

Corrections

BIOPHYSICS AND COMPUTATIONAL BIOLOGY

Correction for “Surface residues dynamically organize water bridges to enhance electron transfer between proteins,” by Aurélien de la Lande, Nathan S. Babcock, Jan Řezáč, Barry C. Sanders, and Dennis R. Salahub, which appeared in issue 26, June 29, 2010, of *Proc Natl Acad Sci USA* (107:11799–11804; first published June 14, 2010; 10.1073/pnas.0914457107).

The authors note that Table 1 appeared incorrectly. The corrected table appears below.

Additionally, the authors note that on page 11803, right column, first paragraph, lines 7–10, “A friction coefficient of

15 ps⁻¹ and a bath temperature of 298 K were used to propagate the equations of motion within the Langevin approach. Periodic boundary conditions were applied to simulate a continuous medium.” should instead appear as “A friction coefficient of 10 ps⁻¹ and a bath temperature of 298 K were used to propagate the equations of motion within the Langevin approach. No boundary conditions were imposed; the system freely evolved in vacuum.”

These errors do not affect the conclusions of the article.

Table 1. Expectation values for $\langle \epsilon_{\text{tot}} \rangle$ and the ratios $r_k^{\text{mut}} = \langle \epsilon_{\text{tot}}^2 \rangle^{\text{mut}} / \langle \epsilon_{\text{tot}}^2 \rangle^{\text{wt}}$ and $r_k^{\text{mut}} = k_{\text{ET}}^{\text{mut}} / k_{\text{ET}}^{\text{wt}}$ obtained from packing density and pathway analyses*

		Wild type	M51L	M51K	M51A	M51C
r_k^{mut}	(Experiment)	1.0	0.68	0.49	0.13	—
$\langle \epsilon_{\text{tot}} \rangle \times 10^3$	(Pathway analysis)	0.90 ± 0.03	0.47 ± 0.03	0.61 ± 0.02	0.65 ± 0.02	0.73 ± 0.02
r_e^{mut}	(Pathway analysis)	1.0	0.36 ± 0.04	0.52 ± 0.04	0.57 ± 0.04	0.76 ± 0.05
$\langle \epsilon_{\text{tot}} \rangle \times 10^3$	(Packing density)	0.70 ± 0.03	0.42 ± 0.04	0.51 ± 0.03	0.62 ± 0.05	1.03 ± 0.05
r_e^{mut}	(Packing density)	1.0	0.56 ± 0.09	0.76 ± 0.07	0.89 ± 0.15	2.29 ± 0.26
P_{hb}		0.53	0.15	0.19	0.18	0.16
τ (ns ⁻¹)		0.23	0.45	1.20	0.50	2.25

*The uncertainties account for the sampling errors of the computational protocol (see *SI Text*). Experimental rates k_{ET} were obtained from k_3 (at 30 °C) in table 3 of ref. 15 (M51C was not reported). P_{hb} is the unit-normalized likelihood that a water molecule is simultaneously hydrogen bonded to both the MADH Ser β 56 O and amicyanin His 95 HE2 atoms during our simulations. The turnover τ of the bridging water molecule is defined as the number of different water molecules that participate in pathway A_1 divided by the length of the simulation in nanoseconds.

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MEDICAL SCIENCES

Correction for “Misconduct accounts for the majority of retracted scientific publications,” by Ferric C. Fang, R. Grant Steen, and Arturo Casadevall, which appeared in issue 42, October 16, 2012, of *Proc Natl Acad Sci USA* (109:17028–

17033; first published October 1, 2012; 10.1073/pnas.1212247109).

The authors note that Table 3 appeared incorrectly. The corrected table appears below.

Table 3. Most Cited Retracted Articles

First author	Journal	Year published	Year retracted	Times cited*	Reason for retraction
Wakefield	<i>Lancet</i>	1998	2004; 2010	758	Fraud
Reyes	<i>Blood</i>	2001	2009	740	Error
Fukuhara	<i>Science</i>	2005	2007	686	Error
Nakao	<i>Lancet</i>	2003	2009	626	Fraud
Chang	<i>Science</i>	2001	2006	512	Error
Kugler	<i>Nature Medicine</i>	2000	2003	494	Fraud
Rubio	<i>Cancer Research</i>	2005	2010	457	Error
Gowen	<i>Science</i>	1998	2003	395	Fraud
Makarova	<i>Nature</i>	2001	2006	375	Error
Hwang	<i>Science</i>	2004	2006	368	Fraud
Potti	<i>The New England Journal of Medicine</i>	2006	2011	361	Fraud
Brugger	<i>The New England Journal of Medicine</i>	1995	2001	336	Fraud
Van Parijs	<i>Immunity</i>	1999	2009	330	Fraud
Potti	<i>Nature Medicine</i>	2006	2011	328	Fraud
Schön	<i>Science</i>	2000	2002	297	Fraud
Chiu	<i>Nature</i>	2005	2010	281	Error
Cooper	<i>Science</i>	1997	2005	264	Fraud
Le Page	<i>Cell</i>	2000	2005	262	Error
Kawasaki	<i>Nature</i>	2004	2006	243	Fraud
Hwang	<i>Science</i>	2005	2006	234	Fraud

*As of June 22, 2012

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Misconduct accounts for the majority of retracted scientific publications

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A detailed review of all 2,047 biomedical and life-science research articles indexed by PubMed as retracted on May 3, 2012 revealed that only 21.3% of retractions were attributable to error. In contrast, 67.4% of retractions were attributable to misconduct, including fraud or suspected fraud (43.4%), duplicate publication (14.2%), and plagiarism (9.8%). Incomplete, uninformative or misleading retraction announcements have led to a previous underestimation of the role of fraud in the ongoing retraction epidemic. The percentage of scientific articles retracted because of fraud has increased ~10-fold since 1975. Retractions exhibit distinctive temporal and geographic patterns that may reveal underlying causes.

bibliometric analysis | biomedical publishing | ethics | research misconduct

The number and frequency of retracted publications are important indicators of the health of the scientific enterprise, because retracted articles represent unequivocal evidence of project failure, irrespective of the cause. Hence, retractions are worthy of rigorous and systematic study. The retraction of flawed publications corrects the scientific literature and also provides insights into the scientific process. However, the rising frequency of retractions has recently elicited concern (1, 2). Studies of selected retracted articles have suggested that error is more common than fraud as a cause of retraction (3–5) and that rates of retraction correlate with journal-impact factor (6). We undertook a comprehensive analysis of all retracted articles indexed by PubMed to ascertain the validity of the earlier findings. Retracted articles were classified according to whether the cause of retraction was documented fraud (data falsification or fabrication), suspected fraud, plagiarism, duplicate publication, error, unknown, or other reasons (e.g., journal error, authorship dispute).

Results

Causes of Retraction. PubMed references more than 25 million articles relating primarily to biomedical research published since the 1940s. A comprehensive search of the PubMed database in May 2012 identified 2,047 retracted articles, with the earliest retracted article published in 1973 and retracted in 1977. Hence, retraction is a relatively recent development in the biomedical scientific literature, although retractable offenses are not necessarily new. To understand the reasons for retraction, we consulted reports from the Office of Research Integrity and other published resources (7, 8), in addition to the retraction announcements in scientific journals. Use of these additional sources of information resulted in the reclassification of 118 of 742 (15.9%) retractions in an earlier study (4) from error to fraud. A list of 158 articles for which the cause of retraction was reclassified because of consultation of secondary sources is provided in Table S1. For example, a retraction announcement in *Biochemical and Biophysical Research Communications* reported that “results were derived from experiments that were found to have flaws in methodological execution and data analysis,” giving the impression of error (9). However, an investigation of this article conducted by Harvard University and reported to the Office of Research Integrity indicated that “many instances of data fabrication and falsification were found” (10). In another example, a retraction notice

published by the authors of a manuscript in the *Journal of Cell Biology* stated that “In follow-up experiments . . . we have shown that the lack of FOXO1a expression reported in figure 1 is not correct” (11). A subsequent report from the Office of Research Integrity states that the first author committed “research misconduct by knowingly and intentionally falsely reporting . . . that FOXO1a was not expressed . . . by selecting a specific FOXO1a immunoblot to show the desired result” (12). In contrast to earlier studies, we found that the majority of retracted articles were retracted because of some form of misconduct, with only 21.3% retracted because of error. The most common reason for retraction was fraud or suspected fraud (43.4%), with additional articles retracted because of duplicate publication (14.2%) or plagiarism (9.8%). Miscellaneous reasons or unknown causes accounted for the remainder. Thus, for articles in which the reason for retraction is known, three-quarters were retracted because of misconduct or suspected misconduct, and only one-quarter was retracted for error.

Temporal Trends. A marked recent rise in the frequency of retraction was confirmed (2, 13), but was not uniform among the various causes of retraction (Fig. 1A). A discernible rise in retractions because of fraud or error was first evident in the 1990s, with a subsequent dramatic rise in retractions attributable to fraud occurring during the last decade. A more modest increase in retractions because of error was observed, and increasing retractions because of plagiarism and duplicate publication are a recent phenomenon, seen only since 2005. The recent increase in retractions for fraud cannot be attributed solely to an increase in the number of research publications: retractions for fraud or suspected fraud as a percentage of total articles have increased nearly 10-fold since 1975 (Fig. 1B).

Geographic Origin and Impact Factor. Retracted articles were authored in 56 countries, and geographic origin was found to vary according to the cause for retraction (Fig. 2). The United States, Germany, Japan, and China accounted for three-quarters of retractions because of fraud or suspected fraud. China and India collectively accounted for more cases of plagiarism than the United States, and duplicate publication exhibited a pattern similar to that of plagiarism. The relationship between journal impact factor and retraction rate was also found to vary with the cause of retraction. Journal-impact factor showed a highly significant correlation with retractions because of fraud or error but not with those because of plagiarism or duplicate publication (Fig. 3A–C). Moreover, the mean impact factors of journals retracting articles

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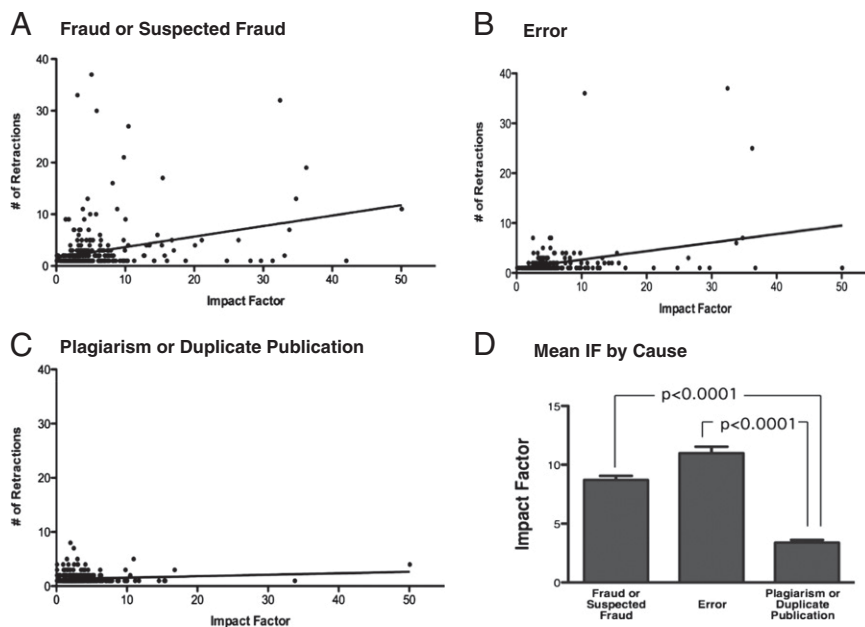


Fig. 3. Relation of journal-impact factor to retractions for fraud or suspected fraud, error, and plagiarism, or duplicate publication. Journal-impact factor showed a highly significant correlation with the number of retractions for fraud or suspected fraud (A) ($n = 889$ articles in 324 journals, $R^2 = 0.08664$, $P < 0.0001$) and error (B) ($n = 437$ articles in 218 journals, $R^2 = 0.1142$, $P < 0.0001$), and a slight correlation with the number of retractions for plagiarism or duplicate publication (C) ($n = 490$ articles in 357 journals, $R^2 = 0.01420$, $P = 0.0243$). The mean journal-impact factor of articles retracted because of fraud/suspected fraud or error was significantly different from that of papers retracted because of plagiarism or duplicate publication (D) (error bars \pm SEM, $P < 0.0001$).

of Research Integrity, *Retraction Watch*, news media, and other public records. The US Office of Research Integrity was formed in 1992 and is charged with the oversight of misconduct allegations involving federally sponsored research. As the consideration of secondary sources led to changes in the perceived cause of retraction in 158 instances (Table S1), we conclude that for many retractions, the retraction notice is insufficient to ascertain the true cause of a retraction.

We further note that not all articles suspected of fraud have been retracted. The *Lancet* and *British Medical Journal* expressed serious reservations about the validity of the Indo-Mediterranean Diet Heart Study after the primary author was unable to present original records to document ethics review and informed consent (18, 19), yet the original articles have not been retracted (20, 21). Several articles authored by Mark Spector when he was working in the laboratory of Efraim Racker remain in the literature (22, 23), despite documentation that Spector committed data fabrication (24). R. K. Chandra was found to have committed fraud in the performance of clinical trials, but only a single article was retracted (25), even though considerable evidence was obtained to suggest that other publications were also fraudulent (26). Therefore, the current number of articles retracted because of fraud represents an underestimation of the actual number of fraudulent articles in the literature.

Although some retraction announcements are specific and detailed, many are uninformative or opaque. In 119 instances, no information regarding the reason for retraction was provided by the journal. Announcements are often written by the authors of the retracted article themselves (27), who may be understandably reluctant to implicate themselves in misconduct. Furthermore, investigation of suspected misconduct is a lengthy process, and retraction notices are frequently made before the full results of investigations are available. Among 285 investigations concluded by the Office of Research Integrity from 2001 to 2010, the length of investigation averaged 20.48 mo in duration and ranged up to more than 9 y (28). Policies regarding retraction announcements vary widely among journals, and some, such as the *Journal of Biological*

Chemistry, routinely decline to provide any explanation for retraction. These factors have contributed to the systematic underestimation of the role of misconduct and the overestimation of the role of error in retractions (3, 4), and speak to the need for uniform standards regarding retraction notices (5).

Differences in the temporal and geographic patterns of retraction according to cause (Figs. 1A and 2) militate against a simple explanation for retractions. One factor is the increased detection of misconduct. The first discernible increase in retractions followed the formation of the Office of Scientific Integrity (the predecessor of the Office of Research Integrity) and passage of the Whistleblower Protection Act in 1989. The recent increase in the incidence of retractions and the differing patterns by region (Fig. 2) argue that incentives may vary with the type of misconduct. Most articles retracted for fraud have originated in countries with longstanding research traditions (e.g., United States, Germany, Japan) and are particularly problematic for high-impact journals. In contrast, plagiarism and duplicate publication often arise from countries that lack a longstanding research tradition, and such infractions often are associated with lower-impact journals (Fig. 3 and Table 1). A highly significant correlation was found between the journal-impact factor and the number of retractions for fraud or suspected fraud and error (Fig. 3A and B); the mean impact factor was found to be significantly higher for articles retracted for fraud, suspected fraud, or error, compared with those retracted for plagiarism or duplicate publication (Fig. 3D). An association between impact factor and retraction for fraud or error has been noted previously (4, 6, 29, 30). This finding may reflect the greater scrutiny accorded to articles in high-impact journals and the greater uncertainty associated with cutting-edge research. Alternatively, the disproportionately high payoffs to scientists for publication in prestigious venues can be an incentive to perform work with excessive haste (31) or to engage in unethical practices (4). The modest correlation between impact factor and time-to-retraction argues against an explanation based on increased scrutiny alone, but the higher proportion of fraud in highly

Table 2. Mean time-to-retraction by category

Cause of retraction	<i>n</i>	Months to retract (Mean)	SD
All causes*	2,047	32.9	34.2
Fraud (fabrication/falsification)	697	46.8	38.4
Suspected fraud	192	29.4	30.0
Plagiarism	200	26.0	32.6
Duplicate publication	290	27.0	30.1
Error	437	26.0	28.0
Other	108	19.8	31.1
Unknown	182	22.1	25.4

*Some articles fall into more than one category.

between time-to-retraction and impact factor (Fig. 4B) suggests that the greater visibility and enhanced scrutiny of high-impact journals may contribute to more rapid retraction of fraudulent papers by these journals, although the effect appears to be quite modest.

Most articles by authors with large numbers of retractions (Table S2) were retracted because of misconduct, and these include some of the most notorious cases in the history of research ethics. The Mori case (Fig. S2) demonstrates that fraudulent articles can go undetected for many years. Such cases may be revealed only fortuitously when exposed by an attentive reviewer or whistleblower (40). Twelve of Mori's retracted articles had been in the literature for 5 y or more, demonstrating that the impact of serial retractions on the average time-to-retraction can be substantial.

In conclusion, a comprehensive review of 2,047 articles retracted from the biomedical literature reveals that misconduct has played a more prominent role than previously appreciated. Our findings underscore the importance of vigilance by reviewers, editors, and readers, and investigations by institutions, government agencies, and journalists in identifying and documenting research misconduct. Furthermore, our findings suggest a need for increased attention to ethics in the training of scientists. However, this attention alone is unlikely to be successful in curbing poor research practices.

The rise in the rate of retractions raises concern about the health of the scientific enterprise itself (32). Although articles

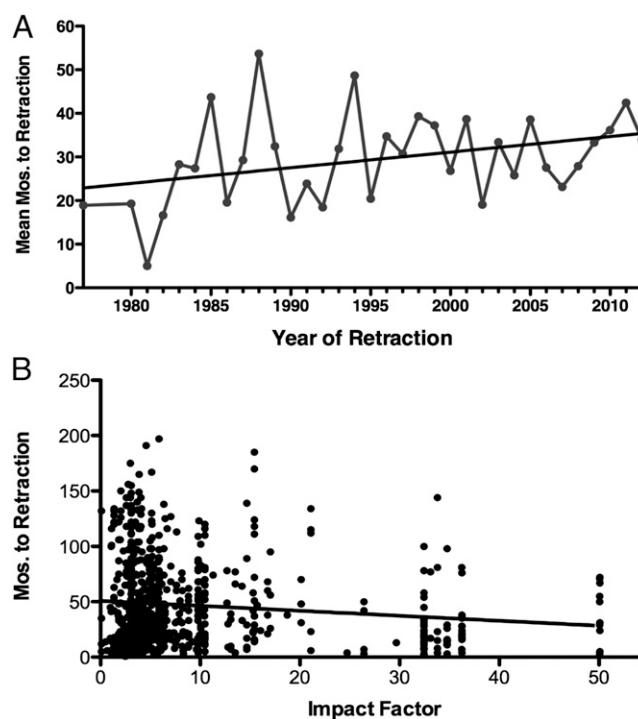


Fig. 4. (A) Time-to-retraction as a function of year of retraction. $R^2 = 0.1236$, $P = 0.0414$. (B) Time-to-retraction as a function of impact factor. Journal-impact factor correlated inversely with time-to-retraction for articles retracted because of fraud ($n = 697$, $R^2 = 0.01441$, $P = 0.0015$) but not other causes.

retracted because of fraud represent a very small percentage of the scientific literature (Fig. 1B), it is important to recognize that: (i) only a fraction of fraudulent articles are retracted; (ii) there are other more common sources of unreliability in the literature (41–44); (iii) misconduct risks damaging the credibility of science; and (iv) fraud may be a sign of underlying counterproductive incentives that influence scientists (45, 46). A better

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Le Page	<i>Cell</i>	2000	2005	262	Error
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*As of June 22, 2012.

understanding of retracted publications can inform efforts to reduce misconduct and error in science.

Given that most scientific work is publicly funded and that retractions because of misconduct undermine science and its impact on society, the surge of retractions suggests a need to reevaluate the incentives driving this phenomenon. We have previously argued that increased retractions and ethical breaches may result, at least in part, from the incentive system of science, which is based on a winner-takes-all economics that confers disproportionate rewards to winners in the form of grants, jobs, and prizes at a time of research funding scarcity (32, 46, 47). We have also proposed a set of reforms to strengthen the scientific enterprise, ranging from improved training of scientists to the identification of mechanisms to provide more consistent funding for science (32, 46). Solutions to address the specific problem of retractions may include the increased use of checklists by authors and reviewers, improved training in logic, probability and statistics, an enhanced focus on ethics, the formation of a centralized database of scientific misconduct, the establishment of uniform guidelines for retractions and retraction notices, and the development of novel reward systems for science (32). Dedicated national agencies, such as the US Office for Research Integrity, can play an invaluable role in supporting and overseeing institutional investigations of alleged misconduct. We hope that the

present study will prompt discussion among scientists and the society they serve to find measures to improve the quality and reliability of the scientific literature.

Methods

The database used for this study was compiled from a search of all articles indexed by PubMed as retracted publications in English on May 3, 2012. Articles were classified according to cause of retraction as fraud, suspected fraud, error, plagiarism, duplicate publication, other, or unknown on the basis of retraction announcements. In addition, retracted articles were cross-checked against the annual reports of the Office of Research Integrity. An internet search using the Google search engine was performed to seek additional information regarding retracted articles for which the reason for retraction remained unclear, and included *Retraction Watch*, news media, and other public records. In one case, an author was contacted to clarify a published retraction notice. Each classification decision was independently reviewed by all authors and any discrepancies were resolved. Impact factors were based on the 2011 edition of *Journal Citation Reports Science Edition* (Thomson Reuters, released June 28, 2012) (48), and 5-y impact factors were used when available. In one case (*Acta Crystallographica A*), the 2011 impact factor (2.076) was used instead of the 5-y impact factor (30.646), because the latter was felt to be anomalous. Journals without an impact factor were assigned a value of 0.1. Statistical analyses were performed using Prism (GraphPad Software).

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