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EMILIO VERATTI AND THE FIRST APPLICATIONS OF THE «BLACK REACTION» TO MUSCLE RESEARCH: A HISTORICAL ACCOUNT

Abstract. — At the end of the nineteenth century the application of the black reaction to muscle tissue led Santiago Ramón y Cajal and Romeo Fusari to observe a reticular structure inside the muscle fibre. A century ago Emilio Veratti, at that time an assistant of Camillo Golgi at the Institute of General Pathology of the University of Pavia, was able to develop this approach so as to obtain a precise morphological characterization of the reticulum in various animal species. Only after the introduction of electron microscopy, more than fifty years later, was this structure identified as the muscle T system and as part of the sarcoplasmic reticulum.

Key words: Veratti; Ramón y Cajal; Fusari; Black reaction; Sarcoplasmic reticulum.

Riassunto. — *Emilio Veratti e le prime applicazioni della «reazione nera» alle ricerche sul muscolo: un approccio storico.* Alla fine del XIX secolo le prime applicazioni della «reazione nera» allo studio del muscolo condussero Santiago Ramón y Cajal e Romeo Fusari all'osservazione di una struttura reticolare nella fibra muscolare striata. Cento anni fa Emilio Veratti, all'epoca assistente di Camillo Golgi all'Istituto di Patologia Generale dell'Università di Pavia, sviluppando ulteriormente queste ricerche, giunse ad una descrizione straordinariamente precisa dei caratteri morfologici di questa formazione in molte specie animali. Soltanto dopo l'introduzione della microscopia elettronica, più di cinquanta anni dopo la pubblicazione del lavoro di Veratti, questa struttura venne identificata come appartenente al sistema T della fibra muscolare striata e come parte del reticolo sarcoplasmatico.

Introduction

A persistent pattern in the history of science is that generation of knowledge occurs in episodic bursts or even explosions of factual discoveries and theoretical breakthroughs, interspersed between lapses of complete or near-complete stagnation which sometimes may last for decades. Far from reflecting a linear process of gradual and continuous accumulation of learning, the development of science follows an irregular course that looks more similar to the fractal profile of a mountain with jagged edges and gorges than to a smoothly sloping plane. Periods in which knowledge grows with remarkable speed, based on a variety of fresh empirical and theoretical approaches, alternate with periods in which scientific creativity seems exhausted and the available techniques appear doomed to clash with insuperable difficulties. Often the peaks of science progress coincide with the introduction of new technologies whose multiple applications generate a wealth of original data and stimulate novel ways of thinking in various areas of science. Among the countless examples that attest the dependence of science on technological advances, one can cite Galileo Galilei's telescope which allowed him to discover the satellites of Jupiter, the phases of Venus, the craters of the Moon and the Sun spots. In general, the introduction of a newly invented research instrument, if successful, opens up fresh territories for investigation that can be defined as experimental «habitats» or «niches», but these territories are naturally destined for barrenness if they are not consistently fertilized by vigorous innovation.

An interesting *case-story* of the influence of a methodological break-through on the progress of science is offered by the discovery of the *black reaction* by Camillo Golgi in 1873 (Pannese, 1996; Mazzarello, 1999), an achievement which promoted the development of many fields of neurobiology and created a number of important experimental «niches». The discovery of the selective precipitation of silver chromate in nerve cells was the crucial event that changed the outlook of science on the fine structure of the central nervous system. But the method of Golgi had a substantial impact on science areas outside neurobiology as well, as exemplified by the discovery of the Golgi apparatus, which revolutionised cytology, and the identification of the *Muller-Golgi canaliculi* in the parietal cells of the stomach, which provided a potent morphological cue to the understanding of gastric secretion. The black reaction was fruitfully applied by Veratti to the study of muscle, resulting in a paper that was judged by qualified experts to be by far the best contribution of light microscopy to the elucidation of the morphology of the *sarcoplasmic reticulum* (Veratti, 1902*a*). This structure is concerned with the release of calcium in muscle fibres, thus constituting an essential element in the excitation-contraction couplig mechanism (Bennett, 1960; Smith, 1961; Huxley, 1977; Berlucchi, 2002). In spite of its high quality, Veratti's work (1902*a*) occupied a marginal position in muscle research for more than fifty years, before achieving a new significance only in the 1950s due to the new ultrastructural research and the developments of electrophysiology. This is a good example of an important discovery which did not gain much attention in the scientific context in which it was produced, but was resurrected much later when it could be fit into a new experimental and theoretical «niche».

Muscle reticula before the black reaction

Historically the study of muscle tissue has constituted a research area with considerable cultural implications. Since muscle tissue is responsible for one of the most fundamental phenomena which characterises life, *i.e.* movement, the understanding of its structure can perhaps lead to the understanding of its function. Especially after the introduction of the achromatic microscope in the first half of the nineteenth century, most of those who looked at muscle tissue through the microscope felt forced to formulate some hypotheses about muscle function on the basis of the structural data. Obviously it was the striping, the most typical morphological characteristic of muscle tissue, that first suggested itself as the most probable basis for the muscle's ability to contract and produce movements. The work which marks the beginning of modern myological research is William Bowman's description of the myofibrils as the main constituents of muscle fibres, along with his interpretation of their characteristic striations as an orderly alternation of stripes with different densities (Bowman, 1840). Bowman was the first to regard the fibrils as the contracting element of the muscle fibre, and many of those who followed him concentrated on the dimensional variations of the stripes during contraction in the hope to obtain direct information on the basic mechanism of muscle function (Smith, 1961; Huxley, 1977). However, in the decade 1880-90 the importance of stripes for muscle contraction began to be disputed for two fundamental reasons, one theoretical and the other experimental. From the theoretical viewpoint, movement was known to occur not only in striated muscle, but also in smooth muscle fibres, in amoeboid leukocytes, in ciliated and flagellated cells, all of which are devoid of striations. From the experimental point of view, histological studies using gold chloride staining methods had revealed that in addition to myofibrils, muscle fibres contained a structure potentially related to movement because it was common (even if not exclusive) to other cells with capacity to move: the *intra-cytoplasmic reticulum*.

The *intra-cytoplasmic reticulum* was probably observed for the first time by G. Thin between 1874 and 1876 in striated muscle fibres of the frog (Thin, 1876). This experimental finding matched the epistemological concept of the uniformity of nature (Huxley, 1977), a concept which reduced the apparent differences of cell organization to a fundamental and substantial architectural and functional uniformity, bringing to mind the old aphorism of William of Ockham, *Entia non sunt multiplicanda praeter necessitatem*. This concept seems too simplistic to be true if applied to such complex phenomena as biological movements, but in the 1880's many scholars of histology and muscle physiology began to believe that aside from occasional morphological differences, the same structural element, *i.e.* the reticulum, could underlie all fundamental bio-kinetic phenomena.

As remarked by Sir Andrew Huxley, the principle of uniformity of nature applied to the muscle was very clearly expressed from a physiological viewpoint by B. Melland, a young researcher at Owens College, Manchester, when he wrote:

Everyone who has considered the subject must admit the essential identity from a physiological point of view of all those tissues which possess in a special degree contractility. The contraction of a white blood-corpuscle or amoeba is essentially the same phenomenon as the contraction of an involuntary fibre-cell or a striped muscle-fibre (Melland, 1885).

Thus, the substantial physiological identity of cells capable of movement was inferred from a shared structural feature, namely the possession of a reticulum.

Another researcher at Owens College, C.F. Marshall, clearly reiterated this concept in the first of two articles published in the *Quarterly Journal of Microscopical Science*, the most important English journal of microscopic research:

Striped muscle has long been known to occur widely distributed in the animal kingdom, but the details of the structure of the striped muscle-cell have been subject of much controversy. Various descriptions have been given, widely differing from one another, and none of them affording a satisfactory basis of comparison with other cells. The demonstration of an intracellular network in the muscle-fibre by several recent observers appears to afford the most rational clue to its structure, for it not only explains all the appearances seen in the muscle-fibre (...) *but it also renders possible a comparison with other cells, and shows that a muscle-fibre is to be regarded as of essentially the same structure as an ordinary cell, and must not be considered as an enigmatic structure, the details of which do not correspond to those of any other cell in the animal economy* (Marshall, 1888).

Fig. 1. – Arthur van Gehuchten.

The muscle fibre, paradigmatically endowed with mobility, was thought to be comparable in all respects to many other ordinary cells, and the intra-cytoplasmic reticulum was regarded as the common element underlying the muscle cell's physiological characteristics. In the light of this theory the typical striations of muscle fibers lost their importance, and were considered to be illusory images produced either by optic artefacts or by *post-mortem* coagulation.

By contrast, the reticulum became one of those *passé-partout* words which in the history of science are not rarely used to provide nominalistic pseudo-answers to unsolvable problems.

Among those who adhered to the theory of the reticulum, the Belgian Arthur van Gehuchten (fig. 1) published two long memoirs (van Gehuchten, 1886, 1888) directly inspired by his mentor J.B. Carnoy, one of the proponents of the reticulum theory. Another supporter of the theory was an as yet unknown Santiago Ramón y Cajal (Ramón y Cajal, 1888), who later regretted this juvenile «infatuation», as attested by a frequently cited excerpt from his autobiography (*e.g.* Huxley, 1977; Shepherd, 1991):

There was current in histology at that time one of those diagrammatic conceptions which temporarily fascinate the mind and influence young workers decisively in their inquiries and opinions. I refer to the reticular theory of Heitzmann and Carnoy, which was applied very ingeniously to the constitution of the striated substance of muscles by Carnoy himself (...) *and afterwards by the Englishman, Melland, and the Belgian, van Gehuchten. Impressed by the ability of these scientists and by the prestige of the Theory, I had the weakness to regard the*

Fig. 2. – Santiago Ramón y Cajal.

contractile substance, as they did, as a tiny lattice of delicate fibres (the pre-existent filaments seen in preparation with acids and with gold chloride) united transversely by the net postulated at the level of the line of Krause. As for the primitive fibrils, they were supposed to be the result of post mortem coagulation. Later on I changed this opinion, which was vigorously criticised by Rollet, Kölliker, and others, who declared rightly that the so-called artifacts could be observed even in the living muscles of certain insects.

I insist upon these details because I wish to warn young men against the invincible attraction of theories which simplify and unify seductively. Ruled by the theory, we who were active in histology then saw networks everywhere. What captivated us specially was that this speculation identified the complex structural substratum of the striated fibre with the simple reticulum or fibrillar framework of all protoplasm. Whatever the cell might be, amoeba or contractile corpuscle, the physiological basis or rather the active factor was always represented by the network or elementary skeleton.

From these illusions no histologist is free, least of all the beginner. We fall into the trap all the more readily when the simple schemes stimulate and appeal to tendencies deeply rooted in our minds, the congenital inclination to economy of mental effort and the almost irresistible propensity to regard as true what satisfies our aesthetic sensibility by appearing in agreeable and harmonious architectural forms. As always, reason is silent before beauty (Ramón y Cajal, 1996).

The theory of the reticulum was attacked and refuted by Kölliker (1888), Rollet (1888), Mingazzini (1888) and other researchers. It was perhaps at that time that Ramón y Cajal (fig. 2), upset by the critiques, developed his *horror reticulorum*, a proverbial idiosyncrasy for all kinds of biological networks.

Fig. 3. – Camillo Golgi in 1889.

A new reticulum

However Ramón y Cajal's rejection of the theory of Carnoy, Melland and van Gehuchten did not clear all the debts he had incurred in regarding the reticula. The method which was going to change his scientific life, the chromo-silver staining (black reaction) of Camillo Golgi (fig. 3), allowed him to see a new reticulum in muscle fibers. After observing some histological preparations of the central nervous system obtained with the black reaction in the home of his colleague Louis Simarro in Madrid, Ramón y Cajal decided to base his scientific research on a systematic employment of the extraordinary but capricious method created by his colleague from Pavia. Obviously he began with the central nervous system, but the enthusiasm stemming from his many discoveries that were destined to change neurobiology convinced him to apply Golgi's staining method to other tissues, like the typically striated limb and wing muscles of insects. In his re-encounter with the reticulum Ramón y Cajal observed two very fine parallel nets, linked by longitudinal lines and arranged transversally around each muscular segment (sarcomere) at the transition between the mono-refractive and bi-refractive bands (fig. 4). These very fine reticula seemed to be continuous with the fine terminal ramifications of the tracheal canals typically found in insect tissues (Ramón y Cajal, 1890*a, b, c*). A fact that evidently was in agreement with the necessity to assure an adequate distribution of oxygen to these energy consuming tissues. This disposition was thus a reasonable and acceptable new physiological interpretation which avoided the previous criticisms of Kölliker and others to the theory of the reticulum as a basis for contraction. Satisfied with the results of this study, Ramón y Cajal did not extend his observations to the muscles to other animals, or did so only marginally.

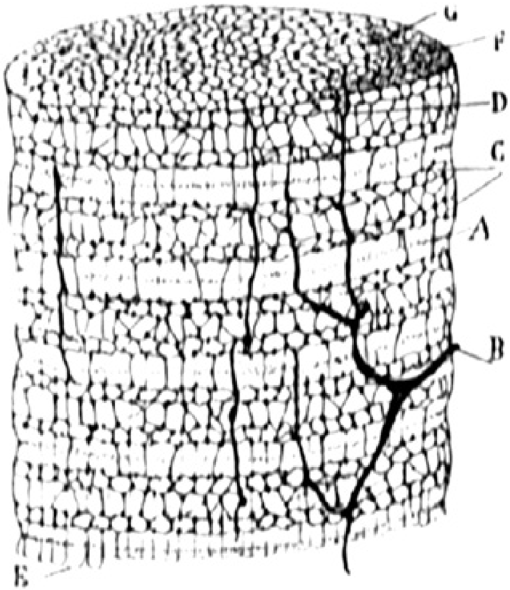

Fig. 4. – Early application of the black reaction to the muscle. Illustrations from the work of Ramón y Cajal (1890*b*). In insects the reticulum is associated with the tracheae penetrating the fiber.

In that same year, the Swedish histologist and anatomist Gustav Retzius published a study on the structure of muscles fixed with a chromo-osmium-acetic mixture and stained with aniline colorants. He found in the sarcoplasm, a term introduced by Rollett in 1888, some granules and fibrils in the vicinity of the Z band (named at the time Amici or Krause line), which perhaps were part of the same structure identified by Ramón y Cajal (Retzius, 1890).

The study of muscle tissue was taken up again in Italy by Romeo Fusari (fig. 5), an expert utilizer of the black reaction who had been a favourite student of Camillo Golgi at the Institute of General Pathology in Pavia (Bruni, 1919; Moiraghi 1991; Mazzarello, 1999). Fusari, a Professor of Anatomy at the University of Ferrara since 1890, applied the chromo-silver staining method to the study of the structure of tongue muscle in mammals. On the 26th of November 1893 he read a communication at the Academy of Medical and Natural Sciences of Ferrara in which he described the preliminary results he had obtained. After having emphasized how the black reaction had been a «very clear aid for the study of the central and peripheral nervous system» he predicted that it would also be «precious for the study of the complicated structure of the striated muscle fibre». And he described some images of striations in longitudinal fibre sections which consisted of a series of granules linked by thinner filaments located «at the limit between the bi-refractive and the mono-refractive stripes» of the sarcomere. In transversal muscle sections the granules appeared to be linked by filamentous bridges, which gave origin to a reticule. The communication of Fusari concluded by asking whether the structure he had described had any relation with the conspicuous reticulum stained with gold

Fig. 5. – From the right, first row: Romeo Fusari, Albert von Kölliker and Edoardo Perroncito; second row: Camillo Golgi and Giulio Bizzozero.

chloride which had interested Melland, van Gehuchten and Ramón y Cajal (Fusari, 1893). Fusari took up the subject again on the following 21 January 1894 with a new communication read at the academy of Medical and Natural Sciences of Ferrara (Fusari, 1894*a*). In this report, based on the application of the black reaction to muscle fibres of insects, amphibians, birds and some mammals, Fusari confirmed his previous results and further described the presence of a reticulum at the level of Z line. However he seemed to believe in a substantial identity between the reticulum he had observed with the chromo-silver method and the one stained with gold chloride. In concluding he announced the publication of a more extensive study as well as of a third communication at the same Academy «on the muscular fibre in a state of contraction and development».

A few months later a major scientific event monopolized the attention of medical doctors. The eleventh International Congress of Medical Science, held in Rome from March 29 to April 5, attracted thousands of scientists and clinicians from all over the world. In the anatomy section, in front of international authorities such as Wilhelm Waldeyer from Berlin, Charles Debierre from Lille and Auguste Eternod from Geneva, Fusari presented a communication «on the structure of the striated muscular fibre with the presentation of histological preparations» (Fusari, 1894*b*, *c*). He claimed that «the striped muscular fibres are formed by bundles of primitive fibrils joined together by reticula of transverse filaments, placed in correspondence of the Z line and at the border between the mono-refractive disk and the bi-refractive disk». Furthermore Fusari asserted that the black reaction of Golgi applied to the muscle gave «interesting results revealing many details [that is the different aspects of the reticule] that account for the various striations of the fibres when they are examined freshly cut». Fusari's communication was considered as a defence of the old theory of the reticulum of Melland and van Gehuchten and produced the resented attacks of Pio Mingazzini, one of those who had contested the theory since its formulation. He noted that «the alleged reticule had been demonstrated to be only a metallic precipitation in the sarcoplasm» and criticized Golgi's black reaction which «though useful for demonstrating many details of the nervous system does not serve the same purpose for other tissues». According to him the theory of the reticule «now re-proposed by Fusari, was victoriously fought by Mingazzini himself, by Kölliker and by Rollet, since 1888, and the authors who supported the theory of the reticule (...) have now changed their mind». Fusari tried to answer and defend himself by remarking that he considered the fibrils «as functional parts of the striated muscle fibres» which do exist «in reality» (in opposition to van Gehuchten and Melland who conceived them as artefacts produced by some sort of «coagulation» in the protoplasm). Nevertheless this defense was evidently unsuccessful, considering that Giovanni Paladino of Naples advised Fusari to perform further studies on «such complex elements as the striated muscle fibres» by using other histological methods «in order to obtain stronger results».

The following 8 July Fusari presented a third communication to the Academy of Ferrara, where he added some morphological details, such as the disappearance of the double transversal reticule (*i.e.* the fusion of the two bands at the border between the bi-refractive and the mono-refractive stripe of the sarcomere) when contraction reached its maximum, and suggested that these nets were constituted by the sarcoplasm of Rollet (Fusari, 1894*d*).

He published the translations of the communications to the Academy of Ferrara in the important journal *Archives Italiennes de Biology* (Fusari, 1895*a*, *b*, *c*) which was printed in French and was known abroad. But the critiques received in Rome probably quenched Fusari's enthusiasm for this research theme, and perhaps for this reason he never kept his promise of a full paper «enriched by illustrations», repeatedly proffered in his communications. Fusari's contributions left, however, some traces in the subsequent muscle research literature [1].

(1) For example the two first communications to the Academy of Medical and Natural Sciences of Ferrara were summarized by P. Schiemenz on *Zeitschrift für wissenschaftliche Mikroskopie und für mikroskopische Technik*, 11: 385-386, 1894. The French summary of the communication to the XI International Congress of Medical Sciences (Fusari, 1894*b*) was quoted in the *Anatomischer Anzeiger*, 10: 7-8, 1895. One of the three French versions of the communications to the Academy of Medical and Natural Sciences of Ferrara published in the *Archives Italiennes de Biologie* was quoted by Heidenhain (1898), even if countersigned by an asterisk indicating that the author of the article did not read Fusari's original work. After 1902 the name of Fusari was cited in relation to studies of muscle nets with the black reaction along with those of Santiago Ramón y Cajal and Emilio Veratti. Some authors also used the eponym «Cajal-Fusari reticulum»

In 1899, in a summary of his research work presented with his *curriculum vitae* as a candidate to the chair of anatomy at the University of Turin, Fusari wrote that the application of the black reaction to the muscle is useful « … because it shows many details of muscle fibres of mammals which cannot be seen with other methods». Perhaps with a certain regret he added that although he had not been able to publish an extensive study on this subject, he nevertheless felt that his contribution did not lack some interest (Fusari, 1899).

Emilio Veratti

The work barely begun by Ramón y Cajal and Fusari was resumed on a grand scale at the beginning of the nineteenth century by Emilio Veratti, at that time assistant of Histology at the Institute of General Pathology at the University of Pavia lead by Camillo Golgi (Locatelli, 1967; Mazzarello, 1999; Berlucchi, 2002). On the basis of what Veratti himself wrote in his publication, his research on muscle structure originated from the casual observation of some «images of singular fineness in neck muscles of newly born mice, treated for other purposes with the black reaction», which tempted him «to extend my work to other muscles and other animals» (Veratti, 1902*a*). At that time the discovery of the internal reticular apparatus or Golgi apparatus (Mazzarello and Bentivoglio, 1998; Bentivoglio and Mazzarello, 1998) had aroused the interest of biologists for all kinds of intracellular reticula. Veratti had played an important role in the development of knowledge about the Golgi apparatus because his modification of the black reaction had allowed an easily reproducible visualization of the apparatus (Veratti, 1899). As a result, some young students and post-docs working on this elusive intracellular organelle at the Institute of General Pathology (fig. 6) were able to demonstrate its presence in many cells in non-nervous tissues (Pensa, 1899, 1901; Gemelli, 1900; Negri, 1900). Veratti had graduated in Medicine at the University of Bologna in 1895 with a thesis supervised by Fusari, and therefore he was aware of the latter's work on muscle fibres. Further, Veratti's experience with the Golgi apparatus had convinced him that the black reaction was a «precious cytological method» (Veratti, 1902*b*), contrary to the diffuse belief that it stained only the outside cell surface. If one adds to these contingencies Veratti's serendipitous observations on neck muscles of rats, it is not hard to understand why he eventually aimed at a systematic investigation of the structure of muscle fibres with the black reaction.

The preliminary results of this investigation were communicated by Veratti at the Istituto Lombardo di Scienze e Lettere, and then published in an extensive memoir read at the same Institute on 13 March 1902 (Veratti, 1902*a*, *b*). Veratti had applied the black reaction, as well as Apáthy's gold chloride method and Heidenhain's iron haema-

to refer to the muscle fibre net, which was often confused with the Golgi apparatus. The Golgi apparatus was observed for the first time in muscle fibres by Luna (1911); see also Smith (1961). However Veratti (1930) explicitly denied the identification of the muscle fibre reticulum with the Golgi apparatus. Among the quotations of the Fusari's work in Italy we found: Varenna (1922); Levi (1927); Pensa (1961).

Fig. 6. – Camillo Golgi's school around 1900. Emilio Veratti is the second from the right, first row. Antonio Pensa is the second from the left, first row. Adelchi Negri and Edoardo Gemelli are the first and the third from the left, second row.

toxylin method, to muscle fibers of many animals including mammals, birds, reptiles, amphibians, fish, crustaceans, and insects. This systematic employment of the black reaction revealed without ambiguity and very clearly the presence of «a true reticular apparatus constituted by filaments» distributed in the sarcoplasm of muscle fibres with an extraordinary geometrical regularity (fig. 7). Comparative analysis in the various animal groups confirmed the widespread presence and uniformity of this apparatus, from insects to mammals, even though some interspecies differences regarding its intracellular location and minor structural modifications could be noted. Veratti's careful microscopic examination of insect muscles allowed him to exclude the existence of a continuity between the apparatus and the terminal branches of the tracheoles, in obvious contrast with the previous interpretation of Ramón y Cajal. Veratti's findings confirmed and extended those of Fusari insofar as the existence of transversal and longitudinal reticula with a precise structure was demonstrated in all muscle fibres. At least in mammals, birds and reptiles, this geometrical regularity appeared to be established after birth, since during development the reticular apparatus of muscle fibres is, in Veratti's words, «formed by anastomosing filaments running in the interstitial sarcoplasm at random in all directions; in fully developed fibers, on the contrary, the direction and the arrangement of the filaments that form the reticular apparatus are regulated according to a generally precise and constant architectonic plan». While Fusari believed that the reticula impregnated with gold chloride coincided at least in part with those evidenced by the black reaction, Veratti resolutely affirmed that «there only seems to be

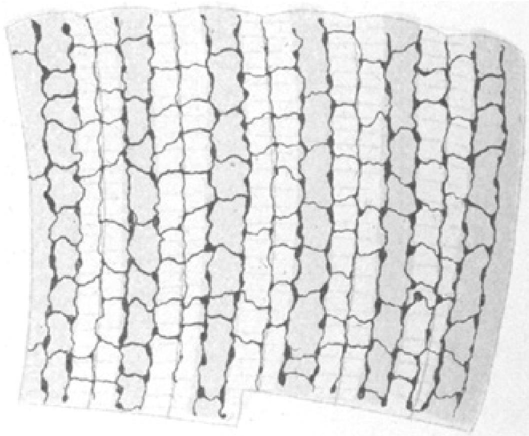

Fig. 7. – Veratti's reticulum. From Veratti (1902*a*).

a similarity between these two series of nets». Thus the apparatus described by Veratti presented itself as a new structure, common to all animal groups, and certainly unrelated to the old reticula of Melland and van Gehuchten.

Veratti clearly described different types of muscle fibres on the basis of location of their reticulum relative to the sarcomeric components: muscle fibres with only one reticulum with a transversal component at the level of the Z band (amphibians); fibres with two transversal reticula at the border between the mono-refractive and the bi-refractive zone; fibres with three reticula (crustacean), one at the level of the Z band and the other two again between the mono-refractive and bi-refractive zones. Actually Veratti did not believe that these differences were real, because he thought that the last type of reticulum was common to all muscle fibres, while the other less extensive types were solely the results of incomplete impregnations. Modern evidence showed that he was clearly in error on this count (Bennett, 1960).

In contrast to Fusari's opinion, Veratti observed that the two reticula never fused and always remained separated during muscle contraction. Fusari also thought that his reticular apparatus occupied the entire sarcoplasm, but Veratti came to the conclusion, based especially on observations on bat muscles, that the reticulum was restricted to a portion of the sarcoplasm, and that it could be clearly set apart from the muscle fibrils and the nuclei, with which it only had «a contiguity relationship».

With regard to the relationship between the reticulum and the cell membrane, Veratti made the very important observation that the reticulum could establish «a more intimate relationship with the sarcolemma on the internal surface of which single filaments of the apparatus occasionally implant themselves by means of triangular enlargements», an observation documented by beautifully accurate drawings. These drawings were used in 1960 by Stanley H. Bennett of the University of Washington at Seattle for providing a morphological counterpart to the physiological data of Huxley and Taylor (1955*a, b*) and Huxley (1957), who had found «sensitive spots» on the sarcolemma

Fig. 8. – Veratti's family and some friends (1921).

Fig. 9. – Veratti in the year 1960.

surface for producing local contractions with subliminal depolarizing stimuli (Bennett, 1960; Berlucchi, 2002). The projections of Veratti's reticulum to the cell membrane were thus identified with the tubules of the T system that are continuous with the extracellular space.

The work of Veratti did not gain much attention from subsequent students of muscle structure and functions. It was rarely cited, mostly *en passant*, and always without sufficient consideration of the precision and beauty of its results (2). Many years later Veratti himself refused to admit the importance of his own findings (Berlucchi, 2002), stubbornly adhering to the understatement of the potential of his work and the exaggerated awareness of its limitations that he had expressed at the end of the memoir presented at the Istituto Lombardo.

In his own words:

From the considerations so far brought to light one can see that my own investigations occupy a secondary position in the larger scheme of investigations on striated muscle fiber. My work does not touch on the weighty questions of the intimate structure of the contractile substance, nor does it gives any new data to explain the mechanism by which the muscle fibers contract (Veratti, 1902*a*, 1961).

Perhaps this bashful and modest style of presentation of a scientific paper was one of the factors that limited its impact. Only the rediscovery by electron microscopy of the reticulum so beautifully illustrated by Veratti made it possible for the experts to understand that he had exploited light microscopy to its limit by providing the most comprehensive description of the structures that were later identified as the T system and the sarcoplasmic reticulum proper (Smith, 1961; Franzini-Armstrong, 2002). Eventually Veratti's work came indeed to the attention of an international audience when it was translated into English and published in 1961 in a supplement in the *Journal of Biophysical and Biochemical Cytology* (Veratti, 1961) and thus (3), from that moment, the name of this modest and proud scientist (Berlucchi, 2002) gained an appreciation from muscle researchers that had been lacking for too long.

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(2) For some works which quote Veratti's paper see Smith (1961). For other quotations see Fusari (1909); Holmgren (1920); Lee (1921); Varenna (1922).

(3) I have recently obtained from the nephew of Veratti, Giuseppe G. Pietra MD, Professor Emeritus of Pathology at the University of Pennsylvania, School of Medicine, the correspondence between Veratti and the editorial staff involved in the translation of his paper (Veratti, 1961) and the publications of a supplement of *The Journal of Biophysical and Biochemical Cytology* dedicated to the Sarcoplasmic Reticulum (see vol. 10, n. 4, part 2, 1961). It appears from these letters that Veratti explicitly denied the identification of his reticulum with the sarcoplasmic reticulum as described by Keith R. Porter and George E. Palade (Porter and Palade, 1957).

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