long as he's a good boy and loves his momma."
 Koestler, A. *The Logic of Laughter*, in *The Act of Creation*, 1964.

The creative act of the humorist consists in bringing about a momentary fusion between two habitually incompatible matrices. In the little story above, the cheerful woman's statement is ruled by the logic of common sense: if Jimmy is a good boy and loves his momma, there can't be much wrong. But in the context of Freudian psychiatry the relationship to the mother carries entirely different associations. Scientific discovery can be described, in very similar terms, as the permanent fusion of matrices of thought previously believed to be incompatible. A problem, when looked at from two or more points of view, may be understood and solved more easily. One reference frame may be, say, strictly biological, while another may be purely mathematical. They tend to enlighten each other so

favoring the intellectual act of creation. It is like taking photographs of a landscape from different positions. Some may show aspects that others may not. The creative act, by connecting previously unrelated dimensions of experience, enables the scientist to attain a higher level of mental evolution. It is an act of liberation, the defeat of the habit by originality. This is a theory put forward by Arthur Koestler—an Austrian journalist (who tragically died some years ago), also philosopher and thinker—in his book entitled *The Act of Creation* (1964). Koestler starts with a Theory of Humor: A joke would lead to laugh when two reference frames collide. An expert joke-teller should carefully prepare the first frame to suddenly exit into a totally unexpected situation, causing the collision and, thus, triggering laughter; in short, the stronger the collision, the higher the laugh intensity. Bioengineering, by its very definition and nature, favors all kinds and sorts of intellectual collisions. It brings together the improbable and the apparently unrelated, biology and mathematics, physiology and physics, medicine and engineering. Thus, through such cross-fertilization, it supplies a good culture broth or scenario for comprehension, discovery and invention. Is this not another strong *attractor* for the youngsters, enlightened by the *Lampas Poesis*?

Question for the curious inquisitive mind: What is an attractor? Where does this term come from? Does it have applications in biology?

1.6. Guiding Philosophy of this Book: The Recording Channel

‘Verba volant, scripta manent’, which means words fly, scriptures remain.

Johannes Gutenberg’s printing machine (1398–1468) with movable types represented an essential step forward in the advancement of culture for it permitted permanent and easily obtained records of the human thought. By digging into historical accounts, Koestler found out that this invention sprang out as a bisociation or collision product of two unrelated practical concepts, namely, the wine-press (well-known in those days) and a coin or lead seal which, owing to pressure, would leave a trace on paper.

Before 1847, the physiological message given off by an animal or by man himself could not be graphically registered. Stephen Hales had to tell the ups and downs of the blood column (as it slowly and blandly coagulated), in a lengthy description, when he measured arterial blood pressure for the first time from a non-anesthetized mare, back in 1728. James Hope, in 1830, called for the presence of witnesses to certify (thus, “record”) his description of the heart sounds, to prove their valvular nature, during experiments made in donkeys.

Suggested study subjects: Find out about Hales’ and Hopes’ doings. Questions: When did anesthesia show up? What was its origin? Any collision of frames? How important was it in the development of medicine? Do you see any possible engineering inputs to these subjects?

To pick up biological signals is essential because they carry, if not all, most of the information needed to understand the behavior of the system and, eventually, to take a decision (say, a therapy). Thus, the **recording channel** appears as a second system (a technological one) to be implemented, coupled to the biological system. **This book takes it as its blueprint.** Figure 1.1 explains its parts: The biological system, either as

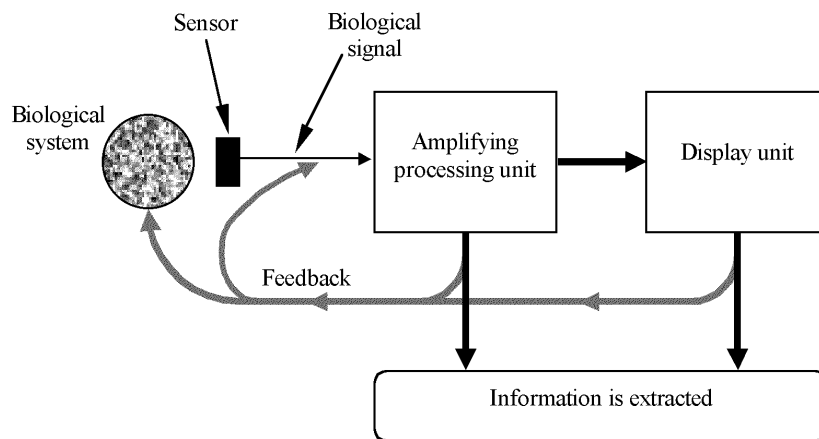


Figure 1.1. THE RECORDING CHANNEL. The biological system produces signals, which are picked up by specific sensors. They are amplified, processed and displayed. Eventually, feedback signals modify different input levels according to information obtained from the different outputs.

an individual, organ or cell, is the source producing signals (Chapter 2), **live signals**, which are picked up by specific sensors. There are very many biological signals (Chapter 3), however, their nature can always be summarized in a few kinds: electrical, mechanical, chemical and thermal. Accordingly, electrodes and transducers represent a key critical bottleneck (Chapter 4), permanently opened to research and new developments. Most of the time, if not always, the signal requires amplification and processing. This basic unit needs to fulfill unique characteristics not covered by the amplifier usually applied in other fields (Chapter 5). Once the signal is faithfully displayed (by and large, there is always some kind of visualization, on paper, oscilloscope screen or monitor), we have to read it to obtain a meaningful interpretation. This is, in simple words, all what signal analysis is about (Chapter 6). But do not get too excited about the content of the chapter, for we merely want to offer you a lead. You will need specific courses to go deeper. The information produced by the analysis of the biological signals, hopefully, will offer a variety of messages leading to one or more decisions: the signal pick up must be improved, signal processing has to be changed, stimulation of some kind is advisable to isolate a given response, a therapy is instituted, a relationship is uncovered or discovered, a mathematical model can be set, thus starting a fruitful feedback loop (Chapter 7). Thus, feedback is meant here in a very wide sense and context. The final chapter will try to put things together, if possible, to jet you off into higher levels with the help of your inspiration, sweat and, perhaps, some light from the *Seven Lamps*.

1.7. Objectives

Set always the goal. It will be easier to find the way. Be a Pathfinder!

Leslie A. Geddes has been one of the outstanding contributors to Bioengineering. When I was a graduate student at Baylor College of Medicine, he told me: “Start the sentence with an infinitive. It means you are going to act. The sentence should be short and concise. If it is too long, either

you do not know well what you want to do or you have to split the objective in two or three.” Let me follow the advice:

The general objective of this book is **to offer an overview of Bioengineering**. This is why it is simply an **introduction** at most, and more likely a **primer**, that is, a take off platform.

The **specific objectives** are:

1. **To describe somewhat critically the basic sections of Bioengineering. The rest springs up from them.**
2. **To give a historical feeling. It teaches humility, it may show the way and avoids repetitions.**
3. **To show you how much you can learn by yourself. It is extremely difficult, but let us try. Your personal effort is indispensable.**

In other words, after finishing it (perhaps a full semester work course), you should have the feeling of having caught almost everything and yet realizing that the true meat and potatoes and full taste of it is still to come, for the book is aimed at the **undergraduate bioengineering student**. Some mathematics is used, say, at the level of calculus, differential equations, and the concept of transform.

In the meantime, learn and put into practice as soon as possible the ABC of science (Bishop, 1997). The authors, believe me, are also trying hard in this respect. Unfortunately, the human being (scientists and engineers are also human beings) is not always too willing to comply with these nice suggestions:

Accept criticism graciously

Become focused and organized

Cope with the burgeoning scientific literature

Develop critical thinking and logical sequence of ideas

Experience satisfaction and joy from your endeavors

Finish tasks undertaken

Give the best at all times

Hone communication skills in writing and speaking.

Even though the word BIOENGINEERING may have conflicting meanings when its detailed coverage is required, as briefly referred to above, it is widely and loosely used in the daily language, probably because it is

shorter and powerfully says what the *métier* is. Therefore, we will stick to it in the text. From here on, it will not be capitalized, as the names of other disciplines will not either.