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Science Communication 1995 16: 304 DOI: 10.1177/1075547095016003004

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>> Version of Record - Mar 1, 1995
What is This?

This article describes examples of influential and/or highly cited papers that were initially rejected by one or more scientific journals. The work reported in eight of the papers eventually earned Nobel prizes for their authors; six papers later became the most cited of the journals in which they were published. Also described are influential and highly cited scientific books whose authors encountered problems in publishing them. These case studies suggest that, although rejection may subsequently result in an improved manuscript, on other occasions referees may simply have failed to appreciate a paper's importance. Many of these rejected papers also reported unexpected findings or discoveries that challenged conventional models or interpretations.

Commentary

On Influential Books and Journal Articles
Initially Rejected Because of Negative Referees' Evaluations

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Scientific journals are both the means by which the scientific community certifies additions to its body of accepted knowledge and the means by which scientists compete for prestige and recognition (Hagstrom 1965; Hargens 1988; Merton 1957). They also can be a source of resistance to new ideas and discoveries. Most scientific journals have editorial boards, editors, and external referees or reviewers which filter and select manuscripts for publi-

Author's Note: I would like to thank Carol Fox Warren, Instituto de Ciencias de la Educación, Universidad de Alcalá; Eugene Garfield, publisher of *The Scientist* and founder of the Institute for Scientific Information; and two anonymous *Science Communication* referees for their helpful comments. I also would like to thank David P. Horrobin, editor of *Medical Hypothesis*, and Magoroh Maruyama, from Aoyama Gakuin University, for encouragement and support. The Institute for Scientific Information (ISI®) has given permission for use of data cited in this article; however, ISI® should not be held responsible for the data's accuracy, use, or interpretations in this article. Address correspondence to Professor Juan Miguel Campanario, Departamento de Física, Universidad de Alcalá, 28871 Alcalá de Henares, Madrid, España; telephone: 34-1-885-4926; fax 34-1-885-4942; Internet: fscampanario@alcala.es.

Science Communication, Vol. 16 No. 3, March 1995 304-325 © 1995 Sage Publications, Inc.

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cation. These "gatekeepers of science" form the peer review system and play an important role in the process of communication in science. (In this article, the term "peer review" will refer to the pre-publication refereeing system, rather than to proposal or project review or to the review that papers receive at meetings.)

There is a vast literature full of criticism of the peer review system (see, for example, Biggs 1990; Crandall 1982; Garfield 1986a; Meadows 1977; Peters and Ceci 1982; Rodman 1970; Singer 1989; Travis and Collins 1991).¹ Study of the agreement between referees' assessments of papers has shown generally low levels of consensus within the system (Cicchetti 1991). Rustum Roy, a materials scientist at Pennsylvania State University, argues that peer review in general is a terrible process: It is "'too slow and too leaky'" and it " 'allows peer reviewers to gain research advantages unfairly' " (Amato 1992). Referees' misconduct also has been discussed by journalists (Broad 1981; Maddox 1992). Redner (1987) went so far as to observe that "one of the roles of journals almost appears to be to shift out and reject really original contributions," and medical editor David Horrobin (1974) has asserted that "there is objective evidence that some referees, and even some highly respected ones in top academic positions, are at best ignorant and careless and at worst deliberately obstructive." Finally, Magoroh Maruyama (1992) has worried that "the present tendency for conceptual inbreeding among academics is not only counterproductive and counterrevolutionary, but also contrary to human rights."

Some analysts have looked at specific examples of referees' mistakes. Horrobin (1990) has presented a set of cases of important, highly cited, or innovative papers rejected by editors because of negative evaluations by referees. Other cases have been mentioned by Astin (1991), Barber (1961), and McCutchon (1991).

Using data compiled by the Institute for Scientific Information (ISI®, I have analyzed instances of important or highly cited papers whose authors encountered difficulties in publishing them in scientific journals. The work reported in seven of these papers eventually earned a Nobel prize. I also have analyzed some instances of scientists who encountered problems in publishing their books.

The reasons for negative evaluation of a manuscript—even one that is later highly cited or very influential—can be diverse. Sometimes referees simply may fail to appreciate a paper's importance. Sometimes the referees' and editor's negative comments may force authors to revise their papers in ways that substantially strengthen and therefore improve them. Thus it is interest-

ing to collect and to analyze instances of important papers and books that were rejected because of negative referees' evaluations and to ascertain the influence of referees on the process of publication of these papers.

Most of my examples have been collected from commentaries written by authors of highly cited papers taken from the Citation Classics® feature of Current Contents; a few cases also have been drawn from other sources. A Citation Classics® article is a paper or book which stands out because of the large number of citations it has received after publication. The selection criteria for nominating a paper or book to be a "citation classic" are diverse (Garfield 1984a; Garfield 1989b). Once an author consents to write a commentary for Current Contents, then the paper or book becomes a Citation Classics®. In the essay, the author explains the work, the details that prompted the research, the contributions of co-authors, and any obstacles encountered during both research and publication, that is, what Garfield (1981a) calls "the human side of science." By the end of 1993, close to 5,000 such commentaries had been published in Current Contents (Garfield 1993). This interesting database has been used in some studies on the sociology of science (Astin 1991; Cano and Lind 1991; Chubin, Porter, and Rossini 1984; Garfield 1989c; Garfield 1990a; Schulz-DuBois 1984), but it deserves more attention from sociologists and historians of science.

Citation data on articles, books, and journals are computed by the Institute for Scientific Information and can be obtained from the Science Citation Index (SCI) and the Social Sciences Citation Index (SSCI). Although a typical paper is cited an average of 15 times, the distribution of citations is quite skewed; a few papers are highly cited and many articles are rarely cited (Seglen 1992). Thus 55 percent of the articles published in 1981 had yet to be cited five years after their publication. Only 2 percent of the more than 32 million papers which were cited at least once between 1945 and 1988 were cited more than fifty times (Garfield 1990b; D. Hamilton 1990). These data highlight the transcendence of the papers and books described below.

Table 1 gives the bibliographic data on the papers described in the text; Table 2 gives the bibliographic data for books that encountered problems in getting into print. For Citation Classics® papers or books, citation data are provided as of the time the author's commentary was published. Citations to these papers or books are higher than average the norm. Next, the papers and books are analyzed in more detail using data obtained from the ISI® prologue to each Citation Classics® commentary and from the commentary itself.

TABLE 1 Total Number of Citations Received (at the Time the "Citation Classics®" Commentary Was Published) for Papers Identified as Having Had Problems in Being Published

Number of		
Citations	Bibliographic Data	
680	Albersheim, P., D. J. Nevins, P. D. English, and A. Karr. 1967. A method for the analysis of sugars in plant cell-wall polysaccharides by gas-liquid chromatography. Carbohydrates Research 5:340-345. [50/1979/PC&ES]	
810	Arright, F. E., and T. C. Hsu. 1971. Localization of heterochromatin in humans chromosomes. <i>Cytogenetics</i> 10:81-86. [7/1983/LS]	
210 ^a	Barten, A. P. 1969. Maximum likelihood estimation of a complete system of demand equations <i>European Economic Review</i> 1:7-73. [40/1992/S&BS]	
b	Belusov, B. P. 1959. In Sbornik referatov po radiatsonni meditsine 1958. Moscow, CCCP: Medgiz. p. 149.	
b	Bednorz, J. G., and K. A. Müller. 1986. Possible high Tc superconductivity in the Ba-La-Cu-O system. Zeitschrift für Physik-B-Condensated Matter 64:189-193.	
	Bessman, M. J., I. R. Lehman, E. S. Simms, and A. Kornberg. 1958. Enzymatic synthesis of DNA: II General properties of the reaction. <i>Journal of Biological Chemistry</i> , 233:171-177.	
b	Binning, G., H. Rohrer, C. Gerber, and E. Weibel. 1982. Surface studies by scanning tunneling microscopy. <i>Physics Review Letters</i> 49:57-61.	
b	Burbidge, E. M., G. R. Burbidge, W. A. Fowler, and F. Hoyle. Synthesis of the elements in stars. <i>Review of Modern Physics</i> 29:547-650.	
100 ^b	Cherenkov, P. A. 1934. Visible light from clear liquids under the action of gamma radiation. (C. R. Doklady) Academy of Sciences of the URSS 2:451-454. [34/1991/PC&ES]	
	Cohn, M., and T. R. Hughes. 1962. Nuclear resonance spectra of adenosine di and triphosphate. <i>Journal of Biological Chemistry</i> 237:176-181.	
265	Cram, D. J., and F.A.A. Elhafez. 1952. Studies in stereochemistry. 10. The rule of "steric control of asymmetric induction" in the synthesis of acyclic systems. <i>Journal of the American Chemical Society</i> 74:5825-5835. [13/1978]	
	Davis, B. D. 1948. Isolation of biochemically deficient mutants of bacteria by penicillin. <i>Journal of the American Chemical Society</i> 70:4267.	
	Davis, B. D. 1985. Sleep and the maintenance of memory. <i>Perspectives in Biology and Medicine</i> 28:457-464.	
435	Englman, R., and J. Jortner. 1970. The energy gap law for radiationless transition in large molecules. <i>Molecular Physics</i> 18:145-164. [31/1988/PC&ES]	
	Eyring, H. 1935. The activated complex in chemical reactions. <i>Journal of Chemical Physics</i> 3:107-115.	
555	Ford, K. W., and J. A. Wheeler. 1959. Semiclassical description of scattering. Annals of Physics 7:259-286. [40/1993/PC&ES]	

Continued

TABLE 1 Continued

Number of	
Citations	Bibliographic Data
550	Foreman, J. C., J. L. Mongar, and B. D. Gomperts. 1973. Calcium ionophores and movement of calcium ions following the physiological stimulus to a secretory process. <i>Nature</i> 245:249-251. [20/1987/LS]
240	Gold, T. 1968. Rotating neutron stars as the origin of the pulsating radio sources. Nature 218:731-732. [8/1993/PC&ES]
4410 ^a	Gorman, C. M., L. F. Moffat, and B. H. Howard. 1982. Recombinant genomes which express chloramphenicol acetyltransferase in mammalian cells. <i>Molecular and Cellular Biology</i> 2:1044-1051. [22/1993/LS]
380	Gruber, K. A., J. M. Whitaker, and V. M. Buchalew. 1980. Endogenous digitalis-like substance in plasma of volume-expanded dogs. <i>Nature</i> 287:743-745. [2/1993/LS]
140 ^a	Hamilton, W. D. 1963. The evolution of altruistic behavior. <i>American Naturalist</i> 7: 345-346. [40/1988/LS]
	Heildelberger, M., A. C. Aisenberg, and W. Z. Hassid. 1954. Glycogen as immunologically specific polysaccharide. <i>Journal of Experimental Medicine</i> 99: 343-353.
2325	Holmes, D. S., and M. Quigley. 1981. A rapid method for the preparation of plasmids. <i>Analytical Biochemistry</i> 114:193-197. [36/1993/LS]
610	Hurlbert, S. H. 1984. Pseudoreplication and the design of ecological field experiments. <i>Ecological Monographs</i> 54:187-211. [12/1993/AB&ES]
600	Jacobowitz, D. M., and M. Palkovits. 1974. Topographic atlas of catecholamine and acetylcholinesterase-containing neurons in the rat brain. I. (Forebrain telencephalon, diencephalon). <i>Journal of Computational Neurology</i> 157:13-28. [34/1993/LS]
870	Jacobowitz, D. M., and M. Palkovits. 1974. Topographic atlas of catecholamine and acetylcholinesterase-containing neurons in the rat brain. II. (Hindbrain mesencephalon, rhombencephalon). <i>Journal of Computational Neurology</i> 157: 29-42. [34/1993/LS]
255 ^a	Kováts, E. S. 1965. Gas chromatographic characterization of organic substances in the retention index system. <i>Advances in Chromatography</i> 1:229-247. [16/1988/PC&ES]
1570	Kozak, M. 1986. Point mutations define a sequence flanking the AUG initiator codon that modulates translation by eukaryotic ribosimes. <i>Cell</i> 44:283-292.
1060	Kozak, M. 1987. An analysis of 5' encoding sequences from 699 vertebrate mRNAs <i>Nucleic Acids Research</i> 18:8125-8148. Lederberg, J., and N. Zinder. 1948. Concentration of biochemical mutants of
b	bacteria with penicillin. <i>Journal of the American Chemical Society</i> 70:4267-4268. Lehman, I. R., M. J. Bessman, E. S. Simms, and A. Kornberg. 1958. Enzymatic synthesis of DNA I: Preparation of substrates and partial purification of an enzyme
450	from E. coli. <i>Journal of Biological Chemistry</i> . 233:163-170. Lindell, T. J., F. Weinberg, P. W. Morris, R. G. Roeder, and W. J. Rutter. 1970. Specific inhibition of nuclear RNA polymerase II by a-amanitin. <i>Science</i> 170: 447-449. [29/1984/LS]
	Maiman, T. H. 1960. Stimulated optical radiation in rubi. Nature 187:493-495.

Continued

TABLE 1 Continued

Number of Citations	Bibliographic Data
	21011081.441.110.2.411
230	Maruyama, M. 1963. The second cybernetics: Deviation-amplifying mutual causal processes. <i>American Scientist</i> 51:164-179. [8/1988/S&BS]
490	Mayer, D. J., T. L. Wolfle, H. Akil, B. Carder, and J. C. Liebeskind. 1971. Analgesia from electrical stimulation in the brain stem of the rat. <i>Science</i> 174:1351-1354. [14/1993/LS]
425 ^a	Nelson, C. R., and C. I. Plosser. 1982. Trends and random walks in
	macroeconomic time series: Some evidence and implications. <i>Journal of Monetary Economy</i> 10:139-162. [28/1993/S&BS]
175	Neu, C. W., C. R. Byers, and J. M. Peek. 1974. A technique for analysis of
	utilization-availability data. Journal of Wildlife Management 38:541-545. [22/1992/AB&ES]
205	Olson, D. R. 1977. From utterance to text: The bias of language in speech and
	writing. Harvard Educational Review 47:257-281. [49/1988/S&BS]
165	Perlman, R., and I. Pastan. 1968. Cyclic 3',5'-AMP: Stimulation of galactosidase
	and tryptophanase induction in E. coli. Biochemical and Biophysical Research Communications 30:656-664.
175	Perlman, R., and I. Pastan. 1968. Regulation of galactosidase synthesis in
	Escherichia coli by byclic adenosine 3',5'-monophosphate. Journal of Biological Chemistry. 243:5420-5427.
150	Phillis, J. W., and G. K. Kostopoulos. 1975. Adenosine as a putative transmitter in
	the cerebral cortex. Studies with potentiators and antagonists. <i>Life Sciences</i> 17: 1085-1094. [36/1993/LS].
250	Porsolt, R. D., M. Le Pichon, and M. Jalfre. 1977. Depression: A new animal model sensitive to antidepressant treatments. <i>Nature</i> 266:730-732. [36/1993/LS]
590	Pulay, P. 1969. Ab initio calculation of force constants and equilibrium geometries in polyatomic molecules. I. Theory. <i>Molecular Physics</i> 17:197-204. [18/1988/PC&ES]
	Snell, E. E., and F. M. Strong. 1939. Microbiological assay for riboflavin.
ь	Industrial and Engineering Chemistry, Analytical Edition 11:346-350.
	Stark, B. C., R. Kole, E. J. Bowman, and S. Altman. 1978. Ribonuclease P: An enzyme with an essential RNA component. <i>Proceedings of the National Academy</i>
300 ^b	of Sciences—USA 75:3717-3721. Taube, H. 1952. Rates and mechanisms of substitution in inorganic complexes in
	solution. Chemical Reviews 50:69-126. [51/1988/PC&ES]
165 ^a	Wiley, R. H., and D. G. Richards. 1978. Physical constraints on acoustic communication in the atmosphere: Implications for the evolution of animal vocalizations. <i>Behavioral Ecology and Sociobiology</i> 3:69-94. [48/1992/LS]

NOTE: Following the bibliographic data for each article is the issue, year, and edition of the *Current Contents* in which the commentary was published. Editions: LS = Life Sciences; S&BS = Social and Behavioral Sciences; PC&ES = Physical, Chemical and Earth Sciences; AB&ES = Agriculture, Biology and Environmental Sciences. Reprinted with permission from ISI®. Copyright 1993, ISI®.

a. This paper has been identified by ISI® as the most cited paper from its journal.

b. One or more authors earned the Nobel prize for the work in which the paper was based.

TABLE 2
Total Number of Citations Received (at the Time the "Citation Classics®" Commentary Was Published) for Academic Books Identified as Having Had Problems in Being Published

Author and Title
Lineberry, R. L. 1977. Equality and urban policy: The distribution of municipal
public services. Beverly Hills, CA: Sage. [29/1988/S&BS]
Maddala, G. S. 1983. Limited dependent and qualitative variables in econometrics. Cambridge, England: Cambridge University Press. (30/1993/S&BS]
Williamson, O. E. 1975. Markets and hierarchies: Analysis and antitrust implications. New York: Free Press. [10/1988/S&BS]
Pianka, E. R. 1974. Evolutionary ecology. New York: Harper & Row. [25/1988/LS]

NOTE: Data include the number of citations received and, in brackets, the issue, year, and edition of *Current Contents* in which the commentary was published. LS = Life Sciences; S&BS = Social and Behavioral Sciences; PC&ES = Physical, Chemical and Earth Sciences; and AB&ES = Agriculture, Biology and Environmental Sciences. Reprinted with permission from ISI®. Copyright 1993, ISI®.

Initial Rejection, Later Citation

In some instances, papers whose authors encounter problems in getting them accepted eventually become the most-cited papers of the journals that finally published them. An important paper displaced to a secondary journal because it had been rejected by a primary journal may well become a heavily cited paper for the secondary journal. However, in some of the instances studied, the journal that finally published the paper was not a secondary one. For example:

- In 1988, ISI® declared the paper by E. S. Kováts on gas chromatographic characterization of organic substances as the most-cited paper published to date by Advances in Chromatography. This paper originally was presented by invitation at the Fourth International Chromatography Symposium in Houston, Texas. Although it had been planned that the lectures presented would be published in Analytical Chemistry, the paper by Kováts was rejected. However, Roy Keller, editor of Advances in Chromatography, rescued the paper and it was published in that journal in 1965.
- In the 1970s, the journal Advances in the Study of Behavior rejected a paper by R. Haven Wiley and D. G. Richards on sound transmission through the atmosphere, in which the authors suggest that adaptations in animals' vocalizations reduce the effects of frequency-dependent attenuation refraction amplitude fluctuations and reverberation. Later, in his Citation Classics® commentary, Wiley speculated that he probably would not have pursued the matter if a

- second journal, Behavioral Ecology and Sociobiology, had rejected his manuscript.
- Charles R. Nelson and C. I. Plosser were convinced that their 1982 work on trends and random walks in macroeconomics was important; it later stimulated a series of papers in macroeconomical theory. The *Journal of Monetary Econ*omy eventually accepted the manuscript, which had been rejected earlier by the editors of the *Journal of Political Economy*.
- A humiliatingly negative referee report was all that economist Anton P. Barten
 obtained from the first journal to which he submitted his paper on the estimation
 of a system of demand equations. Fortunately, Barten showed his paper to Jean
 Waelbroeck, who accepted it after minimal revision for the European Economic
 Review. This was the first article in the first issue of the European Economic
 Review and has been very highly cited.

Avoidable Rejections

Referees' negative verdicts sometimes can be turned into acceptance. It is the editor's responsibility to monitor referees' work to allow a bit of originality and dissent. Sometimes, however, rejection prompts a thorough revision before a manuscript is submitted to the same or another journal. In this section, I describe examples of papers that received negative reports from referees or were rejected, then finally were accepted by the journal's editors. Such case studies can help us to understand the role of referees in facilitating or inhibiting communication of ideas in science.

- C. W. Neu, C. R. Byers, and J. M. Peek developed a new technique for the analysis of preference avoidance by species of a given habitat or forage. When the authors sent a manuscript describing this new procedure to the *Journal of Wildlife Management*, one reviewer recommended rejection because a procedure was already available in the statistical literature. However, from its publication in 1974 until 1992, this paper has been cited in more than 175 publications, confirming the usefulness of the new procedure.
- A first manuscript by Donald J. Cram and F.A.A. Elhafez on the rule of "steric control of asymmetric induction" in the synthesis of acyclic systems was rejected by the prestigious *Journal of the American Chemical Society*. This initial manuscript was sent for fast publication as a communication to the editor. Fortunately, the full paper was accepted. Cram believes that this 1952 publication is frequently quoted because it deals with a problem encountered in many syntheses and the rule is useful in designing synthetic sequences. Nine years after the publication of Cram's Citation Classics® commentary, the Nobel Prize in chemistry was awarded to his work on crown ethers, a related topic.
- The editors of Carbohydrates Research forced Peter Albersheim and his colleagues to delete about half of the data from a paper on a chromatographic method, but Albersheim feels that this decision was a serious mistake. The paper

- was later identified by Eugene Garfield (1987a) as one of the most influential papers in the plant sciences field. In addition, the 1967 paper is a core document in a 1986 research front identified by the ISI® (Garfield 1987a).
- The first detailed and complete neurochemical maps developed by using coronal serial sections throughout the whole brain in rats were not appreciated by one referee for the *Journal of Computational Neurology*. The maps were reported in two separate papers, but the referee stated that he could not see "that [the papers] add to the existing literature." After both articles were published in 1974, D. M. Jacobowitz and M. Palkovits had much feedback from other scientists who found these maps very useful. The high number of citations to these papers confirm this usefulness.
- Getting two highly cited papers into print was not easy for Marilyn Kozak. The editor of *Nucleic Acid Research* wondered if anyone would use the results of her first paper on an analysis of 5' encoding sequences from 699 vertebrate mRNAs. The 1,060 citations received by the paper from 1986 until 1993 are enough to dispel all uncertainty about the quality of the work. In addition, a referee had judged that a study reported in another Kozak paper submitted to *Cell* "could not be of compelling interest to the broad audience" of that journal. Again, the 1,570 citations it eventually received show that the paper was very interesting to the readers of *Cell*.
- According to Stuart H. Hurlbert, massive amounts of incorrect statistical
 analyses exist in the experimental ecological literature. In a 1984 paper, Hurlbert
 describes three of the commonest errors and cites numerous examples of each.
 The paper was submitted to Ecological Monographs, where one reviewer
 opined that "there is nothing new here." Fortunately, editor Nelson Harlston
 decided to accept it.

Rejections by Science and Nature

The journals *Science* and *Nature* are widely considered to be the most prestigious multidisciplinary journals in the world (Garfield 1981b; Garfield 1987b); publication in these journals is commonly accepted as a sign of excellence. Very important discoveries have been published in the pages of these journals. However, cases of error (Maddox 1988), fraud (Weinstein 1979), and duplicate publication in these journals (DuShane et al. 1961; Garfield 1980) have been documented. *Science* and *Nature* have also sometimes rejected significant papers. *Nature* has even rejected work that eventually earned the Nobel Prize ("Criteria for Science" 1993; Anonymous 1988). The editors of *Nature* argue that they receive many more papers than they could possibly publish. In this section, I present cases in which referees from *Science* and *Nature* criticized significant papers and even recommended their rejection. As can be seen in the following stories, in some instances the negative verdict stimulated improvement in the manuscript.

- Electrical stimulation at several brain stem sites has been found to abolish responsiveness to intense pain in rats. An interpretation of these results was the key point of a paper by David J. Mayer and co-workers published in Science in 1971. Before the final acceptance of the report, Science rejected a previous version, probably because it was mostly phenomenological. The final paper included a theoretical explanation for the observed phenomena and it has since been cited in more than 490 publications, demonstrating its importance. Interestingly, as Mayer points out, the origin of the discovery reported in the paper was a serendipitous observation.
- The revision of a manuscript submitted to *Nature* by Kenneth A. Gruber and colleagues providing evidence for an endogenous digitalis-like substance in volume-expanded plasma from dogs was also problematic. According to Gruber, the reason was that one of the reviewers tried to change the requirements he had laid down for acceptance in his first review. Fortunately, the editors challenged this decision. Previously, an abstract describing the findings was eventually published in *Nature*, although it had been rejected for presentation at an American Society of Nephrology meeting in 1979.
- The first submission to *Nature* of a short paper by W. D. Hamilton on the evolution of altruistic behavior was also rejected. In an account of these episodes, Hamilton suggests that the return address of "Department of Sociology, London School of Economics" may have weighed against the manuscript. Hamilton discovered the theme of this paper (the condition for the evolution of genetical altruism) when he was an undergraduate student at the University of Cambridge in 1958. The rejected paper eventually appeared in *American Naturalist* (1963) and, according to the ISI® database, it has been cited in more than 150 publications. Another paper by Hamilton on this topic was published in the *Journal of Theoretical Biology* and it has been cited in more than 1,335 publications, making it this journal's most-cited paper (Hamilton 1964). The elevated number of citations illustrates the transcendence of this topic.
- By 1984, the 1970 paper by Lindell and his colleagues on specific inhibition of nuclear RNA polymerase had been cited in more than 450 publications. Previously, this paper had been rejected by *Nature*. The senior author, William Rutter, was able to convince the editor of *Nature* to reconsider the paper, but it was again rejected. It was later published by *Science*.
- In his Citation Classics® commentary on a review paper on adenosine and its
 nucleotides in central synaptic transmission, J. W. Phillis recalled that the initial
 report he wrote with G. K. Kostopoulos on adenosine action was promptly
 rejected by *Nature*. Adenosine action was an idea that contradicted the theories
 of the 1970s. Indeed, it was widely believed that only 3',5'-cyclic AMP—and
 not adenosine—could depress neuronal firing.
- In 1976, Science rejected a manuscript by R. D. Porsolt, M. Le Pichon, and M. Jalfre on a simple new behavioral model for testing antidepressant drugs. The referees' verdict was that the paper was "not sufficiently interesting." Nature published the manuscript in 1977 and since then the method reported in it has become a standard antidepressant test in pharmaceutical laboratories worldwide. According to the authors, the main reason for its impact is probably its procedural simplicity and its high reproducibility.

- Despite referees' reports that were both favorable and enthusiastic, the editorial staff of *Nature* did not want to publish a paper by J. C. Foreman, J. L. Mongar, and B. D. Gomperts on the movement of calcium ions following physiological stimulus to a secretory process. The authors had to fight to get this highly cited paper into print in that journal.
- A paper by biologist Bernard D. Davis, suggesting that during sleep we
 consolidate waning memories by firing sets of neurons, was rejected by *Nature*and appeared in 1985 in *Perspectives in Medical Biology*, a less prominent
 journal. However, in an autobiographical account, Davis (1992) mentions his
 pleasure at seeing his previously rejected idea acquire increasing acceptance.
- Referees judged that a manuscript by G. M. Gorman, L. F. Moffat, and B. H. Howard was "not of wide enough interest for publication in *Nature*." The manuscript described the development of the first mammalian expression vectors producing the chloramphenical acetyltransferase (CAT) protein and was eventually accepted by *Molecular and Cellular Biology*. Since 1982, it has received more than 4,410 citations, making this paper the most-cited paper published in that journal.

Rejecting Nobel-Class Papers

On some occasions, referees have advised editors to reject papers which reported findings that eventually earned the Nobel Prize for their authors. Documented cases of such rejection include Severo Ochoa's work on polynucleotide phosphorylase (Ochoa 1980); Hans Krebs' account of the citric acid cycle (Dixon 1989); Rosalind Yalow's initial work on radioimmunoassay (Yalow 1982); Murray Gell-Mann's work on quarks (Crozon 1987); and Harmut Michel's research on photosynthetic processes (Garfield 1989a). The above cases have been studied with detail by other authors. Here are some examples that may be less well-known.

- A paper by Russian physicist Pavel Alekseevich Cherenkov, reporting observations of previously unknown properties of visible radiation was rejected in the 1930s by Nature. According to an account by John H. Hubbel (1991), the editors of Nature did not take the work seriously, but the editors of Physical Review accepted and published the paper in 1934. In 1958, P. A. Cherenkov, I. M. Frank, and I. Y. Tamm shared the Nobel Prize in physics for the discovery and explanation of the Cherenkov effect.
- The 1987 Nobel Prize in physics was awarded to Johannes Georg Bednorz and Karl Alex Müller for their discovery of high-temperature superconductivity in ceramic materials. The paper reporting this discovery was rejected by some journals until it was accepted by Zeitschrift für Physik (Combescot 1988). Although the paper was received with widespread skepticism (Combescot 1988; Garfield 1988; Waldrop 1987), the findings were later confirmed by other authors, and the work reported by Müller and Bednorz stimulated worldwide interest in superconductivity.

- Even at the beginning of their research, Gerd Binning and Heinrich Rohrer knew the scanning tunneling microscope would be a significant development (Robinson 1986). However, a referee from the first journal in which they attempted to publish the results of their first experiments found the paper "not interesting enough" (Robinson 1986) and advised rejection (Armstrong and Hubbard 1991). The scanning tunneling microscope has important implications in microelectronics and other fields. Using this device, it is possible to "see" complex surface structures atom by atom. A share in the 1986 Nobel Prize in physics re-awarded the work of Rohrer and Binning in this field.
- William A. Fowler shared the 1983 Nobel Prize in physics for his studies of nucleogenesis. Fowler's best-known contribution to understanding the origin of the elements is a 1957 paper generally known as "BBF&H," after the names of the authors (Burbidge, Burbidge, Fowler, and Hoyle). According to the Swedish Academy of Sciences, the paper "is the basis of our knowledge in the field (of nucleosynthesis)" (Garfield 1984b). However, the original version of the BBF&H paper was rejected by the first American journal to which it was sent (Maddox 1983).
- Some of the ten referees that reviewed two 1957 papers submitted by Bessman and colleagues and by Lehman and colleagues (including senior author Arthur Kornberg) to the *Journal of Biological Chemistry* advised against acceptance. In those papers, authors accounted the enzymatic synthesis of DNA. After some interchange of correspondence, Kornberg decided to withdraw the papers. However, John Edsall, who was about to become editor of that journal, asked him to wait and the papers were finally published in 1958 (Kornberg 1989). A share of the 1959 Nobel Prize in physiology of medicine was awarded to Kornberg for his work on enzymes and on synthesis of DNA.
- In making the discovery that RNA can catalyze reactions, Sidney Altman needed to overcome his own preconceptions as well of those of most chemists and biochemists (Baum 1989; Lewin 1989). Indeed, Altman, who shared the 1989 Nobel Prize in chemistry for this discovery, recognized that his research team encountered difficulties publishing the original report (along with Stark and other colleagues) on the RNA component of RNase-P (Baum 1989). This discovery is one of the most unexpected breakthroughs of the 1980s and challenged the old dogma of proteins only as catalysts.
- Henry Taube admitted that he was a bit naive in sending a paper on rates and mechanism of substitution in inorganic complexes in solution to the prestigious Chemical Reviews, which is comprised only of invited papers. Despite this policy, the contribution was reviewed—and the decision was to reject. Luckily, before the manuscript was actually rejected, it was sent to Jake Kleinberg, who advised its acceptance. The prestige of this inorganic chemist was the only reason the manuscript was accepted and published in 1952. The paper studies the correlation between ligand substitution rates and electronic configuration for coordination compounds of the transition metals. Today, this correlation dominates the way chemists think about the reaction chemistry of coordination compounds (Gray and Collman 1983). Taube received the 1983 Nobel Prize in chemistry for this pioneering work on the mechanisms of inorganic oxidation-reduction (redox) reaction.

Further Examples

- Adenosine was the research topic of R. Perlman and I. Pastan. Unpublished results by these authors were well-known by the academic community. In fact, many scientists were studying the same problem. However, three journals rejected papers on this topic. Finally, papers submitted to Biochemical and Biophysical Research Communications and to the Journal of Biological Chemistry were accepted. In his Citation Classics® commentary, Pastan states that he believes their discoveries would have been more easily accepted if they had not contradicted the orthodox view on gene expression.
- The paper by Robert Englman and J. Jortner on the energy gap law for radiationless transitions in large molecules featured in the decision to award several prestigious prizes (the Israel award in 1982 and the Wolf prize in 1988) to Jortner. However, as Englman recalled in his 1988 Citation Classics® commentary, one of the referees wanted a shortened version and the other recommended rejection. The 435 citations to this paper from 1970 to 1988 demonstrates this referee's mistake.
- In 1960, Theodore Maiman demonstrated the first operation of a laser, which used a ruby crystal pumped by a helical xenon discharge flashlamp. Maiman submitted a paper reporting the above findings to the *Physical Review Letters*, but it was rejected. A probable reason for this rejection was the editorial policy of rejecting papers on MASERS that did not "contain significant contributions to basic Physics" (Bloembergen 1993). *Nature* published an abbreviated form of his manuscript in 1960.
- Physical Review rejected two papers by K. W. Ford and J. A. Wheeler on the semiclassical description of scattering. According to the editor, the papers were too long and too pedagogical. Ford and Wheeler assembled the papers, sent off the new manuscript to the new journal, Annals of Physics, and it was promptly accepted by the editors.
- Physicist P. Pulay received a rejection letter from *Theoretical Chimica Acta* when he submitted his highly cited paper on ab initio calculation of force constants. The paper was sent to and accepted by *Molecular Physics* (1969) where it was ignored by the quantum chemistry community, probably because it was published in a physics journal. Only a later review paper made the computational technique widely known. This is a very instructive example of how a referee's mistake could delay and retard the development of a discipline.
- A paper by David S. Holmes and M. Quigley, reporting a rapid method for the preparation of plasmids, was initially rejected by *Nucleic Acid Research*. The discovery reported in this paper was done serendipitously when Holmes heated a solution beyond the temperature at which the DNA contained in such solution would eventually denature. Surprisingly, the procedure worked and it was incorporated into a very popular compendium of recipes for molecular biology, receiving 2,325 citations from its publication in 1981 through 1993.
- The prestigious Journal of Chemical Physics initially rejected Henry Eyring's classical 1935 paper on the activated complex in chemical reaction. The referee summarized his conclusions with these words: "I have given considerable

thought to the problems involved, and although I have not been able to resolve my uncertainties I have nevertheless become convinced that the method of treatment is unsound and the result incorrect" (Laidler and King 1983). This paper was finally published in that journal and since then it has been highly influential. In addition, Laidler and King (1983) tell us the development of the theory of activated complex was not smooth: some scientists attacked the theory in terms that were offensive to Eyring. This is an instructive example of how scientists themselves can resist scientific discovery.

- A 1977 paper by David R. Olson addressed four basic questions about language
 and its use: its structure, its meaning, the nature of comprehension, and the
 nature of reasoning. As Olson says, the people to whom he showed the paper
 were unenthusiastic and the journal Cognitive Psychology rejected it. A colleague who had been invited to contribute to a special issue of the Harvard
 Educational Review told Olsen about its forthcoming special issue on language.
 Olson submitted the unsolicited manuscript and it was finally published in 1977.
- In an autobiographical account, biochemist M. Heildelberger recalled how the *Journal of Biological Chemistry* rejected a paper describing some of his findings (Heildelberger 1979). In that paper, synthetic polyglucoses were proposed as possible blood-extenders. Heildelberger's research found that certain fractions precipitated heavily with antipneumococcal sera of several types. Then glycogens of various origins were found to react in this way. The referees of the journal recommended that the paper be rejected on the grounds that it was not biochemistry.
- That same reason was given to Esmond Snell and Frank Strong when the *Journal of Biological Chemistry* rejected a manuscript describing an assay for riboflavin. However, the method was highly successful and widely used, and has served as the prototype for many similar methods later devised for other B-vitamins and amino acids. A consequence of this rejection is that it served to Snell as a caution in his years on editorial boards of other leading journals, "not to interpret the subject matter of biochemistry too narrowly" (Snell 1993, 7).
- According to Robert K. Merton, multiple discoveries are the norm and not the exception in science (Merton 1961). What about the multiple rejection of multiple discoveries? In the 1940s, Joshua Lederberg (who later received a Nobel Prize) and his co-worker, Norton Zinder, submitted a manuscript to the Journal of Biological Chemistry, reporting a new idea on bacterial mutations; a manuscript describing parallel work was also submitted by biochemist Bernard Davis. The journal rejected both papers because, according to the referees, they were of insufficient biochemical interest. The Journal of the American Chemical Society later published both papers in 1948. This case also offers an incidental lesson about collegiality, since Lederberg and Zinder offered to hold up their manuscript if Davis sent his immediately (Davis 1992).
- The Journal of Biological Chemistry once rescued a paper that had been rejected first by another journal. Early in 1960, Mildred Cohn, a biochemist, and Tom Hughes, a graduate student, submitted a paper on the results of the metal ion effects on the ³¹P-NMR spectrum of adenosine triphosphate to the Journal of the American Chemical Society. The paper was rejected and it was not until two years later that it appeared. This paper eventually became very influential in its field (Cohn 1992).

- - One of the fastest-growing areas of chemical research deals with oscillating chemical reactions. Some chemical reactions behave strangely: they fluctuate over time so as to alternately consume and then produce the same substance. Although reports of oscillating chemical reactions have been published since 1828, it was not until the 1950s that Soviet biochemist B. P. Belusov serendipitously observed the now famous oscillating reaction that is named after him. The existence of these oscillating reactions apparently completely violated the existing basic rules of chemistry, so it is not strange that two journals rejected Belusov's papers; he finally had to publish his results in an obscure compilation (Vidal 1990). This type of incident shows how the stereotype of scientists as open-minded people clashes frequently with reality.
 - On another occasion, *Nature* rescued a paper by American physicist Thomas Gold on the nature of pulsars. The paper interpreted pulsars as rotating neutron stars. It was submitted to a May 1968 conference on pulsars organized in New York, but the referee's report stated that "if the suggestion was admitted there would be no end to the number of other suggestions that would equally have to be allowed." In October and November of that year, two discoveries confirmed Gold's theory.
 - By 1983, a classic paper by Frances E. Arrighi and T. C. Hsu had been cited in more than 810 publications since its publication in 1971. This paper describes a procedure to localize heterochromatin in human chromosomes. However, the first journal to which the paper was submitted rejected it on the grounds that the method had no medical application. Fortunately, Arrighi and Hsu eventually published their paper in Cytogenetics and, since then, it has been much cited.
 - Probably the world record for rejections is held by Magoroh Maruyama's article that appeared in 1963 in American Scientist. In this paper, the author discusses why some causal loops amplify change, while other loops counteract it, and how similar initial conditions may lead to dissimilar results in social, physical and biological processes. According to the author's account, this paper was rejected by ten different U.S. journals.

Highly Cited Academic Books

Sometimes it is also hard to get books into print. Table 2 shows the bibliographic data for four scientific books that eventually received a high number of citations.

- In Markets and Hierarchies, published in 1975, Oliver E. Williamson examines alternative forms of economic organization from a comparative institutional point of view in which transaction cost economizing is emphasized. This book took shape after the Brookings Institution, which had rights of first refusal, declined it. The book was published by the Free Press, whose staff projected small sales and planned to discontinue production after the first run.
- The book, Limited Dependent and Qualitative Variables in Econometrics, by G. S. Maddala was rejected by MIT Press, Academic Press, McGraw-Hill, and

- two other publishers until it was finally accepted by Cambridge University Press for publication in 1983. The book has had a strong impact in econometrics.
- According to Robert L. Lineberry, publication of his book, Equality and Urban Policy: The Distribution of Municipal Public Services, in 1977 involved an unusual "catch-22." Efforts to obtain funding from the National Science Foundation failed and so he only got money to study one of the three cities that he wanted to examine. When Princeton University Press referees read the manuscript, they advised against publication because the author had studied only one city. Sage eventually published this very influential book.
- Eric R. Pianka's Evolutionary Ecology, published in 1974, describes how to use
 the theory of natural selection in population biology to explain numerous
 phenomena that, until relatively recently, biologists merely accepted as immutable. When Pianka assembled his original outline and sent it off to several
 publishers, all but one rejected it. One of the reasons given was that Pianka was
 an unknown. This book is now in its fourth edition and has been translated into
 four languages.

Conclusion

Derek J. de Sola Price ([1963] 1986) once suggested the establishment of a hypothetical Journal of Really Important Papers; Eugene Garfield (1990b) has proposed a Journal of Citation Classics®; and, as an extension, I have proposed a Journal of Previously Rejected Important Papers. ² These suggestions reflect a more serious concern about neglect and error in the review process and they take on new urgency as we observe a profound change in the patterns of scientific publishing, especially through the challenge of electronic journals. In some areas of physics, few people now want to wait to read articles in the "old" paper journals; their main communication channel is electronic mail (Taubes 1993). Doubtless, when anyone may criticize or comment on-line about an article published by an electronic journal, the role of editors and referees as "author guardians" (Garfield 1986b) will change. Electronic journals will make it possible for a large number of people to express freely their opinion on a given paper. It would be unfortunate if electronic journal publishing used the latest technological devices but continued to play the same old tune.

A related question is the relative frequency with which subsequently highly cited papers are rejected because of negative referee evaluations. This question should be addressed with care and to do so is beyond the scope of this paper. One approach would be to use a database of highly cited papers that is truly comparable. At present, the accounts by authors are scattered throughout the literature in autobiographical accounts, historical narratives, historic introductions on a given topic, Nobel lectures, and so forth. As

Garfield has pointed out, the Citation Classics® commentaries are intended to fill this void (Garfield 1993); however, not all authors of highly cited papers have written commentaries for the Citation Classics® feature. In addition, the Citation Classics® do not cover all important papers. Some very influential papers are not highly cited because of the phenomenon of "obliteration": the papers are integrated into a body of knowledge in a given field and scientists no longer cite them explicitly (Garfield 1983, 10). Thus the data obtained from these sources alone cannot be representative of the whole population of published papers.

One obvious way to ascertain the relative frequency of rejection of influential or highly cited papers would be to examine confidential journal files. However, this method encounters resistance from most editors, even if it is possible to keep referees' names anonymous. Using this method, Gottfredson (1978) found only low to moderate correlations between reviewers' ratings of psychological research papers and the number of citations received by these papers. However, I have studied the relative frequency of rejections of highly cited papers using a different approach and discovered that 23 influential papers from a set of 205 highly cited papers (none of them once discussed in this article) had problems in publication because of negative referees' evaluations. These 205 papers were among the most cited papers of all times.³

Another important question is whether the peer review system can achieve its main goal: to promote original ideas, valuable approaches, or new methods, and to reject mediocre ones. The case stories listed in this article illustrate how perseverance sometimes is necessary to publish good scientific work. As noted above, in some instances negative evaluations may have forced authors to revise their papers, and the contributions therefore may have been strengthened. Sometimes editors may have recommended rejection because a manuscript is not appropriate for a given journal or because it is too long (for example, the 1959 paper by Ford and Wheeler cited above). We could probably suggest more explanations for other cases of rejection. For example, the 1963 Hamilton paper cited above might have been less significant than his most important paper and did not deserve publication in a leading journal. Perhaps one paper was subsequently cited only after the more substantial work was published (I am grateful to an anonymous referee for this interpretation).

However, in other instances referees' and editors' negative evaluations demonstrate that they did fail to appreciate the importance of a potentially influential manuscript. Sometimes authors are "guilty" of challenging in their papers the current views or paradigms of a given discipline, and referees are "guilty" of judging these contributions too narrowly. These referees' mistakes

may even delay the development of a given discipline or dissemination of a new technique, as was true for the 1969 Pulay paper cited above. Something is wrong with the peer review system when an expert considers that a manuscript is not of enough interest and it later becomes a classic in its discipline (or, even worse, when the work reported in a rejected paper earns the Nobel Prize).

I believe that we should seriously consider profound changes in the philosophical foundations of the peer review system. Contrary to reports by the American Association for the Advancement of Science and the National Academy of Sciences, publication in a peer-reviewed journal is not necessarily the best means of identifying valid research (Marshall 1993). Inversely, rejection letters from journals should not mean bad science. And, contrary to the editorial opinion of The New England Journal of Medicine (Kassirer 1992), the rejection of papers is not only explained by a "paper's lack of originality, its doubtful scientific accuracy, its lack of originality or its lack of interest to readers." As shown in the case studies listed above, scientists are correct to argue with editors about their rejected papers or to send a previously rejected manuscript to another journal. In a study of papers published in the American Sociological Journal, Simon, Bakanic, and McPhail (1986) found that a complaint prompted the editors to reconsider a paper for publication. Some of the complainants (13 percent) managed to have their rejection changed to an acceptance. In fact, most leading journals assume that authors of rejected manuscripts will submit them elsewhere, and so editors may even suggest submission elsewhere to the authors of rejected papers (see, for example, the latest guidelines to authors of Science and Nature and Stossel, 1985).

To avoid the "editor's nightmare" of rejecting important papers, journals should be accountable for their refereeing practices. To allow more scrutiny of the review process by readers, it has been suggested that journals should add a "speculations" section to journal articles (Brandt 1987) or that scientific journals should send articles to two experts and one "non-expert" (Wolman 1987). According to Wolman, this process would more easily accept unorthodox opinion. Making room for innovative work that falls outside conventional paradigms presents a challenge to all journals (Davis and Ben-Sasson 1993). Other authors have proposed that four or five years after any article appears in print referees' names should be disclosed (Müller 1993). In addition, I propose that five or six years after the publication of every paper journals should publish a short abstract (maybe 15 or 20 lines) of the referee's report on that article, together with a list of its citations. This system eventually would help readers to check the wisdom of referees for their favorite journal. To avoid extra costs to journals, these referee reports could

be filed in a computer database (perhaps named the Electronic Journal of Referee Reports). This database would be open to users via electronic mail. Using this system, referees' names could be kept anonymous and journals would be responsible for adding their referees' reports. Alternatively, with permission by referees and editors, names and affiliations could be disclosed in those instances in which referee commentaries had been useful in improving the original manuscripts. These important contributions to science could then be listed in vitaes and the referees could be recognized for tenure, grant proposals, or academic promotion.

Notes

- 1. Two papers forthcoming from the author ("The competition for journal space among editors, referees and other authors," and "As referees rejected some of the most cited papers of all times") discuss this point as well.
- 2. This proposal is expanded in my forthcoming article ("As referees rejected some of the most cited papers of all times").
 - 3. Ibid.

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