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Camillo Golgi: the conservative revolutionary

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Abstract

This article outlines the fundamental phases of the scientific life of Camillo Golgi, the first Italian to win a Nobel Prize and one of the protagonists of European biomedical research between the 19th and 20th centuries.

Keywords

Camillo Golgi, Cesare Lombroso, Giulio Bizzozero, neuroanatomy, cytology, malaria, black reaction, Golgi apparatus.

In August 1873 a thirty-year-old Lombard medical doctor, Camillo Golgi, published in the journal *Gazzetta Medica Italiana – Lombardia* a brief note from the modest title *Sulla struttura della sostanza grigia del cervello* ("On the structure of the grey substance of the brain"). The paper gave a hasty description of a new histological procedure for the study of the microscopic morphological structure of the central nervous system. It also provided a quick account of some substantial scientific novelties that the method had allowed to obtain. Making the silver nitrate act on pieces of brain previously hardened with potassium dichromate in succession, Golgi had succeeded in realizing the dream of all the histologists who had previously posed the problem of clarifying the spatial disposition and the remote projections of the cellular elements of which the central nervous system is composed. The miraculous and mysterious contact between the potassium dichromate and the silver nitrate, in fact, determined the precipitation of a brown salt (the silver chromate) that, in a completely unexpected and unpredictable way, occupied the body of the cell and all its extensions, up to the most remote distances. But what most impressed was the randomness of the reaction: only a minority of the cellular elements, present in the microscopic field, were stained in black. At first sight what could have been considered a partiality (and therefore a defect) of the method, was instead his great strength. The cells, and their projections, clearly emerged with respect to the surrounding structures, thus creating almost a "microdissection" of the single elements that were like "extracted" from the tangled neurocytological interweaving within which they were

1 This work collects the results of many researches on Camillo Golgi and his school that I published in the last thirty years. In particular I refer to Mazzarello 2002; 2010; 2011; 2018; 2019; Mazzarello and Bentivoglio 1998; Mazzarello et al. 2001; Mazzarello et al. 2003; Mazzarello et al. 2004; Mazzarello et al. 2006; Mazzarello et al. 2009; Galliano et al. 2010; Raviola and Mazzarello 2011; Shepherd et al. 2011; Bentivoglio et al. 2019.

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imprisoned. It was as if one had succeeded in removing an entire, intact tree, with all its branches and roots, from an inextricable forest. The reaction began to be known as a "chrome-silver reaction" or the "black reaction" or even the "Golgi method". It was a significant scientific contribution destined to change forever the microscopic neuroanatomy but also the professional perspectives of the doctor who had created it. It was not the first time that Golgi's fate had changed compared to the rigid tracks that seemed to constrain the early course of his life.

1. From clinical medicine to basic research

Camillo Golgi was born in Corteno (now Corteno Golgi), a small mountain village in upper Valcamonica in the extreme north of Austrian Lombardy. He was the third of four children of the local doctor, Alessandro, of Pavia origins. After his primary and high school studies, he enrolled at the University of Pavia with the "sole aspiration to regularly obtain the [...] professional degree" to practice medicine as his father had done so many years before. On August 7th 1865 Golgi became medical doctor but could not immediately find his way. He had had the good fortune of being reformed by the military service due to frailty, he then began to operate as a civilian doctor for military health services and was employed in the fight against cholera with an operational base in Zavattarello (a small village in the province of Pavia); for a short period he worked in the Novara Hospital as a surgeon, and in the end he managed to get a modest job as "secondary" doctor (in essence, a low-paid doctor employed both for welfare activities and, occasionally, also for research) at the ancient Hospital of San Matteo in Pavia. Depending on the sanitary requirements, he was also employed in the surgical department, in the small psychiatric ward and in the "syphilocomy" (the dermatological ward where syphilis patients were admitted). An experiment that Golgi did on himself at the time, indicative of the degree of positivist scientific fanaticism, was aimed at finding the solution to the problem of transmissibility of syphilis from mother to child, through mother's milk. According to a testimony, Golgi went so far as to self-inoculate the milk of an infected woman. A singular experiment of which, unfortunately, no known scientific report exists.

Meanwhile, Golgi entered the scientific orbit of Cesare Lombroso, a professor at the University of Pavia and head of the psychiatric department, who was to become internationally known for his anthropological theories on genius, madness and criminality. The meeting with Lombroso certainly constituted a turning point in Golgi's scientific life. The psychiatrist was a man of marked originality, known since he published an essay *On the madness of Cardano* at the age of twenty, in which he already outlined some themes that will make him become, in a few years, one of the leading figures in psychiatric and forensic Italian medical culture. The passion for the scientific research of the brilliant professor had to have a contagious effect because it opened on boundless horizons. After so much speculation it seemed then to be at hand a work program that promised enormous developments in the knowledge of the encephalon, the most fascinating organ of the entire biological domain. Neuropsychiatric illnesses freed themselves of the ballast of "metaphysics"; the brain ceased to be "the organ of the soul" to become, more modestly, "the organ of the psyche". Thus the structural element, the anatomical and anthropometric data, became

Figure 1. Cesare Lombroso, around 1860, in military uniform (Historical Museum, University of Pavia).

the way through which to explore the biology of "mental alienations". Interests that soon caught Golgi still uncertain of the way to follow.

Lombroso often referred to Golgi around 1867-68, mentioned in the publications as a zealous collaborator and sometimes as "the friend Golgi", who took on much of the routine work of the psychiatric ward. However, Lombroso's star then began to set from the horizon of the young doctor; the psychiatrist stated one thing and did another, declaring himself firmly adherent to the experimental method, but his way of proceeding was without methodological rigor. Everything was used to confirm his theories. Instead of proceeding on an inductivistic basis, "gathering the facts", and then constructing interpretations, as the positivistic epistemology of the time wanted, Lombroso was struck by brilliant intuitions, but often outlandish, which became the "filter" through which to select the experimental data. Golgi, who had the practical sense, or we could say common sense, of the mountaineers, could certainly not approve these methods, indeed this lack of method. The sunset of Lombroso was accompanied by the rise of a new scientific star in the Pavia of the time: Giulio Bizzozero.

Born in Varese, three years younger than Golgi, Bizzozero graduated in medicine in 1866, at the age of twenty, passing quickly from the student bench to the professorship of general pathology to replace the professor Paolo Mantegazza, who had been elected deputy in the national parliament. Bizzozero had the magnetic ability to attract anyone interested in scientific research into the orbit of his powerful personality. Everything in him impressed: the speech, the quick gestures, the fascinating way to teach lessons by presenting the topics as a knowledge in progress, in this aspect extraordinarily different from an academic environment where science was still taught as a truth *ex cathedra.* The meeting with Bizzozero was certainly the decisive event for the development of the future scientific personality of Camillo Golgi. From the very young lecturer, soul and guide of the Laboratory of Experimental Pathology (later General Pathology) located in the Palace of the Botanical Garden, he acquired the knowledge of the histological techniques he will adopt and will not abandon for the rest of his life.

If it was Lombroso who ignited in Golgi a passion for the nervous system, it was nevertheless Bizzozero who catalysed his scientific personality, endowing it with a working method and making him discover the *histological path* to neurobiology. From that moment, and for several years, the nervous system became a favoured destination of his studies, just as histological techniques were a privileged (though not exclusive) means of his way of doing research.

In the time that Golgi was free from his hospital clinical commitment, he began to attend the Laboratory of Experimental Pathology under the guidance of Bizzozero. Thus the first scientific publications appeared including the essay written under the influence of the new Lombrosian anthropological doctrines *Sull'eziologia delle alienazioni mentali* ("On the etiology of mental alienations"). However, the relationship with Bizzozero became increasingly narrow; the two also lived in the same building (Lombroso also lived there for a while) and it is likely that those candlelight evenings would pass quickly with the young scholars discussing science at a time when Charles Darwin had upset the world cultural environments important with his theory of evolution. Under the guidance of Bizzozero, Golgi published histological works: a remarkable study on the glia, which represents his first relevant contribution to histology and neurobiology, and a work on the lymphatic of the brain in which he used, in addition to potassium dichromate, silver nitrate for the study of brain membranes. They are the two reagents that, used in succession, would have allowed him to set up the "black reaction" his most precious methodological invention.

Having enrolled at the university with the "sole aspiration to regularly obtain the [...] professional degree" to practice medicine as his father Alessandro had done so many years before, Golgi had by now profoundly changed his life interests and scientific research was become a deeply felt vocation. Unfortunately, there were no important job opportunities in the academic environment of Pavia. The medical faculty, it is true, gave him a teaching assignment in "Clinical Microscopy" and scientific satisfactions were not lacking; his first works had been cited and summarized in German and English literature, the "Rivista Clinica" of Bologna included him in the editorial committee since 1870. But what was missing, above all in the consideration of his father Alessandro, was a properly paid job. So at the age of twenty-eight, pressed by that worried parent, Camillo Golgi felt forced to find a safe and well-paid place to stay, even at the cost of abandoning the University's mirage and betraying his passion for scientific research.

2. Make the invisible visible

In January 1872 a competition was published for a post of primary doctor at the "Pia Casa degli Incurabili", an old hospice for the chronically ill, of Abbiategrasso, a town twenty-five kilometres from Pavia. Alessandro Golgi had also worked in the same hospital about fifteen years earlier, always keeping a good memory of his activity in this hospital.

It was therefore natural for that father to push the son Camillo, who earned little and, moreover, spent money in order to publish his works, to participate in the Abbiategrasso competition. Thus, reluctantly, Golgi took part in it and, naturally, obtained the position of primary doctor, starting the activity on 10 June 1872. He had reached a point in his life where everything gave the premonition of the total and permanent abandonment of the research. The institute did not possess scientific instruments and no costs were foreseen for an experimental activity. Immediately after his arrival in Abbiategrasso, Golgi then experienced a first period of uncertainty in which he accused "slight disturbances" which caused him "intellectual dullness so great" as to "completely inhibit the possibilities of work".

The link with the vast world of research was however maintained, albeit at a distance, by the letters of his friends Bizzozero and those of the ophthalmologist Nicolò Manfredi. By the end of 1872 he had recovered and organized a tiny histological laboratory in the kitchen of the small apartment that had been assigned to him in the Pia Casa.

Many years later, remembering that period, he will write:

Educated in working with the minimum of means, rich in the sacred fire of scientific work, even if I find myself in a kind of isolation, I had no difficulty in continuing to still occupy

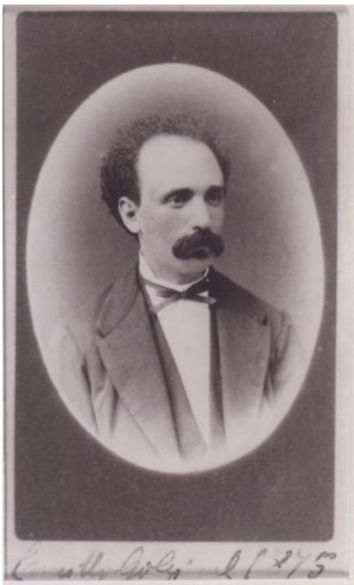

Figure 2. Camillo Golgi in 1875 (Historical Museum, University of Pavia).

myself with microscopic research in the rudimentary laboratory I organized in the kitchen of the small apartment that I had been assigned in the Pio Luogo.

The "sacred fire of scientific work" had taken over again.

On February 16, 1872, a letter from Golgi sent to Manfredi contained this communication:

Now I have regained the energy that for a few months I had completely lost. I spend long hours at the microscope. I am happy to have found a new reaction to demonstrate even to the blinds the structures of the interstitial stroma of the cerebral cortex. I let the silver nitrate act on the pieces of brain hardened in potassium dichromate I have already achieved very good results and I hope to get more.

This is the first announcement known to us, of the discovery (or invention) of the "black reaction" which, as it is easy to imagine, had an electrifying effect on the young Camillo. It had come at the right moment, just when the part-time researcher needed an intellectual medicine to fight the sense of abandonment from the wider world of scientific research, the intellectual horizon to which to hold on.

The black reaction consists of a first phase of "fixation" of the nervous tissue in potassium dichromate (2.5%), for a period varying from 1 to 45 days (and sometimes even more), followed by a second phase of immersion in a solution of silver nitrate. The result obtained is the selective precipitation of a salt, the silver chromate that goes to occupy every part of the neuron and glia including all their extensions. But the singularity of this intracellular reaction is given by its partiality: only a few nerve cells among those included in the microscopic field (in a percentage between 1 and 5%) are stained in black and stand out clearly compared to all the others. A bit like if you could extract a single tree, with all its extensions, from an inextricable forest. It is therefore precisely the partiality of the precipitation of silver chromate that provides the incredible cognitive power of this method that became the fundamental means for studying the structure of the nervous system. To date, the chemical-biological principle underlying this selective precipitation is still unknown. According to some histologists it would depend on the functional state of the cell when the precipitate develops. With regard to the black reaction, one can therefore speak of both discovery (because it is a new biological chemical phenomenon) and the invention of a research method.

An aspect that should be emphasized is the "biotechnological" character of the method developed by Golgi, which realizes a sort of morphological amplification of the histological structures caused by the deposition of an insoluble compound around or in structures so fine that they are not otherwise appreciated. A technique that, appropriately varied and refined, has found application in many areas of biological research allowing, among other things, the discovery of the internal reticular apparatus (Golgi apparatus), the discovery of the system of intracellular canalicular secretion of parietal cells (delomorph) of the gastric glands producing hydrochloric acid (Müller-Golgi canaliculi), the discovery of the pericellular nerve network (Golgi-Netz) and the discovery of the T system linked to the functions of the sarcoplasmic reticulum (by Golgi's pupils Romeo Fusari and Emilio Veratti). But the applications of silver methods related to the "black reaction" have extended to research fields as distant as the highlighting of the hepatic network of the intralobular bile canaliculi, or the identification and analysis of the diffuse endocrine system in the pre-electron microscopy and pre-immunohistochemical era, or the study of biological structures with the electron microscope.

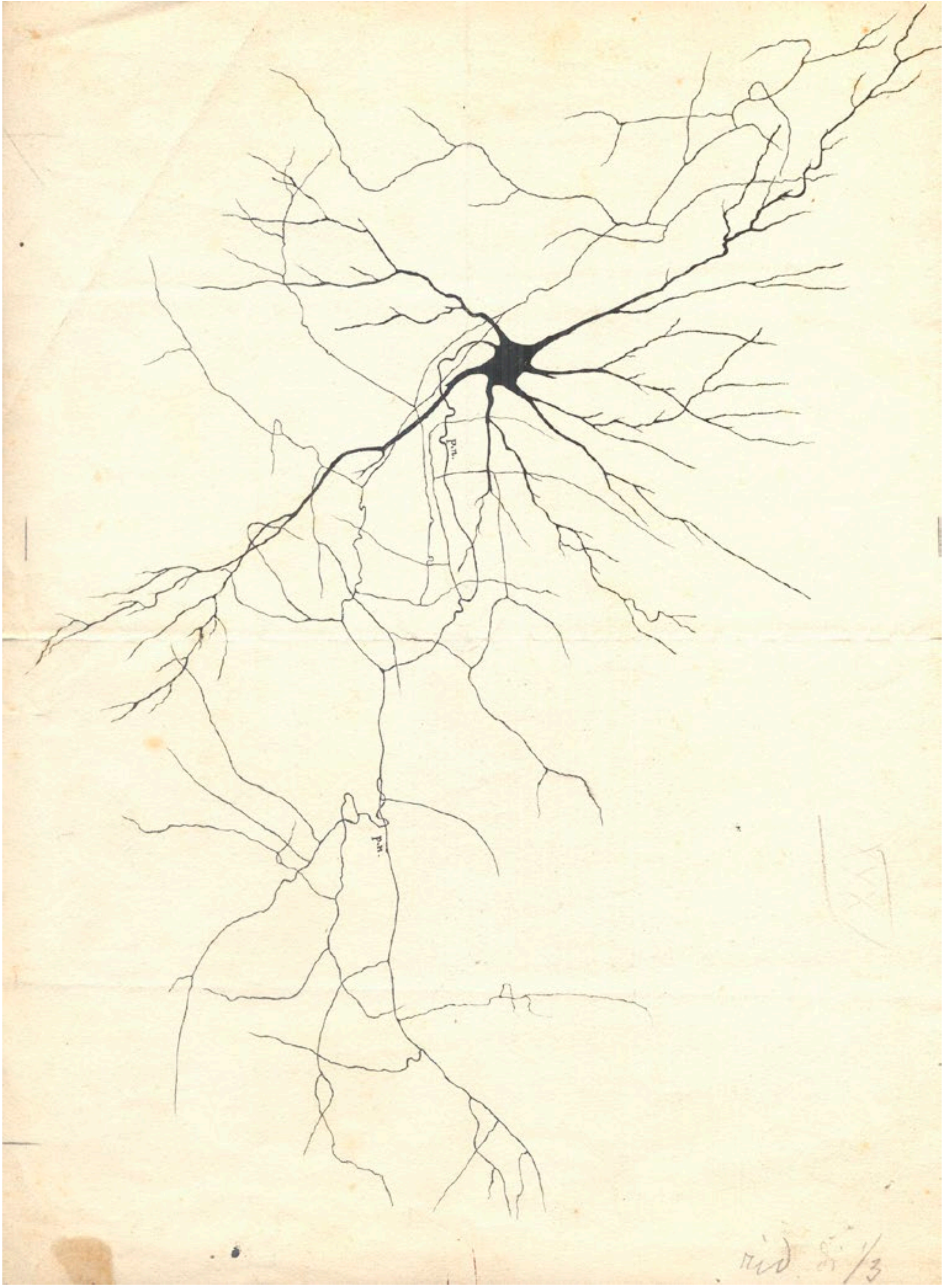

Figure 3. A nerve cell drawn by Golgi (Historical Museum, University of Pavia).

Golgi immediately understood the importance of the extraordinary instrument he had created. In due proportion, someone argued that as Galileo had discovered new stars in any celestial region explored with his telescope, so Golgi saw new nerve architectures in any brain region studied with the black reaction. The young researcher was thus in one of those positions that rarely occur in the history of science, that of the privileged explorer of a new continent. In the isolation of Abbiategrasso his research activity became so hectic. A few months later he had the first scientific communication ready based on the new method: *Sulla struttura della sostanza grigia del cervello*, a work that marks a watershed compared to the previous neurobiological tradition. Immediately afterwards, works appeared on the neuropathological alterations in the nervous system in a case of chorea (in which Golgi described some lesions in the striatum and the frontal cortex), on the structure of the cerebellum (where, among other things, he described the cells bearing his name) and on the morphology of the olfactory bulbs.

Each of these was a seminal work destined to open new perspectives to neuroanatomical and neuropathological research. The work on chorea, in particular, was a pioneering research on the presence of structural alterations in the brain of a patient with a neurodegenerative disease.

3. From neurocytological discoveries to the "diffuse nervous network"

Golgi's neurocytological discoveries were fundamental, reversing the concepts of nerve cell physiology of the time. According to the dominant model of Joseph von Gerlach, a well-known German histologist who introduced new methods of staining tissues with carmine and, subsequently, with gold chloride, the nerve cells were anastomosed in a labyrinthine syncytia, through the fusion of their dendrites, called at that time protoplasmic extensions (Gerlach protoplasmic network). This gigantic interdendritic reticulum would have created an anatomical connection system between the different nervous elements, through an intercellular continuum. Myelinated nerve fibres could originate in two ways: either directly from the interdendritic reticulum, or directly from the axon (called at the time "cylinder axis" or "nervous extension") emerging from the cellular body. It was a model that placed itself in explicit contrast with the cellular theory: the nervous system was not the result of the assembly of so many elementary "bricks" juxtaposed like pieces of a mosaic, but it had the appearance of a gigantic frame of "wires" that encompassed many cell bodies.

Thus the anatomists of the time began to think that at the base of the nervous functions there was a reticular structure, and this idea was well suited to the metaphor of the telegraphic network referred to the nervous physiology, suggested by Hermann von Helmholtz, Emil du Bois-Reymond and other explorers of the border area between physics and biology.

Golgi showed that dendrites did not merge into a network and discovered that the axon was an element *constantly* present in nerve cells. The fundamental neurocytological discovery, only vaguely intuited previously, was however the branching of the axons. These observations undermined Gerlach's reticularism. It was therefore the axon, according to Golgi, the way through which the transmission of the nerve impulse occurred at a distance, and not the dendrite to which he tentatively assigned trophic

Figure 4. The first drawing of a nervous territory observed under a microscope with the black reaction: the olfactory bulbs (1875) (Historical Museum, University of Pavia).

functions. However, the inventor of the black reaction did not abandon the reticularist "paradigm". Around 1870, the "holistic" or "globalistic" neurophysiological vision, supported by Marie Jean Pierre Flourens from the first half of the century, was still influential, according to which the cerebral cortex, in exercising its functions, would have carried out a "unitary" action. This hypothesis was in tune with a cellular model with "communicating vessels" where each element was in diffuse relationship with all the others through a syncytial network. When Golgi observed the slides obtained with the black reaction he had to think that if the net did not exist among the dendrites – to account for the complex relationships inside the nervous system - it must certainly exist between the branches of the newly discovered axons. And the observations that highlighted the tangle of nerve extensions seemed to confirm this assumption. Thus was born the theory of the *diffuse nervous network* within which nerve transmission was not "isolated" along very specific and extremely selective routes, but propagated to the whole nervous system. At the base of this nervous network there had to be either the fusion of the axons or their intimate weaving; the fundamental physiological factor of the model was constituted by the diffused transmission of the nervous impulses. However, these propagations would not have been isotropic, without any order, but able to ensure "prevalent or elective pathways of transmission". Thus, according to Golgi, in the nervous system, there had to be regions "not rigorously delimited, which, as they are prevalently or selectively excited, predominantly responding in a direction corresponding to the actual excitation". In some ways Golgi conceived *fields* of elective or prevalent propagations. A gigantic frame would therefore have served as a support for communication between the various parts of the nervous system. The novelty of Golgi's "reticularist" model, however, was - in addition to the role assigned to axons as a substrate in communication within the nervous system - the functional connotation of the network, conceivable as a true *physiological organ* capable of accounting for the complexity of brain properties. And perhaps for the first time, in the history of science, this concept was *explicitly* related to a complex function. What escaped Golgi was that the only concept of network was insufficient to account for neurological functions; in fact, without a node destined to compartmentalize the nervous energy through a valve mechanism present between cell and cell, able to channel and make the impulses unidirectional, thus preventing their dispersion and decay, the system could not have ensured the division of labour and the order of succession of neuropsychic functions. For Golgi, these functions, were perhaps assured by the differential density of the network between zone and zone, the fact that in certain regions it was richer or more lax. Perhaps, in his view, this idea could have justified the articulated functional differentiation from province to province, within the nervous system.

Golgi maintained this view of cellular relationships within the nervous system that developed in his mind in the 1870s and early 1880s throughout his life. When in 1886-87 he had almost completely abandoned neuroanatomical studies, devoting himself to other subjects of study, the idea emerged that even the nervous tissue was composed of single cells isolated and not fused into a network: the *theory of neuron* was born. First proposed explicitly in 1886-87 by two Swiss scientists, the embryologist Wilhelm His and the psychiatrist Auguste Henri Forel, and also hinted by the Norwegian biologist (and subsequently polar explorer and diplomat) Fridtjof Nansen, was officially baptized by the German anatomist Wilhelm Waldeyer in 1891 and fully developed by the great Spanish histologist and neurobiologist Santiago Ramón y Cajal.

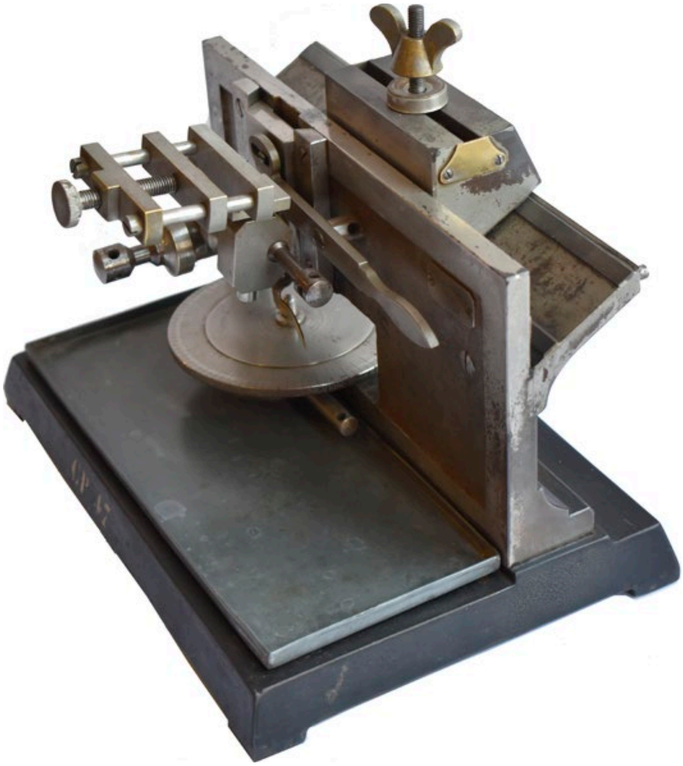

Figure 5. Schanze microtome purchased in 1905 from the Golgi laboratory (Golgi Museum, University of Pavia).

4. Discoveries

With the discovery of the black reaction, Golgi's talent was recognized. At the beginning of 1876 he became professor "straordinario" of histology in Pavia, in May he was promoted to the highest rank of an academic career that of professor "ordinario" (full professor) of anatomy in Siena but after a few months he preferred to return to Pavia on the chair of histology (and starting from 1881 of general pathology).

In Pavia Golgi organized a laboratory that quickly became a reference point for Italian biological research. Here worked, among others, Adelchi Negri whose name is linked to the characteristic lesions of the brain infected with the rabies virus, Antonio Carini who identified in Brasil the fungus *Pneumocystis carinii*, Emilio Veratti, who discovered the T system linked to the sarcoplasmic reticulum functions, Giovanni Battista Grassi who, at the end of the nineteenth century, identified in Rome the vector of human malaria, Carlo Martinotti, whose name is linked to the ascending axon cells of the cerebral cortex, Vittorio Marchi, the inventor of an important myelin staining method that was used in studies on nerve pathways, Aldo Perroncito whose

Figure 6. Laboratory scissors and small tools used by Camillo Golgi (Golgi Museum, University of Pavia).

name has remained linked to studies on peripheral nerve regeneration, after experimental injury.

Golgi himself developed important research in the laboratory, identifying two sensory corpuscles in the thickness of the tendons, the Golgi muscle tendon organs (muscle tension transducers) and the Golgi-Mazzoni corpuscles (sensitive to pressure stimuli), defining new details in the structure of the nerve fibres (horny funnels of Golgi-Rezzonico), discovering that the distal tubule of the kidney enters into relation with the vascular pole of the Malpighian corpuscle (thus clarifying the anatomical basis of what physiologists consider the site of important mechanisms for regulating the arterial pressure), accurately describing the evolutionary phases of the nephron and renal corpuscles.

Furthermore, until the First World War, Golgi maintained the direction of a small clinical department in the San Matteo Hospital of Pavia (as an honorary primary doctor), a circumstance that allowed him to perform important medical observations. An excellent clinician who always refused the practice of private activity, he published papers on intestinal worm infestation, peritoneal transfusions, and the regenerative capacity of renal tissue. Above all, starting from the end of 1885, he developed fundamental clinical-laboratory researches on the evolution of the malarial microbe, the plasmodium, of the quartan and of the tertian form of the disease in the erythrocyte, describing the subsequent morphological modifications (*Golgi cycle*) and establishing the relationship existing between the periodic febrile bouts of patients and the "sporulation" (that is the reproduction) of the protozoan (*Golgi law*). Between 1892 and 1893 he also observed, independently from the Swedish histologist Erik Müller, the canaliculi of the parietal cells of the gastric glands, often called Müller-Golgi tubules.

Naturally this great number of discoveries and the evident international reputation emphasized by acknowledgments and quotations on prestigious publications reverberated also in the Pavia university environment. Thus Golgi was first appointed rector of the University of Pavia in the years 1893-96. During this period it slowed down considerably with scientific research. But between 1897 and 1898 the time came for another revolutionary discovery that would change the structural concepts of the cell.

5. A brick of the cell

In the course of 1897, studying the spinal ganglia with a variant of the classic chromium-silver method, Golgi discovered, in some cells, a convoluted filamentous apparatus arranged in such a way as to form a cytoplasmic network clearly separated from the nucleus and the cell membrane. However the observation was not easily reproducible. So he decided to wait before publishing these preliminary results. When between the end of 1897 and the first months of 1898 his pupil Emilio Veratti succeeded in demonstrating the endocellular formation by studying the cells of origin of the fourth cranial nerve, Golgi decided to make his discovery known. In the meantime he had succeeded in reproducing the reticular structure also in the Purkinje cells of the cerebellum. Thus in April 1898 he communicated the discovery of the internal reticular apparatus to the Pavia Medical-Surgical Society. It was, to use his words, "represented by a fine and elegant reticulum hidden within the cell body and of so

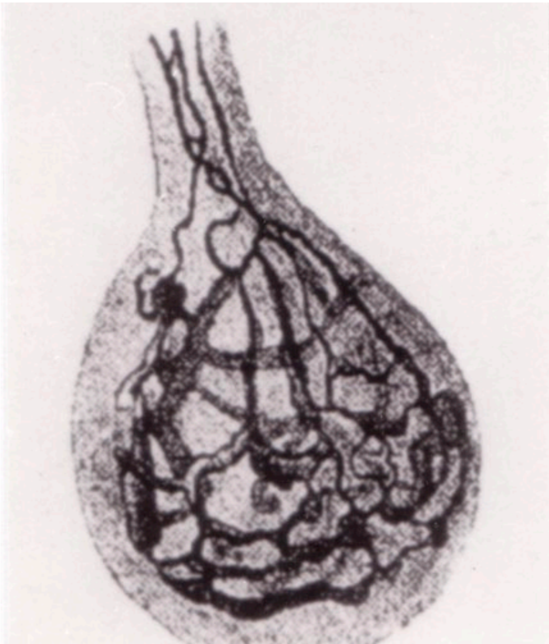

Figure 7. First published illustration (1898) of the Golgi apparatus (Historical Museum, University of Pavia).

characteristic appearance that even small fragments of it, given that the reaction is partial, can safely be recognized as belonging to the same endocellular apparatus [...] But the most characteristic note of the apparatus results from its physiognomy – that is, while it is clearly limited towards the outside, so that [...] the zone of cellular substance comprised between the limit itself and the surface of the cell appears perfectly free and in the form of a regular clear edge, towards the inside, instead, the filaments of the reticulum deepen in different planes".

Shortly after the discovery, Golgi's students Antonio Pensa, Adelchi Negri and Edoardo Gemelli showed their presence also in non-nervous tissues. However for many years the discovery of the internal reticular apparatus was not fully accepted by the international scientific community and in fact did not enter into the official motivation of the conferment of the Nobel Prize to Golgi in 1906. On one hand it was believed that the organelle constituted a part of a wider "lymphatic" canal system extended among several cells, the "Trophospongium", whose existence had been hypothesized by the Swedish histologist Emil Algot Holmgren and who believed himself involved in trophic functions. But in the early decades of the century it was shown that the Trophospongium had nothing to do with the internal reticular apparatus (as Golgi had always claimed) and finally came to consider it an artefact. Others denied the same in vivo existence of the reticular apparatus considering it a fictitious structure secondary to chemical-physical processes of cytoplasm precipitation. The intrinsic uncertainty of the chromo-silver reaction and the difficulty encountered by the researchers in reproducing the results of the Golgian school, had also led to hypothesize (more or less seriously) that some chemical peculiarities of the water of Pavia were the determining factor. The controversy over the existence of the structure discovered by Golgi continued for many years and was definitively resolved in 1954 by Marie Felix and Albert Dalton with the electron microscope.

When, on the basis of his reticular aspect and of its intracellular distribution, Golgi had proposed to call it "internal reticular apparatus", he certainly would not have imagined that it would remain associated with his name making him one the most mentioned biologist in the international scientific literature. Perhaps the first who began to speak of "the Golgi apparatus" was Carlo Besta in 1910. However, the eponymous became internationally known only starting from 1913 after the publication of a seminal work of Jòsef Nusbaum, professor at the University of Lemberg (Lwòw), and the subsequent penetration in the English scientific literature. From the fifties we talk about the "Golgi complex" and in the last forty years we speak of "Golgi" *tout court*. Then there was a clonal terminological amplification of Golgian eponyms: Golgi vesicles, Golgi recycling, Golgi budding, Golgi saccules, Golgi stack, Golgi network, Golgi enzymes etc. The name Golgi, like the fixed part of family surname, is thus always present for any structure or function that refers to the organelle. Thus it has become a mere label without any link to the histologist of Pavia.

Equally variable were the functions attributed to this organelle from the moment when Golgi timidly alluded to a cellular secretory or nutritional functions. In recent years, research developed in laboratories around the world is clarifying its fundamental physiological importance in many cellular processes; the multifunctional role of the Golgi apparatus is increasingly emerging in processes such as the modification, transport and sorting of proteins to the secretory cell surface and the biosynthesis of oligosaccharides and lipids. The communication in which Golgi announced the observation of the internal reticular apparatus contained the description of a second important discovery. The scientist from Pavia in fact observed on the surface of the nerve cells a "very delicate special covering made of a substance clearly differentiable from that of the cell body". This perineuronal reticulum is now recognized as a specific neurocytological entity that has become increasingly important in neurohistological studies.

6. The last years of an experimental genius

With the new century the scientific creativity of Camillo Golgi faded. He continued to publish some work but had to divide himself with the new commitments to the direction of the University of Pavia of which he was dean of the medical faculty (1899-1901), rector again for a second period from 1901 to 1909. He also assumed a political role both locally in the municipality of Pavia and nationally as a senator of the Kingdom of which he became a member since 1900.

In 1906 he reached the apex of his international fame with the awarding of the Nobel Prize for Medicine, ironically won also by his scientific antagonist Ramón y


AFTONBLADET Måndagen den 10 December 1906.

Nobelpristagare år 1906.

I fysik: John Thomson.

I kemi: Henri Moissan.

I medicin: Camillo Golgi.

I medicin: Ramón y Cajal.

I litteratur: Giosué Carducci.

I fredsarbete: Theodor Roosevelt.

Figure 8. The 1906 Nobels seen by the Swedish magazine Aftonbladet.

Figure 9. The Nobel gold medal conferred to Golgi. Historical Museum, University of Pavia.

Cajal, in the same year in which the Italian poet Giosuè Carducci was also recognized for literature.

In addition to the Nobel Prize he obtained other international awards: in 1893-94 the Rinecker prize and medal of the University of Würzburg, in 1894 the Riberi Prize of the Turin Academy of Medicine and in 1907 the Mary Kingsley Prize of the Liverpool School of Tropical Medicine; he also received honorary degrees in Cambridge (1898), Geneva (1909), Kristiania (Oslo, 1911), Athens (1912) and Paris (Sorbonne, 1923).

In the last twenty years of his life, Golgi conducted a tenacious and stubborn battle against the institution of the University of Milan that he considered a threat to Pavia, fearing that it might swallow up the university, sooner or later. During the First World War he headed the Collegio Borromeo military hospital in Pavia and gave impetus to the rehabilitative treatment of war wounded; after the conflict he continued to work in the laboratory, publishing scientific papers until 1923.

But when he died in Pavia on January 21, 1926 this man so full of glory was apparently a loser. He had lost the battle against Ramón y Cajal and the theory of the neuron that was triumphing; he had been defeated in his long war against the institution of the University of Milan whose foundation he bitterly saw.

However after so many years we can say that Golgi was, in reality, one of the most successful researchers in the history of biology: his formidable black reaction had provided the key to opening up the mysterious brain black box, constituting the stele of Rosetta for deciphering the nervous cryptogram and thus helping to found modern neuroscience. The organelle he discovered is one of the building blocks of the cell and a protagonist of cytological research. His malaria studies have inspired generations of researchers.

But it was Golgi's entire scientific work that opened up new fundamental frontiers for biomedical research.

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