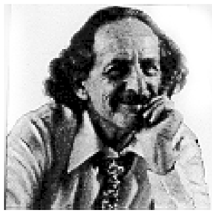
Essays of an Information Scientist, Vol:7, p.326-335, 1984
Current Contents, #42, p.3-12, October 15, 1984



Current Comments®

The Articles Most Cited in 1961-1982. 5. Another 100 *Citation Classics* and a Summary of the 500 Papers Identified to Date

Number 42 October 15, 1984

Over the past few months, we've published a series of essays on the articles most cited from 1961 to 1982 in *Science Citation Index*® (*SCI*®). So far, we've listed the top 400 papers that were cited at least 1,032 times in this 22-year period.[1-4] In this essay, we'll present another 100 *Citation Classics*™. We'll also discuss the distributions by journal, year of publication, and field for all 500 papers identified to date.

It is interesting to note that these lists of high-impact articles are by no means permanent. Science is a dynamic enterprise with a considerable turnover of highly cited research. For example, 10 years ago, we identified the 100 most-cited articles in the 1961-1972 *SCI*.[5] Of these, 55 were still among the 100 most-cited articles for 1961-1982.[1] Another 28 of these "old" classics reappeared in the second through fourth parts of this series.[2-4] However, none of the papers in that 1974 study appear in this essay. Perhaps the remaining 17 papers identified in the 1974 study will resurface when we extend the list to include the top 1,000 papers for 1961-1982.

Table 1 presents bibliographic information on the 100 classics in this study. The papers are arranged in alphabetic order by first author. The number of 1961-1982 citations is shown for each paper. Citations for 1983 are shown in parentheses to give you an idea of how frequently each paper is currently cited. Each of the papers was cited at least 936 times.

Thirty-nine papers have already been featured in *Current Contents*® (*CC*®) as *Citation Classics*. They are indicated by asterisks. After the reference are shown the issue, year, and edition of *CC* in which the author's commentary appeared. We encourage all of the authors listed in Table 1 to submit commentaries on their papers if they have not done so already.

The 100 classics were published in 53 journals. Just six journals account for one-third of these papers: *Biochemical Journal* and *Science* each published six papers. *Biochimica et Biophysica Acta*, *Journal of Biological Chemistry*, *Journal of Chemical Physics*, and *Proceedings of the National Academy of Sciences of the US* each accounted for five papers.

Table 2 lists 25 journals that published at least 5 of the 500 classics we've identified to date. The 500 papers were published in 130 journals, but the top 25 journals account for 69 percent of them; 50 journals account for 83 percent. Table 2 also shows the 1983 impact factor for each journal. Impact is a measure of how frequently a journal's *current* articles are cited. It is calculated by dividing the number of 1983 citations to a journal's 1981 and 1982 articles by the number of articles it published in those

Table 1: The fifth 100 most-cited articles, 1961-1982 *SCI*®, arranged in alphabetic order by first author. A=1961-1982 citations. 1983 citations appear in parentheses. B=bibliographic data. An asterisk (*) indicates that the paper was the subject of a *Citation Classic*™ commentary. The issue, year, and edition of *CC*® in which these commentaries appeared are listed in parentheses. None of these articles appeared in the 1974 list of most-cited articles.

A	B
958 (17)	**Alder K, Bohr A, Huus B, Mottelson B & Winther A.** Study of nuclear structure by electromagnetic excitation with accelerated ions. *Rev. Mod. Phys.* 28:432-542, 1956.
1006 (34)	***Astrup T & Mullertz S.** The fibrin plate method for estimating fibrinolytic activity. *Arch. Biochem. Biophys.* 40:346-51, 1952. (41/84/LS)
973 (23)	**Baltimore D.** Viral RNA-dependent DNA polymerase. *Nature* 226:1209-11, 1970.
958 (70)	**Becchetti F D & Greenlees G W.** Nucleon-nucleus optical-model parameters, $A>40$, $E<50$ MeV. *Phys. Rev.* 182:1190-209, 1969.
994 (35)	**Benacerraf B & McDevitt H O.** Histocompatibility-linked immune response genes. *Science* 175:273-9, 1972.
1000 (7)	**Bogdanski D F, Pletscher A, Brodie B B & Udenfriend S.** Identification and assay of serotonin in brain. *J. Pharmacol. Exp. Ther.* 117:82-8, 1956.
949 (190)	***Bolton A E & Hunter W M.** The labelling of proteins to high specific radioactivities by conjugation to a ^{125}I-containing acylating agent. *Biochem. J.* 133:529-39, 1973. (29/84/LS)
1024 (12)	**Brenner S & Horne R W.** A negative staining method for high resolution electron microscopy of viruses. *Biochim. Biophys. Acta* 34:103-10, 1959.
984 (60)	**Brown B L, Albano J D M, Ekins R P, Sgherzi A M & Tampion W.** A simple and sensitive saturation assay method for the measurement of adenosine 3′:5′-cyclic monophosphate. *Biochem. J.* 121:561-2, 1971.
985 (8)	***Brown J B.** A chemical method for the determination of oestriol, oestrone and oestradiol in human urine. *Biochem. J.* 60:185-93, 1955. (2/83/LS)
950 (9)	**Burn J H & Rand M J.** The action of sympathomimetic amines in animals treated with reserpine. *J. Physiol.—London* 144:314-36, 1958.
989 (3)	**Chamberlin M & Berg P.** Deoxyribonucleic acid-directed synthesis of ribonucleic acid by an enzyme from *Escherichia coli. Proc. Nat. Acad. Sci. US* 48:81-94, 1962.
989 (25)	**Chauveau J, Moule Y & Rouiller C.** Isolation of pure and unaltered liver nuclei: morphology and biochemical composition. *Exp. Cell Res.* 11:317-21, 1956.
1031 (22)	***Chrambach A, Reisfeld R A, Wyckoff M & Zaccari J.** A procedure for rapid and sensitive staining of protein fractionated by polyacrylamide gel electrophoresis. *Anal. Biochem.* 20:150-4, 1967. (40/83/LS)
1004 (77)	***Clegg J B, Naughton M A & Weatherall D J.** Abnormal human haemoglobins. *J. Mol. Biol.* 19:91-108, 1966. (2/82/LS)
980 (4)	***Clewell D B & Helinski D R.** Supercoiled circular DNA-protein complex in *Escherichia coli*: purification and induced conversion to an open circular DNA form. *Proc. Nat. Acad. Sci. US* 62:1159-66, 1969. (8/83/LS)
1014 (156)	***Cohen A S, Reynolds W E, Franklin E C, Kulka J P, Ropes M W, Schulman L E & Wallace S L.** Preliminary criteria for the classification of systemic lupus erythematosus. *Bull. Rheumat. Dis.* 21:643-8, 1971. (11/82/CP)
1002 (45)	***Cole K S & Cole R H.** Dispersion and absorption in dielectrics. I. Alternating current characteristics. *J. Chem. Phys.* 9:341-51, 1941. (3/80/PC&ES)
968 (30)	**Cuatrecasas P, Wilchek M & Anfinsen C B.** Selective enzyme purification by affinity chromatography. *Proc. Nat. Acad. Sci. US* 61:636-43, 1968.
943 (14)	**Dalton A J.** A chrome-osimium fixative for electron microscopy. (Abstract.) *Anat. Rec.* 121:281, 1955.
962 (43)	***Dexter D L.** A theory of sensitized luminescence in solids. *J. Chem. Phys.* 21:836-50, 1953. (38/77)
936 (107)	**Dunnett C W.** A multiple comparison procedure for comparing several treatments with a control. *J. Amer. Statist. Assn.* 50:1096-121, 1955.
1000 (33)	**Elson L A & Morgan W T J.** A colorimetric method for the determination of glucosamine and chondrosamine. *Biochem. J.* 27:1824-8, 1933.
1005 (74)	***Erlanger B F, Kokowsky N & Cohen W.** The preparation and properties of two new chromogenic substrates of trypsin. *Arch. Biochem. Biophys.* 95:271-8, 1961. (4/81/LS)
956 (52)	**Feshbach H.** A unified theory of nuclear reactions. II. *Ann. Phys.—NY* 19:287-313, 1962.
946 (30)	**Feynman R P.** Very high-energy collisions of hadrons. *Phys. Rev. Lett.* 23:1415-7, 1969.
973 (8)	**Feynman R P & Gell-Mann M.** Theory of the Fermi interaction. *Phys. Rev.* 109:193-8, 1958.
965 (26)	***Fisher M E.** The theory of equilibrium critical phenomena. *Rep. Progr. Phys.* 30:615-730, 1967. (46/80/PC&ES)

A	B
948 (40)	**Fleck A & Munro H N.** The precision of ultraviolet absorption measurements in the Schmidt-Thannhauser procedure for nucleic acid estimation. *Biochim. Biophys. Acta* 55:571-83, 1962.
1019 (23)	**Folin O & Ciocalteu V.** On tyrosine and tryptophane determinations in proteins. *J. Biol. Chem.* 73:627-50, 1927.
964 (21)	•**Fredrickson D S, Levy R I & Lees R S.** Fat transport in lipoproteins—an integrated approach to mechanisms and disorders. *N. Engl. J. Med.* 276:34-44, 1967. (3/78)
979 (36)	**Garen A & Levinthal C.** A fine-structure genetic and chemical study of the enzyme alkaline phosphatase of *E. coli*. I. Purification and characterization of alkaline phosphatase. *Biochim. Biophys. Acta* 38:470-83, 1960.
983 (41)	**Gold P & Freedman S O.** Demonstration of tumor-specific antigens in human colonic carcinomata by immunological tolerance and absorption techniques. *J. Exp. Med.* 121:439-62, 1965.
1005 (42)	•**Gold P & Freedman S O.** Specific carcinoembryonic antigens of the human digestive system. *J. Exp. Med.* 122:467-81, 1965. (48/80/CP)
1002 (41)	•**Good N E, Winget G D, Winter W, Connolly T N, Izawa S & Singh R M M.** Hydrogen ion buffers for biological research. *Biochemistry—USA* 5:467-77, 1966. (40/83/LS)
943 (60)	•**Greenfield N & Fasman G D.** Computed circular dichroism spectra for the evaluation of protein conformation. *Biochemistry—USA* 8:4108-16, 1969. (26/82/LS)
990 (24)	**Hager R S & Seltzer E C.** Internal conversion tables. Part I: *K*-, *L*-, *M*-shell conversion coefficients for $Z=30$ to $Z=103$. *Nucl. Data Sect. A* 4:1-235, 1968.
1020 (131)	•**Hamilton M.** A rating scale for depression. *J. Neurol. Neurosurg. Psychiat.* 23:56-62, 1960. (33/81/CP)
979 (124)	**Helenius A & Simons K.** Solubilization of membranes by detergents. *Biochim. Biophys. Acta* 415:29-79, 1975.
977 (29)	**Hinze J & Jaffe H H.** Electronegativity. I. Orbital electronegativity of neutral atoms. *J. Amer. Chem. Soc.* 84:540-6, 1962.
1029 (50)	•**Hubbard J.** Electron correlations in narrow energy bands. *Proc. Roy. Soc. London Ser. A* 276:238-57, 1963. (22/80/PC&ES)
962 (67)	**Hummel B C W.** A modified spectrophotometric determination of chymotrypsin, trypsin, and thrombin. *Can. J. Biochem. Physiol.* 37:1393-9, 1959.
993 (41)	•**Johns E W.** Studies on histones. 7. Preparative methods for histone fractions from calf thymus. *Biochem. J.* 92:55-9, 1964. (11/79/LS)
975 (29)	•**Johnson C E & Bovey F A.** Calculation of nuclear magnetic resonance spectra of aromatic hydrocarbons. *J. Chem. Phys.* 29:1012-4, 1958. (23/79/PC&ES)
1007 (78)	**Johnson H L.** Astronomical measurements in the infrared. *Annu. Rev. Astron. Astrophys.* 4:193-206, 1966.
961 (28)	•**Kalckar H M.** Differential spectrophotometry of purine compounds by means of specific enzymes. III. Studies of the enzymes of purine metabolism. *J. Biol. Chem.* 167:461-75, 1947. (26/84/LS)
1029 (64)	**Kane E O.** Band structure of indium antimonide. *J. Phys. Chem. Solids* 1:249-61, 1957.
967 (17)	•**Kay E R M, Simmons N S & Dounce A L.** An improved preparation of sodium desoxyribonucleate. *J. Amer. Chem. Soc.* 74:1724-6, 1952. (24/80/LS)
996 (18)	**King E J.** The colorimetric determination of phosphorus. *Biochem. J.* 26:292-7, 1932.
949 (44)	**Kluver H & Barrera E.** A method for the combined staining of cells and fibers in the nervous system. *J. Neuropathol. Exp. Neurol.* 12:400-10, 1953.
967 (28)	**Koshland D E, Nemethy G & Filmer D.** Comparison of experimental binding data and theoretical models in proteins containing subunits. *Biochemistry—USA* 5:365-85, 1966.
972 (31)	**Kubo R & Tomita K.** A general theory of magnetic resonance absorption. *J. Phys. Soc. Jpn.* 9:888-919, 1954.
977 (98)	•**Lacy P E & Kostianovsky M.** Method for the isolation of intact islets of Langerhans from the rat pancreas. *Diabetes* 16:35-9, 1967. (8/81/LS)
975 (35)	**Lamb W E.** Theory of an optical maser. *Phys. Rev. A* 134:1429-50, 1964.
1021 (31)	**Lane A M & Thomas R G.** R-matrix theory of nuclear reactions. *Rev. Mod. Phys.* 30:257-353, 1958.
942 (12)	•**Lipmann F & Tuttle L C.** A specific micromethod for the determination of acyl phosphates. *J. Biol. Chem.* 159:21-8, 1945. (46/80/LS)
969 (37)	**Lyon M F.** Gene action in the *X*-chromosome of the mouse (*Mus musculus* L.). *Nature* 190:372-3, 1961.
966 (24)	**McDaniel D H & Brown H C.** An extended table of Hammett substituent constants based on the ionization of substituted benzoic acids. *J. Org. Chem.* 23:420-7, 1958.
964 (63)	•**Melzack R & Wall P D.** Pain mechanisms: a new theory. *Science* 150:971-9, 1965. (23/82/LS)

A | B

956 (33) *Metcalfe L D & Schmitz A A. The rapid preparation of fatty acid esters for gas chromatographic analysis. *Anal. Chem.* 33:363-4, 1961. (2/81/LS)

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1028 (11) Monod J, Changeux J-P & Jacob F. Allosteric proteins and cellular control systems. *J. Mol. Biol.* 6:306-29, 1963.

985 (156) Moretta L, Webb S R, Grossi C E, Lydyard P M & Cooper M D. Functional analysis of two human T-cell subpopulations: help and suppression of B-cell responses by T cells bearing receptors for IgM or IgG. *J. Exp. Med.* 146:184-200, 1977.

1009 (13) Morgan J F, Morton H J & Parker R C. Nutrition of animal cells in tissue culture. I. Initial studies on a synthetic medium. *Proc. Soc. Exp. Biol. Med.* 73:1-8, 1950.

951 (19) *Moruzzi G & Magoun H W. Brain stem reticular formation and activation of the EEG. *Electroencephalogr. Clin. Neuro.* 1:455-73, 1949. (40/81/LS)

999 (129) Palade G. Intracellular aspects of the process of protein synthesis. *Science* 189:347-58, 1975.

981 (1) Pedersen C J. Cyclic polyethers and their complexes with metal salts. *J. Amer. Chem. Soc.* 89:7017-36, 1967.

1002 (48) Pople J A & Gordon M. Molecular orbital theory of the electronic structure of organic compounds. I. Substituent effects and dipole moments. *J. Amer. Chem. Soc.* 89:4253-61, 1967.

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970 (23) Rasmussen H. Cell communication, calcium ion, and cyclic adenosine monophosphate. *Science* 170:404-12, 1970.

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944 (95) Roberts B E & Paterson B M. Efficient translation of tobacco mosaic virus RNA and rabbit globin 9S RNA in a cell-free system from commercial wheat germ. *Proc. Nat. Acad. Sci. US* 70:2330-4, 1973.

940 (42) Roothaan C C J. Self-consistent field theory for open shells of electronic systems. *Rev. Mod. Phys.* 32:179-85, 1960.

974 (19) *Sanger F, Brownlee G G & Barrell B G. A two-dimensional fractionation procedure for radioactive nucleotides. *J. Mol. Biol.* 13:373-98, 1965. (3/81/LS)

983 (48) *Schenkman J B, Remmer H & Estabrook R W. Spectral studies of drug interaction with hepatic microsomal cytochrome. *Mol. Pharmacol.* 3:113-23, 1967. (9/84/LS)

974 (8) *Scherrer K & Darnell J E. Sedimentation characteristics of rapidly labelled RNA from HeLa cells. *Biochem. Biophys. Res. Commun.* 7:486-90, 1962. (50/80/LS)

985 (19) Schneider W C. Intracellular distribution of enzymes. III. The oxidation of octanoic acid by rat liver fractions. *J. Biol. Chem.* 176:259-66, 1948.

1018 (38) *Sharon N & Lis H. Lectins: cell-agglutinating and sugar-specific proteins. *Science* 177:949-59, 1972. (21/82/LS)

1013 (83) Siegel L M & Monty K J. Determination of molecular weights and frictional ratios of proteins in impure systems by use of gel filtration and density gradient centrifugation. Application to crude preparations of sulfite and hydroxylamine reductases. *Biochim. Biophys. Acta* 112:346-62, 1966.

941 (36) Solomon I. Relaxation processes in a system of two spins. *Phys. Rev.* 99:559-65, 1955.

994 (19) *Spies J R & Chambers D C. Chemical determination of tryptophan in proteins. *Anal. Chem.* 21:1249-66, 1949. (25/77)

937 (50) *Spizizen J. Transformation of biochemically deficient strains of *Bacillus subtilis* by deoxyribonucleate. *Proc. Nat. Acad. Sci. US* 44:1072-8, 1958. (19/84/LS)

1029 (59) *Stanier R Y, Palleroni N J & Doudoroff M. The aerobic pseudomonads: a taxonomic study. *J. Gen. Microbiol.* 43:159-71, 1966. (31/77)

962 (75) Steck T L. The organization of proteins in the human red blood cell membrane. *J. Cell Biol.* 62:1-19, 1974.

948 (10) *Steelman S L & Pohley F M. Assay of the follicle stimulating hormone based on the augmentation with human chorionic gonadotropin. *Endocrinology* 53:604-16, 1953. (21/84/LS)

1003 (10) Sutherland E W & Rall T W. The relation of adenosine-3',5'-phosphate and phosphorylase to the actions of catecholamines and other hormones. *Pharmacol. Rev.* 12:265-99, 1960.

964 (25) Sutherland E W, Robison G A & Butcher R W. Some aspects of the biological role of adenosine 3',5'-monophosphate (cyclic AMP). *Circulation* 37:279-306, 1968.

988 (97) Swank R T & Munkres K D. Molecular weight analysis of oligopeptides by electrophoresis in polyacrylamide gel with sodium dodecyl sulfate. *Anal. Biochem.* 39:462-77, 1971.

A	B
1019 (24)	***Temin H M & Mizutani S.** RNA-dependent DNA polymerase in virions of Rous sarcoma virus. *Nature* 226:1211-3, 1970. (47/77)
984 (88)	***Tilley J M A & Terry R A.** A two-stage technique for the *in vitro* digestion of forage crops. *J. Brit. Grassland Soc.* 18:104-11, 1963. (15/80/AB&ES)
988 (19)	**Tiselius A, Hjerten S & Levin O.** Protein chromatography on calcium phosphate columns. *Arch. Biochem. Biophys.* 65:132-55, 1956.
969 (90)	**Udenfriend S, Stein S, Bohlen P, Dairman W, Leimgruber W & Weigele M.** Fluorescamine: a reagent for assay of amino acids, peptides, proteins, and primary amines in the picomole range. *Science* 178:871-2, 1972.
1019 (57)	**van de Kamer J H, ten Bokkel Huinink H & Weyers H A.** Rapid method for the determination of fat in feces. *J. Biol. Chem.* 177:347-55, 1949.
1026 (72)	**van der Pauw L J.** A method of measuring specific resistivity and Hall effect of discs of arbitrary shape. *Philips Res. Rep.* 13:1-9, 1958.
993 (79)	**Weibel E R.** Stereological principles for morphometry in electron microscopic cytology. *Int. Rev. Cytol.* 26:235-302, 1969.
955 (63)	**Westphal O, Luderitz O & Bister F.** Uber die Extraktion von Bakterien mit Phenol/Wasser. (Extraction of bacteria with phenol/water.) *Z. Naturforsch. Sect. B* 7:148-55, 1952.
1006 (67)	***Winter C A, Risley E A & Nuss G W.** Carrageenin-induced edema in hind paw of the rat as an assay for antiinflammatory drugs. *Proc. Soc. Exp. Biol. Med.* 111:544-7, 1962. (6/83/LS)
1028 (31)	**Wolfsberg M & Helmholz L.** The spectra and electronic structure of the tetrahedral ions MnO_4^-, CrO_4^{--}, and ClO_4^-. *J. Chem. Phys.* 20:837-43, 1952.
964 (72)	**Zacharius R M, Zell T E, Morrison J H & Woodlock J J.** Glycoprotein staining following electrophoresis on acrylamide gels. *Anal. Biochem.* 30:148-52, 1969.
1006 (36)	***Zubarev D N.** Double-time Green functions in statistical physics. *Sov. Phys. Usp.—Engl. Tr.* 3:320-45, 1960. (23/81/PC&ES) (Dvukhvremennue funkstii Greena v statisticheskoi fizike. *Usp. Fiz. Nauk SSSR* 71:71-116, 1960. 918 citations, 1961-1982. 24 citations, 1983.)

Table 2: Journals that published at least 5 of the 500 papers most cited from 1961 to 1982, *SCI*®. A = journal title. B = number of papers. C = 1983 impact factor.

A	B	C
J. Biol. Chem.	60	5.8
Biochem. J.	28	3.2
Nature	22	9.3
J. Chem. Phys.	21	3.0
Phys. Rev.	18	2.8
J. Cell Biol.	17	9.2
J. Amer. Chem. Soc.	16	4.5
J. Mol. Biol.	16	6.7
Proc. Nat. Acad. Sci. US	14	8.7
Science	14	7.4
Anal. Biochem.	11	2.9
Anal. Chem.	11	3.4
Biochim. Biophys. Acta	11	2.4
Arch. Biochem. Biophys.	10	2.4
J. Exp. Med.	10	11.1
Acta Crystallogr.	9	1.1
J. Pharmacol. Exp. Ther.	9	3.5
Biochemistry—USA	8	4.1
Meth. Enzymology	7	1.3
Eur. J. Biochem.	6	3.5
J. Histochem. Cytochem.	6	3.9
Proc. Soc. Exp. Biol. Med.	6	1.4
Rev. Mod. Phys.	6	19.9
Exp. Cell Res.	5	2.9
N. Engl. J. Med.	5	16.5

two years. As you can see, the journals that published many classics in the past continue to produce high-impact work.

It is interesting to note that a Russian journal has appeared for the first time in this series. D.N. Zubarev, Steklov Institute of Mathematics, Academy of Sciences of the USSR, Moscow, published his paper, "Double-time Green functions in statistical physics" in 1960. The English translation appeared in *Soviet Physics Uspekhi* that same year. It was cited about 2,000 times in this 23-year period. About half of these citations were to the Russian version published in *Uspekhi Fizicheskikh Nauk*. However, 390 papers cited both versions. Keep in mind that the editors of some journals require authors to cite *all* versions of translated papers, thereby inflating citation counts through "redundancy."

We can use these journal data to get a rough idea of how the 500 classics are

Table 3: Field distributions for the 500 most-cited articles, 1961-1982 *SCI*®

FIELD	TOTAL	Part 1	Part 2	Part 3	Part 4	Part 5
Life Sciences	384	85	77	80	72	70
Biochemistry	147	38	30	26	26	27
Biomedicine	96	17	13	24	21	21
Clinical Medicine	93	16	26	20	14	17
Molecular Biology	43	12	8	9	10	4
Biology	5	2	—	1	1	1
Physics	59	6	11	7	15	20
Chemistry	49	9	10	10	13	7
Mathematics	4	—	1	2	—	1
Engineering/Technology	3	—	1	1	—	1
Earth/Space Sciences	1	—	—	—	—	1
TOTAL	500	100	100	100	100	100

distributed by field. For example, 70 of the papers in this study were published in life-sciences journals, 20 in physics journals, 7 in chemistry journals, and 1 each in mathematics, engineering/technology, and earth/space-sciences journals. Table 3 shows the field distributions for all 500. As we've pointed out before, life-sciences papers dominate this and other citation-based studies, accounting for 384 papers or 77 percent of the 500 classics. Physics follows with 59 papers (12 percent), and chemistry with 49 papers (10 percent). But as the series was extended from 100 to 500 papers, the proportion of life-sciences papers declined from 85 percent to 70 percent. Physics papers increased their share from 6 percent in part one to 20 percent in this study. The proportion of chemistry classics has remained relatively stable, accounting for 7 to 13 percent of the papers in each part of this series. However, biochemistry has been categorized here as a life science. This decision may be considered arbitrary by some chemists, but it is relevant for readers of *CC/Life Sciences*.

It is more difficult to classify papers in this series as being methodological or theoretical. In fact, Leonard Hayflick, University of Florida, Gainesville, recently informed me[6] that his paper on the serial cultivation of human diploid cell strains[7] was mistakenly identified as a methods paper in the second part of this series.[2] Some papers clearly state in their titles that they are discussing a method, technique, or procedure. But other papers refer to measurement, estimation, preparation, isolation, and other terms that may not necessarily be synonymous with "method." Nevertheless, even if we use a broad definition of methods, the proportion of methods papers is declining as this series is extended. About 70 methods papers appeared in part one, 65 in part two, 60 in part three, 55 in part four, and about 50 in this essay.

Table 4 shows the publication-year distributions for both the 100 papers in this study and all 500 classics identified to date. These distributions have been remarkably stable over all five parts of this series. Sixty-one percent of the 500 classics were published in the 1960s and 1970s. Thirty-eight percent were published from 1930 to 1959. It will be interesting to see if this distribution remains stable after we identify the 1,000 most-cited articles. Keep in mind that the citation data reported in this series cover the 22-year period from 1961 to 1982. Additional citations to papers published in 1961 and earlier may be retrieved from the recently published 1955-1964 *SCI* cumulation.

The oldest paper in this study was published in 1927 in the *Journal of Biological Chemistry*. Otto Folin and Vintila Ciocalteu, Harvard Medical School, Boston, Massachusetts, presented a critical analysis of the methods for determining tyrosine and tryptophan that were first described by Folin and J.M. Looney in 1922 in the same journal.[8] In the 1927 paper, the authors noted, "A number of investigators have found the Folin-Looney methods satisfactory, but others have condemned them on general principles, and some have been utterly unable to get any reasonable figures with them.... In these circumstances it seemed well worthwhile to try to clear up any uncertainties or flaws that may legitimately be ascribed to these methods." Folin and Ciocalteu's efforts were indeed worthwhile—their paper became a "kiloclassic" that was cited more than 1,000 times from 1961 to 1982. In 1983, it was still cited explicitly in 23 publications.

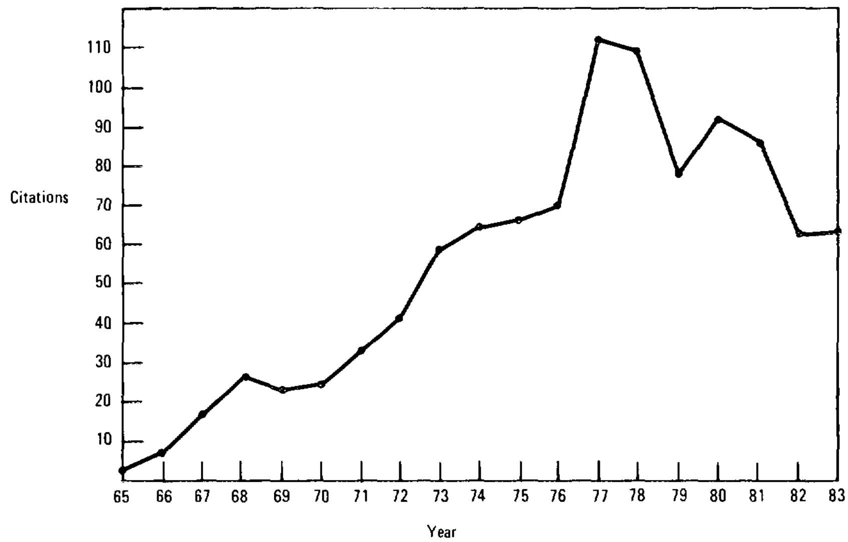
The newest paper, by Lorenzo Moretta and colleagues, University of Alabama, Birmingham, was published in 1977 in the *Journal of Experimental Medicine*. The authors examined and discussed the functions of two types of human T cells. T cells are thymus-dependent leukocytes that play an important role in cell-mediated immunity. The paper was cited for having demonstrated two subpopulations of T cells. Each type of T cell has a specific receptor for either immunoglobulin M (IgM) or IgG, which are distinct antibodies, that is, proteins involved in immune reactions. In addition, the paper was cited for having shown that each type of T cell has a different biological function, to either help or suppress immune reactions. Year-by-year citation data indicate that the explicit citation of this paper has peaked. Though still highly cited, in 1977 it received only 7 citations, 87 in 1978, 186 in 1979, 227 in 1980, 260 in 1981, 218 in 1982, and 156 in 1983.

Table 4: Publication-date distributions for the 100 most-cited papers in this study and all 500 classics identified to date. A = publication date. B = number of papers in this study. C = number of papers from all five parts of this series.

A	B	C
1920s	1	4
1930s	2	14
1940s	7	45
1950s	27	131
1960s	47	227
1970s	16	78
1980s	—	1

Throughout this series, we have commented on various aspects of the classic methodology and theory papers—serendipitous events, initial rejections by journal editors, reasons for citations, and so on. One important aspect that we haven't yet discussed is the resistance of the research community to new theories, particularly when these theories are at odds with established dogma. Ronald Melzack, McGill University, Montreal, Canada, and Patrick D. Wall, University College London, England, elaborated on this point in a *Citation Classic* commentary on their 1965 *Science* paper, "Pain mechanisms: a new theory." They said, "A small number of original thinkers had fought hard to replace the old concept of a specific pain pathway by a more dynamic conception in which pain is determined by many factors in addition to injury—by past experiences, culture, attention, and other activities in the nervous system at the time of injury. This small band of courageous people hammered away at the established, traditional theory. But despite occasional lip service to their ingenuity, the field continued unchanged, holding tenaciously on to Descartes' idea, proposed in 1664, that pain is like a bell-ringing alarm system whose sole purpose is to signal injury to the body."[9]

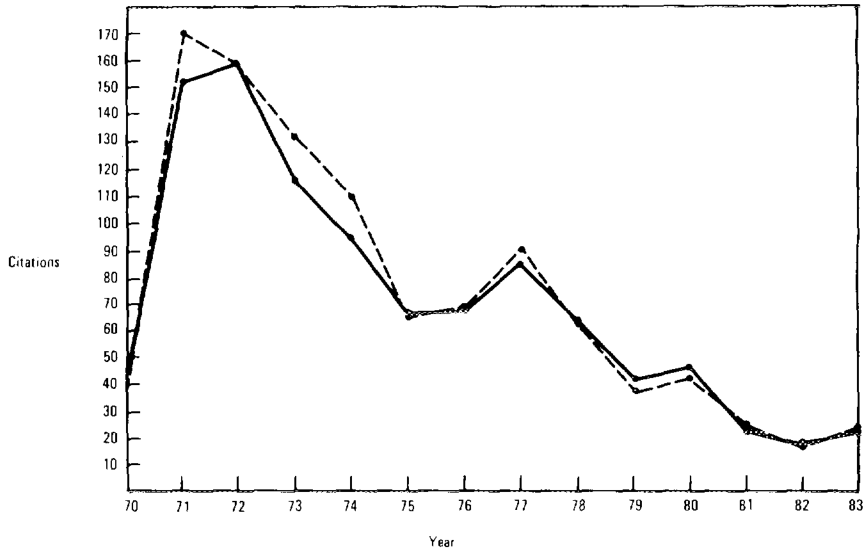
Figure 1: Year-by-year citations to R. Melzack and P.D. Wall, *Science* 150:971-9, 1965.



The citation record for Melzack and Wall's paper illustrates the initial resistance to their new theory of pain mechanisms. Figure 1 provides a graph of the citations to this paper from 1965 to 1983. As you can see, the citations gradually increased from 3 in 1965 to peak at 112 in 1977, after which they trail off to 63 in 1983. The paper was cited 1,027 times in this 19-year period. The authors commented, "When we proposed the gate-control theory in 1965, we hardly expected the astonishing increase in research studies and new therapeutic approaches that were stimulated by it.... Naturally, acceptance was not immediate or total, but in spite of continuing controversy about details, the *concept* that injury signals can be radically modified and even blocked at the earliest stages of transmission in the nervous system is now virtually universally accepted. A fortunate aspect of our publication...is the use of the phrase 'gate-control.' It evokes an image that is readily understood even by those who do not grasp the complex physiological mechanisms on which the theory is based. The fact that the theory had relevance to a wide variety of fields in medicine, psychology, and biology also led to its frequent citation."[9]

In a *Citation Classic* commentary on his 1970 *Nature* paper, Howard M. Temin also noted a general resistance to his hypothesis that the replication of RNA tumor viruses involved information transfer from RNA to DNA via an enzyme.[10] In a companion paper published side-by-side with Temin's paper in *Nature*, David Baltimore, Massachusetts Institute of Technology, Boston, reported the simultaneous identification of the enzyme, now called reverse transcriptase. Temin commented, "Since 1963-1964, I had been proposing that the replication of RNA tumor viruses involved a DNA intermediate. This hypothesis, known as the DNA provirus hypothesis, apparently contradicted the so-called 'central dogma' of molecular biology and met with a generally hostile reception. The hypothesis was not generally accepted until the publication of

Figure 2: Year-by-year citations to H.M. Temin and S. Mizutani, *Nature* 226:1211-3, 1970 (broken line) and D. Baltimore, *Nature* 226:1209-11, 1970 (solid line).



this and the accompanying paper by David Baltimore. These papers demonstrated the existence of an enzyme associated with an RNA template in particles of RNA tumor viruses that could carry out information transfer from RNA to DNA. This result might have been predicted from the previous discovery of polymerases in virus particles and the DNA provirus hypothesis. That the discovery took so many years might indicate the resistance to this hypothesis."[10]

Temin's paper was cited 1,043 times from 1970 to 1983. Baltimore's paper received 996 citations in that 14-year period. Both papers have an almost identical "track record," which can be seen by the graph of their 1970-1983 citations in Figure 2. This should not be surprising, given the nearly identical content of these "companion" papers. In 1970, Temin's paper was cited 40 times and peaked the following year at 170 citations, after which the citations began to decline. Baltimore's paper received 41 citations in 1970, peaked in 1972 with 159 citations, and nearly paralleled the decline in citations observed for Temin's paper. Both papers reached a second peak in citations in 1977. Perhaps this burst of citations is due to Temin and Baltimore having shared the 1975 Nobel prize for physiology or medicine with Renato Dulbecco.

It should come as no surprise that the papers by Temin and Baltimore are highly *co*-cited, when you consider their nearly identical citation records. In fact, these two papers make up the "core" of several current research fronts identified through ISI®'s clustering techniques. For example, they were the core papers in the 1982 research front entitled "Structural Organization and Cellular Origin of Transforming Genes for RNA Tumor Viruses," the 1981 specialty entitled "Alpha-2 Macroglobulin Protease Interactions," and the 1980 research front entitled "DNA and RNA Tumor Viruses."

In addition to Temin and Baltimore, 16 other Nobel laureates are included among the authors listed in Table 1: K.

Alder, C.B. Anfinsen, B. Benacerraf, P. Berg, A. Bohr, H.C. Brown, R.P. Feynman, M. Gell-Mann, F. Jacob, W.E. Lamb, F. Lipmann, J. Monod, B. Mottelson, G. Palade, F. Sanger, and A. Tiselius. In an upcoming essay, we'll report data on the number of classics that the Nobel laureates have authored.

This concludes our essay on the fifth 100 most-cited articles for 1961 to 1982. I'd like again to invite the authors listed in Table 1 who have not yet contributed *Citation Classic* commentaries to do so. These brief comments provide a wealth of insights into high-impact research that students, administrators, and colleagues alike find interesting. In future essays, we'll continue to report on additional groups of 100 most-cited papers until we've covered the top 1,000 at least.

* * * * *

My thanks to Thomas Atkins and Alfred Welljams-Dorof for their help in the preparation of this essay.

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