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JACQUES LOEB AND HIS PERIOD[1]

JACQUES LOEB was born in Germany in 1859, within a few miles of Strasbourg, or in a region in which French and German culture had long mingled. His forebears were among the intellectuals who during the persecutions attendant on the Inquisition were driven out of Portugal and compelled to seek asylum in a more liberal country. They migrated from Lisbon to Amsterdam, and in later and quieter times settled in Alsace. Thus, along with an inheritance distinctly intellectual, Loeb profited by contact with one of the richest European cultures during his formative period. The intellectual cosmopolitanism which moulded his growth into physical maturity served him well throughout his varied life. He was easily at home in the sophisticated intellectual atmosphere of Europe and in the younger but rapidly developing intellectual atmosphere of the United States, where he passed the years from 1891 to 1924.

The influence of the French environment on Loeb's mental growth is shown by the part the writings of Voltaire and the French encyclopedists played in it; and the influence of German surroundings is shown equally by the German *Gymnasium* and university training. Loeb attended three German universities—Berlin, Strassburg and Würzburg. It was at Strassburg and Würzburg that he met the conditions which were to guide his subsequent scientific undertakings. But his emotions were profoundly stirred and his inclination toward humanitarianism was fed by the French philosophers, and he always looked to these writers as among the great intellectual and spiritual liberators of all time. In his book, "The Organism as a Whole," published during the great war, his tormented mind returns to them in the search for an anchor and haven of hope. "This book is dedicated to that group of free thinkers, . . ., who first dared to follow the consequences of a mechanistic science, . . ., to the rules of human conduct and thereby laid the foundations of that spirit of tolerance, justice, and gentleness which was the hope of our civilization . . .," until swept away by the great war.

But it was the advanced system of scientific training

[1] Based on an address made at the exercises held at the Marine Biological Laboratory, Woods Hole, Massachusetts, on August 4, 1927, in connection with the erection of a tablet to Jacques Loeb.

of the German university which emancipated Loeb intellectually by providing him with a foundation for his experimental studies. Loeb entered upon his university career at a propitious time; the German laboratories were filled with eager investigators and their thought was dominated by many fundamental problems in physics, chemistry and biology. For a person like Loeb this fortunate circumstance could not fail to yield a significant result. His natively strong, perspicacious, inquiring mind, already colored by the writings of the French philosophers and naturally tending away from superstition and metaphysical conceptions, readily found a resting place in the growing physico-chemical beliefs of the time.

Loeb received the M.D. degree at Strassburg in 1884. To one looking backward in a desire to follow the story of his intellectual development it would seem natural that he should soon discover that it was not medicine as an art so much as medicine as a science to which his tastes turned. Medicine has in the past served as the doorway leading into science for not a few conspicuous men: through it passed Galileo, Gilbert, Young, Helmholtz, and in our day and country Ira Remsen. Even during Loeb's novitiate, as it were, less than to-day was medicine to be counted among the objective experimental sciences. But if experimental medicine, as such, was still woefully backward, physiology, that basic science of biology and medicine, had already made significant progress. During Loeb's student days, Claude Bernard had just ceased his colossal labors and Johannes Müller had hardly more than completed his extraordinary career as leader and modernist in physiology, pathology and clinical medicine, and had left to extend his influence the brilliant pupils Helmholtz and du Bois-Reymond. Moreover Ludwig was already started on the remarkable undertaking to develop quantitative physical physiology which was to produce a generation of investigators and teachers in that field.

It was very good fortune which directed Loeb to Strassburg and a fortune doubtless connected with his Alsatian birth. Into that French-German environment, the German government projected after 1870 a center of higher learning staffed by a group of brilliant investigators and teachers. To the medical faculty it sent such men as Hoppe-Seyler, von Recklinghausen, Schmiedeberg, Naunyn and Goltz. These are names to conjure with in biological chemistry, pathology, pharmacology, medicine and physiology. Loeb was attracted to Goltz, the pupil of Helmholtz, who was adding conspicuously to the then beginning knowledge of cardiac pressure, the mechanism of shock, functions of the semicircular canals, and the effects of excision of the brain and spinal cord in the frog and dog. That the last-mentioned subject should be the one to claim Loeb's special interest is not perhaps remarkable in view of his philosophic prepossessions. It was at this time that Loeb experimented on the chain reflexes and overthrew Munk's thesis that the Rolandic area is composed of cellular "sensory spheres," by showing that the particular paralyses occasioned by each cortical excision are abolished as soon as the wound has healed. The interest in the centers of brain activity thus aroused was to be continued in his later investigation of tropisms with which he concerned himself at Naples, and which led him to substitute for the anthropomorphic conception of the responses of animals according to supposed desires directing voluntary effort, the operation of tropisms or physico-chemical attraction, on the basis of which there was to arise a mechanistic conception of comparative psychology.

At this point it is desirable to retrace a few steps in order to follow the particular events which were to influence so greatly Loeb's scientific development. Like other discoverers in science, Loeb was the product of his period. This central fact in his notable career will become increasingly evident as we proceed. At the threshold of his life's work circumstances brought Loeb from Strassburg to Würzburg, to be the assistant of Fick, a pupil of Ludwig, then professor of physiology, whose contributions to knowledge in the domain of physical physiology are significant. The investigation of such problems as the physiology of the irritable substances, dissipation of energy and heat production in muscle, as well as the publication of larger works on medical physics, would appear to be sufficient to have attracted the quantitatively minded student of physiology to this particular master.

But whatever the benefit derived from this connection, it was small compared with the rewards in store from the chance association with Sachs which it brought about. The association produced admiration and led to friendship as well as to an impulse of direction in scientific pursuit which was to remain essentially fixed throughout Loeb's exceptionally rich and varied career. It was the fortunate chance encounter with Sachs which turned Loeb's talents into the broad channel of general physiology. Has not Claude Bernard[2] said that general physiology is the basic biological science toward which all others converge? Loeb was to find the truth of this axiom for himself and through his discoveries reveal it to a generation of investigators in a far distant land.

The botanist Sachs's personality and discoveries may be said to have dominated the field of plant

[2] Bernard, Claude, "An Introduction to the Study of Experimental Medicine," The Macmillan Co., 1927, p. 65.

physiology for more than thirty years, between 1857 and 1890, and his influence continues up to the present time. The physiology developed by Sachs was based on chemical and physical actions which he described under the term tropisms: heliotropism, chemotropism, geotropism—or reactions to light, chemicals and gravity. Loeb's alert mind grasped the significance of these phenomena, not only for plants but probably also for animals, so that we find him spending the winter months from 1889 to 1891 at the Naples Zoological Station, where the ideas he had formed could be subjected to experimental test. It was this period and under these particular circumstances that yielded Loeb's discoveries in the animal tropisms and in heteromorphosis.

In a recent biographical sketch,[3] one of his distinguished pupils ascribes the studies leading to the idea of heteromorphosis to a desire on Loeb's part to combat the vitalistic conception of orderly animal development. This purpose may well have had a part in the planning of the experiments, since at a later date Loeb became a warm antagonist of all mystical biological beliefs. Be this at it may, Loeb would seem to have been moved also by the conviction that the physico-chemical forces acting on living matter are one and the same, both for plants and animals. In other words, he applied by means of sharp, ingenious experiments the discoveries made by Sachs in plants to animals as well. Later Loeb extended the observations into the field of psychology and found them to hold there, so that he came to apply his deductions to the explanation of certain phenomena of animal behavior. This line of investigation would have been approved by Claude Bernard who wrote: "I am persuaded that the obstacles surrounding the experimental study of psychological phenomena are largely due to difficulties (associated properties) of this kind; for despite their marvelous character and the delicacy of their manifestations, I find it impossible not to include cerebral phenomena, like all other phenomena of living bodies, in the laws of scientific determinism.[4]

Just as scientific men are made by their time, so extraordinary scientific men make their time what it is. Loeb is now definitely launched on his life's work which was, as far as was possible to him and with the knowledge available, to reduce biological appearances, the so-called manifestations of life, to the status of physico-chemical reactions. It is in connection with the investigation of the physico-chemical relations of vital phenomena that Loeb has exercised so great an influence on his generation. This is, of course, not the occasion on which to enter into a discussion of the controversy, not yet wholly adjusted, on vitalism *versus* determinism. Early in Loeb's scientific career, far more so than at present, the nature of vital phenomena was a subject of eager debate. In this early period, the emancipation from mystical notions had not yet come to some great minds. Was not Johannes Müller, the German colossus who bestrode all there was of medical science in his day and who was the master of Helmholtz, a confessed vitalist? He believed in the existence of something in vital processes which does not admit of mechanical expression; his strongly objective mind forced him, none the less, to hold that the mechanical explanation of physiological phenomena was to be pushed to the limit "so long as we keep to the solid ground of observation and experiment."

Fortunately, natural science had progressed further in France in the first half of the nineteenth century than in Germany. The influence of the discoveries of chemists such as Dumas and Berthelot and of others penetrated into physiology. The times brought forward the extraordinary figure of Claude Bernard, of whom Dumas said: "He was no mere physiological experimenter, but physiology itself." Like Magendie and Johannes Müller, he made his bow to vitalism, but gave it the widest possible berth.[5] Paul Bert, pupil and successor to his chair at the Sorbonne, said that, thanks to Claude Bernard, "the scientific method, respect for whose laws leads to certainty in the sciences of dead matter, assumed equal authority in the sciences of living beings." The stage was set for the new era in biology which was now to be established on the rapidly expanding sciences of physics and chemistry.

A succession of remarkable men appeared and their accomplishments were destined to transform the outlook on the natural sciences. Thus, Loeb's generation of biologists was called upon to sustain a weight of investigative genius in physics and chemistry of hitherto unknown magnitude; and to his lasting credit Loeb was to perceive the trend of events and to sense the extraordinary influence which these sciences were to exert on physiology. Hence he threw his splendid talents into the study of biological phenomena along the lines of their physical and chemical activities, with results of which you are aware and which proved to be of the first importance for the subject of general physiology as now conceived. How great this weight of investigative influence was can

[3] Robertson, T. B., *Science Progress*, July, 1926–27, xxi, p. 114.

[4] Bernard, Claude, "An Introduction to the Study of Experimental Medicine," The Macmillan Co., 1927, p. 91.

[5] Garrison, F. H., "Introduction to the History of Medicine," Edition II, Philadelphia, 1917, p. 576.

best be seen from a tabulation, somewhat arbitrarily constructed, which I present. The remarkable effect which the development of that composite science we call physical chemistry—a union of mathematics, physics and chemistry—was to exercise on biology and in the application of which to the interpretation of phenomena of living matter Loeb was an outstanding figure, is presaged in the fundamental discoveries of Gibbs, Pfeffer, van't Hoff, Ostwald, Arrhenius and J. J. Thomson, with whose period Loeb's is in immediate contact.

Faraday	1791–1867
Liebig	1803–1873
Wöhler	1800–1882
J. Müller	1801–1858
Bernard	1813–1878
Ludwig	1816–1895
du Bois-Reymond	1818–1896
Helmholtz	1821–1894
Virchow	1821–1902
Pasteur	1822–1895
Fick	1829–1901
Maxwell	1831–1879
Sachs	1832–1897
Goltz	1834–1902
Gibbs	1839–1903
Pfeffer	1845–1920
Emil Fischer	1852–1919
van't Hoff	1852–1911
Ostwald	1853–
Ehrlich	1854–1915
J. J. Thomson	1856–
Arrhenius	1859–
Loeb	1859–1924
Nernst	1864–
Donnon	1870–
Einstein	1879–

It was characteristic of Loeb's agile mind that he should so surely and quickly catch the drift of thought and feeling, or the *Zeitgeist,* of the period and proceed to bend the new physico-chemical knowledge to the uses of physiology. This was only repeating what he had already done with Sach's tropisms, and is something which fertile minds are always doing or striving to do. A mathematician has told me that the growth of mathematics in the last fifty years made possible Einstein's calculations, which corrected and extended Newton's discoveries. Taken all in all, physical chemistry constituted for Loeb the bright silver thread on which are strung the brilliant beads of his discoveries. What the chief of these beads are may be read on the bronze tablet erected to-day to his imperishable memory: "Brain Physiology; Tropisms; Regeneration; Antagonistic Salt Action; Duration of Life; Colloidal Behavior." A remarkable list truly of significant titles, and more remarkable even in that these complex phenomena should have been brought so largely within the definition of physico-chemical action.

* * * * *

Jacques Loeb has been among us so recently that many of us recall as of yesterday his vivid personality —his scholarly, slightly stooped figure, his noble head with strongly marked, reflective features, his thoughtful and somewhat pensive eyes, and the hearty, merry peal of laughter with which he lightened passing events of a world to him not always devoid of depressing moments and anxious thoughts.

The man Loeb was the scientist, ever pursued by an inner demon demanding of him the solution of the next problem. It is of men like Loeb that Priestley said that each discovery shows many other discoveries that should be made, and Pascal invented the paradox that, "We are in search never of things, but of the search for things." Loeb gave himself no respite; each succeeding year he drove, if possible, with greater intensity toward a goal always being approached and yet always eluding. Possessed of that vigorous quality of imagination which goes by the name of intuition or even inspiration, and which in essence consists of a feeling in the mind that amounts to a presentiment of truth, he was a remarkably fruitful inventor of ideas or hypotheses, the experimental verification of which is the chief means of extending scientific knowledge. His prescience reminds an associate of Faraday, because of Loeb's uncanny gift of knowing the truth before the experiment was made. "I know what it is; the question is how to prove it."[6] The proof might be long in coming, but it would come and then the result would be startling. Loeb's habit was to ponder, sometimes for years, chance findings, until the mode of attack of the problem appeared, and he then moved with precision and celerity. In this way fragmentary observations, partly his own and partly others, on artificial fertilization led to the discovery of its production at will, and artificial parthenogenesis was discovered.

Newton said that he made his discoveries "by always thinking unto them . . . till the first dawnings open slowly little by little into a full clear light." The power of long thought is something that goes with the highly original gift which we associate with genius. Buffon said that genius is patience, and Newton attributed his discoveries to "nothing but industry and patient thought." Claude Bernard's definition is more searching: "Genius is revealed in a

[6] Northrop, J. H., "Jacques Loeb—1859 to 1924," *Ind. Eng. Chem.,* 1924, xvi, 318.

delicate feeling which correctly foresees the laws of natural phenomena; but this we must never forget, that correctness of feeling and fertility of idea can be established and proved only by experiment."[7] "Genius is patience? No, it is not quite that, or rather it is much more than that; but genius without patience is like fire without fuel—it will soon burn itself out."[8] Loeb possessed the patience and he had the industry; alas, his industry was in excess of his physical constitution, so that he burned out his life before he consumed his talents.

In 1910 Loeb exchanged a professorship at the University of California for membership in The Rockefeller Institute for Medical Research. He organized at the Rockefeller Institute the Division of General Physiology, the first department of the kind to be created in the United States. It was fitting that Loeb, whose discoveries had so enriched general biological science, should have been the pioneer of general physiology in this country. The growth of the new establishment was such that in 1918 a *Journal of General Physiology* was called for and Loeb undertook the task of founding and editing such a journal. His removal to New York called for modification of the research program. As may be observed from his discoveries in the field of colloid chemistry, his fertile mind met the new conditions. By dividing the year between New York and Woods Hole, Loeb's working facilities were enlarged; and this happy arrangement filled his last years with scientific opportunity commensurate with his needs, sympathetic scientific association, and although grudgingly given with those recreative enjoyments which his intense nature required.

Loeb was of the type of the intensive individual investigator; hence his immediate pupils are not numerous. But if Loeb's direct influence was reserved for a favored few, his wider influence has been shared by a large body of students and investigators and even by the educated lay public. His personal contact with successive groups of scientific workers at Woods Hole, the Rockefeller Institute, and elsewhere has been of incalculable value. Loeb's profound scientific learning and experience, wide reading, liberal views often warmly expressed, vivid imagination widely dispensed, and his fund of sparkling wit made him at all times a stirring and delightful companion. No one could have been kinder than Loeb in his human relations; and fortunate were those who came under the reign of his genial, many-sided personality. It is unhappily too true of him "that he may be succeeded, but can not be replaced."

[7] Bernard, Claude, "An Introduction to the Study of Experimental Medicine," The Macmillan Co., 1927, p. 43.

[8] Lodge, Sir Oliver, "Pioneers of Science," London, The Macmillan Co., 1893, p. 202.

Jacques Loeb's life was spent in an ardent desire to interpret nature. It was peculiarly true of him, as has been said, that knowledge is at once the sole torment and the sole happiness. He knew as few come to know the joy of discovery, which is one of the liveliest the mind of man can feel. He knew also, almost too well, that this joy of discovery, to which his inner demon impelled him, is no sooner found than lost; that it is but a flash, whose gleam discovers fresh horizons, toward which our insatiate curiosity repairs with still more ardor. This is research: the search for truth which, if never found in its wholeness, is yet secured in significant fragments; and these fragments of universal truth are precisely what constitutes science.[9] To this search for fragments of universal truth in living matter Jacques Loeb devoted his great talents and his rich life.

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CHEMISTRY IN RELATION TO BIOLOGY AND MEDICINE WITH ESPECIAL REFERENCE TO INSULIN AND OTHER HORMONES

II

ORGANS OF INTERNAL SECRETION

I may now be permitted to call your attention to a field of knowledge that has occupied experimenters for more than half a century—a field of great importance not only to the biologist in general, but to those who are associated in any way with medicine, as the bio-chemist, the physiologist, pharmacologist, the numerous representatives of the medical and surgical professions—a field that is concerned with a study of the functions, both normal and abnormal, of the organs of internal secretion. To the chemist is given a unique opportunity in this field and here, as is so often the case in biology, the last word is his. In saying this I have particularly in mind the obvious chemical aspects of the problems here presented, as, once they are cleared up, the physiologist and the physician are enabled to outline their own problems relating to the function of these organs with greater precision.

The significance of the interdependence of the various mechanisms of the animal body, of their admirably regulated activity and the harmonious manner in which these mechanisms cooperate in the development and growth of the individual from the moment when they first become apparent in early embryonic life to

[9] Bernard, Claude, "An Introduction to the Study of Experimental Medicine," The Macmillan Co., 1927, p. 222.