— V.F. Loeb, Jacques

In a niche overlooking the East River at the extreme northeast corner of the Institute, the President's House is the center of the gracious hospitality of President and Mrs. Bronk. The cover sketch by Vincent Furno shows the intimate garden, facing the river, where Institute faculty, students, and guests attend receptions and garden parties. Behind the curved stone entry is an interior of breath-taking yet quiet beauty, scene of many treasured and stimulating intellectual and cultural discussions.

JACQUES LOEB: RECOLLECTIONS OF HIS CAREER AS A SCIENTIST

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I HAVE, over the years, evolved some concept as to what constitutes a proper biography of one, who, as a leader, has contributed greatly to a field of study. According to this concept it is at first essential to outline the state of knowledge antecedent to such contributions, not only in the specialized fields, but in contiguous scientific fields. It is next essential to indicate in a broad fashion the general character of the chief contributions of the biographee. The third step requires that one indicate what qualities of education, experience, training he possessed and more especially by what particular endowments the biographee was, by his timely appearance, led to make the contributions. With such a background it is then possible, logically and chronologically, to accompany the biographee along the interesting, often exciting, sometimes tedious, difficult and frustrating trail which culminated in his ultimate success with a great discovery. In a considerable measure this has been accomplished by Osterhout in his sketch in the *Journal of General Physiology* (Volume 8, 1928).

MECHANISTIC DETERMINISM

In a short talk such as this, however, it is obviously impossible to do more than touch lightly on only a few of the salient points in Jacques Loeb's scientific career. For this career was one of exceptional, great achievements embracing several fields but unified by a guiding principle that virtually comprised a new philosophy of thought and procedure leading to what is today called experimental biology. In what follows I shall stress primarily the scientific career of Jacques Loeb against the background of his times, attempting to show how the mechanistic conception evolved. After this I shall mention those salient personal characteristics which made his success possible.

The physical sciences, essentially chemistry and physics, had, by 1880, passed through several interesting phases since the work of Galileo laid the foundation of sound scientific advance by means of controlled quantitative investigation. First came the instrumental period in which measuring devices were perfected and data were rapidly accumulated. These were recast into a more useful form in virtue of the systematization following Newton's generalizations defining force. With the unification and direction to experimentation afforded by this system, data and relations between physical manifestations followed so rapidly that in less than one hundred and fifty years the stage in the physical sciences was set for the great period of generalizations described as the systematic period. This led to the enunciation of the great principles of the conservation of matter and of energy; the second law of thermodynamics; the theorems of Laplace, Green, Gauss, Clausius, Boltzmann and Maxwell; the kinetic theory of gases; and culminating, among other things, in Maxwell's electromagnetic theory relating light and electricity. This theory was dramatically confirmed by Heinrich Hertz in 1888 with the discovery of electromagnetic waves. Organic chemistry had been sent on its rapid advance by Kekulé in 1865 and great advances in the syntheses of substances associated with living processes were being made. Arrhenius was developing his theory of electrolytic solutions and physical chemistry in such capable hands as Nernst, and his school was making rapid progress. Willard Gibbs was beginning his investigations. This successful culmination of the basic Newtonian mechanistic system had led to its general acceptance, and all thinking was carried out in its terms. In fact, the success was so striking that physicists believed that, given enough time and mathematical skill, from the state of a system at a given time, its future state could be computed with precision. It was further asserted by some that the future of experimental physical discovery lay in the fourth significant figure.

BIOLOGICAL REACTIONARIES

In the life sciences things had also begun to move. Bacteriology had been well launched through the work of Louis Pasteur and was already exerting its influence in redirecting the course of medical advance. Physiology, especially vertebrate physiology, was making rapid progress. The classification of species in the fields of Botany and Zoology had culminated in the development of Darwin's evolutionary concepts which placed evolution on a more rational basis. Mendel's work was being revived and De Vries was developing his theory of mutations. Work on lower organisms was beginning at the Naples and Woods Hole Marine laboratories. Sachs, the botanist, was developing his theory of tropisms of plant behavior and growth.

However, the reaction to Darwinism and the great complexity of the behavior of living systems had consolidated the vital-

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ists and others who would today be called reactionaries. Experimental controls were not adequate and work and issues were confused. Thus the life sciences were riven with controversies and polemics in these areas with much confusion. It was onto the scene at this stage that the active scientific career of Jacques Loeb began.

Deterred from conventional schooling owing to the ill health of his parents, Jacques Loeb found himself at loose ends when his father died. After a short venture in banking, which he thoroughly disliked, he was encouraged to undertake a neglected education by his uncle, Professor Harry Breslau, a noted historian at Berlin. Entering the Askanische Gymnasium, he threw himself wholeheartedly into his schooling. Graduating with a purely classical training and noted for his proficiency in speaking Latin, he so impressed his teachers that in an unusual gesture they presented him with a volume of Zeller's *Philosophie der Griechen* with the admonition not to become too liberal. His reading and studying had led him to seek an understanding of the human mind and the role of instinct in human behavior. It was his hope that, understanding these problems, mankind could achieve a happier state. He spent one term at the University of Berlin in 1880 listening to lectures in philosophy which convinced him that the solution to his problems was not in that field. In fact, he formed a distaste for the subject that lasted throughout his life. The only philosophy that impressed him was that of the physicist, Mach, oracle of the Newtonian mechanism. This philosophy was to help direct his thinking in later years. The next semester at Munich hearing lectures in the psychology of that era again convinced him that the way to understanding mind and instinct lay more likely in direct experimentation with the brain. He therefore went to Strasbourg to work with R. F. Goltz, then studying localization of functions in the brain. Goltz urged him to obtain his medical degree as a preparation to working in this field. He obtained his M.D. in 1884 and passed his state examination in 1885. He then became assistant to Zuntz in Berlin in further studies in brain physiology. Here he published his first paper based on his earlier work with Goltz purporting to disprove assertions of Hitzig and Munck. This resulted in a prompt denunciation of his work by those workers which did much to dishearten him. However, William James at Harvard wrote him a kind letter endorsing his work, thus starting a long friendship between the two men. It must be recalled that as life sciences were then evolving often with inadequate data, scientific polemics were frequent, violent, and often descended to the level of personalities. This attitude in all sciences was particularly bad in Germany. The more senior professors encouraged their students to carry the onus of attack in such cases and this training exerted its influence on the young physiologist in several ways. An avid and fearless seeker after truth, the effect of these early polemics taught the young scientist the necessity of so conducting his experiments and checking his results that there was no chance of error. Thus it transpired in later controversy that irrespective of differences in interpretation, Jacques Loeb's experimental results were irrefutable.

At the Jacques Loeb Centennial Commemoration held at the Hopkins Marine Station in Pacific Grove, California, on July 12, 1959, Dr. Leonard B. Loeb presented the review of his father's scientific career published here. Jacques Loeb left California in 1910 to come to the Rockefeller Institute where he remained until his death in 1924. During that period he founded the *Journal of General Physiology,* now in its forty-second volume, and he exerted a profound influence on the physicochemical study of biological systems. Leonard Loeb is Professor of Physics at the University of California.

Jacques Loeb throughout his life was an avid reader of the sciences. Thus, from his library dating back to his early years of study when he turned over his books on physics to me from time to time, it is clear that he was well acquainted with the developments of physics and chemistry of the era earlier alluded to. There is no doubt that such books as Clausius' *Mechanische Wärmetheorie* (based on pure mechanism) and the many other books of its kind exerted a very strong influence on the mind of Jacques Loeb. Analogously his acquaintance with Arrhenius' theory of electrolytic solutions was to appear and direct much of his later work. While never properly schooled in mathematics essential to formal training in the physical sciences, except that little he got in medical school, he had a most amazing feeling for an insight into the nature of the physical processes. Thus as his work progressed in those early years he realized that truth could be found only via the contemporary scientific methods of physics and chemistry as typified by the mechanistic constructs of Newtonian physics. It was through truth arrived at by such means that he felt one could emancipate humanity from ignorance and superstition. While his intense humanism which characterized his whole life was certainly a factor in motivating the young scientist as Osterhout claims, the search after truth, the excitement of discovery and the joy of successful solution to a problem were the dominating factors in his life as they are in that of all good scientists.

In 1886 he became assistant to Fick at Würzburg. There he came under the influence of the botanist Sachs, who, though quite senior, became his close friend and mentor. This was the turning point of his life. He was fascinated by the studies of Sachs on the effect of light on plants and with his vivid imagination, which was perhaps another of his outstanding assets, he saw a parallel to the supposed instinctive movements and behavior of animals. Thus began his famous experiments on the tropisms in the study of the Porthesia Caterpillars. This new line of work in the study of animal tropisms was a great relief, for at this juncture he had begun to feel that studies such as those with operations on the brain were not too suggestive and with his humanistic feelings continued operations on warm-blooded animals had become most repugnant to him. In the fall of 1888 he was again at Strasbourg as assistant to Goltz, but his studies were taking him into other fields. In 1889-1890 he spent the winter at Naples. There he began studies in regeneration with hydroids and of the depth migrations of certain lower forms. Here again the influence of the studies of Sachs and others on plants can be seen, for in his studies of heteromorphosis and regeneration he was again applying to the animal kingdom those principles amenable to mechanistic physicochemical interpretation which Sachs had observed in plants. At Naples he laid other foundations for his future when he became acquainted with H. B. Ward and Norman, two young American biologists whose investigations interested him. Perhaps more fortunate among his Naples contacts was his acquaintance with F. P. Mall, the anatomist at Johns Hopkins. It was, in fact, F. P. Mall who, impressed with Loeb's brilliance, obtained for him his position at Bryn Mawr and a year later impressed R. F. Harper, talent scout for his brother, William R. Harper, the newly appointed President at Chicago to get Whitman to bring Jacques Loeb to Chicago.

WOODS HOLE SUMMERS

In consequence of his marriage in 1890 to Anne Leonard, an American girl who had just obtained a Ph.D. at Zürich whom he met at the home of her sister who had married Justus Gaule, the physiologist at Zürich, it became urgent to take a position to augment his limited income from inheritance. Thus in November 1891 he came to America to teach Systematic Botany at Bryn Mawr. The following summer he began his work at Woods Hole. From there he was called to the newly organized University of Chicago, initially as a member of Whitman's department, and later as the head of the Department of Physiology. His summers from then on were largely spent at Woods Hole.

At Chicago that first year the University buildings were not completed. Thus he shared a laboratory in an old apartment building with the physicist, A. A. Michelson. Michelson had the sink in the bathroom for his needs in making mirrors while Jacques Loeb had the bathtub for his frogs. The two formed a close friendship which lasted throughout their lives. Loeb's interest and study in the physical sciences throughout his life brought him close personal friendships with most of the leaders in those fields, such as W. Ostwald, S. Arrhenius, Ernest Rutherford, Albert Einstein, and there is little doubt about the influence of these workers on his mechanistic thought.

It was in Woods Hole, however, that his newly developed interests in tropisms and heteromorphosis led him to much further understanding of the processes at work through physical and chemical actions. Thus in the period 1891 to 1899 he began to study the effects of ions on marine organisms and eggs. These led to the discovery that with CO_2, a change in hydrogen ion concentration in water could reverse the tropistic movements of certain lower swimming forms. He applied the Bunsen-Roscoe law to orientations of animals to a single source of light at different intensities. It was the experiments with ions on sea urchin eggs that led to the discovery of antagonistic salt action and parthenogenesis. The latter gave him a scientific notoriety which he heartily deplored. For despite his brilliance, his sometime aggressiveness and his many achievements he was one of the most modest and humble men I have known. His unwillingness to cooperate with the press, however, did not stand him in good stead.

With the success of his many different lines of investigation using the physicochemical techniques on problems of living organisms, Jacques Loeb became more and more convinced of the validity of the mechanistic conception of life as opposed to the vitalistic school. This viewpoint was perhaps best summed up in his small book entitled *The Mechanistic Conception of Life.* Needless to say, such views, asserted with assurance and buttressed by sufficient data to make them appear sound, aroused much opposition and such open hostility from the camp of the vitalistic school that life was not always a bed of roses for him.

One other notable trait of Jacques Loeb was his perseverance in seeking answers to vital questions. If with his keen scientific intuition a given line of attack was not profitable at the time, it was laid aside to be taken up again as new avenues of attack appeared open. Following the success of the effect of chemical agents in studies on artificial parthenogenesis, further studies, including fertilization of eggs of one species with sperm of unrelated species and production of twins by changes in chemical environment both at Woods Hole and at Pacific Grove, inevitably led to the study of penetration of ions through membranes. Such investigations brought him to the study of protein chemistry starting with the swelling of gelatine and the discovery of the importance of the isoelectric point while at the Rockefeller Institute. In this field Jacques Loeb entered the most brilliant and significant phase of his scientific evolution, among other things applying the Donnan equilibrium to such systems. This excellent series of investigations into protein chemistry initiated in the closing years of his active life belies the common superstition that a man's greatest productivity and originality occurs early in life. In fact, he was still making rapid progress in this field at the time of his death.

In consequence of a trip to Bermuda he discovered the Bermudian "Life Plant," *Bryophyllum calicinum,* and with it saw a chance to resume his regeneration and growth experiments in a quantitative fashion. Notable also during this period were his experiments on the life span of banana flies as a function of temperature, performed together with Northrop. These proved that the life span of animals kept in a sterile environment follows the well known van't Hoff temperature law of chemical reaction.

It is hoped that this brief sketch of the evolution of Jacques Loeb's scientific career and philosophy as related to the times has proved of interest. It is now perhaps fitting to summarize some of his personal attributes that led to his success.

ATTRIBUTES OF SUCCESS

His phenomenal memory has already been mentioned. Such a memory coupled with a very active, enquiring mind with a high degree of originality was undoubtedly responsible in a large measure for his success. Beyond this he had that rare gift of scientific intuition, recognizing where progress was significant and feasible and where further study was futile. He had enormous basic self-control and self-discipline in which from boyhood up he had deliberately schooled himself. To those who knew his general lack of interest in physical activity it may be a surprise that as a young man he did a good deal of rowing and later in life made some of the more difficult Alpine ascents. He was an omnivorous reader in science generally. Literature as such had little interest or appeal for him. In fact, it is from his extensive reading that he developed many of his new, simple and useful techniques in solving problems. His stimulating interest in much that he read was imparted to all those around him. In fact, his enthusiasm for cataphoretic and electrical endosmosis studies

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as well as his interest in Lenard's studies on spray electrification were passed on to the writer in such measure that he and his students carried on studies in the area which after some twenty years of research were summarized in the first general book on *Processes of Static Electrification,* published in 1958. In consequence of his extensive reading, his broad range of interests and scientific observations, his need for self-expression led to a steady flow of publications in the form of papers and books. In this way his scientific audience extended far beyond the range of those few students who were privileged to hear his lectures. One characteristic that most of his acquaintances did not know of was the percentage of his waking hours devoted to his thinking about his work. In this writer's extensive acquaintance with the leading physicists of the atomic era he knows of no one, with the possible exception of J. J. Thomson, who spent a greater proportion of his waking hours thinking of his work. The writer must confess that at home in Woods Hole after final examinations it was at times a bit of a chore to keep up with his father's continual discussion of his problems. Finally there is one more characteristic of scientific work that was vital to his success. This was the exacting and intelligent but meticulous care he used in repeating and checking all his observations before publication. The writer knows of few physicists with the possible exception of Rutherford who made as sure of the accuracy of experimental data published as did Jacques Loeb.

These are the salient features of Jacques Loeb as a leading scientist that the writer wishes to recall. Of his other personal characteristics, his humanism, his moral courage, his crusading spirit, his generosity and sense of humor, others can better testify.

This presentation began by describing Jacques Loeb's development and achievements in relation to the scientific background of his times. Inspired by humanistic principles and scientific curiosity, he carried over the highly developed physical chemical concepts of the Newtonian mechanistic determinism of the end of the 19th century to the life sciences. In so doing the concepts shaped his philosophical viewpoint as exemplified in his book, *The Mechanistic Conception of Life.* It is ironical that while these principles as applied to biology were achieving their greatest success, a success which is even more brilliantly carrying over to the present era, Newtonian mechanistic determinism was being ushered out by the newly discovered principles of relativity, quantum mechanics and uncertainty. Strangely enough, although closely associated with the leaders establishing this newer physics, Jacques Loeb, to the time of his death, did not seem perturbed by the implications of the indeterminancy inherent in the new advances. For at this period the inherent predictability of the future status of a sequence of events from some initial situation was in the newer physics being replaced by generalized mathematical formulations of relativistic and quantum mechanics. These denied such predictability but yielded exceptionally accurate estimates of the *relative probabilities of occurrence of the many possible* situations resulting from the previous single sequence of events. Thus Newtonian predictability and determinism were forced to give way to an inherent indeterminancy and thus unpredictability in detail, quite inconsistent with the mechanistic philosophy of the past. Fortunately, when dealing with the enormous numbers of sequences involved with the myriads of particles associated with physical chemical systems amenable to thermodynamical study the probabilities in the quantum mechanics became quite consistent with the thermodynamical predictions which are so vital to physical chemistry as applied to living organisms. That Jacques Loeb was aware of the radical trend of the times is certain. Svante Arrhenius had visited him in 1911 after Arrhenius' participation in the important Solvay Congress of that year. At this conference the leading physicists, convinced by Planck's study of the radiation laws, Einstein's analyses of specific heats and the law of photoelectric emission as well as studies of others, had formally accepted the quantum which is definitely a non-Newtonian principle. Arrhenius, a staunch mechanist at that time, predicted to the writer that the whole future of physics and chemistry were bound to be dominated by quantum principles—a prediction amply borne out as time went on.

The reason that the abandonment of the basic principles of Newtonian mechanistic determinism did not disturb Jacques Loeb's

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LOUISE PEARCE

Member of the faculty of the Institute from 1913 to 1951, Louise Pearce died at the age of 74 on August 9, 1959.

Nearly fifty years ago Dr. Pearce and Dr. Wade Hampton Brown embarked on a study of the chemotherapy of African sleeping sickness. After six years of studies with animals, Dr. Pearce undertook to carry out tests on humans in the Belgian Congo. Dr. Peyton Rous has written: "The tests required great physical strength and courage as well since they would be done at personal peril...Dr. Pearce was vigorous and forthright, resolute and intrepid. Laboring amidst natives who were hopelessly ill, and helped by the Congo doctors, she brought about one of the most shining and spectacular of the early purposeful achievements of the Institute, the conquest of sleeping sickness."

Later, Dr. Pearce and Dr. Brown encountered a transplantable rabbit cancer during their studies of syphilis. Today this cancer, the Brown-Pearce Carcinoma, is still widely studied. Dr. Pearce found the virus cause of rabbit pox, and still later, with Dr. Brown, studied hereditary disease in rabbits, discovering facts of wide significance.

A native of Winchester, Massachusetts, Dr. Pearce studied at Stanford University and in Boston. She received her M.D. degree from The Johns Hopkins University in 1912. In 1953 the King of the Belgians honored her by conferring on her the King Leopold II Prize of $10,000 and making her an officer of the Royal Order of the Lion. She had received innumerable honors, and served as Visiting Professor of Medicine at the Peiping Union Medical College and President of the Women's College in Philadelphia.

In 1951 Dr. Pearce retired to Trevenna Farm in Skillman, New Jersey, where she made her home in recent years with the novelist, Miss I. A. R. Wylie. She is survived by her brother, Ronald Pearce, of New York City.

RECOLLECTIONS OF JACQUES LOEB *continued from page four*

faith in his Newtonian-based Mechanistic Conception may stem from two conditions. The first lay in the fact that in 1924 the wave mechanics, the dual character of electrons and atoms as waves and particles, and the principle of indeterminancy of Heisenberg which touched off the more intensive philosophical and other controversies lay two to four years in the future. The second and probably more important factor was that aside from the philosophical implications the experimental techniques and in many cases the grosser physical chemical aspects and laws were generally unaffected by indeterminancy. Thus, as proven by the rapid advance of the life sciences under application of the earlier classically Newtonian methods of physics and chemistry, there was little doubt but that, except for more philosophical aspects, the mechanistic conception in experimental application to biology appeared to be the correct procedure for studying basic biological problems. This fact may have sufficiently masked the more philosophical aspects at that time so that Jacques Loeb was not faced with the necessity of altering his philosophy. How seriously the later, more clearly stated philosophical aspects of quantum mechanical indeterminancy as opposed to Newtonian determinism with their humanitarian implications would have upset the mechanistic faith of Jacques Loeb is hard to estimate. With his intolerance and distrust of philosophical polemic it is probable that he would have been content with the continued application of the physicochemical approach. Thus he would have accepted and welcomed the new research potentialities of modern physical chemistry in his pursuit of truth and understanding about vital processes leaving speculations as to the deeper significance of indeterminancy to the philosophers.