

The Fessard's School of neurophysiology after the Second World War in France: globalization and diversity in neurophysiological research (1938-1955)

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Abstract

In France, neurophysiology emerged after the Second World War as a dynamic discipline in different schools, Toulouse, Lyons, Montpellier, Marseilles, and Paris, where Lapique was loosing credit with his studies on the excitability of nerves. Parisian neurophysiologist, Alfred Fessard (1900-1982) was a key figure in establishing a new school of neurophysiology on the model of Edgar Adrian's department in Cambridge, where he worked a few months in the late thirties. Fessard was initially a student of Henri Piéron involved in experimental psychology. He also made parallel oscillographic studies on elementary activities in various animal and plant preparations. His school trained leading French neurophysiologists in Paris until recently and Fessard was instrumental in the creation of IBRO in 1961.

After the Second World War, major French figures in neurophysiology emerged from different traditions in Toulouse, Lyons Montpellier, Strasbourg, Marseilles, and Paris. Alfred Fessard (1900-1982) is recognized today as a most talented neurophysiologist in the 1940's and 1950's who was able to create his own school near Paris, in the former *Institut Marey* (Barbara, 2004, 2007, 2010). Many of his students were among the most renowned French scholars from the early 1960's until very recently.

The story of the Marey Institute is closely linked with the emergence of physiology as an international enterprise. The famous physiologist, Etienne-Jules Marey (1830-1904), was also a leading maker of physiological recording instruments. During the 1898 International Physiological Congress in Cambridge, Marey suggested the creation of an International Commission for the control of graphical instruments devoted to physiology. A new cottage named *Institut Marey* was built near the Physiological Station Marey had planned for his studies on movement in Boulogne-Billancourt, *Parc des Princes*, near Paris. Since it fulfilled a crucial need for collecting and standardizing instruments, the institute was a key element in the construction of European physiology. Nevertheless, after Marey's death in 1904, it progressively lost its international commitments and French neurophysiologists progressively ceased scientific collaborations with foreign countries.



- Figure 1 near here –
Lapicque's Yacht, "L'Axone"

In the 1920's and 1930's, Parisian neurophysiology was dominated by a prominent figure, Louis Lapicque, professor at the Sorbonne University. His conceptions of nerve and muscle excitability, measured in agreement with the concept of *chronaxie*¹, were his main theoretical background to the understanding of nervous system activities. Lapicque built refined concepts, such as *isochronisme*, *chronaxie de subordination* and *métachronaxie* which explained how nervous impulses were adapted to their effector organs, both in space and time. Higher centres were viewed as regulating the frequencies and paths of motor nerve impulses.

Lapicque had started his career examining nerve excitability in the early 1900's and he progressively built his concepts from intensity-duration strength curves, similar to those of French biophysicist Georges Weiss and Dutch biophysicist Jan Leendert Hoorweg². However, Lapicque's work was performed in the context of German physiology, and in close contact with British and

¹ chronaxie, or chronaxy is the minimum time required for excitation of a structure (as a nerve cell) by a constant electric current of twice the threshold current.

² Jan Leendert Hoorweg (1841-1919) and Georges Weiss (1859-1931).

American physiologists (Dale, Hill, Fulton, Gasser). In 1930s, after Rushton challenged Lapique at the Fourteenth Congress of Physiology (1933) on his interpretation of the action of curare on nerves, the *Journal of Physiology* invited Lapique to publish his own results. Rushton later refuted Lapique's interpretations of the blocking effect of curare as the establishment of a different chronaxie between the pre and postsynaptic elements. According to Lapique, synaptic transmission required similar pre and post chronaxie values (*isochronisme*). When this controversy raged, Archibald Hill invited Lapique to cross the channel with his own yacht *L'Axone* to discuss their views on Rushton's results (1937) (Harvey, 1994; Dupont, 1994; Barbara, 2005) (Figure 1). In Plymouth, Hill was surprised to finally meet Lapique who replied: "You never believe me". Both men did not come to any agreement and Lapique became progressively isolated. The way Lapique envisaged international relations involved friendly meetings and scientific discussions (Mrs Lapique was famous for her French style cuisine). However, Lapique developed his research and ideas alone and made very little concessions to others.



- Figure 2 near here –
Alfred Fessard (1900-1982). Photo Jean Fessard.

Alfred Fessard (1900-1982) started his own career in neurophysiology during this period (1930's), when French neurophysiology was radically opposed to the Cambridge school. Fessard was the son of a local printer in Montmartre (Paris). His father thought he would take over his printing house and Fessard entered a business school near Paris (Figure 2). A customer of his father, psychologist Jean-Maurice Lahy (1872-1943), noticed the clever young boy and convinced his father to give him higher education. Alfred Fessard was sent to the *Ecole Normale de la Seine* (Auteuil), he obtained degrees in physics, chemistry and physiology (1924) at the *Faculté des Sciences* (Paris) and his Ph.D. on the excitation of nerves in 1936. During this period, Fessard was assistant at the *Ecole Pratique des Hautes Etudes* (EPHE) in the applied psychological laboratory of the Henri Rousselle hospital in Sainte-Anne, where he started research under the guidance of Henri Laugier (1888-1973), a pupil of Lapique. He then joined his teacher in psychology, Henri Piéron (1881-1964), when he moved from the laboratory of physiological psychology of EPHE at the Sorbonne to the *Collège de France*, where Fessard became his assistant-director.

Fessard was mainly trained by Lapique and Piéron, when Lapique and his students were highly impressed by the early oscillographic studies on nerve fibre conduction from American physiologist Joseph Gasser (Nobel prize in physiology or medicine, 1944). On a trip to Europe, Gasser had most enjoyed his visit to Lapique's laboratory, where he discussed the role of fibre diameters on their conduction rates, which led to a joint paper by Gasser and Lapique (Gasser et al., 1925). At the *Collège de France*, Fessard also adopted oscillography as a new tool with the help of Henri Piéron and funds from the Rockefeller Foundation and the *Fondation Singer-Polignac*.

Piéron was an independent scientist who developed scientific contacts and collaborations with British neurophysiologists, especially Charles Sherrington in Oxford and Edgar Adrian in Cambridge. He was a psychophysicist, holding the chair of sensory physiology at the *Collège de France* in Paris, and he made some reflex studies similar to those of Sherrington. Also, he performed some investigations on vision close to those of Adrian. Piéron supported the work of Fessard who was one of the first French scientists, together with Alphonse Baudouin, to perform electroencephalographic recordings on man (Durup and Fessard, 1936).

Fessard was an open minded scientist and various aspects of brain and muscle physiology interested him. Since the early 1920's, he performed psychophysiological tests based on electrophysiology in Sainte-Anne hospital. In 1926, after he entered Piéron's laboratory at the *Collège de France*, he studied muscle fatigue with electromyography. Together with Georges Durup, Fessard demonstrated conditioning of the blocking of alpha rhythm (Durup and Fessard, 1936). Fessard also collaborated from 1925 to the 1940's with the plant physiologist Daniel Auger on oscillographic recordings of action potentials at the same time as American plant physiologist and biophysicist Winthrop Osterhout (Fessard and Auger, 1935). It appears that during the 1930's and 1940's, Fessard was able to follow the oscillographic revolution in the context of Lapique's hegemony. However, from the very beginning of his career, Fessard always collaborated with others, taking advantage of new tools and new approaches (Barbara and Debru, 2009). Although his first papers using oscillography were officially aimed at confirming Lapique's views (Fessard and Auger, 1932), his personal approach of science was radically opposed.

Besides Fessard's personality, the development of new instruments, as the cathode ray oscilloscope, was a major factor in exchanges of technical skills and ideas. New measurements always led to discussions on how they should be made and what particular property should be taken as proofs for the establishment of facts. Fessard's use of cathode ray oscilloscope led him to measure latencies, central latent periods, elementary circuits, synaptic delays and the synchronization of elementary activities and to adopt the style of Edgar Adrian's research. Thus the oscillographic revolution was a major factor bridging together French, British and American physiology.

Did the choice of Torpedo fish as a model contributed to collaboration with foreign scientists? Interest and research on Torpedo fish have so long a history that relevant epistemological questions must be asked in very specific scientific contexts. Torpedo fish had been studied by Etienne-Jules Marey together with many previous XIXth c. scientists, including du Bois-Reymond. It offered a natural source of animal negativity which could be easily recorded with galvanometers. Torpedo entered Lapique's physiology with studies by the Chauchards in 1925 and 1926. Their results confirmed Lapique's ideas on excitability and the action of curare. Fessard and Auger followed the same general trend, when they confirmed in Torpedo Lapique's concept of *isochronisme* (Fessard and Auger, 1932) (Figure 3). However, it must be emphasized that their approach was already influenced by Edgar Adrian, since they aimed at isolating elementary units of the torpedo's electric organ as Adrian had done on single fibres in the late 1920s. Adrian had established the all-or-none principle of elementary nervous electric activities by devising a clever recording system including a current triode valve amplifier, a capillary galvanometer and a microcinematographic system. He was able to understand how complex nervous waves recorded in nerve centres could appear with simultaneous asynchronous elementary activities and study how synchronous activities could lead to large amplitude potentials.

Similarly to Adrian's experiments, the oscillographic measurements of Fessard and Auger (1928-1935) from pieces of electric tissue were concerned with the isolation of unitary activities, the temporal isolation of a central latency, and the study of the synchronisation of individual motor nerve impulses propagating to the electric organ.



- Figure 3 near here –
Fessard dissecting a torpedo in Arcachon Marine Station

Therefore, if Torpedo was chosen as a means to fit current data with Lapicque's concepts, the use of oscillographic recordings and the emphasis on unitary events led Fessard to adopt the dominant style of research in the field, which Adrian had created. In Fessard's work, Torpedo fish became an interesting model of nerve centre, in the same way Adrian had studied insect's ganglia and the isolated brain stem of the goldfish.

Fessard's research was progressively being influenced by Adrian. Yves Laporte reported that during this period, French physiologist, Camille Soula³ from the *Faculté de médecine et de pharmacie* in Toulouse, deplored French physiology lost its tradition of international collaborations since the Great War (1914-1918). Soula had built close relations with great physiologists of his time, including Ivan Pavlov, Charles Sherrington or Walter Cannon. He dedicated his physiology handbook to Sherrington, written while in prison after being arrested by the Second World War official secret police of Nazi Germany, Gestapo (as Lapicque who also wrote his book *La machine nerveuse* being imprisoned by Gestapo). Similarly to Adrian, Soula developed new recoding devices, such as his sphygmograph with a magnetic recording unit. He acquired new and expensive pieces of equipment, such as a Palmer cylinder, a Schuster-Dale pump and a Van Slyke manometer (Montastruc, 1992). Besides, Soula was the uncle and master of Louis Bugnard, future director of INH (*Institut national d'hygiène*) and master of Yves Laporte in neurophysiology.

However, in the broader domain of biology and medicine, some international collaborations took place thanks to Rockefeller fellowships awarded in the 1920s to selected research fellows. A group of those fellows belonged to the *Institut de Biologie Physico-Chimique* (IBPC) in Paris with Boris Ephrussi (stays abroad in 1926, 1934, 1936) and René Wurmser, a biophysicist studying photosynthesis (1924). Also, the neurologist Alphonse Baudouin, a pioneer in electroencephalography, received funds in 1926. In the 1930s, the policy of fellowships and funding was extended to other research domains, such as nervous physiology (Alexandre Monnier, Paris, Sorbonne ; Louis Bugnard, Toulouse ; Alfred Fessard, Paris), neurosurgery (psychosurgery, Clovis Vincent, Paris) and histology (Pol Bouin, Charles Oberling, Strasbourg ; Christian Champy, *Faculté de médecine de Paris*). This selection is explained by the locating of young promising research fellows, with no intention to dismiss any research school, and by funding mature scientists developing new research domains.

The international relations of their masters Soula and Piéron, facilitated the awards of the Rockefeller fellowships to Fessard and Bugnard. They both stayed in the laboratories of prestigious British physiologists in the 1930s. Fessard worked a few months in the physiology department of Edgar Adrian (Nobel prize of physiology or medicine in 1932), and Bugnard joined the laboratory of Archibald Hill (Nobel prize of physiology or medicine in 1922).

³ Camille Soula (1888-1963).

Fessard obtained two grants from the Rockefeller foundation, one in 1936, for six months, to work in the laboratory of the Marine Biological Association in Plymouth with Dr. Sand on electrical responses of the stretch receptor of pelvic fin Ray muscles using the B.H.C Matthews oscillograph (Fessard and Sand, 1937). In 1939, Fessard obtained a second four months grant from the Rockefeller foundation to join Adrian's physiology department to work with Brian Matthews on unitary dorsal root potentials. During these studies, they both coined the term "synaptic potential" (Fessard and Matthews, 1937).

A radical change was occurring in the relations between Paris, Oxford and Cambridge schools of physiology. Fessard was escaping from Lapique's circle. During the same period, Lapique's results on the action of curare were being refuted by William Rushton. Lapique had chosen Alexandre Monnier to succeed him at the Sorbonne and Fessard was sent abroad in this context. Although Fessard tried to make Lapique and British scientists talk (especially with Hill), he had already chosen the foreign side of science. The following year, when Fessard returned to the nearly abandoned building of the Marey Institute, he was able to set up his own laboratory. This period was crucial to Fessard since he made important scientific contacts. Both his technical skills in oscillographic recordings and his open minded views on synchronization and neurotransmission had allowed him scientific interactions with British physiologists.

The next step towards closer international relations between Fessard and leading European scientists occurred in Arcachon, France (1939) (Figure 4). Fessard invited David Nachmansohn and Wilhelm Feldberg, two German Jewish scientists established respectively in Dale's Laboratory in London (and then in New York) and at the Sorbonne in Paris. Nachmansohn, a biochemist from Meyerhof's laboratory, had first joined the laboratory of René Wurmser (1933). After attending lectures from Henri Dale, he moved to the field of biochemistry of acetylcholine and acetylcholinesterase. He made an impressive number of studies on the localization of enzymatic activities in muscles and nervous system, with the collaboration of the histologist René Couteaux and Annette Marnay. Nachmansohn found acetylcholinesterase activity was higher in innervated portions of muscle. With the chemist Edgar Lederer from Wurmser's laboratory at the *Institut de Biologie Physico-Chimique*, he discovered Torpedo extracts yielded high acetylcholinesterase activity. Fessard was intrigued by these results and invited Nachmansohn to work with him on the subject at the *Station biologique d'Arcachon*. Biological stations including Arcachon always facilitated meetings and collaborations between scientists. In 1937, Lapique and Hill had met at Plymouth, where Fessard worked. Besides these friendly discussions, marine stations favoured joint experimental work on marine animals and contributed to numerous cases of close scientific interactions both in France and abroad.

In Arcachon, Nachmansohn and Fessard discovered high levels of acetylcholinesterase in nerves and synapses from Torpedo. With Feldberg, they further planned to examine whether acetylcholine was involved in the neurotransmission of the electric organ of torpedo, in the context the discovery of its role three years previously at the neuromuscular junction by Dale, Feldberg and Vogt. Feldberg was also invited in Arcachon for his technical skills in the perfusion of organs with acetylcholine, eserine and curare. The question of chemical versus electrical transmission raged. Feldberg, Fessard and Nachmansohn were able to manipulate transmission pharmacologically providing strong physiological and biochemical evidences supporting the role of acetylcholine in torpedo's electric organ neurotransmission. Their results were published in separate papers by Nachmansohn on one side and Feldberg and Fessard on the other. The paper by Feldberg and Fessard (1942) from the *Journal of Physiology* is considered today as a landmark paper. This exemplary collaboration shows how members of the community of neurophysiologists could react together to a specific problem, merging together different approaches and technical skills. However, a common theoretical background was needed and Fessard, unlike many of his electrophysiologist colleges, adopted an open view on chemical neurotransmission. Therefore, the role of Fessard (and

Wurmser) in inviting Nachmansohn and Feldberg and Fessard's idea of international collaborations were a major contribution and a step in the development of an international neurophysiology.

This episode demonstrate how three local traditions from three different sub-disciplines, neuropharmacology (Feldberg), biochemistry (Nachmansohn) and neurophysiology (Fessard) collaborated successfully in the context of the modern theory of chemical neurotransmission.



- Figure 4 near here -

Torpedo fish research collaboration set up by Fessard in Arcachon. From left to right, A Chweitzer (Paris), W. Feldberg (Cambridge), H. Blaschko (Cambridge), R. Sigalas (Arcachon, director of biological station), D. Nachmansohn (New York), A. Fessard (Paris).

In the same years (1938-1947), Fessard was collaborating on electric fish not only in Europe, but also with Brazilian scientists. The son of the famous bacteriologist Carlos Chagas came to study biophysics in France with René Wurmser and Alfred Fessard. Soon after, he visited Archibald Hill and Edgar Adrian. At his return to Brazil, he set up his own laboratory of biophysics at the University of Brazil, in Rio de Janeiro, which became a world famous Institute of Biophysics after 1945. As a model, Chagas chose for his first research the electric eel of the Amazonian fauna, *Electrophorus electricus* to perform studies close to those of Auger and Fessard (1928-1940s). In 1939, Auger, Fessard and Chagas made contributions to the electrogenesis in electric fish at a meeting dedicated to Alvaro and Miguel Osorio de Almeida. In 1946, Chagas defended his thesis in Paris on the same subject. Chagas' early career shows Fessard not only collaborated with famous colleagues in Britain (Adrian), from different disciplines (Nachmansohn and Feldberg), but also with foreign scientists in search of scientific advice. Soon after, Chagas proposed Fessard's wife, Denise Albe-Fessard to join him during summers to Rio de Janeiro to pursue their work on electric fishes. Albe-Fessard was an engineer converted to physiology by Fessard and Auger. The close collaboration with Chagas led Albe-Fessard to defend her thesis in 1950 on the electrogenesis of both electric eel and torpedo and to numerous joint publications (Albe-Fessard et al., 1951). Also, Fessard, Albe-Fessard and Chagas organised seven scientific trips to Brazil on electric fishes, one in

French Guyana and three in Equatorial Africa. Chagas and Albe-Fessard also published several high quality studies both together and independently until the 1960's.

Fessard's work on electric fishes with Feldberg, Nachmansohn, Chagas and his wife are exemplary cases of scientific collaborations in the 1940's and 1950's. The Fessard's also worked with Antonio Moreira Couceiro, His Martins-Ferreira from Chagas' laboratory and Thomas Szabo, a Hungarian anatomist who joined the Marey Institute in the early 1950s. This intense collaboration made Fessard and Chagas among the leading electric fish physiologists, on a highly selective topic, in competition with the groups of Feldberg, Nachmansohn and Grundfest.

Fessard's career can be examined in parallel to that of Alexandre Monnier, the successor of Louis Lapicque at the Sorbonne. Fessard and Monnier both visited Great-Britain and the United-States. Monnier worked with Joseph Gasser and was a close friend of Herbert Jasper, an early electroencephalographer. Monnier became a distinguished biophysicist. However, although he established many scientific friendships abroad, his work dealt exclusively with excitable membrane physiology. He organized famous lectures at the Sorbonne, inviting speakers to famous restaurants, but never was engaged in serious scientific collaboration. His teaching in neurophysiology at the Sorbonne was a mirror of this personal attitude centred on old Lapicquian concepts. In this view, can we further understand how Fessard's conceptions of international scientific relations contributed to the rise of French neurophysiology.

A second technical revolution occurred in 1952, when John Eccles (Nobel prize in physiology or medicine, 1963) made his first intracellular recordings of single neurones from the cat's spinal cord in Canberra, Australia (see Barbara, 2006). Unsurprisingly, Fessard's and Chagas' laboratory were among the first to adopt the new technique with the experiments of Ladislav Tauc, a Czech plant physiologist, Albe-Fessard and Buser from Fessard's laboratory and Richard Keynes, a collaborator of Alan Hodgkin visiting Chagas' laboratory. Once again, the new technique favoured collaborations between scientists. Tauc learned the technique he adapted on plant and muscle cells. Albe-Fessard asked Pierre Buser, a young graduate student of Fessard, to help her record from torpedo fish and the cortex of the cat. All these works led to an international meeting on the microphysiology of excitable elements in Gif, near Paris (1955), where most world famous neurophysiologist were invited (Tasaki, Eccles, Fatt, Hodgkin, Matthews, Amassian, Morruzi, Jung and Baumgarten, Lundberg). Fessard viewed the meeting as a means to develop scientific interactions. He wrote in the introduction to the proceedings: "[...] participants to the colloquium prolonged free discussions in small groups which greatly contributed to the success and usefulness of the meeting."

The base of Fessard's school was established. In all, Fessard had published more than fifty articles, his Ph.D., and a few reviews on nerve excitability, action potentials and auto-rhythmic activities, mostly in the thirties, and mainly with D. Auger and A. Arvanitaki. In the same period, he published thirty studies of psychophysics on sensory and motor functions with G. Durup, H. Laugier, or J. Paillard (Ph.D.), associated with fifty articles on biometry and human biotypology. Ten studies, and an important review (Fessard and Posternak, 1950) were devoted to synaptic transmission. Fessard's studies on electric fishes (26) led to important international collaborations and to the Ph.D. of D. Albe-Fessard and T. Szabo. Fifteen publications (1935-1959) dealt with cerebral micro- and macrophysiology (Ph.D. of P. Buser). More than ten articles and reviews concerned biophysics, and twenty books, book chapters or reviews were devoted to general questions or theoretical essays. For example, Fessard focussed on theoretical aspects of neuroscience regarding consciousness in a pre-cognitive perspective (Fessard, 1954; Barbara, 2008; Romand, 2008).

Most of his students had collaborations abroad and had international recognition. Albe-Fessard pursued her work with Chagas. Buser visited Moruzzi's and Magoun's laboratory. Ladislav Tauc invited Hersch Gerschenfeld from Argentina, and then Eric Kandel (Nobel prize, 2000) to join him. The success of all these collaborations relied on the adoption of new techniques, a common evolving framework, including a theoretical background and novel experimental norms. But most of

all, collaborating required personal skills, strong friendships between scientists and the acceptance of criticisms from distinguished elder personalities.

In the 1950s, the need for international collaboration required to create an international organisation oriented exclusively towards brain research. With Russian scientists and officials, Henri Gastaut from Marseilles organised an international meeting in the House of Scientists in Moscow on October 6-11, 1958. Gastaut and Fessard presented the final resolutions of the Moscow colloquium, in particular related to the creation of an international organisation. Fessard and Herbert Jasper were to write them and they were favourably accepted by UNESCO. Initially, Gastaut wished the foundation of a committee for the study of cerebral mechanisms in the framework of the federation of societies⁴. However, Fessard insisted on the necessity to think IBRO in a broader context in affiliation with UNESCO and the CIOMS. Fessard had been involved with Laugier in previous non successful attempts to create an international structures devoted to Brain research. He thought the goals of IBRO should be to fund “fellowships for exchange of individual workers”, “temporary working teams”, missions, conferences, particular in the field of fundamental science, including all aspect of brain researches (anatomy, neurophysiology, ...). The period of the creation of IBRO was pivotal for international neurophysiology, where France was at the heart of the revival of East-West scientific exchanges.

We conclude that the career of Alfred Fessard is an interesting case with international collaborations being central to the making of a high quality French community devoted to neurophysiology after 1945 in the international context. An open minded view of international research led to joining foreign laboratories and inviting scientists to France. This shows how scientists progressively took advantage of the diversity of local schools during a period of intense globalization of science, both in its technological and theoretical aspects. The fact that Monnier’s school at the Sorbonne is never mentioned today and the success of Fessard’s school both show how international relations were vital to the creation of XXth c. science as an international network.

⁴ He clearly formulated his idea at the first session of IBRO in Paris at the *Maison de l’UNESCO*, 4-7 October, 1960. IBRO first session. NS/IBRO/2, WS/0161.55.

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