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Introduction to A Century of Neuroscience Discovery: Reflecting on the Nobel Prize Awarded to Golgi and Cajal in 1906.

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By the late 1830s, when the cell theory was articulated by Theodor Schwann (1810–1882) and Matthias Schleiden (1804–1881), virtually everything we know today about human brain macroanatomy—what can be seen with the naked eye and scalpel, or in a functional MRI—had already been discovered. The great problem faced by nineteenth century neuroscience was the exact microanatomical relationship between one adult nerve cell and another. Drama at the Nobel Prize ceremony in 1906 centered on diametrically opposite theories about the essential nature of this interneuronal relationship, based, incredible as it may sound, on key evidence derived from the same technique. The players were, of course, Camillo Golgi (1843–1926) and Santiago Ramón y Cajal (1852–1934), and the critical method was the “black reaction” that Golgi first briefly documented in 1873.

Golgi published his monumental book *Sulla fina anatomia degli organi centrali del sistema nervoso* in 1885, just before Cajal began using the method, and in it supported the reticular theory of nervous system organization. Importantly, however, he did narrow the then current view that all neuronal processes (axons and dendrites) form a continuous anastomotic network, to the claim that axons alone participate in the reticulum, assigning instead a nutritive, non-conductive role to dendrites. Cajal summarized his much more extensive, systematic, and incisive research in the masterpiece *Textura del sistema nervioso del hombre y de los vertebrados* (1899–1904), where he argued that neurons interact by way of contiguity rather than continuity, and that under normal circumstances conduction usually proceeds from dendrites and cell body to axon and its terminals. The first conclusion became known as the *neuron doctrine* and, unlike the reticular theory, allowed for control points between neurons in a circuit—the junctions soon to be named synapses by Charles Sherrington (1857–1952). And the second conclusion was refined as the *functional polarity theory* or law: generally speaking, neural impulses are rectified or travel in one direction: they are received by dendrites and cell body, and transmitted via the axon to the next cell in a network—although, importantly, he cited retinal amacrine cells, olfactory interneurons, and interstitial autonomic neurons as possible exceptions.

Cajal’s evidence and interpretations received overwhelming support in the decades to follow, and the electron microscope was used in the 1950s to prove that axons do not form a continuous anastomotic reticulum, and to prove that there is a very narrow intercellular cleft (below the light microscope’s resolution limits) at synapses between axon terminals and dendrites and cell bodies. But the other major contributions to twentieth century neuroscience could hardly have been even imagined by pioneers like Golgi and Cajal—the cellular and molecular basis of electrical impulse conduction along neuronal plasma membranes, exocytosis and ligand-receptor interactions at chemical synapses, gap junctions, genomic involvement in day-to-day neuronal function, and so on.

The Cajal Club has played an important role in analyzing the key contributions of Golgi and Cajal—which are nicely summarized in their 1906 Nobel lectures. The Club was founded in 1947, and later generously endowed, by the innovative neuroanatomist Wendell J.S. Krieg of Northwestern University, and so is the oldest neuroscience organization in North America (<http://cajalclub.org>). The Club's first international meeting was held in 2001, under the Presidency of Charles E. Ribak, at the Cajal Institute in Madrid, to celebrate the 150th anniversary of the namesake's birth. One result was the publication of a collection of 37 chapters on the theme of a resulting book, *Changing Views of Cajal's Neuron*, edited by Efrain C. Azmitia, Javier DeFelipe, Edward G. Jones, Pasko Rakic, and Charles E. Ribak (Elsevier, Amsterdam, 2002).

The centenary of Golgi and Cajal's Nobel Prize offered another wonderful opportunity for the Club to celebrate, and the perfect solution arrived via a letter from Gunnar Grant to then Secretary/Treasurer Peter J. Ralston, offering the Nobel Forum's facilities at the Karolinska Institute in Stockholm to host a meeting of the Cajal Club in 2006. As President of the Club at the time this seemed to me our best choice of venue, a view heartily supported by the other Club Officers and Cajal Club Foundation Corporation Board Members. Gunnar Grant, Sten Grillner, and Tomas Hökfelt of the Department of Neuroscience at the Karolinska Institute acted as the local organizing committee and arranged for the conference to be held on June 11–13—with an opening reception hosted by the Embassy of Spain, through the generosity of Juan José Sanz (Cultural Counsellor to the Embassy), and the Instituto Cervantes in Stockholm, through the good graces of Gaspar Cano (Director of the Instituto).

The first morning session on Developmental and Evolutionary Neuroscience (chaired by Larry Swanson) featured lectures by Pasko Rakic (Making a map of the mind: from silver impregnations to genetic engineering), Andrew Lumsden (Brainstem development: early patterning by segmentation and local organizers), Liqun Luo (Exploring neural circuits using genetic mosaics in flies and mice), and Harvey Karten (Cells, circuits, and genes: evolutionary origins of neocortex). This was followed by a spectacular exhibition of *Art in Science: Cajal, Golgi, Retzius*, organized by Ove Hagelin (Curator of the Högströmer Medico-Historical Library, Karolinska Institute), who also arranged a display of books and articles inscribed by Golgi and Cajal to Gustav Retzius, the great Swedish neuroanatomist. The afternoon session consisted of history and named lectures (chaired by Larry Swanson, President-Elect Edward G. Jones, and Tomas Hökfelt) and featured Gunnar Grant (How Golgi shared the 1906 Nobel Prize in Physiology or Medicine with Cajal), the Wendell J.S. Krieg Lifetime Achievement Award winner Anders Björklund (Use of stem cells for brain repair), the Cajal Club's annual Pinckney J. Harman Lecturer Bert Sakmann (Cortical microcircuits and maps: structure and function), and Hans Jörnvall, Secretary of the Nobel Assembly (The Nobel Prize: a history).

The second morning session was on Systems Neuroscience (chaired by Edward G. Jones) and featured lectures by Apostolos Georgopoulos (Dynamic brain mechanisms of cognitive processing), Sten Grillner (Intrinsic functioning of neuronal networks controlling a goal-directed behavior: pattern generation, steering, and initiation), Leo Chalupa (Synapses of the retinogeniculate system) and Kevan Martin (Canonical circuits of neocortex). This was followed by an excellent poster session organized by Marina Bentivoglio, with a Cajal Club prize for the best to Andreas Montelius. The final session, on Cellular and Molecular Neuroscience, was chaired by Past-President John H. Morrison. Speakers included Seth Grant (Molecular network organization of the synapse proteome and the emergence of behavior), Patrik Ernfors (Transcriptional control of neuronal subtype specification in the neural crest), Catherine Woolley (Hormonal control of synaptic structure and function), and Larry Swanson (The organization of neural systems controlling motivation and emotion). The closing Banquet was held at the Karolinska Institute's Svarta Räfven and featured after dinner presentations on Cajal by Javier DeFelipe and on Golgi by Marina Bentivoglio.

For this Special Issue of *Brain Research Reviews*, the Guest Editors decided to expand the list of invited participants from symposium speakers to Club Officers and Board Members, Symposium Organizers, and Past Club Presidents. The charge to authors was to write an essay of substance and lasting value that reflects on how one's field has changed since the end of the nineteenth century, especially in relation to Golgi's and Cajal's work, with an eye on where the field may be headed in the future.

The symposium could not have been a success without the very generous support of Elsevier (special thanks to Paul Carton) and AstraZeneca (special thanks to Christer Köhler). Gratitude is also warmly extended to the International Brain Research Organization (IBRO) for providing a substantial grant to support student travel to the symposium, and to the Instituto Cervantes Stockholm and Embassy of Spain for hosting the opening reception. And finally, words cannot express my thanks to Secretary/Treasurer Chuck Ribak and Tomas Hökfelt for the extraordinary amount of time and effort they put into making the symposium a success. Speaking for all of the Guest Editors, we hope that the collection of essays presented here contributes in some small way to our understanding of the tremendous advances made by neuroscience in the century following the pioneering research of Golgi and Cajal.

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