The Organic Physics of 1847 and the Biophysics of Today*

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"I cherish the firm conviction that the physico-mathematical research method correctly applied, is in a position to do a great service to organic physics."[1]

Emil du Bois-Reymond, 1848

THE great dream of Emil du Bois-Reymond and his famous colleagues, to found a new physiology consisting of biochemistry and biophysics, seems to have gone astray sometime during the last hundred years. Not only is biophysics springing up as a new science largely unaware of the goals or even the existence of the organic physics of 1847, but also it is largely springing up outside the main line of classical physiology. Since that main line was in great part established by the biophysicists of 1847, Carl Ludwig, Hermann von Helmholtz, Ernst von Brücke, and Emil du Bois-Reymond, it seems worthwhile to investigate the goals and fate of the 1847 program.

It is convenient to refer to these men as the 1847 group and to their program as the 1847 program. The basis for selecting this year is that in 1847 Ludwig became acquainted with the other members of the group. Brücke and du Bois-Reymond had been friends for years, and du Bois-Reymond and Helmholtz had met in 1845. The latter three were students of Johannes Müller. Ludwig, slightly older, had been a pupil of Ludwig Fick. Since the movement as a whole is identified with all four of its members and since most authors characterize it by quoting Ludwig's statement about the 1847 meeting in Berlin: "We four imagined that we should constitute physiology on a chemico-physical foundation, and give it equal scientific rank with Physics . . .,"[2] 1847 seems an appropriate date to attach to the movement. In mid-year of 1847 Ludwig was thirty and fairly well started on his career, having several important publications and holding an appointment as a.o. Profes-

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1 Emil du Bois-Reymond, *Untersuchungen über thierische Elektricität,* Berlin, G. Reimer, 1848, p. xxvi. Part of the Vorrede was republished by du Bois-Reymond in his *Reden,* and is better known in that context under the title "Über die Lebënskraft." All translations in this paper are my own unless otherwise indicated.

2 Quoted from Burdon Sanderson's "Ludwig and modern physiology" as reprinted in *Sir John Burdon Sanderson,* by Lady Burdon Sanderson, Oxford, 1911, p. 281.

sor at Marburg. The others were still working with Müller. Brücke and du Bois-Reymond were 28 and Helmholtz was 26.[3]

The 1847 group expressed their views about the nature of physiology during the ten years centering around 1847. In 1841 du Bois-Reymond wrote "I am gradually returning to Dutrochet's view 'The more one advances in the knowledge of physiology the more one will have reasons for ceasing to believe that the phenomena of life are essentially different from physical phenomena,'"[4] and in 1842, "Brücke and I have sworn to make prevail the truth that in the organism no other forces are effective than the purely physical-chemical . . .,"[5] and in 1845, "I have made the acquaintance of Helmholtz. . . . This is (*sauf la modestie*) to Brücke and my humble self the third organic physicist in the group. A stout fellow who has lapped up chemistry, physics, mathematics, entirely sharing our philosophical point of view and rich in thought and new viewpoints."[6]

In 1848, in the preface to his *Untersuchungen über thierische Elektricität,* du Bois-Reymond discussed the problem in much greater detail. It was this book and its preface which, along with Ludwig's *Lehrbuch* of 1852, made the greatest contemporary impression as propaganda for the physical viewpoint. Adolf Fick refers, in his eulogy of du Bois-Reymond, to "the epoch making effect which the appearance of du Bois-Reymond's *Untersuchungen* had produced"[7] and goes on to say: "I still remember exactly the strong impression which that noteworthy book made upon me as a young student almost fifty years ago when my unforgettable teacher Ludwig handed it to me to report on in a physiological colloquium. One understands even today that this book must make an overpowering impression if one observes the monumental labor put into it and in particular realizes that here for the first time a broadly planned investigation of an extensive field of physiological phenomena was carried out in accordance with the most rigorous physical methods."[7]

In this preface we find such statements as that at the head of this paper and, "The true nucleus of the method, therefore, the

[3] These dates and much of the information on "geneologies" have been taken from K. E. Rothschuh, *Geschichte der Physiologie,* Berlin, Springer, 1953.

[4] Estelle du Bois-Reymond, *Jugendbriefe von Emil du Bois-Reymond an Eduard Hallman,* Berlin, Reimer, 1918, p. 98. Several of the following quotations are to be found in Owsei Temkin, "Materialism in French and German physiology of the early nineteenth century." *Bull. Hist. Med.,* 1946, *20,* 322-7. I am greatly indebted to this short but extremely suggestive paper.

[5] *Jugendbriefe,* p. 108.

[6] *Ibid.,* pp. 122-3.

[7] Adolf Fick, *Gesammelte Schriften,* Würzburg, Stahel, 1904, v. 3, p. 492.

root of the physical mathematical technique, lies . . . in the effort to determine the basic connections of the natural phenomena beneath the mathematical structure of their relationships,"[8] and the assertion that "it cannot fail that . . . physiology . . . will entirely dissolve into organic physics and chemistry. . . ."[9] Equally remarkable and entirely characteristic of its author is the statement: "I have succeeded, unless I am completely deceived, in awakening to vigorous reality, although in a somewhat altered form, that hundred year dream of physicists and physiologists of the identity of the nerve process [Nervenwesens] and electricity."[10]

The boldest statement of the absolute scope of the physical method is one which du Bois-Reymond spent the next few decades explaining, his famous remarks on the freedom of the will: ". . . those who are of one mind with me will not permit themselves to be shaken in the conviction, that nevertheless, if only our methods sufficed, an analytical mechanics of the general life process would be possible. This conviction rests on the insight, possessed even by Aristotle, that all changes in the material world within our conception reduce to motions. Therefore even that process cannot be anything but motions. But again, all motions may ultimately be divided into such as result in one direction or the other along the straight line connecting two hypothetical particles. Therefore to such simple motions must even the processes within the organic state ultimately be reducible. This reduction would indeed initiate an analytical mechanics of those processes. One sees, therefore, that if the difficulty of the analysis did not exceed our ability, analytical mechanics fundamentally would extend even to the problem of personal freedom. . . ."[11]

In his "Ueber die Grenzen des Naturkennens"[12] of 1872 du Bois included freedom of the will among the "transcendental" problems of which he said "ignorabimus." Still later, in "Die Sieben Welträtsel"[13] of 1880, he partially retracted his retraction, having been annoyed by the success of "ignorabimus" in the hands of people he disapproved of, and offered the more cautious "dubitemus." In terms of the goals of 1847 it is the initial sweeping assertion that is of interest, especially since it emphasizes the degree

8 *Untersuchungen,* p. xxix.
9 *Ibid.,* p. l.
10 *Ibid.,* p. xv.
11 *Untersuchungen,* p. xxxv.
12 Emil du Bois-Reymond, *Reden,* Leipzig, Veit, 1912, v. 1, pp. 441-73.
13 *Ibid.,* v. 2, pp. 65-98.

to which mechanistic explanation meant just that, explanation in terms of the motion of material particles.

Ludwig's view and practice at this time can be gauged from the frequently quoted first sentence of the *Lehrbuch* of 1852: "Scientific physiology has the task of determining the functions of the animal body and deriving them as a necessary consequence from its elementary conditions,"[14] and, "This summer I have again ridden mathematics very hard and become tolerably firm in the saddle, up to the partial integral equations (Francoeur). Now I shall study Poisson, in order next summer to resume my experiments on the flow in elastic tubes."[15] Ludwig had taken an anti-vitalistic position in his Habilitationschrift, before he had met the others of the 1847 group: "Rei peritos minime miraturos mihi persuadeo cur hisce pagellis de vi vitali haud multum disseratur, fusius contra conditiones physicae et chemicae illustrentur."[16]

In his eulogy of Ludwig, Fick summarizes the position of the 1847 group by saying that although certain isolated problems in physiology had been treated in a physical manner, by such men as E. H. Weber, Volkmann, and Müller, the 1847 group were the first to assert as a general law that "a vital phenomenon can only be regarded as explained if it has been proven that it appears as the result of the material components of living organisms interacting according to the laws which those same components follow in their interactions outside of living systems."[17]

This then was the program of 1847—in particular the program of Ludwig, the same Ludwig who was to become at Leipzig a father of modern physiology, the man who had more numerous and more influential pupils than any of his contemporaries or successors in physiology. How did physiologists feel about this program some eighty years later?

Writing in 1930, Fulton said:

> . . . it is . . . possible to distinguish two main groups of investigators . . . in some respects opposed. There are those who cherish the independence of

[14] C. Ludwig, *Lehrbuch der Physiologie des Menschens,* Heidelberg, Winter, 1852, v. 1, p. 1. The sympathy between Ludwig and the other members of the 1847 group is emphasized by the fact that the *Lehrbuch* is dedicated to "Den Freuden E. Brücke, E. du Bois-Reymond, H. Helmholtz."

[15] Estelle du Bois-Reymond and Paul Diepgen, *Zwei grosse Naturforscher des 19 Jahrhunderts. Ein Briefwechsel zwischen Emil du Bois Reymond und Karl Ludwig,* Leipzig, Barth, 1927, pp. 27-28.

[16] C. Ludwig, *De viribus physicis secretionem urine dajuvantibus,* Marburgi, Cattorum, 1842, p. 1. Quoted from *Leben und Werk des deutschen Physiologen Carl Ludwig,* by Dr. Heinz Schröer. I am indebted to Dr. Schröer's kindness in sending me a typescript of his unpublished dissertation, and to his generosity in permitting me to quote from it.

[17] Adolf Fick, *Gesammelte Schriften,* Würzburg, Stahel, 1904, v. 3, p. 767.

physiology . . . they tend to set themselves apart under the designation 'general physiologist'. . . . Their viewpoint is quantitative and physical, and they seek to investigate 'vital' processes by restricting themselves to the methods of physical and electrochemistry. Their interest in many cases is centered upon fluids and substances derived from living things, rather than upon the living organism itself. The contribution to physics and chemistry of this relatively small group of workers has been great. . . .

There is another and larger group of physiologists who . . . feel that the true objective of their science is the human body. . . . It were perhaps better for science that many of the so-called 'general physiologists' recognize that they are not physiologists at all, and that it would be preferable to style themselves by more accurate descriptive terms such as "biophysicists,' 'protein chemists,' or 'electrochemists,' as the case may be. . . . Physiology has leaned heavily in the past upon the more exact sciences, . . . at present, however, physics and chemistry have outdistanced the students of vital function, and it is likely in the future that the bearing upon physiology of discoveries of physicists and chemists will be less immediate than in former times. . . . One hopes in the future that physiology will aim to treat of the organism as a whole.[18]

A viewpoint expressed in Germany in 1949 is also of interest. Dr. Heinz Schröer says: "Ludwig's research displayed a general characteristic . . . his physical viewpoint [Anschauung]. A purely mechanistically pursued biology would of course today no more be held up as an ideal. However, the method of today's physiology is in essence physical in the broader sense and must necessarily be so . . . . modern physiology has outgrown the mechanistic age."[19]

There is ample indication that during the last few decades physiologists in all countries have not considered the elucidation of molecular mechanisms, the dissolving of physiology into biophysics and biochemistry as their immediate practice goal. The publications to be found in the leading journals testify well enough to that point. As for the theoretical bias of modern physiology, it is still common to define physiology as the physics and chemistry of life and to assume that the mechanistic stand is correct. Nevertheless, a position sometimes called organicism holds a very wide popularity today: the position that is identified with the frequent use of such concepts as homeostasis, integration, adaptation, organization, and whole organism. These biological concepts are essentially neutral and descriptive but to some they carry a flavor of vitalism. This position is associated with Haldane, Barcroft, and Cannon, and is often represented, perhaps not quite correctly, as the position of Bernard. It is perfectly sound and scientific to con-

[18] John F. Fulton, *Physiology* (Clio Medica), New York, Hoeber, 1931, pp. 110-12.
[19] Heinz Schröer, *op. cit.* (see note 16), p. 78.

sider the problems of the whole organism, but the level of abstraction represented by the above terms is anything but mechanistic.

Among contemporary biophysicists the feeling is often found that it is difficult if not impossible to obtain biophysical training in physiology departments, partly because there is no one to give the training, partly because individual efforts to study mathematics and physics are viewed askance, and finally because where biophysics is encouraged, it is most often conceived of in terms of electronic instrumentation and work with radioactive tracers. It is not easy to document the above statement from printed papers, but it is very easy to do so by personal communication. It is certainly true that the men now recognized as biophysicists in this country have often been trained as physicists, and are working in departments of physics, in departments of biophysics, and in research institutes rather than in departments of physiology.

If we accept the thesis that in the last two or three decades physiology has not been enthusiastically receptive toward biophysics, it will immediately seem probable that the biophysics movement of today did not originate as a revival within physiology of the goals of 1847. We can gain further evidence for this, as for the similarity of the goals of today's biophysics to the goals of 1847 by turning to statements of modern biophysicists. "At the present time biology is overcharged with facts—indocile creatures which need that 'mysterious Priest' the mathematical physicist to lead them to the altar. . . . What prodigious services such a one can render is already abundantly clear. . . . The difficulty . . . is the want of courage in the physicist to come over the way, to leave his home in the physical laboratory and venture among strangers."[20] So was du Bois-Reymond echoed in 1930 by Sir William B. Hardy. A physicist tells how he was drawn into biophysics by the unexpected ease with which he solved a particular biological problem and says: ". . . I was quite sure at that time that the lack of progress of biologists and physiologists in their science was entirely due to the fact that they did not know how to apply the beautifully precise and quantitative measurements that we physicists knew about, and that all I had to do was enter the field and in a few years I could clear up the whole science for them."[21] In a semi-popular article Prof. Pollard says: "Perhaps the time is ripe for applying physics to biology. Can physical principles shed light on the phenomena

[20] Sir William B. Hardy, "Conclusion to the discussion on colloid science applied to biology." *Trans. Faraday Soc.*, 1930, *26*, 864.

[21] *Symposium on shock.* N. Y., Josiah Macy, Jr. Fdn., 1953, p. 21.

of life as they have on so many other fundamental questions? More specifically can the laws of quantum mechanics, electricity and statistics explain living systems?"[22] In his *Four Lectures on Biophysics* K. S. Cole remarks that in the history of the field one can find such men as Poiseuille, Mayer, Fick, Helmholtz, Maxwell, H. Weber, and L. Hermann. He names, therefore, one member of the 1847 group, Helmholtz, and two pupils, Fick, who was a pupil of Ludwig, and Hermann who was a pupil of du Bois-Reymond. He then remarks: "But now we may ask, what about the progress of biological physics in the present century? It has been limping along not getting much of anywhere not at all certain of where it is going. But perhaps it is not so much worse than it was in the 19th century—if we exclude Helmholtz, that is."[23]

If, as the above quotations suggest, modern biophyicists tend to be unaware of, or uninfluenced by the 1847 program, and if the physiological heirs to 1847 have tended to be unsympathetic to biophysics, the least we may conclude is that the 1847 group did not succeed in creating a movement toward biophysics at all comparable in influence to that attained by the sister science of biochemistry, and that even the impetus toward biophysical investigation diminished over the years. There are many obvious reasons why this should have been so, the most obvious and the most important being that the state of physical knowledge of 1847 was such as to make biophysics a decidedly premature venture. The dominant branch of physics was mechanics, the new fields were heat and electricity. Most of physical chemistry, biochemistry, thermodynamics, spectroscopy, and most molecular theories in physics lay in the future. Some of these sciences in fact grew out of the work Helmholtz did after he had largely abandoned physiology for physics.

One would naturally assume that the high goals of 1847, being unattainable, gradually fell from sight and were completely lost track of after the death of their propounders. As a matter of fact, the reaction seems to have set in much sooner as is shown by various statements of Adolf Fick. Fick was a pupil of Ludwig and a strong adherent of all of the goals of 1847. Not only that, but he, more than any of the members of the 1847 group, made some progress toward those goals. His work on diffusion (Fick's Law), on muscle contraction, on muscle thermodynamics, and on blood

22 E. C. Pollard, "The physics of viruses," *Sci. Amer.*, Dec. 1954, p. 63.

23 K. S. Cole, *Four lectures on biophysics.* Instituto de Biofisica, Universidade do Brasil, Rio, 1947, pp. 9-17.

flow (Fick's Principle) represents some of the finest achievement in pure and applied biophysics in the nineteenth century. When he speaks of biophysics he does not do so unsympathetically.

In 1874 Fick[24] pointed out that twenty-five years earlier a remarkable development had occurred. The concept that the phenomena of life were to be explained in chemico-physical and physico-mathematical terms had been introduced and gained absolute ascendency. Trail-blazing discoveries of the forties and early fifties, such as those made in studying the electrical and chemical phenomena in nerve and muscle, in combination with the successful use of mathematics in a number of applied problems (the mechanics of the circulation, the mechanism of the ear, the dioptrics of the eye) had had a brilliant success. Not only young men but also research workers grown grey in other pursuits turned to the study of mathematics in order to do justice to the new orientation. No one could doubt that from that time onward all physiologists would be thoroughly trained in physics and mathematics.

But "the absolute dominance of the mechanistic-mathematical orientation in physiology has proved to be an Icarus flight, and unhappily in this case, the wax of the wings was not melted by too great a nearness to the sun of knowledge but through the heating which the unaccustomed effort brought with it."

Fick pointed out that the mechanistic explanation of vital processes still received acceptance as the ultimate goal of physiology, but the immediate daily research in 1874 was directed to practical problems: the question of which nerves innervate the heart or blood vessels was receiving as much attention as the problem of the molecular nature of the nerve impulse. Many workers who were strongly oriented toward the physical approach in 1850 had by 1874 turned to other methods of study, e.g. histological. This Icarus flight Fick attributed to the extreme difficulty of both theory and practice met with in the biophysical realm. Few were able or willing to take the time to learn physics and mathematics. The young physician "imagines mathematical studies, for one provided with the necessary rudiments ought to be just as easy as medical studies are for an accomplished physician." On the laboratory side, the physically oriented experiments are far more difficult than ordinary vivisections or histological researches. "Considering this

[24] Adolf Fick, "Methoden und Richtung der physiologischen Forschung" in *Gesammelte Schriften*, v. 4, pp. 389 ff. The following three paragraphs are freely translated and condensed from Fick. Where quotation marks are used exact translation has been carried out.

great difficulty which progress in the mechanistic direction offers, it can be no surprise if it is no more as generally taken up as it was in the time when it added the stimulus of novelty to the attractive force which it always through its nature must exert on logical minds."

Years later, in dedicating his institute at Würzburg Fick said that of the three sections, vivisectional, chemical, and physical, the smallest space was "for my own research orientation—the physical" and explained this by the fact that the need for space is determined more by the amount of instruction than the amount of research and "In physically oriented physiological practical courses a large crowd cannot be expected. Lively interest for this experimental orientation presupposes a degree of mathematical and physical development which the students of medicine . . . only very exceptionally are able to gain."[25]

This evidence for the Icarus flight and downfall of the biophysical movement in Germany correlates very well with our other observations. In particular, if the biophysical approach died down as a practical working approach as soon as Fick implies, then we see that it was quite possible for physiologists from the United States to work with Ludwig in the 1870's,[26] and even to become disciples of Ludwig, without partaking of the extreme biophysical philosophy but only of the physiological working approach. Incidentally, Ludwig was famous for matching the problem to the student and would certainly not have forced a physical problem on a person unprepared for it. Thus there is nothing to cause surprise when we find American physiology many years later thinking of itself as descendant from Ludwig and at the same time holding rather cool views toward the biophysical and even the general physiological approaches. Similarly, we find that the most ardent biophysicists of the next generation were pupils during the early, ambitious years of the 1847 program: in particular Adolf Fick, Julius Bernstein, and Ludimar Hermann. It is worth noting that these men became well known for their research in the two fields in which almost pure biophysics has continued to be of importance in classical physiology to this day, the fields of the nature of muscular contraction as studied mechanically and thermodynamically, and of the nature of the nerve impulse as studied electrically. These

25 Adolf Fick, "Rede Zur Einweihung des Physiologischen Instituts in Würzburg." Mai 1888. *Loc. cit.*, v. 4, pp. 486-96.

26 George Rosen, "Carl Ludwig and his American Students." *Bull. Hist. Med.*, 1936, *4*, pp. 609-50.

areas have always, when treated physically, seemed on the verge of revealing their secrets, and for the last hundred years physiologists with physical interests have been drawn to them. They naturally represented the stronghold of the 1847 group.

A quite separate problem is posed by the field of general physiology. This discipline, which could logically have been the bridge between the biophysics of today and that of 1847 but in general was not, requires an entire study in its own right. The whole question of the relation of the goals of general physiology to those of the 1847 movement, of the attitude within the field toward the problem of the reduction of physiology to physics and chemistry, and the associated philosophical question of whether or not general physiology represents a valid level of abstraction between that of physiology *qua* physiology and physiology *qua* physics and chemistry is very complex. Some of the names prominent in this field are those of men academically descended from 1847, e.g. Jacques Loeb was a pupil of Adolf Fick, and Christian Bohr was a pupil of Ludwig and the teacher of Krogh. On the other hand Höber is found, again with Jacques Loeb, among the pupils of Goltz, of whom Rothschuh quotes Ewald as saying, "He was and remained a biologist in the period when people wanted to reduce physiology to applied physics and chemistry."[27] Anyone who wishes to be satisfied that the general physiology which was becoming popular before the first world war was quite different from the 1847 movement need only glance at Loeb's *The Mechanistic Conception of Life*[28] with its emphasis on parthenogenesis and tropisms, or at the prefaces to the various editions of Bayliss' *Principles*[29] to see how biological much of the conceptualization was and how far removed from the spirit of du Bois-Reymond's *Vorrede*.

To gain a more detailed impression of the nature of the scientific activity of the 1847 group it is convenient to consider its members individually with reference to biophysics and physiology. Ernst Brücke is today the least well known of the four, although du Bois-Reymond runs him a close race for this distinction. Neither is likely to be mentioned in a course in physiology even if it is taught by someone interested in the history of the field. Only Helmholtz and Ludwig are represented in the magnificent portrait gal-

27 Rothschuh, *op. cit.*, p. 187.

28 Jacques Loeb, *The mechanistic conception of life*, Chicago, University of Chicago Press, 1912.

29 Sir William Maddock Bayliss, *Principles of general physiology*, 4th ed., London, Longmans, Green, and Co., 1924. The 4th edition retains the prefaces to the preceding three editions.

lery included in Bayliss' *Principles,*[80] nor does Bayliss even credit Brücke with one of his more important investigations, and one of a biophysical nature—the observations on the singly and doubly refractive bands in skeletal muscle. Rothschuh finds only twelve contributions of Brücke of sufficient importance to be included in his tables[81] and of these perhaps only the one mentioned above is biophysical. Others are biochemical, such as the demonstration of a reducing substance in normal urine and the preparation of crystalline pepsin. But the general picture of his research is physiological. As a matter of fact the most famous of Brücke's pupils, Sigmund Freud, spent most of his time with Brücke working on histological problems.[82] Brücke had some successful students, e.g. Cyon and Kühn, but none of his followers can be considered strongly physically oriented.

With du Bois-Reymond the situation is quite different. Of the four, he remained the most faithful to biophysics throughout his life and trained well-known students with a physical orientation, in particular Ludimar Hermann and Julius Bernstein. It is natural that electrophysiology, the life work of du Bois-Reymond, should remain physically oriented. It can hardly be otherwise. What is not so obvious is why he remained faithful to electrophysiology. His great contributions, the discovery of the negative variation of activity in nerve and muscle (i.e., the action potential) were made by 1849 and it is almost not too harsh to say that he did little of value thereafter. Adolf Fick speaks movingly of his success, influence, and failure: "The last of the four great founders of the German physical-physiology school . . . the representative man of the physical school. . . ." "One understands that this book [the *Untersuchungen*] would be regarded as a prototype, and throughout decades was considered as such and that people had placed on it the most sanguine hope that the explanation of the electromotor activity of muscle and nerve would in the near future permit the solution of the riddle of life." "However, in spite of all expenditure of acumen and effort he did not succeed as he had hoped 'to awaken that hundred year drama of physicists and physiologists to vigorous reality.' On the contrary he had to experience the general abandonment of the theory which he had so fondly con-

80 Bayliss, *op. cit.*

81 K. E. Rothschuh, *Entwicklungsgeschichte physiologischer Probleme in Tabellenform,* München-Berlin, Urban & Schwarzenburg, 1952.

82 Siegfried Bernfeld, *Psychoanal. Quar.,* 1944, *13*, pp. 341-62. *Amer. Imago,* 1951, *8*, pp. 107-27.

ceived and which had originally been accepted with enthusiasm by his colleagues. Du Bois-Reymond to the end was not persuaded by his opponents. It was rather tragic to see how so great a personality fought with all the means of his rich spirit for an early adopted and tenaciously held theory against grounds whose soundness must readily be evident to every unprejudiced person."[33]

Du Bois-Reymond's own judgment is no more cheerful. The *Untersuchungen* was published over a period of thirty-six years, Volume I appearing in 1848, Volume II, part 1 in 1849, Volume II, part 2, pages 1-384 (ending in the middle of a sentence) in 1860, and Volume II, part 2, pages 385-579 in 1884. Twenty-four years seems rather a long time to finish writing a sentence, but in fact much of the last section had already been printed in 1860, and the author says in the Nachwort of March 1884, "So I have at last decided, with heavy heart, to stop where I might just as well have done more than a quarter-century ago. . . . These *Untersuchungen* remain a torso, or even more, a *Monstrum per defectum. . . .*"[34]

The book remained a torso because of the author's inability to write the final section, promised in 1848, "In the fourth section I have allowed myself to discuss certain conjectures on the relation of electrical phenomena of nerve and muscle with the rest of the phenomena of their activity."[35] The impossibility of writing a general theory of electrophysiological activity even today, and Fick's opinions, merely emphasize the fact that du Bois-Reymond, by sticking faithfully to purely biophysical problems ensured that his earliest work was his best and ensured a decline in his once gigantic reputation to its present-day low state. Du Bois-Reymond wrote *finis* to his long attempt to explain electrical events in tissues three years before Arrhenius introduced the concept of the ion into chemistry. Ostwald suggested the possible connection between ionic distributions and electrophysiological phenomena in 1890 when du Bois-Reymond was seventy-two. We see here again the basic difficulty of the 1847 search for a pure physics and chemistry of life, a seeking for molecular explanations in a day when physics and chemistry were predominantly molar.

The greatness of Helmholtz lies partly in the fact that he gave up biophysics and physiology to become one of the greatest physicists of all time. As a physicist he laid the foundation for much of the thermodynamics and physical chemistry that was to play so im-

33 Fick, see note 7.
34 Du Bois-Reymond, *Untersuchungen*, v. II, part 2, p. 501.
35 *Ibid.*, v. I, p. liv.

portant a role in the general physiology and biophysics of the future. Indeed, from the thermodynamics of Helmholtz to that of Ostwald and van't Hoff and from there to the Bernstein membrane theory and the electrochemical theories of excitation which have, in the hands of Hodgkin, raised new hopes of solving the now two-hundred-year-old "dream of physicists and physiologists" there is a very direct line indeed. But if we consider Helmholtz strictly as a biophysicist, we find the usual story: the great contributions were pretty well over by the time the "program" was formulated. Between 1847 and 1852 he contributed the law of the conservation of energy, with its implications for animal heat, the measurement of muscle heat, the measurement of the conduction velocity of the nerve impulse: quite enough to set him up as a great biophysicist. Most of his subsequent work in physiology was on sensory problems and cannot be denied the title of biophysics, but most people would call it applied biophysics, a distinction which must be made in some of Ludwig's work as well. His work on vision and hearing, profound and physically oriented though it was, did not elucidate and did not aim to elucidate molecular mechanisms. Helmholtz did not fall into the error of du Bois-Reymond of continuing to hope that nineteenth century physics and chemistry were sufficient to provide molecular explanations. Perhaps this was so simply because he was so much more able a physicist and mathematician. At any rate the member of the 1847 group best qualified by ability and training to fulfill its goals of reducing physiology to physics and chemistry instead made his greatest contributions in physics and chemistry as such. Nonetheless, the accomplishments listed above and the profundity of his work give him fair claim to being known as one of the greatest physiologists of all time, equalled in the nineteenth century only by Bernard.

Ludwig, a figure of great versatility, whose labors in mathematics testify to his earnest desire to reason physically, is always thought of as the physiologist par excellence, the physiologists's physiologist. His career began with a physically oriented study, the filtration theory of urine formation. He had some biophysically oriented pupils, in particular Fick. Never at any time in his career was physically oriented work completely absent from his laboratory—work on filtration, diffusion, blood pressure, hemodynamics, blood gases appears and reappears. He stood fast by his mechanistic philosophy throughout the years. And yet—and correctly—he is thought of as a physiologist, often as *the* physiologist. Many physiologists who recognize the superior ability of Helmholtz feel that somehow Bernard and Ludwig are the representative men of the nineteenth century.

We need only examine the purely physiological contributions of Ludwig to find the basis for this feeling: he introduced the kymograph and the recording manometer, he studied the depressor nerve and demonstrated reflex slowing of the heart, he studied the function of the vasomotor center and the splanchnic nerves, elucidated the nature of Traube's waves, worked on secretion and the secretory nerves, studied the heart sounds and cardiac excitability, automaticity and fibrillation. We may also examine the publications of the Leipzig Institute and find the occasional physically oriented paper balanced by the occasional purely anatomical paper, the rest—the majority—being typical, elegant, modern physiology in reasoning and method.

It is especially interesting in considering Ludwig as a biophysicist to look at the German physiologists of 1930 in *Minerva,* make a list of the most obvious candidates for the title of biophysicist and find that the top contenders are not pupils of the 1847 group: Höber, Cremer, and Frank. Rothschuh remarks that Frank did not like Ludwig and left his institute for that of Voit. It is especially striking that this modern representative of the rigorous physical treatment of cardiovascular problems left Ludwig, dissatisfied. The rigorous and severe physical-mathematical orientation did not dominate the institute of the "genial" Ludwig or the work of Bowditch, Pavlov, or many other great physiologists of the next generation who were pupils of Ludwig.

Rothschuh claims that the shift to a Physico-chemical orientation in physiology occurred not with Müller but with Ludwig.[86] It cannot be claimed here that the shift never occurred at all, but it can be suggested that the influence of the 1847 group is better understood in terms of what we now call the scientific method and that the great growth of physiology in the nineteenth century was a result of active experimentation rather than the result of success in reducing physiology to physics and chemistry. Never at any time did any member of the 1847 group succeed in reducing a vital phenomenon to physics and chemistry. A general survey of their work might divide it into physiology and applied biophysics, where by applied biophysics is meant the use of physical devices or measurements in physiological problems. Most of du Bois-Reymond's work

[86] *Op. cit.,* p. 119.

in electrophysiology comes under the category of applied biophysics, as does much of Helmholtz's, especially the work on the physics of vision and hearing. The measurement of the heat produced by an active muscle, or of the conduction velocity of a nerve impulse, though elegant technical achievements are applied physics not molecular explanation.

It is important to remember that the use of physical techniques and modes of thinking was not introduced into physiology by the 1847 group. It had been part of physiology at least since Borelli, and even as this group met in Berlin in 1847 physics had been actively and successfully applied to physiology for two decades by such a man as E. H. Weber. We cannot set the 1847 group aside and honor them for introducing the ideas of weighing and measuring and reasoning physically into physiology. What they did do was proclaim as an article of faith the idea that physiology could be reduced to physics and chemistry and they proclaimed their intention to do it. It was this proclamation which won them so much attention and it was this intention which they failed to carry off. Indeed, it is not possible today to give an explicit and detailed reduction of any complex physiological phenomenon in terms of physics and chemistry.

The attempt to explain the life process in terms of physics, chemistry, and mathematics fell from grace during a time when physiological knowledge was increasing sensationally. Even if we regard all of du Bois-Reymond's work and some of Ludwig's and Helmholtz's as biophysical, the contributions to physiology *qua* physiology of this group represent an enormous development in the field, a development founded primarily on the techniques of histology and vivisection. Rothschuh characterizes the earlier part of the nineteenth century (Müller, Magendie) as experimental, biological, and vivisectional, and the era of Ludwig as physical-chemical. A survey of all the evidence suggests that the great success of the 1847 group was based on methods which may justly be called experimental, biological, and vivisectional, rather than on a theoretical bias toward the physical and chemical. Because the announced program of the 1847 group was physical and chemical and because the 1847 group were so successful as physiologists, it does not follow that they were successful in terms of their own goals.

The introduction of certain devices such as the galvanometer, the use of certain measurements, such as that of blood pressure, does not argue for a biophysical triumph. Had the movement of

1847 been really successful and productive in biophysical terms, it would, as Fick implies, have continued to draw young men trained in physics and mathematics and it would have seized at every new advance in physics and chemistry. In fact, the kymograph remains a symbol of physiology today. There can be no doubt that a considerable and important change in the direction of physiology *qua* physiology occurred around 1850, an infusion of physical thinking and methodology. There is equally little doubt that the infusion found the science biological and left it biological. In all probability the progress made in experimental physiology in the period 1850-1950 owes as much or more to the use of anesthesia in vivisection as it does to the application of physics and chemistry.

Another aspect of the 1847 movement which was of great importance in its success and influence and which stemmed directly from its philosophical opinions was its vigorous anti-vitalism and determinism. The assertion of du Bois-Reymond's *Vorrede* that the explanation of life processes must be sought in the ordinary laws of inorganic nature is an important belief for the experimentalist because of its implication of causality, and more than that, of accessible causality. Although purely mechanistic research methods can be used by a quasi-vitalist such as Haldane or by a man indifferent to the philosophical problems involved, such as Weber, at least a firm belief in causality is indispensible. As Helmholtz said in 1869, "In physiology particularly scientific work had been crippled by doubts respecting the necessary conformity to law, which means, as we have shown, the intelligibility of vital phenomena, and this naturally extended itself to the practical science directly dependent on physiology, namely medicine. Both have received an impetus, such as had not been felt for thousands of years, from the time that they seriously adopted the method of physical science, the exact observation of phenomena and experiment,"[87] and, "The attack was made wherever a way could be perceived of understanding one of the vital processes, it was assumed that they could be understood, and success justified this assumption."[88]

The mechanistic assertions of 1847 had a triple implication: firstly, the anti-vitalist position, with its accompanying idea of intelligible causality; secondly, an argument for the use of observation and experiment; these two implications formed the basis for

[87] Hermann von Helmholtz, "The aim and progress of physical science" (1869) in *Popular lectures on scientific subjects,* trans. by E. Atkinson, London, Longmans, Green, 1898, v. 1, p. 345.

[88] Helmholtz, "On thought in medicine," *op. cit.,* v. 2, p. 224.

the progress made by the group.[39] The third implication, that it was practical and worth attempting to reduce physiology to physics and chemistry, was of value in drawing attention to the other two. If the scientific practice of the 1847 group is considered in terms of the first two implications, it will be seen to have a great deal in common with the practice of its predecessors such as Müller and Magendie, Purkinje, and Weber, with Bernard and with modern physiology. The apparent discontinuity in the realm of theory is seen to be just that—philosophical assertion, of the utmost importance, of necessity relegated to the position of a remote goal.

The 1847 group was vastly successful in experimental physiology, temporarily successful in putting across mechanism as against vitalism, and reasonably successful in popularizing applied physics and chemistry as techniques in physiological research. But Ludwig, Helmholtz, du Bois-Reymond and Brücke had for a short time held most of German physiology to a much bolder task, that of dissolving physiology into physics and chemistry. It was this task which Ludwig himself admitted proved "much more difficult than we had anticipated."[40]

39 Compare Paul Bert on Bernard: "I must repeat that Claude Bernard, therefore, proved himself, almost from the outset, superior to both Magendie and Bichat, since he felt not only the endless multiplicity of unknown data in physiology, but also their subordination to the general laws of matter and their obedience to the experimental method." Quoted from Bernard, *An introduction to the study of experimental medicine,* trans. by H. C. Greene. New York, Macmillan, 1927, p. xiv.

40 See note 2.