Ranvier, Louis

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Louis Ranvier (1835-1922)

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The contribution of microscopy to physiology and the renewal of French Anatomie Générale

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Louis Antoine Ranvier was born in Lyons (1835), in a family devoted to politics and public affairs, including hospital administration. He naturally took up medical studies at the Ecole Préparatoire de Médecine et de Pharmacie in Lyons, which soon led him to Paris (1860), after he succeeded in the highly competitive examination for the internship of Parisian hospitals. During his medical training, Ranvier became acquainted with normal and pathological anatomy, and soon turned to microscopy as a means for further studies on tissues. This attitude was not popular among French scholars, after Bichat had inspired Henri Ducrotay de Blainville (1777-1850) and Auguste Comte (1798-1857) in their attacks over microscopy (see Canguilhem, 1952, pp. 63-64; Bichat, 1799, p. 35). However, the French context of medical microscopy was changing. Since the early 1830s, physicians trained in Paris, including Alfred Donné (1801-1878), Hermann Lebert (1813-1878), David Gruby (1810-1898), Louis Mandl (1812-1881), and later Charles-Philippe Robin (1821-1885), Paul Broca (1824-1880), Eugène-François Follin (1823-1867) and Aristide Verneuil (1823-1895) devoted some of their research and teaching to microscopical studies (La Berge, 2004). Donné and Robin had published memoirs and microscopy manuals, some of them addressed to students, which may have influenced Ranvier (Foucault & Donné, 1844-1845; Robin, 1849, 1854, 1856). Nevertheless, Ranvier was probably more influenced by German studies, including the French translations he would later quote (Kölliker, 1856; Virchow, 1858; see Jolly, 1922, p. 10, Jolly, 1932, p. 213).

Figure 1: Louis Ranvier (1835-1922) (Courtesy of Collège de France)

Between 1860 and 1865, Cornil and Ranvier devoted part of their time to microscopy. Besides observing tumors and other pathological tissues, Ranvier focused on bone preparations, which led him to study cartilage and bone lesions for his medical thesis (Ranvier, 1865). By 1865, they had started collaborating on epithelial tumors. They developed a small private laboratory on rue Christine in Paris, which soon attracted young interns, among whom were Malassez, Joseph-Louis Renaut, Georges Maurice Debove (1845-1920), and Jacques-Joseph Grancher (1843-1907). From 1866 to 1867, Cornil and Ranvier's one-semester course in microscopy had no equivalent in France (Jolly, 1922). It ended when Ranvier agreed to join Claude Bernard at the Collège de France. This course was published in three parts, as an authoritative manual, two years later (Cornil & Ranvier, 1869). It was translated into English, with notes and additions both in England and the United-States (Cornil & Ranvier, 1880; 1882). It represented a well-written and useful modern textbook for medical students interested in normal and pathological histology. In the early 1870s, microscopical studies had gained academic recognition at the Faculté de Médecine de Paris. A chair of histology had been created in 1862 for Robin. However, according to Broca, the vast majority of French medical micrographers remained opposed to cell theory. They did not accept the concept of the cell, but rather recognized the "specificity of diverse cells", meaning that different histological entities should replace the German unitary concept (La Berge, 2004, p. 438; Canguilhem, 1952, pp. 66-67).

Ranvier was influenced by Virchow's extension of cellular theory to pathology. In Ranvier's introductions to studies on cartilage and bone, Virchow's observations are emphasized (Cornil & Ranvier, 1869, pp. 19-29; Ranvier, 1863). While Cornil further investigated pathological tissues, Ranvier focused on normal histology. He was not only concerned with cell theory, but also, as a student of Bernard, with development, nutrition and functions of normal tissues.

Ranvier learnt from Bernard how histology could serve physiology. He followed Bernard's lectures at the Collège de France: Leçons sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme (Bernard, 1859), and Leçons sur les propriétés des tissus vivants (Bernard, 1866), both being relevant to microscopy. In the 1860s, French experimental physiology encouraged histologists to localize the function of organs at the level of tissues and cells. This physiological approach contrasted with the static descriptive histology of Robin, which refused generalization and theorizing, as practiced in German schools (see Jolly, 1922, p. 12). Ranvier was to fill in this gap between Bichat and Bernard, by adopting what Bernard would later call experimental histology.

The Collège de France and the Ecole Pratique des Hautes Etudes were necessary institutions for the development of such original programs. Both French institutions functioned as a balance to the Faculties by favouring marginal researchers such as Ranvier. They played a dominant role in France in accepting cell theory, and fulfilled their mission in teaching new scientific ideas, while Faculties tended to teach established facts (see Bernard, 1877, pp. 23-26, p. 215). Thanks to Bernard, Ranvier settled into a small histological laboratory, founded in the Ecole Pratique des Hautes Etudes, and later established in Ranvier's lodgings at the Collège de France (1867), where many of his colleagues followed his research.

Ranvier's first studies are often regarded as a synthesis between histology and physiology, since both were relevant to defining functions of organs (see Jolly, 1922; Jolly, 1932; Appel, 1978). However, Bernard's and Ranvier's conceptions of function differed on the role of generalized anatomical observations used as norms in the determination of function.

The French epistemologist Georges Canguilhem (1904-1995) has analyzed some of the reasons why Bernard accepted cell theory. He emphasized how it justified experimental physiology, providing Bernard with a new organization of living organisms and escaping both materialism and vitalism (Canguilhem, 1994a). Bernard's theory defined parts both as independent units and by their relations to the organism, with function localized into histological elements (Bernard, 1877, p. 135). For Bernard, function could be revealed by experimental physiology, whereas histology was only concerned with localization. He discounted anatomical deductions of function, believing that cells of similar appearance could have radically different functions. Conversely, cells with different morphologies and sizes might have similar functions, a view supported by Ranvier, in his work on small and large spinal cord neurons (Ranvier, 1875a, p. 1061).

Nevertheless, Ranvier developed an apparently opposed and radical view based on his faith in assigning functions to particular cell types by histological criteria. In Bernard's view (1872), such criteria were to be established by physiology, since anatomy alone could not directly derive function. Nevertheless, Ranvier was to prove functions could be proposed by experimental histology.

Ranvier further extended this conception to tissues and cellular elements (Ranvier, 1872a, p. 443). For him, experimental histology was a way to study cellular physiology. Ranvier's studies on nerves showed he was able to follow this path and accordingly his biographer Justin Jolly (1870-1953) later defined Ranvier as a physiologist (Jolly, 1922; Jolly, 1932).

For Bernard, nutrition was a general cellular function to be studied by the methods of experimental physiology (Bernard, 1877, p. 85). The concept of nutrition was adopted in Ranvier's work after 1869 (Ranvier, 1869a; 1969b). His description of nerve fibre nodes was made in a search for how nutrients were continuously exchanged with the blood for nerve cell function (Ranvier, 1871a, p. 1168). Physiology had demonstrated a loss of motor nerve function by interruption of blood flow and a return to function by perfusion of oxygenated blood. An acidic reaction and a rise in temperature, noticed by Ugo Schiff (1834-1915), suggested nerve fibers might be a locus for oxygen consumption (Ranvier, 1871a, pp. 1168-1169). The question was then clear to Ranvier: what is the path for oxygen between oxygenated blood and nerve fibers? For Ranvier, the continuous and impermeable myelin sheath of nerve fibres prevented exchange of fluids and thereby nutrition. He demonstrated the point histologically showing that soluble carmine could not penetrate isolated myelinated nerve fibers (Ranvier, 1871b, p. 131). However, Ranvier showed picrocarminate could penetrate fibres, at localized sites identified as interruptions of the myelin sheath, and later marked with silver nitrate (Ranvier, 1871a, pp. 1169-1170; Ranvier, 1871b, p. 133). Ranvier had discovered what was soon called the "nœuds de Ranvier". Nodes discovered in the context of Bernard's ideas on nutrition were localized subcellular elements, Ranvier suggested they were involved in the physiological exchange of nutrients between fibers and blood. Although the function of nodes remained an open question for decades, Ranvier demonstrated experimental histology could propose hypothetical physiological functions at the level of cells and cell parts.

With the aim of correlating histological observations to physiology, Ranvier favoured studies examining the loss of nervous function induced by nerve lesions (Ranvier, 1872a). According to Ranvier, nerves were surrounded by perifascicular conjunctive tissue and contained intrafascicular conjunctive tissue. For both, function was defined in the context of nutrition. While the first supported blood and lymphatic vessels delivering nutrients, the second was an elastic protection against mechanical forces and a chemical barrier permitting access to nutrients by a colloid path (Ranvier, 1871a, p. 1171; Ranvier, 1872a, p. 443). When this latter was destroyed by lesion, Ranvier observed the effect of introducing water in the wound of a living animal. Nodes disappeared and the myelin sheath was swollen at their former sites (Ranvier, 1872a, p. 444). The effect of water therefore paralleled the loss of nerve function, and later paralysis of the nerve itself. Ranvier inferred nodes of nerve fibers were necessary for nervous conduction.

This approach was replicated in studies on nerve degeneration, where Ranvier precisely defined histological norms for nerve fiber nodes (Ranvier, 1872b). Ranvier observed a single Schwann cell with a single nucleus was located between each two successive nodes. Thus, he recognized as a norm the cellular nature of interannular segments. This led him to the first precise account of nerve degeneration, where morphological changes were noticed in Schwann cells of injured fibres, while newly formed fibres were normal (Tello, 1877-1887, Part I, p. 102). The disappearance of nodes in pathological conditions or the multiplication of nuclei in Schwann cells were deviations from a norm, which caused nerve fiber malfunction. Hence, Ranvier's work showed how histological norms, derived from minute anatomical details, could help understand loss of function in response to pathological lesions.

Ranvier's research on nerve degeneration was made in the Bernardian perspective of nervous elements, seen as regulators of the activity of tissues. Sectioning nerves was believed to relieve negative nervous regulations of all sorts, including regulation of growth and development, thereby inducing morphological changes in surrounding tissues. Multiplication of nuclei in Schwann cells of injured fibers was interpreted in this way, as a loss of control in cell division. Cell theory was also important in recognizing newly formed fibers originating from cellular and central parts of cut fibers. Thus, Ranvier's new histological techniques allowed observations in agreement with his heuristic theoretical background.

As a general goal, as seen in his studies on the effect of water on nerve sections, Ranvier searched for histological explanations of physiological observations. In this perspective, he adopted a mechanistic approach to explain the loss of function of degenerated fibers. Three days after section of a nerve, loss of function was correlated with multiplication of nuclei and swelling of Schwann cells. Ranvier concluded that swelling of protoplasm exerted pressure on nerve fibers, thereby preventing conduction. Nevertheless, Ranvier's approach and interpretations were sometimes contradicted. Joseph Jules Déjerine (1849-1917), and later Ramón y Cajal contradicted Ranvier, demonstrating protoplasm invaded gaps initially formed by myelin sheath fragmentation prior to any mechanical constraint (Barbara, 2005; Ramón y Cajal, 1913, p. 70). Furthermore, his mechanical theory of nerve fiber growth along a line of least resistance was similarly refuted in 1900 (See Ramón y Cajal, 1913, p. 70). However, both Ramón y Cajal and his pupil Jorge Francisco Tello Muñoz (1880-1958) were indebted to Ranvier for his remarkably precise observations. Ranvier was first to recognize fatty accumulations along Schwann cells as migrating leucocytes, which he had observed in experimental lesions of conjunctive tissue (Ranvier, 1971c, p. 124). Ranvier gave the first account of the exaggeration of node striation in living central fibers (Ramón y Cajal, 1913, p. 138). Spiral structures were described as aberrant new structures (Ramón y Cajal, 1913, p. 159).

The successes of Ranvier were intimately linked to the perfection of his techniques, including precise manipulations, careful dissociations by hand, and special uses of acids and stains (see Ranvier, 1872b, for technical details). Ranvier's use of silver nitrate reduction by light to observe nodes revealed new details of nerve fibers and surrounding cells (Ranvier, 1871a, p. 1169).

According to DeFelipe and Jones, the improvement of that same technique by Ramón y Cajal in 1903 was crucial in his last confrontation with reticularism (DeFelipe & Jones, 1991, p. 6). Although Ranvier did not become involved in the controversy over neurone doctrine, Ramón y Cajal considered him an early monogenist, together with His and Forel.

Ranvier's general aim was to recognize the cellular nature of specialized histological elements. In this perspective, he studied both bone corpuscles and cellular elements of conjunctive tissues (1869), where "plasmatic channels" for nutrition were described (Ranvier, 1869a). This study was published as a full article in the *Quarterly Journal of Microscopical Science*, the first journal entirely devoted to microscopy (Ranvier, 1869b; Ranvier, 1870).

During the early 1870s, Ranvier had the opportunity to work on ray and torpedo in the marine laboratory of Victor Coste (1807-1873) in Concarneau. In a note of anatomie comparée, he described nodes and sheaths in the motor nerve of the torpedo's electric organ (Ranvier, 1872c). In 1875, observations on torpedo motor nerve endings were communicated by Bernard to the Académie des Sciences as being relevant to anatomie générale. This shift from comparative to general anatomy occurred in parallel with Ranvier's appointment by Bernard in 1875 to a chair of anatomie générale at the Collège de France.

Although Ranvier wrote further notes on histology and physiology, most of his subsequent papers concerned anatomie générale, previously illustrated by authors such as Robin and Virchow in the Comtes Rendus Hebdomadaires de l'Académie des Sciences. This turn to general anatomy was based on elegant and refined studies on the anatomical independence of nerve fiber terminals as a general refutation of fibre nets. In the notes he added to his translation of the *Handbuch der Histologie und Histochemie des Menschen* by Heinrich Frey (1822-1890), Ranvier described his first studies on nerve endings in salivary gland, cornea and skin (Frey 1859; Frey 1871). Together with most histologists, he had been impressed by the gold chloride staining technique of Julius Cohnheim (1839-1884), which allowed unequivocal demonstrations of free nerve endings in cornea and skin (Frey, 1871, pp. 717, 735). However, Ranvier first preferred his chromic acid technique (Frey, 1871, p. 711). Only, when he succeeded in Concarneau to combine Cohnheim's technique with chromic acid, was he able to refute fibre nets in the electric organ of torpedo, previously described by Rudolf Albert von Kölliker (1817-1905), Max Schultze (1825-1874) and Franz Christian Boll (1849-1879) (Ranvier, 1875b). Ranvier's success in this field was based not only on his use of refined staining procedures, but also on new immersion objectives, such as number 12 of Hartnack and Prazmowski, which allowed a magnification of x1000 (see Ranvier, 1875a, p. 789). Furthermore, the technique of Joseph von Gerlach (1820-1896) enabled Ranvier to visualize branching fibers, prior to endings, similar to a chiasma.

Ranvier's move to general anatomy was possible after he could reproduce his general observations on nerve fiber terminals in various structures. Following Franz von Leydig (1821-1908) and Friedrich Sigmund Merkel (1845-1919), he made a precise study of Grandy's tactile end organs of the papillæ of the beak and tongue of the duck (Ranvier, 1877). Ranvier described a disk-like nerve ending similar to Merkel's tactile disk, occurring in the epidermis of the pig's snout. The generalization of these finding to tactile end organs of skin, cornea and smooth muscle, was published as Leçons d'Anatomie Générale (Ranvier, 1878a; Ranvier, 1880a; Ranvier, 1881). Similarly, Ranvier demonstrated free nerve endings in his studies on smooth muscle. However, Ranvier's conception of nerve plexi was far more complex. The existence of free endings was not for Ranvier a radical argument against fiber nets, which according to him did occur in some preparations before nerve fibers ended. Ranvier's careful examination of plexi required an improvement of Cohnheim's and Löwit's techniques, replacing formic acid with lemon juice. Ranvier's method was published as a novel contribution to the Quarterly Journal of Microscopical Science (Ranvier, 1880b). Plexi were demonstrated as small peripheral nerve centers in particular tissues. They were suggested to mediate non-voluntary movements, as in the mammalian esophagus and arthropod's digestive tract (Ranvier, 1878a, p1144; Ranvier, 1879, p. 1088). Thus, Ranvier was also concerned with the functional significance of plexi, which he felt represented terminal arborizations of single fibers.

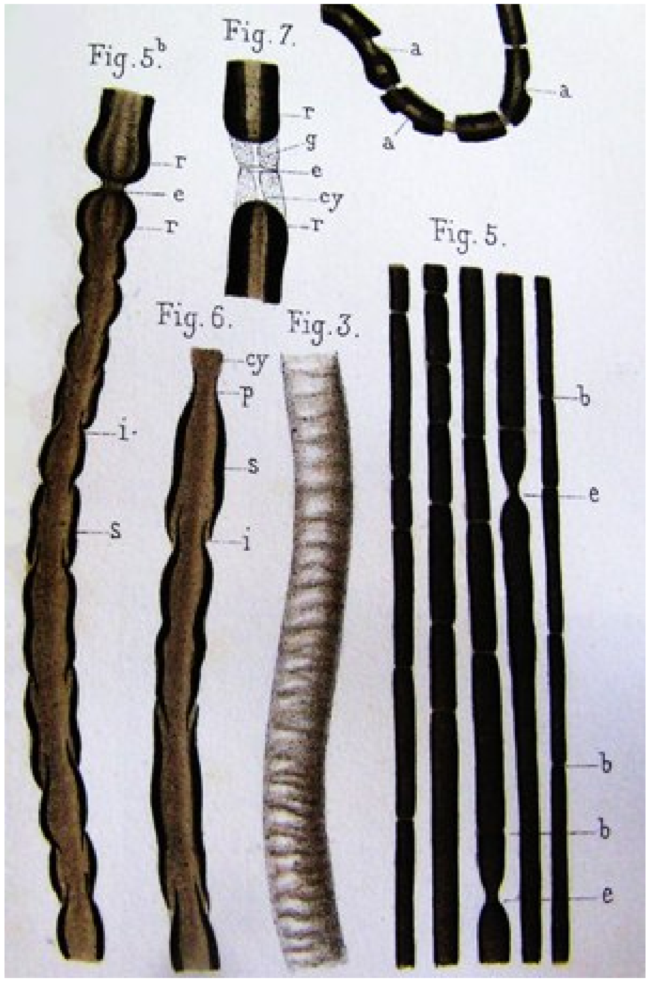

Figure 2: Sciatic nerve tubes fixed in osmic acid (1%) when physiologically extended. Dissociation was made in water. A whole sciatic nerve is shown as seen with a magnifying glass (fig. 3). Other figures show nerve tubes observed through a microscope, a, neck when "Schwann's membrane" is removed, b, incision provoked by myelin retraction, cy, "axis cylinder" (flowing out in fig. 6), e, "étranglement annulaire", "annular constriction" or "node of Ranvier", g, granular mass, p, thinning of "cylindroconical segment" on axis cylinder's surface, r, terminal nerve tube bulge (bulges are extended in fig. 7), s, "cylindroconical segment". Reprinted from Ranvier (1878b, Plate I, volume 1).

Using this approach, Ranvier came to a major discovery, while examining another minute nervous structure. Observations made from 1870 to 1875 in studies of different ganglia, with the aim to find a common internal structure, led to the discovery of the T structure of nerve fibers from sensory ganglion cells (Ranvier, 1875c). He concluded that nervous conduction in sensory and motor neurons should not be seen as linear chains. Although Ranvier could not ascribe a direction to the circulation of nervous impulses in T structures, he suspected complex fiber branching might occur in nerve centers and modify current views on their physiology.

These studies portray Ranvier as a rather pragmatic scientist, more concerned with facts and precise descriptions of histological elements with refined techniques, than with new ideas on the nervous system. While some of his observations were relevant to the polemic on the neuron doctrine, Ranvier did not participate in the polemic, but rather founded French general anatomy as a joint anatomical and histological discipline.

While he gained limited international recognition, Ranvier should be remembered for three major achievements. Certainly, he lives on as the discoverer of the "nœuds de Ranvier". His and Arthur Van Gehuchten (1861-1914) paid tribute to Ranvier's first observation of T structures of fibers from dorsal root ganglion cells (see Shephered, 1991, p. 108; Van Gehuchten, 1897, p. 210). Ranvier was honored by Ramón y Cajal for his precise description of nerve fiber degeneration and regeneration (see Ramón y Cajal, 1913). Besides, he was also respected for his talented teaching on histological techniques (see Fernandez and Breathnach, 2001; Ranvier, 1875a). In particular, Ramón y Cajal paid tribute to Ranvier's manual, referred to as his "technical bible of those days [1887]" (Ramón y Cajal, 1917, p. 307). When speaking of the preparation for his competitive exams in 1879 he wrote:

"Conscious of my defects, I had endeavoured to overcome them so far as possible. I perfected myself in histological technique, using as a guide the admirable book entitled Manuel technique d'histologie, written by Ranvier, the illustrious professor at the Collège de France [...]" (Ramón y Cajal, 1917, p. 255).

In contrast to his teaching manuals, which were widely translated, Ranvier's research was little known and quoted in the specialized international literature. Ranvier's nodes and T structures were generally described as anatomical details, without mention of his observations. Similarly, his studies on nerve fibre degeneration and regeneration were only properly recognized many years later (Ramón y Cajal, 1913). The functional significance of both observations was not fully appreciated at the time of Ranvier's work. Today, Ranvier's nodes and the study of axon regeneration are two fascinating and active fields of inquiry (Ishibashi et al., 2003; Sherman & Brophy, 2005; Clark et al., 2005).

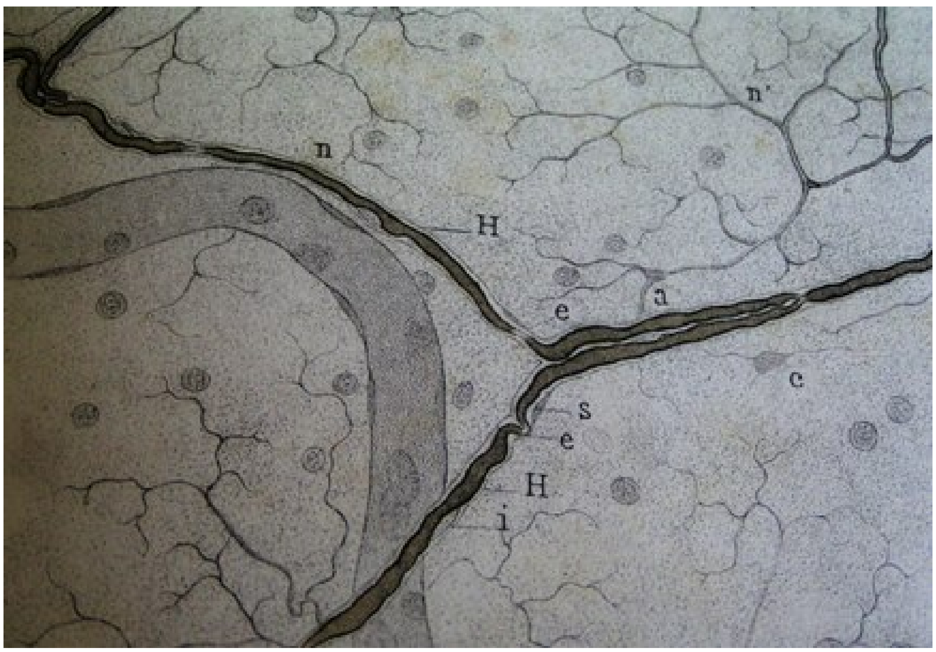

Figure 3: Ventral side of electric organ of torpedo after injection of osmic acid (2%) and maceration for 24 hours. A blood capillary is shown with red and white blood cells, a, recurrent ramifications from a myelin nerve tube, c, "stellate cell" of "muquous tissue" between "electrical lamellae", e, "annular constriction" or "node of Ranvier", H, secondary sheath, i, nucleus of "interannular segment", n, nerve tube with myelin, n', second order nerve fibers with no myelin, s, nucleus of secondary sheath. Reprinted from Ranvier (1878b, Plate IV, volume 2).

Another reason for the relative obscurity of Ranvier's research was that it was published in French journals, and never as translated treatises. His published lessons, primarily devoted to students, were also little read and quoted by experts. Although, Ranvier was known as an eminent professor in histological techniques, his rough personality and the tedious nature of his lectures did not encourage foreign medical students. However, Luis Simaro Lacabra (1851-1921) attended Ranvier's lessons, where he learnt Golgi's method, which he later demonstrated to Ramón y Cajal in Madrid (Fernandez and Breathnach, 2001). Thus, Ranvier's influence was rather limited to a small circle of French histologists, to colleagues at the Salpêtrière hospital (Barbara, 2005), and to foreign students and colleagues praising his techniques, on which Ramón y Cajal commented:

"In my systematic explorations through the realms of microscopic anatomy [...] I examined [the

Nervous System] eagerly in various animals, guided by the books of Meynert, Huguenin, Luys, Schwalbe, and above all the incomparable works of Ranvier, of whose ingenious technique I made use with conscientious determination" (Ramón y Cajal, 1917, p. 304).

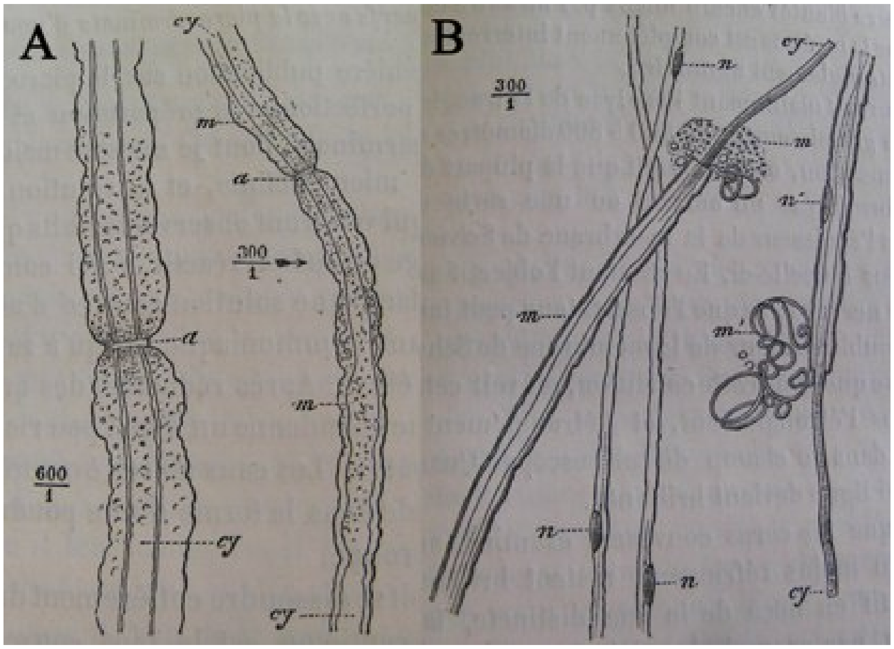

Figure 4: Large sciatic nerve tube dissociated in picrocarminate ammonium (1%). Tubes were drawn after 1 hour incubation. A, Axis cylinder is stained in red near annular constriction, indicating picrocarminate penetrates the nerve tube at this level. Staining is illustrated by dots, x 600 magnification. B, Axis cylinder and myelin flow outside the sheath. Red picrocarminate staining is indicated by hatched lines. Picrocarminate stains the extruded axis cylinder and invades the inner portion of the nerve tube, showing myelin is impermeable to picrocarminate, a, "annular constriction" or "node of Ranvier", cy, "axis cylinder" stained, m, myelin, n, nucleus of "interannular segment". Adapted from Figures 1 and 2 from Ranvier (1872a).

Ranvier's approach has often been neglected by some neuroscience historians, perhaps due to his physiological research style he followed in the 1870s and the 1880s. Ranvier was scarcely involved in the history of the neurone doctrine, since he simply defined a nerve cell as a cell body with continuous contacts with nerve fibers and neglected Golgi's method for its unreliability (Ranvier, 1875a, p. 1062). While he certainly recognized the beauty of silver chromate deposits, he felt the technique could not reliably demonstrate relations between nerve cell processes and nerve fibers (Ranvier, 1875a, p. 1097). In retrospect, a convincing demonstration of contiguity between neurons did not emerge before the advent of electron microscopy. In these respects, Ranvier was a typical French figure, in the line of Magendie and Bernard, more concerned to rectify outdated theories and ideas and to construct histology as a new discipline on a solid base of unquestionable facts, derived by a rigorous experimental approach.

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Bibliography

Appel TA (1978): Louis Ranvier. In: Gillispie CC, ed., *Dictionary of Scientific Biography*. New York, Scribner's Sons.

Barbara JG (2004): Les étranglements annulaires de Louis Ranvier (1871). *Lettre des Neurosciences* 28: 3-4.

Barbara JG (2005): Louis Antoine Ranvier (1835-1922). *Journal of Neurology* (in press).

Béclard PA (1827): *Elémens d'anatomie générale ou description de tous les genres d'organes qui composent le corps humain*. Paris, Béchet jeune.

Bernard C (1858): *Leçons sur la physiologie et la pathologie du système nerveux*. Tome I. Paris, Baillière.

Bernard C (1859*): Leçons sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme*. Paris, Baillière.

Bernard C (1866): *Leçons sur les propriétés des tissus vivants*. Paris, Cours de médecine du Collège de France.

Bernard C (1872): De la physiologie générale. In: *La science expérimentale*. Paris, Baillière.

Bernard C (1877): *Principes de médecine expérimentale*. Paris, PUF.

Bichat X (1799): *Traité des membranes*. Paris, Richard, Caillé et Ravier.

Bichat X (1801): *Anatomie générale appliquée à la physiologie et à la médecine*. Paris, Brosson, Gabon.

Bouchet A (1982): Histoire de l'anatomie à Lyon. In: Ollier L, ed., *Conférences d'histoire de la médecine, cycle 1981-1982*. Lyon, Fondation Mérieux.

Canguilhem G (1952): *La Connaissance de la vie*. Paris, Hachette.

Canguilhem G (1994a): *Etudes d'Histoire et de Philosophie des Sciences*. Paris, Vrin.

Canguilhem G (1994b): Claude Bernard et Bichat. In: Canguilhem G, ed., *Etudes d'Histoire et de Philosophie des Sciences*. Paris, Vrin.

Caullery M (1941): Les Sciences biologiques dans la France contemporaine. In: *La France et la civilisation contemporaine. Bibliothèque de Philosophie scientifique*. Paris, Flammarion.

Clark BA, Monsivais P, Branco T, London M, Hausser M (2005): The site of action potential initiation in cerebellar Purkinje neurons. *Nature Neuroscience* 8:137-139.

Cornil V, Ranvier L (1869, 1873, 1876): *Manuel d'histologie pathologique*. Paris, Baillière.

Cornil, V, L Ranvier (1880): *A Manual of Pathological Histology*. Translated and with notes and additions by E O Shakespeare and J Henry C Philadelphia, Henry Lea.

Cornil, V, L Ranvier (1882): *Manual of Pathological Histology*. Translated by A M Hart London, Smith, Elder & Co.

DeFelipe J and Jones EG (1991): *Cajal's Degeneration and Regeneration of the Nervous System*. Oxford, Oxford University Press.

Deiters OFK (1865): *Untersuchungen über Gehirn und Rückenmark des Menschen und der Säugetiere*. Braunschweig, Vieweg.

Duval M (1900): *Précis d'Histologie*. Paris, Masson.

Fernandez N, Breathnach CS (2001): Luis Simarro Lacabra [1851-1921]: from Golgi to Cajal through Simarro, via Ranvier? *Journal of the History of the Neurosciences* 10:19-26.

Flourens P (1858): *De la vie et de l'intelligence*. Paris, Garnier frères.

Foucault L, Donné A (1844-1845): *Cours de microscopie complémentaire des études médicales. Anatomie microscopique et physiologie des fluides de l'économie*. Paris, Baillière.

Frey H (1859): *Handbuch der Histologie und Histochemie des Menschen*. Leipzig, Verlag von Wilhelm Engelmann.

Frey H (1871): *Traité d'histologie et d'histochimie*. Translated from the German third edition by P Spillmann, with notes and one appendix by Ranvier. Paris, Savy.

Ishibashi T, Ikenaka K, Shimizu T, Kagawa T, Baba H (2003): Initiation of sodium channel clustering at the node of Ranvier in the mouse optic nerve. *Neurochemical Research* 28:117-125.

Jolly J (1910): Notice sur la vie et les travaux de Louis Malassez. *Comptes-Rendus de la Société de Biologie* 68: 1-18.

Jolly J (1922): Louis Ranvier (1835-1922): Notice biographique. *Archives d'Anatomie microscopique* 19: 1-72.

Jolly J (1932): Ranvier et la méthode expérimentale. In : Abel Lefranc ed., *Le Collège de France, 1530-1930, livre jubilaire composé à l'occasion de son quatrième centenaire*. Paris, Presses universitaires de France.

Kölliker A (1856): *Éléments d'histologie humaine*. Translated by MM. J. Béclard and M. Sée, revised by the author. Paris, Masson.

La Berge A (1994): Medical microscopy in Paris, 1830-1855. In: La Berge A, Feingold M, eds., *French Medical Culture in the XIXth Century*. Amsterdam, Rodopi.

La Berge A (2004): Debate as Scientific Practice in Nineteenth-Century Paris: The Controversy over the microscope. *Perspectives on Science: Historical, Philosophical, Social* 12: 424-453.

Laguesse E (1902): Revue anuelle d'anatomie générale. *Revue générale des sciences pures et appliquées* 13: 1088-1099.

Landouzy TJ (1871): Lymphadénie cutané. Mycosis fongoïde. *Comptes-Rendus de la Société de Biologie* 23: 184-185.

Michaut P (1899): *Pour devenir médecin*. Paris, Reinwald et Schleicher.

Michel P (1856): Du microscope et de ses applications à l'anatomie pathologique, au diagnostic et au traitement des maladies. *Mémoires de l'Académie de Médecine* 21: 241–442.

Pallulault F (2003): *Medical Students in England and France, 1815-1858. A Comparative Study*. D. Phil, Oxford.

Papillon F (1829): L'Anatomie Générale et les travaux de M. Charles Robin. *Revue des deux mondes* 88: 330-361.

Ramón y Cajal S (1913): *Estudios sobre la Degeneración y Regeneración del Sistema Nervioso. Vol. 1. Degeneración y Regeneración de los Nerviosos. Vol. 2. Degeneración y Regeneración de los Centros Nerviosos*. Madrid, Moya. English translation by May (1928), Oxford, Oxford University

Press, *Degeneration and Regeneration of the Nervous System*. New edition (1991), *Cajal's Degeneration and Regeneration of the Nervous System*, DeFelipe J & Jones EG, eds., *Cajal's Degeneration and Regeneration of the Nervous System*. Oxford, Oxford University Press.

Ramón y Cajal S (1917): *Recuerdos de mi vida, historia de mi labor científica*. Madrid, Moya. English translation by Craigie and Cano (1937), Recollections of My Life. *American Philosophical Society Memoirs*, VIII, Philadelphia, University of Philadelphia. New edition (1989) Cambridge, MA, MIT Press.

Ranvier L (1863): De quelques modes de préparation du tissus osseux. *Journal de Physiologie de l'Homme et des Animaux* 6: 549-553.

Ranvier L (1865): *Considérations sur le développement du tissu osseux et sur les lésions élémentaires des cartilages et des os*. Thèse inaugurale. Paris.

Ranvier L (1869a): Des cellules et des noyaux tubulaires des tendons. *Comptes Rendus de l'Académie des Sciences* 68: 274-276.

Ranvier L (1869b): Des éléments cellulaires des tendons et du tissu conjonctif lâche. *Archives de Physiologie* 2: 471-487.

Ranvier L (1869c): Des cellules du tissu conjonctif. *Comptes Rendus de l'Académie des Sciences* 68:1478-1479.

Ranvier L (1870): On the cellular elements of tendons and of loose connective tissue. *Quarterly Journal of Microscopical Science* 10: 367-380.

Ranvier L (1871a): Contributions à l'histologie et à la physiologie des nerfs périphériques. *Comptes Rendus de l'Académie des Sciences* 73: 1168-1171.

Ranvier L (1871b): Séance du 11 novembre. *Comptes-Rendus de la Société de Biologie* 23: 130-134.

Ranvier L (1871c): Des lésions du tissu conjonctif lâche (tissu cellulaire) dans l'œdème. *Comptes Rendus de l'Académie des Sciences* 73: 124-126.

Ranvier L (1872a): Recherches sur l'histologie et la physiologie des nerfs. *Archives de Physiologie Normale et Pathologique* 4: 129-149, 427-446.

Ranvier L (1872b): De la dégénérescence des nerfs après leur section. *Comptes Rendus de l'Académie des Sciences* 75: 1831-1835.

Ranvier L (1872c): Des étranglements et des segments interannulaires chez les Raies et les Torpilles. *Comptes Rendus de l'Académie des Sciences* 75: 1129-1132.

Ranvier L (1873): Sur les éléments conjonctifs de la moelle épinière. *Comptes Rendus de l'Académie des Sciences* 77: 1299-1302.

Ranvier L (1875a): *Traité technique d'histologie*. Paris, Savy, 1875.

Ranvier L (1875b): Sur les terminaisons dans les lames électriques de la Torpille. *Comptes Rendus de l'Académie des* Sciences 81: 1276-1278.

Ranvier L (1875c): Des tubes nerveux en T et de leurs relations avec les cellules ganglionnaires. *Comptes Rendus de l'Académie des Sciences* 81: 1274-1276.

Ranvier L (1877): De la terminaison des nerfs dans les corpuscules du tact. *Comptes Rendus de l'Académie des Sciences* 85: 1020-1023.

Ranvier L (1878a): De la méthode de l'or et de la terminaison des nerfs dans le muscle lisse.

Comptes Rendus de l'Académie des Sciences 86: 1142-1144.

Ranvier L (1878b): *Leçons sur l'histologie du système nerveux*. Paris, Savy.

Ranvier L (1879): Recherches expérimentales sur la signification physiologique du plexus nerveux terminal de la cornée. *Comptes Rendus de l'Académie des Sciences* 88: 1087-1089.

Ranvier L (1880a): Nouvelles recherches sur les organes du tact. *Comptes Rendus de l'Académie des Sciences* 91: 1087-1089.

Ranvier L (1880b): On the terminations of nerves in the epidermis. *Quarterly Journal of Microscopical Science* 20: 456-459.

Ranvier L (1881): Terminaisons nerveuses sensitives: cornée. In: *Leçons d'anatomie générale faites au Collège de France*. Paris, Baillière.

Robin, CP (1849): *Du Microscope et des injections dans leurs applications à l'anatomie et à la pathologie*. Paris, Baillière.

Robin, CP (1854): *Sur un nouveau microscope approprié aux besoins des démonstrations anatomiques et permettant à plusieurs personnes d'observer ensemble*. Paris, Thunot.

Robin, CP (1856): *Mémoire sur les objets qui peuvent être conservés en préparations microscopiques transparentes et opaques, classés d'après les divisions naturelles des trois règnes de la nature*. Paris, Baillière.

Shepherd GM (1991): *Foundation of the neurone doctrine*. Oxford, Oxford University Press.

Sherman DL, Brophy PJ (2005): Mechanisms of axon ensheathment and myelin growth. *Nature Reviews Neuroscience* 6: 683-690.

Tello JF (1877-1887): Cajal y su labor histológica. In: DeFelipe J & Jones EG (1991), eds., Cajal's *Degeneration and regeneration of the Nervous System.* Oxford, Oxford University Press.

Van Gehuchten A (1897): *Anatomie du système nerveux de l'homme: leçons professées à l'université de Louvain*. Louvain, Uystpruyst-Dieudonné.

Virchow R (1858*): Die Cellularpathologie in ihrer Begründung auf physiologische und pathologische Gewebelehre*. Berlin, Hirschwald.