Cambridge University Press
978-0-521-84112-2 - Introductory Biomechanics: From Cells to Organisms
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Excerpt
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1 Introduction

Biomechanics is a branch of the field of bioengineering, which we define as the application of engineering principles to biological systems. Most bioengineering is applied to humans, and in this book the primary emphasis will be on *Homo sapiens*. The bioengineer seeks to understand basic physiological processes, to improve human health via applied problem solving, or both. This is a difficult task, since the workings of the body are formidably complex. Despite this difficulty, the bioengineer's contribution can be substantial, and the rewards for success far outweigh the difficulties of the task.

Biomechanics is the study of how physical forces interact with living systems. If you are not familiar with biomechanics, this might strike you as a somewhat esoteric topic, and you may even ask yourself the question: Why does biomechanics matter? It turns out that biomechanics is far from esoteric and plays an important role in diverse areas of growth, development, tissue remodeling and homeostasis. Further, biomechanics plays a central role in the pathogenesis of some diseases, and in the treatment of these diseases. Let us give a few specific examples:

- How do your bones "know" how big and strong to be so that they can support your weight and deal with the loads imposed on them? Evidence shows that the growth of bone is driven by mechanical stimuli [1]. More specifically, mechanical stresses and strains induce bone cells (*osteoblasts* and *osteoclasts*) to add or remove bone just where it is needed. Because of the obvious mechanical function played by bone, it makes good sense to use mechanical stress as the feedback signal for bone growth and remodeling. But biomechanics also plays a "hidden" regulatory role in other growth processes, as the next example will show.
- How do our arteries "know" how big to be so that they can deliver just the right amount of blood to their distal capillary beds? There is good evidence that this is determined in large part by the mechanical stress exerted on the artery wall by flowing blood. Endothelial cells lining the inner arterial surface sense this shear stress and send signals to cells deeper in the artery wall to direct the remodeling of the artery so as to enlarge or reduce its caliber [2].

- What about biomechanics in everyday life? Probably the most obvious application of biomechanics is in locomotion (walking, running, jumping), where our muscles generate forces that are transferred to the ground by bones and soft connective tissue. This is so commonplace that we rarely think about it, yet the biomechanics of locomotion is remarkably complex (watch a baby learning to walk!) and still incompletely understood.
- Locomotion happens on many scales, from whole organisms all the way down to individual cells. Unicellular organisms must be able to move so as to gather nutrients, and they have evolved a variety of clever strategies to accomplish this task [3]. In multicellular organisms, the ability of single cells to move is essential in processes such as repair of wounds, capture of foreign pathogens, and tissue differentiation. Force generation at the cellular level is a fascinating topic that is the subject of much active research.
- Cells can generate forces, but just as importantly, they can sense and respond to forces. We alluded to this above in the examples of bone remodeling and arterial caliber adjustment, but it is not only endothelial and bone cells that can sense forces. In fact, the ability of mechanical stress to elicit a biological response in cells seems to be the rule rather than the exception, and some cells are exquisitely specialized for just this task. One remarkable example is the hair cells in the ear. These cells have bundles of thin fibers (the *stereocilia*) that protrude from the apical cell surface and act as sensitive accelerometers; as a result, the hair cells are excited by sound-induced vibrations in the inner ear. This excitation produces electrochemical signals that are conducted by the auditory nerve to the auditory centers in the brain in a process that we call hearing [4,5].[1]
- The examples above show that biomechanics is important in homeostasis and normal function. Unfortunately, biomechanics also plays a role in some diseases. One example is glaucoma, an ocular disease that affects about 65 million people worldwide [6]. Normally the human eye is internally pressurized, a fact that you can verify by gently touching your eye through the closed eyelid. In most forms of glaucoma, the pressure in the eye becomes elevated to pathological levels, and the resulting extra biomechanical load somehow damages the optic nerve, eventually leading to blindness [7]. A second example is atherosclerosis, a common arterial disease in which non-physiological stress distributions on endothelial cells promote the disease process [8].
- What about biomechanics in the treatment of disease and dysfunction? There are obvious roles in the design of implants that have a mechanical function,

[1] Actually, the function of the hair cells is even more amazing than it first appears. The outer hair cells are active amplifiers, changing their shape in response to mechanical stimulation and thus generating sounds. The net effect is to apply a frequency-selective boost to incoming sounds and hence improve the sensitivity of the ear.

such as total artificial hips [9], dental implants [10], and mechanical heart valves [11]. In the longer term, we expect to treat many diseases by implanting engineered replacement tissue into patients. For tissues that have a mechanical function (e.g., heart valves, cartilage), there is now convincing evidence that application of mechanical load to the tissue while it is being grown is essential for proper function after implantation. For example, heart valves grown in a bioreactor incorporating flow through the valve showed good mechanical properties and function when implanted [12]. Cartilage subjected to cyclic shearing during growth was stiffer and could bear more load than cartilage grown without mechanical stimulation [13]. We expect that biomechanics will become increasingly important in tissue engineering, along the way leading to better fundamental understanding of how cells respond to stresses.

The above examples should give a flavor of the important role that biomechanics plays in health and disease. One of the central characteristics of the field is that it is highly interdisciplinary: to be called biomechanics, there must be elements of both mechanics and biology (or medicine). Advances in the field occur when people can work at the frontier of these two areas, and accordingly we will try to give both the "bio" and the "mechanics" due consideration in this book.

Another characteristic feature of biomechanics is that the topic is fairly broad. We can get a sense of just how broad it is by looking at some of the professional societies that fall under the heading of biomechanics. For example, in Japan alone, at least six different professional societies cover the field of biomechanics.[2] Obviously we cannot, in a single book, go into detail in every topic area within such a broad field. Therefore, we have given an introduction to a variety of topics, with the hope of whetting readers' appetites.

1.1 A brief history of biomechanics

We can learn more about the field of biomechanics by looking at its history. In one sense, biomechanics is a fairly young discipline, having been recognized as an independent subject of enquiry with its own body of knowledge, societies, journals, and conferences for only around 30–40 years. For example, the "Biomechanics and Human Factors Division" (later to become the "Bioengineering Division") of the American Society of Mechanical Engineering was established in late 1966. The International Society of Biomechanics was founded August 30, 1973; the European

[2] These are the Japanese Society of Biomechanics, the Bioengineering Division of the Japan Society of Mechanical Engineers, the Japan Society of Medical Electronics and Biological Engineering, the Association of Oromaxillofacial Biomechanics, the Japanese Society for Clinical Biomechanics and the Japanese Society of Biorheology.

Society of Biomechanics was established May 21, 1976, and the Japanese Society of Biomechanics was founded December 1, 1984. On the other hand, people have been interested in biomechanics for hundreds of years, although it may not have been called "biomechanics" when they were doing it. Here we take a quick look back through history and identify some of the real pioneers in the field. Note that the summary below is far from exhaustive but serves to give an overview of the history of the field; the interested reader may also refer to Chapter 1 of Fung [14] or Chapter 1 of Mow and Huiskes [15].

Galileo Galilei (1564–1642) was a Pisan who began his university training in medicine but quickly became attracted to mathematics and physics. Galileo was a giant in science, who, among other accomplishments, was the first to use a telescope to observe the night sky (thus making important contributions in astronomy) and whose synthesis of observation, mathematics, and deductive reasoning firmly established the science that we now call mechanics.[3] Galileo, as part of his studies on the mechanics of cantilevered beams, deduced some basic principles of how bone dimensions must scale with the size of the animal. For example, he realized that the cross-sectional dimensions of the long bones would have to increase more quickly than the length of the bone to support the weight of a larger animal [17]. He also looked into the biomechanics of jumping, and the way in which loads are distributed in large aquatic animals, such as whales. However, Galileo was really only a "dabbler" in biomechanics; to meet someone who tackled the topic more directly, we must head north and cross the English Channel.

William Harvey (1578–1657) was an English physician who made fundamental contributions to our understanding of the physiology of the cardiovascular system, and who can be rightly thought of as one of the first biomechanicians (Fig. 1.1). Before Harvey, the state of knowledge about the cardiovascular system was primitive at best, being based primarily on the texts of the Roman physician Galen (129–199?). Galen believed that the veins distributed blood to the body, while arteries contained pneuma, a mixture of "vital spirits," air, and a small amount of blood. It was thought that the venous and arterial systems were not in communication except through tiny perforations in the interventricular septum separating the two halves of the heart, so the circulatory system did not form a closed loop. Venous blood was thought to be produced by the liver from food, after which it flowed outward to the tissues and was then consumed as fuel by the body.[4]

Harvey was dissatisfied with Galen's theories, and by a clever combination of arguments and experimentation proved that blood must travel in a closed circuit

[3] Charles Murray, in his remarkable survey of human accomplishment through the ages [16], ranks Galileo as the second-most accomplished scientist of all time, behind (who else?) Newton.

[4] It is easy to look back and ask: How could Galen have been so wrong? The answer is that he was influenced by his predecessors; prior to Galen it was thought that arteries were filled with air and that the veins originated in the brain, for example. The lesson to be learned: question dogma!

Figure 1.1

Portraits of Drs. William Harvey (left) and Stephen Hales (right). Both were early biomechanicians; Harvey was a noted English physician, while Hales was a Reverend and "amateur" scientist. Both portraits, courtesy of the Clendening History of Medicine Library and Museum, University of Kansas Medical Center [18].

in the cardiovascular system. For example, he carried out careful dissections and correctly noted that all the valves in veins acted to prevent flow away from the heart, strongly suggesting that the function of the veins was to return blood to the heart. For our purposes, his most intriguing argument was based on a simple mass balance: Harvey reasoned that the volumetric flow of blood was far too large to be supplied by ingestion of food. How did he do this? Using a sheep's heart, he first estimated the volume of blood pumped per heart beat (the stroke volume) as two ounces of blood. Knowing the heart rate, he then computed that the heart must be pumping more than 8600 ounces of blood per hour, which far exceeds the mass of food any sheep would be expected to eat! In his words (italics added) [19]:

> Since all things, both argument and ocular demonstration, show that the blood passes through the lungs and heart by the force of the ventricles, and is sent for distribution to all parts of the body, where it makes its way into the veins and porosities of the flesh, and then flows by the veins from the circumference on every side to the center, from the lesser to the

greater veins, and is by them finally discharged into the vena cava and right auricle of the heart, *and this in such a quantity or in such a flux and reflux thither by the arteries, hither by the veins, as cannot possibly be supplied by the ingesta, and is much greater than can be required for mere purposes of nutrition*; it is absolutely necessary to conclude that the blood in the animal body is impelled in a circle, and is in a state of ceaseless motion.

By these and additional arguments [20], Harvey deduced the closed nature of the cardiovascular system (although he was unable to visualize the capillaries). For our purposes, Harvey is notable because he was one of the first physicians to use a combination of *quantification*, deductive reasoning, and experimentation to understand a clinically important medical topic. Such approaches are commonplace today but were revolutionary in Harvey's time and even caused him to be strongly criticized by many prominent physicians.

Giovanni Alfonso Borelli (1608–1679) is variously described as a mathematician, physicist, and physiologist, which is surely a testament to the breadth of his interests. He worked at various universities throughout Italy, coming in contact with Galileo. Notably, he spent 10 years in Pisa, where he worked with the famous anatomist Malpighi (responsible for the discovery of the capillaries). Later in his career, Borelli became interested in the mechanics of animal motion, and is best known for his two-volume work on this topic, *On the Movement of Animals* (*De Motu Animalium*), published posthumously in 1680 (Volume I) and 1681 (Volume II). In addition to the novelty of the material in these books, they are notable for their wonderfully detailed figures illustrating biomechanical concepts such as locomotion, lifting, and joint equilibrium (Fig. 1.2). Borelli used the principles of levers and other concepts from mechanics to analyze muscle action. He also determined the location of the center of gravity of the human body and formulated the theory that forward motion involved the displacement of the center of gravity beyond the area of support and that the swinging of the limbs saved the body from losing balance [21]. Further, he considered the motor force involved in walking and the location of body support during walking. Borelli was also interested in respiratory mechanics: he calculated and measured inspired and expired air volumes. He was able to show that inspiration is driven by muscles, while expiration is a passive process resulting from tissue elasticity. In honor of his seminal contributions in the field of biomechanics, the career accomplishment award of the American Society of Biomechanics is known as the Borelli Award.

Another early biomechanician was the Reverend Stephen Hales (1677–1761), who made contributions to both plant and animal physiology (Fig. 1.1). He is best known for being the first to measure arterial blood pressure, now a staple of all clinical examinations. He did this by direct arterial cannulation of his horse (in his back yard, no less)! In his words [22,23]:

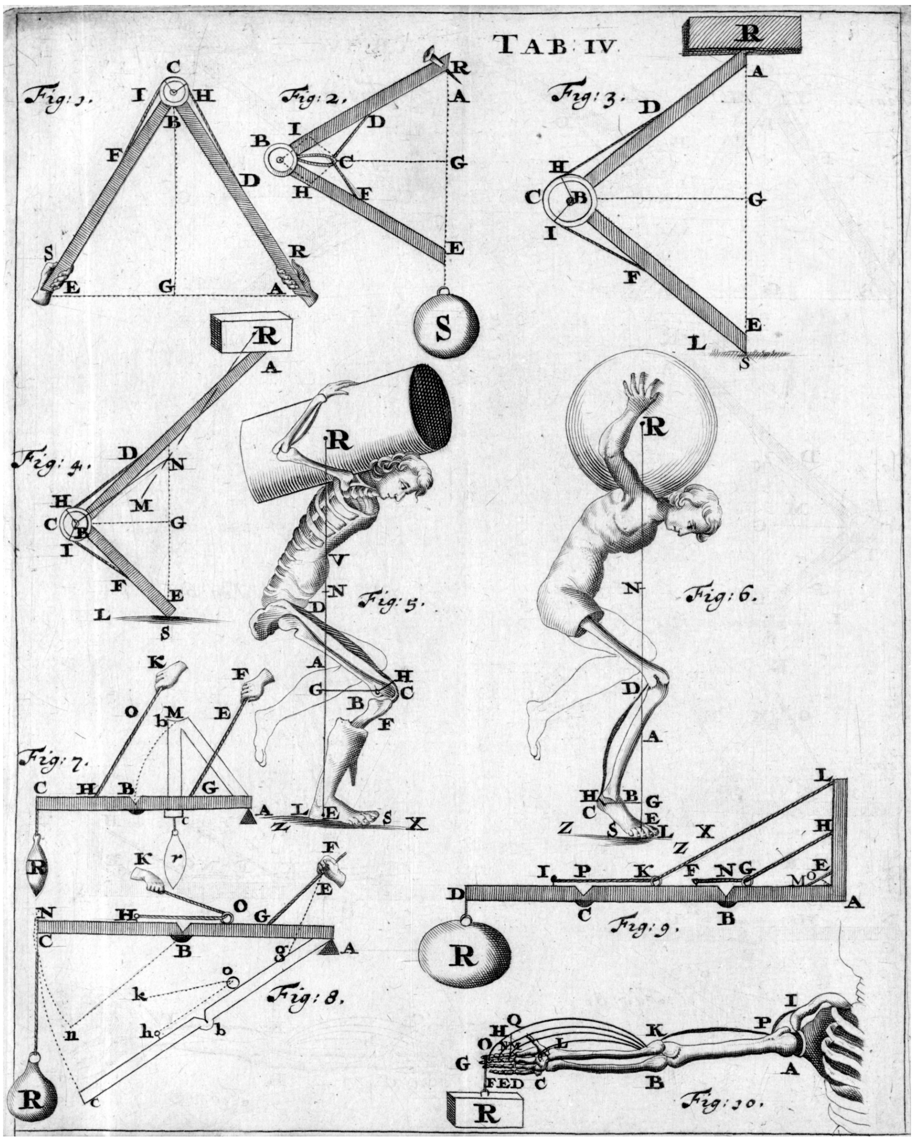

Figure 1.2

Figure from Borelli's classic work, *De Motu Animalium* (*On the Movement of Animals*). Panels 1–4 show how elastic bands (representing muscles) can interact with two pivoting levers (representing bones) in a variety of geometric configurations. Panels 5 and 6 demonstrate how the muscle and bone configurations act in humans carrying loads. Panels 7 and 8 show various pulley arrangements, while panels 9 and 10 show how muscle action in the human arm supports a weight R. (We will revisit this subject in Ch. 8.) The concepts may not seem advanced to modern students, but to put things into context, it should be remembered that the first volume of *De Motu Animalium* was published seven years before the appearance of Newton's *Principia*.

I caused a mare to be tied down alive on her back . . . having laid open the left crural [femoral] artery about 3 inches from her belly, I inserted into it a brass pipe whose bore was 1/6 of an inch in diameter; and to that, by means of another brass pipe . . . I fixed a glass tube of nearly the same diameter, which was 9 feet in length; then untying the ligature on the artery, the blood rose in the tube 8 feet 3 inches perpendicular above the level of the left ventricle of the heart . . . when it was at its full height, it would rise and fall at and after each pulse 2, 3, or 4 inches.

Hales also improved Harvey's estimate of cardiac stroke volume by pouring wax at controlled pressure into the heart's main pumping chamber (the left ventricle) to make a casting. He then measured the volume of the wax cast by immersing it in water, and measured its surface area by carefully covering it with small pieces of paper covered with a measuring grid. Together with his measurements of blood pressure, Hales then used these results to provide the first estimate of left ventricular systolic (pumping) pressure, and a remarkably accurate estimate of the blood velocity in the aorta (0.5 m/s).

Jean Léonard Marie Poiseuille (1797–1869; Fig. 1.3) was a French engineer and physiologist who was also interested in blood flow [25]. In his thesis [27], he described how he simplified and improved the measurement of blood pressure. His contributions were two-fold: first, he developed the U-tube mercury manometer, which did away with the need for an unwieldy 9 foot-long tube. Second, he used potassium carbonate as an anticoagulant [28]. He was surprised to discover that the pressure drop from the aorta to arteries with diameters as small as 2 mm was negligible [29]; we know now that most of the pressure drop in the circulatory system occurs in vessels with diameter smaller than 2 mm. Poiseuille then became interested in laminar flow in small tubes and carried out experiments on the flow of water through artificial glass capillaries with diameters as small as 30 μm. His results allowed him to deduce the relationship between flow, tube dimensions, and pressure drop, which we know today as the Hagen–Poiseuille law [30]. We will explore the implications of this law for blood flow in Ch. 3.

Thomas Young (1773–1829) was an English physician and physicist (Fig. 1.3). He was remarkably prodigious as a child, having learned to read "with considerable fluency" at the age of two, and demonstrating a knack for languages, such that he had knowledge of English, Greek, Latin, French, Italian, and Hebrew by the age of 13 [26]. He studied medicine and practiced in London while developing and maintaining expertise in a staggering range of areas. For example, he demonstrated the wave theory of light, deciphered some of the first Egyptian hieroglyphics by analysis of the Rosetta stone, helped to establish actuarial science, and lectured on the theory of tides, surface tension, etc. In the biomedical area, he established, with von Helmholtz, the theory of color, discovered and measured astigmatism in the

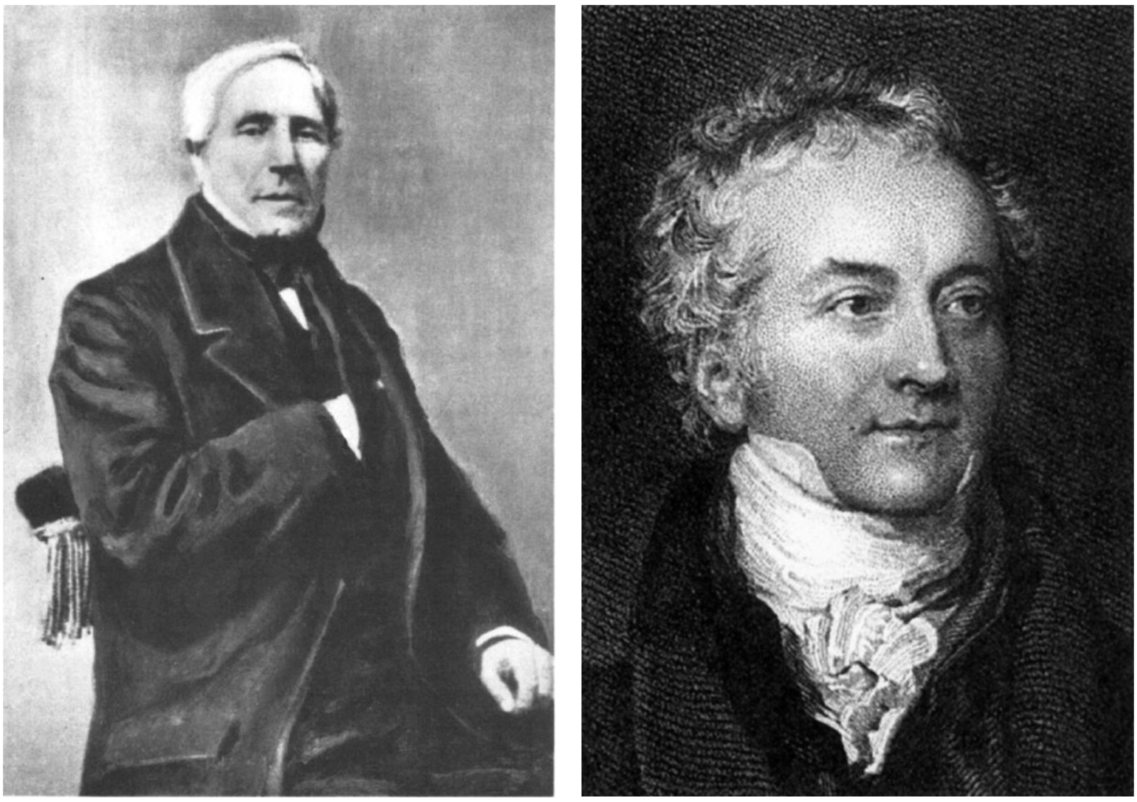

Figure 1.3

Portraits of Drs. Jean Poiseuille (left) and Thomas Young (right). Both men did important work in physiology and medicine, yet are familiar to engineering students: Poiseuille for his work on steady laminar incompressible flow in a tube of uniform circular cross-section (Hagen–Poiseuille flow) and Young from his work on the elasticity of bodies (Young's modulus of elasticity). Poiseuille portrait reproduced with permission from [24] as modified by Sutera [25]; Young portrait by Sir Thomas Lawrence, engraved by G. R. Ward, as shown in Wood [26].

eye, and deduced that the focussing power of the eye resulted from changes in the shape of the lens. He devised a device for measuring the size of a red blood cell, with his measurements showing a size of 7.2 μm [26], a value that is remarkably accurate (see Ch. 3). He also studied fluid flow in pipes and bends, and the propagation of impulses in elastic vessels, and then applied this to analysis of blood flow in the arteries. He correctly deduced that peristaltic motion of the artery wall did not contribute to the circulation of blood, and instead that the motive power must come from the heart [31]. He is most familiar to engineering students for defining the modulus of elasticity, now known as Young's modulus in his honor.

Julius Wolff (1836–1902) and Wilhelm Roux (1850–1924) were German physicians (Fig. 1.4). Of the two, Wolff is better known to biomedical engineers because

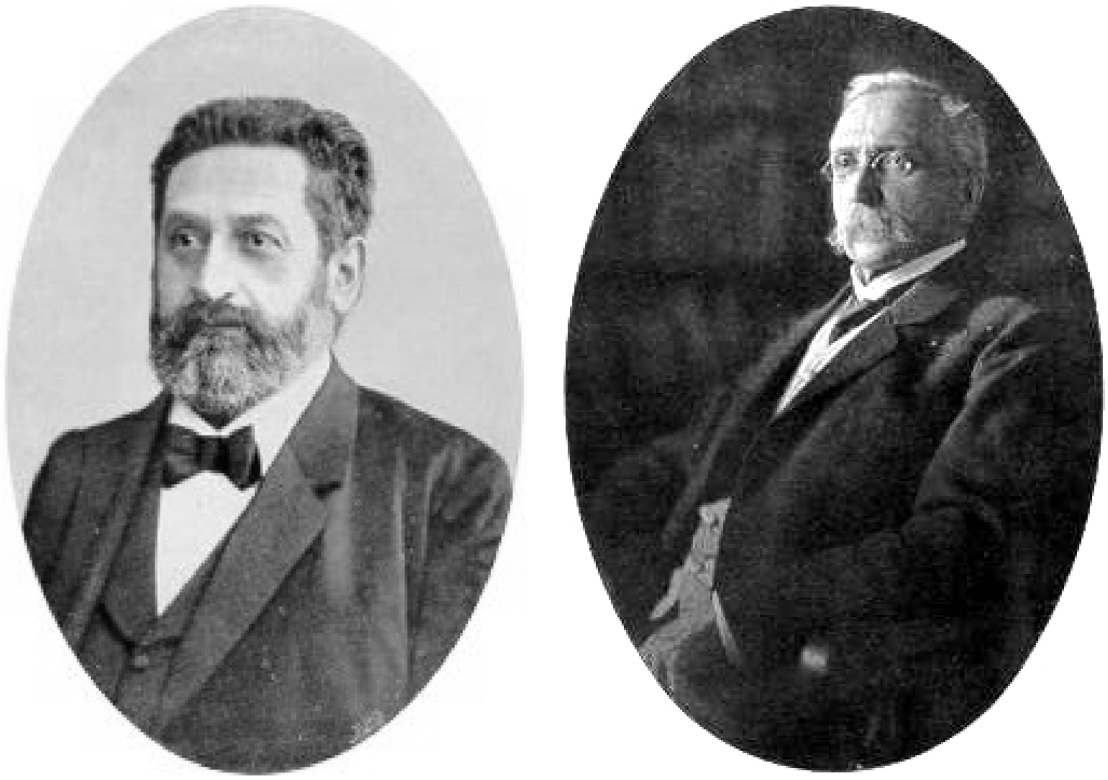

Figure 1.4
Portraits of Drs. Julius Wolff (left) and Wilhelm Roux (right). Both were German physicians who were interested in how mechanical forces could influence the structure and development of bone. Both portraits, courtesy of the Clendening History of Medicine Library and Museum, University of Kansas Medical Center [18].

of his formulation of "Wolff's law" of bone remodeling. Legend has it [32] that the structural engineer Karl Culmann saw a presentation by the anatomist Hermann von Meyer, in which von Meyer described the internal architecture of the bone in the head of the femur. Culmann was struck by the similarity between the pattern of solid elements in the cancellous ("spongy") bone of the femur and the stress trajectories[5] in a similarly shaped crane that he was designing (Fig. 1.5).[6] Based on von Meyer's paper describing this similarity [33], as well as other data available at the time, Wolff hypothesized that bone was optimized to provide maximum strength for a minimum mass. He then went on to formulate his "law" of bone

[5] A stress trajectory is an imaginary line drawn on a surface that is everywhere tangent to the principal stress directions on the surface. Stress trajectories help to visualize how the stress is carried by an object, and they can be used as the basis of a graphical procedure for determining stress distributions in bodies. This graphical solution method is now obsolete, having been replaced by computational methods.

[6] This certainly emphasizes the importance of interdisciplinary interaction in biomedical engineering!