Analysis and Correction of Inappropriate Image Duplication:

2	The Molecular and Cellular Biology Experience
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19 Abstract

The present study analyzed 960 papers published in Molecular and Cellular Biology (MCB) from 20 2009-2016 and found 59 (6.1%) to contain inappropriately duplicated images. The 59 instances 21 22 of inappropriate image duplication led to 42 corrections, 5 retractions and 12 instances in which 23 no action was taken. Our experience suggests that the majority of inappropriate image duplications result from errors during figure preparation that can be remedied by correction. 24 25 Nevertheless, ~10% of papers with inappropriate image duplications in MCB were retracted. If 26 this proportion is representative, then as many as 35,000 papers in the literature are candidates 27 for retraction due to image duplication. The resolution of inappropriate image duplication concerns after publication required an average of 6 h of journal staff time per published paper. 28 29 MCB instituted a pilot program to screen images of accepted papers prior to publication that 30 identified 12 manuscripts (14.5% out of 83) with image concerns in two months. The screening 31 and correction of papers before publication required an average of 30 min of staff time per problematic paper. Image screening can identify papers with problematic images prior to 32 33 publication, reduces post-publication problems and requires significantly less staff time than the 34 correction of problems after publication.

36 Introduction

37 Recently we reported an analysis of 20,000 papers from 40 biomedical journals, published over a period of 20 years, in which approximately 1 in 25 papers contained at least one 38 39 inappropriately duplicated image (1). The frequent occurrence of inappropriate image 40 duplication in published papers is a major concern, because it reduces the integrity and credibility of the biomedical literature. At one end of the spectrum, inappropriate image 41 42 duplications caused by simple errors in constructing figures raise concerns about the attention given to the preparation and analysis of data, while at the other end of the spectrum, problems 43 resulting from deliberate image manipulation and fabrication indicate misconduct. Increased 44 45 awareness of such image duplications has resulted from post-publication peer review websites such as PubPeer and discussions on social media (2). Whereas simple errors found in 46 47 published studies can be addressed by a correction, deliberate image manipulation or 48 fabrication can lead to retraction of a paper (3).

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Inappropriate image duplications undermine the quality of the literature and can necessitate a 50 51 considerable investment of time and resources by authors and journals when discovered after 52 publication of a scientific paper. However, we presently lack information on the causes for the inappropriate image duplications, since neither cause nor intent can be reliably inferred from 53 54 inspecting images in published articles. We categorized inappropriate image duplications as 55 simple duplications (category 1), shifted duplications (category 2) or duplications with alterations (category 3), with category 1 most likely to result from honest error, while categories 2 and 3 56 57 have an increased likelihood of resulting from outright falsification or fabrication. A follow-up analysis of a subset of these papers found that several variables including academic culture. 58 59 peer control, cash-based publication incentives and national misconduct policies were 60 significantly associated with duplications in categories 2 and 3, suggesting that these variables

might affect scientific integrity (4). In the present study, we sought to determine whether an
investment by a journal to scan images in accepted manuscripts prior to publication could
resolve image concerns in less time that was required to address these issues after publication.

65 The mission of the journals published by the American Society for Microbiology (ASM) is to publish high-quality scientific articles that have been rigorously peer reviewed by experts and 66 evaluated by academic editors (5). In 2013, the ASM journal Molecular and Cellular Biology 67 68 (MCB) instituted a program to analyze the figures in all accepted manuscripts before publication 69 (6), modeled after a similar program used by the Journal of Cell Biology (7, 8). In this study, we 70 applied the approach used previously (1) to published papers in the journal MCB, and followed 71 up the findings with a process that included contacting the authors of the papers. Consequently, 72 we are now able to provide information as to how inappropriate image duplications occur. In 73 addition, a set of manuscripts accepted for publication in MCB was inspected prior to publication for spliced, beautified, or duplicated images. For both sets of papers, the time and effort spent 74 75 on following up on these papers was recorded. The results provide new insights into the 76 prevalence, scope and seriousness of the problem of inappropriate image duplication in the 77 biomedical literature.

78 Methods

Published papers set. Papers published in 2009-2016 in MCB were inspected visually for
inappropriate image duplication. For each year, issues 1-12 (January-June) were selected, and
the first 10 papers in each issue containing photographic images were screened. Thus, 120
papers were inspected per publication year, resulting in a total of 960 papers screened. Since
almost all MCB papers contain photographic images, no specific search term was used, but
papers were only counted if they contained photographic images.

86 Image inspection. Published papers were scanned using the same procedure used in our prior 87 study (1). Briefly, one person (EMB) scanned published papers by eye for image duplications in any photographic images or FACS plots. Problematic images were also inspected by two 88 additional authors (AC and FCF). Such duplicated images fell into three general categories: 89 90 simple duplications, duplications with repositioning, and duplications with alterations (1). As in 91 the previous study (1), cuts and beautifications were not scored as problematic. EMB was not 92 aware of the year in which MCB started increased screening (see below) for image problems 93 while she screened journals. The image allegations were confirmed using ORI forensic 94 software by the MCB Production Department. Decisions as to whether to pursue the allegations by contacting authors were based on this analysis. Each published paper containing suspected 95 image duplication problems was reported to the Editor-in-Chief of MCB. The EIC then 96 97 requested clarification from the corresponding author(s) regarding concerns with the figure 98 using the category classification described above. The EIC followed up on all concerns from 2010 and on potential concerns in Categories 2 & 3. Category 1 concerns were handled by 99 100 ASM staff.

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Prospective screening of manuscripts before publication. Starting in January 2013, all MCB manuscripts accepted for publication were screened for image duplications and other problems, including undisclosed cuts and beautifications (which were not counted in the screen of the published papers described above). For this study, the time to inspect these figures in manuscripts accepted from January 14, 2013 to March 21, 2013 was recorded. In the case of image problems, the authors were contacted and asked to explain and/or remake the figure. Corrections and retractions followed COPE guidelines

109 (https://publicationethics.org/resources/guidelines).

110 **Results**

112	Inappropriate duplications in MCB published papers. A set of 960 papers published in MBC
113	between 2009 and 2016, including 120 randomly selected papers per year, was screened for
114	image duplication. Of these, 59 (6.1%) papers were found to contain inappropriately duplicated
115	images. The distribution of these showed a decline since 2013, when the screening of accepted
116	manuscripts was introduced (Figure 1). From 2009-2012, the average percentage of image
117	duplication was 7.08%, while after the introduction of screening accepted manuscripts in 2013,
118	the percentage was 3.96%, a significant decrease (t test; p<0.01).
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120	Investigation by ASM staff into published papers with image duplication. The 59 papers with
121	inappropriate image duplications in MCB were investigated by contacting the corresponding
122	authors and requesting an explanation for the apparent problem. The 59 instances of
123	inappropriate image duplications led to 42 corrections, 5 retractions and 12 instances in which
124	no action was taken (Table 1). The reasons for not taking action included origin from
125	laboratories that had closed (2 papers), resolution of the issue in correspondence (4 papers),
126	and occurrence of the event more than six years earlier (6 papers), consistent with ASM policy
127	and Federal regulations established in 42 CFR § 93.105 for pursuing allegations of research
128	misconduct. Of the retracted papers, one contained multiple image issues such that a correction
129	was not an appropriate remedy, and for another retracted paper, the original and underlying
130	data was not available, but the study was sufficiently sound to allow resubmission of a new
131	paper for consideration, which was subsequently published.
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133	Analysis of inappropriate image duplications. Authors who were contacted about image
134	irregularities most frequently reported errors during assembly of the figures. The most
135	commonly reported error was the accidental inclusion of the same blot or image twice. Other

commonly reported mistakes were the selection of the wrong photograph, the assembly offigure panels with mock photographs that were not properly replaced, etc.

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Time effort for published papers. For the 59 papers published with potential image duplication 139 140 concerns, the ASM publication staff members recorded ~580 emails pertaining to these cases, or an average of ~10 emails per case (range 4-103). In addition, at least two phone 141 conversations with authors took place, each approximately 1 h. The Production Editor and 142 Assistant Production Editor handled ~800 emails in their folders regarding these corrections. In 143 144 addition, for 20 papers the Editor in Chief (EIC) was involved in communications with the authors, which involved a total of 244 emails (range per paper 4-29) or an average of 12.2 145 messages per paper. Including the EIC time would add another 61 h (~15 min x 244 emails). 146 147 The exact content of these emails was not disclosed to any individuals outside of the MCB 148 ethics panel. The breakdown of the Production Staff emails were: correspondences with staff members to keep them apprised of what had been received, discussions about wording (since 149 150 each item needed individual assessment of the appropriate approach), or logistical details 151 regarding retracted or republished papers. Correspondences with authors comprised the next 152 largest category (less than half the amount of staff correspondence), followed by 153 correspondences with the EIC. Correspondences with the printer was the smallest category. Hence, the problem of inappropriate image duplication after publication imposed a large time 154 155 burden on the journal, with an average of 6 h of combined staff time (1400 emails estimated to 156 take 15 min each to write and follow up per 59 papers) spent to investigate and follow-up each 157 paper.

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Screening of manuscripts prior to publication. Analyzing the papers with inappropriately
 duplicated images as a function of time revealed a decline in incidence beginning in 2013, which
 coincided with a change in the editorial process to include pre-publication screening for image

162 problems (Figure 1). During a period of 2 months in the beginning of 2013, 83 papers were 163 accepted with 452 images inspected. In this recording period, 12 papers (14.5%) were detected 164 in which an image concern (duplication or undisclosed cuts) was identified. The percentage of papers flagged during pre-publication screening was higher than the frequency of duplicated 165 166 images detected in published papers, because beautification or undisclosed cuts were flagged 167 as well. Prior to this time, no manuscript was rejected by MCB because of image duplication, but starting in 2013, after the introduction of pre-publication screening, the percentage of 168 169 manuscripts rejected for image problems steadily increased (Figure 2). 170 Outcome of pre-publication screening of manuscripts. During the recording period in 2013, 84 171 manuscripts were screened, and 12 manuscripts were flagged for containing duplications or 172 173 other irregularities. The authors of each manuscript were contacted for follow-up by the handling 174 editor. In 11 cases, the problem could be corrected by the submission of a new version of the figure, while in 1 instance, the authors provided the original data to show that the figure did not 175 misrepresent the original data. 176 177 178 Time effort for manuscripts. When image screening was first instituted by MCB in 2013, time 179 records were maintained for approximately two months to ascertain the time cost of this procedure. The total time required to inspect all images in the 84 manuscripts screened during 180 181 this period was 687 minutes (8.3 minutes per screened paper). The total time required for 182 reporting and following up of ethical concerns found in 12 papers was 375 minutes of ASM staff time, not counting the time devoted by the EIC to addressing these problems. Thus, the time 183 effort of ASM staff/editors translated into 31.3 minutes per manuscript. 184

185 **Discussion**

186 Here we report the first detailed investigation of inappropriate image duplications in biomedical 187 research papers and a systematic process for their correction. By focusing on one journal 188 within the ASM journals portfolio, we were able to determine the outcome of image concerns. The most reassuring outcome of our findings is that the majority of inappropriate image 189 190 duplications resulted from errors during figure construction that could be easily corrected by the 191 authors. The finding that 5.5% of MCB articles had inappropriate image duplications is a 192 percentage consistent with prior findings involving over 40 journals (1). This confirmation is 193 noteworthy because the approach used in the current study differs from prior work in that it 194 focused on a single journal with a 120-paper sample for each of six publication years. Of concern is that approximately 10% of the papers containing problematic images required 195 196 retractions after the adjudication process, due to apparent misconduct, an inadequate author 197 response, or errors too numerous for an authors' correction. Other efforts to investigate causes 198 of inappropriate image duplication for papers published at two other American Society of Microbiology journals, Journal of Virology and Infection and Immunity, including some from a 199 200 prior study (1), produced retraction rates ranging from 2.9 (1 of 35) to 21% (4 of 19), 201 respectively, which yields an average of $10.6 \pm 8.1\%$ for the three journals.

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203 Research misconduct has always existed, but this topic has been of increasing concern in 204 recent years in view of several high profile scandals, a perceived reproducibility crisis and an 205 epidemic of retracted papers, most of which are due to misconduct (9). The actual number of 206 compromised papers in the extant literature is unknown, but our observations permit some 207 estimates. Although extrapolation from three American Society of Microbiology journals to the 208 general biomedical literature must be made with caution, our study allows a rough estimate of 209 the number of seriously compromised papers in print. Based on the average percent retraction 210 from the three journals, the 95% confidence interval ranges from 1.5-19.8%. If 3.8% of the 8,778,928 biomedical publications indexed in PubMed from 2009-2016 211

212 (http://dan.corlan.net/medline-trend.html) contain a problematic image (1), and 10.6% (CI 1.5-213 19.8%) of that group contain images of sufficient concern to warrant retraction, then we can 214 estimate that approximately 35,000 (CI 6,584-86,911) papers are candidates for retraction due to image duplication. These numbers are almost certainly an overestimate since not all papers 215 216 in the literature have images of the type studied here. On the other hand, we only screened for 217 visible duplications, and papers might contain additional problems in graphs, tables, or other 218 datasets that are less easy to find, suggesting that this could also be an underestimate. 219 Whatever the actual number, it is clear that the number of compromised papers in the literature 220 is significant. The continued presence of compromised papers in the literature could exert pernicious effects on the progress of science by misleading investigators in their fields. 221 222 Nevertheless, even the most liberal estimates the total number of papers that are candidates for 223 retraction represent a very small percentage of the literature. Our findings are consistent with 224 other studies reporting that a significant number of papers in the literature have problems associated with misconduct (10, 11). 225 226

227 Our study also documents the potential value of increased journal vigilance for reducing 228 inappropriate image duplications in published papers. A significant reduction in the number of 229 inappropriate image identified in MCB papers was observed after initiation of dedicated image inspections by the journal in 2013 (6). Increased vigilance reduces problematic images by 230 231 identifying and correcting errors before publication and by heightening awareness among 232 authors to prevent such problems. However, such efforts come at considerable time and 233 financial costs to the journal. The time invested in inspecting manuscripts pre-publication was 234 approximately 8.3 minutes per paper, and the identification of a problematic image resulted in 235 additional time investment in communicating with authors and deciding if a problem raised an 236 ethical concern. Additional costs to science include the time taken by the authors to correct 237 figures and the delays in publication. However, these costs may be significantly lower than the 238 overall cost associated with discovery of image duplication after publication, which triggers an 239 investigation by the journal that consumes considerable time, as is evident from the average of 240 10 emails per case, to outcomes including publication of corrections and retractions. In our analysis, we found that following up on problematic images before publication costs about 30 241 242 min per problematic paper, whereas the time spent to follow up similar issues after publication. 243 not including EIC time, was 6 h per paper, which is twelve times greater. Hence, even though the majority of inappropriate image duplications result from simple errors in assembling figures, 244 245 their occurrence once identified imposes considerable costs to journals and authors, and by 246 extension, to the scientific enterprise. Identifying image problems before publication, even though this requires additional time for journal staff, might save journals time in the end by 247 preventing problematic images from appearing in published papers. In addition, identifying 248 249 potential problems before publication protects authors' reputations and prevents the collateral 250 damage to the reputations of all authors of a retracted paper (12).

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Peer review is a cornerstone of science (13, 14), which is primarily designed to look for 252 253 fundamental errors in experimental setup and data analysis. Most peer reviewers do not have 254 the expertise to analyze papers for scientific misconduct. Consequently, the responsibility of 255 screening for plagiarism, falsification, fabrication, and other forms of science misconduct often lies with editors (15). Although sloppiness and misconduct have always existed in science, the 256 257 problem may be becoming more acute because of advances associated with the information 258 revolution. The ability to cut-and-paste text or images combined with availability of software to 259 manipulate and generate photographic images gives authors powerful tools that can be 260 misused. Our prior study noted that the problem of inappropriate image duplications was largely 261 a 21st century phenomenon temporally associated with the proliferation of software for image 262 construction (1). However, the information revolution has also provided tools to reduce error and abuse. Some publishers, including ASM, already perform routine screening of manuscripts 263

264 using plagiarism-detection software. Combined with manual curation and supervision, these 265 tools work reasonably well (11, 16). However, identifying image duplication of the types reported 266 here and in our prior study (1) is more challenging and dependent on individuals capable of spotting suspicious patterns. We noted that the pre-screening process at MCB is quite good at 267 268 picking up spliced images but poor at finding image duplications of the type reported in this 269 study. Hence, without routine screening by individuals who are gifted at identifying image 270 duplications and modifications, it is likely that the type of image problems identified here will 271 continue (1). Although detecting image problems is difficult, the recent development of 272 improved software tools appears promising (17).

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274 The finding that most inappropriate image duplications result from sloppiness and error during 275 figure construction but impose large costs to authors and journals for their correction indicates 276 that greater efforts to prevent such errors should be instituted by research laboratories. Given that most figures are currently constructed by authors themselves, it may be possible to reduce 277 278 the prevalence of image problems by asking others in the laboratory that are not directly 279 involved with the current research to participate in figure construction or review. Prior to the 280 availability of image editing software, figures for research papers were usually made by 281 individuals who specialized in this activity and were not involved in data collection. We note that in our previous study we found no instances of inappropriate image duplication prior to 1997 (1). 282 283 We hypothesize that prior to the availability of software that allowed authors to construct their 284 own figures, the discussions between photographers or illustrators and authors combined with the separation of data generation from figure preparation reduced the likelihood of these types 285 of problems. 286

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In addition, providing clear guidelines for the preparation of photographic images as part of a
journal's instructions for authors is helpful. For example, instructions might include rules about

- 290 how to disclose cuts in Western blots, the requirement of each experiment to have their own
- 291 control (e.g. β -actin or globin) protein control blots (no re-use of these blots allowed), etc.
- 292 Examples of such guidelines currently exist (18). ASM maintains an ethics portal in its website
- 293 with information that may be helpful to authors
- 294 (http://journals.asm.org/site/misc/ethicsportal.xhtml)
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In summary, we confirmed our prior results by inspecting a single journal using a systematic

approach and provide insights into the causes of inappropriate image duplication in research

- 298 papers. The results provide both reassurance and concern regarding the state of the
- biomedical literature. We are reassured that the majority of duplication events result from errors
- that do not compromise validity of the scientific publication and are amenable to correction,

301 notwithstanding the cost of considerable time investment on the part of the journal staff, editors

and authors. However, of concern is the significant minority of papers with inappropriate image

303 duplications that result in retractions, suggesting that the current biomedical research literature

304 contains many such publications that warrant retraction. At the very least, our findings suggest

the need for both authors and journals to redouble their efforts prevent inappropriate image

306 duplications.

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308 **Conflict of interest statement**

- 309 Elisabeth Bik is an employee of uBiome, but conducted this work outside of working hours.
- 310 uBiome did not sponsor this research. AC, FCF and RJD are either current or former editors of
- the ASM journals *mBio*, *Infection and Immunity*, and *Molecular and Cellular Biology*,
- respectively. AK is the publishing ethics manager in the ASM journals department and
- 313 participated in this research in a retrospective capacity. This paper reports on an effort by ASM
- journals to review the integrity of figures in a subset of published manuscripts. That effort was

315	not initially intended as a study but rather as due diligence in maintaining the integrity of the
316	scientific record. However, since the results of this effort provided important information that
317	could inform future efforts at improving the reliability of the literature, a decision was made to
318	present the data in a publication. The views expressed in this article do not necessarily reflect
319	the views of this journal or the ASM.
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369 Figure 1. Percentage of papers published in ASM's Molecular and Cellular Biology

containing duplicated images. Inspection of manuscripts pre-publication started in 2013.



Figure 2. Percentage of accepted MCB manuscripts that were found to have problematic

images, 2013-2016. No screening for problematic images was done before 2013 and NA means

375 non-applicable.

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Table 1. Summary of results and comparison of image duplication problems in

379 published MCB papers and accepted MCB manuscripts.

		Papers with Image duplication problems	
		Post publication (59, 6.1%) ¹	Pre-publication (12, 14.5%) ²
Action	Explanation		
None	Duplication could not be confirmed	3 (5.1%)	0
	or not a strong case		
	Duplication was legitimate	1 (1.7%)	0 (0%)
	Lab had closed after submission of	2 (3.3%)	0 (0%)
	paper, not pursued		
	Older than 6 years	4 (6.8%)	0 (0%)
	Authors did not reply	2 (3.3%)	0 (0%)
	Authors provided original blot	1 (1.7%)	0 (0%)
	showing no duplication		
Correction	Simple duplication during figure	40 (67.8%)	11
	assembly		
	Error in figure assembly	1 (1.7%)	14
Retraction (or	Too many errors for simple	3 (5.1%)	0
rejection of	correction		
manuscript)	Intention to mislead suspected	2 (3.3%)	0
Staff effort	Emails sent to resolve problems	1400-1600 ³	N.A. ⁵
	Average time spent per paper	6 h	1.5 h

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381 ¹ Published papers (n=960), 2009-2016

- 382 ² Accepted papers (n=83), 2 months in 2013
- 383 ³ Email estimate includes EIC correspondence.
- 384 ⁴Analysis revealed potential case of non-uniform enhancements

385 ⁵N.A. means not available



