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Current Comments®

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The Most-Cited Papers of All Time, *SCI* 1945-1988. Part 1B. Superstars New to the *SCI* Top 100

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The top 100 papers cited in the 1945-1988 *Science Citation Index®* (*SCI®*) are presented. Seventeen did not appear on an earlier list of most-cited papers for 1961-1982. These are discussed using *Citation Classic®* commentaries by the authors. Three papers among the *SCI* Top 100 appear to be cases of delayed recognition. Their annual citations are graphed. Overall, molecular biology papers, especially on molecular cloning and polymer sequencing, dominate the recent additions to the top 100 list.

Newcomers to the *SCI* Top 100

Table 1 lists the *Science Citation Index®* (*SCI®*) Top 100 papers, 1945-1988, that were presented in the first part of this essay.[1] The papers are ranked now by total citations, shown in column A, rather than alphabetically by first author as in Part 1A. Column B shows the average annual citations for each paper, which is calculated by dividing total citations by the paper's age. Column C shows the number of citations each paper received in 1988. Whether a paper in 1988 was rising or falling against its average annual citation rate is indicated by comparing columns B and C.

Column D gives full bibliographic references for the *SCI* Top 100. An asterisk preceding a reference indicates that the paper was the subject of a *Citation Classic®* commentary, and the *Current Contents®* (*CC®*) issue, edition, and year of publication follows the reference in parentheses.

A dagger preceding a reference indicates that it is one of 17 papers that did *not* appear in our earlier study of the most-cited papers of 1961-1982.[2] Most of the 83 holdovers from the earlier study have already been discussed in previous *CC* essays. Here I'll focus on the newcomers and let the authors themselves describe their works from their published *Citation Classic* commentaries. They are listed in Table 2 in order of total citations, with their 1988 citations and rankings also shown.

Three New Statistics Papers

The most-cited statistics paper in Table 1 is a 1955 *Biometrics* paper by David B. Duncan, Virginia Polytechnic Institute, Blacksburg, on "Multiple range and multiple *F* tests." It was included on the list of most-cited papers for 1961-1982 and was the only pure statistics paper identified in that study.

In addition to the Duncan paper, three other statistics papers are among the *SCI* Top 100 of 1945-1988, none of which appeared on the 1961-1982 list. A 1958 paper from the *Journal of the American Statistical Association* (*JASA*) by Edward L. Kaplan, University of California Radiation Laboratory, and Paul Meier, University of Chicago, Illinois, is the second most-cited statistics paper on the list. In his 1983 *Citation Classic* commentary,[3] Kaplan recalled that the paper was inspired by quite disparate interests of the two authors. Kaplan was curious about the lifetimes of vacuum tubes in the repeaters of underwater telephone cables while Meier was interested in cancer duration. Both submitted separate manuscripts to *JASA*, whose editors recommended a joint contribution. After four years of correspondence between the coauthors, the now *Citation Classic* paper was published. Kaplan explained:

> The product-limit formula estimates the proportion of organisms or physical devices surviving beyond any age *t*, even

> when some of the items are not observed to die or fail, and the sample is rather small.... Presumably this paper is frequently cited because it gives a good presentation of a simple solution to a problem often encountered by researchers. (It has also been used in a seminar intended to introduce students to the use of the literature.)[3]

Kaplan and Meier's paper has been cited over 4,750 times, averaging 153 citations per year. Its annual citation rate continues to increase, with more than 780 citations in 1988, its highest citation year to date. Interestingly, the paper's year-by-year citations seem to indicate that its recognition was long delayed—from 1959 through 1968, the paper was cited between one and five times per year. Ten years after that, in 1977, the paper received 102 citations and has quickly and steadily increased since then. Later in the essay, we present graphs of annual citations to this paper and several other possible cases of delayed recognition identified on the *SCI* all-time *Citation Classics* list.

A 1963 paper by Donald W. Marquardt, Department of Engineering, E.I. du Pont de Nemours & Company, Wilmington, Delaware, entitled "An algorithm for least-squares estimation of nonlinear parameters," was published in the *Journal of the Society for Industrial and Applied Mathematics*. It has received over 3,400 citations, averaged 132 citations per year, seems to have peaked at 337 citations in 1987, and was cited 316 times in 1988. In his 1979 *Citation Classic* commentary, Marquardt wrote:

> It was clear from the beginning that this was a real breakthrough. At first by plotting and then by algebraic calculation, I had observed that the gradient and Taylor-series methods invariably gave correction vectors whose included angle γ is nearly a right angle. Recognition of the orientation of these vectors in the sum-of-squares contours explained for the first time the apparently anomalous behaviors of the previous methods.[4]

Marquardt also learned a valuable lesson from his paper about footnoting, a practice that I feel journals should discourage in their guidelines for authors. Marquardt explains:

> A small but very critical part of the algorithm...is described in a footnote. [It] is included in our...computer program, which has been supplied to many requestors.... Many others have programmed the algorithm on their own, but a number of such users have not included [the footnoted detail] and have not achieved nearly as good results. I've eschewed footnotes ever since![4]

The remaining statistics paper among the *SCI* Top 100 is by David R. Cox, Imperial College, London, UK, on "Regression models and life-tables," published in 1972 in the *Journal of the Royal Statistical Society. Series B (Methodological)*. In a 1986 *Citation Classic* commentary, Cox explained that the paper is concerned with "the analysis of a common type of failure (or survival) data in which the dependence on explanatory variables is studied."[5] He examined the usual approach of preparing a "likelihood function" but found that it "gave only an expression of virtually useless complexity." Some years of mulling over the problem led him to the realization that "most of the likelihood was irrelevant to the main purpose and that if only relevant factors were retained, quite simple procedures of analysis were achieved." The author noted that, shortly after the 1972 paper was published, the method was included in a number of statistical packages and had, by 1986, found application in many fields of study "from econometrics to animal breeding."[5]

Cox's paper was cited about 3,400 times and averaged 200 citations per year over its 17-year life to date. Its annual citations have steadily increased from 9 in 1973 to 540 in 1988.

Highest Ranking and Fastest Rising Newcomers

The highest ranking paper new to the list is the 1979 *Proceedings of the National Academy of Sciences of the USA (PNAS)* paper by Harry Towbin, Friedrich Miescher Institute, Basel, Switzerland; T. Staehelin,

Table 1: Bibliography of the 100 most-cited papers from the *SCI*®, 1945-1988. Papers are arranged in order of total citations. A=1945-1988 citations. 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 *Current Contents*® issue, year, and edition of the commentary follow the bibliographic reference. A dagger (†) indicates that the paper did *not* appear on the 1961-1982 top 100 list.

A	B	C		D
187,652	4,938	9,750	1.	***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)
59,759	3,145	8,896	2.	**Laemmli U K.** Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* 227:680-5, 1970.
24,366	1,874	4,303	3.	**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.
20,672	1,034	575	4.	**Weber K & Osborn M.** The reliability of molecular weight determinations by dodecyl sulfate-polyacrylamide gel electrophoresis. *J. Biol. Chem.* 244:4406-12, 1969.
20,505	641	945	5.	**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.
17,928	690	44	6.	***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)
17,510	700	504	7.	**Davis B J.** Disc electrophoresis—II. Method and application to human serum proteins. *Ann. NY Acad. Sci.* 121:404-27, 1964.
17,247	269	335	8.	**Fiske C H & SubbaRow Y.** The colorimetric determination of phosphorus. *J. Biol. Chem.* 66:375-400, 1925.
16,382	1,170	2,295	9.	**Southern E M.** Detection of specific sequences among DNA fragments separated by gel electrophoresis. *J. Mol. Biol.* 98:503-17, 1975.
13,782	345	1,050	10.	**Scatchard G.** The attractions of proteins for small molecules and ions. *Ann. NY Acad. Sci.* 51:660-72, 1949.
13,487	409	483	11.	***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)
11,763	294	297	12.	***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)
11,344	1,134	2,887	13.	***†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)
10,739	384	126	14.	***Luft J H.** Improvements in epoxy resin embedding methods. *J. Biophys. Biochem. Cytol.* 9:409-14, 1961. (20/77)
10,718	893	3,258	15.	***†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)
10,414	336	182	16.	**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.
9,922	342	49	17.	***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)
9,741	295	611	18.	**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.
9,639	321	781	19.	***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)
9,531	397	314	20.	**Mancini G, Carbonara A O & Heremans J F.** Immunochemical quantitation of antigens by single radial immunodiffusion. *Immunochemistry* 2:235-54, 1965.
9,390	171	172	21.	***Lineweaver H & Burk D.** The determination of enzyme dissociation constants. *J. Amer. Chem. Soc.* 56:658-66, 1934. (11/85/LS)
9,068	648	883	22.	***O'Farrell P H.** High resolution two-dimensional electrophoresis of proteins. *J. Biol. Chem.* 250:4007-21, 1975. (51/82/LS)
8,995	999	1,258	23.	**†Maxam A M & Gilbert W.** Sequencing end-labeled DNA with base-specific chemical cleavages. *Meth. Enzymology* 65:499-560, 1980.

A	B	C		D
8,985	264	429	24.	*Duncan D B. Multiple range and multiple *F* tests. *Biometrics* 11:1-42, 1955. (4/77)
8,877	423	713	25.	*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)
8,628	288	399	26.	*Bartlett G R. Phosphorus assay in column chromatography. *J. Biol. Chem.* 234:466-8, 1959. (4/85/LS)
8,575	715	1,177	27.	†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.
8,079	337	292	28.	*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)
7,829	154	23	29.	Reed L J & Muench H. A simple method of estimating 50 percent endpoints. *Amer. J. Hyg.* 27:493-7, 1938.
7,627	293	378	30.	*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)
7,589	169	187	31.	*Nelson N. A photometric adaptation of the Somogyi method for the determination of glucose. *J. Biol. Chem.* 153:375-80, 1944. (3/77)
7,516	501	387	32.	*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)
7,411	371	389	33.	*Spurr A R. A low-viscosity epoxy resin embedding medium for electron microscopy. *J. Ultrastruct. Res.* 26:31-43, 1969. (50/79/LS)
7,084	394	247	34.	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.
6,472	162	249	35.	*Litchfield J T & Wilcoxon F A. A simplified method of evaluating dose-effect experiments. *J. Pharmacol. Exp. Ther.* 96:99-113, 1949. (7/77)
6,294	233	341	36.	*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)
6,236	223	214	37.	Marmur J. A procedure for the isolation of deoxyribonucleic acid from micro-organisms. *J. Mol. Biol.* 3:208-18, 1961.
6,228	208	331	38.	Ellman G L. Tissue sulfhydryl groups. *Arch. Biochem. Biophys.* 82:70-7, 1959.
6,190	155	311	39.	Arnon D I. Copper enzymes in isolated chloroplasts. Polyphenoloxidase in *Beta vulgaris*. *Plant Physiol.* 24:1-15, 1949.
6,081	203	160	40.	*Warren L. The thiobarbituric acid assay of sialic acids. *J. Biol. Chem.* 234:1971-5, 1959. (36/77)
6,041	263	288	41.	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.
5,995	428	633	42.	†Köhler G & Milstein C. Continuous cultures of fused cells secreting antibody of predefined specificity. *Nature* 256:495-7, 1975.
5,904	227	25	43.	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.
5,904	246	250	44.	*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)
5,880	218	659	45.	*Murashige T & Skoog F. A revised medium for rapid growth and bioassays with tobacco tissue cultures. *Physiol. Plant.* 15:473-97, 1962. (43/78)
5,792	276	342	46.	Cromer D T & Mann J B. X-ray scattering factors computed from numerical Hartree-Fock wave functions. *Acta Crystallogr. A* 24:321-5, 1968.
5,734	229	371	47.	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.
5,474	196	122	48.	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.

A	B	C		D
5,463	166	206	49.	*Chen P S, Toribara T Y & Warner H. Microdetermination of phosphorus. *Anal. Chem.* 28:1756-8, 1956. (9/77)
5,365	158	34	50.	Scheidegger J J. Une micro-méthode de l'immuno-électrophorèse (A micromethod for immunoelectrophoresis). *Int. Arch. Allergy* 7:103-10, 1955.
5,178	432	362	51.	Maxam A M & Gilbert W. A new method for sequencing DNA. *Proc. Nat. Acad. Sci. USA* 74:560-4, 1977.
5,167	517	1,602	52.	†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.
5,104	510	937	53.	*†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)
5,050	561	896	54.	†Thomas P S. Hybridization of denatured RNA and small DNA fragments transferred to nitrocellulose. *Proc. Nat. Acad. Sci. USA* 77:5201-5, 1980.
4,756	153	781	55.	*†Kaplan E L & Meier P. Nonparametric estimation from incomplete observations. *J. Amer. Statist. Assn.* 53:457-81, 1958. (24/83/LS)
4,648	273	654	56.	†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.
4,589	242	118	57.	Gilman A G. A protein binding assay for adenosine 3′:5′-cyclic monophosphate. *Proc. Nat. Acad. Sci. USA* 67:305-12, 1970.
4,583	327	246	58.	*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)
4,468	248	176	59.	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.
4,380	77	126	60.	*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)
4,372	156	292	61.	*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)
4,269	109	83	62.	*Trevelyan W E, Procter D P & Harrison J S. Detection of sugars on paper chromatograms. *Nature* 166:444-5, 1950. (6/77)
4,255	177	76	63.	*Venable J H & Coggeshall R. A simplified lead citrate stain for use in electron microscopy. *J. Cell Biol.* 25:407-8, 1965. (10/77)
4,232	169	70	64.	Andrews P. Estimation of the molecular weights of proteins by Sephadex gel-filtration. *Biochem. J.* 91:222-33, 1964.
4,111	171	57	65.	Cromer D T & Waber J T. Scattering factors computed from relativistic Dirac-Slater wave functions. *Acta Crystallogr.* 18:104-9, 1965.
4,101	85	23	66.	*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)
4,077	163	73	67.	Ornstein L. Disc electrophoresis—I. Background and theory. *Ann. NY Acad. Sci.* 121:321-49, 1964.
4,045	253	251	68.	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.
4,014	211	280	69.	Cromer D T & Liberman D. Relativistic calculation of anomalous scattering factors for X-rays. *J. Chem. Phys.* 53:1891-8, 1970.
4,009	121	35	70.	Dole V P. A relation between non-esterified fatty acids in plasma and the metabolism of glucose. *J. Clin. Invest.* 35:150-4, 1956.
3,994	285	197	71.	*Laskey R A & Mills A D. Quantitative film detection of ^{3}H and ^{14}C in polyacrylamide gels by fluorography. *Eur. J. Biochem.* 56:335-41, 1975. (13/83/LS)
3,945	127	39	72.	Watson M L. Staining of tissue sections for electron microscopy with heavy metals. *J. Biophys. Biochem. Cytol.* 4:475-8, 1958.
3,913	170	206	73.	*Laurell C-B. Quantitative estimation of proteins by electrophoresis in agarose gel containing antibodies. *Anal. Biochem.* 15:45-52, 1966. (51/80/LS)
3,890	130	39	74.	*Eagle H. Amino acid metabolism in mammalian cell cultures. *Science* 130:432-7, 1959. (5/77)
3,885	134	33	75.	*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)

A	B	C		D
3,784	223	112	76.	*Singer S J & Nicolson G L. The fluid mosaic model of the structure of cell membranes. *Science* 175:720-31, 1972. (46/77)
3,766	171	70	77.	*Conney A H. Pharmacological implications of microsomal enzyme induction. *Pharmacol. Rev.* 19:317-61, 1967. (3/79/LS)
3,761	209	144	78.	*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)
3,727	196	359	79.	*†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)
3,722	109	284	80.	*†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)
3,715	84	52	81.	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.
3,708	98	220	82.	Hamburger V & Hamilton H L. A series of normal stages in the development of the chick embryo. *J. Morphol.* 88:49-92, 1951.
3,666	147	46	83.	Yphantis D A. Equilibrium ultracentrifugation of dilute solutions. *Biochemistry—USA* 3:297-317, 1964.
3,594	300	339	84.	*†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)
3,591	103	66	85.	Dulbecco R & Vogt M. Plaque formation and isolation of pure lines with poliomyelitis viruses. *J. Exp. Med.* 99:167-82, 1954.
3,565	71	68	86.	Bratton A C & Marshall E K. A new coupling component for sulfanilamide determination. *J. Biol. Chem.* 128:537-50, 1939.
3,525	147	100	87.	Monod J, Wyman J & Changeux J-P. On the nature of allosteric transitions: a plausible model. *J. Mol. Biol.* 12:88-118, 1965.
3,515	95	156	88.	*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)
3,507	95	145	89.	Somogyi M. Notes on sugar determination. *J. Biol. Chem.* 195:19-23, 1952.
3,488	129	172	90.	Bitter T & Muir H M. A modified uronic acid carbazole reaction. *Anal. Biochem.* 4:330-4, 1962.
3,478	158	123	91.	Weinberg S. A model of leptons. *Phys. Rev. Lett.* 19:1264-6, 1967.
3,441	132	316	92.	*†Marquardt D W. An algorithm for least-squares estimation of nonlinear parameters. *J. Soc. Ind. Appl. Math.* 11:431-41, 1963. (27/79/ET)
3,434	156	41	93.	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.
3,392	200	540	94.	*†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)
3,328	76	20	95.	*†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)
3,306	69	31	96.	Warburg O & Christian W. Isolierung und Kristallisation des Gärungsferments Enolase (Isolation and crystallization of the enzyme enolase). *Biochem. Z.* 310:384-421, 1941.
3,278	96	88	97.	*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)
3,274	88	6	98.	Palade G E. A study of fixation for electron microscopy. *J. Exp. Med.* 95:285-97, 1952.
3,231	129	193	99.	*†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)
3,204	188	49	100.	*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)

Department of Pharmaceutical Research, Hoffman-La Roche, Basel; and J. Gordon, Friedrich Miescher Institute, "Electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets: procedure and some applications." It is the 13th most-cited paper in the 1945-1988 *SCI* database, with more than 11,300 citations. It averaged 1,134 citations per year since 1979 and received nearly 2,900 citations in 1988.

In a 1988 *Citation Classic* commentary,[6] Towbin explained that the paper grew out of his interest in identifying and characterizing protein-specific antibodies. Gels used at that time for protein suspensions were too dense to allow antibodies to diffuse readily to the proteins. Towbin's idea was to fix proteins instead on nitrocellulose filters, and he discovered a way to transfer them from gels to the more effective medium for antibody-protein binding. Towbin wrote:

> The idea of using replicas of gels...was certainly inspired by the example of DNA-blotting introduced by E.M. Southern [#9 in Table 1].... We discussed various methods of obtaining replicas, and the idea of some electrophoretic elution transpired. In Gordon's laboratory an electrophoretic destainer was used.... Since protein stains are charged, the excess dye moves out of the gel in the electric field maintained by the apparatus. Hence, the gel clears in...minutes, as compared to hours by simple diffusion. This impressive acceleration gave me the idea of... trying to elute proteins by transverse electrophoresis.[6]

Towbin suggested several possible reasons for the paper's extraordinary impact:

> The rapid acceptance of our procedure and its frequent citation may be due to its technical simplicity, its publication in a widely read journal, and the "snowball" effect provided by important publications quoting our method. Methods papers in immunochemistry are of interest to an extremely wide range of potential users, reflecting the spread of immunochemical techniques to all areas of the medical and biological sciences.[6]

The most rapidly rising paper new to the *SCI* Top 100 was coauthored by double Nobelist Frederick Sanger, S. Nicklen, and A.R. Coulson, Medical Research Council Laboratory of Molecular Biology, Cambridge, UK, and describes a DNA sequencing method. Although it ranks 15th in Table 1 with slightly more than 10,700 citations, this *PNAS* paper received over 3,250 citations in 1988, more than any paper other than the top three most-cited papers, by Oliver H. Lowry, School of Medicine, Washington University, St. Louis, Missouri, and colleagues (1951); Ulrich K. Laemmli, Department of Biochemistry, University of Geneva, Switzerland (1970); and Marion M. Bradford, Department of Biochemistry, University of Georgia, Athens (1976).

In his December 1988 *Citation Classic* commentary,[7] Sanger described the DNA sequencing breakthrough that permitted fast characterization of primary DNA structure:

> From the scientific point of view, the 1975 paper[8] [which has received more than 405 citations through 1988] was probably more important than this one since it described an entirely new approach and represented a turning point in DNA sequencing that led to the vast amount of data that is being obtained today. The present paper is more widely cited because it describes the actual method that is being used.
>
> Another rapid DNA sequencing technique was developed about the same time by A.M. Maxam and W. Gilbert [see #51 in Table 1], and the two methods led to a surge of interest and activity in DNA sequencing. The scope and use of the "dideoxy" method was greatly increased by the introduction of a cloning procedure by J. Messing and his colleagues.[9] This made it possible, at least in theory, to sequence any DNA, however large, and most of the papers published today on DNA sequences use this system.[7]

The 1977 papers by Sanger and colleagues and by Allan M. Maxam and Walter Gilbert, Department of Biochemistry and Molecular Biology, Harvard University, Cambridge, Massachusetts, and the 1980 papers by Maxam and Gilbert and by Patricia S. Thomas, Fred Hutchinson Cancer Research Center, Seattle, Washington, represent in Table 1 the surge of DNA sequencing research during the last 12 years. Sanger men-

Table 2: Bibliography of the 17 papers on the *SCI*® Top 100 list that did not appear in the 1961-1982 most-cited articles study. Papers are ranked by total citations through 1988. A = 1945-1988 citations, with 1945-1988 rank in parentheses. B = number of 1988 citations, with rank on this list by 1988 citations in parentheses. C = abbreviated bibliographic data. An asterisk (*) indicates that the paper was the subject of a *Citation Classic*® commentary. The *Current Contents*® issue, year, and edition of the commentary follow the bibliographic reference.

A	B	C
11,344(#13)	2,887(#5)	*Towbin H, Staehelin T & Gordon J. *Proc. Nat. Acad. Sci. USA* 76:4350-4, 1979. (11/88/LS; 11/88/CM)
10,718(#15)	3,258(#4)	*Sanger F, Nicklen S & Coulson A R. *Proc. Nat. Acad. Sci. USA* 74:5463-7, 1977. (50/88/LS)
8,995(#23)	1,258(#8)	Maxam A M & Gilbert W. *Meth. Enzymology* 65:499-560, 1980.
8,575(#27)	1,177(#9)	Rigby P W J, Dieckman M, Rhodes C & Berg P. *J. Mol. Biol.* 113:237-51, 1977.
5,995(#42)	633(#20)	Köhler G & Milstein C. *Nature* 256:495-7, 1975.
5,167(#52)	1,602(#7)	Chirgwin J M, Przybyla A E, MacDonald R J & Rutter W J. *Biochemistry—USA* 18:5294-9, 1979.
5,104(#53)	937(#12)	*Birnboim H C & Doly J. *Nucl. Acid. Res.* 7:1513-23, 1979. (45/88/LS)
5,050(#54)	896(#13)	Thomas P S. *Proc. Nat. Acad. Sci. USA* 77:5201-5, 1980.
4,756(#55)	781(#15)	*Kaplan E L & Meier P. *J. Amer. Statist. Assn.* 53:457-81, 1958. (24/83/LS)
4,648(#56)	654(#19)	Aviv H & Leder P. *Proc. Nat. Acad. Sci. USA* 69:1408-12, 1972.
3,727(#79)	359(#34)	*Sternberger L A, Hardy P H, Cuculis J J & Meyer H G. *J. Histochem. Cytochem.* 18:315-33, 1970. (4/83/LS)
3,722(#80)	284(#87)	*Havel R J, Eder H A & Bragdon J H. *J. Clin. Invest.* 34:1345-53, 1955. (46/83/LS)
3,594(#84)	339(#37)	*Cleveland D W, Fischer S G, Kirschner M W & Laemmli U K. *J. Biol. Chem.* 252:1102-6, 1977. (41/84/LS)
3,441(#92)	316(#40)	*Marquardt D W. *J. Soc. Ind. Appl. Math.* 11:431-41, 1963. (27/79/ET)
3,392(#94)	540(#23)	*Cox D R. *J. Roy. Statist. Soc. Ser. B Metho.* 34:187-220, 1972. (42/86/AB; 42/86/A&H; 42/86/S&BS)
3,328(#95)	20(#99)	*Schneider W C. *J. Biol. Chem.* 161:293-303, 1945. (8/77)
3,231(#99)	193(#60)	*Hakomori S. *J. Biochem. Tokyo* 55:205-8, 1964. (23/80/LS)

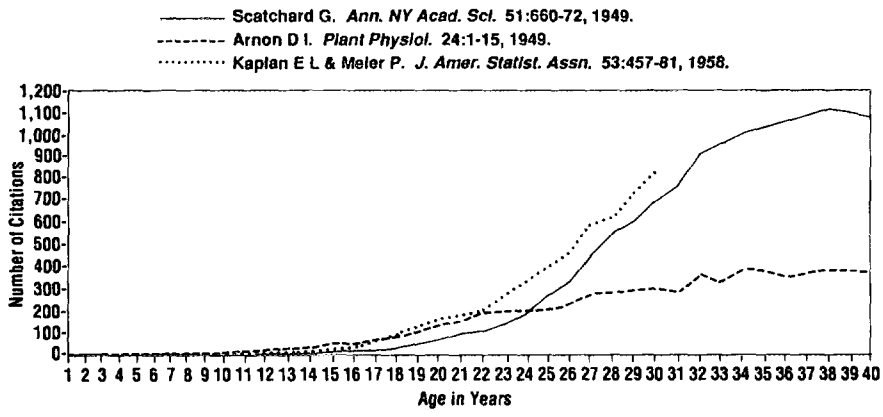
tioned the work of Joachim Messing, Department of Biochemistry, University of Minnesota, St. Paul, in his *Citation Classic* commentary quoted earlier.[7] Indeed, four papers by Messing, Jeffrey Vieira, also at the Department of Biochemistry, University of Minnesota, and colleagues[9-12] received 200 to 700 citations each in 1988, for a total of more than 1,700 citations. In addition, *Molecular Cloning*,[13] a 1982 laboratory manual by Tom Maniatis, Department of Biochemistry, Harvard, received more than 5,200 citations in 1988 alone. This work will be discussed in a future essay on the *SCI* most-cited books for 1945-1988.

The appearance of these dominating publications signals a shift in biochemistry from analysis of nucleotides, proteins, and lipids to separation and identification of long sequences of polymeric molecules. The protein methods papers still outrank all others. But the fastest rising superstar papers today are in molecular cloning and DNA sequencing.

Quantitative Criteria for Delayed Recognition

Three papers in the *SCI* Top 100 deserve special comment as apparent cases of delayed recognition, a subject discussed several times during the last year.[14-16] The most obvious example is the 1949 paper by George Scatchard, Department of Chemistry, Massachusetts Institute of Technology, Cambridge, "The attractions of proteins for small molecules and ions," published in the *Annals of the New York Academy of Sciences*. It received 13,782 citations, averaged 345 citations per year, peaked at 1,167 citations in 1986, and received 1,050 1988 citations. The second classic case of delayed recognition is the 1958 statistics paper by Kaplan, discussed earlier. The third example among the *SCI* Top 100 is a 1949 paper from *Plant Physiology* by Daniel I. Arnon, University of Cambridge, UK, on copper enzymes in isolated chloroplasts. It has about 6,200 citations, averaged 155 per

Figure 1: Distribution of *SCI*® citations to papers from the list of 100 most-cited papers displaying characteristics of delayed recognition. Year one represents the year each paper was published, and citation growth is measured year-by-year for each paper through 1988.



year, peaked at 379 citations in 1982, and received 311 citations in 1988.

Figure 1 presents a graph of the citation "trajectories" of these three papers. Delayed recognition was defined quantitatively as follows: at age 10, the paper was still cited infrequently, in the single digits or low teens; sometime at or after age 20, the paper's annual citation rate was *at least 10-fold* higher than at age 10.

The *SCI* database of over 175 million citations in about 15 million source items published from 1945 to 1989 is an excellent source for quantifying and identifying possible cases of delayed recognition. Several of these papers are likely to describe methods whose *application* may have become widespread after many years but whose recognition, as such, was not necessarily delayed. In an upcoming essay on delayed recognition, we'll discuss several apparent cases of delayed recognition from the *SCI* files, present and graph a few of the more obvious examples, and invite *CC* readers to comment on these cases.

The DNA Methods Anomaly

Two papers among the *SCI* Top 100 are anomalies. A 1945 paper by Walter C. Schneider, University of Wisconsin Medical School, Madison, in the *Journal of Biological Chemistry* describes a method for the extraction of nucleic acids from tissue. It overlaps significantly in application with another paper in the *SCI* Top 100, by Gerhard Schmidt, Boston Dispensary, Joseph H. Pratt Diagnostic Hospital, Massachusetts, and S.J. Thannhauser, Tufts College Medical School, Boston, published in the same issue of the journal. One might have expected that one or the other paper would have been cited preferentially over time. But both papers have achieved very similar citation patterns. One might also expect that the two papers would have been frequently *co*-cited—that is, cited together in the same bibliography of a citing paper. But in 1988, 72 distinct papers cited the Schneider or Schmidt and Thannhauser papers but only two of these cited both works.

In a 1977 *Citation Classic* commentary, Schneider said:

> Imagine my surprise and chagrin upon opening the journal in which my paper appeared to find a paper on the same subject by Gerhard Schmidt and S.J. Thannhauser. Their paper permitted the separation of DNA from RNA, which mine did not, but not the separation of DNA from protein, which mine did. It was immediately obvious to me that the ideal method for measuring nucleic acids would combine the best features of the two methods. I hurried to the laboratory to work out the details and the results were published[17] the following year in the same journal.[18]

The Schneider paper received over 3,300 citations from 1945 to 1988, averaged 76 citations per year, peaked at 127 in 1964, and was cited 20 times in 1988. The Schmidt and Thannhauser paper has more than 3,700 cites, averaged 84 citations per year, peaked at 140 citations in 1973, and received about 50 cites in 1988.

It is also curious that the "ideal method" Schneider published the following year[17] has received only 30 cites to date. In a recent *Citation Classic* commentary,[19] Masatoshi Nei, Center for Demographic and Population Genetics, University of Texas Health Science Center, Houston, described a citation phenomenon that may apply to Schneider's case.

Nei discussed his 1978 *Genetics* paper,[20] which received over 490 citations, and contrasted it with another paper he published in the *American Naturalist* in 1972,[21] cited over 1,300 times and the subject of a separate *Citation Classic* commentary.[22] Nei noted:

> When I published [the *Genetics*] paper, I thought that future researchers would cite it more often than my 1972 paper. This prediction proved to be wrong. Although this paper has been cited reasonably well, researchers have cited the 1972 paper more often. It seems that they want to cite the first original paper, even if they are actually using a method given in a later paper.[19]

Perhaps the same phenomenon is working with Schneider's 1945 and 1946 papers. Researchers may prefer to cite the "first original" paper even when a later paper represents a significant refinement. However, Sanger came to the *opposite* conclusion about two papers in a similar situation in his *Citation Classic* commentary, quoted earlier in this essay.[7] Even though he considered it the more important paper, Sanger's "first original" paper was cited much less frequently than a subsequent publication. The later paper was cited more often, Sanger suggested, because it described the actual method.

The Next Member of the *SCI* Top 100?

Earlier I mentioned several papers by Messing, Vieira, and colleagues[9-12] whose annual citation rates may propel them into a future list of the *SCI* Top 100. But there is another paper with a phenomenal annual citation record that will probably make it to such a list first.

A 1984 *Nature* paper by Yasutomi Nishizuka, Kobe University School of Medicine, and Department of Cell Biology, National Institute for Basic Biology, Okazaki, Japan, on "The role of protein kinase C in cell surface signal transduction and tumour promotion,"[23] received slightly more than 3,100 citations through 1988, just 100 citations less than the threshold for inclusion in the *SCI* Top 100, 1945-1988. It averaged over 600 citations per year and was cited over 800 times in 1988. If its current citation trend continues, the paper may receive over 900 citations in 1989. Thus, by the time this essay is published, Nishizuka's paper may well qualify for the top 100 papers of 1945-1989.

The Second 100 All-Time *Citation Classics*

In Part 2 of this series, we'll present a list of the second 100 papers in the 1945-1988 *SCI* all-time *Citation Classics* list. They include seven physics and astrophysics papers and two more papers published in the 1920s. Several papers will be highlighted and discussed by the authors themselves from their *Citation Classic* commentaries.

The essay will also present citation data on the second 100 papers—total, average annual, peak, and 1988 citations. These data will also be cumulated for the *SCI* Top 200. We'll continue to identify papers whose annual citation profiles quantitatively indicate a premature discovery. We'll also discuss other distinct and quantitatively defined citation patterns that emerge. For example, certain papers may be considered "perennials" because they achieve medium-to-high citation rates that remain fairly stable over 20 or more years. Other papers may be labelled "shooting stars," achieving spectacular citation levels early but then fading quickly. Then there are papers that may be called "rockets" because they start out with a bang and keep rising rapidly. As the series continues and more data are cumulated, we may find "signature" citation patterns for

high-impact papers from different research specialties.

CC readers are invited to send us comments on the lists published in this series. You may also request a preview list of the next group of 100 papers to be featured. Simply address your letters to All-Time Citation Classics, Editorial Services, ISI, 3501 Market Street, Philadelphia, Pennsylvania 19104.

* * * * *

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