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Putting Isotopes to Work:

Liquid Scintillation Counters, 1950–1970

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PUTTING ISOTOPES TO WORK: LIQUID SCINTILLATION COUNTERS, 1950-1970[1]

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1. INTRODUCTION

Perhaps no other instrument has symbolized the techno-myth of an avant-garde science, that was so widespread in the expanding community of molecular biology and radiomedicine in the 1960s and 1970s, more powerfully than the liquid scintillation counter. It was a piece of apparatus that effectively comprised three key technologies of the twentieth century: mechanical automation, electronics, and radioactive tracing. Yet - in contrast to other instruments and techniques characteristic of modern biology and medicine such as electrophoresis, ultracentrifugation, electron microscopy, NMR (Nuclear Magnetic Resonance), and PCR (Polymerase Chain Reaction)[2] - liquid scintillation counters have so far not received any attention from historians of science and technology.

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1 I thank Mr. Rainer Stangl, a Viennese Product Manager for Packard, for his help in contacting former representatives of Packard Instrument Company. My special thanks go to Professor Eugene Goldwasser, Dr. Gerhard Kremer, Lyle E. Packard, Edward Polic, and Dr. Edward Rapkin for kindly allowing me to interview them, and their responses to further requests. Jean-Paul Gaudillière, Myles Jackson, Lily Kay, Robert B. Loftfield, Patricia Nevers, Xavier Roqué, and Sahotra Sarkar are acknowledged for valuable comments on drafts of the manuscript. To appear in: Bernward Joerges and Terry Shinn (eds.), Instrumentation Between Science, State, and Industry. Harwood Academic Publishers, Reading, in press.

2 Lily Kay, The Tiselius electrophoresis apparatus and the life sciences, 1930-1945, History and Philosophy of the Life Sciences 10 (1988), 51-72; Boelie Elzen, Two ultracentrifuges: A comparative study of the social construction of artefacts, Social Studies of Science 16 (1986), 621-662; Nicolas Rasmussen, Picture Control. The Electron Microscope and the Transformation of Biology in America, 1940-1960. Stanford University Press, Stanford 1997; Timothy Lenoir, Instituting Science. The Cultural Production of Scientific Disciplines. Stanford University Press, Stanford 1997, Chapter 9 (in collaboration with Christophe Lécuyer), Instrument makers and discipline builders: The case of Nuclear Magnetic Resonance, pp. 239-292; Paul Rabinow, Making PCR. A Story of Biotechnology. The University of Chicago Press, Chicago 1996.

This paper intends to exemplify the coming into being and development of a research-enabling instrument. As I will show below, in 20 years liquid scintillation counters developed from a clumsy technology for specialized cases of radiation measurement in the 1950s into a generic technology that became ubiquitous in molecular biology and medicine laboratories in the 1970s. From a few early models, it was particularly Packard's Tri-Carb liquid scintillation spectrometer that made its way into university institutes, national laboratories, hospitals, and research departments of companies. A Packard Tri-Carb, with its calculator data output connected to an IBM typewriter-printer, became the sign of an up-to-date biomedical laboratory in the 1960s and 1970s (Fig. 1).

In this study, I briefly discuss the introduction of emitters of low energy ß-particles (electrons) such as ^{35}S (sulfur), ^{14}C (carbon), and ^{3}H (tritium) to biomedical research during the 1940s and early 1950s. The technologies initially available to monitor these biological tracer elements in biochemical reactions were of very limited efficiency. I then show how several epistemological, technological, and cultural factors came to interact in the aftermath of World War II, which contributed to the establishment of liquid scintillation counting as an alternative to traditional methods, such as solid sample counting or gas counting based on ionization.

The first commercial liquid scintillation counter that became the prototype of a continuous production series was built for the University of Chicago by Lyle E. Packard in 1953. I have chosen the story of this prototype as an example of the development of a piece of research technology, without aiming to describe the complete history of liquid scintillation counting in all its bewildering technical details and scientific ramifications. Between 1953 and 1970 the design of the instrument underwent a cascade of technical changes that, after much exploratory tinkering, made its generic application possible. This in turn opened new epistemic dimensions for radioactive experimentation in biology and medicine. I follow the main events in the development of sample preparation, data processing, and the instrument's circuitry - a development that exemplifies the commercialization of nuclear energy in postwar America and beyond. Finally, I look at how the relations between producer and customers took shape as Packard Instrument grew from a one-man home business into an international corporation.

Radioactive tracing is an example of what Gerhard Kremer, a former president and now retired executive of the International Bureau of Packard Instrument in Zurich, calls a "research-enabling technology," i.e. a technology that opens new fields of investigation.[3] According to Kremer, it is characteristic of such technologies that they paradoxically permit questions to be answered that have not yet been posed.

3 Interview with Dr. Gerhard Kremer, Zurich, 2 April, 1996.

Basically, radioactive tracing has three components. The first is the production of suitable radioactive isotopes and the incorporation of these isotopes into a variety of organic molecules. It is a feature of radioactive tracers that they do not noticeably alter the chemical or biological characteristics and functions of the compounds into which they are incorporated. The second component of radioactive tracing is the development of experimental systems in which particular metabolic reactions are represented and visualized, preferably in vitro, through the addition of radioactive molecules as tracers. The third component is the development of appropriate measuring devices. This paper will be largely confined to the third aspect of radioactive tracing.[4]

2. Radiolabels in Biological and Medical Research

Biological and medical research began to change during the 1920s and 1930s. It was in effect revolutionized during World War II and immediately thereafter through the advent of artificial radioactive isotopes.[5] Of special importance to this paper are the radioactive isotopes of those elements that represent major constituents of biological molecules, such as hydrogen, carbon, phosphorus, and sulfur. Radioactive phosphorus (^{32}P) was one of the first cyclotron-produced radioactive isotopes. In 1939 Luis Alvarez and Robert Cornog, using the cyclotron at the Radiation Laboratory (Rad Lab) of the University of California at Berkeley's Department of Physics, obtained radioactive hydrogen (^{3}H) by bombarding deuterium gas with deuterons.[6] Ernest Lawrence, head of the Rad Lab, immediately realized the potential of the finding: "Radioactively labeled hydrogen opens up a tremendously wide and fruitful field of investigation in all biology and chemistry."[7] He began negotiations with the Rockefeller Foundation for a large grant. Less than a year later, Samuel Ruben and Martin Kamen, using Lawrence's machine, obtained radioactive carbon (^{14}C) by bombarding graphite with deuterons.[8] The construction of

4 Elsewhere, I have given an example of the second aspect, i.e. the construction of appropriate experimental systems. See Hans-Jörg Rheinberger, Toward a History of Epistemic Things. Synthesizing Proteins in the Test Tube. Stanford University Press, Stanford 1997.

5 For an early overview see Georg von Hevesy, Historical sketch of the biological application of tracer elements, Cold Spring Harbor Symposia on Quantitative Biology 13 (1948), 129-150; for the production of biologically and medically relevant istotopes in the first particle accelerators see, e.g., John L. Heilbron and Robert W. Seidel, Lawrence and His Laboratory: A History of the Lawrence Berkeley Laboratory, vol. I. University of California Press, Berkeley 1989, especially Chapter VIII; for the revolution of biomedicine in the wake of the Manhattan Project see Timothy Lenoir and Marguerite Hays, The Manhattan Project for Biomedicine, in Philip R. Sloan (ed.), Controlling Our Destinies: Historical, Philosophical, Social and Ethical Perspectives on the Human Genome Project. University of Notre Dame Press, South Bend, Indiana, in press (1999).

6 Luis W. Alvarez and Robert Cornog, Helium and hydrogen of mass 3, The Physical Review 56 (1939), 613.

7 Quoted in Heilbron and Seidel 1989, p. 373.

8 Samuel Ruben and Martin D. Kamen, Radioactive carbon of long half-life, The Physical Review 57 (1940), 549; Martin D. Kamen and Samuel Ruben, Production and properties of carbon 14, The Physical Review 58 (1940), 194; see also Martin D. Kamen, Early history of carbon-14, Science 140 (1963), 584-590. This paper was widely circulated; it appeared also in the Journal of Chemical Education (1963), and as an introduction to Seymour Rothchild (ed.), Advances in Tracer Methodology. Vol. 3, Plenum Press, New York 1965.

powerful particle accelerators, and later, controlled fission, were crucial for the production of a large variety of new isotopes.[9] In the aftermath of World War II, ^{3}H, ^{14}C, ^{32}P, and ^{35}S, derived in particular from production in nuclear reactors, became widely available for biological and medical experimentation from the Isotope Distribution Program of the Atomic Energy Commission.

Like phosphorus and sulfur, hydrogen and carbon are ubiquitous constituents of organic matter. And like phosphorus-32 and sulfur-35, their radioactive isotopes - hydrogen-3 and carbon-14 - emit ß-particles in their decay and have a half-life long enough to offer the prospect of being used as tracers in metabolic studies. Typically in such experiments, the in vivo distribution or incorporation of these atoms into biological molecules is monitored. As an alternative, the metabolic fate of molecules isotopically labeled prior to their application began to be followed in vitro. With the exception of phosphorus, however, their radiation energy was not high enough to be measured reliably by the conventional Geiger-Müller counting tubes in use at the end of World War II, which recognized carbon-14 only poorly and tritium not at all because its low energy ß-particles could not penetrate the walls of the tubes.

The huge war efforts of the United States, under the auspices of the Manhattan Project, resulted in an unprecedented expansion of radiation research and expertise, as well as its diagnostic and therapeutic application in nuclear medicine, including human experimentation.[10] As a byproduct of nuclear reactor development, radioisotopes came to abound. When the war was over, the United States concentrated its atomic research in a network of national laboratories, among them Los Alamos, Berkeley's Radiation Lab, Oak Ridge, and Argonne. They were supervised by the Atomic Energy Commission (AEC), which was set up in 1947 as a civilian, governmental agency to coordinate the military, economic, political, and scientific work in atomic energy. Promoting the production of fissionable material and atomic devices for military use was top priority, but part of AEC's mission was also to succeed in "giving atomic energy a peaceful, civilian image" and, therefore, to promote research in such areas as radiobiology and radiomedicine.[11] In its first year, the AEC expanded to include a biology and medicine division. Within the first few postwar years, radioisotopes flooded the laboratories and hospitals. In 1947 the isotopes produced in the Oak Ridge nuclear reactor alone were "the equivalent of thousands of years of cyclotron production."[12] In the summer of 1946, the Oak Ridge laboratory began delivering radioisotopes to hospitals and universities nationwide as part of the Isotope Distribution Program of the AEC initiated by its director Paul Aebersold who had done his PhD with

9 W. J. Whitehouse and J. L. Putman, Radioactive Isotopes. An Introduction to their Preparation, Measurement and Use. Clarendon Press, Oxford 1953, especially chapter IV on the production of radioactive isotopes.
10 Lenoir and Hays 1999; Heilbron and Seidel 1989, chapter VIII.
11 For the changing images of nuclear energy, see Spencer R. Weart, Nuclear Fear. A History of Images. Harvard University Press, Cambridge 1988.

Ernest Lawrence in Berkeley.[13] In 1947 AEC sold phosphorus-32 for $ 1.10 per millicurie, iodine-131 for $ 1.70, sulfur-35 for $ 35.00, and carbon-14 for $ 50.00.[14] In 1948 isotopes for biomedical research, cancer diagnostics and therapy even became free of charge, as part of the atoms-for-peace campaign.[15] Phosphorus-32 and iodine-131 had already been used in cancer diagnostics and therapy for a decade,[16] and sulfur-35 and carbon-14 held promise to become ideal tracers for biochemical assays. The impact of this ready supply of isotopes was massive. Between 1945 and 1956 the percentage of the total number of studies published in the American Journal of Biological Chemistry which used radioactive isotopes increased from 1 to 39%.[17] A brief sampling suggests that at this percentage, a saturation level had been reached for the years to come.[18] In 1966, more than 5000 shipments with a total of 2.5 million curies left Oak Ridge.[19]

The virtually ubiquitous presence of radiation research and application in military as well as in civilian, environmental, and medical contexts called for new, sensitive and reliable detection, monitoring, and measurement devices. Postwar declassification of investigations in radiation instruments also stimulated the search for alternative counting methods.[20] Companies such as Radiation Counter Laboratories (Chicago), Instrument Development Laboratories (Chicago), North American Philips Company (New York), Victoreen Instrument Company (Cleveland), General Radio Company (Cambridge), Cyclotron Specialties Company (Moraga, CA), Engineering Laboratories (Tulsa), Geophysical Instrument Company (Arlington), soon produced counters of all types and sizes which were widely advertised in the scientific and technical literature.[21] The beginnings of the commercial nuclear industry enhanced the trend.[22]

12 Richard G. Hewlett and Oscar E. Anderson, Jr., A History of the United States Atomic Energy Commission. Volume I, The New World 1939/1946 and Volume II, Atomic Shield 1947/1952. The Pennsylvania State University Press, University Park, Pennsylvania 1962. Volume III was added later. See Richard G. Hewlett and Jack M. Holl, Atoms for Peace and War, 1953-1961. University of California Press, Berkeley 1989. The quotes are from Vol II, pp. 96 and 109.
13 Lenoir and Hays 1999.
14 A.E.C. Radioisotopes, Nucleonics 1 (No. 1) (September 1947), 64-69.
15 Hewlett and Anderson II 1962, p. 253.
16 Heilbron and Seidel 1989, chapter VIII; Lenoir and Hays 1999.
17 Engelbert Broda, Radioactive Isotopes in Biochemistry. Elsevier, Amsterdam 1960, p. 2.
18 In the first quarter of 1959, the number was 39%, in 1961, 43%, and in 1963, 33%.
19 Waldo E. Cohn, Introductory remarks by chairman, in Seymour Rothchild (ed.), Advances in Tracer Methodology. Vol 4, Plenum Press, New York 1968, pp. 1-10.
20 Hewlett and Anderson II 1962, p. 247.
21 These companies are a sample taken from the first issues of Nucleonics in 1947.
22 Brian Balogh, Chain Reaction. Expert Debate and Public Participation in American Commercial Nuclear Power, 1945-1975. Cambridge University Press, Cambridge 1991.

3. Early Steps in Radiation Measurement

In the early years of radiation research around the turn of this century one of the first methods for quantifying the activity of radioactive samples was based on the phenomenon of scintillation. Sir William Crookes in London developed a method for counting what he called the "emanations" of radium based on the scintillations, or light flashes, that these emanations provoked on a screen of zinc sulfide.[23] The light flashes were counted visually by using a simple microscope. Crookes' observation was very soon confirmed by Julius Elster and Hans Geitel from Wolfenbüttel.[24] Five years later, Erich Regener in Berlin recorded the α-particles of polonium using the scintillation method.[25] This method was widely used in nuclear physics for about two decades, although it had major disadvantages resulting from the fact that the "counters" were humans: "Rapid fatigue of the observer and subjective influences require a frequent change of observers. They can only observe for half a minute up to a minute, and need long intervals in between. During a whole week, the time in which they can reliably observe amounts to two hours at best. The net effect is poor; good and useful computations can only be expected for 20 to 40 scintillations per minute."[26]

The scintillation method gradually fell into oblivion when Geiger-Müller counters came into use in the late 1920s.[27] These instruments were based on the ionizing capacity of the emitted particles and the ensuing discharges produced in an electrical field in a gas-filled tube. Geiger-Müller counters proved useful for the detection of ß-particles of higher energy: γ-rays could be measured, albeit with low efficiency, through the secondary electrons which they produced when penetrating the walls of the tube. Later versions of the Geiger-Müller counting tubes were supplied with a thin mica end-window in front of which a solid sample could be mounted after plating it directly on aluminum planchets. With this device, which remained in use well into the 1950s, ß-particles emitted by radioactive carbon could be measured with an efficiency of about 10%. The weak ß-emissions of tritium, however, remained beyond the scope of this technique.

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23 William Crookes, The emanation of Radium, Proceedings of the Royal Society of London 71 (1903), 405-408.

24 Julius Elster und Hans Geitel, Über die durch radioaktive Emanation erregte scintillierende Phosphoreszenz der Sidot-Blende, Physikalische Zeitschrift 4 (1903), 439-440.

25 Erich Regener, Über Zählung der a-Teilchen durch die Szintillation und die Größe des elektrischen Elementarquantums, Verhandlungen der deutschen physikalischen Gesellschaft 10 (1908), 78-83.

26 "Schnelle Ermüdbarkeit des Beobachters und subjektive Einflüsse erfordern häufigen Wechsel der Beobachter, die nur, mit langen Zwischenpausen, für eine halbe bis eine Minute zählen und pro Woche nicht mehr als zwei Stunden insgesamt zuverlässig beobachten können. Der Nutzeffekt ist sehr gering; gute, brauchbare Zählungen gelingen nur bei 20 bis 40 Szintillationen pro Minute." Adolf Krebs, Szintillationszähler, Ergebnisse der exakten Naturwissenschaften 27 (1953), 361-409, p. 362.

27 More details on the early history of radioactivity research and measurement can be found in J. A. Hughes, The Radioactivists: Community, Controversy, and the Rise of Nuclear Physics. PhD Thesis, University of Cambridge, 1993; Thaddeus J. Trenn, The Geiger-Müller counter of 1928, Annals of Science 43 (1986), 111-135; Thaddeus J. Trenn, Die Erfindung des Geiger-Müller-Zählrores, Deutsches Museum, Abhandlungen und Berichte 44 (1976), 54-64; Friedrich G. Rheingans, Hans Geiger und die elektrischen Zählmethoden, 1908-1928. D.A.V.I.D. Verlagsgesellschaft, Berlin 1988.

Another technique based on ionization consisted in converting the sample into gaseous form - for example, by oxidizing ^{14}C-labeled compounds to produce radioactive carbon dioxide and water - and then using ionization chambers to monitor the decay events. This method of gas counting worked in principle, but one of the big disadvantages was the very tedious sample preparation procedure and the difficulties of quantifying the probes to be measured.

At the beginning of the 1940s scintillation counting was taken up again as a result of developments in another field: photoelectricity. Peter Galison, distinguishing an "image" tradition from a "logic" tradition in the history of monitoring methods in particle physics, describes this development as follows: "What transformed the scintillator's flash and Cerenkov's glow into basic building blocks of the logic tradition was the electronic revolution begun during the war. When attached to the new high-gain photomultiplier tubes and strung into the array of amplifiers, pulse-height analyzers, and scalers that emerged from the Rad Lab and Los Alamos, then and only then did the scintillator and Cerenkov radiation become part of the material culture of postwar physics."[28] The physicist and biophysicist Adolf Theodor Krebs, who had been a staff member of the Kaiser Wilhelm Institute for Biophysics in Frankfurt from 1937, and who in 1947 became director of the Division of Radiobiology of the U.S. Army Medical Research Laboratory at Fort Knox, was probably the first to develop an instrument in which the human counting component was replaced by a highly sensitive, quick-responding photoelectric device for detecting and counting scintillations.[29] Attempts to improve combined scintillation and photoelectric gadgets intensified toward the end of the war, mainly because of the construction of efficient and reliable photomultipliers. Radio Corporation of America in the United States and E.M.I. in Britain soon became leaders in this technology, which was essential for weapons control and guidance systems as well as for civilian mass communication. Scintillation counters are usually understood as consisting of an appropriate scintillating crystal in conjunction with a photomultiplier.[30] Devices were constructed to measure α-particles[31] as well as ß-particles and γ-rays.[32] Alternatively, the Geiger-like photon tube counting devices - essentially a combination of the classical scintillation arrangement with a photosensitive Geiger tube of special design - became popular. They could be used for α-/ß-/γ- surveys, for the selective detection of α-particles in the presence of ß-particles and γ-ray background, for ß-particle detection alone,

28 Peter Galison, Image and Logic. A Material Culture of Microphysics. The University of Chicago Press, Chicago 1997. p. 454.

29 Adolf Krebs, Ein Demonstrationsversuch zur Emanationsdiffusion, Annalen der Physik 39, 5. Folge (1941), 330-332; see also Adolf T. Krebs, Early history of the scintillation counter, Science 122 (1955), 17-18.

30 Samuel Crowe Curran and W. R. Baker, A photoelectric alpha particle detector, U.S. Atomic Energy Commission Rpt. MDDC 1296, 17 November 1944, declassified 23 September 1947.

31 J. W. Coltman and Fitz-Hugh Marshall, Photomultiplier radiation detector, Nucleonics 1 (No. 3) (November 1947), 58-64.

32 Immanuel Broser and Hartmut Kallmann, Über die Anregung von Leuchtstoffen durch schnelle Korpuskularteilchen I, and Über den Elementarprozess der Lichtanregung in Leuchtstoffen durch alpha-Teilchen, schnelle Elektronen und gamma-Quanten II, Zeitschrift für Naturforschung 2a (1947), 439-440 and 642-650.

or for γ-ray detection.[33] The main problem with the former type of instruments was to contain the dark current of the photomultiplier, that is, the spurious activity of the device; the latter type of instruments had the disadvantage of having a finite dead time of the Geiger tube between the discharges. Together with new solid scintillators for accurately counting α-particles, γ-rays, and ß-particles,[34] these technologies were recognized by contemporaries as "one of the most important advances in devices for the detection of nuclear radiations since the invention of the Geiger-Müller counter,"[35] and as heralding a "new era" of nuclear development and research,[36] both because of the high resolution and efficiency of the counting process, and because of the applications involving low specific activity. In 1949 the first conference on scintillation counting was held at Oak Ridge.

4. Liquid Scintillation Counting

A new and different direction in counting technology was charted when Hartmut Kallmann from the Physics Department of New York University,[37] in collaboration with Milton Furst, seriously began to work on his earlier observation that certain organic substances, such as anthracene, in aromatic solvents such as toluene, worked as scintillators, and when used in conjunction with an electron-multiplier phototube should be suitable for liquid scintillation counting.[38] At Princeton University, George Reynolds and his colleagues worked on the new technology as well.[39] As in the case of solid scintillation, the process basically involved the conversion of radioactive decay events into photons, and the photons into photoelectrons that

33 C. E. Mandeville and M. V. Scherb, Photosensitive Geiger counters: their applications, Nucleonics 7 (No.5) (November 1950), 34-38.

34 Robert Hofstadter, Alkali halide scintillation counters, The Physical Review 74 (1948), 100-101; Robert Hofstadter, The detection of gamma-rays with thallium-activated sodium iodide crystals, The Physical Review 75 (1949), 796-810.

35 G. A. Morton and J. A. Mitchell, Performance of 931-A type multiplier as a scintillation counter, Nucleonics 4 (No. 1) (January 1949), 16-23, p. 16.

36 Robert W. Pringle, The scintillation counter, Nature 166 (1950), 11-14.

37 Kallmann did his thesis under Max Planck and had been a staff member of the Kaiser Wilhelm Institute for Physical Chemistry and Electrochemistry in Berlin-Dahlem from 1920. In 1933, he was dismissed after the Nazis came to power. However, he was not allowed to leave the country but was forced to work with I.G. Farben throughout the war (Gerald Oster, A Young Physicist at Seventy: Hartmut Kallmann, Physics Today [April 1966], 51-54). Working as professor (1945-1948) at the Technical University of Berlin, he had already announced in 1947 his version of a scintillation counter (Broser and Kallmann 1947). A year later, he came to the United States, joining the U.S. Army Signal Corps Laboratories in Belmar, New Jersey, as a research fellow before being appointed as professor and director of the Radiation and Solid State Laboratory at New York University's Physics Department in 1949.

38 Hartmut Kallmann and Milton Furst, Fluorescence of solutions bombarded with high energy radiation (Energy transport in liquids), Part I, The Physical Review 79 (1950), 857-870; Hartmut Kallmann and Milton Furst, Fluorescence of solutions bombarded with high energy radiation (Energy transport in liquids), Part II, The Physical Review 81 (1951), 853-864; Milton Furst and Hartmut Kallmann, Fluorescence of solutions bombarded with high energy radiation (Energy transport in liquids), Part III, The Physical Review 85 (1952), 816-825.

39 G. T. Reynolds, F. B. Harrison, and G. Salvini, Liquid scintillation counters, The Physical Review 78 (1950), 488.

could be amplified and counted. The energy of the decay events was absorbed by the scintillator solvent, which then transferred the energy to the scintillator solutes causing them to emit photons. These in turn were collected in a photomultiplier tube and amplified. The energy transfer processes in the solvent system were only poorly understood at the beginning, and it took years to elaborate the physical details. The early work in this completely new field of liquid scintillation counting concentrated on the external counting of high energy radiation emitted from sources such as radium (Kallmann) or cobalt-60 (Reynolds).

In 1951, M. S. Raben from the New England Center Hospital and Tufts College Medical School in Boston, and Nicolaas Bloembergen from the Nuclear Laboratory of Harvard University, suggested "that a simple and geometrically ideal counting system might be obtained by dissolving the material to be counted directly in [the] liquid. This method would facilitate particularly the counting of soluble compounds labeled with a weak ß-emitter, such as C^{14}."[40] First measurements showed that with such internal sample counting, it might be possible to trace even nanocurie amounts of carbon-14. This finding promised a gain in sensitivity, efficiency and accuracy of measuring the radioactivity of other weak ß-emitters such as ^{35}S, and, for the first time, even ^{3}H. The reason was the homogeneous distribution of the radioactive sample and the virtually complete absorption of the emitted energy by the scintillator.

Some early internal sample liquid scintillation counters were basically adaptations of the crystal scintillation spectrometers available at the end of the 1940s. They consisted of the sample in a glass bottle, surrounded by a reflector and made contiguous to the photomultiplier tube by an optical coupling fluid such as silicon oil, glycerin, or Canada balsam. This arrangement was connected to a preamplifier, an amplifier, a pulse-height analyzer, and a scaler element. The expectation was that tritium could be measured by such an instrument with an efficiency of up to 20%. However, the "dark current" (spontaneous thermionic emissions from the photomultiplier cathode) became prohibitively strong at the high voltages required to attain maximum efficiency.[41] The noise could be somewhat reduced but not suppressed by the selection of appropriate multiplier tubes, by pulse-height discrimination, and by refrigeration. The latter in turn put constraints on the scintillator solutes in terms of the temperature-dependence of their solubility. The single photomultiplier liquid scintillation spectrometer remained a transient adaptation of the previous solid scintillation counter.

A major advance was made by the group working at the Los Alamos Scientific Laboratory, especially Newton Hayes and R. Hiebert, toward establishing internal sample liquid scintillation

40 M. S. Raben and Nicolaas Bloembergen, Determination of radioactivity by solution in a liquid scintillator, Science 114(1951), 363-364.

41 F. Newton Hayes, R. D. Hiebert, and R. L. Schuch, Low energy counting with a new liquid scintillation solute, Science 116 (1952), 140.

counting as the preferred method for measuring the activity of low energy ß-emitters. They accomplished this by exploring the potential of various scintillator solutions to meet typical applications in biology and medicine, and by developing improved and robust coincidence-type counting equipment.[42] The principle of coincidence counting went back to the days of Walther Bothe and Hans Geiger,[43] and it had been adapted by engineers at the Radio Corporation of America, R.C.A. Laboratories Division in Princeton, for use in a solid scintillation counter in 1949 (Fig. 2).[44] The method was adapted by Kallmann as well as Reynolds to external liquid scintillation counting in 1950, and by Raben and Bloembergen to internal liquid scintillation counting in 1951.[45] In simple terms, the noise generated by the electronic equipment was virtually eliminated by placing two photomultipliers opposite each other that simultaneously examined the same sample. After amplification, only those pulses were counted that arrived "in coincidence" at the pulse height analyzer and therefore could be assumed to arise from one and the same scintillation event caused by a decay electron rather than by system noise. Under these conditions, a single tube noise rate of tens of thousands of counts per minute (cpm) could be reduced to the acceptable order of tens of counts per minute.

Between 1952 and 1957, six internal liquid scintillation counting coincidence counters were built for use in Wright Langham's Biomedical Research Group at the Health Division of Los Alamos Scientific Laboratory.[46] Other people at Los Alamos thought more in terms of external liquid scintillation counting. Ernest Anderson built a machine for externally monitoring whole human bodies with naturally occurring potassium-40 for such things as gross body composition or for measuring the accumulation of radioactivity in the bodies of people exposed to radioactive fallout. In 1957, he duly noted the "sharp rise in public concern over the effects of low intensity radiation on man over the past few years." Exposure to radioactivity, its measurement, control, and prevention had become a vehemently debated issue with the spread of atomic power from weapon research, development and production - including weapon testing - to industrial plants and the biomedical sector. In a deliberately polemic and apologetic tone Anderson mocked that there might soon be "a legal prohibition of some of our most popular materials of construction, notably concrete and brick, on the basis of their high concentration of natural ra-

42 Hayes, Hiebert and Schuch 1952; R. D. Hiebert and R. J. Watts, Fast-coincidence circuit for H3 and C14 measurements, Nucleonics 11 (No. 12) (December 1953), 38-41.
43 Galison 1997, pp. 438-454.
44 G. A. Morton and K. W. Robinson, A coincidence scintillation counter, Nucleonics 4 (No. 2) (February 1949), 25-29.
45 Reynolds, Harrison and Salvini 1950; Hartmut Kallmann and Carl A. Accardo, Coincidence experiments for noise reduction in scintillation counting, Reviev of Scientific Instruments 21 (1950), 48-51; Raben and Bloembergen 1951.
46 R. D. Hiebert and F. Newton Hayes, Instrumentation for liquid scintillation counting at Los Alamos, in Carlos G. Bell and F. Newton Hayes (eds.), Liquid Scintillation Counting. Pergamon Press, New York 1958, pp. 41-49; Wright H. Langham, Application of liquid scintillation counting to biology and medicine, ibid., pp. 135-149.

dioactivities such as radium and potassium."[47] Meanwhile, a colleague of Anderson, Frederick Reines, was engaged in making giant liquid scintillation detectors for neutrino and neutron detection.[48]

In the context of a discussion of instrumentation for research and production of generic, multipurpose devices, this constellation of instrument development is particularly interesting. For at the beginning the new technology of internal liquid scintillation counting served fairly special purposes in the whole context of radiation measurement, and the associated equipment had quickly become a rather sophisticated assembly of different physical, organochemical, and technical parts into which biological, and other, material happened to be inserted. There appeared to be a long way to go, if indeed there was such a way, to achieving the objective of producing an instrument for routine laboratory work that could be operated by inexperienced personnel. The prospect for "ease of preparing counting samples by simply dissolving the substance in solvent in a bottle" was not on the horizon.[49] The possibility of a generic use of the new devices that could appeal to a wide variety of laboratory workers concerned with isotope production, monitoring and waste management in materials research and in medical diagnostics, biology, chemistry and pharmacology was remote. Additional technical challenges included sample vial geometry, the elimination of luminescence, the appropriate choice of vial glass type, the optimization of photocathode sensitivity and the emission spectrum of the scintillator, and many more. The sample material in turn had also to meet certain preconditions. It had to be soluble in the organic liquid scintillation solvents, which was not a trivial matter; and it needed to be minimally colored in order to avoid quenching, that is, the depression of the photon-yield induced by the probe itself.

5. Testing a Commercial Prototype

The first generation of commercial liquid scintillation coincidence counters did not originate from Los Alamos. They came from the University of Chicago, another of the centers of nuclear technology research and development during and after World War II. It was here that Arthur Compton established the Metallurgical Laboratory (Met Lab) in 1941, where Enrico Fermi, Walter Zinn, and their colleagues built the world's first nuclear reactor - Chicago Pile-1 - which produced a self-sustaining nuclear chain reaction late in 1942. In 1946 Met Lab became part of

47 Ernest C. Anderson, The Los Alamos human counter, in Carlos G. Bell and F. Newton Hayes (eds.), Liquid Scintillation Counting. Pergamon Press, New York 1958, pp. 211-219, p. 211.

48 Frederick Reines, Giant liquid scintillation detectors and their applications, in Carlos G. Bell and F. Newton Hayes (eds.), Liquid Scintillation Counting. Pergamon Press, New York 1958, pp. 246-257; Galison 1997, pp. 460-463.

49 Jack D. Davidson and Philip Feigelson, Practical aspects of internal-sample liquid-scintillation counting, International Journal of Applied Radiation and Isotopes 2 (1957), 1-18, p. 3.

Argonne National Laboratory, which was a center for nuclear reactor technology and nuclear propulsion engines.[50] At the University of Chicago, too, Willard Frank Libby pioneered the use of naturally occurring radioactive carbon as a means of carbon dating of organic matter.

Lyle E. Packard had earned a degree in mechanical engineering from the Illinois Institute of Technology in Chicago. During the war, he was recruited into the Navy, where he received training in electronics and became involved in work on radio, radar, and sonar. After the war, in the spring of 1946, he was hired as an engineer for the Institute of Radiobiology and Biophysics at the University of Chicago by its director Raymond Zirkle. The Institute was one of three new research bodies (the two others being the Institute for Nuclear Studies, now the Enrico Fermi Institute, and the Institute for the Study of Metals, now the James Franck Institute) that were established by the University's President Robert Maynard Hutchins in the context of the University's peacetime program initiated immediately after the war.[51] They took over the parts of the Manhattan Project that had been operating under the umbrella of the University of Chicago. Hutchins wanted the new Institutes "to advance knowledge and not primarily to develop the military or industrial applications of nuclear research." He pondered that "for the past six years the United States has abandoned both basic research and the training of a new generation of scientists. It is essential to our progress and our welfare that we overcome that deficiency."[52]

Besides designing and overseeing the construction of temporary laboratory space during the first few years of the Institute's work, Packard supervised a small staff of engineers, technicians and machinists whose role was designing and building special instrumentation and installing and maintaining equipment for the various research groups in the Institute. This involved a wide variety of very specialized items. For example, there was physiological equipment for studying axon cells in squids for a group headed by Kenneth Cole and George Marmont. Raymond Zirkle and William Bloom required customized systems for time-lapse photomicrography and various radiation equipment, including a Van de Graff generator for basic radiobiological studies.

Along with several other individuals, the physicist Leo Szilard had a number of special requirements. Together with Aaron Novick, Szilard was at this time "retooling" in biology and thought about building a "chemostat," an instrument that would keep a bacterial population growing over an indefinite period of time in order to enable study of their behavior subsequent to muta-

50 Jack M. Holl, Argonne National Laboratory, 1946-96. University of Illinois Press, Urbana and Chicago 1997, especially chapters 1 and 2; Argonne National Laboratory, Argonne News 30, 5 (1986), 3-15; see also Hewlett and Anderson Vols. I and II 1962.

51 William H. McNeill, Hutchins' University. A Memoir of the University of Chicago 1929-1950. The University of Chicago Press, Chicago 1991, pp. 123-124, 158.

52 One in Spirit. A Retrospective View of the University of Chicago on the Occasion of its Centennial. The University of Chicago Publications Office, Chicago 1991, p. 105.

tion.[53] After reluctantly leaving Columbia in 1942 and joining Compton's Met Lab in 1942, Szilard took an indefinite leave of absence without pay from the Manhattan Project in Chicago in the fall of 1945, following his unsuccessful attempt to convince President Truman not to use the atomic bomb against Japan. In October 1946 President Hutchins appointed him professor of biophysics at the Institute of Radiobiology and Biophysics.[54] Packard recalls: "When Szilard joined the University he had a number of patentable ideas, things that he wanted to preserve for himself and he excluded those from his contract. It was on one of those things in particular that I have worked personally with him, after-hours, weekends and so on. So I got to know him a little bit. Very, very interesting experience." Szilard's laboratory was designed by Packard and was located in the basement of the former synagogue of a Jewish orphanage. The building was taken over by the University of Chicago and was ready by January 1948.[55] The first chemostats were placed in a thermostatically controlled room at 37 °C. "We did that at Szilard's request in a very inexpensive way by controlling banks of commercial 1500 Watt heaters."[56]

In 1948, Packard also came into contact with a group of researchers at the Institute for Nuclear Studies who were using mica end-window Geiger counters for counting ^{14}C. The efficiency of these counters was very poor. Packard recounts that it was of the order of 10%. Nathan Sugarman at the Institute had devised an instrument without a window, and Packard engaged in efforts to construct a workable windowless counter of the sort where the sample could be pushed right into the counting chamber. The aim was to yield a higher counting efficiency, by avoiding the absorption of ß-particles in the thin, but not thin enough, mica plate of the window. The use of low energy radioisotopes, whose electrons had only a very short range and which were thus difficult to monitor, was expanding at a rapid pace due to the activities of the Isotope Distribution Program. The reason was that low energy isotopes could be used to label a whole range of organic molecules and so had potentially unlimited application in metabolic studies in vivo and in vitro. In addition, an urgent need for monitoring contamination arose. And the more the use of these labeled compounds (among them nucleotides, amino acids, fatty acids, sugars, antibiotics) spread, the more counting devices were needed, apparent in requests from visitors. "At that point we had so many visitors coming to the University, visiting these new Institutes, and they would invariably come around and ask: 'Where could I get one of these?' 'Well, you can't get one, we make them here.'"[57]

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53 Bernard T. Feld and Gertrud Weiss Szilard, eds., The Collected Works of Leo Szilard. Scientific Papers, Volume I. The MIT Press, Cambridge, MA 1972, see especially Part IV, Published Papers in Biology (1949-1964), with an introduction by Aaron Novick, pp. 389-524.

54 David A. Grandy, Leo Szilard. Science as a Mode of Being. University Press of America, Lanham, MD 1996, especially chapters 5 and 6; William Lanouette, Genius in the Shadows: A Biography of Leo Szilard; the Man Behind the Bomb. Scribner's, New York 1992.

55 Feld and Weiss Szilard 1972, p. 389.

56 Interview with Lyle E. Packard, Chicago, November 5, 1996.

57 Packard, Interview 1996.

In 1949, as a result of this demand, Packard began to think about starting a company part-time. With the permission of the University administration, he set up a company, together with a partner, called "Research Equipment and Service." Their first product was a windowless counter that Herbert Anker had designed in the Biochemistry Department. It had a rather slow transfer mechanism with one sample position to push in and pull out. Packard sold these to customers from other institutions as well as from other departments at the University. A variation of the windowless counter soon followed, with a much more efficient circular sample device that had three positions: an internal counting position, a pre-flushing position, and a loading and unloading position exposed to the air. Another of the company's early products was not directly related to monitoring radioactivity. It was an unspectacular fraction collector.

At the Institute of Nuclear Studies, Packard had become friends with James Arnold, a former student and colleague of Willard Libby. Libby served as a member of the General Advisory Committee of the AEC (1950-1954) and, a decade later in 1960 received a Nobel Prize for developing the concept and method of carbon-14 dating of organic matter.[58] Libby had obtained his first results with a solid sample Geiger-Müller counter, "a big thing about 4 inches in diameter, with all kinds of shielding around it."[59] James Arnold had heard of the potential of liquid scintillation counting as advocated by Kallmann and Furst from New York University and by Reynolds from Princeton. He set out to explore the prospects for internal liquid scintillation counting in Libby's carbon-dating project. His instrument had a coincidence circuit of the sort that Hayes was building for Langham's Biomedical Research Group at Los Alamos. Arnold maintained good contacts with Hayes and Anderson who gave him access to unpublished data and new scintillation materials. Furthermore, he attempted to push the internal sample idea to its extreme by actually making his very low activity samples the solvent for the scintillator.[60] The Los Alamos work also captured the interest of George Leroy from the Argonne Cancer Research Hospital at the University of Chicago who consulted with Los Alamos on medical matters. While working at the University, Packard followed Arnold's work with great interest. Leroy knew this, and he knew that Packard was working in his own company in 1952. So he asked him to design and build a liquid scintillation system for him.[61] The Argonne Cancer Research Hospital had been founded in 1948 with money from the AEC and was operated by the University of Chicago, as part of AEC's first efforts to fight "America's number-two killer disease."[62]

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58 Willard Frank Libby, Radiocarbon Dating. University of Chicago Press, Chicago 1952.
59 Packard, Interview 1996.
60 "A method for converting samples to aliphatic hydrocarbon is being worked out, so that solutions of good efficiency can be prepared that are 80% sample." James R. Arnold, Scintillation counting of natural radiocarbon: I. The counting method, Science 119 (1954), 155-157.
61 Packard, Interview 1996; Packard to Rheinberger, August 26, 1998.
62 Holl 1997, p. 75.

By that time, in 1952, Packard had left the University in order to work full-time in his company. His business was soon renamed "Packard Instrument Company,"[63] and together with a newly hired colleague Packard started to build a prototype liquid scintillation coincidence system in the front part of his apartment which he transformed into a workshop. It took him about a year to build the first unit, and it was delivered to the Argonne Cancer Research Hospital in 1953 (Fig. 3). None of the basic components of this machine were completely new, but Packard knew how to engineer research equipment. And through his previous experience at the University, he was aware of what biomedical users would require from such an instrument: versatility and easy operation. George Leroy and his colleagues planned to evaluate double-label experiments with tritium and ^{14}C in this machine.[64] "That's when I came up with the idea of designing the production model especially for these two isotopes and naming it the Tri-Carb for ^{3}H and ^{14}C and gave it the model number 314." This requirement determined the unique design of the electronic circuitry for the production units that were to follow.[65] We are faced with the paradoxical situation that what later became a generic device resulted from a deliberate narrowing down of the application range of the instrument at the beginning.

The sale price of the prototype, including the refrigeration unit that basically consisted of an adapted commercial freezer, was $ 6500, about five times the cost of a Geiger counter and a scaler at that time. Eugene Goldwasser, a biochemist who had become associated with Leroy in 1952 after two postdoctoral years with Hermann Kalckar in Copenhagen, recalls: "It was one of those peculiar times of history, at least from my perspective, when we had all the money we needed for research and George could go on and ask Lyle to build (an instrument) without worrying about where to get the money to pay for it. I came to Chicago from Copenhagen, and the first thing I had to do was sit in an unfinished room with stacks and stacks of catalogues and start a lab from nothing. And I figured roughly in 1952 I spent about a million dollars. [This] was all AEC money; there seemed to be no end to it. [That] was part of the original AEC charter from the Congress. They were to promote the use of radioactivity in research and therapy, and to promote the development of instrumentation for study of radioactivity. So that my work, which had little to do with atomic energy or cancer research, [was] funded under their umbrella because I used isotopes."[66] In Denmark he had experimented with radioactive adenine handmade by his mentor Kalckar.[67] Now, he got his labeled compounds from Berkeley's Rad Lab.[68]

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63 His earlier partnership had been limited to work on the windowless Geiger counters.

64 Jon J. Kabara, George T. Okita, and George V. LeRoy, Simultaneous use of H^3 and C^{14} compounds to study cholesterol metabolism. in Carlos G. Bell and F. Newton Hayes (eds.), Liquid Scintillation Counting. Pergamon Press, New York 1958, pp. 191-197.

65 Packard, Interview 1996.

66 Interview with Eugene Goldwasser, Chicago, November 5, 1996; Goldwasser, letter to Rheinberger, November 4, 1998.

67 Eugene Goldwasser, The incorporation of adenine into ribonucleic acid in vitro, Journal of Biological Chemistry 202 (1953), 751-755.

On the one hand this was a very typical story, but on the other hand, it clearly comprised a particular epistemic and technical configuration. There was a mechanical engineer with electronics experience working in close contact with academic researchers on a piece of advanced research technology that held the promise of very specific, local uses in archaeological dating and double-label experiments. When asked about the characteristics of such interaction between researchers and instrument engineers, Packard replied: "I don't think I can generalize my thoughts on the interactions of scientists and engineers. Based on nearly five decades of developing and manufacturing scientific instruments - as well as five years at the University of Chicago functioning in somewhat varying roles, but all generally facilitating the requirements of scientists - I found extreme variations. To a certain extent it depends on the field of science. As might be expected, physicists typically are more concerned with technical specifications and details of the mechanics and electronics of what they want from engineers. Biological and medical researchers, I have found, usually interact with engineers on the basis of the function they wish to accomplish - how easily, how fast, how precisely, etc. - and typically are not interested in details of the equipment as long as it performs what it is supposed to do reliably. There are exceptions and, particularly in earlier times, I have seen extreme cases. For example, I've seen biological scientists who like to play at engineering spend months of their laboratory time improvising something like a homemade fraction collector."[69] Packard's company grew out of these variegated laboratory contacts, and his products were initially purchased principally with federal AEC and Public Health Service money to which there seemed to be virtually no limit in these first years of the Cold War.

Soon Packard relocated his business. He moved out to LaGrange, Illinois, in the suburbs of Chicago. Right after having built the prototype machine for Leroy, he received orders for two more machines. One of them was from Jack Davidson of the Presbyterian Hospital at Columbia University, of which machine Packard said, "That was really the first which I would call a production unit."[70] Davidson used his instrument to do a lot of optimization with respect to sample size and different mixes of solvents, primary and secondary solutes - such as 2,5-diphenyloxazole (PPO) and 1,4-di(2-[5-phenyloxazolyl])benzene (POPOP) - which came to be called "cocktails" in laboratory jargon.[71] As a result, he rated liquid scintillation counting to be "a useful new technique," although "by no means the panacea for all counting problems."[72] Its main advantages were its the excellent sensitivity for very weak decay electrons, high precision, high absolute efficiency, and relative ease of sample preparation. Surveying the early literature, one

68 Eugene Goldwasser, Incorporation of adenosine-5-phosphate into ribonucleic acid, Journal of the American Chemical Society 77 (1955), 6083.
69 Packard to Rheinberger, letter of February 25, 1998.
70 Packard, Interview 1996.
71 Davidson and Feigelson 1957.
72 Davidson and Feigelson 1957, p. 17.

gains the impression that these first commercial machines were themselves mainly part of exploring the scope of the field. They were components of a very small, but self-amplifying circuit. Basically, the application of the methodology consisted in its own optimization.

Clearly, in the early 1950s the liquid scintillation counter was not perceived as being a potentially universal piece of equipment in the world of biomedicine. Nuclear-Chicago, one of the biggest and most experienced instrument builders in the field of radiation technology, had put its bets on solid sample or gas counting fulfilling such a role. According to a user's testimony, the Nuclear Chicago D-47 Micromil gas flow counter, with its ultra-thin Mylar window, reached approximately 40% efficiency for ^{14}C, had a low background count due to its anti-coincidence circuitry, and its sample changer was "nearly fail-safe."[73] But although Nuclear-Chicago only entered liquid scintillation counting at the beginning of the 1960s,[74] Packard's Tri-Carb system was not completely without direct commercial competition in those early years. Tracerlab in Waltham, MA, a company that also produced radioactive biochemicals, undertook some efforts in liquid scintillation counter construction, as did Technical Measurement Corporation in New Haven, CT.[75] Packard recalls an early and fierce competitive test at the National Institutes of Health (NIH) in Bethesda: "Our biggest competition in the early days came at the NIH. It seemed to us, in a much smaller way of course, like something they sometimes had in military procurement, where two companies would be requested to provide special-purpose airplanes for a fly-off to see which one was better. In this case, NIH requested one of our Tri-Carb systems and one of the TMC [Technical Measurement Corporation] units for side-by-side comparisons. After extensive testing, our Tri-Carb system was selected and purchased as the first of dozens that NIH would acquire during the next few years."[76] Edward Rapkin, one of Packard's later colleagues, comments that one of the special features of the Packard unit was that its system logic was "unsymmetrical." That is to say, the two photomultipliers were assigned different functions. One was used for pulse height analysis, the other one monitored coincidences (Fig. 4). This arrangement required only one good phototube and one good amplifier, a distinct advantage in the days of vacuum tubes.[77] In 1956, Packard was working with 25 employees and sold some 20 systems.[78]

73 Loftfield, letter to Rheinberger, September 24, 1998.
74 Edward Rapkin, Development of the modern liquid scintillation counter, in Edwin D. Bransome (ed.), The Current Status of Liquid Scintillation Counting. Grune & Stratton, New York 1970, pp. 45-68, p. 47.
75 For this instrument, see Utting 1958.
76 Packard, Interview 1996.
77 Rapkin 1970, p. 48.
78 Packard Instrument Company, Annual Report 1965, Ten Year Financial Highlights.

6. Automation: Making the Instrument Work for "Inexperienced Personnel"

The early Packard Tri-Carb Spectrometer Model 314 was operated manually, timing was mechanical, there was one single sample position, and the electric circuitry was entirely based on vacuum tubes (Fig. 5). Although "the user of this apparatus [did] not need to understand all of the electronics involved," Davidson contended that "any intelligent use of the technique [required] familiarity with the general principles of the electronic equipment."[79]

The first major change of design was introduced in 1957. It consisted of incorporating an automatic 100 sample changer (Fig. 6).[80] Prior to this, changing a sample had been a tedious and time-consuming exercise. Even the high voltage had to be switched off before removing one sample and inserting another one. "Take it out, put the next sample in, close the light-tight chamber, close the lead shield, close the freezer door, turn the high voltage on. And then wait a little bit and then start your count. And your count was manual. So, you sat there and you watched the clock go around for a minute or two minutes or five minutes or whatever."[81] The sample vial was a large fifty millimeter diameter glass vessel that was immersed in silicon oil to make a good optical connection with the phototubes. The first prerequisite for automation was reducing the size of the vials, which also made the silicon oil connection unnecessary. Packard and his associate Soderquist did the detailed design of a circular sample changing device. The previous sample shield had been a horizontal cylinder. It was changed to a vertical iron cylinder, and the turn-table sample-changing device was put on top of it. This model sold: in 1958 some 80 employees produced and delivered close to 100 units. At this point, TMC had discontinued its production of internal liquid scintillation counters, and Packard had a market share of near 100%.

If there is one thing in particular which made the liquid scintillation counter really attractive, it is its transformation into an automatic machine. With the conventional counters that were in operation immediately after World War II, "even when efficiently organized, each assay must have consumed an hour of professional time."[82] The new possibility of the machine conducting serial counts involving hundreds of samples unattended and overnight, opened the prospect of performing experiments of hitherto unheard-of dimensions that required frequent measurements and combined different types of assays. For instance kinetic experiments assaying the association of molecules require probes to be taken at as many time intervals as possible. In addition, these assays usually have to be performed at different temperatures and, in order to be

79 Davidson and Feigelson 1957, p. 3.
80 Lyle E. Packard, Instrumentation for internal sample liquid scintillation counting, in Carlos G. Bell and F. Newton Hayes (eds.), Liquid Scintillation Counting. Pergamon Press, New York 1958, pp. 50-66.
81 Packard, Interview 1996.
82 Loftfield to Rheinberger, September 24, 1998.

reliable, carried out in duplicate or triplicate, which can easily necessitate hundreds of samples. The automatic machine also allowed for the testing of long series of fractions derived from e.g. chromatographic purification, separation columns or preparative ultracentrifugation runs; and it allowed laboratory workers to include in the design of their experiments as many controls as they deemed necessary for reliable results. Packard comments: "Putting this turntable on, and making it automatic, just opened up the possibility for what then were massive studies, I mean, you would take a rat and sacrifice it, and take all the parts of the rat. [It] made it possible for people to design different types of experiments than they ever could have designed before. Previously you never would have designed an experiment for a thousand samples. [Well] I don't know how many times, but certainly many times I have had people come up to me at trade shows, really prominent names in the field and say, 'you know, Lyle, all the work I have done in the last five years I could not have done if I hadn't had a Tri-Carb'."[83]

Initially liquid scintillation counters had just been a potentially promising technology that would allow researchers to introduce tritium labels in their biomedical tracing tools and to exploit carbon-14 labels more efficiently, but the automated variant enabled them to set up experimental systems of previously unthinkable dimensions and design, and to scale up routine monitoring by orders of magnitude. On the epistemic side, the scope of the instrument broadened from locally enhancing sensitivity to gaining a generic impact on the way biomedical research could be conducted. On the experimental side, a quantum leap in monitoring capacity was achieved. Thus, automated liquid scintillation counting became one of the instrumental bridges joining the biochemical and biophysical work on a preparative scale to the small analytical world of molecular biology.

As Wright Langham from the Los Alamos Biomedical Research Group put it toward the end of the 1950s: "Biological and medical investigations by nature call for counting systems with the greatest of versatility. Among the requirements are (a) analyses of large numbers of samples with a minimum of processing; (b) high sensitivity; (c) wide adaptability as to variations in sample size; (d) accommodation of wide variations in nature and chemical composition of the sample; [and] (f) dependable operation with a minimum of servicing." The requirement for large sample numbers results from the necessity of doing multiple counts because of the inherent variability of biological probes, as well as from doing serial experiments of the kind mentioned above. A minimum of processing is necessary to minimize the chances of accidental loss of activity. Every experimenter in the field knows that each processing step between the assay and the counts is principally is one step too much. High sensitivity allows for the low doses of radioactivity often needed to avoid damaging the biological sample. The nature and size of sam-

83 Packard, Interview 1996.

ples often vary because of intrinsic necessities of experiment design. With the new automated machines, liquid scintillation counting promised to match all these needs. Langham went so far as to conclude: "Liquid scintillation counting is the most important recent development in the applications of radioisotopes to biology and medicine."[84]

Edward Rapkin, who joined Packard's company in 1957, recalls: "It did also make the counter business very good. [Because] the thing that converted everything from an occasional sale of three or four a month to some months fifty was the automatic counter."[85] In 1961, more than 700 Tri-Carb spectrometers had been installed all over the world since the delivery of the first production unit in 1954.[86] Around 1960, direct sales to the United States government and its agencies accounted for about 15% of the total sales. The rest were to the universities, the hospitals, and the industry.

In 1959 Tracerlab made a second brief attempt to enter the market, this time with a 40-sample automatic counter. Tracerlab was the first company to use the new E.M.I. photomultiplier that soon became standard in the field, and it was the first to introduce transistorized preamplifiers which, however, in 1959 could not yet match the quiet performance of good vacuum tubes. These innovations notwithstanding, the Tracerlab machine lacked "important user requirements" such as high sample capacity and a light-tight detector.[87] This electronic innovation alone could not outdo convenience and smoothness in operation. In 1960 Packard introduced the 314A Tri-Carb which was entirely transistorized except for the preamplifiers. In 1961, the 314E Tri-Carb series came on the market. It was a completely transistorized liquid scintillation counter exhibiting an improvement of the system logic such that two different isotopes present in one sample could be counted simultaneously with separation efficiencies that had previously required successive counts. Also in 1961, Nuclear-Chicago entered the liquid scintillation market. In 1962, it offered an instrument with a serpentine sample transport and a sample capacity of 150 vials. This machine was able to perform repeated counting cycles, and it allowed grouping of samples such that the counting output could accommodate different users. The instrument provided three counting channels and thus allowed for channel ratio quench monitoring. A mechanical calculator could perform some data processing. Introduction of this Nuclear-Chicago counter was a challenge for Packard, who offered a new model 200 sample capacity Tri-Carb at the same time. Within five years, Nuclear-Chicago's market share rose to an estimated 20%, whereas Packard Instrument's went down from 85 to 63%.[88]

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84 Langham 1958, pp. 136-137.
85 Rapkin in Packard, Interview 1996.
86 Packard Instrument Company, Liquid Scintillation Counting Systems, Advertisement, September 1961.
87 Rapkin 1970, p. 50.
88 Estimates by Edward Rapkin. Packard to Rheinberger, August 26, 1998.

The market expanded rapidly. A glimpse through the publications in the Journal of Biological Chemistry is revealing in this respect. In 1959 roughly one out of ten experiments performed with ^{14}C or ^{3}H was conducted with a liquid scintillation counter. Conventional end-window Geiger-Müller counters, vibrating reed electrometers, and gas flow counters dominated the scene, especially the Nuclear-Chicago D-47 windowless gas flow counter. Only four years later, almost every third experiment involved a liquid scintillation counter of which more than 80% were Packard Tri-Carbs, and by the end of the 1960s virtually every ^{14}C or ^{3}H-based experiment relied on a liquid scintillation counter. By that time, the application of the method had become so ubiquitous that it was no longer mentioned in the "Methods" section of a paper.

Concomitantly, competition became fierce, and system logic innovations and user-friendly improvements to the operating and recording equipment became mandatory.[89] In 1962 a couple of people who had left Packard started a company called Vanguard which advertised a bench-top automatic liquid scintillation counter, but went out of business after delivering a few units. In March 1963 Rapkin left Packard and started a small company to produce a liquid scintillation counter he called ANSitron. It became the first unit in production to incorporate automatic external standardization. Packard had started developing ideas for automatic standardization to correct for quenching, and in June 1965 was issued a U.S. patent.[90] In 1966 Picker Nuclear acquired the patent for ANSitron, but shortly went out of business. Also in 1966, low cost models of liquid scintillation counters were introduced by Nuclear-Chicago, Packard, Picker and Beckman. In 1967 both Packard and Beckman announced different and rather sophisticated systems that utilized their automatic standardization equipment to offset the effects of quenching before counting each sample, as opposed to just measuring how much the quench effect is.[91] Packard's company had grown from 50 employees in 1957 to over 500 in 1966, and the corresponding net sales had risen from $ 0.5 million to $ 14 million, which represented well under a thousand units per year. However, a still expanding market was able to accommodate all these competitors (Fig. 7). Liquid scintillation counters began to crowd the laboratory spaces.

The combination of improved system logic, of facilitated operation for multiple users engaged in different experiments in large laboratory settings, of versatility in raw data processing, plus increasingly sophisticated scintillation cocktails for various kinds of probes, made liquid scintillation counting ubiquitous in molecular biological research, in biomedical diagnostics, in

89 Packard to Rheinberger, August 26, 1998.

90 The patent was for Method and Apparatus for Automatic Standardization in Liquid Scintillation Spectrometry. It covered both automatic internal and external standardization, and subsequently it was licensed to the major companies in the field and became an essential requirement for every top liquid scintillation counter.

91 Packard had its own Absolute Activity Analyzer (AAA) which actually printed out the disintegrations per minute (dpm) after counting each sample. And Beckman had its Automatic Quench Calibration (AQC) which adjusted system gain to restore the counting efficiency of each quenched sample to that of a previously measured reference sample.

clinical settings, and in pharmaceutical firms. The production of ever improved liquid scintillation counters in the 15 years between 1952 and 1967 coincided with the exponential growth of biochemical and biophysical research and the simultaneous increase in the commercial production of radiochemicals, with the huge programs of fighting cancer,[92] and with the whole complex of nuclear medicine and the industry related to it. Yet we have to see this as a two-way connection in which the fields contributed to cross-fertilize each other. Without the massive advent of radioactive biomolecular tracers in general, among other important technical feats, the molecularization of biology and medicine would have been different; and the technology of liquid scintillation counting - in particular, the extended in vitro assay designs and experimental systems - made work such as deciphering the genetic code between 1961 and 1965 feasible. It is not that this technology opened up a specific new field of investigation, rather it had a more general impact on assay design and the potential range of metabolic analysis.

In this context, it is equally important to stress the ever more diversified synthesis of ^{3}H and ^{14}C labeled molecular compounds. Initially they were mainly supplied by the National Laboratory at Oak Ridge. But soon commercial producers took over, among them Tracerlab, New England Nuclear Corporation, Isotopes Inc., and the Radiochemical Center Amersham in England. Robert Loftfield recalls: "New England Nuclear set up a tritiation service: send us your compound, we will tritiate it over a one week period and return it to you for purification or experimental use."[93] But the tritiation process was tricky because it frequently involved highly labeled byproducts, and the tritium exchange with the solvent was difficult to control. This required rigorous checks that opposed routine application. The development of liquid scintillation counting and the synthesis, purification and application of tritium and carbon-14 labeled molecules proceeded in parallel and had to be mutually adapted over an extended period of time. Without mastering the "software" problems of the compounds, it would not have been possible to put the hardware of the machines to much use in molecular biology and biomedical research. There was a constant mutual shaping and reshaping between the instrument, the molecular probes, and the epistemic agendas into which they were inserted.

92 See Jean-Paul Gaudillière, The molecularization of cancer etiology in the postwar United States: Instruments, politics, and management, in Soraya de Chadarevian and Harmke Kamminga (eds.), Molecularizing Biology and Medicine: New Practices and Alliances 1910s - 1970s. Harwood Academic Publishers, Amsterdam 1998, pp. 139-170.

93 Loftfield, letter to Rheinberger, September 24, 1998.

7. Between Industry and Customers

In the previous sections I have shown that liquid scintillation counter prototypes arose from an interaction between researchers and engineers at universities and national laboratory research sites. There was a direct correspondence between the users' needs and the technical solutions that the engineers offered in terms of an assemblage of scintillation physics and chemistry, of photoelectronics, and of mechanical automation. Manufacturing and research virtually coincided both in time and in space. In fact, Packard's colleague Leo Slattery continually serviced Leroy's machine and gave advice on particular uses of the instrument in particular experiments.[94] A similar relationship between engineer and scientific customer is documented for George Utting from the Technical Measurement Corporation.[95]

As soon as the instruments began to be produced and sold as commercial items, this symbiotic and reciprocal relationship changed. Packard insists that from then on most of the instrument improvements came from "inside," meaning from inside the company and from what other companies introduced into the market. But that does not mean that trying to find out what scientists were doing with the instrument and getting a feeling for what they needed ceased to be significant. The interaction was taken over by a system of reporters who were both salespersons and service and repair personnel in one. Packard recalls: "We called them combination people." He insists that separating these functions was counterproductive and would have been disastrous. "If we had ever tried to do this through reps, it just would not have worked. [I] think our own people could give the best installation, the instructions and the theory of operation, and all of that necessary support."[96] Rapkin stresses that "the salesmen were all hired to be servicemen" and added: "One thing I think may have been the strength of the Packard Instrument Company in those days was its sales force. And they were good about reporting back new requirements and problems."[97]

Gerhard Kremer summarized his experience in the field of liquid scintillation counting by emphasizing that the relations between research, technological refinement, customer, and marketing were decisive. He generalized his observations by stating that research and development engineers on the one hand and customers on the other tend to have different visions of perfecting an instrument. The necessary interaction between them has largely to be mediated by the salesmen who are competent servicemen at the same time. These mediators need to be scientif-

94 George T. Okita, Jon J. Kabara, Florence Richardson and George V. LeRoy, Assaying compounds containing H^3 and C^{14}, Nucleonics 15 (No. 6) (June 1957), 111-114. Here, Slattery is acknowledged for "suggesting the discriminator-ratio method."

95 See Monte Blau, Separated channels improve liquid scintillation counting, Nucleonics 15 (No. 4) (April 1957), where Utting is acknowledged "for help and advice."

96 Packard, Interview 1996.

97 Rapkin in Packard, Interview 1996.

ically and technically up to date and have a feeling for the customers' needs, involving a whole "psychology of competence." Paradoxically, the more the technology becomes black-boxed for routine use, the more competence a salesperson must bring with him or her in order to be convincing. It is not uncommon therefore for engineers and scientists qualified to PhD level to enter the sales business.[98]

There was one part of the business, however, in which the know-how clearly traveled from the customers to the manufacturer. The refinements of sample preparation, including new recipes for scintillation cocktails, were largely due to tinkering in the diverse laboratories where people were struggling with their idiosyncratic experimental problems and trying to exploit the machines for their individual purposes. Much of the early work of Newton Hayes at Los Alamos, James Arnold at the University of Chicago, and Jack Davidson at Columbia was devoted to this task. This is also the way plastic vials came into use. Rapkin reports: "A customer [Herbert Jacobsen, University of Chicago] told me that they were using plastic vials. And we tried it and it worked very well. [I] think by having a wall that was diffusing the light, there was a better chance the photomultipliers would get the light. So for tritium counting, the improvement was significant as a percent of the total count."[99] Although plastic has the disadvantage that it does not prevent the organic scintillation cocktail from diffusion and thus has to be disposed of quickly, cheap polyethylene vials partially replaced the glassware with its additional inherent drawback of exhibiting at least some naturally occurring radioactivity.[100]

Eugene Goldwasser gives another example of customer-derived innovation - that of dual label counting, in which he had been involved with George Leroy at the Argonne Cancer Research Hospital: "It's a two-directional kind of thing. Once it became known to experimenters that you could discriminate isotopes based on the magnitude of the pulse you get, then they would sort of talk to the people developing instrumentation saying: 'This is really what we would like to be able to do.'"[101] Despite the early promises, dual label counting went through a decade of trouble-shooting and deceptive experiences before it became a routine procedure based on the mutual adjustment of sample preparation and counting features.

The interaction between appliers and supplier was indeed vital. According to Robert Loftfield, Packard realized in 1958 or 1959 that many of his Tri-Carb machines, often purchased by inexperienced customers with generously distributed federal research money, were standing around

98 Kremer, Interview 1996.
99 Rapkin in Packard, Interview 1996.
100 Edward Rapkin and Lyle E. Packard, New accessories for liquid scintillation counting, in Guido H. Daub, F. Newton Hayes, and Elizabeth Sullivan (eds.), Proceedings of the University of New Mexico Conference on Organic Scintillation Detectors, August 15-17, 1960. U.S. Government Printing Office, Washington 1961, pp. 216-231.
101 Goldwasser, Interview 1996.

in hospitals either unused or at best generating unimpressive data. Packard managed "to persuade the Atomic Energy Commission to set up an award sufficient to place Tri-Carbs in some 20 reputable laboratories where problems could be uncovered and applications developed that would increase the usefulness of the Tri-Carb for other hesitant scientists."[102] One of these machines - "a beautiful machine: coincidence counting, automatic sample changing, cooled to about -10 °C, automatic print-out, pre-selectable voltage gates, etc." - was located at the John Collins Warren Laboratories of the Huntington Memorial Hospital at the Massachusetts General Hospital in Boston, where Loftfield explored the pitfalls involved in the direct counting of paper chromatography strips.[103]

Thus various interfaces between the laboratory and industry are generated in such an epistemic-technical interplay. Highly developed research-enabling technologies require special product management. This process is best carried out by people who operate and are at home at these interfaces, and it is typically materialized in objects and accessories that connect to the core machinery and make it a generic device. On the other hand, without the cooperation of experienced researchers familiar with particular experimental systems, these connections inevitably collapse. Liquid scintillation counting is a good example of this reciprocal interaction. Ultracentrifugation with its different types and sizes of tubes and rotors is another. The salesmen/ reporters carry the new products into the laboratories, search for new applications in the laboratories, divine the upcoming needs of the customers, and suggest product modifications that feed back into the company's research and development program. A Common Shares prospectus of the Packard Instrument Company dating from 1961 notes: "The Company [maintains] a laboratory to study product applications, to handle trial samples for prospective customers and to devise and test techniques for utilizing both its existing products and new products under development. The Engineering Department devotes its efforts to the development of new products and improvement of existing models. During the year 1960 the Company had approximately fifteen employees engaged in research and development and spent approximately $ 210,000 for this purpose, exclusive of quality control and normal product testing. Consultants are utilized where special skills and knowledge can be more effectively obtained than with full-time staff members."[104] Thus the proportion of R&D amounted to slightly less than 10% of the net sales ($ 2,964,161) and slightly more than 10% of the total number of employees (125).

102 Loftfield, letter to Rheinberger, September 24, 1998.
103 Robert B. Loftfield and Elizabeth A. Eigner, Scintillation counting of paper chromatograms, Biochemical and Biophysical Research Communications 2 (1960), 72-75.
104 Packard Instrument Company, Inc., Common Shares Offer, 1961, pp. 6-7.

8. An Interdisciplinary and International Network

There is one more aspect to this story of research-enabling technologies, that is, networking. On the technical side, liquid scintillation counting depended upon pure and reliably quantified sources of various isotopes for testing instrument circuitry and solutions, for calibrating the counting procedure, and for suitable standard samples. On the biological side, suitably labeled compounds were necessary. Packard maintained close connections with Edward Shapiro and Seymour Rothchild of New England Nuclear Corporation, a company that had been founded by former Tracerlab employees and that produced and purchased labeled compounds. Tracerlab had been one of the first private companies to be approved to receive isotope shipments from Oak Ridge as an agent for the purchaser and for synthesizing a variety of labeled molecules.[105]

Besides contacts to the isotope industry, Packard also sensed the need to be visible at the level of publications. "When Edward Rapkin came to work with us, what we wanted was for him to become the leading liquid scintillation oracle and publish little newsletters for us, which he did. So from that time on, the person who knew everything that was being done, all the techniques, all those solvents, and all the cocktails, was Dr. Rapkin."[106] Rapkin was in the U.S. Army working with a mass spectrometer located in the Argonne National Laboratory when he first encountered the Packard Tri-Carb. After leaving the Army, but before joining Packard's Company in 1957, he had already run experiments for Packard on the alkaline digestion of proteins with hyamine at Armour & Co., in an effort to make samples containing proteins soluble in toluene-based scintillation mixtures.[107] Solubilizing proteins was a major problem since most of the biological samples contained variable amounts of proteins.

The publication and dissemination of a newsletter - the Technical Bulletin - was, however, only one part of organizing publicity.[108] A more extended task was organizing conferences to bring together scientists and engineers, research institutes and application laboratories, and thus make the company part of a circuit of communication that included instrument makers and instrument users, both academic and commercial. To this effect, starting in 1957 Packard, together with New England Nuclear's Seymour Rothchild and Atomic Associates, sponsored a long series of symposia on "Advances in Tracer Methodology" later edited by Rothchild and published in four volumes.[109] Packard himself gave papers at a large conference on liquid scintillation counting held at Northwestern University in August 1957, sponsored by the National Science Foundation and the Technological Institute of Northwestern University, and at a conference with over two

105 See, e.g., the advertisement in the October 1947 issue of Nucleonics, p. 85.
106 Packard, Interview 1996.
107 Edward Rapkin, Hydroxide of hyamine 10-X, Technical Bulletin Number 3, Revised June, 1961.
108 18 of these Technical Bulletins appeared between 1961 and 1969, one third of which were signed by Edward Rapkin.

hundred participants on organic scintillation detectors held at the University of New Mexico in August 1960, sponsored by the University of New Mexico, the National Science Foundation, and the U.S. Atomic Energy Commission.[110]

The 1957 Northwestern conference, in a nutshell, reflects many facets of liquid scintillation counting as an explosively expanding research technology towards the end of the 1950s. Participants came from university research institutes including Princeton University, Columbia University, New York University, the University of Chicago, and the University of California at San Francisco; from national laboratories including Los Alamos, Argonne, and Brookhaven, the National Bureau of Standards, and the National Institutes of Health; from hospitals such as the Veterans Administration Research Hospital; from laboratories in France (Saclay, Gif sur Yvette), England (Atomic Energy Research Establishment, Harwell), and Israel (Weizmann Institute, Rehovoth); and from companies including Packard Instrument Company, Technical Measurement Corporation, Shell Oil Company, and Tracerlab. The constituency shows the wide range of interest in the new technology at that stage and the scope of its customers, ranging from the epistemic core of physical, chemical and biomedical research to the wider realm of hospital diagnostics, precision measurement, standardization, and radiation control. Consequently, the conference brought together experimental physicists, chemists, radiologists, biochemists, archaeologists, medical researchers, electronics engineers, mechanical engineers, and instrument builders. All these disciplines either contributed to the physical, chemical, or engineering parts of the machine, or they used it in their research, or participated in both these aspects. As Eric Schram and Robert Lombaert write, with a tone of understatement, in the introduction to their textbook: "The field of organic scintillation detectors may be said to extend to several sciences, physics, electronics, organic and biological chemistry."[111]

The liquid scintillation counter was on its way to becoming the central point for a transdisciplinary, temporary and informal community of researchers, engineers and industrialists. James Arnold, who was among the participants at the Northwestern conference, remarked: "As one of the early workers in the field, I am made rather complacent by the fact that it has ramified in so many unexpected directions. This is actually a rather good case history of the unexpected applications which result from 'pure' research. I do not think that either the people at Los Alamos

109 Between 1957 and 1966, a total of eleven conferences were sponsored in New York, Chicago, Washington, Los Angeles, San Francisco, Zürich, and Boston. See Proceedings of the Symposium on Tritium in Tracer Applications, sponsored by New England Nuclear, Atomic Associates, Packard Instrument, NY City, November 22, 1957; Proceedings of the Symposium on Tritium in Tracer Applications, sponsored by New England Nuclear, Atomic Associates, Packard Instrument, NY City, October 31, 1958; Seymour Rothchild (ed.), Advances in Tracer Methodology. Plenum Press, New York 1963 (Vol. 1), 1965 (Vol. 2), 1966 (Vol. 3), and 1968 (Vol. 4).

110 Packard 1958; Rapkin and Packard 1961.

111 E. Schram and R. Lombaert, Organic Scintillation Detectors. Counting of Low-Energy Beta Emitters. Elsevier, Amsterdam 1963, p. v.

or the others who were working in the field at that time would have been much more successful in predicting all the applications represented at this conference."[112] However, it should also be stated that the development of liquid scintillation counters is a rather good example of a case for which the distinction between pure research and its application does not help us much to frame its history. But this contemporary remark of one of the founders of the technology makes us aware once again of the fact that in the exploratory phase of the technology between 1950 and 1955, liquid scintillation counting did not amount to more than one option among other, much more established, procedures and counting devices. What made liquid scintillation counting really work and finally take over was the result of a techno-epistemic conjunction of heterogeneous factors of different origin: a physico-chemical principle (liquid scintillation) of a potentially generic use in bioassays; a photoelectronic industry driven by weapons production and mass communication; the pervasive use of weak ß-emitters with all their intricacies throughout the biomedical complex in the aftermath of atomic fission; and mechanical automation effectively matching users' demands. Above all, an inherent disposition to "wet" experimentation in biochemistry made a "liquid" boundary between the measuring device and the probe a very adaptable and versatile assembly.

Rapkin recalls: "It used to be a very active field for discussions of technique. And so there were many, many conferences in the early days. Discussions about the best counting solutions, how do you measure steroids, all that kind of thing. It was a fairly active thing at one time."[113] Journals such as Nucleonics (1947) were founded which aggressively promoted and advertised the spread of technology and its industrialization. Its resonant name was taken from a 38-page classified "Prospectus on Nucleonics," featuring postwar nuclear policies, that was passed to Arthur H. Compton by a group of scientists chaired by Zay Jeffries and including Enrico Fermi in November 1944.[114] The journal was announced as a "medium for the cross-fertilization of technical advances in all phases of nuclear technology, [a] meeting place for the exchange of ideas between engineers, physicists, chemists, life scientists and teachers."[115] The International Journal of Applied Radiation and Isotopes (1956) and the Journal of Nuclear Materials (1959) followed. In addition, there were countless smaller meetings on scintillation counting over the years, such as the Symposia on Tritium in Tracer Applications already mentioned, and certainly more than a dozen big conferences, besides the Northwestern conference, including the Scintillation and Semiconductor Counter Symposia in Washington, the Annual Symposia on Advances in Tracer Methodology, the University of New Mexico Conference on Organic Scintillation

112 James R. Arnold, Archaeology and chemistry, in Carlos G. Bell and F. Newton Hayes (eds.), Liquid Scintillation Counting. Pergamon Press, New York 1958, pp. 129-134, on p. 129.
113 Rapkin in Packard, Interview 1996.
114 Jerome D. Luntz, The story of a magazine and an industry, Nucleonics 15 (No. 9) (September 1957), 78-83, p. 79.
115 What is nucleonics? - The magazine, Nucleonics 1 (No. 1) (September 1947), p. 2.

Detectors in Albuquerque in 1960, the International Atomic Energy Association (I.A.E.A.) Symposium on the Detection and Use of Tritium in the Physical and Biological Sciences in 1961, the I.A.E.A. Conferences on Nuclear Electronics in 1958 and 1961, a conference on liquid scintillation counting at the Massachusetts Institute of Technology in 1969,[116] and an international conference on organic scintillators and liquid scintillation counting at the University of California, San Francisco, in 1970.[117] Soon monographs came to complement the conference proceedings.[118]

One of the conferences jointly sponsored by Packard and New England Nuclear was organized in Switzerland and took place at the Züricher Kunsthaus. "The biggest [conference] I think we ever put on was in Zurich. God, they made a real deal out of that. [The] Bürgermeister came and talked, and we had one of the great big halls, right downtown in Zurich. It was a two or three day seminar, and then a big dinner. [People] from all over Europe came to that."[119] Packard's company had expanded internationally. The first foreign sale was to France in 1957, to Saclay, Gif sur Yvette, the French atomic energy research site. Sales all over Europe followed, including to Yugoslavia and Hungary, and even the Soviet Union. The company acquired a chemical plant in Holland to produce scintillation chemicals. The company even installed a few whole body counters for monitoring radioactivity in living bodies, one of them at the University of Hamburg, Germany. Together with Niilo Kaartinen from the University of Turku, Finland, Packard constructed a sample oxidizer machine.[120] The Packard-Kaartinen combustion machine helped to convert otherwise insoluble material into gaseous and then liquid form, and as a physical side effect of the combustion of organic materials to CO_2 and H_2O, it provided an elegant and very efficient means of separating tritium and carbon-14 in critical dual label experiments with, for example, low ^{3}H and high ^{14}C content. The machine was widely used, although its mechanical operation remained somewhat troublesome because of frequent soot deposits and the delicacy of the mechanics of closing and opening the combustion chamber.

To promote international business, Packard set up Packard Instrument Sales Corporation in 1957, and in 1959 a wholly owned foreign subsidiary called Packard Instrument International S.A. Under the direction of James Kriner, and with its headquarters located in Zurich, a widespread network of international offices began to be established. By the end of the 1960s Gerhard

116 To this meeting, Rapkin contributed a valuable historical paper. See Rapkin 1970.
117 Donald L. Horrocks and Chin-Tzu Peng (eds.), Organic Scintillators and Liquid Scintillation Counting. Academic Press, New York and London 1971.
118 Schram and Lombaert 1963; Yutaka Kobayashi and David V. Maudsley, Biological Applications of Liquid Scintillation Counting. Academic Press, New York 1974.
119 Packard, Interview 1996.
120 Niilo Kaartinen, Packard Technical Bulletin No. 18. Packard Instrument Co., Inc., Downers Grove, Illinois 1969; see also L. J. Everett, N. Kaartinen, and P. Kreveld, An advanced automatic sample oxidizer - new horizons in liquid scintillation sample preparation, in Philip E. Stanley and Bruce A. Scoggins (eds.), Liquid Scintillation Counting. Academic Press, New York and London 1974, pp. 139-152.

Kremer, who had started at the German office, became Director of International Operations in Zurich.[121] "We had the most advanced sales and service arrangement in our field, by having a base in Sweden, a base in Italy, a base in Belgium, a base in Germany, in France, in England, in Israel. And each of these bases had a local person who was the top man. Whether he was the president or the director general or whatever other title, it was always a local person, with local staff, and everybody was bilingual, at least bilingual: their own language and English. And, all the business was done in the local currency with local bank accounts and it worked out just really beautifully."[122] In contrast, it was general business practice in those times to use distributors; operating directly with clients was unusual in the scientific instrumentation business. The high value of the dollar helped to keep costs low. In 1969 Packard Instrument's worldwide sales and service network included, in addition to those just mentioned, representatives and sales engineers in Australia, Canada, Denmark, Japan, Norway, and in the Republic of South Africa.

Packard sold his company in 1967. When I asked him why he did this, he answered: "Basically, the reason for selling the company was that we needed additional financial support to continue to expand, compete and maintain our dominant market position. An undesirable alternative would have been to retrench both technical and marketing development and concede the leading market share to the bigger companies, Searle and Beckman, that had entered our market with acceptable products by acquiring our smaller competitors, Nuclear-Chicago and Sharp Laboratories. [The] merger (with American Bosch Arma Corporation) did provide us with the necessary financial support to compete with the larger companies we were facing in 1967. [It] is very tough to compete when big companies buy their way into a business and are willing to lose money until they win or drop out."[123]

9. Instead of a conclusion

Lyle Packard stayed with the business for three and a half more years and then left at the end of 1970. He then bought a couple of islands in the Caribbean and enjoyed life, sailing extensively. Later, he became engaged in the work of several smaller companies and is currently the Chairman and Chief Executive Officer of Advanced Instrument Development, Inc. (AID), a firm that produces special X-ray equipment for medical diagnostics. Packard Instrument Company, today part of Packard Bioscience Company (formerly Canberra Industries, Inc.), has kept its leading position in the technology of liquid scintillation counters, sample preparation solu-

121 Years later Kremer became President of the parent company and operated out of the corporate headquarters near Chicago, while still retaining his permanent residence in Zurich, where he returned to work as a corporate director and senior executive for a few years before finally retiring from the Company in 1997.
122 Packard, Interview 1996.
123 Packard, letter to Rheinberger, February 25, 1998.

tions, and other accessories to this day.[124] But the company now increasingly focuses on developing a new generation of microplate fluorescence and luminescence technologies.

The overwhelming dominance of radioactive tracing in molecular biology and medicine is beginning to recede now at the end of the millennium. The days of almost unlimited growth in nuclear research technology are past. Alternative tracing methods based on fluorescence or luminescence, and other tracing tools that circumvent the use of radioactivity altogether are the order of the day. An advertisement of Packard Instrument Company from June 1998 reads: "Make the move to non-isotopic assays!" Although there is a range of fundamental applications where radioactive tracing may remain indispensable for a long time to come, many competing options for visualization through labeling have become available. Research technologies, even comparatively long-lived ones, have their historical highs and lows. Scientific objects and the ways they are manipulated, likewise, come and go with the technologies. And companies only stay in business if they keep abreast of these epistemic moves in the changing technoculture of research.

124 Dr. Kremer proudly insists that the actual Packard Model 2700 Tri-Carb Liquid Scintillation Spectrometer is probably the best liquid scintillation counter which has been built in 45 years.

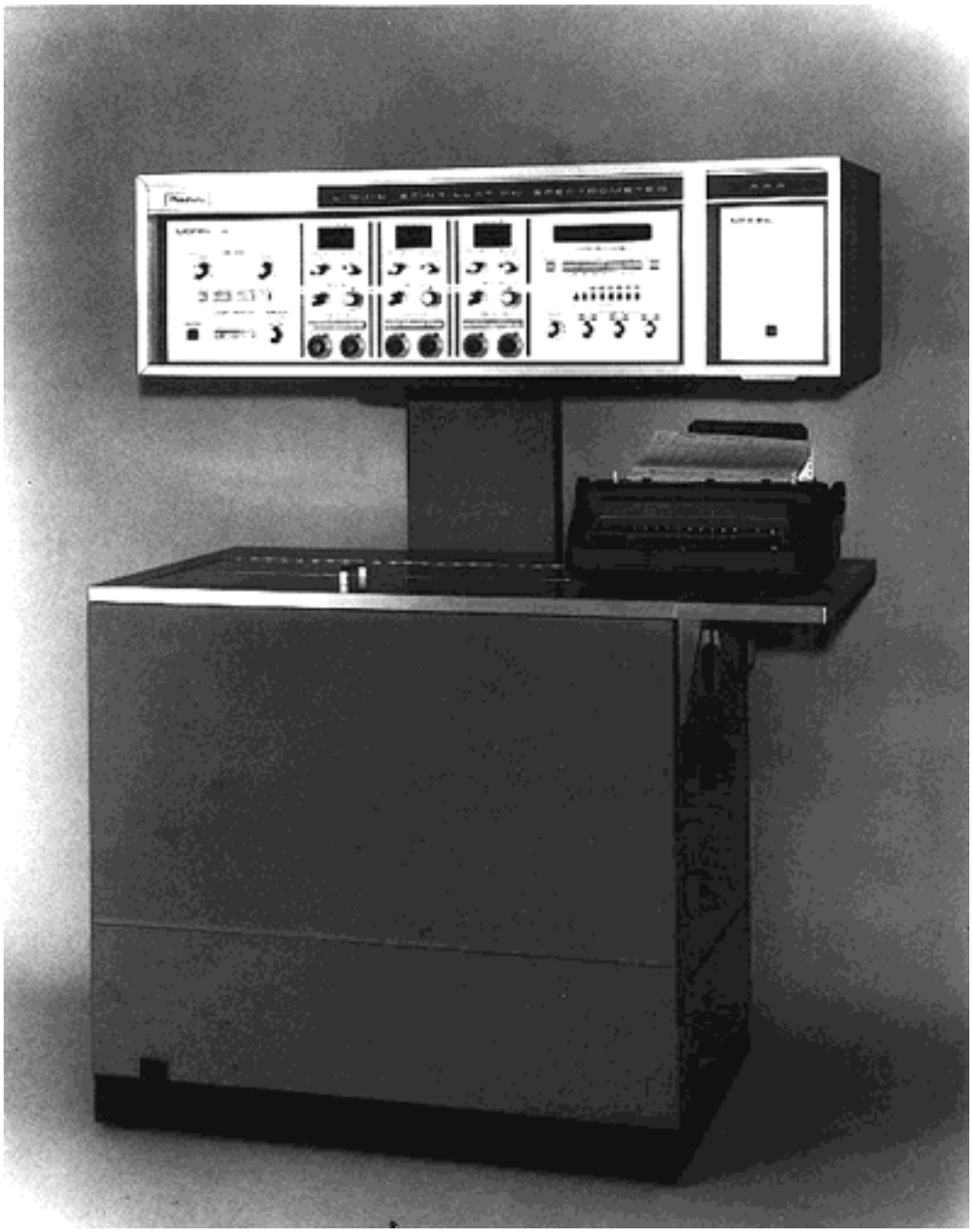

Figure 1:

First liquid scintillation counter with an absolute activity analyzer
(collection of Edward F. Polic, 702 Glenn Court, Milpitas, CA 95035-3330)

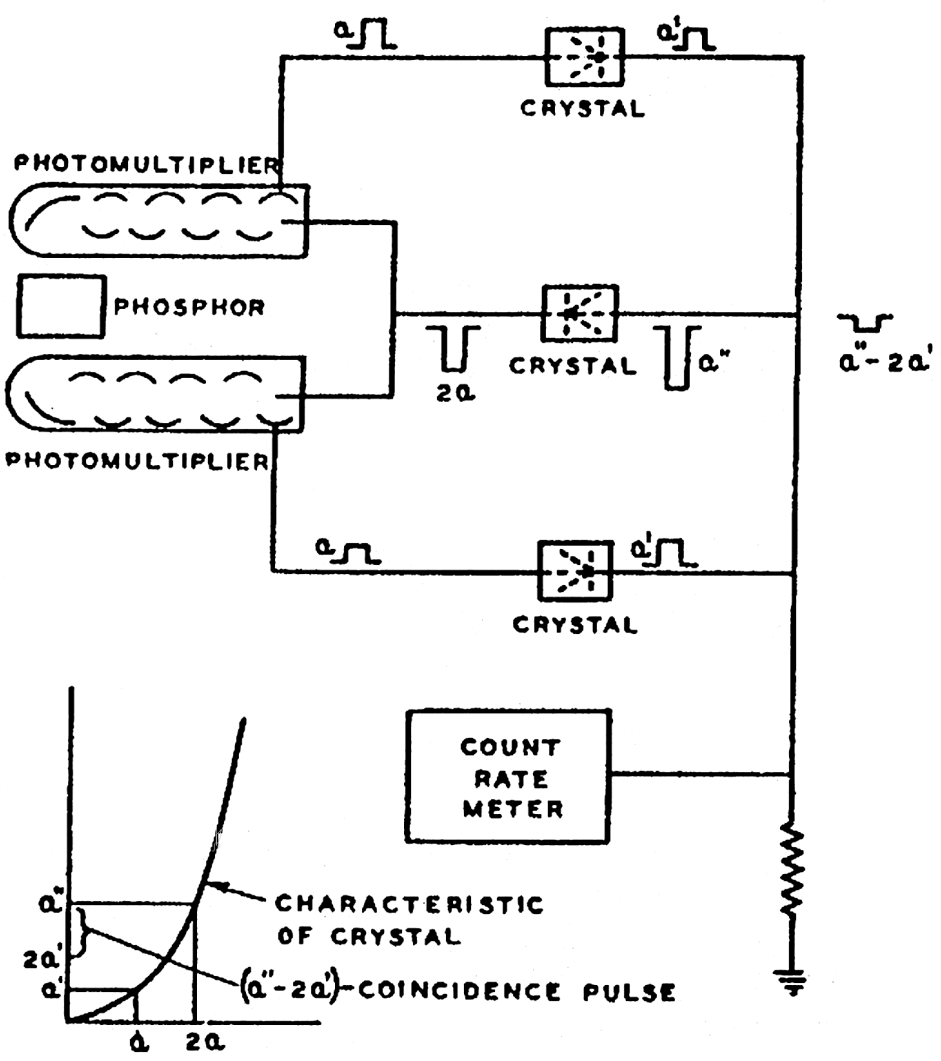

Figure 2:

Coincidence circuit using crystal diodes (Morton and Robinson 1949)

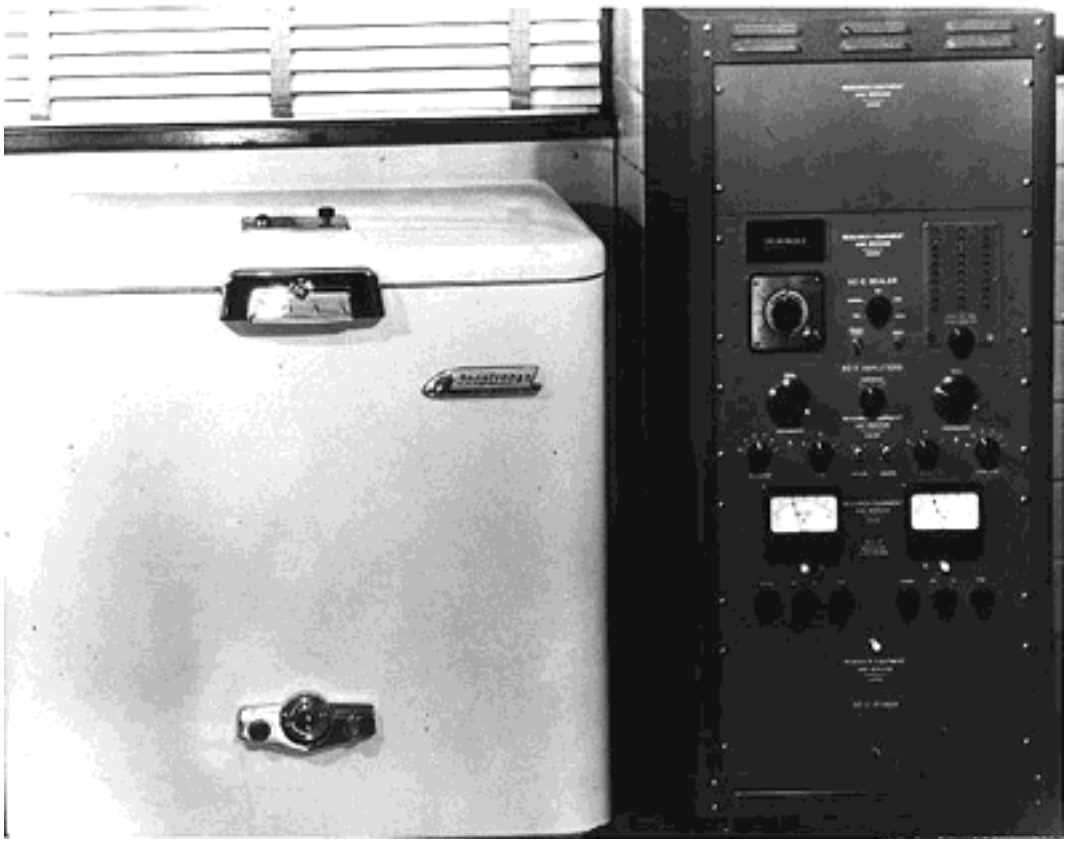

Figure 3:

First commercial liquid scintillation counter made by Packard, sold to Argonne Cancer Research Hospital, circa 1953 (collection of Edward F. Polic)

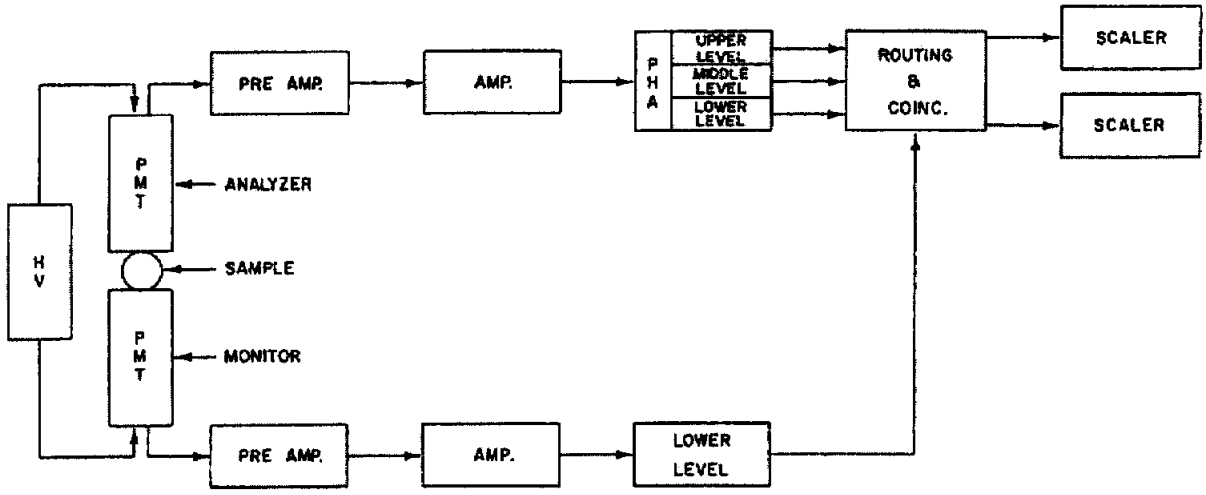

Figure 4:

Packard Model 314 block diagram, 1954 (Rapkin 1970)

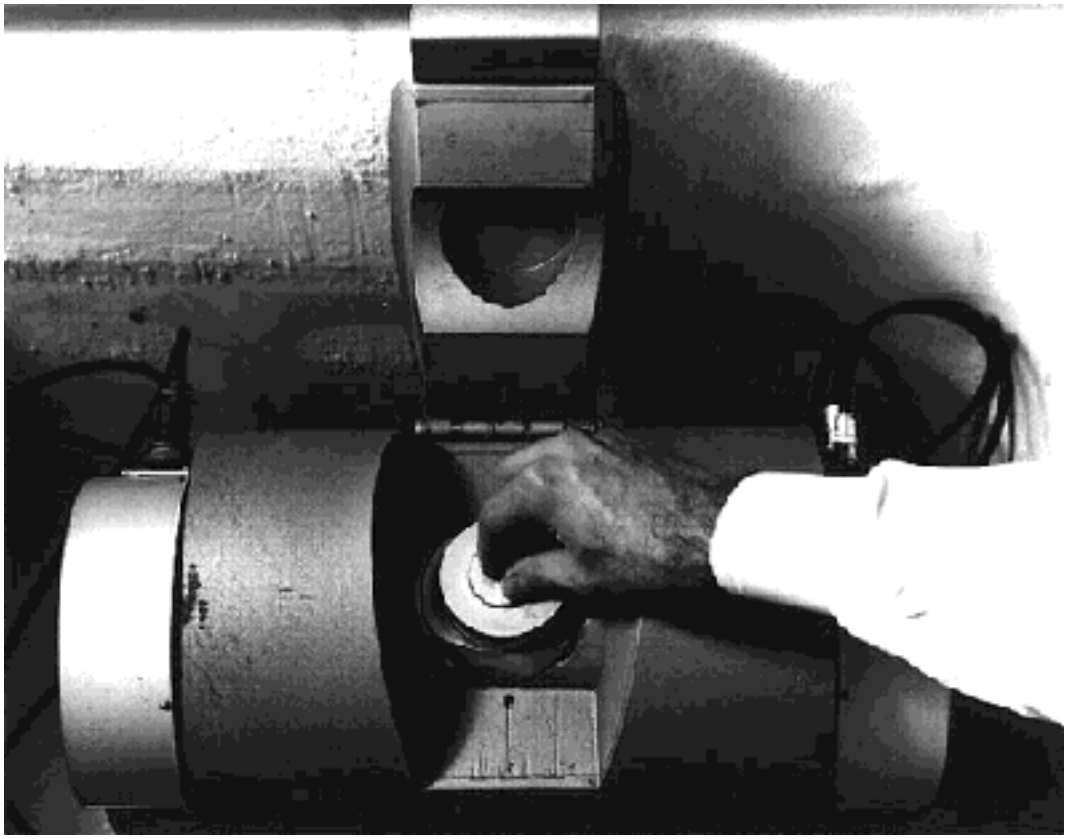

Figure 5:

First production Tri-Carb liquid scintillation counter with light tight shutter - for 50ml sealed ampoule samples or 20ml vial samples, circa 1954 (collection of Edward F. Polic)

Figure 6:

First automated liquid scintillation counter, with steel shielding, dual elevators, 100 20ml vial samples in four circular rows, 1957 (collection of Edward F. Polic)

% Dollar Market Shares (estimated)

	1955	1960	1965	1970
Packard Instrument Company Inc.	95	85	63	45
Nuclear-Chicago: Searle (first sale - 1960)	-	10	20	15
Beckman (first sale - 1965)	-	-	5	20
Wallac ; LKB	γ counters	only	appproximately	1973
Ansitron (first sale - 1964)	-	-	10	5 (Picker)
Intertechnique (first sale - 1968)	-	-	-	15
Philips				
Picker Nuclear	-	-	2	acquired Ansitron 1966
Sharp Laboratories never sold l.s.c. (see Beckman)	-	-	-	-
TMC	5	discontinued		
Tracerlab	-	5	discontinued	
Vanguard	sold	< 5 units	total	
Nuclear Enterprises (Scotland)	very few	units sold,	none outside	UK
Berthold (Germany)	-	-	-	3 (Germany only)
Aloka ? (Japan)	-	-	-	
???? (Russia)	no	commercial	counters, only	home built
Belin (France)	sold a	few units to	French AEC	1958-62

Figure 7:
Estimated % dollar market shares of main purchasers of liquid scintillation counters (estimate from Edward Rapkin, 1998)