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Update on the Most-Cited Papers in the *SCI*, 1955-1986. Part 1. Highlighting Another 100 *Citation Classics*

Number 12 March 21, 1988

Following up on two previous studies based on data from the *Science Citation Index*® (*SCI*®), we have identified 200 additional papers that were highly cited between 1955 and 1986. These papers, predominantly from the life sciences, were *not* included in our series on the 1,000 most-cited papers in the *SCI*, 1961-1982, nor in our study of 250 highly cited papers, 1955-1964. In Part 1 the first group of 100 papers is presented.

In 1986 we completed a 10-part series on the 1,000 papers most cited in the 1961-1982 *Science Citation Index*® (*SCI*®).[1] In a 1985 essay we also published a study of 250 highly cited papers from the "essential decade," 1955-1964.[2] In this two-part essay, we'll be extending these studies, examining a broader time span and obtaining a more up-to-date picture. To prepare this study, we identified 200 highly cited papers from the 1955-1986 *SCI*—papers that were *not* included in the aforementioned essays.

As with our series on the top 1,000 papers, we have divided these papers into groups of approximately 100 each. Appearing here is the first group, consisting of papers that have received at least 963 citations. The second group, cited at a level slightly below that threshold, will be discussed in the next part of this essay. These groups constitute a ranked listing based purely on number of citations. As such, they do not reflect differences in the sizes and citing populations of various disciplines. For example, we have not controlled for the larger population of chemists as compared to physicists. Occasionally in these citation studies we do single out various fields and subject areas for close-up analysis. In those essays, such matters as citing population and literature size do come into play. The groups of papers in this study, however, form an absolute ranking based on citation frequency.

The first group of papers appears in the Bibliography, listed in alphabetic order by first author. As was the case in our previous studies on the *SCI*, papers in the life sciences predominate in this group.

Techniques/Technologies vs. Theories/Hypotheses

There are also a number of methods papers, which, as we've remarked in earlier essays, tend to make strong showings in these lists of highly cited papers. The papers in this group demonstrate the importance of methodology and technology in propelling scientific research—a theme often expounded by the late science historian Derek J. de Solla Price, Yale University, New Haven, Connecticut. At a memorial meeting at Yale shortly after Derek's death, Belver C. Griffith, School of Library and Information Science, Drexel University, Philadelphia, remarked on Derek's support of the view that instrumentation was of far greater importance than suspected in scientific achievement.[3] As Derek himself explained in his article "Of sealing wax and

Table 1: Journals that published at least two articles in the first group of articles most cited in the 1955-1986 *SCI*®. A=journal title. B=number of papers. C=1986 impact factor.

A	B	C
Proc. Nat. Acad. Sci. USA	10	9.16
Nature	10	15.25
Anal. Biochem.	6	2.46
Cell	4	20.09
Phys. Rev.	4	*
Annu. Rev. Biochem.	3	31.62
J. Biol. Chem.	3	6.31
J. Chem. Soc.	3	**
Science	3	12.43
Gene	2	4.15
J. Histochem. Cytochem.	2	4.01
J. Mol. Biol.	2	6.59
J. Pharmacol. Exp. Ther.	2	3.54
Life Sci.	2	2.89
Meth. Enzymology	2	1.65
N. Engl. J. Med.	2	17.75
Nucl. Acid. Res.	2	6.05

*Superseded by Phys. Rev. A—Gen. Phys., Phys. Rev. B—Condensed Matter, Phys. Rev. C—Nucl. Phys., and Phys. Rev. D—Part. Fields.

**Superseded by J. Chem. Soc. Chem. Commun., J. Chem. Soc. Dalton Trans., J. Chem. Soc. Faraday Trans. I, J. Chem. Soc. Faraday Trans. II, J. Chem. Soc. Perkin Trans. I, and J. Chem. Soc. Perkin Trans. II. Each has its own impact factor.

string," it is often techniques and technologies, rather than theories or hypotheses, that originate scientific breakthroughs. "The simple truth," he wrote, "is that one uses a technique, rather than an idea, to do something to something else."[4]

Journals

The most-cited paper in this group received approximately 5,830 citations; the least-cited, approximately 960. The average number of citations was 1,261. The papers were published in 55 journals. Nine of these journals account for approximately 46 percent of the papers. Journals that published two or more papers in this study appear in Table 1. Many of these, including the *Journal of Biological Chemistry*, *Proceedings of the National Academy of Sciences of the USA* (*PNAS*), *Physical Review*, and *Science*, have appeared frequently in our studies of highly cited papers from the *SCI*. *PNAS* accounted for 10 of the papers in this study, as did *Nature*. Table 2 is a chronologic distribution of publication dates for the papers in the Bibliography. As the table shows, the largest number of papers appeared in the years between 1975 and 1979.

In fact, approximately 78 percent of the papers in the Bibliography were published during the 1970s and 1980s. Of the papers in the second part of this essay, roughly 50 percent were published in these decades. In our study of the top 1,000 papers, 1961-1982, we found that over 45 percent of the articles were published in the 1960s. The present study, as mentioned above, encompasses a greater time span than the top 1,000 series—further back in time as well as more recent. It is interesting to note the higher percentage of papers from the 1970s and 1980s.

Nobel Laureates

Of the 226 unique authors in this study, 9 have won the Nobel Prize. These laureates include Georges J.F. Köhler, Max Planck Institute for Immunobiology, Freiburg, Federal Republic of Germany; Niels K. Jerne, Basel Institute for Immunology, Switzerland; and César Milstein, Medical Research Council (MRC) Laboratory of Molecular Biology, Cambridge, UK, who shared the 1984 Nobel Prize in physiology or medicine for their work in immunology. Köhler and Milstein's "Derivation of specific antibody-producing tissue culture and tumor lines by cell fusion," a 1976 paper cited over 1,070 times, is included in the Bibliography. As we noted in our discussion of the 1984 Nobel Prizes, Köhler and Milstein's production of monoclonal antibodies using the hybridoma technique was a methodological breakthrough with broad practical applications.[5] One example is provided by another paper in the Bibliography, "Monoclonal antibodies defining distinctive human T cell surface antigens," by Patrick C. Kung, Ortho Pharmaceutical Corpora-

tion, Raritan, New Jersey, and colleagues. This 1979 paper from *Science* has been cited over 1,000 times.

Jerne is represented by "Towards a network theory of the immune system," a 1974 paper cited around 1,250 times. Two other corecipients of the medicine prize, Joseph L. Goldstein and Michael S. Brown, University of Texas Health Science Center, Dallas, who shared the 1985 prize for their research in cholesterol metabolism, have two papers in this study: "The low-density lipoprotein pathway and its relation to atherosclerosis," a 1977 paper cited nearly 1,200 times, and "Coated pits, coated vesicles, and receptor-mediated endocytosis" (with coauthor R.G.W. Anderson), cited 1,220 times since its publication in 1979. In our study of Goldstein and Brown's work, we identified these papers as the authors' most cited.[6]

Frederick Sanger, MRC Laboratory of Molecular Biology, who received the Nobel in chemistry in 1958 and again in 1980, is coauthor of a 1980 paper in the Bibliography, "Cloning in single-stranded bacteriophage as an aid to rapid DNA sequencing." This paper was cited in approximately 1,080 publications.

Another Nobel laureate in this study is a cowinner of the physics prize, Eugene Wigner, Princeton University, New Jersey. Wigner was honored in 1963 for his work in the principles governing the interaction of protons and neutrons in the nucleus of the atom. The Bibliography includes his 1932 paper, "Quantum correction for thermodynamic equilibrium," which has been cited in roughly 980 publications. Wigner wrote a commentary on this *Citation Classic*® in 1983.[7] Many of the older papers in this study, we've noted, are in physics.

Peter Mitchell, Glynn Research Laboratories, Cornwall, UK, who won the Nobel Prize in chemistry in 1978, wrote a *Citation Classic* commentary on his 1966 paper, "Chemiosmotic coupling in oxidative and photosynthetic phosphorylation." As Mitchell notes, his chemiosmotic hypothesis did not win immediate acceptance and was subjected to considerable experimental scrutiny. "That may partly explain the frequency of citation of my 1966 review," he writes, "which has acted as a source of the chemiosmotic conjecture that numerous experimentalists rightly sought to test to destruction. The survival of this conjecture has led to the general acceptance of the chemiosmotic principles in membrane bioenergetics."[8] In Figure 1 we present a year-by-year graph of citations to Mitchell's 1966 paper. It has now been cited in over 1,600 publications.

Geoffrey Wilkinson, Imperial College, London, winner of the 1973 Nobel in chemistry, is also included in the Bibliography.

Table 2: Chronologic distribution of publication dates for the first group of articles in the updated most-cited articles in the 1955-1986 *SCI*®.

Publication Year	Number of Papers
1920-1924	1
1930-1934	1
1940-1944	2
1945-1949	1
1950-1954	3
1955-1959	4
1960-1964	2
1965-1969	8
1970-1974	17
1975-1979	42
1980-1984	19

Citation Classic Authors

In addition to Wigner and Mitchell, 12 other authors have written *Citation Classic* commentaries on papers in the Bibliography. John M. Bennett, University of Rochester Cancer Center, New York, for example, commented in 1984 on "Proposals for the classification of the acute leukaemias," published in the *British Journal of Haematology* in 1976. Bennett and his six coauthors—hematologists affiliated with French, American, and British institutions—made an extensive study of acute leukemia and defined nine subgroups of leukemic morphologic variants. The project, as Bennett writes, was

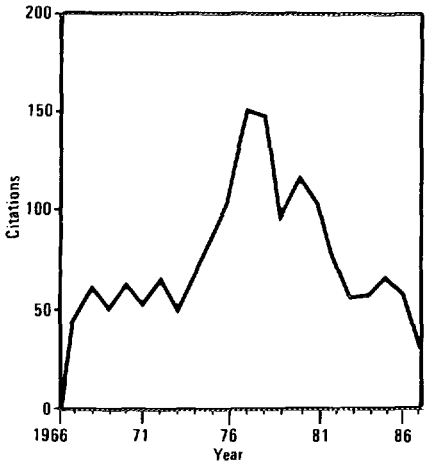

Figure 1: Year-by-year citations to the *Citation Classic*® paper by Mitchell P. *Biol. Rev. Cambridge Phil. Soc.* 41:445-502, 1966 (1,619 cites 1955-1986 *SCI*®, 32 cites 1987 *SCI*).

designed to address "differences in concepts and practice in the diagnosis of the acute leukemias." As Bennett concludes, "The acceptance of the 'proposals' indicates that the provision of an international classification provides a basis for useful discussion and comparative research."[9] As we noted at the time of Bennett's commentary, this was the most-cited paper ever published in the *British Journal of Haematology*. It has now been cited over 1,400 times.

Another commentary was provided by W.Y. Cheung, St. Jude Children's Research Hospital, Memphis, Tennessee. Cheung discusses his 1980 paper from *Science*, "Calmodulin plays a pivotal role in cellular regulation." As he notes in his commentary, his paper reviews various aspects of the "ubiquitous protein" calmodulin, which mediates the action of calcium ions in many cellular processes. The paper's "wide-ranging coverage," says Cheung, "coming at a time when interest in calmodulin was building rapidly, may be the reason for the paper's frequent citation."[10] This paper was cited in over 1,470 publications.

In another *Citation Classic* commentary, Michael J.S. Dewar, Department of Chemistry, University of Texas, Austin, discusses his 1977 paper from the *Journal of the American Chemical Society*, "Ground states of molecules. 38. The MNDO method. Approximations and parameters." This paper, coauthored with colleague W. Thiel, discusses quantum mechanical treatment of organic molecules. In his commentary Dewar describes the development of MNDO—modified neglect of diatomic overlap. This technique, as Dewar puts it, is "a practical chemical tool for studying molecular properties and reactions, as a large and increasing number of organic chemists have discovered."[11] This paper has received approximately 1,170 citations.

Other Selected Papers

The oldest paper in this study is from 1920, by A.A. Griffith, Royal Aircraft Establishment, London. "The phenomena of rupture and flow in solids," published in *Philosophical Transactions of the Royal Society of London Series A—Mathematical and Physical Sciences*, has been cited over 1,000 times. In Figure 2 we present a year-by-year graph of citations to this paper. Griffith investigated the effect of surface

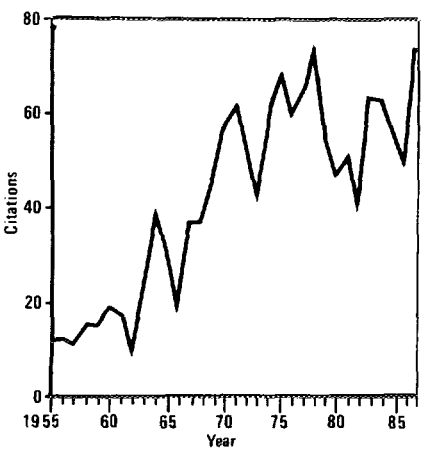

Figure 2: Year-by-year citations to the oldest article listed in the Bibliography, Griffith A A. *Phil. Trans. Roy. Soc. London A* 221:163-98, 1920 (1,041 cites 1955-1986 *SCI*®, 74 cites 1987 *SCI*).

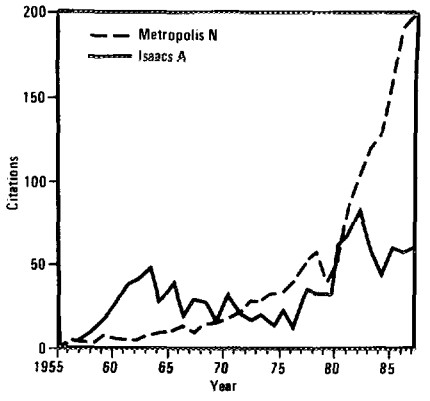

Figure 3: Year-by-year citations to two classic papers from the 1950s. **Broken line**=Metropolis N. *J. Chem. Phys.* 21:1087-92, 1953 (1,251 cites 1955-1986 *SCI*®, 198 cites 1987 *SCI*). **Solid line**=Isaacs A. *Proc. Roy. Soc. London Ser. B* 147:258-67, 1957 (965 cites 1955-1986 *SCI*, 60 cites 1987 *SCI*).

scratches on the mechanical strength of solids. As can be seen from Figure 2, the paper continues to be acknowledged as a seminal work in materials science.

The most recent paper is from 1984: "The role of protein kinase C in cell surface signal transduction and tumour promotion," by Yasutomi Nishizuka, Department of Chemistry, Kobe University, Japan. (We discussed Japanese science in a recent essay.[12]) Nishizuka's review article, published in *Nature*, summarizes evidence relating to the activation of the enzyme protein kinase C and to the importance of that activation for subsequent cellular responses. The author also discusses evidence that protein kinase C serves as a receptor for tumor promoters, such as phorbol ester.

According to our data this paper was cited over 1,350 times from its publication in 1984 to 1986. Such a rapid accumulation of citations, of course, attests to the paper's immediate impact and to the intensity of research in this area.

In Figure 3 we have graphed year-by-year citations to two highly cited papers from the 1950s. One is "Virus interference. I. The interferon," by A. Isaacs and J. Lindenmann, National Institute for Medical Research, London. This 1957 paper, published in *Proceedings of the Royal Society of London Series B—Biological Sciences*, reports the discovery of interferon, which the authors identified following incubation of heated influenza virus with the chorioallantoic membrane of a chick embryo. This paper was cited in 965 publications. Figure 3 shows a surge of citations to the paper in the early 1980s.

The second paper shown in Figure 3, also from the 1950s, is "Equation of state calculations by fast computing machines," by Nicholas Metropolis, Los Alamos Scientific Laboratory, New Mexico, and colleagues, from the *Journal of Chemical Physics*. This 1953 paper describes an algorithmic method of calculating the properties of any substance composed of interacting individual molecules. As can be seen from Figure 3, the paper displays a slowly rising level of citations from its publication until the late 1970s, when the rate of citations begins a nearly vertical climb. This sharp rise in citations reflects a new application for the technique described in this paper. The algorithm developed by Metropolis and colleagues, originally devised for use in physics, has in recent years become highly useful in work being done by computer scientists. The widespread use of high-speed computers, which 35 years ago were available only at labs like Los Alamos, is another factor in the paper's recent surge in citations. Areas in which the algorithm is being applied include neural network theory, learning machines, and optimization studies.

One of the coauthors on the Metropolis paper, incidentally, is Edward Teller, now a research fellow at the Hoover Institution, Stanford University, California. Teller discussed the Strategic Defense Initiative and other issues last fall in an interview in *THE SCIENTIST*™.[13]

Methods Dominate Most-Cited Papers

As mentioned earlier, methods papers play a prominent role in this study. The most

highly cited paper in the Bibliography, for example, is a methods paper: "Electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets: procedure and some applications," by Harry Towbin, Friedrich Miescher Institute, Basel, Switzerland, with colleagues Julian Gordon and Theophil Staehelin, Hoffmann-La Roche, Basel. This 1979 paper from *PNAS* describes a method for detecting and analyzing proteins. The procedure involves transferring proteins from a polyacrylamide gel to a sheet of nitrocellulose in such a way that a faithful replica of the original gel pattern is obtained. The immobilized protein can then be subjected to a variety of analytical procedures. This paper received more than 5,830 citations—over 2,500 more than the next most-cited paper in this study.

That paper, which appeared in *Nucleic Acids Research*, also discusses a method—in this case a procedure for extracting plasmid DNA from bacterial cells. Coauthored by H.C. Birnboim and J. Doly, Institute for Research in Molecular Biology, Paris, this paper has been cited over 3,200 times. The third most-cited paper, "Hybridization of denatured RNA and small DNA fragments transferred to nitrocellulose," is by Patricia S. Thomas, Fred Hutchinson Cancer Research Center, Seattle, Washington. As the title implies, this paper describes a method for transferring RNA from agarose gels to nitrocellulose paper for blot hybridization. This article has been cited in over 3,100 publications.

Another of the methods papers in the Bibliography was written by W. Neal Burnette, Fred Hutchinson Cancer Research Center. This paper describes "Western blotting," a procedure for identifying DNA sequences and proteins. This method is a refinement of Southern blotting (after which "Western blotting" and another refinement, "Northern blotting," were somewhat facetiously named). Southern blotting was the invention of Edwin M. Southern, University of Edinburgh, UK.[14] All these methods are now essential tools in molecular biology and biotechnology.

In Part 2 of this study, we will examine the next most-cited group of highly cited papers from the *SCI*, 1955-1986. This second group, in addition to papers from the life sciences, features a larger representation of papers from physics, chemistry, and mathematics.

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My thanks to Christopher King and Elizabeth Fuseler-McDowell for their help in the preparation of this essay.

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