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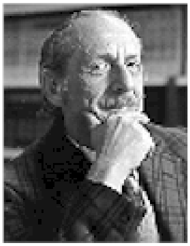

Current Comments®

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The Most-Cited Papers of All Time, *SCI* 1945-1988. Part 1A. The *SCI* Top 100—Will the Lowry Method Ever Be Obliterated?

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The 100 most-cited papers in the 1945-1988 *Science Citation Index®* (*SCI®*) are identified. For each paper the list shows total citations, average annual citations, and 1988 citations. *Citation Classic®* commentaries on 50 of the *SCI* Top 100 have been published to date. Don T. Cromer, University of California, Los Alamos Scientific Laboratory, New Mexico, is first author of three papers on the list, and nine other authors appear twice. The *Journal of Biological Chemistry* leads the list of journals ranked by the number of *SCI* Top 100 papers published.

Introduction

In previous essays we have identified the most-cited articles for 1961-1972[1] and 1961-1982[2] that, at the time of their publication, represented virtually the entire *Science Citation Index®* (*SCI®*) file. Since then we have extended the *SCI* files back through the crucial postwar period to 1945, a time when major scientific and technical advances were made and science began its explosive growth. With the publication of the 1945-1954 10-year cumulation,[3] the *SCI* today represents a continuous record of about 15 million source items published from 1945 through 1989, and over 175 million cited references.

As Derek J. de Solla Price first observed in 1963, "Eighty to 90 percent of all the scientists that have ever lived are alive now."[4] The list of the 100 most-cited articles in 1945-1988 presented in this essay may therefore be considered an honor roll of papers that have had the highest impact on the greatest number of scientists. In future essays we will continue to identify additional 100 "all-time" *Citation Classics®* until the top 1,000-1,500 have been listed.

How the List Was Prepared

To generate the master list of all-time *Citation Classics*, we started with about 175 million citations in the 1945-1988 *SCI* database. A total of about 33 million items were cited, including articles, books, patents, and other publications. These items were then ranked in order of the total number of citations received during the 44-year period.

Table 1 shows the frequency distribution for items cited from 1945 through 1988. About 500,000 were cited 50 or more times, and they represent about 2.0 percent of the entire file. The top 1,400 papers and books cited at least 1,000 times are a very select sample representing just 0.004 percent of all cited publications in the 1945-1988 *SCI* database. The top 100 papers included in this essay are an infinitesimally small fraction of the 1945-1988 *SCI* file—0.0003 percent. These data ought to discourage invidious comparisons between individual papers based on their relative citation ranking among the top 100 or top 1,000.

Books have been removed from the list for now. This is a temporary expedient. Since citations to books are less standard-

Table 1: Citation frequency distribution for papers in the *SCI*®, 1945-1988. A=number of citations. B=number of items receiving that number of citations. C=percent of entire *SCI* file.

A	B	C
>10,000	20	*
5,000-9,999	47	*
4,000-4,999	23	*
3,000-3,999	54	*
2,000-2,999	181	*
1,000-1,999	1,051	*
900-999	325	*
800-899	438	*
700-799	727	*
600-699	1,073	*
500-599	1,828	*
400-499	3,406	0.01
300-399	7,736	0.02
200-299	21,952	0.07
100-199	112,299	0.34
50-99	348,537	1.06
25-49	842,950	2.58
15-24	1,089,731	3.33
10-14	1,207,577	3.69
5-9	2,955,984	9.03
2-4	7,877,213	24.07
1	18,255,577	55.78
TOTAL	32,728,729	100.00

*=less than 0.01 percent of the *SCI* file, 1945-1988.

ized than article citations, considerable editing is required to unify the data. Books are often published in several editions, sometimes in several languages, and each edition may be cited differently. Furthermore, specific pages or chapters of a book are often cited. Since the *SCI* has deliberately kept these as separate entries, it is a painstaking task to unify all these "variant" citations. The most-cited books during 1945-1988 will be the subject of separate essays in the future.

The *SCI* Top 100, 1945-1988

Table 2 presents the top 100 papers in alphabetical order by first author's name. Column A shows how often each paper was cited in the 1945-1988 *SCI* database, followed by its rank among the top 100. Column B shows the average annual citations for each paper, which is calculated by dividing total citations by the paper's age. For example, the first paper listed in Table 2, by Bruce N. Ames and colleagues, Department of Biochemistry, University of California, Berkeley, received 4,583 citations. Dividing total citations by 14, the paper's age from publication in 1975 through 1988, gives an average annual citation rate of 327. Column C shows the number of citations each paper received in 1988. Comparing columns B and C will give an indication of whether a paper in 1988 was rising or falling against its average annual citation rate.

Column D provides a full bibliographic reference for each work. An asterisk preceding a reference indicates that the paper was the subject of a *Citation Classic* commentary, and the *Current Contents*® (*CC*®) issue, year, and edition in which the commentary was published follows the reference in parentheses. A dagger preceding a reference indicates that the paper did *not* appear on the previously published list of 100 most-cited papers for 1961-1982.[2]

The oldest of the *SCI* Top 100 papers is by Cyrus H. Fiske and Yellapragada SubbaRow, Harvard Medical School, Boston, Massachusetts, published in 1925 in the *Journal of Biological Chemistry*. It describes a method for the colorimetric determination of phosphorus and has received 17,247 citations through 1988. The paper averaged 269 citations per year over its 64 years, reached a peak of 597 citations in 1975, and has since declined to 335 in 1988.

The two youngest papers were published in 1980 by Allan M. Maxam and Walter Gilbert, Department of Biochemistry and Molecular Biology, Harvard University, Cambridge, Massachusetts, in *Methods of Enzymology* and by Patricia S. Thomas, Fred Hutchinson Research Center, Seattle, Washington, in the *Proceedings of the National Academy of Sciences of the USA*. (*PNAS*). The Maxam and Gilbert paper on a DNA-sequencing method was cited about 9,000 times, with an annual citation average of just under 1,000 and 1,258 citations in 1988. The Thomas paper on an RNA-hybridization method received over 5,000 citations

Table 2: Bibliography of the 100 most-cited papers from the *SCI*®, 1945-1988. Papers are arranged alphabetically. A = 1945-1988 citations, with 1945-1988 rank in parentheses. B = average number of annual citations. C = 1988 citations. D = bibliographic data. An asterisk (*) indicates that the paper was the subject of a *Citation Classic*® *commentary*. *The issue, year, and edition of the commentary follow the bibliographic reference.* A dagger (†) indicates the paper did *not* appear on the 1961-1982 top 100 list.

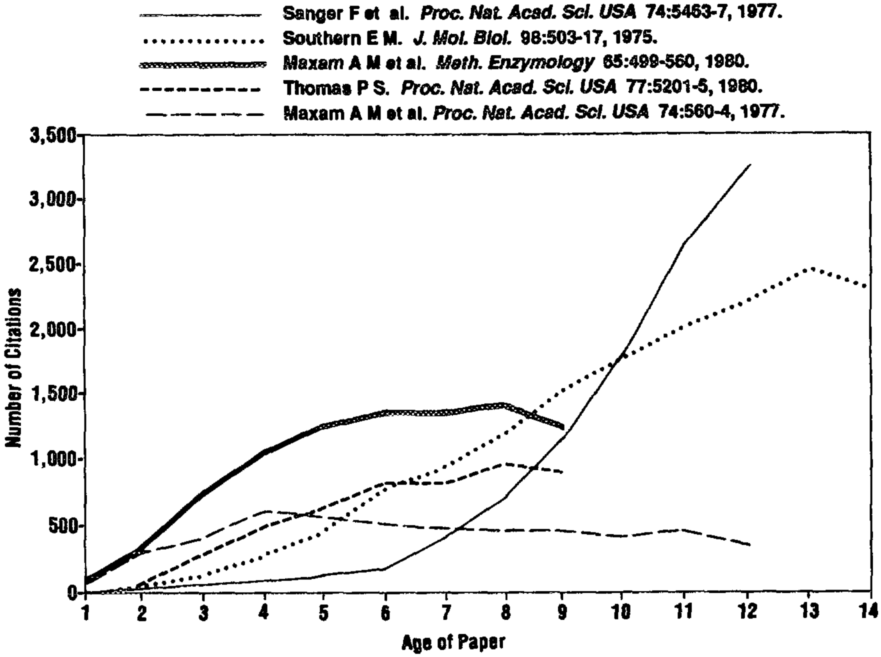
A	B	C	D
4,583(#58)	327	246	***Ames B N, McCann J & Yamasaki E.** Methods for detecting carcinogens and mutagens with the salmonella/mammalian-microsome mutagenicity test. *Mutat. Res.* 31:347-64, 1975. (12/84/LS)
4,232(#64)	169	70	**Andrews P.** Estimation of the molecular weights of proteins by Sephadex gel-filtration. *Biochem. J.* 91:222-33, 1964.
6,190(#39)	155	311	**Arnon D I.** Copper enzymes in isolated chloroplasts. Polyphenoloxidase in *Beta vulgaris. Plant Physiol.* 24:1-15, 1949.
4,648(#56)	273	654	**†Aviv H & Leder P.** Purification of biologically active globin messenger RNA by chromatography on oligothymidylic acid-cellulose. *Proc. Nat. Acad. Sci. USA* 69:1408-12, 1972.
4,101(#66)	85	23	***Barker S B & Summerson W H.** The colorimetric determination of lactic acid in biological material. *J. Biol. Chem.* 138:535-54, 1941. (46/83/LS)
8,628(#26)	288	399	***Bartlett G R.** Phosphorus assay in column chromatography. *J. Biol. Chem.* 234:466-8, 1959. (4/85/LS)
5,104(#53)	510	937	***†Birnboim H C & Doly J.** A rapid alkaline extraction procedure for screening recombinant plasmid DNA. *Nucl. Acid. Res.* 7:1513-23, 1979. (45/88/LS)
3,488(#90)	129	172	**Bitter T & Muir H M.** A modified uronic acid carbazole reaction. *Anal. Biochem.* 4:330-4, 1962.
9,639(#19)	321	781	***Bligh E G & Dyer W J.** A rapid method of total lipid extraction and purification. *Can. J. Biochem. Physiol.* 37:911-7, 1959. (52/78)
7,516(#32)	501	387	***Bonner W M & Laskey R A.** A film detection method for tritium-labelled proteins and nucleic acids in polyacrylamide gels. *Eur. J. Biochem.* 46:83-8, 1974. (1/83/LS)
8,877(#25)	423	713	***Böyum A.** Isolation of mononuclear cells and granulocytes from human blood. *Scand. J. Clin. Lab. Invest.* 21(Supp.97):77-89, 1968. (45/82/LS)
24,366(#3)	1,874	4,303	**Bradford M M.** A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal. Biochem.* 72:248-54, 1976.
3,565(#86)	71	68	**Bratton A C & Marshall E K.** A new coupling component for sulfanilamide determination. *J. Biol. Chem.* 128:537-50, 1939.
9,922(#17)	342	49	***Bray G A.** A simple efficient liquid scintillator for counting aqueous solutions in a liquid scintillation counter. *Anal. Biochem.* 1:279-85, 1960. (2/77)
13,487(#11)	409	483	***Burton K.** A study of the conditions and mechanism of the diphenylamine reaction for the colorimetric estimation of deoxyribonucleic acid. *Biochem. J.* 62:315-22, 1956. (26/77)
5,463(#49)	166	206	***Chen P S, Toribara T Y & Warner H.** Microdetermination of phosphorus. *Anal. Chem.* 28:1756-8, 1956. (9/77)
5,167(#52)	517	1,602	**†Chirgwin J M, Przybyla A E, MacDonald R J & Rutter W J.** Isolation of biologically active ribonucleic acid from sources enriched in ribonuclease. *Biochemistry—USA* 18:5294-9, 1979.
3,594(#84)	300	339	***†Cleveland D W, Fischer S G, Kirschner M W & Laemmli U K.** Peptide mapping by limited proteolysis in sodium dodecyl sulfate and analysis by gel electrophoresis. *J. Biol. Chem.* 252:1102-6, 1977. (41/84/LS)
3,766(#77)	171	70	***Conney A H.** Pharmacological implications of microsomal enzyme induction. *Pharmacol. Rev.* 19:317-61, 1967. (3/79/LS)
3,392(#94)	200	540	***†Cox D R.** Regression models and life-tables. *J. Roy. Statist. Soc. Ser. B Metho.* 34:187-220, 1972. (42/86/AB; 42/86/A&H; 42/86/S&BS)
4,014(#69)	211	280	**Cromer D T & Liberman D.** Relativistic calculation of anomalous scattering factors for X-rays. *J. Chem. Phys.* 53:1891-8, 1970.
5,792(#46)	276	342	**Cromer D T & Mann J B.** X-ray scattering factors computed from numerical Hartree-Fock wave functions. *Acta Crystallogr. A* 24:321-5, 1968.
4,111(#65)	171	57	**Cromer D T & Waber J T.** Scattering factors computed from relativistic Dirac-Slater wave functions. *Acta Crystallogr.* 18:104-9, 1965.
17,510(#7)	700	504	**Davis B J.** Disc electrophoresis—II. Method and application to human serum proteins. *Ann. NY Acad. Sci.* 121:404-27, 1964.

A	B	C	D
3,278(#97)	96	88	***de Duve C, Pressman B C, Gianetto R, Wattiaux R & Appelmans F.** Tissue fractionation studies. 6. Intracellular distribution patterns of enzymes in rat-liver tissue. *Biochem. J.* 60:604-17, 1955. (12/77)
4,009(#70)	121	35	**Dole V P.** A relation between non-esterified fatty acids in plasma and the metabolism of glucose. *J. Clin. Invest.* 35:150-4, 1956.
9,741(#18)	295	611	**Dubois M, Gilles K A, Hamilton J K, Rebers P A & Smith F.** Colorimetric method for determination of sugars and related substances. *Anal. Chem.* 28:350-6, 1956.
3,591(#85)	103	66	**Dulbecco R & Vogt M.** Plaque formation and isolation of pure lines with poliomyelitis viruses. *J. Exp. Med.* 99:167-82, 1954.
8,985(#24)	264	429	***Duncan D B.** Multiple range and multiple F tests. *Biometrics* 11:1-42, 1955. (4/77)
3,890(#74)	130	39	***Eagle H.** Amino acid metabolism in mammalian cell cultures. *Science* 130:432-7, 1959. (5/77)
6,228(#38)	208	331	**Ellman G L.** Tissue sulfhydryl groups. *Arch. Biochem. Biophys.* 82:70-7, 1959.
4,372(#61)	156	292	***Ellman G L, Courtney K D, Andres V & Featherstone R M.** A new and rapid colorimetric determination of acetylcholinesterase activity. *Biochem. Pharmacol.* 7:88-95, 1961. (22/77)
7,084(#34)	394	247	**Fairbanks G, Steck T L & Wallach D F H.** Electrophoretic analysis of the major polypeptides of the human erythrocyte membrane. *Biochemistry—USA* 10:2606-17, 1971.
17,247(#8)	269	335	**Fiske C H & SubbaRow Y.** The colorimetric determination of phosphorus. *J. Biol. Chem.* 66:375-400, 1925.
20,505(#5)	641	945	**Folch J, Lees M & Sloane Stanley G H.** A simple method for the isolation and purification of total lipides from animal tissues. *J. Biol. Chem.* 226:497-509, 1957.
4,468(#59)	248	176	**Germain G, Main P & Woolfson M M.** The application of phase relationships to complex structures. III. The optimum use of phase relationships. *Acta Crystallogr. A* 27:368-76, 1971.
4,589(#57)	242	118	**Gilman A G.** A protein binding assay for adenosine 3′:5′-cyclic monophosphate. *Proc. Nat. Acad. Sci. USA* 67:305-12, 1970.
11,763(#12)	294	297	***Gornall A G, Bardawill C J & David M M.** Determination of serum proteins by means of the biuret reaction. *J. Biol. Chem.* 177:751-66, 1949. (13/79/LS)
6,041(#41)	263	288	**Graham R C & Karnovsky M J.** The early stages of absorption of injected horseradish peroxidase in the proximal tubules of mouse kidney: ultrastructural cytochemistry by a new technique. *J. Histochem. Cytochem.* 14:291-302, 1966.
7,627(#30)	293	378	***Greenwood F C, Hunter W M & Glover J S.** The preparation of ^{131}I-labelled human growth hormone of high specific radioactivity. *Biochem. J.* 89:114-23, 1963. (15/77)
3,231(#99)	129	193	***†Hakomori S.** Letter to editor. (A rapid permethylation of glycolipid and polysaccharide catalyzed by methylsulfinyl carbanion in dimethyl sulfoxide.) *J. Biochem.—Tokyo* 55:205-8, 1964. (23/80/LS)
3,708(#82)	98	220	**Hamburger V & Hamilton H L.** A series of normal stages in the development of the chick embryo. *J. Morphol.* 88:49-92, 1951.
3,722(#80)	109	284	***†Havel R J, Eder H A & Bragdon J H.** The distribution and chemical composition of ultracentrifugally separated lipoproteins in human serum. *J. Clin. Invest.* 34:1345-53, 1955. (46/83/LS)
3,515(#88)	95	156	***Hodgkin A L & Huxley A F.** A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol.—London* 117:500-44, 1952. (28/81/LS)
6,294(#36)	233	341	***Hunter W M & Greenwood F C.** Preparation of iodine-131 labelled human growth hormone of high specific activity. *Nature* 194:495-6, 1962. (26/89/LS; 26/89/CM; 26/89/ET; 26/89/PC)
3,204(#100)	188	49	***Jondal M, Holm G & Wigzell H.** Surface markers on human T and B lymphocytes. I. A large population of lymphocytes forming nonimmune rosettes with sheep red blood cells. *J. Exp. Med.* 136:207-15, 1972. (24/85/LS)
4,045(#68)	253	251	**Julius M H, Simpson E & Herzenberg L A.** A rapid method for the isolation of functional thymus-derived murine lymphocytes. *Eur. J. Immunol.* 3:645-9, 1973.
4,756(#55)	153	781	***†Kaplan E L & Meier P.** Nonparametric estimation from incomplete observations. *J. Amer. Statist. Assn.* 53:457-81, 1958. (24/83/LS)

A	B	C	D
5,904(#44)	246	250	***Karnovsky M J.** A formaldehyde-glutaraldehyde fixative of high osmolality for use in electron microscopy. *J. Cell Biol.* 27:137A-8A, 1965. (15/85/LS)
5,995(#42)	428	633	†**Kohler G & Milstein C.** Continuous cultures of fused cells secreting antibody of predefined specificity. *Nature* 256:495-7, 1975.
4,380(#60)	77	126	***Krebs H A & Henseleit K.** Untersuchungen über die Harnstoffbildung im Tierkörper (Studies on urea formation in the animal organism). *Hoppe-Seylers Z. Physiol. Chem.* 210:33-66, 1932. (52/80/LS)
59,759(#2)	3,145	8,896	**Laemmli U K.** Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* 227:680-5, 1970.
3,994(#71)	285	197	***Laskey R A & Mills A D.** Quantitative film detection of ^3H and ^{14}C in polyacrylamide gels by fluorography. *Eur. J. Biochem.* 56:335-41, 1975. (13/83/LS)
3,913(#73)	170	206	***Laurell C-B.** Quantitative estimation of proteins by electrophoresis in agarose gel containing antibodies. *Anal. Biochem.* 15:45-52, 1966. (51/80/LS)
9,390(#21)	171	172	***Lineweaver H & Burk D.** The determination of enzyme dissociation constants. *J. Amer. Chem. Soc.* 56:658-66, 1934. (11/85/LS)
6,472(#35)	162	249	***Litchfield J T & Wilcoxon F A.** A simplified method of evaluating dose-effect experiments. *J. Pharmacol. Exp. Ther.* 96:99-113, 1949. (7/77)
187,652(#1)	4,938	9,750	***Lowry O H, Rosebrough N J, Farr A L & Randall R J.** Protein measurement with the Folin phenol reagent. *J. Biol. Chem.* 193:265-75, 1951. (1/77)
10,739(#14)	384	126	***Luft J H.** Improvements in epoxy resin embedding methods. *J. Biophys. Biochem. Cytol.* 9:409-14, 1961. (20/77)
9,531(#20)	397	314	**Mancini G, Carbonara A O & Heremans J F.** Immunochemical quantitation of antigens by single radial immunodiffusion. *Immunochemistry* 2:235-54, 1965.
6,236(#37)	223	214	**Marmur J.** A procedure for the isolation of deoxyribonucleic acid from micro-organisms. *J. Mol. Biol.* 3:208-18, 1961.
3,441(#92)	132	316	*†**Marquardt D W.** An algorithm for least-squares estimation of nonlinear parameters. *J. Soc. Ind. Appl. Math.* 11:431-41, 1963. (27/79/ET)
5,474(#48)	196	122	**Martin R G & Ames B N.** A method for determining the sedimentation behavior of enzymes: application to protein mixtures. *J. Biol. Chem.* 236:1372-9, 1961.
5,178(#51)	432	362	**Maxam A M & Gilbert W.** A new method for sequencing DNA. *Proc. Nat. Acad. Sci. USA* 74:560-4, 1977.
8,995(#23)	999	1,258	†**Maxam A M & Gilbert W.** Sequencing end-labelled DNA with base-specific chemical cleavages. *Meth. Enzymology* 65:499-560, 1980.
3,525(#87)	147	100	**Monod J, Wyman J & Changeux J-P.** On the nature of allosteric transitions: a plausible model. *J. Mol. Biol.* 12:88-118, 1965.
3,885(#75)	134	33	***Moorhead P S, Nowell P C, Mellman W J, Battips D M & Hungerford D A.** Chromosome preparations of leukocytes cultured from human peripheral blood. *Exp. Cell Res.* 20:613-6, 1960. (7/83/LS)
5,880(#45)	218	659	***Murashige T & Skoog F.** A revised medium for rapid growth and bioassays with tobacco tissue cultures. *Physiol. Plant.* 15:473-97, 1962. (43/78)
7,589(#31)	169	187	***Nelson N.** A photometric adaptation of the Somogyi method for the determination of glucose. *J. Biol. Chem.* 153:375-80, 1944. (3/77)
9,068(#22)	648	883	***O'Farrell P H.** High resolution two-dimensional electrophoresis of proteins. *J. Biol. Chem.* 250:4007-21, 1975. (51/82/LS)
5,734(#47)	229	371	**Omura T & Sato R.** The carbon monoxide-binding pigment of liver microsomes. I. Evidence for its hemoprotein nature. *J. Biol. Chem.* 239:2370-8, 1964.
4,077(#67)	163	73	**Ornstein L.** Disc electrophoresis—I. Background and theory. *Ann. NY Acad. Sci.* 121:321-49, 1964.
3,274(#98)	88	6	**Palade G E.** A study of fixation for electron microscopy. *J. Exp. Med.* 95:285-97, 1952.
7,829(#29)	154	23	**Reed L J & Muench H.** A simple method of estimating 50 percent endpoints. *Amer. J. Hyg.* 27:493-7, 1938.
17,928(#6)	690	44	***Reynolds E S.** The use of lead citrate at high pH as an electron-opaque stain in electron microscopy. *J. Cell Biol.* 17:208-12, 1963. (32/81/LS)
8,575(#27)	715	1,177	†**Rigby P W J, Dieckman M, Rhodes C & Berg P.** Labeling deoxyribonucleic acid to high specific activity *in vitro* by nick translation with DNA polymerase I. *J. Mol. Biol.* 113:237-51, 1977.

A	B	C	D
5,904(#43)	227	25	**Sabatini D D, Bensch K & Barrnett R J.** Cytochemistry and electron microscopy: the preservation of cellular ultrastructure and enzymatic activity by aldehyde fixation. *J. Cell Biol.* 17:19-58, 1963.
10,718(#15)	893	3,258	*†**Sanger F, Nicklen S & Coulson A R.** DNA sequencing with chain-terminating inhibitors. *Proc. Nat. Acad. Sci. USA* 74:5463-7, 1977. (50/88/LS)
13,782(#10)	345	1,050	**Scatchard G.** The attractions of proteins for small molecules and ions. *Ann. NY Acad. Sci.* 51:660-72, 1949.
5,365(#50)	158	34	**Scheidegger J J.** Une micro-méthode de l'immuno-électrophorèse (A micro-method for immunoelectrophoresis). *Int. Arch. Allergy* 7:103-10, 1955.
3,715(#81)	84	52	**Schmidt G & Thannhauser S J.** A method for the determination of deoxyribonucleic acid, ribonucleic acid, and phosphoproteins in animal tissues. *J. Biol. Chem.* 161:83-9, 1945.
3,328(#95)	76	20	*†**Schneider W C.** Phosphorus compounds in animal tissues. I. Extraction and estimation of desoxypentose nucleic acid and of pentose nucleic acid. *J. Biol. Chem.* 161:293-303, 1945. (8/77)
3,434(#93)	156	41	**Shapiro A L, Vinuela E & Maizel J V.** Molecular weight estimation of polypeptide chains by electrophoresis in SDS-polyacrylamide gels. *Biochem. Biophys. Res. Commun.* 28:815-26, 1967.
3,784(#76)	223	112	***Singer S J & Nicolson G L.** The fluid mosaic model of the structure of cell membranes. *Science* 175:720-31, 1972. (46/77)
3,507(#89)	95	145	**Somogyi M.** Notes on sugar determination. *J. Biol. Chem.* 195:19-23, 1952.
16,382(#9)	1,170	2,295	**Southern E M.** Detection of specific sequences among DNA fragments separated by gel electrophoresis. *J. Mol. Biol.* 98:503-17, 1975.
10,414(#16)	336	182	**Spackman D H, Stein W H & Moore S.** Automatic recording apparatus for use in the chromatography of amino acids. *Anal. Chem.* 30:1190-206, 1958.
7,411(#33)	371	389	***Spurr A R.** A low-viscosity epoxy resin embedding medium for electron microscopy. *J. Ultrastruct. Res.* 26:31-43, 1969. (50/79/LS)
3,727(#79)	196	359	*†**Sternberger L A, Hardy P H, Cuculis J J & Meyer H G.** The unlabeled antibody enzyme method of immunohistochemistry: preparation and properties of soluble antigen-antibody complex (horseradish peroxidase-antihorseradish peroxidase) and its use in identification of spirochetes. *J. Histochem. Cytochem.* 18:315-33, 1970. (4/83/LS)
8,079(#28)	337	292	***Stewart R F, Davidson E R & Simpson W T.** Coherent X-ray scattering for the hydrogen atom in the hydrogen molecule. *J. Chem. Phys.* 42:3175-87, 1965. (48/77)
5,050(#54)	561	896	†**Thomas P S.** Hybridization of denatured RNA and small DNA fragments transferred to nitrocellulose. *Proc. Nat. Acad. Sci. USA* 77:5201-5, 1980.
11,344(#13)	1,134	2,887	*†**Towbin H, Staehelin T & Gordon J.** Electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets: procedure and some applications. *Proc. Nat. Acad. Sci. USA* 76:4350-4, 1979. (11/88/LS; 11/88/CM)
4,269(#62)	109	83	***Trevelyan W E, Procter D P & Harrison J S.** Detection of sugars on paper chromatograms. *Nature* 166:444-5, 1950. (6/77)
3,761(#78)	209	144	***Vane J R.** Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. *Nature New Biol.* 231:232-5, 1971. (42/80/LS)
4,255(#63)	177	76	***Venable J H & Coggeshall R.** A simplified lead citrate stain for use in electron microscopy. *J. Cell Biol.* 25:407-8, 1965. (10/77)
3,306(#96)	69	31	**Warburg O & Christian W.** Isolierung und Kristallisation des Gärungsferments Enolase (Isolation and crystallization of the enzyme enolase). *Biochem. Z.* 310:384-421, 1941.
6,081(#40)	203	160	***Warren L.** The thiobarbituric acid assay of sialic acids. *J. Biol. Chem.* 234:1971-5, 1959. (36/77)
3,945(#72)	127	39	**Watson M L.** Staining of tissue sections for electron microscopy with heavy metals. *J. Biophys. Biochem. Cytol.* 4:475-8, 1958.
20,672(#4)	1,034	575	**Weber K & Osborn M.** The reliability of molecular weight determinations by dodecyl sulfate-polyacrylamide gel electrophoresis. *J. Biol. Chem.* 244:4406-12, 1969.
3,478(#91)	158	123	**Weinberg S.** A model of leptons. *Phys. Rev. Lett.* 19:1264-6, 1967.
3,666(#83)	147	46	**Yphantis D A.** Equilibrium ultracentrifugation of dilute solutions. *Biochemistry—USA* 3:297-317, 1964.

Figure 1: Distribution of *SCI*® citations to papers on extraction, isolation, and sequencing of DNA from the list of the 100 most-cited papers in Table 2. Year one represents the year each paper was published, and citation growth is measured year-by-year for each paper through 1988.



for an annual average of 561, compared to 896 citations in 1988. These papers reached citation peaks of 1,404 and 987, respectively, in 1987. Figure 1 presents a graph of the "citation trajectories" of these high-impact DNA methods papers and three others—a 1977 paper by Maxam and Gilbert, a 1977 paper by Frederick Sanger and colleagues, Medical Research Council Laboratory of Molecular Biology, Cambridge, UK, and a 1975 paper by Edwin M. Southern, Department of Zoology, University of Edinburgh, Scotland.

Two papers in Table 2 were published in German—by Hans A. Krebs and Kurt Henseleit, then at the University of Freiburg, Germany, in 1932 (4,380 citations, 1945-1988) and by Otto Warburg and Walter Christian, Kaiser Wilhelm Institute for Cell Physiology, Berlin, Germany, in 1941 (3,306 citations). The Krebs and Henseleit paper is a classic "concepts" rather than methods paper. It explained a biological process in terms of its underlying biosynthetic chemical pathways. The Warburg and Christian paper reports a method for preparing samples of the enzyme enolase. Both papers reached citation peaks at late ages, with 185 citations in 1980 for the Krebs paper and 150 citations to Warburg in 1972. One might have thought that these German-language papers would have been cited more heavily in their early years, when Germany was still a dominant scientific power. In his *Citation Classic* commentary, Krebs reminds us of another, more chilling kind of power when he says that his coauthor, Henseleit, was forced to leave research for medical practice after being told "by the Hitler regime that there was no future for him in academic medicine."[5]

One French-language article is also on the list. The 1955 paper by J.J. Scheidegger, Policlinic of the Medical School, Geneva, Switzerland, describes a micromethod for immunoelectrophoresis. It received 5,365 citations through 1988, averaged 158 citations annually, and reached a peak of 351 in 1970. The paper was cited 34 times in 1988.

One of the *SCI* Top 100 papers is a letter to the editor. In a 1980 *Citation Classic* commentary,[6] Sen-itiroh Hakomori, then at the Department of Biochemistry, Institute for Cancer Research, Tohoku Pharmaceutical School, Sendai, Japan, recalled first submitting his paper to the *Journal of Biochemistry* (Tokyo) in June 1963, but he quickly withdrew it because of criticism from a preprint reviewer. Equally but oppositely impelled by a colleague's forceful encouragement, he resubmitted the manuscript in November 1963, and it was eventually published as a letter in February 1964. It went on to receive 3,231 citations through 1988, achieved an annual average of 129 citations, peaked at 234 in 1981, and was cited 193 times in 1988.

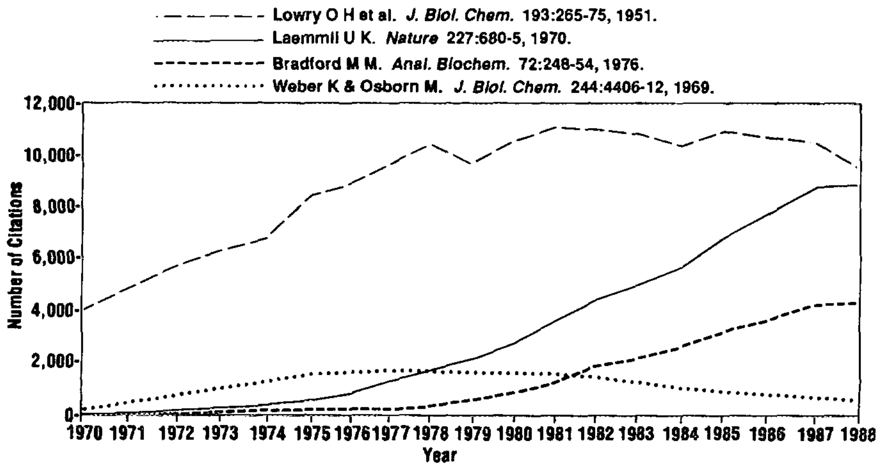
As a final highlight of the list, there is one physics paper among the *SCI* Top 100—a 1967 "concepts" paper by Steven Weinberg, then at the Department of Physics, Harvard, that presents a model of leptons; this paper was cited about 3,500 times through 1988. It averaged 158 citations per year, peaked in 1980 at 333, and was cited 123 times in 1988. We'll present citation trajectory curves of high-impact physics papers later in this series, when their numbers are more significant, and compare them with graphs from other fields.

Citation Classics Superstars

Since 1977 ISI® has published over 3,000 *Citation Classic* commentaries on frequently cited papers and books in virtually all the fields represented in the *SCI* and the *Social Sciences Citation Index*® databases. In these commentaries the authors themselves describe what their landmark papers are about and suggest their own reasons why these works have gone on to become so highly cited. Indeed, personal commentaries on exactly half of the 100 papers listed for 1945-1988 have been published. These 50 papers are indicated in Table 2 by an asterisk. One more *Citation Classic* commentary in Table 2, on the paper by Richard C. Graham and Morris J. Karnovsky, Department of Pathology, Harvard Medical School, is in production as we go to press.

That means there are still 49 papers we believe ought to be represented in the *Cita-*

Figure 2: Year-by-year distribution of citations from the *SCI*®, 1970-1988, for the four top cited works from the list of the 100 most-cited papers in Table 2.



tion Classics series. This essay is an open invitation to the coauthors, or their colleagues, of papers in Table 2 not already published as *Citation Classic* commentaries (those without an asterisk) to contact us. With their help, we welcome the opportunity to extend the record of personal "biographies" of *Citation Classic* papers.

Has Lowry Peaked?

It was entirely appropriate that Oliver H. Lowry, School of Medicine, Washington University, St. Louis, Missouri, and colleagues' landmark paper on protein determination was the subject of the first *Citation Classic* commentary,[7] published in *CC* in 1977. In the history of science, there has never been another paper that has come close in terms of total or annual citation counts. Whatever accounts for this phenomenon, explicit citations to the Lowry method seem to be declining somewhat but are still higher than any other.

Figure 2 presents a graph of citations per year to Lowry's seemingly immortal contribution, and three other classic protein methods papers: by Marian M. Bradford, Department of Biochemistry, University of Georgia, Athens (1976), Ulrich K. Laemmli, Department of Biochemistry, University of Geneva (1970), and Klaus Weber and Mary Osborn, Max Planck Institute for Biophysical Chemistry, Göttingen, Federal Republic of Germany (1969). These papers are the four most-cited papers in Table 2.

The Lowry paper seems to have reached and passed its citation peak. The more modern methods and microtechniques for protein identification and quantitation are being cited at fast and rising rates. The Laemmli paper, "Cleavage of structural proteins during the assembly of the head of bacteriophage T4," is now approaching Lowry and may eventually surpass it in annual citations.

Don W. Cleveland, Department of Biochemical Sciences, Princeton University, New Jersey, the first author of another paper by Laemmli on the list (see Table 2), tied together two of the top-cited papers in Table 2 in a *Citation Classic* commentary:

> As a result of its speed, resolving power, adaptability, and ease of use, polyacrylamide gel electrophoresis in the presence of the detergent sodium dodecyl sulfate is the most widely utilized method for the determination of both the purity and molecular mass of polypeptides in protein samples. This simple, but powerful, technique, first popularized by Weber and Osborn [1969, see Table 2] and improved by Laemmli [1970, see Table 2], remains the centerpost of available methods for polypeptide analysis and characterization more than 16 years after its introduction.[8]

Laemmli's "improvement" paper has received more than 59,000 citations, nearly 9,000 in 1988 alone, while Cleveland's 1977 paer (see Table 2) has received about 3,600 citations, with nearly 340 in 1988. Weber and Osborn's 1969 paper (see Table 2) received more than 20,600 citations between 1969 and 1988, with 575 in 1988.

Multiple Representation in the Top 100

Ten authors are represented more than once on the list of top 100 papers: Don T. Cromer, University of California, Los Alamos Scientific Laboratory, New Mexico, is first author of three crystallography papers. Authors represented twice are Ames; George L. Ellman, Langley Porter Neuropsychiatric Institute, University of California, San Francisco; Gilbert; Frederick C. Greenwood and W.M. Hunter, Division of Chemistry and Biochemistry, Imperial Cancer Research Fund, London; Karnovsky; Laemmli; Ronald A. Laskey, Laboratory of Molecular Biology, University Medical School, Cambridge University; and Maxam.

The two papers by Greenwood and Hunter on the list deserve special comment. In 1977 we published Greenwood's commentary[9] on his 1963 *Biochemical Journal*[10] paper.

Table 3: Chronological distribution of the 100 most-cited papers from the *SCI*®, 1945-1988. Data in parentheses for 1950s papers reflect exclusion of the Lowry method paper.

Decade	Number of Papers	Total Cites	*Average* Citations Per Year	*Average* 1988 Cites
1920s	1	17,247	269	335
1930s	4	25,164	118	97
1940s	9	60,246	160	247
1950s	24	337,652	398	677
	(23)	(150,000)	(201)	(283)
1960s	34	222,525	276	231
1970s	26	228,429	597	1,205
1980s	2	14,045	780	1,077
TOTAL	100	905,308	371	553

However, last year we published another commentary[11] on his 1962 paper in *Nature*.[12] When we graphed the citation curves for the two papers, we expected to see a good deal of co-citation (source articles citing both the Greenwood and Hunter papers in the same bibliography). After all, the two papers were published almost simultaneously and on the same subject, a procedure for preparation of radioiodinated human growth hormone.

However, we discovered that, out of the 378 and 341 citations to the two Greenwood and Hunter papers in 1988, there are 715 distinct citing papers. Only four papers in the 1988 *SCI* cited both the Greenwood and Hunter papers.

We asked Greenwood what he thought about the low level of co-citation in 1988. He indicated that he thought some people prefer to cite the more general *Nature* report while others prefer to cite the more technical *Biochemical Journal* paper. He also indicated that one of the papers included J.S. Glover, Radiochemical Centre, Amersham, Buckinghamshire, UK, as a third author. He speculated, perhaps tongue-in-cheek, that some people might choose to cite a paper with two authors instead of three.

Does this mean that if Hunter, Greenwood, and Glover had written only one paper, it would have received nearly 13,800 citations by now? Possibly so.

In addition to the multiple representations mentioned above, there are also two papers in a series that were written by different authors, both then at the Cell Research Laboratory, Mt. Sinai Hospital, New York. L. Ornstein is the sole author of "Disc electrophoresis—I. Background and theory," with more than 4,000 cites; Baruch J. Davis is the sole author of "Disc electrophoresis—II. Method and application to human serum proteins," with more than 17,000 cites. Both were published in the *Annals of the New York Academy of Sciences* in 1964.

Chronological Distribution of Papers by Decade

Table 3 shows the distribution of the top 100 papers by decade, from the two 1980 papers on DNA sequencing methods discussed earlier to the 1925 paper of Fiske and SubbaRow on phosphorus determination. Also shown are the total citations received by all papers within each decade, the group's average annual citation rates, and average 1988 citations. As the series progresses through the *SCI* Top 1,000-1,500 papers, we will update and cumulate the information shown here and plot citation trajectory curves by decade.

Of the *SCI* Top 100, 84 were published from 1950 through 1979. The average annual citation rate for 1950s papers is inflated by Lowry's exceptional citation record. When the Lowry paper is removed, the citation data on the group of 23 papers from

Table 4: The journals that published the 100 most-cited *SCI*® papers. A=title, with founding year in parentheses. B=number of most-cited articles appearing in the journal.

A	B
J. Biol. Chem. (1905)	17
Proc. Nat. Acad. Sci. USA (1915)	6
Nature (1869)	5
Anal. Biochem. (1960)	4
Biochem. J. (1906)	4
J. Cell Biol. (1962)	4
J. Mol. Biol. (1959)	4
Acta Crystallogr. (1948)	3
Anal. Chem. (1929)	3
Ann. NY Acad. Sci. (1877)	3
Biochemistry—USA (1964)	3
J. Exp. Med. (1896)	3
Eur. J. Biochem. (1967)	2
J. Biophys. Biochem. Cytol. (1955)	2
J. Chem. Phys. (1931)	2
J. Clin. Invest. (1924)	2
J. Histochem. Cytochem. (1953)	2
Science (1880)	2
Amer. J. Hyg. (1921)	1
Arch. Biochem. Biophys. (1942)	1
Biochem. Biophys. Res. Commun. (1959)	1
Biochem. Pharmacol. (1958)	1
Biochem. Z. (1906)	1
Biometrics (1945)	1
Can. J. Biochem. Physiol. (1929)	1
Eur. J. Immunol. (1970)	1
Exp. Cell Res. (1950)	1
Hoppe-Seylers Z. Physiol. Chem. (1877)	1
Immunochemistry (1964)	1
Int. Arch. Allergy (1950)	1
J. Amer. Chem. Soc. (1879)	1
J. Amer. Statist. Assn. (1888)	1
J. Biochem.—Tokyo (1922)	1
J. Morphol. (1931)	1
J. Pharmacol. Exp. Ther. (1909)	1
J. Physiol.—London (1878)	1
J. Roy. Statist. Soc. Ser. B Metho. (1934)	1
J. Soc. Ind. Appl. Math. (1953)	1
J. Ultrastruct. Res. (1957)	1
Meth. Enzymology (1955)	1
Mutat. Res. (1964)	1
Nucl. Acid. Res. (1974)	1
Pharmacol. Rev. (1949)	1
Phys. Rev. Lett. (1958)	1
Physiol. Plant. (1948)	1
Plant Physiol. (1926)	1
Scand. J. Clin. Lab. Invest. (1949)	1

the 1950s falls in line with the general trend toward increasing total and annual average citations over the decades. Also, there is a clear break between papers published before and during the 1970s. The group of 26 papers published during the 1970s averaged 597 citations per year, double that of the 1960s papers. Also, the 1970s papers averaged about 1,200 citations in 1988, five times that of the 1960s papers.

Journals of the Top 100 Papers

Table 4 presents the journals that published the 100 most-cited articles. The journal's first year of publication is shown in parentheses after each title, and the number of *SCI* Top 100 papers it published is shown in column B.

The *Journal of Biological Chemistry*, in which Lowry's paper was published in 1951, heads the list with 17 papers—ahead of *PNAS*, with six. *Nature* is third, with five papers.

PNAS, *Nature*, the *Annals of the New York Academy of Sciences*, and *Science* are the multidisciplinary journals represented by more than one paper. All other journals with more than one are in the fields of biochemistry and cell biology, except *Acta Crystallographica* (three papers) and the *Journal of Chemical Physics* (two papers).

Journal editors and publishers should be interested to know that ISI's database can identify the most-cited papers from any journal cited in over 175 million references published from 1945 to 1988. In addition to providing a reference for each article cited at least 50 times, the cited items from a particular journal are ranked by total citations, the number of citations during each year is detailed, and total and annual citation data are summarized. If you are interested in reviewing a sample of the *Classics Journal* file, simply write or call ISI's director of editorial services, Al Welljams-Dorof, at 1-800-523-1850, ext. 1429.

A Journal of *Citation Classics*?

Price frequently suggested starting a *Journal of Really Important Papers*, a serialized compendium of science's best journal contributions.[13] I have counterproposed a *Journal of Citation Classics*. By publishing the original author's *Citation Classic* article together with the author's *a posteriori* commentary, a variety of research purposes could be serviced. Since they are cited so often, they are requested in libraries quite regularly. Issuing this journal in the form of compact disks would allow it to be easily updated and accessed. Certainly, the papers listed in Table 2 would be the most likely candidates for the first "volume" of this library of *Citation Classics*. Considering that thousands of papers can be stored on a single disk, we could calculate the probability that the average scientist would need to access the disk enough times each year to justify his own personal volume. It's a project worth contemplating.

In the second part of this essay inaugurating our new series on the Most-Cited Papers of All Time, we will focus on those 17 papers on the *SCI* Top 100 that did *not* appear on the previous list for 1961-1982. They are indicated in Table 2 by daggers preceding the reference. The discussion of these "newcomer" superstars will incorporate *Citation Classic* commentaries where available.

* * * * *

My thanks to C.J. Fiscus and James Mears for their help in the preparation of this essay.

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