

The Scientific Method through the Lens of Neuroscience; From Willis to Broad

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Abstract:

In an age of unprecedented scientific achievement, I argue that the neurosciences are poised to transform our perceptions about life on earth, and that collaboration is needed to exploit a vast body of knowledge for humanity's benefit. The scientific method distinguishes science from the humanities and religion. It has evolved into a professional, specialized culture with a common language that has synthesized technological forces into an incomparable era in terms of power and potential to address persistent problems of life on earth. When Willis of Oxford initiated modern experimentation, ecclesial authorities held intellectuals accountable to traditional canons of belief. In our secularized age, science has ascended to dominance with its contributions to progress in virtually every field. I will develop this transition in three parts.

First, modern experimentation on the brain emerged with Thomas Willis in the 17th Century. A conscientious Anglican, he postulated a "corporeal soul," so that he could pursue cranial research. He belonged to a gifted circle of scientifically minded scholars, the *Virtuosi*, who assisted him with his *Cerebri anatome*. He coined a number of neurological terms, moved research from the traditional humoral theory to a structural emphasis, and has been remembered for the arterial structure at the base of the brain, the "Circle of Willis."

Second, the scientific method is briefly described as a foundation for understanding its development in neuroscience. Scientists now are necessarily professionals, who are credentialed and are engaged in scientific specialties. This section of the paper is sometimes referred to as the "heroic period" for its noteworthy pioneers. Their accomplishments paved the way for unprecedented growth in the neurosciences at the end of the 20th Century. Two illustrations demonstrate a preoccupation with brain (neuron doctrine) and mind (development of psychology) throughout the maturation stage. The neuron doctrine was formulated by creative use of cellular stains and improved microscopy: Ramón y Cajal, Golgi, Nissl, Weigert, Waldeyer, and Sherrington. Early options for the subject of psychology as science were consciousness (Wundt, James) and unconsciousness (Freud, Jung). In their wake were Gestalt (Wertheimer, Koffke, Köhler), behaviorism (Watson, Skinner), and mechanical intelligence. In the mid-20th century psychologists questioned a partitive approach to the mind and non-empirical theories. Governmental support for scientific research led to technology that dramatically expanded the neurosciences. The issues of the mind and neurophysiology have synthesized into the cognitive neurosciences, which are concerned with the biological substrates of mental processes and their behavioral manifestations.

Third, how does the world marshal neuroscientific and genetic breakthroughs to serve its urgent problems? The collaborations of the past point to the need for an institutional hub to coordinate the resources at our disposal. The Broad Institute was founded in 2004 to transform medicine through molecular knowledge. Its goals are holistic, so it adds a bodily dimension to the traditional mind/brain focuses of neuroscience. This collaborative model is very promising for the kinds of challenges that we face today. The paper has presented some information to show us that the scientific method has created distinctive academic disciplines with a common language. Accordingly, a neuroscientist is a professional practitioner in a specialty that seeks to advance our understanding of mind/brain/body connections through research, medicine, and the affiliations that sponsor collaboration in the field.

Introduction

My topic concerns the scientific method as viewed through the lens of neuroscience. I will present it with a view to the round table's subject, "Religion and Science after Darwin." My experience at gatherings like this and Templeton's Metanexus Institute has impressed me with the fact that modern differences between science and the humanities in general can be traced to the modern scientific method and its social implications. Science has had an abiding commitment to the derivation of knowledge about nature through its experimental method. Scientific disciplines have evolved with a standard procedure for their open-ended discoveries of natural principles. The humanities and religions have argued competing claims differently, because of their concerns about traditional texts and authorities, interpretive methods, differing concepts of deity, intangible values, and elusive goals have usually lacked the empirical anchors of scientific

research. At least from the early-modern setting of Galileo, scientific theories should not be equated with religious dogma.

I come to this presentation with indebtedness to academic and charitable experiences. First, I earned a doctorate in humanities at the University of Texas at Dallas, a program that mandates inter-(or cross-) disciplinary learning. I left the doctoral program with a conviction that the 20th Century was an unprecedented age of scientific achievement. It witnessed advances from a quantum view of reality to quantum chromodynamics, from Rutherford's "solar-system" atomic structure to Gell-Mann/Zweig's leptons and hadrons to a search for a "Standard Model" for understanding gravity, from basic telescopes to interstellar exploration, and from telephonic communications to the worldwide web.

Though a humanities professor for about thirty years, I determined to adopt the neurosciences as a personal passion about fourteen years ago. An earlier commitment probably would have led to a different profession. My pleasure has been to watch exponential growth in the neurosciences over the last three decades. Some of the finest minds of the century have given me a sensitivity to human development, learning differences, addictive behaviors, and neural pathologies that have promoted my self-understanding as well as my attempts to reach out to my students and family.

Second, I have been involved for thirty-six years with medical and educational endeavors in India and America's inner cities. These involvements have impressed me with the power of social environment and nurturing influences in the formation of our brains and our lives. I wish that we could analyze humanity and our problems without an exhausting interplay between genetics, relationships, and environments. But we can't!

Thus, I will argue that the neurosciences are poised to transform our perceptions about life on earth, and that collaboration is needed to exploit a vast body of knowledge, personal and social, for humanity's benefit. This has involved significant changes, which I will try to simplify. Religious dominance over the sciences around the 17th Century has given way to science's ascendancy over religion and the humanities in this century. I will develop this transition in three parts. Firstly, in my opinion, modern neuroscience that is based on experimentation began with Thomas Willis of Oxford, who was careful to mollify ecclesial authorities as he formed his views of the brain. Secondly, I will briefly discuss the dynamic growth and maturing methods of the neurosciences in the late nineteenth and twentieth centuries. The period could be subdivided, but the notions of formation under Willis and maturation of science's common method and language must suffice for our purpose. Thirdly, I will argue that the proliferation of knowledge in genetics and neurosciences raises the need for collaboration, if we are to use the knowledge for our world's critical needs. The scientific method has allowed for complementary expertise and calls for resources, financial and otherwise, that will facilitate our expanding knowledge of the most complex entity in the universe. I doubt that methods in the humanities and religion can match the global potential of collaborative science.

Formation, Willis and the *Virtuosi*

Thomas Willis (1621-75) is considered by historians of neuroscience as “the founder of modern neuroanatomy.”¹ A prominent physician in a transitional generation, he witnessed an implicit decline in the church’s influence over scientific research and an explicit rise in experimentation over tradition as a source of physiological knowledge. He received his Bachelor of Medicine in 1646, served as a royal physician to Charles I, and became a Doctor of Medicine in 1660. Willis was born a mere twenty-five years after René Descartes, but he replaced “the great Cartes”’ emphasis on humoral theory and the pineal gland with an hypothesis about the correlation of neural structures and functions. Oxford itself was in transition from a preserver of Aristotelian traditions to a center of new ideas.

Willis was a conscientious Anglican, who hosted a congregation in the 1650s. He dedicated his *Cerebri anatome* (1664) to the Archbishop of Canterbury, for “it was by your means (Most Noble Prelate) that I obtained the votes in the Famous University for the place of Sidly Professor.”² The congregation included John Fell, brother of his first wife Mary and one of his biographers-to-be. In the epilogue of *Cerebri anatome*, he promised a second book on the “body and soul” relationship, so that there would be no ecclesial offense over his research. His *De anima brutorum* (1672) distinguished two souls, an “immortal soul” and a “corporeal soul.”³ The former distinguished humanity from the beasts, while the latter was the material brain that was shared with other animals.⁴ Thus, in Willis’ view, the corporeal brain would be incapable of surviving the body and could be studied by scientists. The Archbishop of Canterbury viewed Willis’ position as acceptable, thus freeing him to pursue his research on neural functions.

His associations at Oxford promoted his growing interest in the brain. After receiving his doctorate, he was appointed Sedleian Professor of Natural Philosophy at Christ Church. He used the position to study the senses and nerves.⁵ William Harvey (1578-1657) resided in Oxford between 1642 and 1646 and was instrumental in replacing the traditional view of blood as humoral “sludge” with a scientific theory in which heart valves continuously circulated it through arteries and veins.⁶ Robert Boyle (1627-1691), a fellow member of the “experimental

¹ Louise Marshall and Horace Magoun, *Discoveries of the Human Brain* (Totowa, NJ: Humana Press, 1998), 46. For a complete biography, the reader may consult Hansruedi Isler, *Thomas Willis, ein Wegbereiter der Modernen Medizin, 1621-1675* (Stuttgart: Wissenschaftliche Verlagsgesellschaft, 1965). In English, *Thomas Willis; Doctor and Scientist, 1621-75* (New York: Hafner, 1968).

² Thomas Willis, *The Anatomy of the Brain, The 1681 edition, reset and reprinted, with the original illustrations by Sir Christopher Wren* (Tuckahoe, NY: USV Pharmaceuticals, 1971), 1-2. The original title was *Cerebri anatome, cui accessit nervorum descriptio at usus* (London: J. Martin and J. Allestry). The volume was initially published in Latin in 1664 and was translated into English by Samuel Pordage in 1681. Cf. Kenneth Dewhurst, *Thomas Willis as a Physician* (Los Angeles: Clark Memorial Library, UCLA, 1964), 7-10.

³ The treatise was reprinted as “Two Discourses Concerning the Soul of Brutes,” in *Practice of Physick*, trans. S. Pordage (London: Dring, Harper, and Leigh, 1684).

⁴ Contrary to Descartes, Willis held that animals have rudimentary perception, cognition, and memory. On this point he sided with Pierre Gassendi, whose ideas were discussed by the *Virtuosi*. Gassendi held that animals could learn at a subhuman level.

⁵ The Sedleian position required lectures, at least twice weekly, on the Aristotelian tradition. Willis shifted the opportunity to scientific investigations of the “affections of the soul.” By “soulful affections” he meant studies of the brain. Kenneth Dewhurst, ed., *Thomas Willis’s Oxford Lectures* (Oxford: Sandford Publishers, 1980).

⁶ Harvey’s *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus* was published in 1628. His work was formed under the tutelage of Hieronymus Fabricius at Padua, and his experimental method paralleled Willis and kindred scientists at Oxford.

philosophical clubbe” (or “Invisible College”) was laying the groundwork of modern chemistry at the same time.⁷

These men were members of the *Virtuosi*, scientifically inclined academics who played an important role in forming the Royal Society of London. Founded in 1660, the prestigious society was dedicated to the promotion of “natural knowledge.” Willis was one of the original forty names on the role of the founders.⁸ He was also honored by recognition as a fellow of the Royal College of Physicians in 1664.

Other members of the *Virtuosi* assisted Willis with *Cerebri anatome*. Richard Lower, an inseparable friend and talented experimentalist, assisted with the dissections. Thomas Millington, a fellow physician who succeeded Willis as Sedleian Professor, contributed anatomical knowledge as well. And Christopher Wren, the noted architect of St. Paul’s Cathedral, helped with the dissections and drew most of the anatomical plates in the book, which were generally acknowledged as the most advanced yet produced. The landmark volume was a collaborative effort that bore the name of Willis:

Willis, Wren, Lower, and others in this circle of talented men not only worked together, but strove for a new spirit of cooperation. They felt it important not to compete and preached the sharing of thoughts and skills....By collaborating, they believed, researchers could more ably advance the cause of science.⁹

Willis’ writings reflected his commitment to the experimental method as the source of his understanding of the brain. Though “it may have been the spirit of the times to experiment,” Willis excelled.¹⁰ His research involved extensive dissections, chiefly corpses from the gallows and a wide variety of animals and insects.¹¹ Few anatomists at the time even cared about invertebrates as the objects of scientific research. His clinical observations stimulated fresh thinking about the nervous system among his peers, who proceeded to test and improve his findings, a motivation that was one of his significant contributions according to some scholars.

Charles Sherrington, 1932 Nobel laureate, praised Willis as the one who “practically refounded anatomy and physiology of the brain and nerves.”¹² Among many notable accomplishments, Willis’ language and observations about structure and function will be noted here. First, he coined “neurologie” to refer to the cranial, spinal, and autonomic nerves as

⁷ Boyle published his experiments with the air pump in 1660 under the title *New Experiments Physico-Mechanicall, Touching the Spring of the Air, and Its Effects*, which first mentioned his law that the volume of a gas varies inversely to its pressure. He published *The Sceptical Chemist in 1661*, in which he viewed the elements as undecomposable constituents of material bodies.

⁸ Thomas Sprat, *The History of the Royal Society of London for the Improving of Natural Knowledge*, reprint ed. (London: Elibron Classics, 2005), 433, where he appears simply as “Dr. Willis.” In the spirit of Willis and his contemporaries, Sprat noted: “In their *Method of inquiring*, I will observe how they have behav’d themselves in Things that might be brought within their *own Touch and Sight* . . . I fhall lay it down as their *fundamental Law*, that whenever they could poffibly get to *handle* the Subject, the *Experiment* was fill perform’d by fome of the *Members* themselves,” p. 83.

⁹ Stanley Finger, *Minds Behind the Brain* (Oxford: Oxford University Press, 2000), 90

¹⁰ M. Neuburger, “Carl Weigert (1845-1904),” in *The Historical Development of Brain and Spinal Cord Physiology Before Flourens*, trans and ed. by Edwin Clarke (Baltimore: Johns Hopkins University Press, 1981), 17.

¹¹ Willis, *Anatomy of the Brain*, p. 6: “That the perfect knowledge of the Brain and its parts may be gained, it is necessary not only to dissect and look into mens Heads, but all other kind of living Creatures heads.”

¹² C. S. Sherrington, *Man on his Nature* (Cambridge: Cambridge University Press, 1941), 245. Similarly, Stanley Finger wrote in *Origins of Neuroscience: A History of Exploration into Brain Function* (Oxford: Oxford University Press, 1994), 24: “Willis, more than any other person in the post-Renaissance period, provided a sound basis and powerful stimulus for looking at the functional contribution of individual brain parts.”

differentiated from the brain and spinal cord. The term first appeared in the English edition of *Cerebri anatome* in 1681 and later, of course, assumed a much broader meaning. He also coined a number of anatomical terms like lobe, hemisphere, and corpus striatum. Second, he was an important figure in the shift from ventricular to structural interpretation. The dominant view of the Renaissance era was that memory was stored in the posterior ventricle. Willis saw “no reason to discourse on these vacuities.”¹³ Instead he proposed that memory of words and ideas resided in the “utmost [cortical] banks” of the cerebral hemispheres. He noted the smoother cortices of animals and changed the earlier view that cortical “convolutions” were intestine-like masses of random coils. In his Sedeian lectures and in the *Cerebri anatome* he related the convolutions and gyrations to the variety and number of humanity’s higher faculties.¹⁴ He described the “Cerebel” [cerebellum] as the primitive regulator of the autonomic nerves of internal organs in place of the earlier theory that it stored memory.¹⁵ He described and named the corpus striatum accurately for the first time.¹⁶ From evidence in autopsies and newborn pups, he associated the corpus striatum with movement and sensation.

Above all, Willis has been known for his description of the arterial structure at the base of the brain. The basal arteries were depicted first by Guilio Casserio (1561-1616), but Willis improved observation by injecting a dye into a major artery and tracing its distribution in his dissection. In this way he explored the anastomoses of the arteries that form the circle. He was the first scientist to number the cranial nerves in the order in which they are now enumerated by neuroanatomists. A part of this configuration is a cerebral arterial circle, which is referred to as “the circle of Willis” (or the “Willis Polygon”). It is formed by a number of arteries: the anterior cerebral artery (left and right), the anterior communicating artery, the internal carotid artery (left and right), the posterior cerebral artery (left and right), and the posterior communicating artery (left and right).¹⁷ The circle cemented Willis’ reputation in scientific memory.

In summary, Willis used his medical and academic opportunities to experiment extensively on human corpses, animals, and invertebrates. His discoveries replaced the humoral

¹³ Willis, *Anatomy of the Brain*, pp. 65-66.

¹⁴ *Ibid.*, pp. 59-60, Cf. the helpful translation of E. Clarke and C. D. O’Malley, *The Human Brain and Spinal Cord. A Historical Study Illustrated by Writings from Antiquity to the Twentieth Century* (Berkeley, Los Angeles: University of California Press, 1968), 388-89. His explanation of the abundance of blood vessels in the cortex as the source of “ethereal spirits” was borrowed from the past. In a famous critique in the Paris residence of Monsieur Thévenot, the Danish anatomist Nicolaus Steno expressed reservations about Willis’ blind repetition of unconfirmed concepts. Kenneth Dewhurst, “Willis and Steno,” in *Steno and Brain Research in the Seventeenth Century*, ed. G. Sherz, 43-48 (Oxford; Pergamon Press, 1968). Willis received the criticism in a positive spirit and admitted that he was unable to veer from his speculations or his fanciful iatrochemistry.

¹⁵ Willis, *Anatomy of the Brain*, chaps. 16-17. He would have been more correct to associate the cerebellum with involuntary movements of skeletal muscles such as walking and drinking. In the 1800s the role of the medulla in governing autonomic functions became clearer.

¹⁶ *Ibid.*, p. 78. Again, Willis’ thinking was an advance, but he would have been more accurate to relate sensation to the thalamus.

¹⁷ The basilar artery and middle cerebral arteries are not considered part of the circle. Considerable anatomic variation can exist in the circle, about 65% in a study of 1413 cases. A common variation is that the proximal part of the posterior cerebral artery is narrow and its ipsilateral posterior communicating artery is large, so that the internal carotid artery has to supply the posterior cerebrum. The circle creates redundancies in circulation, so that, as in cases of subclavian steal syndrome (a narrowing of the subclavian artery), the circle is called upon to preserve blood flow to upper limbs. Cf. www.anatomyatlases.org/AnatomicVariants/Cardiovascular/Text/Arteries/CircleofWillis.shtml [accessed on May 18, 2009]. Also, C. Uston, “Dr. Willis famous eponym: the circle of Willis,” *Journal of the History of Neuroscience*, 14 (March 2005): 16-21. And R. S. Lord, R. Adar, and R. L. Stein, “Contribution of the circle of Willis to the subclavian steal syndrome,” *Circulation* 40 (December 1969): 871-78.

and ventricular emphases with more accurate descriptions of cerebral structures and functions. But, like others of the time, he worked with a view to ecclesial approval. In centuries that followed, scientists would refine their methods and increase our knowledge of the brain and its dominant role in every area of life.

Maturation, the Neuron Doctrine and Cognitive Science

The modern scientific method is an iterative process by which scientists collectively use standard criteria to construct an accurate understanding of the world.¹⁸ The method begins with an observation, a question, or a problem that has surfaced from cumulative, sophisticated research. These starting points may be creatively new or past findings that need refinement. Research follows to determine to extent of knowledge about the point. An hypothesis is constructed as an operational definition to explain the phenomena, which must be observable and quantifiable. That is, it must be unknown in outcome, testable by experimentation, and as procedurally unbiased as possible. Willis illustrated the importance of experimental testing in the method, even if some of his conclusions were rudimentary. In scientific experimentation all data should be preserved and the procedure should be fully described and replicatable.¹⁹ The scientist must analyze the data and draw conclusion(s) from the experiment. Experimentation continues until the hypothesis has a predictable conclusion. Then, the results must be communicated to professional peers for review. If the appropriate scientific community reaches a consensus about the accuracy of the hypothesis, then it usually attains the status of a theory or a law as a principle of nature. A scientific theory is a demonstrated hypothesis or a group of related hypotheses, which form a conceptual framework that explains existing phenomena and predicts new ones. Only after repeated tests of incompatible phenomena do scientists question or modify theories or formulate new ones.²⁰ A new theory not only assimilates the older one but also extends it, sometimes into a new insight about nature.²¹ Normally, scientists prize the “elegance,” or profound simplicity, of the theory’s expression. This process is exemplified by the evolution of our understanding of the neuron doctrine and the development of psychology, which are described below.

My argument in this section assumes this method and earmarks the practical aspects of background research, peer review, and social applicability as the reasons why science has

¹⁸ The “modern scientific method” can be traced to Francis Bacon’s *Novum Organum* (1620), which outlined a new logical empiricism to replace older syllogistic thinking. René Descartes’ *Discourse on Method* (1637) advanced a framework of guiding principles. In the 19th Century C. S. Peirce proposed the hypothesis/testing foundation that undergirds contemporary practice. Cf. C. S. Peirce, *Essays in the Philosophy of Science*. New York: Bobbs-Merrill, 1957, and *The Essential Peirce: Selected Philosophical Writings*: Bloomington, IN: Indiana University Press, 1998.

¹⁹ Research granting agencies like the National Science Foundation and professional journals like *Nature* and *Science* mandate archival standards that allow experiments to be replicated (cf. www.nature.com/nature/submit/get_published/index.html [accessed November 11, 2008]).

²⁰ *Science* sponsored a “Keystones of Science” project in which various articles were used to exemplify the scientific method. They show how discovery of the structure of DNA exemplify the various aspects of the method. From Mendel’s studies, scientists knew that genetic inheritance could have a mathematical description, but the mechanism was not known. Lawrence Bragg’s laboratory at Cambridge University used x-ray diffractions to try to determine the structure of DNA. Linus Pauling hypothesized that DNA was a triple helix. Francis Crick and James Watson knew that this conclusion was incorrect from experiments that demonstrated that helical structures produced x shapes. They shared their hypothesis with a team from King’s College that included Rosalind Franklin. Her detailed images (specifically photo 51 of the wetter, extended B form) confirmed the helical structure. Watson and Crick were then able to infer the Nobel-winning double helix by modeling the shapes of the nucleotides.

²¹ Thomas S. Kuhn, *The Structure of Scientific Revolutions*, 3rd ed. (Chicago: University of Chicago Press, 1996).

emerged with its distinctive academic disciplines in the modern era. My argument has some significant implications for the subject of this paper. The primary one is that scientists are necessarily professionals, who are credentialed and are engaged in scientific disciplines. I wish that I could be credentialed and placed in a research laboratory, but I am only an informed observer who can help the neurosciences by advocating financial resources in an understandable way to appropriate authorities. This professional recognition is very important because amateurs and pseudoscientists are seemingly innumerable, and they clog media with misinformation and iconic nonsense.²² I will illustrate the argument with two examples from the “heroic period,” so named because of outstanding pioneers who paved the way for our present. I will seek to show how daunting an accurate understanding of contemporary neuroscience has become.

The first example is the “neuron doctrine,” the foundational principle that neurons are the basic structural and functional units of the nervous system.²³ An earlier view was that the nervous system was a reticulum, a weblike network of tissue rather than discreet cells with somata (cell bodies), axons, and dendrites that communicate with one another through synapses.²⁴ Its “Law of Polarization” states that transmissions between neurons move from dendrites as receptive extensions of cell bodies toward axons as transmitters of action potentials. The problem before the doctrine was that cells could not be microscopically distinguished.

The most important breakthrough came in the latter part of the 19th Century, when Santiago Ramón y Cajal (1852-1934) used a technique that was discovered by Camillo Golgi (1843-1926).²⁵ Silver chromate particles were attached to the neurilemma (the neuron membrane) by reacting silver nitrate with potassium dichromate. The silver randomly blackened a small percentage of the neurons, which were sharply contrasted against a yellow background.²⁶ Ramón y Cajal realized that the technique did not stain myelinated cells, so he experimented on younger (less myelinated) brains. With visual clarity, he was able to produce exquisite drawings of neural structures. This ability to see neurons discreetly led to the acceptance of the neuron doctrine.²⁷ Heinrich Wilhelm Gottfried von Waldeyer-Hartz also made a valuable contribution. He used the research of Ramón y Cajal and Golgi to publish and promote the doctrine in the German-dominated field of microscopic anatomy. His highly acclaimed papers in *Deutsche*

²² Of course, the humanities and religion are beset with similar problems, and they too have academic safeguards,

²³ T. H. Bullock, “Neuron doctrine and electrophysiology,” *Science* 129 (1959): 997-1002.

²⁴ E. R. Kandel, J. H. Schwartz, and T. M. Jessell, eds. *Principles of Neural Science*, 4th ed. (New York: McGraw-Hill, 2000), 23. Cf. Santiago Ramón y Cajal, *Neuron Theory or Reticular Theory: Objective Evidence of the Anatomical Unity of Nerve Cells*, trans. M. Purkiss and C. Fox (Madrid: Consejo superior de investigaciones científicas, 1954). The reticular theory is often associated with Joseph von Gerlach, who used carmine stain with nonmyelinated nerves to advance an “interconnected fusion” theory in the 1850s. In 1886 Wilhelm His hypothesized that transmission of nerve impulses did not require fusion.

²⁵ Ramón y Cajal and Golgi shared the Nobel Prize in Physiology or Medicine in 1906. Cf. Juan De Carlos and José Borrell, “A Historical Reflection of the Contributions of Cajal and Golgi to the Foundations of Neuroscience,” *Brain Research Reviews* 55 (August 2007): 8-16. Along with his technique, Golgi also identified the intracellular reticular apparatus in 1898, now known as the “Golgi apparatus.” Cf. A. Dröscher, “The History of the Golgi Apparatus in Neurones from Its Discovery in 1898 to Electron Microscopy,” *Brain Research Bulletin* 47 (October 1998): 199-203. Franz Nissl (1860-1919) used aniline to stain ribosomal RNA purplish-blue, giving the cytoplasm a mottled appearance. His intracellular stains are still used to examine nuclei, since axons do not stain with his method. Karl Weigert (1845-1904) developed a stain for the myelin sheath around axons. The stains and advances in microscopy were invaluable for 20th-century neuroscience.

²⁶ The reason for this random isolation of the cells for visual analysis is still unexplained.

²⁷ Ramón y Cajal also proposed the “Law of Dynamic Polarization” in 1891 with indebtedness to Arthur Van Gehuchten, *Recollections of My Life*, trans. E. H. Craigie and J. Cano (Philadelphia: American Philosophical Society, 1937), 382-92.

medizinische Wochenschrift summarized the doctrine, consolidating it over against the reticular theory and coining the term “neuron” in the process.²⁸

A related discovery with foundational implications concerned neural communication through “synapses,” so named by Charles Sherrington (1857-1952) who shared the 1932 Nobel Prize in Physiology and Medicine with Edgar Adrian.²⁹ As a physiologist, Sherrington noticed that conduction in the brain’s “white matter” (myelinated axons) was faster than in the “gray matter.”³⁰ So, on the basis of a theoretical “hunch,” he hypothesized that neurons were structural units with a space or cleft between them. This was not observed until the early 1950s with electron microscopy. Biologically, there are electrical, immunological, and most commonly chemical synapses. Connecting in a variety of ways, a single neuron may have hundreds of synapses. Typically, chemical synapses pass information axodendritically with neurotransmitters (chemical messengers) across the synaptic cleft. Neurons grade the excitatory and inhibitory signals to determine which potentials will communicate with another neuron. The neurotransmitters, when released from the post-synaptic receptors, are either reabsorbed to be repackaged for future release (endocytosis) or are broken down metabolically (usually through astrocytes). Consistent with advances in the scientific method, synaptic experiments have formed their own specialized field of research in cellular biology.³¹ For example, Shawn Ferguson and associates have demonstrated that synaptic vesicles in the pre-synaptic terminal can resynthesize neurotransmitters in the absence of dynamin 1, a protein that was formerly viewed as necessary for the formation of vesicles.³²

Beyond such micro discoveries, the neuron doctrine has had to be refined repeatedly through the years. First, electrical synapses are more common in the central nervous system than once thought. They not only allow bidirectional transmission of neural communications, but they

²⁸ Heinrich Waldeyer, “Über einige neuere Forschungen im Gebeite der Anatomie des Centralnervensystems,” *Deutsche medizinische Wochenschrift* 17 (1891): 1213-18, 1244-46, 1287-89, 1331-32, and 1350-56. Wilhelm His (1890) and Albrecht Kölliker (1896) introduced “dendrite” and “axon” to neurology respectively. A. Kölliker. *Handbuch der Gewebelehre des Menschen*, 6th ed. (Leipzig: Engelmann, 1896).

²⁹ Sherrington and his colleagues coined the term from the Greek *syn* (together) and *haptain* (to clasp). For an extended discussion of synapses in the context of human living, see Joseph LeDoux, *Synaptic Self: How Our Brains Become Who We Are* (New York: Viking Press, 2002). The complexity of the brain is self-evident. Neurons range in size from four microns (interneurons) to 100 microns (motor neurons). In the adult human brain, estimates are that there are 100 billion neurons and 100 trillion synapses.

³⁰ Willis had noted the phenomena and labeled them “reflections.” Sherrington had derived his insight in the context his research on circuitry of reflexes. He was persuaded by Hermann Helmholtz’s conclusion that reflexes were slower than conduction. Cf. J. P. Swayey, *Reflexes and Motor Integration: Sherrington’s Concept of Integrative Action* (Cambridge: Harvard University Press, 1969), 76. This shows how noteworthy scientific ideas “remain on the table” until they result in satisfactory explanation or plausible prediction. Sherrington concluded his Silliman Lectures at Yale (1904) by stating, “It is then around the cerebrum, its physiological and psychological attributes, that the main interest of biology must turn.” *The Integrative Nature of the Nervous System* (New Haven: Yale University Press, 1906), 390.

³¹ Venkatesh Murthy, Harvard neuroscientist who began his research at the Salk Institute for Biological Studies, recently stated in an interview that only in the past decade have scientists begun to draw a reasonable diagram of how synapses work – how they grow, load up the right chemicals, pass on information, communicate with one another, and get recycled. Corydon Ireland, “How brain cells make good connections,” *Harvard University Gazette* (February 14-20, 2008): 3.

³² Shawn Ferguson et al., “A selective activity-dependent requirement for Dynamin 1 in synaptic vesicle endocytosis,” *Science* 316 (April 2007): 570-74. Cf. Phillip Robinson, “How to fill a synapse,” 316 (April 2007): 551-53. This is a good example of peer validation of a discovery in neuroscience.

also connect neurons directly, cytoplasm-to-cytoplasm.³³ Second, dendrites are no longer viewed as passive recipients of information. Instead we know that they, like axons, have ion channels that can generate potentials to and from the soma.³⁴ Third, we know now that an older view that adult brains cannot generate neurons is incorrect. Adults apparently can generate new neurons in the hippocampus and areas related to the olfactory bulb.³⁵ Fourth, our knowledge of the role of glial cells has developed. Glials are ten times more numerous than neurons. Formerly unappreciated in the neural scheme of things, we now know that they are vital for brain health.³⁶ Among their functions, oligodendrocytes, which are glials in the central nervous system, myelinate axons, so that potentials can move rapidly by saltation. These refinements point to the proliferation of neuroscientific knowledge in recent decades, and, as we look forward, how strangers to the developments are left in the wake of an overwhelming amount of information and its new, technical vocabulary.

Beyond the neuron doctrine with its physiological implications, a second example deals with the “hard problem” of psychology, which concerns the “philosophical question of why and how any kind of brain activity is associated with consciousness.”³⁷ In other words, what is the proper subject of a science of the mind? By the late 19th Century, mind had become the last bastion of human sacredness, the only natural phenomenon that had not been scrutinized by materialistic processes. The issue of the soul had been a lingering deterrent to this kind of research. However, in the latter part of the century, two influential pioneers of psychology were engaged in different explanations of mental processes.

Wilhelm Wundt created the first laboratory for experimental psychology in 1879 in Leipzig. He formed the first journal for psychological research in 1881, and in 1895 he began the first research institute for the new subject.³⁸ For him the subject of psychology is consciousness as understood through examination of perception, memory, learning, and reasoning.³⁹ He requires our acceptance of consciousness as a natural reality. Subjective experience is just as factual as alternations between wakefulness and sleep. Interestingly, his experimentation led him to conclude that people are primarily willful and emotional creatures; we are motivated by what

³³ B. Connors and M. Long, “Electrical Synapses in the Mammalian Brain,” *Annual Review of Neuroscience*, 27 (2004): 393-418.

³⁴ M. Djurisic et al., “Voltage imaging from dendrites of mitral cells: EPSP attenuation and spike trigger zones,” *Journal of Neuroscience* 24 (2004): 6703-14.

³⁵ The cortical issue is still under discussion. However, see E. Gould et al., “Neurogenesis in the neocortex of adult primates,” *Science* 286 (1999): 548-52. Gould, Graziano, and Gross have even suggested that neurogenesis can occur in the neocortex after birth, an area that is vital for cognitive function. Also, D. Kornack and P. Rakic, “Cell proliferation without neurogenesis in adult primate neocortex,” *Science* 294 (2001): 2127-30, and P. Rakic, “Neuroscience. No more cortical neurons for you,” *Science* 313 (2006): 928-29.

³⁶ M. Witcher, et al., “Plasticity of perisynaptic astroglia during synaptogenesis in the mature rat hippocampus,” *Glia* 55 (2007): 13-23.

³⁷ James Kalat, *Biological Psychology*, 6th ed. (New York: Brooks/Cole Publishing, 1998), 444-45.

³⁸ Bringmann, W. G. et al. “Wilhelm Wundt 1832-1920: A Brief Biographical Sketch,” *Journal of the History of the Behavioral Sciences* 11 (July 1975), 287-97.

³⁹ Wundt’s influential work was entitled *Grundzüge der physiologischen Psychologie*. Blumenthal notes: “Lost from view now, as well, is the old German parochialism of the title’s adjective *physiologische* in its 1870s local German usage. That adjective once referred to a methodology rather than a program of reducing psychological processes to physiological mechanisms. . . . we find, however that the book is weighed with theory and philosophy, even to the point of overshadowing its depictions of ‘characteristics of experimental psychology.’” Blumenthal, “A Wundt Primer, The operating characteristics of Consciousness,” in *Wilhelm Wundt in History: The Making of a Scientific Psychology*, eds. Robert Rieber and David Robinson in collaboration with Arthur Blumenthal and Kurt Danziger (New York: Kluwer Academic/Plenum Publishers, 2001), 121-22.

we want before we reason on how to get it. His culminating work was *Principles of Physiological Psychology*, a ten-volume presentation of his system of “internal perception” or the self-examination of mental structures through a person’s desires and choices.⁴⁰ Several of his students became outstanding psychologists in their own right. Among others, Edward Bradford Titchener founded the first psychology laboratory in the United States at Cornell University, and Hugo Münsterberg led a similar laboratory at Harvard University. Münsterberg (1863-1916) is particularly noteworthy as a bridge between Wundt and James. He joined Wundt’s laboratory in 1883, and met William James at the First International Congress of Psychology in 1891. He served at Harvard from the 1890s.

James (1842-1910), like Wundt, was interested in how the mind consciously ordered sensory perceptions. His *The Principles of Psychology* (1890) introduced “stream of consciousness” and “selective attention” to psychological theory.⁴¹ The world, he held, was a mosaic of diverse experiences, which cannot be paused for objective analysis. So, in the stream of life we “selectively respond” to the most useful options. The world is a precarious environment. With a Darwinian twist, we pay attention to beneficial situations according to biological stimuli. The “James-Lange theory of emotion” states counter-intuitively that in experiences of “fight or flight” we are afraid because we flee. We sense a physical stimulus before we express the feeling; or, the mental aspect of emotions are subject to their physiology, not vice versa. Intense experiences are the best view of mental processes, like visual enlargements that can be more clearly analyzed, so James experimented with various drugs to seek clarity on his theories. “Selective attention” in which personal identity is tethered to what we attend to, became an important concept for later thinking about consciousness.⁴²

Contemporaneous with Wundt and James were Freud and Jung. For Sigmund Freud (1856-1939), the unconscious was the subject of psychology.⁴³ People have experiences that they repress, usually infantile sexual trauma.⁴⁴ Repressed memories are dynamic and strive for consciousness, which, he believed, could be facilitated by psychoanalysis (“talking cure”). The goal of Freudian therapy was to free the patient from psychotic symptoms, “hysterical illnesses,” which were caused by unconscious turmoil.⁴⁵ He formulated a famous map of the mind with three aspects to replace his concept of “system unconsciousness.” The id is the source of sexual instincts and drives. It ceaselessly tries to get the ego to do what it wants without regard for consequences. Ego is the reality principle, the values of society (usually taboos) that people internalize and that cause shame and guilt if exposed. It seeks a balance between the id’s

⁴⁰ Wilhelm Wundt, *Principles of Physiological Psychology*, 10 vols. Cambridge: Harvard University Press, 1904.

⁴¹ William James, *The Principles of Psychology*, 2 vols. (London: Macmillan, 1891; reprint New York: Dover, 1950).

⁴² Jon Driver, “A selective review of selective attention research from the past century,” *British Journal of Psychology* 92 (2001): 53-78.

⁴³ Historian Mark Altschule observed, “It is difficult – or perhaps impossible – to find a nineteenth-century psychologist or psychiatrist who did not recognize unconscious cerebration as not only real but of the highest importance,” *Origins of Concepts in Human Behavior* (New York: Wiley, 199).

⁴⁴ In 1895 Freud collaborated with Josef Breuer, his mentor, on *Studies in Hysteria*, which first articulated his theory of repression.

⁴⁵ In October 1885 Freud went to Paris on a traveling fellowship with Europe’s most renowned neurologist of the time, Jean-Martin Charcot. Later in his practice, Charcot had become concerned with hysteria, which encouraged Freud to turn toward psychopathology. Charcot is credited with forming the nascent field of neurology into a modern discipline, in which mental disorders were viewed as signs and symptoms rather than diseases.

hedonism and the super-ego's moralism, a balance that is reflected in social behavior. The super-ego is the moral conscience, which polices the ego's ideals.⁴⁶

Significantly, Freud's theory challenged Descartes' assumption that the human mind knows itself. Willis' contemporary had held that ultimately we cannot comprehend knowledge external to ourselves, but we can "think about ourselves, therefore we are." However, Freud claimed that we can try to understand ourselves, but we cannot know the root causes of our behavior. In a word, our responses are unconscious in their source.

Carl Jung (1875-1961) was a younger follower of Freud until he broke with his mentor in 1911 with a number of contemporaries. Most of them wanted to expand Freud's narrow focus on sexuality. Jung agreed with the unconscious as the subject of psychology, but he expanded Freud's personal theory into a collective unconsciousness, which was inheritable from our common evolutionary history. Our experiences, in his view, are ordered by innate patterns, archetypes that manifest themselves in human behavior such as the individuation of self. Archetypes are common symbols that involve three levels of (un)consciousness. First, the ego is the locus of conscious thought. Second, personal unconsciousness consists of unconscious experiences that can become conscious. Third, collective unconsciousness is never conscious and is not experiential. It is a platonic, instinctual substratum of human life that is reflected in personal consciousness.⁴⁷

The trend of an unconscious basis of psychology was opposed by three nonsequential alternatives that were roughly contemporaneous: Gestaltic, behavioral, and mechanical. Max Wertheimer (1880-1943) with Kurt Koffka (1886-1941) and Wolfgang Köhler (1887-1967) founded Gestalt psychology as a movement. They studied together in Berlin under Carl Stumpf before migrating to American colleges because of the political climate in Germany in the 1920s and '30s.⁴⁸ Their mutual concern was the proper subject of psychology as a science. *Gestalt* means "whole pattern, shape, or form" and refers to the cerebral principle that perceptions are holistic, parallel, and analog. Its fundamental principle of perception is *prägnanz* ("pithiness"), which means that we order percepts in natural situations within an environment that is more than a collection of sensory responses; that is, context forms our perceptions of experience. Methodologically, thinking is analyzed in productive and reproductive ways. "Productive" refers to perceiving experience with spontaneous insight, while "reproductive" refers to perceiving experience on the basis of what is already known. The principle of "psychophysical isomorphism" means that conscious experience correlates with cerebral activity.

Koffka particularly addressed the instability of the scientific method in the first half of the 20th Century. He questioned the partitive approach to questions of perception. Science, he argued, is not the mere accumulation of facts. Scientific research and knowledge is instead

⁴⁶ Sigmund Freud, *The Ego and the Id*, trans. Joyce Crick (London: Hogarth Press, 1927). In *The Interpretation of Dreams*, trans. Joyce Crick (London: Hogarth Press, 1900), Freud called dreams the road to the unconscious and proposed that their analysis was an important method for gaining access to it.

⁴⁷ By platonic, I mean a realm of ideal Forms that are reflected in the shadows of earthly life. Jung's legacy lay in mythography rather than the neurosciences.

⁴⁸ *Gestalt* psychology must be distinguished from Gestalt psychotherapy. One has little to do with the other. Often *Gestalt* is distinguished from structuralism and Wundt. Christian von Ehrenfels introduced the concept *Gestalt* and interpreted it as a secondary quality that emerges from experience. Max Wertheimer insisted that Gestalt is primary to experience, so that the whole is greater than the sum of its parts. Brett King and Michael Wertheimer, *Max Wertheimer and Gestalt Theory* (New Brunswick, NJ: Transaction Publishers, 2005). Köhler and Koffka served as subjects for Wertheimer's studies of the phi phenomenon. Köhler's own studies of chimpanzees extended Edward Thorndike's studies of animal intelligence, stating that they could perceive with spontaneous insight ("aha experiences"). Wolfgang Köhler, *Gestalt Psychology* (New York, London: Liveright, 1947).

“knowledge of the rational system, the interdependence of all facts.” Science, he continued, “is apt to forget that it has not absorbed all aspects of reality, and to deny the existence of those which it has neglected.”⁴⁹

An antithetical alternative was behaviorism as formulated and developed by John Watson and B. F. Skinner. Watson declared that the subject of psychology concerns the prediction and control of behavior rather than consciousness, which is neither empirical nor scientific. In 1913 he declared:

Psychology as the behaviorist views it is a purely objective experimental branch of natural science. Its theoretical goal is the prediction and control of behavior. Introspection forms no essential part of its methods, nor is the scientific value of its data dependent upon the readiness with which they lend themselves to interpretation in terms of consciousness.⁵⁰

Watson’s theory was that people are reactive creatures and that control of behavior was based on an understanding of stimulus and response.⁵¹

Behaviorists were influenced by Ivan Pavlov’s research on conditioned reflexes and Edward Thorndike’s conclusions about animal intelligence. Thorndike had formulated two laws, seemingly obvious but heretofore unstated; namely, animal behavior is reinforced by repetition and keyed to behavioral consequences.⁵² Behaviorism was very prominent for more than a decade, declined briefly, and became resurgent with the work of B. F. Skinner in 1928.⁵³

One can surmise as well that the dominance of behaviorism in mid-20th-Century reflected a desire for a more quantifiable data-driven method. Skinner’s inventive mind was well known.⁵⁴ He invented the operant conditioning chamber to measure interactions between subjects such as rats and pigeons and their environments, the cumulative recorder to measure rate of responses graphically, and a teaching machine to measure learners’ responses to questions.

Skinner labeled his approach “radical behaviorism” to distinguish it from methodological behaviorism that advanced deductively by consensus. He advocated an inductive, data-driven approach that could integrate all perceptual and emotional considerations regardless of an academic consensus. He was introduced to Watson through Bertrand Russell’s *An Outline of Philosophy*, which included the pioneering behaviorist. The idea shifted Skinner’s attention from literature to a scientific study of behavior as a reflection of reinforcing conditioning. His “technology of behavior” used schedules of reinforcement to enhance performance by time (interval) and task (ratio). His “operant conditioning” distinguished him from alternative

⁴⁹ Kurt Koffka, *Principles of Gestalt Psychology* (New York: Harcourt, Brace, and World, 1935), 6-8. Cf. K. Koffka, “Perception: An Introduction to the *Gestalt-theorie*,” *Psychological Bulletin* 19 (1924): 531-85.

⁵⁰ John Watson, “Psychology as the Behaviorist Views It,” *Psychology Review* 20 (1913), 158.

⁵¹ John Watson, *Behavior: An Introduction to Comparative Psychology* (New York: Holts, 1914).

⁵² Edward Thorndike, *Animal Intelligence: Experimental Studies* (New York: Macmillan, 1911).

⁵³ Skinner’s multi-volume autobiography is a valuable view of the state of affairs in the middle of the century by one of its leading scientists. Among his relevant writings for this paper are *Science and Human Behavior* (New York: Free Press, 1953); *Beyond Freedom and Dignity* (New York: Alfred A. Knopf, 1971); *About Behaviorism* (New York: Random House, 1974); and *Upon Further Reflection* (New York: Prentice Hall, 1987). The behaviorists made a significant contribution to the educational theory of the day. For example, Thorndike investigated ways to maximize learning with his “connectionism” as developed in his *Education Psychology* (New York: Routledge, 1913). And Skinner tirelessly promoted more effective education with his emphasis on positive reinforcement as found in his *The Technology of Teaching* (New York: Appleton-Century-Crofts, 1968).

⁵⁴ The *Review of General Psychology* (June 2002), 19-52, concluded from its survey that Skinner was the most influential psychologist of the 20th Century.

behavioral theories in that he distinguished respondent and operant agencies. His focus was on the latter. The rate at which behavior is rewarded or punished will enable the affecting agency to control the pace of change. *Beyond Freedom and Dignity* (1971) argued that traditional values were a barrier to better societies. Since people are culturally conditioned and not autonomous, they should be “dignified” by rewards for what they have done.⁵⁵

In addition to the apparent desire for a more quantifiable, data-driven method, we can also detect in the widespread acceptance of behaviorism, among other phenomena, a growing alliance of industry, university, and the military in governmental sponsorship of science. We pause briefly to note the change from private to public support of scientific research. This funding has been vital for the neurosciences because it was the engine driving phenomenal growth toward the end of the century. The Morrill Land Grant Act (1862) gave large tracts of federal land to states that created engineering colleges to support industrialization. Engineering veered toward scientific disciplines instead the workshop model, and the profession expanded from 13 colleges with engineering in 1862 to 126 in 1917. At the turn of the century, Johns Hopkins and the University of Chicago led universities from their mission as preservers of tradition to a new vision as centers of innovative research through postgraduate credentials and doctorates in science. Industry and academia banded together to promote invention and innovation, but the United States had a unique, long-standing bias against federal funding of research, which in time of war worked to Germany and Japan’s advantage. In the course of World War II, scientific expertise expatriated from Germany and Eastern Europe to the United States. This enriched every area of American science, and we have noted Wertheimer, Koffka, and Köhler above. Vannevar Bush became head of the Office of Scientific Research and Development, which proved its worth in advanced radar technology in the Rad Lab at MIT and related projects. Bush wrote a report on “Science: The Endless Frontier,” in which he argued that the future of America was critically dependent on scientific innovation. Truman accepted his argument. The National Science Foundation was created to distribute peer-reviewed grants. The National Institutes of Health trace their roots to the Marine Hospital Service and the Hygienic Laboratory. But not until 1930 did the Hygienic Laboratory become the National Advisory Health Council, which, in turn, became the National Institute of Health through the Ransdell Act with its own facilities and a system of fellowships. A number of institutes were established in the following decades. In 2007, echoing Bush’s paper, the NIH inaugurated Innovator Awards to ensure the future of medical science, distributing five-year grants of more than \$105 million to 41 scientists. The atmosphere of the country had changed. Of course, this change is a major study in itself, but in contemporary America one never speaks of the separation of society (or state) and science as in ecclesial matters.

A third alternative, a harbinger of the change and contemporaneous with Gestalt and behaviorism, was a mechanical approach to understanding the mind as exemplified by cybernetics and artificial intelligence. In the 1940s Norbert Wiener founded the field of “cybernetics,” and Alan Turing was formulating mechanical knowledge, both of which initiated the idea that human reasoning may be replicated by computation.⁵⁶ The underlying assumption

⁵⁵ Curiously, throughout his long career Skinner distanced himself from the neural substrates of behavior. In his words, he “rejected Sherrington’s physiology, not because, like Jacques Loeb. I ‘resented the nervous system,’ but because I wanted a science of *behavior*,” *The Shaping of a Behaviorist: Part Two of an Autobiography* (New York: Knopf, 1979), 68.

⁵⁶ Later, Turing recorded his thinking in his widely read article, “Computing Machinery and Intelligence,” *Mind* 59 (1950): 433-60.

of mechanical approaches to intelligence was that the mind is reason, so if we could model reason we could create an artificial mind as well. Cybernetics, a term coined by Wiener to refer to mechanical control, is the science of communication, feedback, and control mechanisms that are applied to living systems.⁵⁷ The key for Wiener was the concept of “feedback loops,” which, when appropriately applied in circuits, could make a machine appear adaptive and purposive.⁵⁸ By implication, the circular causality of feedback loops can be used in a system’s ability to accomplish a goal. Cybernetics was linked to Claude Shannon and Warren Weavers’ emerging theory of information, which showed that electrical circuits could implement propositional logic.⁵⁹ Wiener also surfaced the growing problem of the proliferation of knowledge. A person, he held, may have mastered the technical details and jargon of her field, yet regard any other discipline as the domain of a colleague down the hall. Without collaboration the work of science would be hindered. One of his achievements was to inspire a generation of scientists to think of computer technology as a way to extend human capabilities.

Cybernetics was initially disseminated through the Macy Foundation Conferences between 1942 and 1952.⁶⁰ Though the initial goal of the foundation was to explore the prevention of war through gatherings of “the best and the brightest” scientists, the attendees gravitated toward explanations of the mind in material terms. The chairman was Warren McCullough, who is remembered for his work on neural nets with Dusser de Barenne of Yale and chiefly Walter Pitts from the University of Chicago.⁶¹ Neural net architecture is a so-called “bottom up” approach (non-algorithmic) in which memory is trained to respond between neuron nodes.

Meanwhile, John von Neumann was at Princeton University, designing EDVAC as the first stored-program, digital computer. His project was also based on his participation in the Macy conferences and his work with Turing. His architecture, contrary to neural net, was serial processing, meaning that the computer ordered its data “top down” from programs that controlled its functions. The contrasting systems generally co-existed until the 1980s, when the von Neumann architecture could be programmed to simulate neural nets.

In the 1950s experimentation tested the limits of computer intelligence with game theory and solving logical problems.⁶² In 1956 John McCarthy chaired a conference at Dartmouth College, where “artificial intelligence” entered the vocabulary of mechanical thought. In 1963 the Defense Advanced Research Projects Agency (DARPA) gave MIT a grant to establish a center for “machine-aided” cognition. Marvin Minsky became the director of the AI lab, which

⁵⁷ The underlying Greek word [*kubernetes*] means a steersman or pilot. Ampere, before Wiener, used the term to refer the science of government.

⁵⁸ Norbert Wiener, *Cybernetics: Or the Control and Communication in the Animal and the Machine* (Cambridge: MIT Press; Paris: Librairie Hermann & Cie, 1948).

⁵⁹ Claude Shannon and Warren Weaver, *The Mathematical Theory of Communication* (Urbana, IL: University of Illinois Press, 1976).

⁶⁰ The foundation published its edited transactions under the direction of Heinz von Foersten, Margaret Mead, and Hans Lukas Teuber.

⁶¹ McCullough was a founding member of the American Society for Cybernetics. Among his writings with Walter Pitts were “A Logical Calculus of the Ideas Immanent in Nervous Activity,” *Bulletin of Mathematical Biophysics* 5 (1943): 115-33; “A Hierarchy of Values Determined by the Topology of Nervous Nets,” *Bulletin of Mathematical Biophysics* 7 (1945): 89-93; “How We Know Universals: The Perception of Auditory and Visual Forms,” *Bulletin of Mathematical Biophysics* 9 (1947): 127-47. Cf. Warren McCullough, *Embodiments of Mind* (Cambridge: MIT Press, 1965).

⁶² In 1997 “Deep Blue” defeated Garry Kasparov, the world chess champion, in a tournament.

became famous for a “top down” view of the mind as a symbol processor.⁶³ Without understanding the symbols, the machine stored them with the effect of childlike mimicry. Among its accomplishments was INTERNIST, the first diagnostic program for medicine.

We can now approach the end of the century and the rise of cognitive neuroscience. The phenomenal growth of technology and knowledge about the mind, the brain, and their relationship through Gestalt, behavioral psychology, and mechanical innovation came together from the 1980s in the rise of multidisciplinary fields and methods, ranging from molecular biology, to consciousness, and to therapy.⁶⁴ The issues of the mind and neurophysiology synthesized because of the invention of sophisticated instruments and techniques that resulted in an exponential growth of specialties and technical literature. Examples of the instruments are electron microscopy, computed tomography (CT) scans, positron emission tomography (PET) scans, magnetic resonance imaging (MRI), functional MRI (fMRI), magnetoencephalography (MEG), evoked response potential (ERP), and event related optical signal (EROS). Not least, advanced computer technology, software, and the Internet have facilitated both analysis of information and its dissemination worldwide. For example, SPECT imaging uses a gamma camera to acquire multiple 2-D images from multiple angles. A computer then applies a tomographic reconstructional algorithm to the projections, resulting in a 3-D dataset. A remarkable case-in-point is diffusion spectrum imaging, which Van Wedem of Massachusetts General Hospital developed. The technique breaks MRI images into 3-D pixels (“voxels”) to reconstruct an entire, living brain into its fibers for analysis.⁶⁵ Journals cover the obvious topics: *Neuroscience*, *Neuron*, *Brain*, *Mind*, etc. Beyond that are dozens, if not hundreds, of specialized publications, depending on the boundaries of one’s investigations: anatomical parts (e.g., *Hippocampus*, *Amygdala*); specialties (e.g., *Neurophysiology*, *Neurobiology*); national reports (e.g., *European Journal of Neuroscience*); projections (e.g., *Frontiers in Neuroscience*), or functions (e.g., *Visual Neuroscience*, *Auditory Research*).

The long pilgrimage from Willis to Ramón y Cajal and Sherrington, from unconsciousness to behavior as subject of psychology, and from mechanized intelligence to visual explorations of the brain have converged on the cognitive neurosciences. The plural is deliberate, because each strand of our discussion has reemerged in a growing number of specialties that view the mind as physical-chemical activation patterns in the brain.⁶⁶ Cognitive neuroscience, as a representative field of research, is concerned with biological substrates of mental processes and their behavioral manifestations. The coordination of neural activations with genetic and environmental considerations obviously multiplies issues for future research. So too

⁶³ Marvin Minsky and Seymour Papert, *Artificial Intelligence* (Eugene, OR: University of Oregon Press, 1972). Also, Marvin Minsky, *The Society of Mind* (New York: Simon and Schuster, 1987). The reader should consult the insightful study of Daniel Crevier, *AI: The Tumultuous Search for Artificial Intelligence* (New York: Basic Books, 1993).

⁶⁴ Nobel laureate Gerald Edelman, *Wider Than the Sky: The Phenomenal Gift of Consciousness* (New Haven: Yale University Press, 2004), wrote, “The program he [Darwin] established remains to be completed. One of the key tasks in completing that program is to develop a view of consciousness as a product of evolution rather than as a Cartesian substance, or *res cogitans*, a substance not accessible to scientific analysis.”

⁶⁵ Emily Singer, “The Brain Unveiled,” *Technology Review* (Nov./Dec. 2008), 42-7.

⁶⁶ A comprehensive bibliography for contemporary research is too extensive except as a multi-volume collection. For projects like this, the reader can consult a rather complete list of thinkers and sources at www.carbon.cudenver.edu/rmryder/itc_data/cogsci.html or www.infoguides.gmu.edu/content.php?pid=14708&sid=98753 [these resources were accessed on June 9th and 25th, 2009, respectively].

do the conclusions that point to asymmetry, when we have expected further insight into symmetry as the outcome of experimentation.⁶⁷

The neurosciences today have profoundly affected scientific methods. The paper has traced two aspects of the neurosciences to illustrate their longstanding commitment to the brain (the neuron doctrine) and the mind (neuropsychology). There are many aspects of the subject that have not been mentioned: cerebral localization and dominance, the role of electricity, neuropsychopharmacology, and many others. A few of the outstanding women and men who contributed to the field have been noted. Hopefully, enough has been covered to demonstrate the emergence a field with proliferating specialties, yet with common language. With the introduction of this section in view, scientists usually come to a project with an assigned problem in their professional laboratories, whether university or industrial setting. They will face a vast amount of research, which has a bearing on their experimentation. Their hypotheses will be tested by an unprecedented number of researchers worldwide, even for seemingly obscure subjects. In many cases, they will face pressures to protect confidentiality, to bias results, to shorten processes, or to circumvent litigation because of funding issues. But by now the resources are so extensive that impurities and inconveniences are steamrolled in our march toward neuroscientific revolutions in our thinking and treatments.

Projection: the Broad Institute and Beyond

How does the world marshal the personnel, resources and knowledge to address its admittedly urgent concerns? How does it do this, when we cannot stop progress that is based on intense competitions for prestige and funding to sustain laboratories and other research facilities? The answer lies probably in collaboration, which has been a part of neuroscientific development from its modern roots. The *Virtuosi* strove “for a new spirit of cooperation” for the good of science. The Macy Conferences played a vital role in 20th-Century thinking about the mind and brain. Where do we go now on the cusp of revolutionary breakthroughs in the neurosciences and genetics? I would suggest that we consider the past as we contemplate our future.

In 1990 the Whitehead Institute/MIT Center for Genome Research was founded and became an international leader in genomics. In 1995 these scientists began to focus on genomic medicine. In 1998 Harvard Medical School-based scientists established the Institute of Chemistry and Cell Biology to introduce chemical genetics as an academic discipline. In 2002 the ICCB was awarded a grant by the National Cancer Institute, which it used to develop an Investigator-Initiated Screening Program for more than 80 research groups worldwide. The two groups demonstrated the power of enabling scientists to collaborate in addressing major challenges in molecular medicine. A brochure from the Broad Institute states: “It was clear that a new type of formal organization was required – open, collaborative, interdisciplinary, and able to organize projects at any scale. In addition, it was important that the complementary expertise of genomic scientists and chemical biologists across MIT and Harvard be brought together in one place to drive the transformation of medicine with molecular knowledge.”⁶⁸

Eli and Edythe Broad met with MIT/Whitehead and Harvard/hospitals to shape a vision for their new venture. The Broads made a founding gift of \$100 million in 2004; in 2005 they doubled the gift; and in 2008 they gave an additional \$400 million in recognition of the

⁶⁷ Richard Davidson, and Kenneth Huydahl, , eds. *Brain Assemetry*. Cambridge, London: MIT Bradford, 1998.

⁶⁸ “The Broad Institute: History.” The information for this part of the paper was obtained from materials at the Broad Institute during my visit in November of 2008. Most of the information can also be found at www.broad.mit.edu/news/1051 [accessed March 12, 2009].

Institute's early progress.⁶⁹ For example, a research team led by HMS assistant professor and Broad Institute associate member Vamsi Mootha developed a "tool kit" that isolates mitochondrial functions and analyzes how individual drugs affect cells. Mitochondrial dysfunction leads to many neurodegenerative conditions.⁷⁰

Noteworthy is the fact that the neurosciences are not singled out as a focus of research. The Institute specifies "the single goal of transforming medicine with genome-based knowledge in a worldwide biomedical community." It adds to the "lens of Neuroscience" the aspect of body, so that now one frequently encounters professional interest in "mind/brain/body" connections.

One of its programs is the "Psychiatric Disease Program," which "aims to unravel the molecular basis of psychiatric disease, with the ultimate aim of improving diagnosis, treatment and, if possible, prevention." Its focuses are mental illnesses that affect more than three percent of the world's population.

We have noted collaborations in the past, but the Broad Institute brings an unprecedented breadth of expertise to bear on medicine. Its pioneering vision is incarnated in a fully endowed, standalone institution. As such, it can coordinate the wealth of present knowledge on the unforeseeable limits of our finitude. I am not promoting the Institute. It doesn't need my help. I am saying that it is the kind of model that can cohere a scientific "culture" in a field like genomic medicine. Our sincerest hope is that the model can multiply.⁷¹

We conclude with perspective about the subject of this paper. Fifty years ago C. P. Snow delivered his famous Rede Lecture at the University of Cambridge on "The Two Cultures and the Scientific Revolution."⁷² He contended that people in different disciplines rarely have any meaningful communication. The "two cultures" in the lecture were literary intellectuals and scientists. Snow was a polymath, a physicist and novelist, who experienced the progressive polarization that he wrote about.⁷³ Snow expressed "serious concern" over his literary friends' inability to describe entropy. A recent symposium at Harvard commemorated the lecture.⁷⁴ With the exponential growth of science in view, Steven Shapin, historian of science, observed that today Snow would be arguing for more respect for Elizabethan poetry!

Like many of you I live in at least four cultures on a weekly basis: religion, humanities, science, and popular.⁷⁵ Each of the subjects has seemingly limitless sub-categories and

⁶⁹ Other agencies have expanded the Broad's generosity. The NIH granted Broad \$15 million to map epigenomes, an important intersection between genome biology and human disease. The NIH also granted \$86 million to identify and develop molecular tools ("small molecules"), which can probe proteins, signaling pathways, and cellular processes that are crucial in promoting health and healing disease.

⁷⁰ David Cameron, "HMS, Broad Institute team works to better understand mitochondria," *Harvard University Gazette* (Feb. 28–Mar. 5, 2008), 9.

⁷¹ There are other areas where cooperation, if not collaboration is in place. For example, southern California is a "mecca" for neuroscientific research.

⁷² C. P. Snow, *The Two Cultures: and a Second Look: An Expanded Version of the Two Cultures and the Scientific Revolution* (New York: New American Library/Mentor, 1964). Snow argued with an apocalyptic slant; that "the intellectual life of the whole of western society is increasingly being split into two polar groups" (11), who regard one another with "incomprehension" since they are "tone deaf" as they merely "touch their caps" to other-cultured texts (18-20). "There seems to be no place where the cultures meet," (21) he concluded.

⁷³ The neuroscientific people in this paper represent many men and women who were polymathic as well.

⁷⁴ Colleen Walsh, "Still 'two cultures' but who's on top?," *Harvard University Gazette* (May 14-20, 2009), 9.

⁷⁵ Snow's definition of "culture" is a population with a kindred response to understanding life (17). For scientists this common response is based on the scientific method: "At one pole, the scientific culture really is a culture, not only in an intellectual but also in an anthropological sense. That is, its members need not, and of course often do not, always completely understand each other; biologists more often than not will have a pretty hazy idea of

specialties. As I have experienced Snow's lament, I have been motivated to ask questions about the meaning of "communication" and "dialogue." Snow does not tell us how extensive communication and dialogue must be before cultures are bridged. I am not as apocalyptic as Snow about non-communication, for we seem to be surviving in spite of the proliferation of information and knowledge. People may not be able to play "trivial pursuits" across cultures, but this does not necessarily mean that they don't have a vital interest in different cultures. Also, cultures are dynamic, especially in the 20th Century. No doubt, religions have declined in public prestige since the times of Willis. And, as the neurosciences have expanded, they are encroaching on traditional domains such as neurophilosophy and neurotheology.⁷⁶ This may be inevitable when powerful words like "truth" and "reality" are more audible in public discourse.

I would suggest from my experiences that comprehension of a culture outside of one's expertise requires a commitment that very few people are willing to undertake. I have discovered that nothing can promote communication and respect like "crossing the bridge" to seriously engage another culture. I have traveled to India for over thirty years. My involvement in educational and medical programs has been daunting and pleasurable at the same time. After years of struggle with language, religion, and cultural disciplines, I can say that I can now communicate and dialogue with them on very non-American terms. I am not certain about when the line between stranger and friend was crossed, but somehow their needs and my resources met in mutual blessing. Surprising as it may seem, money may not be the critical element in situations like these. For approximately the same length of time, I have engaged in programs in America's inner cities. A number of city-dwellers that I know rarely comprehend the depth of need, crime, and suffering within blocks of their privileged neighborhoods. There are dimensions of depravity that transcend our comfort-seeking imaginations. However, America's inner-cities contain people that are similar in some ways to Indian villagers. Efforts to communicate at a meaningful level involve similar issues of mutual understanding and trust in both cultures. However, very few people have any desire to walk across the bridge.

Regarding science, this paper has been an extended argument that I have tried to cross that bridge for fourteen years. I am still trying to determine whether I have succeeded or not. I have discovered an exciting culture, whose incredible growth has intensified specialization. My conversations in the Society for Neuroscience indicate that I have succeeded. My argument has been that method is the baseline distinction between science and the humanities. The neurosciences have used the scientific method to evolve into a professionalized, specialized "culture" with a common language that has synthesized technological forces into an incomparable opportunity to address persistent problems of life on earth. A vital part of the method is peer review, a task that is impossible without a detailed knowledge of the technical literature that forms the neuroscientific landscape. Perhaps, I am more concerned now that the neuroscientific specialties will evolve into polarizing "cultures" that lose touch with one another, which makes collaboration a necessity as we contemplate the future.

contemporary physics; but there are common attitudes, common standards and patterns of behaviour, common approaches and assumptions" (16).

⁷⁶ A leading exponent of neurophilosophy is Patricia Smith Churchland, *Brain-Wise: Studies in Neurophilosophy* (Cambridge, London: MIT Press, 2002). The *Dallas Morning News* (August 28, 2007), 1, 18A, contained a feature entitled "Scientists rush in where angels may tread." Neuroscientists at the University of Texas Southwestern Medical Center and the Center for Brain Health plan an "unprecedented flood" of science about religion and ethics. The article noted that "forgiveness, gratitude, compassion, prayer, justice, empathy – these key words can be found regularly in top science journals such as *Science*, *Nature*, . . ."

Common ground? As a survivor of two life-threatening illnesses and as a recipient of two serious surgeries, I gravitate to medicine as the most compelling metaphor of mutual human needs. From Dr. Willis to the Broads, I have been validated in this sentiment. Beyond that, my fourteen years of reading in neuroscience have enriched my teaching, my recognition of mental disabilities, my understanding of the biological aspects of life, and my relationships with my family and society.

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