Daniel Frederik Eschricht (1798-1863) Peter Wilhelm Lund (1801-1880): Danish pioneers in experimental physiology

Historians, philosophers and practitioners on Claude Bernard's *Introduction à l'étude de la médecine expérimentale*

By C. Barker Jørgensen

Historisk-filosofiske Meddelelser 92

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Abstracts

D. F. Eschricht was a Danish physiologist, anatomist, and naturalist, who, in particular, is known for his studies of the anatomy of whales and for a comprehensive collection of whale skeletons. According to his biographers, Eschricht lacked the qualifications needed in the new, experimental physiology, adhering to traditional comparative anatomy and speculations on the function of the organs studied. The present article shows that the characterization of Eschricht as a functional morphologist is incorrect. Eschricht was, in fact, trained in experimental physiology, based on vivisection, by François Magendie, who became his teacher and friend, and whom Eschricht assisted in studies of the cranial nerves. The function of the cranial nerves also became the subject of Eschricht's dissertation. Experiments on the relationship between the fifth and seventh cranial nerves were carried out in collaboration with P. W. Lund, who later obtained fame as a paleontologist for his excavations and studies of the bones of extinct mammals, discovered in caves in Brazil. Eschricht's stay in Paris and his relations to Magendie are elucidated in letters to his mother. Eschricht early intensified an old interest in natural history at the expense of the study of physiology. This development from experimental physiologist to naturalist and collector has been followed in his letters to Lund in Brazil.

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The views of historians and philosophers of science on the influence of Claude Bernard's *Introduction à l'étude de la médecine expérimentale* (1865) range from calling it one of the most influential works in physiology to stating that it has been of no consequence because practicing physiologists don't read books on the philosophy of experimental method. The autobiographical prefatory chapters, which outstanding, retiring physiologists wrote to the *Annual Review of Physiology* from 1950 to 1987, seem to support the latter view: none of the autobiographers referred to Bernard's *Introduction.*

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Contents

D.F. Eschricht and P.W. Lund:
Danish pioneers in experimental physiology

Introduction 5
Magendie's assistant: letters to his mother 6
Lund and Eschricht 10
From physiologist to naturalist 15
Professor of physiology 16
Reflex movements 17
Magendie and Claude Bernard about Eschricht 19
References 21

Historians, philosophers and practitioners on
Claude Bernard's Introduction

Introduction 25
Early views 27
An odd document 30
20. century views 31
Retiring physiologists reminisce 34
Peter Medawar 40
References 42

Daniel Frederik Eschricht (1798-1863) Peter Wilhelm Lund (1801-1880): Danish pioneers in experimental physiology

Introduction

D. F. Eschricht was a Danish physiologist, anatomist, and zoologist. He graduated in surgery and medicine in 1822, was trained in experimental physiology by François Magendie (1783-1855) in Paris, 1824-1825, defended a thesis on the anatomy and function of some cranial nerves 1825 and obtained a stipend for 3 years to study with the leading comparative anatomists in Europe, including Cuvier in Paris. On his return to Denmark, he became a teacher of physiology at the University of Copenhagen, from 1830 as a professor of physiology, later also of anatomy.

Eschricht's biographers agree in their low evaluation of him as a physiologist. They observe that in spite of the fact that he was a pupil of Magendie, he never acquired the qualifications needed in the new experimental physiology. To Eschricht, physiology remained functional morphology, i. e., comparative anatomy in connection with speculations on the function of the structures studied (Thornam, 1863; Torup, 1918; Wolff, 1980). The biographers thus disregarded his early contributions to the experimental physiology.

It is the aim of this article to revive Eschricht's contributions to experimental physiology, and to show that it was not lacking qualifications that prevented Eschricht from establishing modern physiology in Denmark but a shift in engagement from physiology to natural history and collection of animals and other natural objects. This development was preceded by his study with Magendie and by his collaboration with his friend, the medical student, P. W. Lund, in investigations of the relations of the fifth cranial nerve to the seventh. The stay in Paris and his relation to Magendie are elucidated in letters home to the mother, and the transition from experimental physiology to anatomy and natural history in letters to Lund.The letters are in the Royal Library, Copenhagen. None of these letters have previously been used to elucidate Eschricht's, and Lund's, roles in the early history of experimental physiology.

Magendie's assistant: letters to his mother

Magendie was at the height of his career and fame when Eschricht was in Paris and became his assistent in the experiments. In 1822, Magendie had shown, by cutting of the roots of the spinal nerves, that the posterior (dorsal) roots of these nerves are sensory and the anterior (ventral) roots mainly motor, a discovery that became one of the foundations of modern neurophysiology. When Eschricht came to Magendie he was engaged in investigations of the cranial nerves, and it was in these investigations that Eschricht assisted, as he related in the letters to his mother. (Eschricht's father died 1819.)

In his letters, Eschricht appears as a vivid and witty narrator, both about the Metropolis and its life, and about his relations to scientists he met, including Alexander von Humboldt who introduced him to Magendie. Obviously, Eschricht rapidly felt at home in Paris, and he is full of praise to Magendie whom he came to admire as a human being and as a scientist. Apparently the feelings were mutual, because Eschricht soon became Magendie's assistent, as described in a letter of September 10, 1824, two months after his arrival in Paris.

Eschricht opened the long letter with the hope that it would give his mother "a happy hour! – So I begin to let the pen run freely. – Voulez vous – oui Monsieur! Thus I always come at once when Magendie begins with voulez vous; knowing that it means to help him in a work from which I get a lot of benefit, or it is about helping him eating a basket of peaches, or going for a walk to see something extra. So voulez vous, Monsieur (it is probably better to continue in Danish) call me tomorrow at 10 o'clock to eat a physiological lunch, and afterwards do experiments? Oui Monsieur, I said a little hesitantly, because I had arranged with my countryman Dr Hohlenberg and a German doctor to go to Versailles to see the fountains, and had even refused an invitation there with my Parisian ladies. Ah! vous voulez peut-être à Versailles? – oui Monsieur? – Eh bien! when we have finished, then I take you out there, we shall see everything, take a good dinner and drive back again. – Well, I'll be damned! Yes, then I had to be a traitor to my countryman. Thus Sunday August 27, at 10 o'clock we began a physiological lunch, which tasted very nice, and where I had to choose the menu which I prefered etc etc, worked then to 2 o'clock."

Eschricht didn't disclose on what they worked, but the letter narrated in detail about the great experience the subsequent visit to Versailles and the lavish meal there had been. And he continued by asking his mother: "But what do you think of such a man like Magendie, a man who is famous on all continents, without doubt the first man in his craft (the physiology), a young man, beautiful man, kind, unselfish, and yet he makes so much of me poor creature."

The letter also gives an interesting glimpse of Magendie's laboratory and of Magendie at work. Thus, Eschricht prepared his mother for what would meet her when she stepped into the laboratory: "Entering into his antechamber, it depends upon whether you go to the left or to the right. To the left: in rooms with beautiful paintings, books etc (he is of course not married). To the right: an ugly room, with a large amount of bad straw chairs and an old long table of beech. On the walls are hanging 3 paintings: a skull, a ? with some birds of prey which are swooping down on others, a crying country boy who has cut himself in the foot. On the floor are standing 2 buckets with water and a big tub, with some 40 frogs and toads. A cage with an owl, a basket with fowls and other birds etc. On the floor – here a rabbit is crawling, continually turning to the left, here then continually to the right. Here a third is continually rolling to one side, here a pigeon is continually flying backwards. Here a cat, which is blind, is prawling ahead, here stands a gaping magpie, in which the brain has been taken out. At the table he is sitting in his shirt sleeves, making his experiments. Your Frits is sitting at his side, helping him in doing them. At the other side a secretary, who is writing down everything that soon printed run about in the whole world. Just opposite him are sitting doctors from Russia, Denmark, Buenos Eires etc etc. In the next room, into which opens a poor door without a lock, some small Indian pigs are heard fighting over their cabbage, or a bunch of rabbits jumping against the wall. Here is, so to speak, a whole menagerie. – However, it is probably better now to say goodbye to Magendie and walk a little around in Paris. Where do you want to go? To Palais royal? Eh bien!" – And then followed a long and interesting account of what to experience on a walk in the garden of Palais Royal and in Paris.

In a letter of October 4, Eschricht is able to tell his mother that he has begun to work with his pen. "That is, I have written a letter to my Magendie, which contains so many good things, that it is

going to be printed, and it gets into his famous Journal. If it goes well I hope to get more courage." Within three months, Eschricht had thus advanced to be Magendie's collaborator.

Letters of December 20 and January 24, 1825, are without scientific interest, but in his last letter from Paris, of March 15, Eschricht writes that he has planned to go to London, presumably because "Magendie, as good as settled, will go there next month on a visit of some weeks, and he wants me as a travelling companion. How much this fine man likes me, is difficult to understand, as he usually has a keen eye, especially if I should only be good for a witch doctor. He is in the very highest esteem and friendship with the greatest English physicians, which people are not to be sneezed at. Last year much was made of him, and he was given fêtes, and hardly less will be done this year, especially because they will try to make good again some outrageous insults to Magendie from a certain Englishman Martin, who held a mad speech in Parliament against Magendie. Well, I am very much looking forward to this journey."

Magendie had visited London in 1824 where he had been invited to demonstrate his experiments on the nervous system to some leading physicians on whom he had made a deep impression. But he had also been invited to give public demonstrations for a large gathering of physicians, where he, among other things, demonstrated the function of the spinal nerve roots. The demonstration divided the English medical world into two camps. The one camp, for which the respected journal *Lancet* acted as a mouthpiece, praised in an editorial Magendie to the skies, whereas the *Medico-chirurgical Review* attacked him for his vivisections. Eschricht's "a certain Englishman Martin" was a MP, "Humanity" Martin, who, in a notorious speech in Parliament, accused Magendie for cruelty to animals: he performed "experiments so atrocious as almost to shock belief" (Olmsted, 1944, p. 140). To the English public, Magendie became the exemplar of the evil scientist, and the continued campaign against him was to a great extent responsible for the clause in the Vivisection Act of 1876 that required special certificates for lecture demonstrations in physiology (Ozer, 1966).

Eschricht wrote two letters home during his stay in London. They disclose that the meeting with London became an anticlimax. He wrote that he had not managed the stay if a friend

from Göttingen, Dr. Himly, had not been there to introduce him to various doctors and professors. He did not have the letters of introduction or persons that apparently were necessary. The second letter ended: "But it's true, I forgot to tell that Magendie did not go to England, and that I went alone."

Lund and Eschricht

P. W. Lund began to study medicine at the University, but gave up surgery and medicine in favour of natural history. Already as a student, he demonstrated great scientific gifts. In 1824 he thus answered both the University's prize subject in medicine and in zoology, and he was awarded the gold medal for both essays.The prize subject in medicine read: *Give an account of the fruits which human physiology has reaped from the large body of vivisections performed during the last decades.* The subject of the zoological prize was an investigation, by means of knife and injection, of the blood circulation in the decapod crustaceans.

The subject of the medical prize is interesting because it shows that the widespread disapproval of vivisection was not shared by the medical faculty at the University of Copenhagen.The aversion to vivisection, also among scientists, was especially predominant in England, exemplified by the attack of the leading anatomist Charles Bell (1774-1843) on the French experimental physiologists, particularly Magendie. Thus, according to Bell (1823, p. 302): "Experiments have never been the means of discovery; and a survey of what has been attempted of late years in physiology, will prove that the opening of living animals has done more to perpetuate error, than to confirm the just views taken from the study of anatomy and natural motions." But the distrust of vivisections was also common among German physiologists. Thus it is interesting to compare Lund's prize essay on modern physiology with a review from the same year by a German, Ignaz Doellinger (1770-1841), on the recent progress in physiology. To Doellinger, physiology was morphology, comparative anatomy, embryology, histology, pathological anatomy, obductions. But he admitted that such physiology, primarily based on observations, only progressed slowly, and that the heights reached by modern physiology was due to the introduction of experiments, to the opening of living animals. But then followed his objections: "The torture to which the animal was subjected brought about a condition in which the normal functions did not occur at all." Doellinger subsequently dealt in detail with the drawbacks of vivisection as a physiological method, concluding that any lesion of the body disturbs the internal balance on which life depends, which prevents safe physiological conclusions to be drawn (Doellinger, 1824).

The great German anatomist and physiologist, Johannes Müller (1801-1858), was in line with Doellinger. Thus, according to Müller, in occupation with the living nature, observations were dependable, and experiments were independable. And he observed that contemporary physiology was characterized by excessive experimentation which only resulted in an accumulation of "facts" nobody could interpret. Obviously, Müller was primarily referring to Magendie (Müller, 1826, cit. Rothschuh (1960, pp. 228-9).

Lund (1824) didn't share Doellinger's or Müller's reservations about vivisection. To him, Magendie indeed represented the Zeitgeist, and vivisection had transformed physiology from a speculative to an empirical science. Lund's essay is a matter-of-fact account of the results of the new physiology, with Magendie as the central person. It was published as: *Physiologische Resultate der Vivisectionen neuerer Zeit* (1825), and it was used as a physiology text in the medical teaching at the Universities of Copenhagen and Vienna. It also appeared in an Italian edition (1828). It is of considerable historical interest as the first, and perhaps only, book that exclusively treated the importance of vivisection in establishing modern, experimental physiology. The most interesting section of the book is two paragraphs on the function of the nervous system. The first of these paragraphs reports on experiments to determine whether there are special sensory and motor nerves. A footnote informs that Lund was indebted to a friend, landphysicus (country medical officer) Eschricht, for extensive information about the physiology of the nervous system. The next paragraph deals with experiments on the functions of the motor nerves. Here a footnote informs that Lund thoroughly reworked this chapter from the prize essay, particularly based on information from Eschricht. The footnote also disclosed that Eschricht visited the English physiologist Herbert Mayo (1796-1852) during his stay in London.

In 1822, Mayo had shown that the fifth cranial nerve was the main sensory nerve of the head, whereas the seventh nerve was motor, but to a smaller degree also sensory. He hypothesized that the pain that he observed on stimulation of the seventh nerve in the cat and dog was due to the existence of a particular muscular sense. The evident difference in the intensity of the pain on the irritation of a cutaneous and a muscular nerve caused Mayo to perform a closer study of the sensation of the various cranial

nerves. The results of this study confirmed him in his theory about the existence of a special muscular pain sense, besides the ordinary sensory innervation of the muscles.

Eschricht had not found the theory convincing, and he had pointed out to Lund that the sensory function of the seventh nerve might be derived from the numerous connections with the fifth nerve. Lund and Eschricht therefore decided jointly to investigate this possibility by cutting the fifth nerve at its root in rabbits. The experiments were made at the "Royal Natural History Museum" in the presence of the curator of the museum, Professor J. H. Reinhardt (1776-1845). It is thus indicated that neither the professor of zoology was an adversary of vivisection. The animal protection and antivivisectionist movements were slow to develop in Scandinavia. Societies to the protection of animals were only established late in Scandinavia, in 1859 in Norway, and in 1875 in Denmark and Sweden. Finally, 1882 was the "Scandinavian Association for the Prevention of Cruelty to Animals in Science" founded (Bronander, 1987).

In order to perform their experiment, Eschricht and Lund had to open the skull of the rabbit and remove the overlaying hemisphere of the brain, a technique Eschricht had learned from Magendie. The section of the nerve eliminated the sensitivity of the same side of the face, and pinching of the anterior part of the seventh nerve only caused contractions of the muscles of the face, without any signs of pain. The posterior part of the nerve, however, remained sensitive, presumably because of anastomoses from the first cervical nerve pair. They therefore concluded that the experiments confirmed Eschricht's theory, that the sensitivity of the seventh nerve was due to the numerous anastomoses it primarily received from the fifth nerve. Mayo's special muscular pain sense did not exist.

The experiments were in time to be included in Lund's *Physiologische Resultate* (1825) as an appendix, and they constituted the first and larger part of Eschricht's dissertation: *De functionibus nervorum faciei & olfactus organi.* Eschricht suggested, without success, to change the old names of *n. facialis* and *n. trigeminus* to *n. motorius* and *n. sentiens faciei.* Magendie published Eschricht's dissertation in his Journal (Eschricht, 1826a,b).

The second part of Eschricht's dissertation was not based on own studies, but is a critical examination of a paper of Magendie

(1824) in which he reported that section of the fifth nerve abolished the sense of smell in dogs, rabbits and other animals. Magendie therefore concluded that smelling was performed by branches of the fifth nerve, and that the first, olfactory, nerve did not take part in this function.

Magendie's criteria for smelling were the reactions of the animals to the odour of ammonia, acetic acid, or oil of lavender. Eschricht pointed out that these test substances, besides being odiferous, also irritated the nasal mucosa. In dogs this was true even for the oil of lavender because of their acute sense of smell. Magendie also made some experiments with meat wrapped in paper, but because of the miserable condition of the animals after the severe operation the experiments were inconclusive. Eschricht therefore concluded that Magendie had not proven that the fifth nerve is the olfactory nerve (Eschricht, cited in Lund 1825, pp. 313-315).

In his standard work, *Handbuch der Physiologie des Menschen*, Johannes Müller gives a detailed account of Eschricht's discovery that the sensitivity of the seventh nerve pair was primarily due to the anastomoses it received from the fifth nerve pair, but also from the first cervical nerve pair (Müller, 1833, I, p. 643). The relationship between the fifth and seventh nerve pair was the main topic in Magendie's lecture-demonstrations of the nervous system, 1838-1839. Thus, in the second section of the course, 12 out of the 20 lectures were based on the cutting of the roots of the fifth nerve in rabbits and dogs and the effects on the face and the facial sense organs (Magendie, 1839). Notably, Magendie did not mention predecessors to his experiments and to the discovery that the sensitivity of the seventh nerve derived from the fifth. But in his memoire of Magendie, Pierre Flourens (1794-1867) stated that "a very fine experiment of M. Eschricht of Copenhagen suggested to M. Magendie an inquiry in order to determine the action of the fifth pair on the seventh" (Flourens, 1858, p. 117), referring to Eschricht's reprinted dissertation (1826a). Flourens, Magendie's perpetual rival (Olmsted, 1944), thus accused Magendie of having appropriated Eschricht's discovery.

A second reference to Eschricht's work on the cranial nerves is found in Eckhard (1888). He erroneously included Eschricht amongst the authors who deserved to be mentioned for "the sake of completeness", because he had confirmed Mayo's finding that

the fifth nerve was the sensory nerve of the face and the seventh the motor nerve. As mentioned above, Eschricht and Lund had in fact tested and confirmed Eschricht's original theory that the sensory function of the seventh nerve primarily derived from anastomoses it received from the fifth pair, and they had rejected Mayo's theory about the existence of a particular muscular pain sense.

Eschricht's (and Lund's) pioneer studies of the cranial nerves were overlooked in Brazier's (1987) and Clarke and Jacyna's (1987) histories of nineteenth century neurophysiology.

From physiologist to naturalist

The young Eschricht's engagement in the experimental physiology is well documented in his letters to the mother, in Lund's *Physiologische Resultate*, and in his dissertation. The letters to Lund elucidate Eschricht's transition from experimental physiologist to primarily naturalist and passionate collector of whale skeletons and other natural objects.

Lund went to the South for reasons of health, and he had left for Brazil on September 28, 1825, before Eschricht had received his dissertation from the printer. He therefore sent a copy of it to Lund, together with a vivid and ironic description of the public defence of the thesis. He ended the long letter by regretting that he had not made any physiological experiments, and he reminded Lund about the Physiological Society they had planned to establish when he came back. In the next letter, of February 25, 1826, Eschricht mentioned that he was missing Lund very much, as a friend and as a companion in the physiological studies, which he had neglected, and he finished the letter by again reminding Lund of their Physiological Society which "shall come off even if it consists of only two members."

Four and a half year passed before the next letter, of October 1, 1830. In this letter there was nothing about physiology. It dealt mostly about Eschricht's mania for collecting. Three times he had sweared to stop it, but in vain, and he enumerated his rich collections. The letter ended by urging Lund also to collect to him. The transition from physiologist to naturalist and collector was thus accomplished since the previous one in the collection of preserved letters.

Professor of physiology

Eschricht, who began a promising career in experimental physiology, could not in the long run remain a good teacher in the subject because he neither remained active in the field nor kept abreast of the developments. He succeeded though in writing a textbook in physiology, the first part of which appeared 1834-1836 and the second in the forties. According to *Dansk biografisk Leksikon* is his broadly written, voluminous book a popular publication rather than a university textbook. The book can, however, hardly be classified as popular science, and its comprehensiveness has increased its historical value. Of special interest here is Eschricht's account of a demonstration of the spinal nerve roots with which he had assisted Magendie during a visit in 1825. He wrote about his experience that "for any observer [it] must be considered as the most conclusive [experiment] that can be shown in the physiology. The whole spinal cord was exposed in a living dog. On the right side did he [Magendie] cut through all posterior, on the left all anterior roots. Every time this animal was pinched on the right side, it showed no sign of feeling it; on the other hand, every time the animal was pinched on the left side, it crawled by means of the right leg, dragging the lame side along the table" (Eschricht, 1834-1836, p. 177).

When Eschricht wrote his textbook there was, as mentioned, a widespread opposition against vivisection as a physiological tool in generel and against Magendie's experiments on the spinal nerve roots in particular. Eschricht understood why: " The consequence of so decisive and in addition important an experiment must always be, that everyone who has seen it cannot listen to any objection; on the other hand, everyone who has not seen it, especially if he is not at all familiar with vivisections, will be very disinclined to accept the truth of it. It is thus explainable that so important a discovery could remain disregarded in several years in Germany, until an excellent anatomist, Prof. Joh Müller, by himself repeating these experiments, became wholly convinced, although he only performed them on frogs, from which the conclusion to man must always be dubious" (Eschricht, 1834-1836, p. 177). Müller was a close friend of Eschricht, and at the time of writing the textbook they jointly published a paper on the retia mirabilia of the tunny liver (Eschricht and Müller, 1835).

Reflex movements

In the annual royal festschrift for 1845, Eschricht wrote a popular treatise, in Danish, on the nervous system, focusing on the reflex movements which had been dealt with in detail by Marshall Hall and Johannes Müller in 1833. The concept of reflex movements can be traced back to Thomas Willis (1622-1675), Jean Atruc (1684-1766), Georg Prochaska (1749-1820) and others, but the localisation of the reflex centre, whether in the brain or the spinal cord, was long a matter of debate (Stirling, 1876; Canguilhem, 1955; Liddell, 1960). Eschricht based his account of the reflexes and of central modulators on observations he made when he assisted Magendie in his experiments on the olfactory function of the cranial nerves. One day Magendie made experiments on a brainless rabbit which, as usual in brainless animals, stayed motionless. Eschricht therefore only expected a slight effect of the olfactory test which consisted of introducing the wane of a quill, dipped in ammonia, into the nostrils of the rabbit. But the reactions were far more violent than in the animals with an intact brain, and the brainless rabbit began to scream loudly.

Eschricht connected this unexpected observation with an experience of his own. Once he had had very cold hands he happened to touch a man in deep sleep with his hands. The action set the person in violent movement. When he woke up, Eschricht again touched him, but now he merely remarked how cold the hand was. This increased reactivity to external stimuli in the sleeping man and the brainless rabbit led Eschricht to the hypothesis that an inhibitory action from the brain on the reaction was lacking in both. He wrote: "The spinal cord is the organ for that principle from which the whole detailed control of the muscular machinery of the body is performed. Every action upon the external as well as the internal organs is transmitted through the posterior roots of the spinal cord (the nerves of sensitivity). The influence that is received from the external organs is immediately transmitted further to the brain, and by this [the brain] may then the counteraction from the spinal cord be retained or at least modified. Otherwise, the counteraction follows from the spinal cord immediately; it becomes a pure unconscious muscular activity; it becomes what the newer physiologists have introduced to call 'a reflex movement'" (Eschricht, 1845, p. 19).

Eschricht's views of reflexes were original and clear-sighted. Müller's (1833) treatment of the reflexes is a detailed account of all movements, conscious as unconscious, which he interpreted as motor responses to sensory impulses to the spinal cord and brain, but he did not mention brain control of the spinal reflexes; neither did Marshall Hall (1833). Moreover, Hall's highly speculative treatise on the function of the spinal cord as a reflex centre was met with violent opposition. Hall thus assumed that the reflex movements depended upon the existence of a special nervous system, different from the voluntary. Even the existence of spinal reflex centres was debated, and according to the predominant view, the spinal cord was merely a string of nerves from the brain where all nerves originated (Liddell, 1960). Magendie, too, may have shared this view on the spinal cord. In his course of the nervous system (Magendie, 1839), there is no mentioning of spinal reflexes, not to mention their central nervous control. In 1839, Magendie may have forgotten the surprise in 1825 over the hypersensitive, brainless rabbit, – or it may only have been Eschricht who was surprised.

The central control of the spinal reflexes was rediscovered by Türck (1851) and Setchenow (1863a,b), both working in Claude Bernard's laboratory. Setchenow observed that the existence of central moderators of reflexes was only half-way proved, based on the intensified reflexes that follow decapitation of an animal. He and Türck established the existence of a central control of the spinal reflexes by hemitransection of the cord and successive dipping of a hind leg in highly dilute sulphuric acid. The time interval between immersion and retraction of a limb was shorter on the operated side, indicating enhanced sensitivity on this side.

Eschricht was also clear-sighted in his view of the importance of vivisection in the solution of the function of the spinal cord. He thus stated that Bell-Magendie's discoveries of the function of the nerves of the spinal cord "gave a new proof of how little we with the help of the anatomy alone are able to fathom this important system [the spinal cord and its nerves] in its whole diversity." And he pointed out that the function of the nervous system can only be explored "by observations on the living body, and whenever these get into conflict with the anatomical, the former ought to carry the greatest weight" (Eschricht, 1845, p. 22). This was, as mentioned above, the opposite of what leading anatomists, with Charles Bell in front, meant.

Magendie and Claude Bernard about Eschricht

Eschricht's opinion of the person and scientist Magendie is well documented in the letters to his mother. Even though Eschricht's later contributions to physiology were modest, they show that he did not forget what he learnt as Magendie's pupil and assistent. Very little is, hovever, known about Magendie's opinion of and feelings for Eschricht. A short letter from Magendie to Eschricht is therefore of interest. The letter, written 1848 and preserved in the archives of the Zoological Museum, Copenhagen, is merely a recommandation of a young French biologist who wished to study with Eschricht. But it ends with the words: "Adieu mon cher et ancien collaborateur. Croyez à mon sincere attachement," consistent with the impression gained from Eschricht's letters to his mother that the sympathy between teacher and pupil was mutual.

Eschricht seems to have had similar feelings for Claude Bernard (1813-1878). In the posthumous *Principes de médecine expérimentale,* Bernard (1947, p. 91) wrote that Eschricht had visited him several times on his journeys to Paris. On the question why Eschricht had changed his scientific course and abandoned physiology, he had answered that physiology was not an exactly defined science; in order to explain the living phenomena it rested, now on the physics, now on the chemistry, now on hypotheses such as those about the vital force. Anatomy is at least a precise science, and you can depend upon the anatomical facts. That was why Eschricht got "l'ambition de devenir un cétologue distingué."

Bernard (1947, p. 91) further gave the interesting information that Eschricht had told him that Tiedemann (F. Tiedemann, 1781-1861) and Müller had been led by the same feelings in their choice of anatomy for physiology. They had all three started successful careers as experimental physiologists, to end as anatomists. In other words, Eschricht's turn away from experimental physiology was not purely accidental but reflected a scheme familiar to other physiologists of the same period.

It seems to have worried Bernard that these three "very eminent physiologists" had abandoned physiology in favour of anatomy. He returned to the subject repeatedly. In the *Cahier Rouge* he thus noted that: "Müller, Tiedemann, Eschricht ont été dégoûtés et se sont jetés dans l'anatomie" (Bernard, 1942, p. 113),

and in the *Leçons de physiologie opératoire* he related how Eschricht, who had started as a successful experimental physiologist, had abandoned physiology for comparative anatomie, and Johannes Müller had at the end of his scientific career, struck by the incoherence of experimental results, turned to dissection of the lower animals. Tiedemann was again cited as a third example (Bernard, 1879, p. 6).

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Historians, philosophers and practitioners on Claude Bernard's *Introduction à l'étude de la médecine expérimentale*

Introduction

François Magendie (1783-1855) and his pupil, Claude Bernard (1813-1878) were pioneers in modern, experimental physiology, based on vivisection. But their approach to the subject differed fundamentally. Magendie declared himself to be a mere collector of experimental facts, even accepting apparently contradictory results. To Bernard the physiological processes were as determined as the processes in physics and chemistry, differing only in complexity. Determinism is the code word in his philosophy of physiological method, as developed in his *Introduction à l'étude de la médecine expérimentale* (1865).

The basic elements of his philosophy of method he formulated in a definition of the true scientist: " (1) He notes a fact; (2) *à propos* of this fact, an idea is born in his mind; (3) in the light of this idea, he reasons, devises an experiment, imagines and brings to pass its material conditions; (4) from this experiment, new phenomena result which must be observed, and so on and so forth. The mind of a scientist is always placed, as it were, between two observations: one which serves as starting point for reasoning, and the other which serves as conclusion" (Bernard, 1957, p. 24). The true man of science is also a doubter: he believes in science, but he doubts himself and his interpretations. "Even when experiment fully proves his preconceived idea, the experimenter must still doubt; ... his reason still demands a counterproof" (Bernard, 1957, p. 52).

In his foreword to the Dover edition of the English translation of the *Introduction,* I, Bernard Cohen stated that this book is an exception to the usual definition of a scientific "classic" as a great work that is venerated, cited, but no longer read. The statement seems supported by the extensive literature that deals with the book, as well as by the numerous editions and translations. It has thus appeared in ten French editions, from 1900 to 1984, and it has been translated into English (1927), Spanish (four editions), Catalan, Italian, German, Czechish, Russian, Turkish, and Japa-

nese (Grmek, 1967). The statement seems, however, contradicted by the general view that scientists, including physiologists, don't read books on the philosophy of scientific method. It was therefore found of interest to see what historians and philosophers of physiology, as well as practicing physiologists have said – or not said – about Claude Bernard's *Introduction.*

The literature dealing with the life and work of Claude Bernard is overwhelming. Grmek's bibliography from 1967 encompasses 502 titles. The titles indicate that 57 of the listed works deal with Bernard's philosophy of scientific method, whereas further 37 may do so. In the following a representative number of the references to Bernard's philosophy, scattered over the century that followed the publication of the *Introduction,* have been selected for inspection.

Early views

Bernard was himself doubtful about the usefulness to scientists of a philosophy of scientific method. He admitted that the "solid union between science and philosophy is useful to both: it lifts the one and confines the other" (Bernard, 1957, p, 224). But this statement he qualified by adding: "if men of science are useful to philosophers, and philosophers to men of science, men of science remain free, none the less, and masters in their own house; as for myself, I think that men of science achieve their discoveries, their theories and their science apart from philosophers." And he referred to J. de Maistre who, in his book on the philosophy of Bacon from 1836, stated that "those who make the most discoveries in science know Bacon least, while those who read and ponder him, like Bacon himself, have poor success." And the *Introduction* ends by emphasizing that philosophy of scientific method is of no use to scientists. Science, including physiology, can only be learned in the laboratory.

Louis Pasteur, Bernard's colleague, friend, and junior by about 10 years, didn't agree in this negative evaluation of the usefulness of philosophy. In a review of Bernard's works from the last 20 years, ending with the *Introduction,* he stated that nobody has written more lucid, more complete, more profound about the true principles of the so difficult art of experimentation. And he envisaged that "the influence it [the *Introduction*] would exert on the medical sciences, on their teaching, their progress, even on their language, would be immense; ..." (Pasteur, 1866).

At the same time the French philosopher, Paul Janet (1866), based a detailed analysis of the experimental method and physiology on Bernard's *Introduction.* He noted that Bernard in his scientific philosophy in many aspects had been anticipated by Francis Bacon. Thus Bernard pointed out the importance of noticing unexpected results of an experiment and of following such fortuitous observations up. But already Bacon had "perfectly seen and signalled the importance of a fact that presents itself accidentally to the observer ... and which the scholar must know to follow up." Bernard stressed the importance of the *crucial* experiment and the necessity of counterproof, both "capital maxims of Bacon." Bernard, moreover, repeated Bacon's rule not to end an experiment prematurely. At one point, however, Bernard dif-

fered from Bacon, namely in the use of hypotheses in science. Janet found Bernard's view that the hypothesis was an absolute necessity in experimental physiology to be one of the most interesting in the book, because of the, at that time, incessantly repeated protests against its use in science ever since Newton's famous motto: "*Hypotheses non fingo,* I do not make hypotheses." Janet observed, though, that statements in favour of hypotheses in the sciences were not absolutely new, and he referred to a number of scientists and philosophers who also defended the use of hypotheses, that is, if they were based on observations. More recently the relationship between hypotheses and observations had been dealt with by Auguste Comte, and Janet pointed out the similarities beween Bernard and Comte in their views on this relationship.

Paul Bert, in a commemorative speech of Bernard, dealt in detail with the *Introduction,* in which Bernard "showed the conditions for scientific doubt, the utility and danger of theories, the rule of observation and experimentation in the biological sciences, the importance, the necessity of intuition, the inner sense, the hypothesis, in order to procreate the experimental idea!" – And Bert recalled a personal – often cited – memory from his first year as Bernard's préparateur. He was about taking off his coat before entering the laboratory when Bernard gave him the advice: "Laissez votre imagination avec votre paletot, au vestiaire, mais reprenez-la en sortant," implying that you enter the laboratory to make your experiments according to your preconceived ideas, but, in some way passively, accepting the results of the experiments, whether these are favorable or unfavorable to the preconceived idea, even with greater pleasure if the latter is the case, because that was the sign of an unknown novelty and therefore for making a discovery. But, on leaving the laboratory, resume your imagination, reflect, conclude if it is time for that, or conceive a new hypothesis for testing (Bert, 1881, p. 79).

A letter from an earlier student of Bernard to Pasteur, and published by him, throws further light on Bernard's experimental method. Bernard advised his students to doubt all theories, and he often repeated that you should always try to refute them (à se demolir). And he let the students understand that theories only deserved confidence to the extent to which they resisted objections and attacks (Pasteur, 1878).

Also the French physician, A. Ferrand (1879), dealt at great length with the *Introduction*, with numerous citations from it. He, as Janet in 1866, referred to Bernard as an empiricist, descending in direct line from Auguste Comte. Bernard's relationship to Comte and the Positivism was once more pointed out by Lenoir (1919). Neither Janet nor Ferrand expressed an opinion on the significance of Bernard's scientific philosophy for the development of physiology, but Lenoir observed that Bernard's ideas did not exert the influence to which they were entitled.

The founder of modern physiology in England, Michael Foster's obituary notice of Bernard is notable by not mentioning the *Introduction* (Foster, 1878). But in his monograph on Claude Bernard and his scientific works twenty years later he noticed briefly that Bernard in the *Introduction* had given an "admirable description of the genesis and growth of a successful experimental inquiry" (Foster, 1899, p. 228).

Also the American physiologist, A. Flint, Jr (1878), wrote an obituary notice that mainly dealt with Bernard's physiological discoveries. It appears from the obituary that Flint had stayed with Bernard in 1861. It is therefore the more surprising that he referred to the *Introduction* as "a volume of lectures." In fact, the *Introduction* was planned to be the preface of a larger work: *Principes de la médecine expérimentale.* Bernard wrote drafts to this work concurrently with writing the *Introduction.* But he never finished the work which Leon Delhoume later edited and published with a detailed account of its history (Bernard, 1947).

An odd document

In 1919, an American librarian, J. C. Bay, published an account of Claude Bernard and his scientific work. He introduced his narrative by referring to "the memories of those of us who studied physiology a quarter of a century ago, ... " He felt that "there is no parallel in life to those times our eyes would brighten at the mere mention of the name of Brücke, Ludwig, Hoppe-Seyler, Pasteur, Claude Bernard, Berthelot, Darwin, Huxley and Burdon-Sanderson. ... We enjoyed the blessing of seeing the red thread which forever connects the name of Aristotle, Theophrastes and Galen through the Middle Ages with ... ," and – after further lists of names – Bay returned to *Claude Bernard* – "one of the immortals" (Bay, 1919a).

Bay further related that at the University of Copenhagen a professor Rasmus Pedersen in 1877 began a course of lectures on comparative physiology which remained unfinished at his death in 1900. It thus appears that Bay was Danish by birth and that he had studied at the University of Copenhagen. He was, in fact, born in Denmark in 1872 and emigrated to USA in 1892.

Bay is wrong in stating that Rasmus Pedersen had lectured on comparative physiology. He was a professor of plant physiology, and he had lectured on plant physiology. Oddly enough, Bay had, in the same year that his paper on Claude Bernard appeared, published a booklet on Rasmus Pedersen (Bay, 1919b). And in this he speaks of Pedersen's perpetual course in plant physiology, which he had followed a year. But he also writes about his close connections with the eccentric professor who had tutored him privately and placed his rich library to his disposition. Presumably it was from these personal contacts with Rasmus Pedersen and his library that Bay became familiar with Bernard's works which he reviewed in detail, but without any mentioning of the *Introduction.* All he wrote about Bernard's scientific philosophy was that "he who wishes to learn what was Claude Bernard's method in work and philosophical contemplation, would best read one or more of his works in the original – particularly the lectures on the nervous system and those on the life activities common to animals and plants."

20. century views

The views on the importance and influence on physiology of Claude Bernard's *Introduction* varied during the 20. century. The French philosopher, Henri Bergson (1936), compared it with R. Descartes' *Discours de la method,* and in a dissertation on Claude Bernard's work and philosophy, M. H. Goldstein (1930) observed that the *Introduction* was a book "the novice and beginner in physiological research would profit immensely by reading." A presidential address by J. L. Miller (1923) on Bernard's influence on medicine consisted practically exclusively of quotations from the *Introduction,* and Miller ended by stating that he knew "of no more appropriate adornment for the walls of a research laboratory than some mottoes of this famous physiologist."

J. M. D. Olmsted's (1939) definitive biography of Claude Bernard deals at length with the *Introduction.* The conclusion was that "it is Bernard's contribution to have described perfectly and out of his own experience the collaboration of mind and nature, of fact and idea, which takes place in the experimental method." And Olmsted (1939, p. 273) cited the German-American historian of medicine, H. E. Sigerist, for having pointed out, in his book *The Great Doctors,* that the *Introduction* is one of the few medical books which have not aged quickly (Sigerist, 1959). (As mentioned above, this was also Cohen's opinion in his foreword to the Dover edition of the book.) At about the same time, a French biographer, the physician Pierre Mauriac (1935), was, however, less laudatory. He noticed that the *Introduction* had become a kind of Bible in the scientific research. But he wouldn't be surprised if some day the book's fortune would seem strange. The style was often slack and the text overwhelmingly repetitious, and he had never believed that it had been of much help to the experimenters. The *Introduction* was only an after-thought. Mauriac ended by admitting that Bernard was a great scientist, but he was an inferior man, lacking "the philosophical spirit." Mauriac's demolition of Bernard's philosophy of the experimental method was countered by the Mexican-Canadian physician J. J. Izquierdo (1947), who translated both a Spanish and a Catalan edition of Bernard's *Introduction.* And when a philosopher of profession, Max Black (1949), was trying to formulate the principles of scientific method, he referred to Claude Bernard's *Introduction,* "a

classic of the philosophy of science which deserves to be better known in the English-speaking countries." He suggested that "its title may have misled readers into expecting a technical treatise on physiology; it is in fact an essay on method not unworthy to be classed with that of Descartes." He consequently reviewed Bernard's views on scientific method, focusing on Bernard's fallibilism and determinism.

Also the French-American nutritionist, hero from the Second World War, humanitarian, President of Tufts University, etc. etc., Jean Mayer (1951) wrote enthusiastically about Claude Bernard. After a characterization of Bernard as a scientist, primarily based on his studies of the sugar metabolism, "the most famous series of physiological investigations ever conducted," Mayer referred to "his Introduction to the Study of Experimental Medicine (1865), the clearest exposition ever written of biological epistemology, and a masterpiece of scientific style." But at about the same time another biographer, Reino Virtanen (1960), was less enthusiastic over the literary qualities of the *Introduction.* He found that it was "not free from faults of composition and expression. In parts [it was] repetitious, sometimes verbally inconsistent, occasionally digressive." He acknowledged, however, that it was "basically consistent throughout, an example of clear, cogent exposition, full of meat and substance." Virtanen excused Bernard for his shortcomings in his lacking "early philosophical training which might have enabled him to formulate his views with more terminological precision." Also Gérard Vassails (1951), obviously a Marxist critic, referred to Claude Bernard as "an autodidact in philosophy," and he blamed Bernard for ignoring the "dialectical materialism" in his *Introduction.* Vassails (1952) noted that Claude Bernard politically remained loyal to the Emperor, and that consequently his philosophical opinions remained "bourgeois."

In a comprehensive, highly critical review of theories of scientific method from Plato to E. Mach, the English historian of science, L. Laudan (1968) observed that Claude Bernard's "discovery [of] the indispensable rôle ... [of] preconceived ideas ... was not Bernard's discovery, ... Notwithstanding its importance, the *Introduction* scarcely merits Leclercq's appelation as "la bible de la méthode experimentale." Laudan thus seems to ignore that it was Bernard who established physiology as an exact science, based on determinism. A German historian of science, Hans

Querner (1975), is more positive in his evaluation of the *Introduction*, a work which he called "die entscheidende programmatische Schrift für die experimentelle Physiologie (und Medizine)."

Two more conflicting views on Bernard's *Introduction* may be added. In an address by Th. v. Uexküll (1958) to mark the centenary of Johannes Müller's death, the author made a strong appeal to present days' physiologists to return from mere collection of facts to Müller's physiology – and to Claude Bernard's, as described in his *Introduction*. This book v. Uexküll found was a "classic" of medicine, meaning a book that was still referred to, but not any longer read. According to the English physiologist, James Fitzsimons (1976), however, Bernard's *Introduction* "was one of the most influential works in physiology ever."

In summary, the biographers' opinion of Claude Bernard's *Introduction* and its influence on the development of physiology have varied from the belief that it would incite a new spirit in the study of physiology to the conviction that it had not been and would never become of any conseqence to the development of physiology because practicing physiologists did not read books on the philosophy of physiological method. But what do the practitioners themselves say? The autobiographical prefatory chapters which outstanding, retiring physiologists wrote to the *Annual Review of Physiology* from 1950 to 1987 seemed to provide an opportunity for answering this question.

Retiring physiologists reminisce

The first author of a prefatory chapter, Eugen F. DuBois (1950), Cornell University, Medical School, mentioned that the Editor in his letter of invitation had stated that the motive behind the invitation was the "desire to make the Review something more than a consideration in detail of the current advances in our science. Physiology is a form of human activity as well as an accumulation of knowledge. As such it has a history of hopes, ambitions, enthusiasms, fashions and phobies." The letter ended by pointing out that "interest in the philosophic basis of science is increasing as we attempt to approach our ultimate task, the revealing of the nature of man." This somewhat cryptic statement seemed to imply that the authors of the prefatory chapters were encouraged to consider the philosophic basis of their research. DuBois, however, did not respond to this part of the invitation. His prefatory chapter outlined fifty years' development of physiology in America. DuBois was worried because he found that physiology had expanded "faster than the supply of trained personnel," with the result that "physiology in the United States had expanded until it somewhat resembles an acromegalic giant."

The author of the next prefatory chapter, Carl J. Wiggers (1951), Western Reserve University, School of Medicine, had attempted to comply with the Editor's request to interpret influences on the development of physiology during the past fifty years. But owing to limitations of time and space he had had to confine the survey to the first two decades of the century. This survey consisted in a compilation of physiological discoveries, based on 95 references, and there was no mention of a philosophy of physiological method. But Wiggers related how, as a student, Cushny (a founder of modern kidney physiology), had granted him "the privilege of assisting him in his experiments on free afternoons. ... it afforded the opportunity to learn how a great experimenter observes, ponders, and deducts from his observations." Wiggers thus learnt basic elements of Claude Bernard's philosophy of experimental physiology in a kind of apprenticeship, which seems to be the standard way of learning physiologcal research.

In the following prefatory chapters, autobiographies or reviews of own scientific activities predominated. One author, Frank C.

Mann (1955), from the Division of Experimental Medicine, the Mayo Clinic, had, however, attempted to write philosophically, but the remembered remnants of his "university courses in philosophy that had not been filtered out by the passing years did not appear to apply to physiology."

Still, Mann had a philosophy of experimental research. Early in his career he conceived that problems should be designed to give answers that were yes or no, or that the methods available could not give a definite answer.

Mann got an opportunity to practice his philosophy by introducing group research in a new experimental laboratory which he had erected. Group research required carefully prepared design, based on a previously discovered guide, and not on pure imagination. The unexpected discovery was therefore not so likely to occur as in researches made by the individual. The object of the research in Mann's laboratory was to train the members of the group in research and to make valuable discoveries. Presumably, an unexpected result of an experiment did not give Mann as much pleasure as it, according to Bert (1881), did Bernard.

Mann's research policy thus approached a tendency in contemporary physiology which several of the contributors deplored: the overestimation of the importance of facts as opposed to ideas. Thus, the American Nobel Laureate, Otto Loewi (1954), observed that "such terms as 'hypothesis' or – even more so – 'speculations' are taboo for many scientists." And the Argentine Nobel Laureate, B. A. Houssay (1956), noticed that "physiology requires more than the mere accumulation of isolated facts; ... Physiology sails its ship between the Charybdis of premature, undocumented generalizations, and the Scylla of unimaginative fear of hypothesis and synthesis." The Swedish physiologist, G. Liljestrand (1957), dealt with the question by quoting a beautiful speech which the Russian Nobel Laureate Pavlov at the age of 87 years delivered to the students of his country. About the relationship between facts and ideas, Pavlov said: "Learn, compare, collect the facts. ... Facts are the air of a scientist. ... Without them your 'theories' are vain efforts. ... But do not become an archivist of facts. Try to penetrate to the secrets of their occurrence, persistently search for the laws which govern them."

The most original prefatory chapter was written by the biophysicist, A. C. Burton (1975), who, too, noted that too much time and

money were spended on accumulating mountains of data with no underlying idea. So he gave a perfect description of how to solve physiological or biophysical problems, – and on verse:

Discovery

Little rivulets of thought
Erode the broad surface of the problem posed,
Idle, wandering and aimless rills
Like garden freshets after heavy rain.

And now the streams have quickened, coalesced,
To eddy round the hillock of a doubt,
Find well-worn channels, ditches study-dug,
and flow with purpose in a common trend.

Ideas break surface with salmon splash,
While from the deep,
Wise intuition adds its hidden flow,
A rhythmic pulse is growing, surge on surge,
Insistent logic in bolero time.

At last the turgid waters will not stay –
Glide swiftly through the gorges of analogy,
Go leaping down the rapids of hypothesis, and break
Into a quiet flood of certainty.

Obviously, Burton might have been inspired by Claude Bernard's *Introduction*, but without mentioning it.

A few of the authors of the prefatory chapters pointed to the importance of noticing odd or unexpected things that turned up during an experiment and of their following up, presumably unaware that this was also an advice of Bernard's. Thus the English physiologist, A. V. Hill's (1959) critical experiments on heat production in muscle and nerve "were not usually thought out in advance, they were certainly not 'planned' as doctrinaires profess to plan research, they arrived quietly by noticing odd things that turned up, by trying to understand them, and then seeing how they could be used."

The Belgian respiration physiologist, C. Heymans (1963), related how in his studies he had followed an advice of his father: "Never kill an animal at the end of a planned experiment, if the animal may still be used for any experimental purpose, and take profit of this animal to perform any experimental trial, even if it looks foolish, but keep your eyes well open in order to catch any unexpected event." Following this advice, Heymans, after finishing an experiment on the carotid sinus baroreceptors in the dog, injected cyanid in the animal – and the carotid chemoreceptors were discovered.

The American physiologist, George H. Bishop's (1965) prefatory chapter was a humorous causerie over his "life among axons." He observed that "most of the answers to the questions that plagued us [Bishop and his coworkers] in earlier days were found by people who were looking for something else."

One author, the pharmacologist Carl F. Schmidt (1961), did refer to Bernard's *Introduction*, not, however, to its philosophy of physiological method, but to Bernard as a pioneer in the study of the action of drugs.

Finally, two autobiographies differed from the norm, those of the neurophysiologist, J. C. Eccles (1977) and the electrophysiologist, A. L. Hodgkin (1983).

Eccles had previously, in his autobiography *Facing Reality* (1970), written about personal experiences with scientific method. Until 1945 he had held the idea "that hypotheses grow out of the careful and methodical collection of experimental data. This is the inductive idea of science deriving from Bacon and Mill" (p. 105). And he added the dubious statement that "most scientists and philosophers still believe this is the scientific method." The statement might perhaps have applied to many English-speaking scientists at the time because, according to Medawar (1967, p. 118), the English had unfortunately "been brought up to believe that scientific discovery turns upon the method ... of *Induction*."

Medawar's observation is supported by an experience which the Austrian philosopher, Karl Popper referred to in his autobiography. After a lecture, which Bertrand Russell gave in 1936 at Bedford College, London, Popper had participated in the discussion and said that he "did not believe in induction at all." This statement the audience took as a joke and laughed. Then he said

that "what we call 'scientific knowledge' was hypothetical, and often not true, ... Again the audience took this for a joke, or a paradox, and they laughed and clapped. I wonder whether there was anybody there who suspected that not only did I seriously hold these views, but that, in due course, they would be widely regarded as commonplace" (Popper, 1986, p. 110).

Eccles "conversion" in 1945 he owed to Karl Popper's teaching (Eccles, 1970, p. 104). He had come under the influence of Popper during the Second World War when the latter was a professor of philosophy in New Zealand. Eccles had heard "about the great stir that Popper was making among the scientists at Canterbury University College," and Popper was consequently invited to give lectures on the philosophy of science. "They were an enormous success among the staff and student body, ... Many people, including myself, had our scientific lives changed by the inspiring new vision on science that Popper gave us. ...

Briefly the message we got in those memorable lectures was that science is not inductive, but deductive. A scientific project starts as a problem, for example with a theory that appears deficient or inadequate. New hypotheses are developed and tested experimentally, either to be falsified or corroborated, but the claim of verification should never be made. Thus there are two aspects of a scientific investigation: first, the development of a hypothesis using creative imagination; second, the rigorous experimental testing of this hypothesis in its most vulnerable aspects in an attempt at falsification."

At the time of Popper's lectures, Eccles was much concerned about the fate that seemed to threaten his electrical hypothesis of synaptic transmission, and he admits that it was certainly a crisis in his life when he, urged by Popper, designed models for the experimental testing and falsification of the electrical hypothesis. Thus it was Popper, and not Bernard, who taught Eccles to devise experiments for the rigorous testing and falsification of hypotheses, indicating that Bernard's *Introduction* was unknown to Eccles. It appears from Popper's autobiography that he seems to have considered the principle his own major philosophical contribution to the experimental sciences (Popper, 1986, p. 110), indicating that Bernard's *Introduction* was unknown to Popper, too.

Hodgkin's prefatory chapter dealt with personal reminiscences of his life as a young physiologist, and concerning his research he

referred to a published lecture (Hodgkin, 1976). This lecture is an informal account of experiments on nerve which he carried out in collaboration with Andrew Huxley and Bernard Katz. Hodgkin relates how they within a month "obtained virtually all the voltage-clamp records that were used in the five papers published in 1952." They had spent over two years analysing and writing up the result, but, although they had obtained much new information the overall conclusion was basically a disappointment. They had started off to test a carrier hypothesis, and they believed that they should be able to "deduce" a mechanism from the massive amount of electrical data they had collected. But the carrier model could not be made to fit certain results and had to be given up. They consequently turned to the sodium hypothesis, which eventually became the generally accepted theory for the propagation of the nerve impuls.

Evidently, Hodgkin's and his colleagues' research was not guided by Bernard's *Introduction,* nor, for that matter, by Potter's falsification principle. But it is a notable example of the fact that pioneering work in physiology can be done without philosophical guidance.

Summing up, the prefatory chapters in the *Annual Review of Physiology* support the general but hitherto undocumented view that modern physiologists usually don't read books on the philosophy of scientific method.

Peter Medawar

The English immunologist, Director of the National Institute for Medical Research, Nobel laureate in medicine and physiology, recipient of 20 odd honorary doctorates, etc. etc. – and admirable essayist – Sir Peter Medawar (1915-1987) is a remarkable exception to the rule that contemporary physiologists are not interested in the philosophy of their profession. In a discussion on the BBC Third Programme broadcast in 1966 Medawar told how his interest in philosophy began when he, as an undergraduate, incidentally came across Bertrand Russell's *Principles of Mathematics*. The opening paragraph of this book had tremendously impressed him. He had kept up his philosophic interests in Oxford where he attended a body called the Theoretical Biology Club. Here he met Karl Popper with whom he made friends and from whom he obtained an insight in the nature of scientific discovery which he thought had been most helpful and probably could be helpful to others too (Medawar, 1990, pp. 3-4).

Medawar (1990, p. 231) considered Popper to be the greatest modern authority on the nature of scientific method, and to his "mind the great strength of Karl Popper's conception of the scientific process is that it is realistic – it gives a pretty fair picture of what goes on in real life laboratories" (p. 100). But, when Medawar 23 years earlier, in his essay "Hypothesis and Imagination", had needed an example to show "the Scientific Method at work," he did not refer to Popper, but to Claude Bernard whose *Introduction* he cited extensively. He pointed out how Bernard over and over again insisted on the use in physiology of hypotheses that could be tested and refuted, and on the virtue of doubt. And he ended by stating that Claude Bernard, in creating experimental physiology, did put medicine on a new foundation. His philosophy *worked* (Medawar, 1967, p. 153).

Medawar took the subject up again in a lecture from 1968 on "Induction and Intuition in Scientific Thought" (Medawar, 1982, p. 79). He introduced the lecture by noticing that it was not usual for scientists to write about the nature of scientific method, despite the fact that the testemony of biologists on their scientific method "should be heard with specially close attention." Yet, "the wisest judgements on scientific method ever made by a working scientist were indeed those of a great biologist, Claude Bernard."

But Medawar also noticed that Bernard's *Introduction* seemed to have made little impact on the English-speaking world. Thus, his name was mentioned in only two of a dozen well-known texts on scientific methodology on Medawar's shelves. Medawar found that the *Introduction* had suffered in translation which might account for its limited influence (Medawar, 1982, p. 73). An alternative explanation might be that historians of scientific methodology may tend to overlook a work written by an amateur in the field.

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