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Rejecting and resisting Nobel class discoveries: accounts by Nobel Laureates

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I review and discuss instances in which 19 future Nobel Laureates encountered resistance on the part of the scientific community towards their discoveries, and instances in which 24 future Nobel Laureates encountered resistance on the part of scientific journal editors or referees to manuscripts that dealt with discoveries that later would earn them the Nobel Prize.

Lack of progress in science is never so much due to any scarcity of factual information as it is to the fixed mindsets of scientists themselves.
[SCHRAM, 1992, P. 357]

A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up that is familiar with it.
[PLANCK, 1949, PP. 33–34]

Introduction

The history of science is dotted with stories documenting how many important discoveries were initially resisted or ignored by fellow scientists [BARBER, 1961]. Some important discoveries were *premature*, in the sense that they did not fit the common paradigms, or their implications could not be connected by a series of simple logical steps to existing scientific knowledge. These discoveries were often rejected and deemed impractical for some time after their initial communication [STENT, 1972] [STENT, 2002]. In other instances, novel theories or discoveries collided with the dominant paradigms in science, and were resisted or scorned with a generous dose of skepticism.

When this happens, papers are rejected, fellow scientists ignore discoveries, articles are not cited, or commentaries are written against the new finding or discovery. In other instances, authors of very innovative papers are criticized and often face stonewalling from their peers. As Nobel Laureate J. Steinberger rightfully observed, "new ideas are not completely easy to accept, sometimes even by the brightest and most open of people" [STEINBERGER, 1997]. A worse scenario can also play out: scientific contributions are sometimes effectively silenced [SOMMER, 2001] and prevented from being

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published for years (for example, one article appeared in 1957 in the *Journal of the American Chemical Society* 25 years after it was initially submitted [KOELSCH, 1957]).

Among the more notorious instances of resistance to scientific discovery are Mayer's difficulties in publishing an initial version of the first law of thermodynamics [COLMAN, 1982], the difficulties experienced by Henry Eyring in publishing his classic 1935 paper on the activated complex in chemical reactions [LAIDLER & KING, 1983] or the resistance Avogadro's hypothesis met with [NISSANI, 1995]. The reader is welcome to review other instances reported elsewhere [BARBER, 1961; CAMPANARIO, 1993; 1995; 1996; 2002; CAMPANARIO & ACEDO, 2007; NISSANI, 1995; SHEPHERD, 1995].

Despite the deluge of documented cases, there has been a relative lack of interest on the part of sociologists, philosophers and science historians in investigating the important topic of scientists' resistance to scientific discovery. It is naturally embarrassing for the scientific community to acknowledge that many important discoveries were neglected, rejected or utterly ignored. As Barber points out, the norm of open-mindedness is one of the strongest values in science, but the episodes of resistance to scientific discovery clash with this institutionalized norm [BARBER, 1961].

Almost all leading journals use a peer review system to evaluate and select contributions. A analysis by Weller on editorial peer review provides an enumeration of the achievements and deficiencies of editorial peer review [WELLER, 2001].A serious charge against the peer review system was raised by Stephen Lock, former editor of a medical journal, who claimed that peer review "favours unadventurous nibblings at the margin of truth rather than quantum leaps" [LOCK, 1985]. Redner claimed that "one of the roles of journals almost appears to be to sift out and reject really original contributions" [REDNER, 1987].

In previous articles I used a systematic approach to study this particular kind of resistance to scientific discovery [CAMPANARIO, 1993; 1995; CAMPANARIO & ACEDO, 2007]. I have relied on commentaries and reminiscences from scientists who wrote highly cited papers – commentaries that were published from 1977 to 1992 in a section of *Current Contents* (available in http://garfield.library.upenn.edu/classics.html). Using this approach I have shown that some of the most cited papers in the history of science were first rejected by journal referees and editors [CAMPANARIO, 1996]. I have also identified a number of important or influential papers and books whose publication was delayed for similar reasons [CAMPANARIO, 1993; 1995]. In some instances the initially rejected papers eventually became the most highly cited works in their respective journals.

The goal of the present study is to extend previous work on the topic of resistance by scientists to scientific discovery by a very select population of scientist: those who won the Nobel Prize in Physics, Chemistry, and Physiology or Medicine. I wished to record the accounts by the scientists themselves of episodes of resistance to new discoveries that eventually earned them a Nobel Prize.

Method

I collected instances of resistance to scientific discovery in which Nobel Prize winners were involved. These instances were taken from autobiographies, personal accounts, Nobel lectures and other written reports. Only documents in which a Nobel Laureate was directly involved were used for the present analysis.[1] I also included data on the papers cited by Nobel Laureates when the authors provided enough information to locate the articles.

I have classified the instances of resistance in two broad categories:

a) Skepticism by part of the scientific community towards a discovery that would eventually be awarded the Nobel Prize.

b) Rejection by journal editors or referees of a paper that reported a discovery or contribution that would eventually be awarded the Nobel Prize.

In two previous papers I identified three additional instances of rejection of Nobel class papers. These instances relate to the work of Severo Ochoa [CAMPANARIO, 1993], Henry Taube and Arthur Kornberg [CAMPANARIO, 1995]. I have been unable to obtain new data on these instances, so interested readers are advised to consult the above articles.

Results

Instances of skepticism by part of the scientific community towards discoveries that were eventually awarded the Nobel Prize are listed in the Appendix. The accounts by Nobel Laureates are self-explanatory. These accounts express the views and feelings of the scientists themselves regarding the reception of their discoveries by the academic community. As can be seen, there are a significant number of instances that cast doubt on simplistic visions and common conceptions of science as an activity in which novelty is welcome, and on the capacity of science to assimilate novel data, facts, observations and theories.

The most interesting instances are those in which a Nobel class paper encountered resistance in the refereeing process or was rejected outright (Table 1). In the excerpts that follow I summarize instances of this problem in papers reporting seminal discoveries or findings that would eventually earn their authors a Nobel Prize.

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[1] I have not included an additional instance in which the journal *Nature* acknowledged that a Nobel class paper had been rejected. The reason is that I have been unable to find any documents in which the Nobel Laureate himself describes the episode. *Nature* rejected a Nobel class article written by Harmut Michel, who shared the 1988 Nobel Prize in Chemistry. The article was eventually published in the *Journal of Molecular Biology*, and a scientometric analysis by the Institute for Scientific Information (ISI) identified it as a core document in two research fronts concerning the topic for which Michel would eventually share the Nobel Prize [GARFIELD, 1989C]. With time Michel was vindicated in a letter by an anonymous writer from *Nature* who wrote expressly to acknowledge this paramount mistake [ANONYMOUS, 1988].

Table 1. Nobel class papers that had difficulties during the peer review process or that were rejected by editors of journals

Nobel laureate	Paper	Journal involved
Binnig, Gerd; Rohrer, Heinrich	Binnig, G.; Rohrer, H.; Gerber, Ch.; Weibel, E. (1982) Surface studies by scanning tunnelling microscopy. *Physical Review Letters*, 49, 57-61.	
Blumberg, Baruch S.	London, W.T.; Sutnick, A.I.; Blumberg, B.S. (1969) Australia antigen and acute viral hepatitis. *Annals of Internal Medicine*, 70, 55-59.	
Boyer, Paul D.	Boyer, P.D.; Cross, R.L.; Momben, W. (1973) A new concept for energy coupling in oxidative phosphorylation based on a molecular explanation of the Oxygen exchange reaction. *Proceedings of the National Academy of Sciences-USA*, 70, 2837-2839.	*Journal of Biological Chemistry*
Cech, Thomas R.	Bass, B.L.; Cech, T.R. (1984) Specific interaction between the self-splicing RNA of Tetrahymena and its Guanosine substrate-Implications for biological catalysis by RNA. *Nature*, 308, 820-826.	*Nature*
Ernst, Richard R.	Ernst, R.R.; Anderson W.A. (1966) Application of Fourier transform spectroscopy to magnetic resonance. *Review of Scientific Instruments*, 37, 93-102.	*Journal of Chemical Physics*
Furchgott, Robert F.	Furchgott, R.F.; Zawadzki, J.V. (1980) The obligatory role of endothelial cells in the relaxation of arterial smooth muscle by acetylcholine. *Nature*, 288, 373-376.	*Nature*
Gell-Mann, Murray	Gell-Mann, M. (1953) Isotopic spin and new unstable particles. *Physical Review*, 92, 833-834.	*Physical Review*
Krebs, Hans	Krebs, H.; Johnson, W.A. (1937) The role of citric acid in intermediate metabolism in animal tissues. *Enzymologia*, 4, 148-156.	*Nature*
Kroemer, Herbert	Kroemer, H. (1963) A proposed class of heterojunction injection lasers. *Proceedings of the IEEE*, 51, 1782-1783.	*Applied Physics Letters*
Laurterbur, Paul C.	Lauterbur, P.C. (1973) Image formation by induced local interactions: Examples employing Nuclear Magnetic Resonance. *Nature,* 242, 190–191.	*Nature*
Lee, David M.; Osheroff, Douglas D.; Richardson, Robert C.	D. D. Osheroff; Gully, W.J.; Richardson, R.C.; Lee D.M. (1972) New Magnetic Phenomena in Liquid He3 below 3 mK. *Physical Review Letters*, 29, 920-923.	*Physical Review Letters*
Mullis, Kary B.	Mullis, K.B.; Faloona, F.A. (1987) Specific synthesis of DNA in vitro via a polymerase-catalyzed chain reaction, *Methods in Enzymology*, 155, 335-350.	*Nature and Science*
Polanyi, John C.	Polanyi, J.C. (1961) Proposal for an infrared maser dependent on vibrational excitation. *Journal of Chemical Physics*, 34, 347-348.	*Physical Review Letters*
Tiselius, Arne	Tiselius, A. (1937) A new apparatus for electrophoretic analysis of colloidal mixtures. *Transactions of the Faraday Society*, 33, 524-531	*"A biochemical journal"*
Wigner, Eugene P.	Wigner, E.P. (1939) On the unitary representations of the inhomogeneous Lorentz group. *Annals of Mathematics*, 40, 149-204.	
Yalow, Rosalyn S.	Berson, S.A.; Yalow, R.S.; Bauman, A.; Rothschild, M.A.; Newerly, K. (1956) Insulin-I131 metabolism in human subjects: Demonstration of insulin binding globulin in the circulation of insulin treated subjects *Journal of Clinical Investigation*, 35, 170-190	*Science*

The 1948 Nobel Prize in Chemistry was awarded to Arne Tiselius "for his research on electrophoresis and adsorption analysis, especially for his discoveries concerning the complex nature of the serum proteins." Tiselius originally published his findings in the *Transactions of the Faraday Society*, where he reported the application of an improved method of electrophoretic analysis to the study of serum proteins. However, this paper was rejected by the biochemical publication to which it was first sent. Apparently the journal's main objection was that the content of the paper was too "physical" [TISELIUS, 1968, P. 7]. Nonetheless, the importance of this article can be deduced from the fact that it is explicitly cited in Tiselius' official biography [ANONYMOUS, 1948]. Despite the initial rejection, and according Tiselius' testimony, "the reaction (to the paper) was immediate and extremely positive" and "I was flooded with letters and requests for reprints and even a telegraphic order" [TISELIUS, 1968, P. 7].

The referees of the journal *Physical Review Letters* also rejected a key paper concerning the discovery of superfluid helium (^{3}He), a discovery which earned Professors David M. Lee, Douglas D. Osheroff and Robert C. Richardson the 1996 Nobel Prize in Physics. The future Laureates spent a great deal of time getting the decision overturned. One referee argued that the system "cannot do what the authors are suggesting it does" [BUCHANAN, 1996]. Eventually the authors managed to convince the editor that they had stumbled on a new and exciting discovery, and as Lee pointed, "ultimately, reason prevailed and the manuscript finally appeared" [LEE, 1997].

A manuscript authored by Murray Gell-Mann and dealing with "strangeness" in elementary particle physics was rejected by *Physical Review* referees in 1953. The editors objected to the use of the main concept Gell-Mann coined ("curious particles"). He had to change this term to "new unstable particles" after "strange particles" was also rejected. The referees also objected to his explanation of the differences between neutral bosons and neutral anti-bosons. It was very difficult for Gell-Mann to convince the referees that he was right [GELL-MANN, 1982]. The work reported in this article was awarded the Nobel Prize in Physics in 1969.

Figure 1 shows a copy of the polite letter Hans Krebs received from *Nature* declining to publish the first report on the citric acid cycle, the discovery for which Krebs would eventually share the 1953 Nobel Prize in Physiology or Medicine. Krebs' commentary, which accompanied the letter, is quite illuminating: "the paper was returned to me five days later accompanied by a letter of rejection written in the formal style of those days. This was the first time in my career, after having published more than fifty papers, that I had rejection or semi-rejection" [KREBS, 1981, P. 98–99]. As can be seen, *Nature* argued that they had sufficient letters to fill the correspondence columns for seven or eight weeks and offered to keep the letter "until the congestion were relieved." Instead of waiting, Krebs forwarded the manuscript to the journal *Enzymologia*, where it was published within two months. Many years later, an anonymous writer from *Nature* came forward and acknowledged this cardinal mistake [ANONYMOUS, 1988].

Figure 2 shows a copy of the rejection letter received by Berson and Yalow from the *Journal of Clinical Investigation*, where the authors intended to publish a singular paper that later was recognized as a great achievement in Medicine and earned Rosalyn Yalow a share of the 1977 Nobel Prize in Physiology or Medicine. The paper was first submitted to and rejected by *Science*, and after an initial rejection by the *Journal of Clinical Investigation* it was published in this journal after a compromise was reached with the editor involving some changes in content [YALOW, 1978].

The discovery for which Thomas R. Cech received the half of the 1989 Nobel Prize in Chemistry conflicted with some well-established ideas in biology. Cech discovered that RNA molecules can act as an enzyme. Nonetheless, in his Nobel Lecture Cech vividly described how contemporary enzymologists felt outraged at the use of words "catalysis" and "enzyme-like" to describe the function of RNA he had recently discovered [CECH, 1989, PP. 666–668]. For example, all three referees who reviewed a manuscript submitted to *Nature* by Bass and Cech strongly criticized the use of these concepts.

Telegraphic Address: PHUSIS, LESQUARE, LONDON.
Telephone Number: WHITEHALL [illegible].

Editorial and Publishing Offices: MACMILLAN & CO. LTD., ST. MARTIN'S STREET, LONDON, W.C.2.

RAG.AH/N. 14th June 1937.

The Editor of NATURE presents his compliments to Mr. H. A. Krebs and regrets that as he has already sufficient letters to fill the correspondence columns of NATURE for seven or eight weeks, it is undesirable to accept further letters at the present time on account of the delay which must occur in their publication.

If Mr. Krebs does not mind such delay, the Editor is prepared to keep the letter until the congestion is relieved in the hope of making use of it. He returns it now, however, in case Mr. Krebs prefers to submit it for early publication to another periodical.

Figure 1. Letter from *Nature* declining to publish the first paper on the citric acid cycle, June 1937. Reprinted with permission from *Nature*. Copyright 1981 Macmillan Magazines Limited

September 29, 1955

Dr. Solomon A. Berson
Radioisotope Service
Veterans Administration Hospital
130 West Kingsbridge Road
Bronx 63, New York

Dear Dr. Berson:

I regret that the revision of your paper entitled "Insulin-I^{131} Metabolism in Human Subjects: Demonstration of Insulin Transporting Antibody in the Circulation of Insulin Treated Subjects" is not acceptable for publication in THE JOURNAL OF CLINICAL INVESTIGATION. – – – – – – – – – – – –

– – – – – – – – – – – – – – – The second major criticism relates to the dogmatic conclusions set forth which are not warranted by the data. The experts in this field have been particularly emphatic in rejecting your positive statement that the "conclusion that the globulin responsible for insulin binding is an acquired antibody appears to be inescapable". They believe that you have not demonstrated an antigen-antibody reaction on the basis of adequate criteria, nor that you have definitely proved that a globulin is responsible for insulin binding, nor that insulin is an antigen. The data you present are indeed suggestive but any more positive cleaim seems unjustifiable at present.

– –

Sincerely,

Stanley E. Bradley

Stanley E. Bradley, M.D.
Editor-in-Chief

Figure 2. Letter of rejection received from the *Journal of Clinical Investigation* concerning discoveries that would eventually be recognized by a Nobel Prize to Rosalind S. Yalow. Reprinted with permission of the Nobel Foundation. Copyright The Nobel Foundation, 1977

One of the two reviewers of *Nature* who read Robert F. Furchgott's highly original article describing "endothelium-dependent relaxation" expressed doubts about the validity of the experimental procedures and conclusions [FURCHGOTT, 1993]. Publication of this paper required considerable rebuttal, and the paper also had to be shortened. Yet as in previous instances, the findings reported in this manuscript turned out to be the discovery that earned its author a share of the 1998 Nobel Prize in Physiology or Medicine.

Paul C. Lauterbur shared the 2003 Nobel Prize in Physiology and Medicine for his work on magnetic resonance imaging. A seminal paper included crude images of two glass capillaries filled with water. The manuscript was initially rejected by *Nature*; however, protests proved successful and the paper was published in *Nature* in 1973 [LAUTERBUR, 2003, P. 248]. Almost thirty years later the journal publicly celebrated the article's appearance in its pages.

Both *Nature* and *Science* rejected one of the first reports by Kary B. Mullis concerning the polymerase chain reaction (PCR), which became the most widespread method for analyzing DNA [MULLIS, 1998, P. 105]. This was the discovery for which Mullis shared the 1993 Nobel Prize in Chemistry. Apparently the editors of *Science* had little faith in the revolutionary technique that was about to modernize DNA analysis with its practical applications, and believed that the paper would be more appropriate for a secondary journal. As a consequence the article appeared later in *Methods in Enzymology*.

Gerd Binnig and Heinrich Rohrer are famous for developing the scanning tunneling microscope, for which they received a share of the 1986 Nobel Prize in Physics. In their Nobel Lecture they remarked how often they had been told that they were addressing something that should "not have worked in principle" [BINNIG & ROHRER, 1986, P. 389]. Actually, their first successful experiment came in the spring of 1981. However, Rohrer told *Science* that the first attempt to publish the results failed when a referee found the paper "not interesting enough" [ROBINSON, 1986, P. 822].

The original publication in which Baruch S. Blumberg related Australia antigen with the etiologic agent of "viral" hepatitis did not elicit wide acceptance. Indeed, as Blumberg noted, there had been many previous reports of the identification of the agent causing hepatitis [BLUMBERG, 1977, P.19]. The referees initially rejected a longer paper by Blumberg and coworkers on the same topic, on the grounds that the authors were proposing another "candidate virus" and that there were already many of these around [BLUMBERG, 1977, P. 19]. This was the discovery for which Blumberg shared the 1976 Nobel Prize in Physiology or Medicine.

Twice in 1965 the *Journal of Chemical Physics* rejected the key paper that led to the 1991 Nobel Prize in Chemistry being awarded to Richard R. Ernst [ERNST, 1991]. The editors claimed that the contents were not original enough for publication in the journal. Consequently, Ernst had to publish his findings in the less known *Review of Scientific*

Instruments. His article described the use of single high-energy pulses of radio waves containing all frequencies, which would make atoms “flip”, instead of a gradual sweep with a spectrum of radio waves as had been used previously [GARFIELD, 1992, P. 5]. Varian, a well-known maker of scientific instruments, was reluctant to build a spectrometer that incorporated the novel Fourier transform concept [ERNST, 1991]. As Ernst would later confirm, even the authors themselves did not foresee that the simple concept they were proposing would revolutionize nuclear magnetic resonance [ERNST, 1983].

The *Journal of Biological Chemistry* declined to publish the Nobel Prize-winning work of Paul Boyer, as he acknowledged in an interview published in his university magazine [OLNEY, 2000] and in his Nobel lecture [BOYER, 1997]. The work awarded the 1997 Nobel Prize in Chemistry was the description of the molecular motor that creates cellular energy, and the biochemical pump that transports energy across cell membrane.

Leading professional journals refused to publish Louis J. Ignarro’s discovery that nitric oxide is crucial to life process, a discovery that was awarded a share of the 1998 Nobel Prize in Physiology or Medicine [OLNEY, 2000]. This discovery triggered an avalanche of research in many different laboratories around the world, Viagra being, perhaps, the best known application of his discovery [OLNEY, 2000].

William N. Lipscomb received the 1976 Nobel Prize in Chemistry for his studies on the structure of boranes. In an interview with E. Thomas Strom, Lipscomb recalled how the *Journal of the American Chemical Society* rejected the first manuscript in which he used the concept of pseudorotation to explain the structure of a boron hydride [STROM, 1989].

According to the Swedish Academy of Sciences, Eugene P. Wigner received a share of the 1963 Nobel Prize in Physics “for his contributions to the theory of the atomic nucleus and the elementary particles, particularly, through the discovery and application of fundamental symmetry principles.” One of his highly cited papers on symmetries dealing with unitary representations of the inhomogeneous Lorentz group was nevertheless rejected when first submitted for publication. Fortunately, John Von Neumann was so impressed that he had it published in the *Annals of Mathematics*. As Wigner pointedly remarked with regard to this unjustified rejection, “not all articles originally rejected by a journal prove to be valueless” [WIGNER, 1979, P. 297]. According to Wigner, the content of the paper proved to be useful both in physics (when applied to elementary particles) and in mathematics.

Herbert Kroemer received a share of the Nobel Prize in Physics in 2000 “for developing semiconductor heterostructures used in high-speed and opto-electronics.” He suggested the principle of the double heterostructure laser in 1963 and published it in the *Proceedings of the IEEE*. However, the paper was previously rejected by the journal *Applied Physics Letters* [KROEMER, 2000].

Richard Martin Willstätter was awarded the 1915 Nobel Prize in Chemistry for his researchers on plant pigments, especially chlorophyll. However, the *Berichte of the German Chemical Society* rejected his first article on this topic. This manuscript was two pages long and contained many analytical results; according to Willstätter the paper was never printed because he "could not accept the editors' stipulation that a section containing the essential conclusions had to be eliminated in order to forestall disagreements" [WILLSTÄTTER, 1965, P. 184].

According the official website of John Polanyi (http://www.utoronto.ca/jpolanyi/), a seminal report that described for the first time a large category of lasers based on vibrational energies in molecules was rejected by the *Physical Review Letters*. The journal rejected the paper as lacking scientific interest. This article was published in 1961 by *Journal of Chemical Physics* (identical text). According the press release from Swedish Academy of Sciences that announced the 1986 Nobel Prize in Chemistry, 'the method which (Polanyi) has developed can be considered as a first step towards the present more sophisticated, but also more complicated, laser-based methods for the study of chemical reaction dynamics' [ANONYMOUS, 1986].

Michael Smith received the half of the 1993 Nobel Prize in Chemistry for his fundamental contributions to the establishment of oligonucleiotide-based, site-directed mutageneis and its development of protein studies. According Smith account in an interview, the technique he used was considered so obscure it was rejected by the editors of the leading journal *Cell* [MUNRO, 2006].

The manuscript that reported findings concerning antibody response by Sir Frank MacFarlane Burnet was rejected by the journal to which it was originally submitted. The reason was that the manuscript lacked sufficient experimental basis [BURNET, 1968, P. 71]. The future Nobel Laureate pursued the topic, collected more data, and published his observations in an unrefereed monograph titled "The production of antibodies" [FENNER & CORY, 1997]. The discovery reported in the second edition of the monograph was awarded a share of the 1960 Nobel Prize in Physiology or Medicine.

Discussion

The above examples of accounts by Nobel Laureates give us an idea of how they perceived the negative reception by the scientific community of work that would eventually earn them a Nobel Prize. Some instances exemplify the phenomenon of delayed recognition [GARFIELD, 1989A; 1989B; 1990]. When this happens the discovery may go unnoticed for years until the scientific community begins to recognize its value or the scope of its implications, reflected in the attention the work receives later – a clear sign that it has been "discovered" by the scientific community. Curiously enough, the article which falls victim to this phenomenon is usually published in widely read journals, therefore the delayed recognition phenomenon cannot be attributed to lack of access to scientific information. For example, the two papers authored by Allan Cormack and published in 1963 and 1964 (see Appendix) were published in the well-known *Journal of Applied Physics*. A citation analysis revealed that these articles, in which Cormack presented his award-winning work, received only 7 citations until 1973. Thereafter the citation rate increased [GARFIELD, 1980, Table 4].

In other instances a Nobel class paper was rejected by journal editors or referees. In some cases rejection by a referee could be considered justifiable and explainable. For example, *Physical Review Letters* rejected the first theory of the fractional quantum Hall effect by Nobel Prize winner Robert B. Laughlin because a referee discovered mistakes [LAUGHLIN, 1998]. Obviously this was not a Nobel class paper, although a future Nobel Laureate wrote it. Professor Furchgott also admitted that the editor of *Nature* was right in advising him to shorten his Nobel Prize manuscript [FURCHGOTT, 1993, V3]. Sometimes scientists choose the wrong journal in terms of topics covered, presentation style, and other factors. Accordingly, there are instances where an initial objection against publishing Nobel class papers seems justified. In addition, initial rejection can stimulate deeper thinking and more careful research. This happened, for example, to Frank MacFarlane Burnet when one of his first papers on the work awarded the Nobel Prize was rejected by the editor of the journal as not having sufficient experimental basis [BURNET, 1968, P. 71]. However, most instances summarized above deal with genuine resistance to scientific discovery, so it is illuminating to ascertain some of the reasons why such resistance exists in the first place.

A possible explanation for peer resistance to scientific discovery lies in the fact that new theories or discoveries often clash with orthodox viewpoints held by the referees. It seems that skepticism towards new theories and discoveries is not rare in science [NISSANI, 1995]. Nobel Laureate Stanley B. Prusiner confirmed this view when he wrote, "while it is quite reasonable for scientists to be skeptical of new ideas that do no fit within the accepted realm of scientific knowledge, the best science often emerges from situations where results carefully obtained do not fit within the accepted paradigms" [PRUSINER, 1997]. In some instances, objections were related with terminological or conceptual problems – objections that reflect viewpoints and theoretical constructs related to paradigms.

In other instances the problem was that referees did not appreciate the potential or the interest of the new discoveries. This can happen, for example, because some discoveries are not clearly derived from accepted knowledge or related to the current body of knowledge. The fact is that some of the articles reporting new findings or discoveries were initially rejected but would later earn their authors much-deserved recognition along with the highest accolade scientists aspire to. This outcome of peer review raises important questions about current publishing policies which govern the dissemination of new information.

Conclusions

A new theory or discovery does not fully exist until it goes beyond the walls of the office or laboratory in which it was conceived or demonstrated. New theories and discoveries need to be announced and then evaluated by other scientists. Thus any scientific discovery involves a social component linked to the communication process. Undeniably, the most common way to communicate a given finding, theory or discovery is through its publication in articles submitted to learned journals. It may happen that the editors and referees who read articles reporting a novel discovery are not able to assess the value of innovative work. However, sometimes it is hard to discern the difference between a potentially useful, innovative discovery or technique and one which is not significant.

Some of the previous instances of resistance demonstrate that the common wisdom concerning the scientific publishing system may sometimes be wrong. For example, in his well known article titled "On the scientific method: its practice and pitfalls", Ayala noted that, "peer review does not thwart new ideas. Journal editors and the 'scientific establishment' are not hostile to new discoveries. Science thrives on discovery and scientific journals compete to publish new breakthroughs" [AYALA, 1994, P. 240]. However, critics often argue that peer review operates to regulate paradigmatic science (in the Kuhnian sense) rather than to welcome brand new knowledge. Peer review has been shown to be plagued with many imperfections. Judging from some of the previously discussed examples and other published findings [SOMMER, 2001], there is a real risk that evidence contrary to the established views can be suppressed or disregarded. Editors and referees of scientific journals should be aware of critical analyses of peer review in order to avoid the "reviewer's nightmare" of rejected discoveries that are later awarded the Nobel prize.

The above instances illustrate the fact that persistence may be needed to obtain recognition for work that is innovative and revolutionary. According to the Kuhnian view, scientists tend to be conservative and to maintain the current paradigm. Discoveries that are awarded the Nobel prize are usually revolutionary, so it is not surprising that the scientific community is often initially skeptical of them. Scientists who challenge dominant paradigms should be prepared to face skepticism and rejection.

Some science sociologists use the term "scientific controversies" to denote scientific conflicts that arise as a result of discrepancy among scientists regarding different theories or different viewpoints on a theory, a certain discovery, or a research field. However, another type of negative outcome of publication that can lead to delayed recognition may be when innovative work receives no reaction and no response, but is simply overlooked, disregarded or ignored. In these cases there is not much room for controversy.

Scientists questioning a widely accepted paradigm can find it difficult to gain a hearing: questions about fundamentals are rarely welcomed. The instances studied here illustrate that scientists with something truly original to communicate often have to fight against the silence, the lack of interest, and as a result the absence of citations and recognition. Silence and lack of attention is even worse than negative reactions because negative reactions, at least, attract the attention of others who, in turn, might find the new paradigm convincing. Delayed recognition is not rare for very important discoveries: peers tend to be slow in recognizing their impact.

Due to the nonsystematic nature of the sample of reactions to rejection used here, the results of this analysis cannot be generalized to all Nobel Laureates. However, this analysis could be extended by exploring the archives of the journals that rejected papers written by Nobel Laureates. The examination of editorial correspondence between the journal and the scientists could yield more insights into the process of evaluation of Nobel class discoveries. However, obtaining this material could be difficult given the confidential nature of the refereeing process. Another source of relevant data for further analysis may lie in the strategies used by Nobel Laureates to overcome the skepticism and resistance by peers to their discoveries. This is the approach we used in a previous analysis of the views of scientists who authored highly cited papers that were originally met with resistance [CAMPANARIO & ACEDO, 2007].

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Appendix
Nobel laureates who experienced scepticism or delayed recognition concerning their award winning discoveries

George W. Beadle (Physiology or Medicine, 1958) *'...In retrospect one wonders how such important findings could be so thoroughly unappreciated and disregarded for so many years. Obviously the time was not ready for their proper appreciation. Even in 1941 when Tatum and I first reported our induced genetic-biochemical lesions in Neurospora few people were ready to accept what seemed to us to be a compelling conclusion...the skeptics were many, the converts few...even at the time of the 1951 Cold Spring Harbor Symposium on Quantitative Biology the skeptics were still many...'* [BEADLE, 1974, p. 11]
Baruj Benacerraf (Physiology or Medicine, 1980) *'Although Kenneth Rock and I provided biological evidence, based in the phenomenon of antigen competition in support of our hypothesis of the specific interaction between processed antigen and MHC molecules, our ideas were initially received with considerable scepticism on the part of MHC geneticists such as Jan Klein.'* [BENACERRAF, 1991, p.15]
Günter Blobel (Physiology or Medicine, 1999) *Interviewer:* Well, over the years there's been some skepticism about your work. Do you feel vindicated now? *Dr. Blobel:* I do *Interviewer:* In what way? *Dr. Blobel:* Well, there was a particular aspect of it for instance, a channel that we postulated that proteins travel across membranes, and that was a concept that was not easily accepted [IFILL, 1999]
Mario R. Capecchi (Physiology or Medicine, 2007) *"In 1980, we submitted a grant proposal to the National Institutes of Health to test the feasibility of gene targeting in mammalian cells; these experiments were rejected on the grounds that there was only a vanishingly small probability that the newly introduced DNA would find its matching sequence within a host cell genome… By 1984 we had good evidence that gene targeting in cultured mammalian cells was indeed possible. At this time I resubmitted our grant to the same National Institutes of Health study section that had rejected our earlier grant proposal and their critique began with the phrase "We are glad that you didn't follow our advice."* [CAPECCHI, 2001, p. 1087]
Allan MacLeod Cormack (Physiology or Medicine, 1979) *'Publication took place in 1963 and 1964. There was virtually no response. The most interesting request for a reprint came from a Swiss Centre for Avalanche Research. The method would work for deposits of snow on mountains if one could get either the detector or the source into the mountain under the snow!'* [CORMACK, 1979, p. 554-555]
Peter C. Doherty (Physiology or Medicine, 1996) *'...at the stage that this review was written, we found ourselves almost totally unable to generate any support at all for the idea that MHC genes were coding directly for the T cell receptor.'* [DOHERTY, 1983, no page number] *'...our ideas both contradicted the accepted North American model for the role of immune response genes, and turned the perception of the transplantation system on its head....Evidently some were also infuriated by what we were saying.'* [DOHERTY, 1996]
Alexander Fleming (Physiology or Medicine, 1945) *'In 1929, I published the results which I have briefly given to you and suggested that it would be useful for the treatment of infections with sensitive microbes. I referred again to penicillin in one or two publications up to 1936 but few people paid any attention. It was only when some 10 years later after the introduction of sulphonamide had completely changed the medical mind in regard to chemotherapy of bacterial infections, and after Dubos had shown that a powerful antibacterial agent, gramicidin, was produced by certain bacteria that my co-participators in this Nobel Award, Dr. Chain and Sir Howard Florey, took up the investigation.'* [FLEMING, 1945, p. 92]

Denis Gabor (Physics, 1971) *'For my part, with my collaborator W.P. Goss, I constructed a holographic interference microscope...The response of the optical industry to this was so disappointing that we did not publish a paper on it until 11 years later, in 1966. Around 1955 holography went into a long hibernation.'* [GABOR, 1971, p. 18]
Sheldon Lee Glashow (Physics, 1979) *'When we spoke, in 1974, of the unification of all elementary particle forces within a simple gauge group, and of the predicted instability of the proton, we were regarded as mad. How things change!'* [GLASHOW, 1979]
Corneille Heymans (Physiology or Medicine, 1938) *'The discovery of peripherally located chemoreceptors acting reflexly on respiration was, however, not accepted without much resistance coming from several sources and we also had to undergo what Claude Bernard predicted: 'Quand vous avez trouvé quelque chose de nouveau, on commence par dire que ce n'est pas vrai, puis lorsque la vérité de ce que vous avez avancé devient absolument évidente, on dit que ce n'est pas vous qui l'avez trouvé'.'* [HEYMANS, 1963, p. 7-8]
Jerome Karle (Chemistry, 1985) *'I also deeply appreciate the supportive atmosphere provided by the Naval Research Laboratory. This was especially helpful during the early 1950's when a large number of fellow-scientists did not believe a word we said.'* [KARLE, 1985]
Rita Levi-Montalcini (Physiology or Medicine, 1986) *'In spite of, or perhaps because of its most unusual and almost extravagant deeds in living organisms and in-vitro systems, NGF did not at first find enthusiastic reception by the scientific community, as also indicated by the reluctance of other investigators to engage in this line of research.'* [LEVI-MONTALCINI, 1986, p. 357]
Barry J. Marshall (Physiology or Medicine, 2005) *"There was interest and support from a few but most of my work was rejected for publication and even accepted papers were significantly delayed. I was met with constant criticism that my conclusions were premature and not well supported. When the work was presented, my results were disputed and disbelieved, not on the basis of science but because they simply could not be true. It was often said that no one was able to replicate my results. This was untrue but became part of the folklore of the period. I was told that the bacteria were either contaminants or harmless commensals."* [MARSHALL, 2005]
Stanley B. Prusiner (Physiology or Medicine, 1997) *'Publication of this manuscript, in which I introduced the term 'prion', set off a firestorm. Virologists were generally incredulous and some investigators working on scrapie and CJD were irate.'* *'Since the press was usually unable to understand the scientific arguments and they are usually keen to write about any controversy, the personal attacks of the nay Sayers at times became very vicious.'* [PRUSINER, 1997]
Ernst Ruska (Physics, 1986) *'Of course, at that time our approach was not taken seriously by most of experts. They rather regarded it as a pipe dream. I myself felt that it would be very hard to overcome the efforts still needed-mainly the problem of specimen heating.'* [RUSKA, 1986, p. 362] *'In spite of these more recent publications, it took us three years to be successful in our quest for financial support through the professional assessment of Helmut Ruska's former clinical teacher, Professor Dr. Richard Siebeck, Director of the I. Medical Clinic of the Berlin Charite.'* [RUSKA, 1986, p. 367]
William Shockley (Physics, 1956) *'The first good junction transistor was presented publicly in 1950 when I described it at an international semiconductor conference. It was a high-power, low-frequency device, and aroused so little interest that it was omitted from the report of the conference.'* [SHOCKLEY, 1972, p. 690-691]

Howard M. Temin (Physiology or Medicine, 1975) *'Since 1963-64, I had been proposing that the replication of RNA tumour 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...that the discovery took so many years might indicate the resistance to this hypothesis.'* [TEMIN, 1977, p. 159]
Charles H. Townes (Physics, 1964) *'One day...Raby and Kusch, the former and current chairmen of the department, both of them Nobel Laureates for their work with atomic and molecular beans and with a lot of weight behind their opinions, came into my office and sat down. They were worried. Their research depended on support from the same source as did mine. 'Look', they said, 'you should stop the work you are doing. You're wasting money. Just stop'.'* [LAMB, SCHLEICH, SCULLY & TOWNES, 1999, p. S266]
Frits Zernike (Physics, 1953) *'With the phase contrast method still in the first somewhat primitive stage, I went in 1932 to the Zeiss Works in Jena to demonstrate it. It was not received with such enthusiasm as I had expected. Worst of all was one of the oldest scientific associates, who said 'If this had any practical value, we would ourselves have invented it long ago.' Long ago, indeed! The great achievements of the firm in practical and theoretical microscopy were all due to their famous leader Ernst Abbe and dated from before 1890, the year in which Abbe became sole proprietor of the Zeiss Works.'* [ZERNIKE, 1953, p. 242]