Aspects of the History of Instrumentation in the Neurosciences at Rockefeller University: Nobelists Herbert Gasser and H. Keffer Hartline

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This examination of the importance of scientific instruments in the history of the neurosciences begins with the premise that the role of instrumentation in the history of medicine and the history of science in general has been underreported. I suggest that the history of science and the history of medicine have overplayed the conceptualization of research projects, and the pursuit of theoretical confirmation, and have underplayed the central role of instrumentation.[1] In fact, two historians of instrumentation have argued that, for the history of science, "the philosophical debate over whether theory drives experiment or experiment drives theory has tended to obscure the independent role of instruments in science."[2] Looking backward into the early modern period, the eminent historian of science Derek de Solla Price stated that "the scientific revolution… was largely the invention […,] improvement [,] and use of a series of instruments of revelation that expanded the reach of science in innumerable directions."[3]

Personally, as a historian of technology, I have been increasingly engaged in research overlapping with the history of science and medicine over the last two decades. In that process I have tended to zero in on the use of tools in the laboratory, and in doing so I have been struck by the general lack of recognition of the importance of the creation and use of instrumentation in 20^{th}-century science. My remarks today are in the form of an extended appreciation of the role of instruments in the work of the two Nobelists, Herbert Gasser and Keffer Hartline.

As an introduction to this exploration of the key role of instrumentation in 20^{th-}century science and medicine, I will begin by reviewing three other significant episodes in the history of the Rockefeller University, the current name for the biomedical research institution in New York City that for most of the 20^{th} century was the Rockefeller Institute for Medical Research. The usefulness of a Rockefeller framework for considering the importance of instrumentation in modern biomedicine is supported by historian and sociologist Rogers Hollingsworth, who in a recent essay titled "Institutionalizing Excellence in Biomedical Research," noted that "more major discoveries occurred in biomedical science at Rockefeller University than at any other research organization during the twentieth century."[4] It is also appropriate to note that "the Rockefeller," as it is often referred to, has had 23 Nobel prizewinners associated with it since its founding in 1901. The chair of the Rockefeller's board of trustees is fond of pointing out that if the University were a nation, this number would give it a rank behind the United States, Britain and Germany, but ahead of France.

1. The Centrifuge and DNA

The first case of instrumentation at the Rockefeller that I want to consider relates to what may be the most significant series of experiments in 20^{th} century biomedicine – the work of Oswald T. Avery, Colin McCloud and Maclyn McCarty on DNA. Avery oversaw this research for more than a decade, culminating in the famous publication of 1944 with his two collaborators that established that DNA was the genetic material.

Avery was on the staff at the Rockefeller Institute for Medical Research's hospital, a hospital dedicated to research on infectious diseases.[5]

Soon after he joined the hospital staff in 1913 Avery focused his studies on pneumococci, a subject that continued to occupy his succeeding 30 years of research. Avery's laboratory was long known for its modest equippage and its reliance on well-known chemical procedures.[6] It was only in his continuing hunt for understanding the nature of the "transforming principle," as the search for the genetic material was known in his laboratory, that Avery began to take advantage of recent developments in research instrumentation. Not until 1938 did he have his laboratory equipped with "centrifuges and other electrical laboratory equipment."[7]

The installation of centrifuges has to be understood in the context of what had gone on at the Rockefeller in recent years. On the campus of the Rockefeller Institute was a laboratory of the International Health Division (IHD) of the Rockefeller Foundation that had a program of developing vaccines for various diseases, including yellow fever, typhus, and influenza. In 1934 the IHD laboratory also began a program of ultracentrifuge development because of the need to concentrate minute quantities of biological materials. In this work the IHD laboratory had the support of the inventor of the ultracentrifuge, Thė Svedberg of Sweden, and the collaboration of the Rockefeller Institute staff, including Alexandre Rothen. It was Rothen's version which proved to be useful to Avery's research.

There was also another device available to Avery, a less-sophisticated centrifuge derived from the cream separators in use by the dairy industry since the late 1800s. The Sharples Company of West Chester, Pennsylvania, a major manufacturer of cream separators, moved into the manufacture of laboratory centrifuges by the mid-1930s. One or more of the Sharples models must have been installed in Avery's updated laboratory in 1938. According to McCarty's memoir, "thousands of liters of pneumococcal culture were passed through this machine" over the next three years, and "the increased yields of starting material had a major impact on progress of the work; one could now try a variety of fractionation and purification procedures without being limited by the amount of crude active extract."[8]

Another important step in Avery's project was the use of Rothen's modified ultracentrifuge in the spring of 1942. This device was in a separate laboratory and, according to McCarty, filled "most of the space in a medium-sized room." Unlike the Sharples centrifuge, which was designed and used to concentrate substantial quantities of fluid, Rothen's ultracentrifuge was analytical.[9] It held "only about one-half [a] cubic centimeter of extract."[10]

Although some additional research was carried out, the studies done with the aid of the Sharples centrifuge and the Rothen ultracentrifuge had by the summer of 1942 convinced the Avery laboratory that DNA was the genetic material.[11] It is useful to note here that Avery's team took the further step of utilizing electrophoresis as another means of confirming that the transforming principle was inherent in DNA. The Rockefeller Foundation had been a supporter of Arne Tiselius's development of the apparatus, and researchers at the Rockefeller Institute were early adopters of the technique.[12] In 1939 it was reported that five of the 14 Tiselius electrophoresis devices in the United States were either at the Rockefeller or in the IHD laboratory on the Rockefeller campus.[13] Thus, although Avery was himself not a very technology-oriented researcher, to confirm the results of his work he had utilized two of the most advanced laboratory techniques of his time – ultra-centrifuging, and electrophoresis.

In February 1944, Avery, MacLeod and McCarty published their landmark paper, "Studies on the chemical nature of the substance inducing transformation of pneumococcal types. Induction of transformation by a desoxyribonucleic acid fraction isolated from pneumococcus type III."[14] Interestingly, major historical works have not focused nearly as much on the role of instrumentation in their accomplishment as did McCarty in his later memoir, *The Transforming Principle*, from which I have quoted above. René Dubos, for example, who had worked in Avery's laboratory, wrote a volume on Avery and the DNA work. He gave only a brief mention each to the Sharples centrifuge and Rothen's ultracentrifuge, although he recognized the importance of advanced techniques in Avery's laboratory's research, and noted that "these technical advances were not published at the time."[15] Robert Olby devoted an early chapter to the history and use of the ultracentrifuge in his classic *The Path to the Double Helix,* but makes no mention at all of its role – or of the role of any instrumentation – in his account of Avery's research.[16] Horace Judson, in *The Eighth Day of Creation,* does mention the role of instrumentation in Avery's project, but without highlighting its significance. In another context, however, Judson quotes Nobelist Sidney Brenner as stating that the availability of a "tremendous technological armamentarium" was one of the critical preconditions for the development of molecular biology.[17]

I shall return later to this matter of the role that is historically accorded to laboratory technology.

3. Counter-current Apparatus

Lyman C. Craig, regarded as a "gifted experimentalist," came to Rockefeller in 1933. During war work in the early 1940s he developed the counter-current apparatus for separating constituents of mixtures otherwise thought to be compounds. Craig continued to improve his apparatus through the 1950s. The counter-current device was particularly important in work on proteins and antibiotics, and its use spread widely in the biomedical research community.[18] For example, Nobel Prize winner Sune Bergström noted that his early work on prostaglandins was aided significantly by the Craig counter-current device that Bergström had brought to Sweden after a fellowship in the United States in the 1940s.[19] Craig himself received the Albert Lasker Award in 1963 for the apparatus and associated methodology "which [according to the award citation] has made possible the isolation and identification of countless substances that occur in nature and that [as a result] can be synthesized in the laboratory for therapeutic purposes."[20]

4. Peptide Synthesizer

Bruce Merrifield won a Nobel Prize in 1984 for creating the peptide synthesizer. He joined Wayne Woolley's laboratory at the Rockefeller in 1949, and a decade later began work on a device that would assemble amino acids into peptide chains.[21] A successful result held the promise of making proteins to order in the laboratory. Merrifield took three years to create a device that would synthesize a nine-amino-acid-long hormone. Then, "Merrifield and his colleagues from his laboratory and Rockefeller's instrument shop began automating the process… By 1965 they had a working model and in 1969 they synthesized ribonuclease… Merrifield's invention… revolutionized protein chemistry."[22] Note here the mention of the role of the instrument shop, another subject to which I will soon return.

5. Neurophysiology: Cathodes and Computers

Herbert S. Gasser

Neurophysiology became a major area of research at the Rockefeller when Herbert Gasser succeeded Simon Flexner as Director in 1935. He brought along a well-developed program of research "that focused on the fundamental properties of nerve cells, dendrites, and the primary synaptic endings of nerve fibers."[23]

Gasser had undergraduate and graduate training at the University of Wisconsin, and an M.D. from Johns Hopkins. His life's work began when he joined Joseph Erlanger's laboratory at Washington University in 1916, beginning a collaboration with Erlanger that eventually led to a shared Nobel Prize.[24] Their research was revolutionized in 1921 by adapting to experimental use the recent development by Western Electric of a suitable "low vacuum Braun tube [i.e., an oscilloscope] with a hot cathode which operated at a low voltage," and which Gasser judged to be "the most important factor in aid of [his] work on the electro-physiology of nerves."[25] This advance was later characterized by a well-informed reviewer of Gasser's work as "like giving sight to the blind."[26]

The effective use of this technology depended, as well, on procuring a suitable amplifier, and a cathode-ray tube: the combination of the three dramatically improved Erlanger and Gasser's ability to identify patterns nerve potentials.[27] Yet the technology was far from perfected. One historian commented that:

> It is difficult in the days of near-universal television to imagine the early difficulties of oscillographic recording. Light intensity was so low that many repetitions of the nerve response were required to produce a photographic image, and [vacuum] tubes lasted but a few hours.[28]

One Rockefeller professor who knew Gasser well has provided another anecdote that suggests the difficulties of those early days. According to his recollection:

> At first Western Electric refused to sell [Erlanger and Gasser] the new Cathode Ray Tube. [They then] constructed their own CRT using an Erlenmeyer Flask by coating the inside with a phosphor and mounting appropriate electrodes inside with terminals coming through the glass to the outside. They exhibited this contraption at the XIII International Physiology Conference [Congress?] in 1929. Perhaps [because] Western Electric fear[ed] further competition, they [then] agreed to sell them one of theirs.[29]

This particular anecdote seems inconsistent with another element of the Erlanger-Gasser story, which is that Western Electric engineers gave critical help to them in the development of an amplifier based on a three-stage vacuum tube.[30] Nonetheless, these elements of the history of neurophysiology show that scientific research is not as divorced from business and industry as most scientific publications would suggest.[31]

Gasser continued his neurological research at Cornell University Medical College, which he moved to in 1931, and then at the Rockefeller. He also had spent 1923-1925 working with A.V. Hill at University College, London, participating in the important British-American network of neuroscientists that flourished in the interwar era. This network was led by Adrian, Dale, Hill, and Sherrington, all of whom became connected with Rockefeller Institute through students and visiting fellowships. As one historian has put it:

> The regular visits and collaborations between physiologists during the first part of the twentieth century broke down the idea of laboratory-based communities and

> instead created a vision of a single community based on an international network of scientists.[32]

Specifically, as this historian notes, the international collaboration focused on the development of experimental techniques that was fostered by trans-Atlantic travel and laboratory stints, such as Gasser's with Hill.[33] When Alan Hodgkin joined Gasser's laboratory in 1937 he immediately "abandoned" the technique he had used at Cambridge "in favor of the Thyratron discharge circuit used in Dr. Gasser's laboratory."[34] While I am getting ahead of myself in regard to the laboratory apparatus, I am including this digression to point out that the importance of instrumentation extended well beyond Gasser's own research agenda to a broader community of neuroscientists.[35]

I am now returning to a focus on Gasser.

For the purpose of this talk Gasser's actions when he took over the directorship of the Rockefeller are very interesting. Although an instrument shop had been created at the Rockefeller in 1920, Gasser greatly expanded it after his arrival there in 1935, specifically to support his research agenda. In his first annual report to the Institute's Board of Scientific Directors he stated that:

> The first step toward the development of a physiological laboratory, in which the utilization of physical methods is contemplated, is the establishment of an instrument shop. A certain amount of standard apparatus is purchasable, but to a very large extent the apparatus which is used in physiological research must be especially designed for the purpose, and provision must be made for continuous alteration and additions as the work progresses.[36]

Critical to the development of the shop was the hiring of Josef Blum, an instrument-maker who was known for his "skill and ingenuity."[37] Blum was a German immigrant, who had twenty years' experience in machine manufacture, in constructing electrical apparatus, in tool-and-die making, in the repair and building of motion-picture projectors, in aeronautics, and in the radio industry. With this variety and wealth of experience he obtained a position as an instrument-maker with the United Research Corporation of Long Island City, New York. After six years he came to Rockefeller, described as "a very excellent and capable mechanic …. [who] also possesses a great faculty for the development of intricate processes and methods."[38]

It was on Blum and others in the instrument shop that Gasser relied as he set up his own laboratory on a substantial scale, including the construction of a large apparatus with which to continue his experimental regime. Two keys to his apparatus were his adoption of two of the latest electronic devices, a new type of vacuum tube, the thyratron, and an improved cathode-ray tube from General Electric.

The thyratron was so important to his laboratory set-up that Gasser used the term "Thyratron Unit" to describe the entire apparatus. The thyratron itself was a vacuum tube invented by Albert W. Hull in 1927 that created intermittent discharges of electrical current, and thus was an ideal device to incorporate into an experimental regime that called for stimulating nervous tissue at specific intervals.[39]

By 1933 thyratrons apparently were in use by several researchers in the neurosciences, and at some point around this time Otto Schmitt's thyratron relay control (or "trigger") began to be incorporated into laboratory apparatus to make it even more effective as a research tool.[40] Schmitt described his invention in an article he and his brother published in *Science* in 1932. He began by asserting that "Modern advances in the field of nerve physiology, involving high amplification of the action potential and its visual recording by means of the cathode ray oscillograph, especially at high rates, are unsatisfactory." Describing the stimulator he had developed, he asserted that his "arrangement is particularly useful for work where the intensity of stimulation must be very accurately adjusted, as in studies on the single axon response."[41] He went on to state that his device could be characterized as "an entirely non-mechanical system by means of which each shock produced by this stimulator may be synchronized automatically."[42] Five years later a researcher could refer casually to "the adaptation of the thyratron oscillator … [for] physiological research," and note that "detailed presentation of the principles of operation" no longer was required when referring to it, presumably because it had been so widely adopted.[43]

Gasser combined the thyratron with advanced cathode-ray tubes made by RCA, manufactured in its Radiotron series. Here is the "Thyratron Unit" in use in the Gasser laboratory in 1938. Among the hundreds of oscillograph photographs in his papers I also found two photographs of the unit, this one showing both the apparatus for fixing nerve fibers and the camera set-up for photographing the oscilloscopes.[44] This is apparently the apparatus proudly described by Gasser in 1937 as capable of taking:

> Six oscillograph records… simultaneously on cinematographic film with different amplifiers designed to prevent cross leads when the potentials are derived from different parts of the same preparation… [although] the pictures may be taken interchangeably on stationary film….[45]

Gasser was awarded the Nobel jointly with Erlanger in 1944. In his Nobel Lecture, given a year later, there is no mention whatsoever of the experimental apparatus.[46] I cannot resist the temptation to recall that, in comparison, when Charles Lindbergh wrote a book about his famous transatlantic flight in 1927, he titled it *We,* recognizing that he was not alone, but was in intimate partnership with a sophisticated machine.[47]

H. Keffer Hartline

Although not a student of Gasser, in the 1950s and 1960s, Haldan Keffer Hartline continued the strong Rockefeller tradition in neurophysiology. A graduate of Lafayette College, Hartline also held an M.D. from Johns Hopkins. Hartline had an appointment at Penn, and then at the Johnson Foundation, where he came to the attention of Detlev Bronk, who could be characterized as Hartline's "patron." Bronk brought him back to Hopkins under his presidency, and then to the Rockefeller when he became president there in 1953.[48]

Hartline already had a considerable record of research on the neurophysiology of vision, which he had begun when he was an undergraduate during summers at Woods Hole. By 1933 he had begun to use the horseshoe crab as a subject for his studies, although he also engaged in studies of the frog's visual system. At Johns Hopkins he established close relationships with an instrument-maker and an electronics engineer to develop effective laboratory techniques. By his own account he adopted oscilliscopy to study "the long optic nerves" of the horseshoe crab, which could be "frayed into thin bundles which are easy to split until just one active fiber remain[ed]."[49]

Among his most notable accomplishments on his way to the Nobel, according to one of his close associates, was his publication in 1949 of:

> his discovery of lateral inhibition – a form of negative feedback – in the retina, in which excitatory activity in one region of the retina diminishes … excitatory activity in neighboring regions. Lateral inhibition serves to enhance contrast and sharpen edges in retinal images.[50]

Hartline was regarded by a close associate as "an outstanding inventor, mechanical designer and later, computer programmer," who was "quick to appreciate the promise of new technology."[51] Accordingly, early in the 1960s he reportedly began working with "a computer owned by a friend at Hopkins" with which "he demonstrated the feasibility of direct computer processing of his experiments."[52]

In 1962 Hartline purchased the Institute's first computer, a Control Data Corporation 160-A, to improve his ability to analyze his data from "the experimental stimulation of nerve fibers" of the eye of the Horseshoe Crab.[53] This computer, priced at $90,000, was described in a Control Data Corporation press release as having "a magnetic core memory of 8,192 12-bit computer words [expandable to 32,768 words] ….and an unusually large and powerful list of ninety-one instructions." Possible peripherals included "a magnetic tape system, high-speed line printer, card reader[card] punch, and [an] electric typewriter."[54] After installation, the Rockefeller electronics laboratory created an interface that "translate[d] the information coming from the experiment into data which [could] be handled by the computer."[55] When the computer was programmed it was possible "while the experiments were in progress, and the [nerve tissue] was still viable, to make changes in the protocol."[56] A colleague remembered that:

> Hartline amused himself on the train [while commuting between his home in Baltimore and his laboratory in New York] writing arithmetic programs in the CDC machine language. With the skill acquired he was able to specify an algorithm for obtaining the instantaneous rate between any two optic nerve impulses to a tenth of a millisecond….[57]

A contemporary article described the value of the computer to the Hartline laboratory:

> An advantage of … the computer is, of course, that experiments can be modified or rerun at the moment on the basis of the information received. Another advantage of such 'on-line' work, in addition to the time-saving feature, is the effect on the investigator – the stimulation of being able to monitor his own experiment as it is going on.[58]

Hartline received the Nobel Prize in 1967 for his accomplishments in understanding vision. His acceptance speech did not mention any of the sophisticated apparatus that he had used to obtain the results that made him prize-worthy.[59]

Even in one major speech in 1964 in which Hartline acknowledged the important role of computers in his work, describing them as "enormously useful" for his studies, he argued that "the basic problem" was a purely intellectual one: "how to think about complex organization, how to develop useful general principles."[60]

So, considering these case studies as a possibly useful approximation of a larger set, we come to the question: Why is the technical background of scientific research omitted or downplayed by the scientists themselves when it comes to giving accounts of their work?

Surely, as I have shown above in the cases of Gasser and Hartline, it is not because the scientists themselves are not technically adept, technically knowledgeable, or interested in the technology of laboratory instrumentation. Before today's era of "big science" most instrumentation was assembled, even invented, right in the laboratories, often by the scientists who put them to use. Even now, when many instruments are commercially available (and here I have to note that Rockefeller University closed its instrument and glassblowing shops in 2000), the vast majority of scientists work closely with the engineers and technicians who operate the equipment that makes their observations possible.

A central reason why technical matters are excused from scientific accounts is that they simply are not easily reducible to words. My mentor Eugene Ferguson, an engineer and an historian, published an important piece in *Science* thirty years ago that grappled in part with this question. In his words:

> Many features and qualities of the objects that a technologist thinks about cannot be reduced to unambiguous verbal descriptions; they are dealt with in his [/her] mind by a visual, nonverbal process.[61]

Further, Ferguson argued that:

> Nonverbal thinking, which is a central mechanism in engineering design, involves perceptions, the stock-in-trade of the artist not the scientist… [and the] intellectual

> component of technology, which is nonliterary and nonscientific, has been generally unnoticed because its origins lie in art and not in science.[62]

In other words, while the course of scientific investigation can be written out as a logical, inductive process, it is very difficult to convey the development of instrumentation, or even the use of instrumentation, in the same way. Utilizing Ferguson's viewpoint one could say that it is a much more difficult matter to explain technology than science, and telling the scientific tale wins out when scientists explain what they are about.

There certainly is another aspect to this that ought to be considered, which is that at the present time science, conceived of as an ideational process, is in most of its aspects is held in higher esteem than technical pursuits, which are conceived as a manual process and lower on the social scale. In short, in modern society the pursuit of ideas is held higher than the making of things. Therefore any account of laboratory science will emphasize thought and not practice.

In my research for this paper I have come across two historical works that are suggestive of this. Eric Kandel's In *Search of Memory* is a best-seller, and for good reason: it is written by a Nobel prizewinner, and describes his intellectual and personal odyssey as a scientist. (Interestingly, Kandel worked in Harry Grundfest's laboratory in the 1950s, and was therefore enmeshed in the same network that Gasser had been in twenty years before.)[63] While Kandel's text by no means ignores the role of scientific instruments, the emphasis is very much on exquisite and elegant formulations of ideas.

The other book is by the late Robert L. Schoenfeld, professor and head of the Laboratory of Electronics at Rockefeller University. His book, *Explorers of the Nervous*

System, includes vivid and telling descriptions of his work with Gasser, Hartline and others, yet is almost a how-to guide to the laboratory instrumentation of neuroscience, complete with circuit diagrams. Needless to say, this book is not a best-seller and I only found out about it by word-of-mouth.

Clearly, Eric Kandel's book will shape our understanding of the history of neuroscience much more than Robert Schoenfeld's, even though they have equal claim to telling important stories. The history of ideas ranks higher in the retelling of science than the history of things.

All together, I come back to my original points: whether looking at the discovery of DNA as the genetic material, or at some of the other leading discoveries over the last century at Rockefeller University, instruments have played a very important, yet seldom-appreciated, role. I will leave the last word to Rockefeller professors Stanford Moore and William H. Stein, who received a shared Nobel Prize in 1972 "for their contribution to the understanding of the connection between chemical structure and catalytic activity of the active center of the ribonuclease molecule." In their Nobel address, after reviewing the experimental procedures that led to their accomplishment, they concluded:

> "The sharing of knowledge among academic scientists and industrial designers of instruments… has played an important role in [the] progress of biomedical research."[64]

ENDNOTES:

[1] However, a recent brief essay provides a counterpoint: Guilano Pancaldi, "Instruments, Biological." In J.L. Heilbron, et al., editors, *The Oxford Companion to the History of Modern Science.* New York: Oxford University Press, 2003, pp. 411-413.
[2] Albert Van Helden and Thomas L. Hankins, "Introduction: Instruments in the History of Science." *Osiris* 9 (1994) p. 6.
[3] Quoted in William J. Broad, "Is Technology the Hero of the Scientific Revolution?" *Plain Dealer*. Cleveland, Ohio, (21 August 1984) p. 1-B. See Derek de Solla Price, "The Science/Technology Relationship, the Craft of Experimental Science, and Policy for the Improvement of High Technology Innovation." *Research Policy* 12 (February 1984) pp. 1-20.
[4] J. Rogers Hollingsworth, "Institutionalizing Excellence in Biomedical Research: The Case of The Rockefeller University." In Darwin H. Stapleton, editor, *Creating a Tradition of Biomedical Research: Contributions to the History of The Rockefeller University.* New York: Rockefeller University Press (2004) p. 17.
[5] Saul Benison, "The Development of Clinical Research at The Rockefeller Institute before 1939." In *Trends in Biomedical Research, 1901-1976.* Proceedings of the Second Rockefeller Archive Center Conference, (December 10, 1976) North Tarrytown, New York: Rockefeller Archive Center 44 pp. 39; E.H. Ahrens, Jr., "Changing Patterns in Clinical Investigation." *Trends in Biomedical Research,* p. 59.
[6] René J. Dubos, *The Professor, the Institute, and DNA.* New York: Rockefeller University Press (1976) pp. 70-71.
[7] Bernard Lupinell to E.B. Smith, 13 June 1938, folder 1, box 1, Oswald T. Avery Papers, RG Av37, Rockefeller University Archives (hereafter RUA), Rockefeller Archive Center (hereafter RAC), Sleepy Hollow, NY, USA.
[8] McCarty, *The Transforming Principle,* p. 104.
[9] "Report of Dr. Rothen." In *Reports to the Scientific Directors* 27 (October 1938-October 1939) p. 131, RUA; "Report of Dr. Rothen." In *Reports to the Scientific Directors* 28 (October 1939-October 1940) p. 36, RUA.
[10] McCarty, *The Transforming Principle,* p. 138.
[11] McCarty, *The Transforming Principle,* p. 142.
[12] Warren Weaver diary, 5 November 1937, 22 September 1939, RG 12.1, RFA; Lily E. Kay, "Laboratory Technology and Biological Knowledge: The Tiselius Electrophoresis Apparatus, 1930-1945." *History and Philosophy of the Life Sciences* 10 (1988) pp. 51-72.
[13] Warren Weaver diary, 22 September 1939, RG 12.1, Rockefeller Foundation Archives, RAC.
[14] O.T. Avery, C.M. MacLeod, and M. McCarty, "Studies on the chemical nature of the substance inducing transformation of pneumococcal types. Induction of transformation by a desoxyribonucleic acid fraction isolated from pneumococcus type III." *Journal of Experimental Medicine* 79 (1944) pp. 137-58.
[15] Dubos, *The Professor, the Institute, and DNA,* pp. 140-141, quote on p. 141. Dubos also stated that "surprising as it may seem, the Avery group never published a complete detailed account of the steps that led them to this remarkable and unexpected conclusion." p. 142, McCarty's volume, *The Transforming Principle*, substantially remedied the situation.
[16] Robert Olby, *The Path to the Double Helix: the Discovery of DNA.* Rev. editor, New York: Dover (1994), pp. 11-21, 181-189.
[17] Horace Freeland Judson, *The Eighth Day of Creation: Makers of the Revolution in Biology.* Expanded editor, Plainview, New York: Cold Spring Harbor Laboratory Press, 1996, p. 183.
[18] Nicole Kresge, Robert D. Simoni and Robert L. Hill, "Lyman Creighton Craig: Developer of the Counter-current Distribution Method." *Journal of Biological Chemistry* 280 (18 February 2005) at *jbc ONLINE*, 7 November 2005; E.H. Ahrens, Jr., "After 40 Years of Cholesterol-Watching." *Cardiovascular Drug Reviews* 20 (2002) p. 245; Corner, *A History of the Rockefeller Institute,* pp. 350-352.
[19] Sune Bergstöm, "The Prostaglandins: From the Laboratory to the Clinic." Nobel Lecture, 8 December 1982.
[20] "1963 Albert Lasker Award for Basic Medical Research: Lyman C. Craig." at http://www.laskerfoundation.org/awards/library/1963b_cit.shtml. Site visited 7 November 2005.
[21] Corner, *A History of Rockefeller Institute,* pp. 378, 592; Bruce Merrifield, "Solid State Synthesis." Nobel lecture, December 8, 1984.

[22] Elizabeth Hanson, *The Rockefeller University: Achievements, A Century of Science for the Benefit of Humankind, 1901-2001.* New York: Rockefeller University Press, 2000, p. 111.
[23] Hollingsworth, "Institutionalizing Excellence in Biomedical Research." In Stapleton, editor, *Creating a Tradition*, p. 36.
[24] Merrill W. Chase and Carlton C. Hunt, "Herbert Spencer Gasser, July 5, 1888–May 11, 1963." *Biographical Memoirs,* National Academy of Sciences 67 (1985), pp. 2-33.
[25] Herbert S. Gasser to William W. Stanhope, 10 January 1962, folder 5, box 4, RG 302.2, Herbert S. Gasser Papers, RUA. This letter gives a date of December 1920 for the time when Gasser heard about the development of this type of oscilloscope; another document gives the date of December 1921: J. Erlanger and H.S. Gasser, "The Beginning of Nerve Oscillography." n.d., folder 1, box 6, RG 302.6, Herbert S. Gasser Papers, RUA.
[26] "The Nature of the Nerve Impulse and its Conduction." *Rockefeller Institute Quarterly* 2 (Winter 1959) p. 4.
[27] Abigail Tierney, "Gasser, Bronk, and the International Network of Physiologists." In Stapleton, editor, *Creating a Tradition*, pp. 241-244; Corner, *A History of the Rockefeller Institute*, pp. 333-335.
[28] David P.C. Lloyd, "Herbert Spencer Gasser." In Charles C. Gillespie, editor, *Dictionary of Scientific Biography.* New York: Charles Scribners' Sons, 5 (1981) p. 291.
[29] Robert L. Schoenfeld, *Explorers of the Nervous System: With Electronics, and Institutional Base, a Network of Scientists.* Boca Raton, Florida: Universal Publishers, 2006, pp. 66-67.
[30] Schoenfeld, *Explorers of the Nervous System*, p. 43.
[31] I have investigated the intersection of science and industry in a particular region in Darwin H. Stapleton, "The Rise of Industrial Research in Cleveland, 1870-1930." In Elizabeth Garber, editor, *Beyond History of Science: Essays in Honor of Robert E. Schofield.* Bethlehem, Pennsylvania: Lehigh University Press, 1990, pp. 231-245.
[32] Abigail Tierney, "Gasser, Bronk, and the International Network of Physiologists." In Darwin H. Stapleton, editor, *Creating a Tradition of Biomedical Research: Contributions to the History of The Rockefeller University.* New York: Rockefeller University Press, 2004, p. 242.
[33] Tierney, "Gasser, Bronk, and the International Network of Physiologists," pp. 243-247.
[34] A.L. Hodgkin, "The Subthreshold Potentials in a Crustacean Nerve Fibre." *Proceedings of the Royal Society of London*, series B, Biological Sciences 126 (23 September 1938) p. 91. See also: Alan Hodgkin, *Chance & Design: Reminiscences of Science in Peace and War*. Cambridge, Massachusetts: Cambridge University Press, 1992, pp. 89-103.
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