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The Fessard's School of Physiology after war in France: globalization and diversity in neurophysiological research on Torpedo fish (1938-1955)

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A research program directed by Claude Debru is devoted to the history of French neuroscience after Second World War, in the international context. The work in progress involves interviews, meetings with elder scientists and study cases of main Institutes. The main purpose of the program is to understand the birth after 1945 of French neurophysiology from various local schools, in relation with one another, in an increasingly global and international scientific network. From these analyses, it is envisaged to demonstrate not only the role of international relations in the evolution of neurophysiology in France, but also the importance of French schools in the making of an international science devoted to the nervous system. Several questions arise. Was there a key event in the re-birth of neurophysiology at the end of the 1930's which contributed to the scientific context from which post-war neurophysiology emerged? What was the role of technological transfers? In what context did international relations become increasingly numerous? How new techniques and scientific collaborations shaped science at a local scale, taking advantage of diversity from local schools? These questions will be asked in a case study: the research on the electric fish torpedo in Fessard's school of neurophysiology.

After war, major French figures in neurophysiology emerged from different traditions in Toulouse, Lyon Montpellier, Marseilles, but

most of all from Paris. Alfred Fessard (1900-1982) is recognized today as the most talented neurophysiologist in the 1940's and 1950's in France. He was able to create since 1947 his own school in the former Marey Institute. Many of his students were among the most renown 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 world famous physiologist Etienne Jules Marey (1830-1904) was 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 Marey Institute was built near the Physiological Station Marey had planned for studies on movement. 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.

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, were the only 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 organ, 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 progressively built his concepts from intensity-duration strength curves similar to that of French biophysicist Georges Weiss. However, Lapicque's work was performed in the context of German physiology, and in close contact with British and American physiologists (Dale, Hill, Fulton, Gasser). In the 1930s, after Rushton challenged Lapicque at the Fourteenth Congress of Physiology (1933), the journal of Physiology invited him to publish his own results on the action of curare. When the controversy raged, the famous biophysicist Archibald Hill invited Lapicque to cross the channel to discuss their views on Rushton's results (1937). Both men did not come to any agreement and Lapicque became progressively isolated. The way Lapicque envisaged international relations involved friendly meetings and scientific discussions (Mrs Lapicque was famous for her French style cuisine). However, Lapicque developed his research and ideas alone and made very little concessions to others.

Fessard's career in neurophysiology was started during this period (1930's), when French neurophysiology was radically opposed to the Cambridge school. However, Lapicque and his students were highly impressed by early studies from Joseph Gasser's group on nerve fibre conduction. On a trip to Europe, Gasser had most enjoyed his visit to Lapicque's laboratory, where he discussed the role of fibre diameters on rates of conduction, which led to a joint paper by Gasser and Lapicque in 1925. Fessard took advantage of this context and adopted oscillography as a new tool. Fessard was nevertheless an open minded scientist, 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 Henri Piéron's laboratory at the Collège de France, he studied muscle fatigue with electromyography. Besides these studies, Fessard also collaborated from 1925 to the 1940's with the plant physiologist Daniel Auger on oscillographic recordings of action potentials in the lines of the American plant physiologist and biophysicist Winthrop Osterhout. It appears that during the

1930's and 1940's, Fessard was able to follow the oscillographic revolution in the context of Lapicque's dogmas. However, from the very beginning of his career, Fessard always collaborated with others, taking advantage of new tools and new approaches. Although his first papers using oscillography were officially aimed at confirming Lapicque's views, 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. Thus the oscillographic revolution was a major factor bridging together French, British and American physiology. In particular, Fessard's research on torpedo led him to adopt the style of Edgar Adrian's research.

Does the choice of torpedo fish as a model contributed to collaboration with foreign scientists? What is the history of this animal model in XXth c. neurophysiology? 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 elder XIXth c. scientists, including du Bois-Reymond. It offered a natural source of animal negativity which could be easily recorded with galvanometers. Torpedo entered Lapicque's physiology with studies by the Chauchards in 1925 and 1926. Their results confirmed Lapicque's ideas on excitability and the action of curare. Fessard and Auger followed the same general purpose, when they confirmed in torpedo Lapicque's concept of isochronism. However, it must be emphasized that their approach was already influenced by Edgar Adrian. Their oscillographic measurements (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 synchronisation of individual motor nerve impulses to the electric organ. 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 isolated brain stem of the Goldfish.

Fessard's research was progressively being influenced by Adrian. When Fessard obtained in 1938 a grant from the Rockefeller foundation to travel to England, Fessard met Adrian and worked with his collaborator Brian Matthews. 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 Archibald 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 thanks to the help of Henri Piéron from the Collège de France and funds from the Rockefeller foundation. 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 France (1939). Fessard invited David Nachmansohn and Wilhelm Feldberg, two German Jewish scientists established respectively in Dale's Laboratory in London 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 the 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 marine d'Arcachon. Biological stations including Arcachon always facilitated meetings and collaborations between scientists. In 1937, Lapique and Hill had met at Plymouth Marine Biological station, 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 neurotransmission in 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 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 in 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 colleagues, 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.

In the same years (1938-1947), Fessard was collaborating on electric fish not only in Europe, but also with Brazil. 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*. He worked in the line of studies by 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 his work on electric fish. Albe-Fessard was an engineer converted to physiology by Fessard and Auger. The close collaboration with Chagas allowed Albe-Fessard to defend her thesis in 1950 on electrogenesis of both Electric eel and torpedo. This led to numerous joint publications. However, both Chagas and Albe-Fessard also published several high quality studies independently and their collaboration was pursued until the 1960's.

Fessard's work on electric fish 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, an 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. The 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 made his first intracellular recordings of single neurones from the Cat's spinal

chord. Unsurprisingly, Fessard's and Chagas' laboratory were among the first to adopt the new technique with the work of Ladislav Tauc, a Czech plant physiologist 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 had adopted on plant and muscle cells to Albe-Fessard. She then asked Pierre Buser, a young undergraduate student of Fessard, to help her record from torpedo fish and Cat's cortex. This work led to an international meeting on microphysiology of excitable elements in Gif sur Yvette, near Paris (1955), where most world famous neurophysiologists 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. 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, then Eric Kandel 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 experimental norms to interpret data. But most of all, collaborating required personal skills such as strong friendships between scientists and the acceptance of criticisms from distinguished personalities.

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. 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.