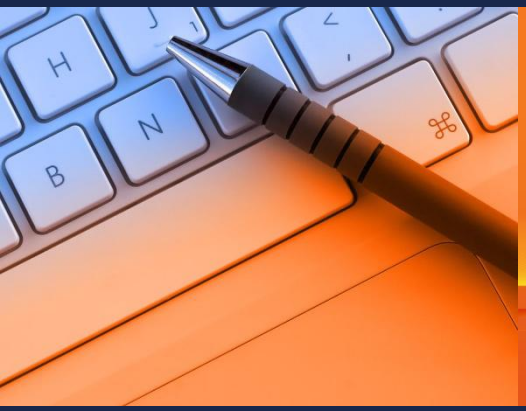
ACCDON

Jesse V. Jokerst is an Assistant Professor in the Department of NanoEngineering at UC San Diego. Prior to UCSD, he received his Ph.D. in Chemistry at the University of Texas at Austin and did research in the Stanford University. Professor Jokerst is also an Associate Editor/Editorial Advisor at two peer reviewed journals, *J. Biomaterials Analysis* and *ACS Applied Nano.* He has published over 50 papers; and completed about 250 peer reviews. Prof. Jokerst is a senior scientific editor at Accdon-LetPub.



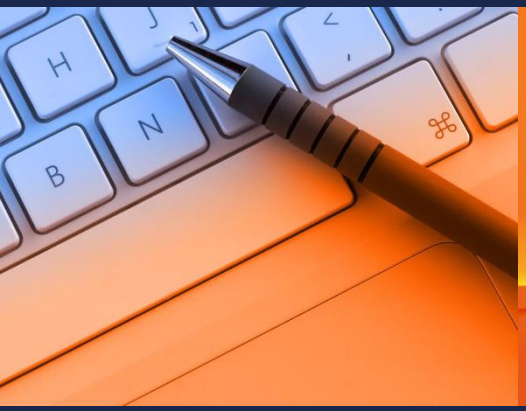
ACCDON

Getting Your Paper Accepted

Jesse V. Jokerst, PhD

Jacobs School of Engineering

University of California, San Diego



Disclaimer and Disclosure #1

- I have a consulting relationship with Accdon/LetPub.
- I do not represent the University of California or any journal or publisher.
- The opinions expressed here are solely my own.

Disclaimer and Disclosure #2

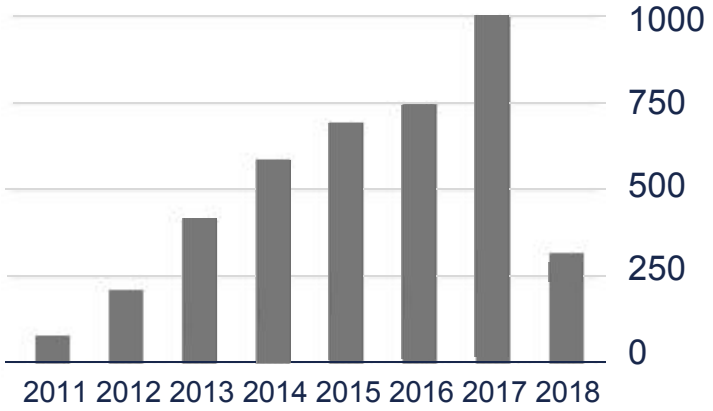
- I only speak English.
- I can not imagine how hard it must be to write about science in a second language.
- I hope this presentation will make it a little bit easier to publish using English.

My Credentials and Background

My Credentials and Background

- Assistant Professor at UC San Diego
- Grants: $3.5M USD in two years
- Training at UT Austin (PhD in Chemistry) and Stanford (Postdoc in Radiology)
- ~ 50 papers; ~ 250 peer reviews
- 10 students/postdocs
- H-index of 22; i10 of 29
- Associate Editor/Editorial Advisor:
  - *ACS Applied Nano*
  - *J. Biomaterials Analysis*

Citations	4141	3775
h-index	22	22
i10-index	28	28

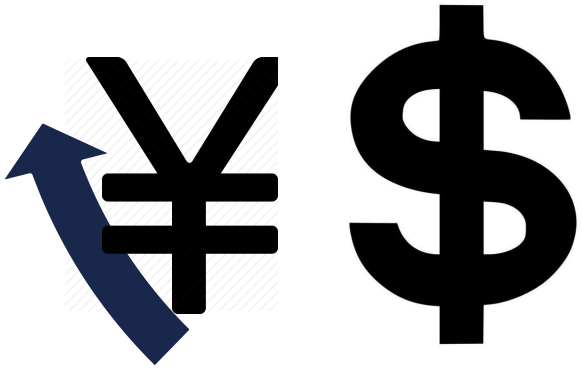


Scope of the Presentation

- The publication process
- How to think like a reviewer
- Tips on clearer writing

Publishing is About Money

Papers → Grants



Results

Publishing is About Science

- Publications are the currency of science/engineering.
- Justification for graduation, promotion.
- Record of your work

So Where to Begin?

- Advice abounds on the internet
- Videos, articles, blog posts produced by publishers
  - does not account for human nature
  - overemphasis on the sanctity of the peer review system
- Inherent asymmetry in the process: you spent a year on a paper; the reviewer spent an afternoon (if you're lucky)
- It is very possible that the reviewer doesn't "get it," but that may be because the author didn't explain it (sell it) well!
- Sometimes the reviewer is just a crank/lazy

What Makes a Good Paper

- We are assuming that the work is worth submitting
  - good science is a necessary *but not sufficient* criterion for acceptance
- The purpose of a paper is to instruct the reader and ultimately to change their behavior
  - to use your technique
  - to interpret their results in light of yours
  - to do *something* different
- Mistake: to assume a paper is archival and to get it out the door just for another paper

When is the Paper Ready?

- Sufficient number of controls
  - Positive and negative controls
- Sufficient number of replicates
- Clear answer to, “What is new?”
- Appropriate references to prior work
- Paper has been read and approved by all authors

How to Write it?

- Think about the question or hypothesis or goal
- I generally start with a sketch of the figures
  - Even if I don't have the data
  - Study y as a function of x
  - Remember your controls!

    (Key Point: Design of experiment)
- Collect data (Key Point: WRITE while you do it)
- Once I have the data, finalize figures and figure captions
- Then make bullet point list of Intro, Results, Discussion
- Finalize. Revise, Revise, Send to co-authors, Revise.

Think like a reviewer

- They are teaching and writing grants and writing their own papers and preparing lectures and have sick children and a cranky husband and needy graduate students and consulting and . . . .
- And then YOUR paper comes across their desk
- And they already have 4 other literature reviews due
- And maybe just this morning they had one of their paper get rejected.
- So how to make it EASY on them?
- How to make it easy to get to “yes?”

So Why do Reviewers Do It?

- They do not get paid.
- Enjoy science.
- Sense of duty to community.
- Like to see what is new.
- See how their work compares to field/competitors.
- Get new ideas for their own work.
- Learn.
- Sense of obligation to the journal/editor.
- Ensure that their work is being cited.

So how to increase your chances?

- Make it easy on them!
- Hint: Reviewers often do not read your entire paper.

1. Clear writing. Nothing can replace this.
2. Abstract, Figures, Figure captions, and last paragraph of introduction

→ This must contain the entire message of the paper.

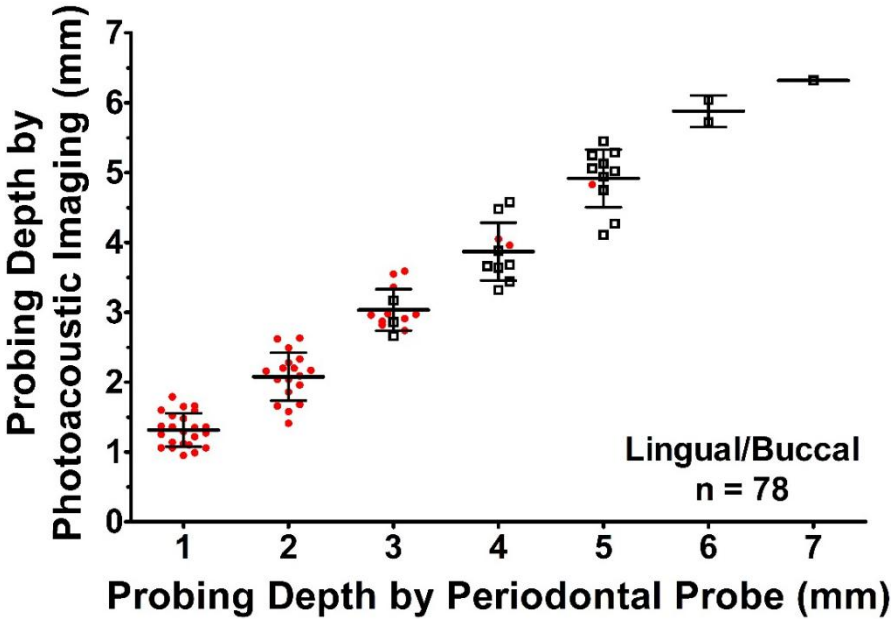
3. Proper controls.
4. Clear statement and illustration of novelty.
5. Minimize jargon and abbreviations

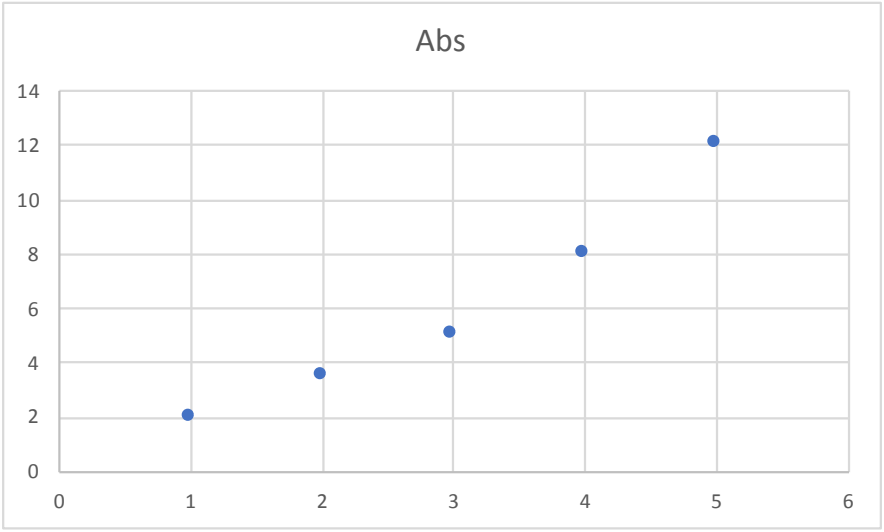
More on Figures

- You will be judged very heavily on the *quality of your figures*
  - the reader is not going to *study* your figures

    → the meaning must be *obvious* since they will look there first
  - use fonts that seem absurdly large until shrunken to one column
  - look at other plots, micrographs, schematics, drawings, etc. from the journal you are targeting.
  - Do yours look like that?
  - If not, then you need to remake them.
- GraphPad, Slide Writer, Adobe Illustrator, etc.

More on Figures





More on Figures

- Big fonts that are consistent throughout.
- Errors bars; scale bars in images.
- Statistical analyses.
- Referenced in the text.
- Figures usually better than tables.
- Minimal use of supplementary information.
  - Why?
  - Hard on reviewer.
- In the submitted version have them embedded in the text

Figure Captions

- HUGE problem in the papers I see.
- Figure caption should include rationale, experimental, results, discussion, and conclusion for that experiment .
- Hard to do that in 3-4 sentences but critical!
- Bad example:

  Figure 1. XRD patterns of the samples synthesized with different amounts of NaCl (a). FTIR spectra of sample 869 and 870 (b).

- This doesn't tell the reviewer anything. What am I supposed to see? Be impressed with? Why did you do this? What did you learn?

How to Write a Better Caption?

Remember C.A.R.:

Context: Why are you doing it?

Action: What did you do?

Result: What did you find? What does it mean?

→ This also applies to presentations, interviews, etc. etc.

Better Example

Figure 5. Influence of SiC on cancer cells. (A) Viability assay shows that the SiCNWs do not decrease cell viability in OV2008 and MCF-7 cells at concentrations up to 400 µg/mL. (B) Proliferation study shows that SiCNW has negligible effect on the proliferation of MCF-7. (C) Migration assay shows the MCF-7 can migrate after labeled with SiCNW. Scale bar presents 200 µm.

Context: Why are you doing it?

Action: What did you do?

Result: What did you find? What does it mean?

Better Example

Figure 5. Influence of SiC on cancer cells. (A) Viability assay shows that the SiCNWs do not decrease cell viability in OV2008 and MCF-7 cells at concentrations up to 400 μg/mL. (B) Proliferation study shows that SiCNW has negligible effect on the proliferation of MCF-7. (C) Migration assay shows the MCF-7 can migrate after labeled with SiCNW. Scale bar presents 200 μm.

Context: Why are you doing it?

Action: What did you do?

Result: What did you find? What does it mean?

Last Paragraph of the Introduction

The last paragraph of the Introduction is a great place to accomplish some key tasks.

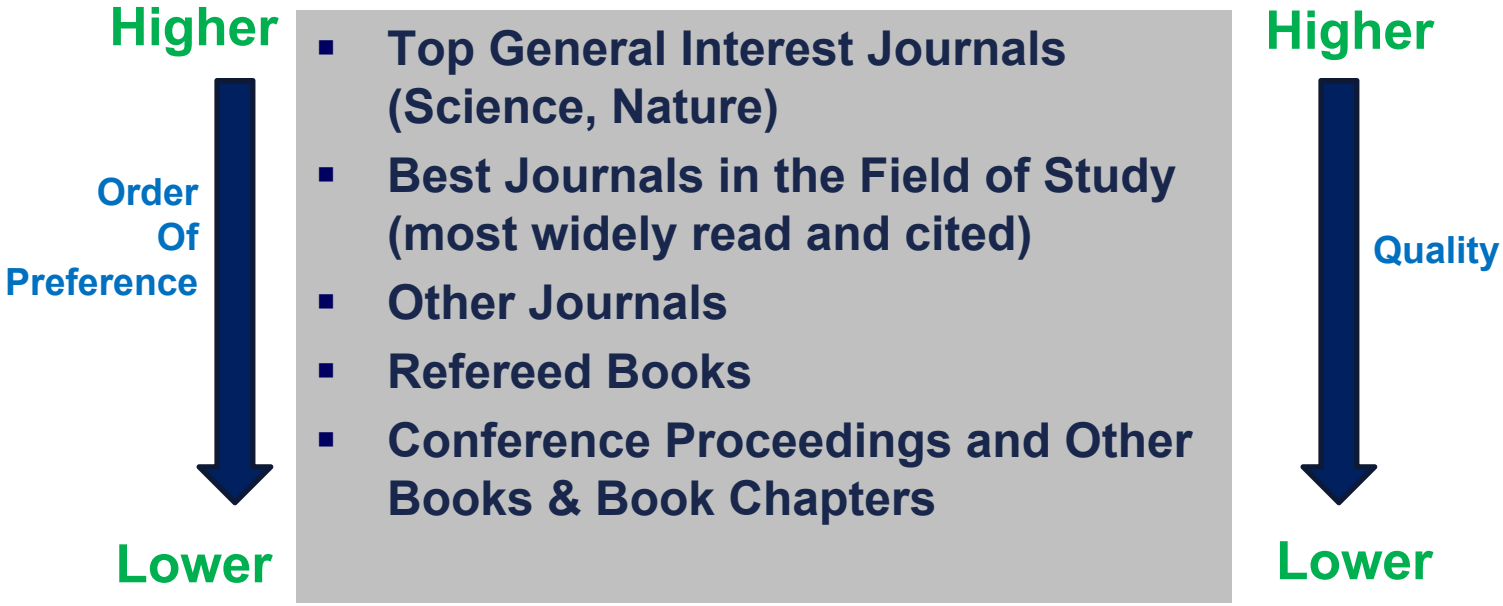
Many authors use this as a mini-abstract in which they:

- **restate the fundamental limitation and motivation of the work (1-2 sentences)**
- **briefly, state the work flow (1-2 sentences)**
- **state the main finding**
- **and then include a statement that "to the best of our knowledge, this is the first (or best) . . . ."**

Ok, So it’s Written. Now What?

Where to send it?

Hierarchy in Scientific Results



Modified From Randal Filer, Iset Policy Institute

Journals versus Book Chapters

Journals

- **Editorial Goals:** Journal editors are looking for something new and original that will receive considerable interest and citations (drives impact factors)
- **Advantages**
  - Peer review typically significant
  - More widely distributed
  - Cited and read more frequently
  - More available online
- **Disadvantages**
  - Page and figure limitations

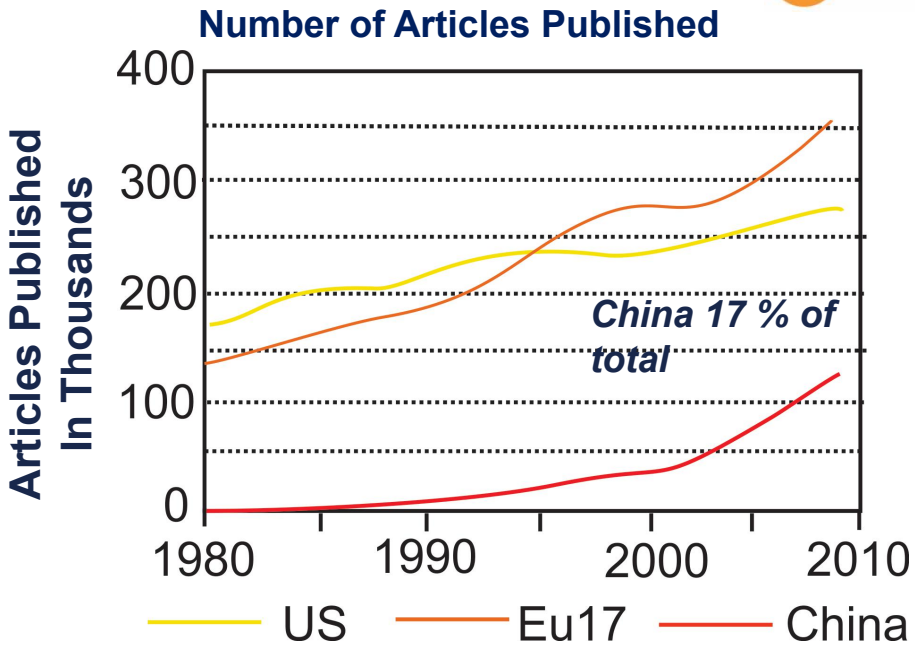
Book Chapters

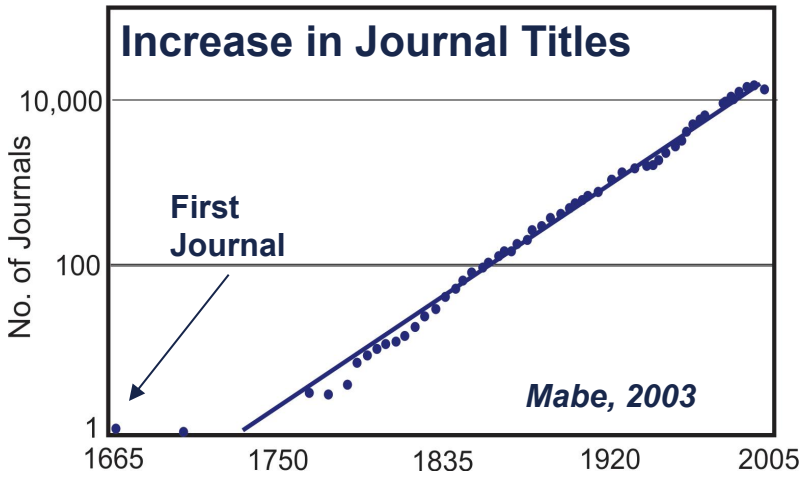
- **Editorial Goals:** Book editors are looking for materials that sells to as large of audience as possible
- **Advantages**
  - Typical less restrictive on length and figures
  - Author association with topic
- **Disadvantages**
  - Lower quality reviews
  - Less reputable
  - Less well distributed
  - Often require longer publication times
  - Less availability online

Peer-Reviewed Journals

English Language Journals

- ~28,100 peer-reviewed journals (all fields) (Plume & Van Weijen, 2014)
- Publish ~2.5 million articles per year
- ~3.5-4.5 % increase in published articles
- CrossRef database includes ~55 million journal articles





Thomson Reuter's Journal Citation Reports (most cited journals)

- 10,900 journals
- 2,550 publishers
- 8,700 are science related
- 3,200 are social science related
- 1.5 million articles published per year collectively

Peer-Reviewed Journals

- Method of sharing data and discoveries
- Maintain quality of science – allow only sound research to be disseminated
- Serve as an archive for scientific data and discovery
- Provide author services
  - Register author's findings/discoveries (precedence)
  - Serves as a indicator of researcher's impacts on field
    - primary reasons for publishing was to obtain funding and furthering author's career.

Publishing: The Perfect Business Model (Scam?)

- Libraries/Universities pay them for access
- Advertisers pay them for ad space
- Authors pay them for pay them for page charges
- Authors do the work (for free)
- Reviewers do the work (for free)
- Pay Editors poorly

- This is why I *strongly* prefer non-profits . . . American Chemical Society, Materials Research Society, American Cancer Society, etc.

Publishers

- Wide range of publishers
  - Globally, 5000-10000 journal publishers
  - ~650 main English-language publishers
    - 73% are not-for-profit
      - Only publish 20% of journals
      - 80% of journals published by for-profit publishers
        - 9,240 journal of total 11,550 (English)
        - Elsevier - ~25% of total science titles
- Revenues are often high – US $25.2 Billion
  - US $10 Billion for journals
  - US $5 Billion in books

Data from STM, 2015

Impact Factor

- Formulated by Eugene Garfield, founder of the Institute of Scientific Information (ISI)
- Produced by Thomson Reuters and Published Annually in the ISI Citations Reports (starting in 1975), for journals indexed in ISI databases (Web of Science/Knowledge)
- It is the average number of times each paper published in that journal is cited during the preceding two years by other indexed journals

Example:

$$\text{Impact Factor 2014} = \frac{\text{\# of times that all papers published in journal in 2012 \& 2013 were cited in indexed journals 2014}}{\text{\# of articles published in that journal in 2012 \& 2013}}$$

Impact of Increased Publication Volume on Scientists

Fallout of digital publishing and distribution

- Access to papers has increased and is dominated by online sources
- A larger number of journals combined with a larger volume of published articles has made it more of a challenge for our papers to get noticed

Not only do we need to get published, but we need to do it in such a way that the papers we publish will get read.

Balancing Quality, Quantity, and Professional Success

Quantity versus Quality

International Standard: To Maximize Quality	↓	↑
Academic/Institutional Demands Quantity	↑	↓

Always Strive to Maximize Quality

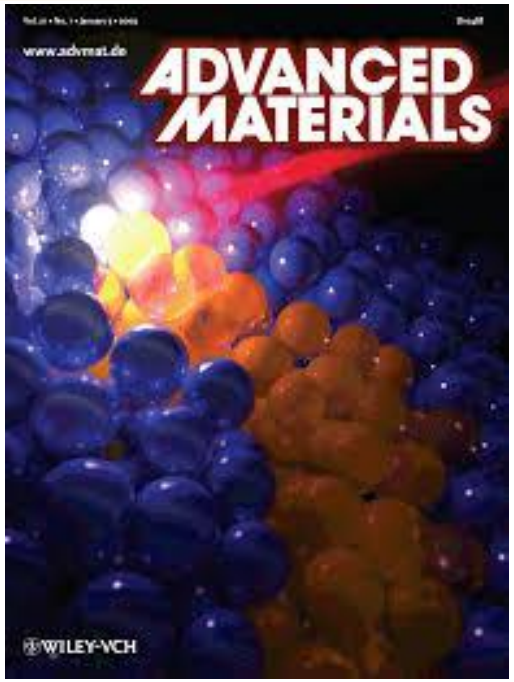
Research I Universities in the US require about 2 papers per year in refereed journals for Promotion & Tenure

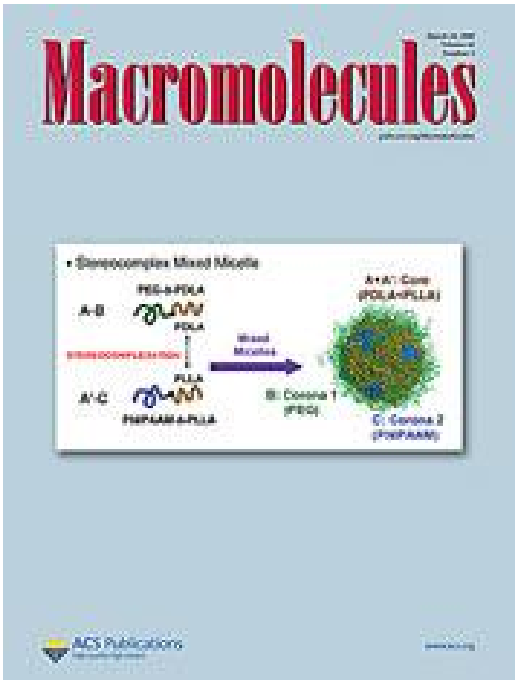
Dreamtime.com

Reasons to Maximize Quality over Quantity

- You can publish a million papers, but if the papers are not of high quality, few other scientists will follow your works
- Good works get lost in the mix of lower quality articles
- First impressions count – especially important for early career scientists

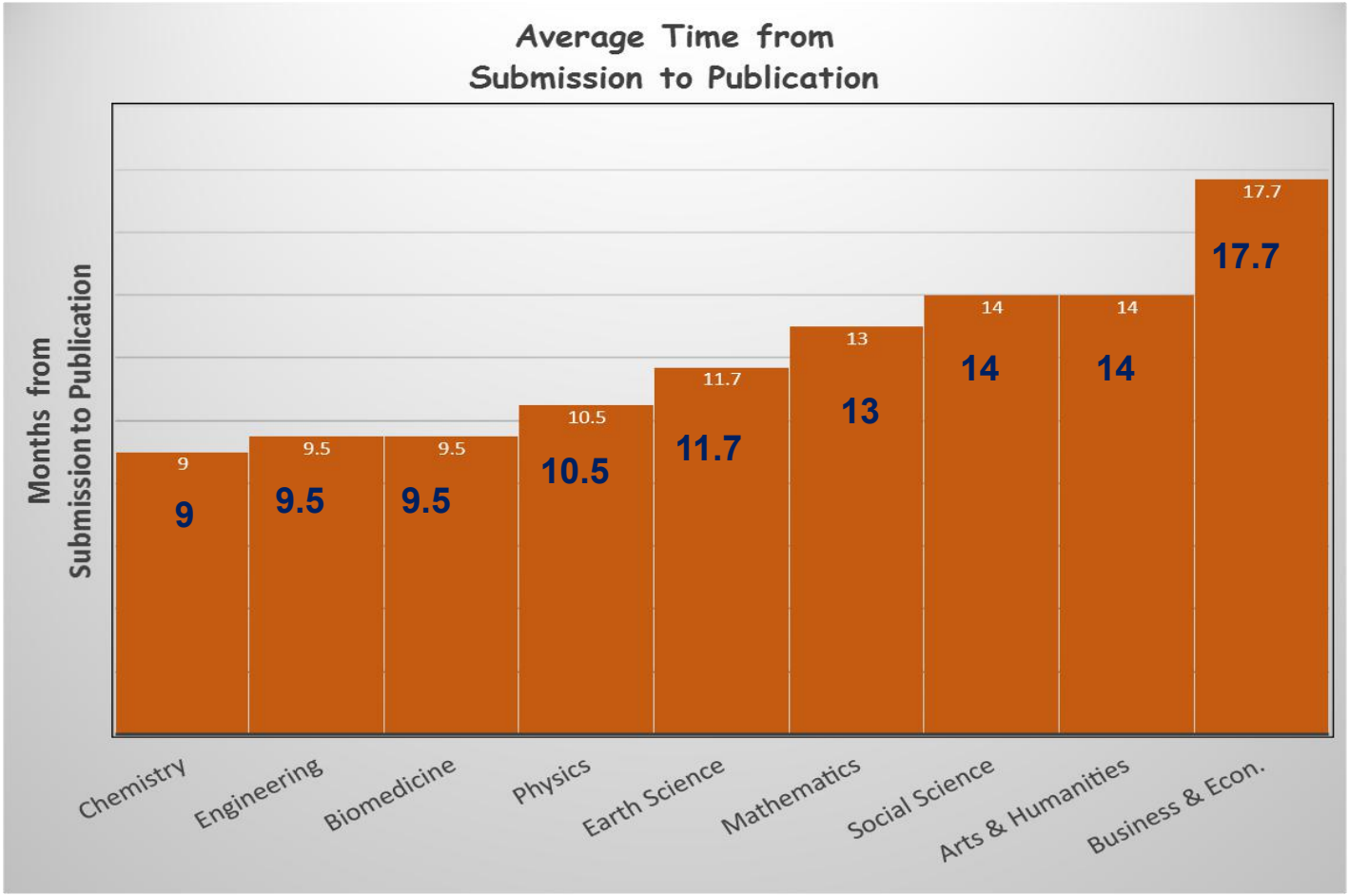
Where to Submit?





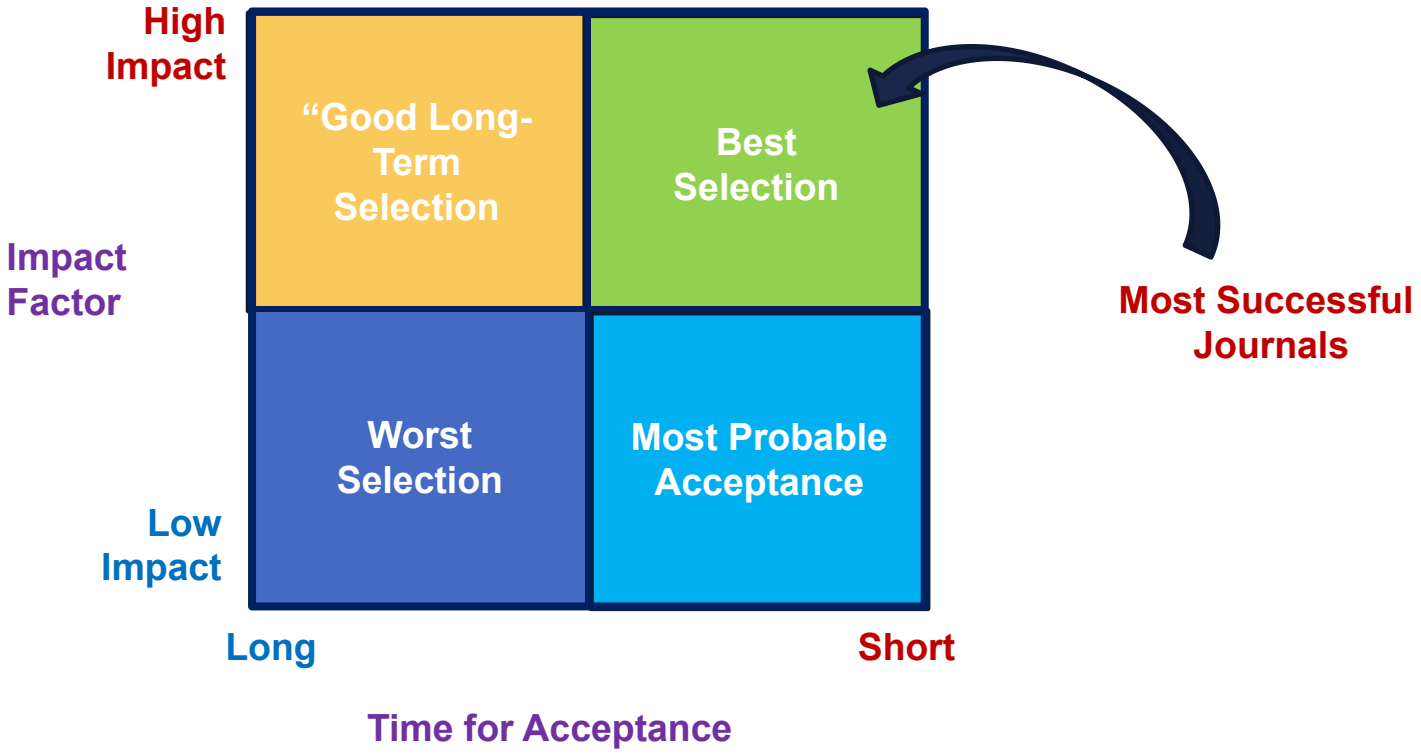
- Choice of journal should be made realistically
- Okay to push the envelope a little bit
- Not every paper belongs in *Science*
- Aiming too high annoys editors and wastes your time

Time Required for Publication



Acceptance times varies by discipline

Journal Selection Model



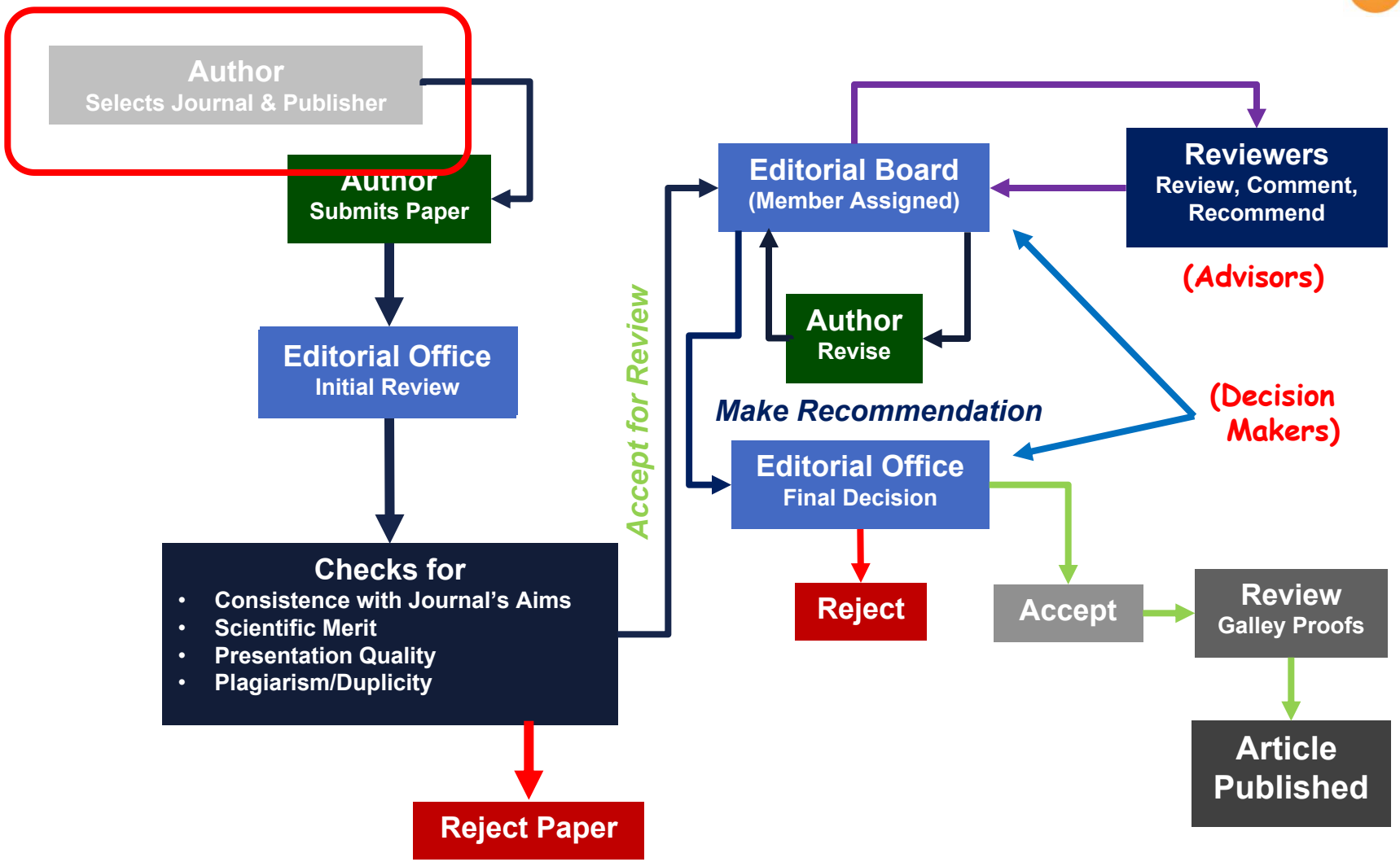
After Linda V. Knight and Theresa A. Steinbach, 2008

Journal Selection Model

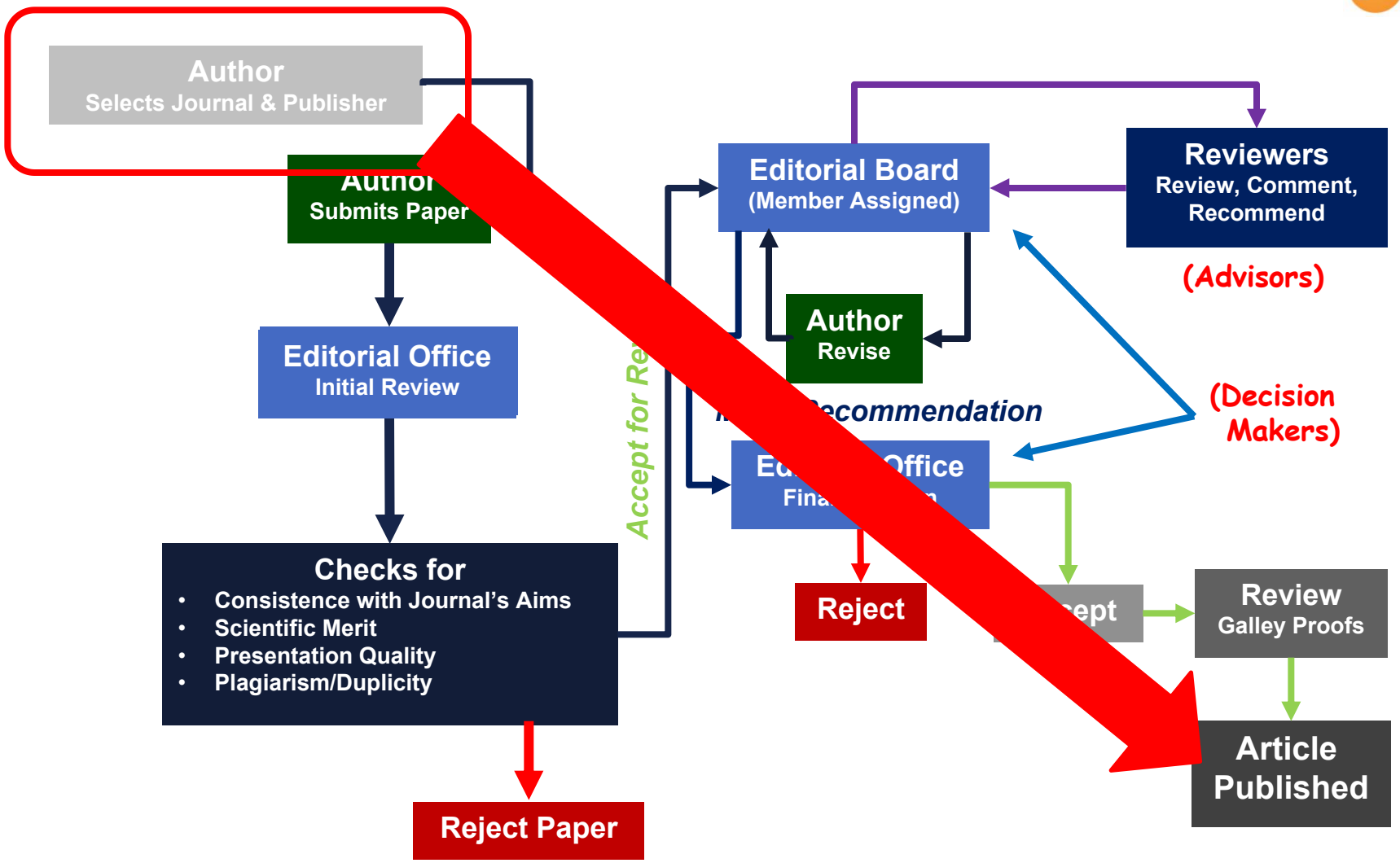
LetPub
Your Manuscript Editor

OK, I've picked a journal and am ready to submit. Now what?

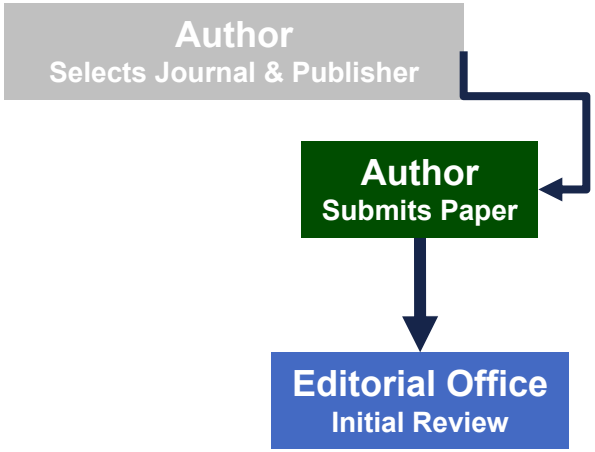
Typical Peer Review Process



Typical Peer Review Process



Journal Editors



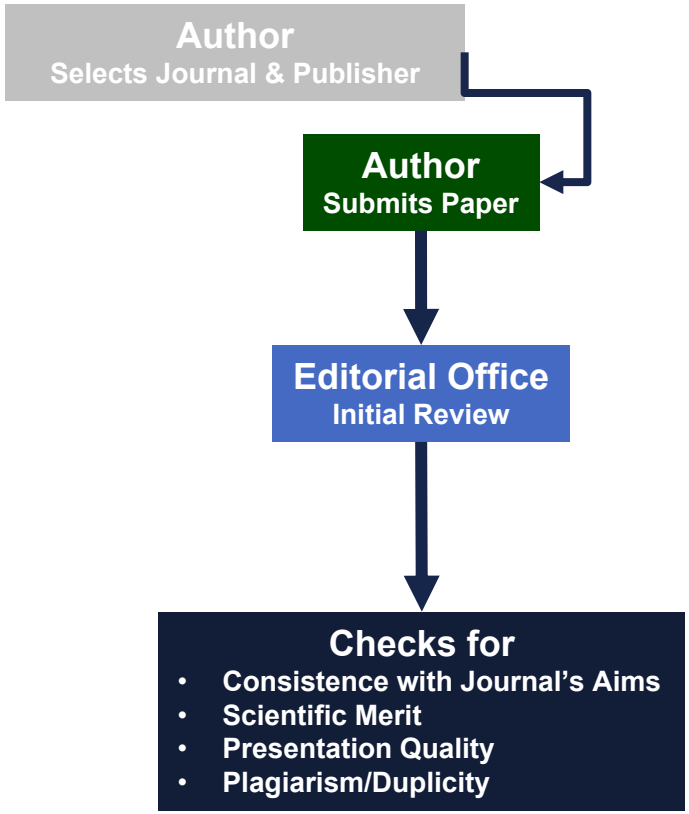
Duties/Tasks

- Find papers to fill journal pages; required to make a profit or kept journal solvent
- Maintain the journal's reputation by accepting high quality papers

- Few financial benefits;
- Editorial duties are just one of many demands on editors' time:
  - Managing manuscript flow (deadlines)
  - Working with authors and reviewers
  - Other teaching, research, and/or managerial responsibilities

The Editor's Job is Made Easier by High Quality Papers – They Want to Accept Your Paper!

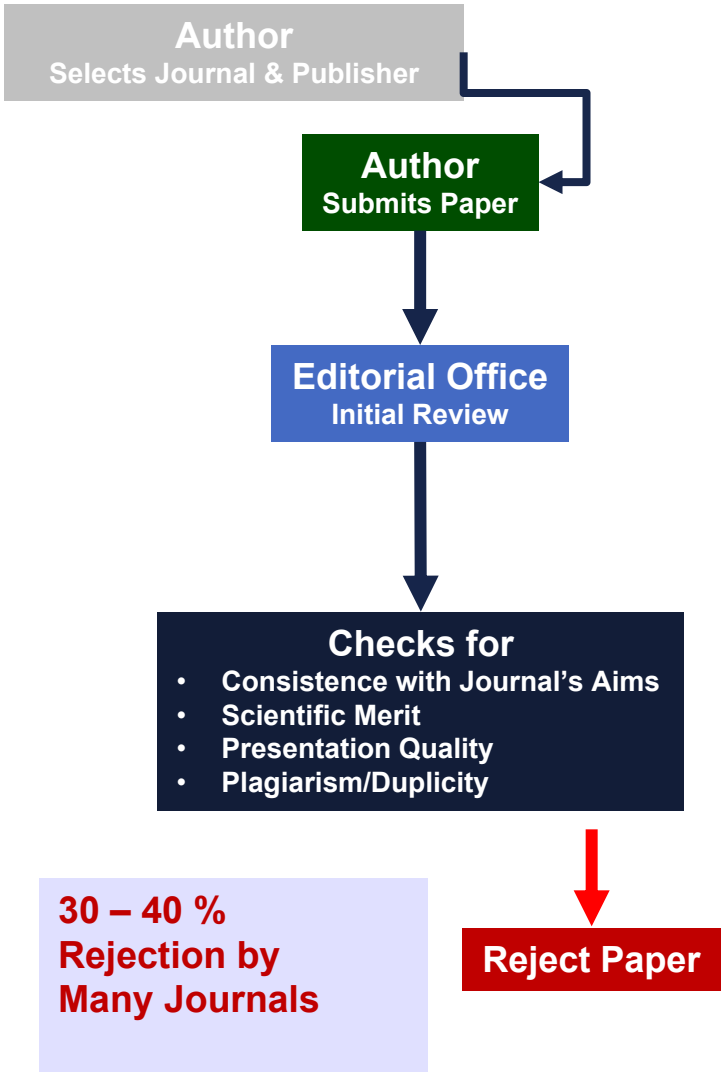
Paper Triage: Appearances Matter



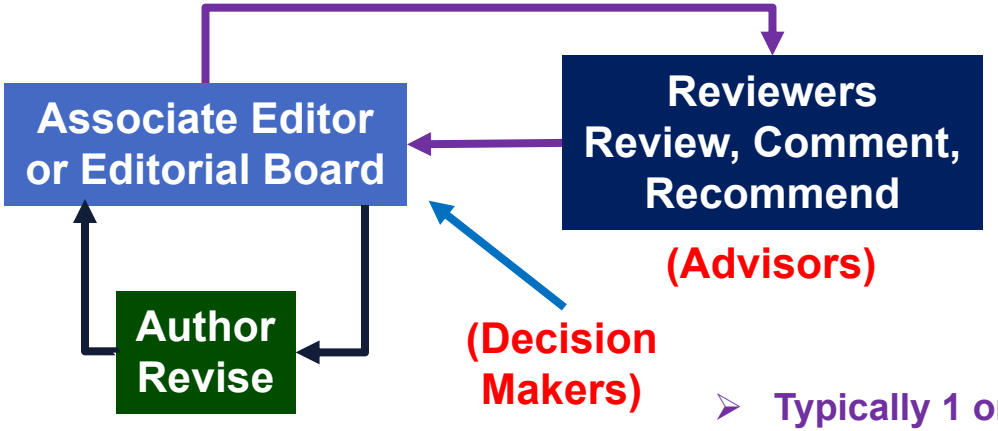
Performed to Save Time and Effort

- Paper inconsistent with journal's aims and goals
- Manuscript does not follow submission guidelines
  - Length, figure number or quality, key elements (e.g., title, key words, section headings)
- Paper has been submitted elsewhere or is very similar to a previously published article
- Manuscript is poorly written or organized such that the paper is difficult to comprehend

Typical Peer Review Process



Identifying a Primary Editor



- Typically 1 or 2 reviewers
- Advisory role only

- **Blind-Review: Authors do not know the reviewers**
- **Double-Blind Review: Authors do not know the reviewers & reviewers do not know the authors**

Journal Reviewer

- Typical review takes 4-5 hours; 8+ hrs for less experienced reviewer (STM, 2015)
- Reviewing is unpaid professional service to the discipline for which there is little reward
  - Editors often ask 6 scientists to find 2 reviewers
- Reviewers want to review papers that are easy to read, well-organized and describe novel “cutting-edge” research
  - They Want to Accept, Not Reject, Your Manuscript
- Advice: Ask your PI to let you peer review a paper

The Players

- Any submission involves the interplay of three roles
  - The author
  - The editor
  - The reviewer(s) (usually 2-4 of them)
- The editor is usually a mid-career or senior scientist
- Some publishers (e.g., Nature, Wiley-VCH) use professional editors, as do some journals within publishers (e.g., *Energy & Environmental Science*)
- Editors are often your colleagues
- The roles revolve; most authors are reviewers several times per paper they submit

Goal of the Cover Letter

- Get it sent out of review
- Make the editor an advocate
- Remember:
  - You have been working on this for 6-24 months.
  - But this is the first the editor is seeing it.
- Thus, the cover letter needs to explain problem AND solution while building enthusiasm

Goal of the Cover Letter

- Novelty and significance of the work
  - What has been done
  - How it was received by the community
  - Fundamental limitation of existing technology
- How the work solves these problems
  - Is it the first or best?
- Why the paper is appropriate for *this* journal
  - Previous papers
  - How were they cited?

The Art of the Cover Letter

I have now served as an Associate Editor at *ACS Nano* for three months. As promised, doing so has provided unique insights into scientific publishing. Interestingly, the biggest surprise has not been something that authors do, but something they frequently neglect to do: constructing a well-written cover letter, including a statement justifying the importance of their work.

http://pubs.acs.org/doi/full/10.1021/nn100907e

Cover Letter for a Paper

- Find a good example from your group
  - Different fields have different conventions
- Same thing as other writing: revise, revise, revise
- Proofread
- Word limits?
- Figures?

The Cover Letter

- Written to the editors; some journals call it the "letter to referees"
- Address them as human beings
- Not a recapitulation of the abstract (the editor has it already)
- What did you *really* do and why did you *really* do it?

Bad Example: Just copy the abstract

Dear Editor,

Heparin anticoagulation therapy is an indispensable feature of clinical care, yet has a narrow therapeutic window and is the second most common ICU medication error. The active partial thromboplastin time (aPTT) monitors heparin, but suffers from long turnaround times, a variable reference range, limited utility with low molecular weight heparin, and poor correlation to dose. Here, we describe a photoacoustic imaging technique to monitor heparin concentration in real time using methylene blue as a simple and FDA-approved contrast agent. We found a strong correlation between heparin concentration and photoacoustic signal measured in phosphate buffered saline (PBS) and in blood (R^2>0.97). Clinically relevant heparin concentrations were detected in blood with a detection limit of 0.28 U/mL. We validated this imaging approach by correlation to the aPTT (Pearson's r = 0.86; p<0.05) as well as with protamine sulfate treatment. This technique also has good utility with low molecular weight heparin (enoxaparin) including a blood detection limit of 72 μg/mL. Finally, we described a nanoparticle-based hybrid material that can immobilize methylene blue for potentially applications as a wearable/implantable heparin sensor to maintain drug levels in the therapeutic window. To the best of our knowledge, this is the first report to use imaging data to monitor anticoagulation and the first use of photoacoustics as a tool for therapeutic drug monitoring.

Sincerely,

Jesse Jokerst

UNIVERSITY OF CALIFORNIA, SAN DIEGO

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO

SANTA BARBARA • SANTA CRUZ

April 25, 2016

Dear Editor,

Problem

Heparin anticoagulation therapy is a cornerstone of surgical and cardiovascular medicine because of its short half-life, reversible nature, and low cost—there are over 500,000,000 doses given annually worldwide. However, heparin therapy also suffers from a narrow therapeutic window and is the second most common medication error. This can result in hemorrhage and bleeding during overdose and emboli and clotting during underdose.

For these reasons, heparin therapy is monitored by the partial thromboplastin time (PTT) test—an *in vitro* test that requires venipuncture and large (>1.5 mL) blood volumes. The PTT suffers from long turnaround times, a variable reference range, limited utility with low molecular weight heparin, and poor correlation to dose. Thus, it can take a very long time for patients to reach the therapeutic window (**Fig. 1**). This is especially problematic in pediatrics because their hemostasis system is rapidly changing, and they do not have sufficient blood volume for repeat testing.

Solution

The work described here solves these major limitations. We identified a solution to monitoring anticoagulation using *imaging* rather than *in vitro* diagnostics and have detailed this in a manuscript entitled, "**Imaging Anticoagulation: Real-Time Photoacoustic-based Measurements of Clotting Time for Therapeutic Drug Monitoring**" submitted for publication in *Nature Communications*. This system is based on the simple, yet remarkable discovery that clinically approved phenothiazinium dyes produce dose-dependent photoacoustic signal when bound to heparin. We first validated this approach in buffer and blood, and then developed a novel nanoparticle-based material that could be coated onto venous catheters. These will not only deliver heparin, but also monitor heparin to quickly titrate the dose into the therapeutic window (**Fig. 1**). The strengths of this approach include a rapid turnaround time, excellent sensitivity, good correlation to hemostasis, and flexibility with both heparin and low molecular weight heparin.

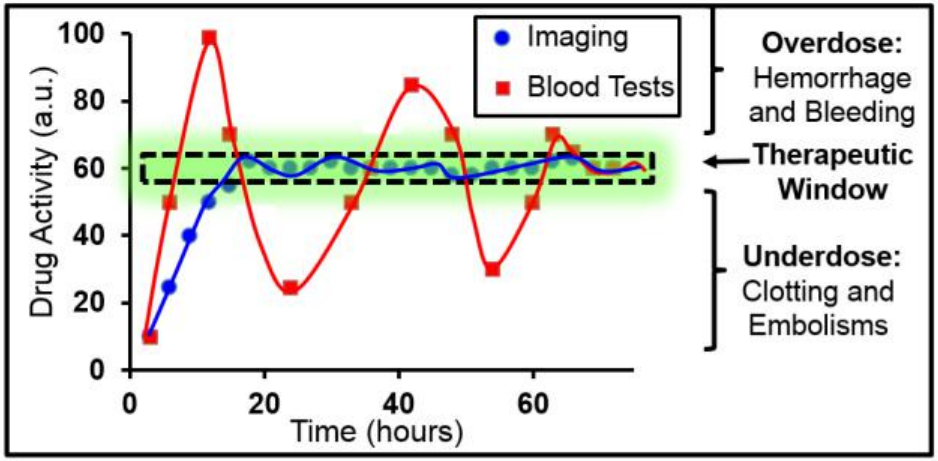


Fig. 1. The use of imaging in drug monitoring. The current approach (red square) to heparin monitoring involves peaks and troughs. Because the frequency of blood-based testing is low, it takes a very long time to reach the therapeutic window (safe and effective; green dashed box). Monitoring heparin via real-time imaging (blue circles) will quickly reach and maintain drug levels in the therapeutic window.

Context and Novelty Rationale

We hope that you find this manuscript suitable for publication in your prestigious journal. We understand that the primary function of *Nature Communications* is to publish the most exciting advances in cross-disciplinary fields. This paper combines nanotechnology, bioengineering, medicine, and imaging, and we think it is ideally suited for the readership of the journal.

We also note that there have been multiple recent publications in *Nature* series journals describing photoacoustic imaging (de la Zerda, Wilson, Pu, Kircher, Conkey, Lai, etc., etc.). These papers have garnered many citations because of the importance of photoacoustic imaging to medicine and biomedical engineering. However, we must emphasize that the work enclosed here is not an incremental extension of our existing work or the community's existing work. Indeed, the main elements of novelty and significance include:

1) the first description of photoacoustics for therapeutic drug monitoring;
2) the first report to use imaging to study anticoagulation therapy; and
3) the first report to describe photoacoustic signal in a device.

We think that these elements—combined with the incredible common use (and misuse) of heparin by the medical community—make this paper very significant to persons studying cardiovascular disease, clotting disorders, imaging, contrast agent development, and biosensors.

On the following page we suggest potential reviewers who may be helpful. We sincerely appreciate your consideration.

Reviewers and Editors

- Usually a journal will allow you to suggest reviewers
  - the editor does not have to take your suggestions
- Suggesting reviewers
  - at least five, but up to ten or more
  - ideally they are independent
    - less than half the list should be your advisor's former students
    - people who will give you a constructive review
- Suggesting editors
  - find the associate editor closest to your topic
  - suggestions are used only sometimes

So You've Submitted Your Manuscript

- After a few days
  - rejected without review
  - assigned to an editor
- Then we wait for 4-8 weeks

Decision on Manuscript…

- Accept as-is (almost never happens)
- Minor revisions (provisional accept)
- Major revisions (almost always accepted in the end)
- Reject and resubmit (major revisions + some hoops)
- Transfer (better than reject)
- Reject
  - they are not trying to destroy your career
  - it does not feel good now, but getting a real reaction is the only way we learn
  - *getting a reaction is key*; it helps refine your arguments

Examples of Referee Reports

Additional Questions:
Is this paper in the top 20% of manuscripts in the field?: No

If this paper is not in the top 20% of manuscripts in the field: It could be improved to be in the top 20% with further work.

Is it appealing to a broad audience?: No

Does the manuscript give a complete description of the procedures that could be reproduced by others in the field?: No

Are the literature references appropriate and up to date?: Yes

Provides significant insight into or the development of an important application: Poor

Work is original and significant: Fair

Conclusions adequately supported by data: Fair

Clarity of presentation: Poor

Potential for impact in materials science and engineering: Poor

Examples of Referee Reports

Recommendation: Other could be revised

Comments:
Decision: Reject

The authors have synthesized Organosilica nanoparticles (OSNPs) using the different ratios of bis(triethoxysilyl) ethane (BTSE) and bis(3-trimethoxysilyl- propyl) amine (TSPA). The nanoparticles have been successfully characterized using TEM and DLS spectra. The surface charge values and surface morphology/ porosity have been ascertained in terms of zeta potential and BET techniques. The as synthesized OSNPs are then used to selectively adsorb anionic dye (phenol red) from its mixture with a cationic dye (methylene blue). The maximum adsorption capacity of the OSNPs is found to be 175.44 mg/g that is claimed to be higher than 67 adsorbents among total of 77 reported adsorbents of its kind. The importance of adsorption parameters such as pH, time, dye concentration, adsorbent dosage, and ionic strength has been studied and optimal conditions have been found. The nanoparticles are found to be reusable for next 10 cycles which further strengthen their applicability. The manuscript lacks in certain ways and can be improved better. Hence it cannot be accepted to ACS Applied Materials & Interfaces with the current format. The below comments can be helpful to the authors to improve this manuscript.

1. Please add supplier details of methylene blue in chemicals section.
2. The author has used the 1:10 and 10:1 ratio of dyes in selectivity experiments. They should also explain the reason for taking such extreme ratios.
3. The time taken for 86% adsorption of phenol red over the OSNPs is very high (3days). The use of nanoparticles in dye adsorption is advantageous when it consumes small fractions of time. In the later sections the authors have stated that 2.4 mg of OSNPs can remove 100% dye. The authors are advised to optimize the parameters (pH, nanoparticles dosage, dye concentration) to obtain least reaction time.
4. Concentrations of salt (NaCl) for ionic strength testing are very high (1,2 and 4M). Authors should describe the reason for choosing such high concentrations.
5. The authors have explained that why the adsorption is lowest at low (1) and high (12, 13) pH values. Whereas no reason for maximum adsorption at pH=2 and 3 has been given. The reason for lowest adsorption at pH=1 is ascertained to higher concentration of H+, that are also present at pH=2 and 3. How the authors have distinguished the two cases in terms of adsorption is absent in the manuscript.
6. Selectivity of anything means that one's tool is specific to that analyte and it will not interact with other identical or near identical analytes. Whereas the other dye used for selectivity testing is a cationic dye. To explain the selectivity of the OSNPs, the authors should use the analytes which have atleast the same charge as their target analyte.
7. Phenol red has been desorbed from the OSNPs using the NaOH solution, which indicates that NaOH can leach the dye from nanoparticles surface. For the quantification of dye using UV spectrophotometer, the authors treated the dye solution with NaOH first in order to maintain the same pH values. Wouldn't such a practice will desorb the dye from the nanoparticles. Certain amendments in this process may lead to increased ad

The Response Letter

- Quote the referee reports verbatim
  - however, correct any typos (even if you would like to make the reviewer appear careless or dumb)
- Don't be emotional → if you want, write what makes you feel good just for fun, and then delete the mean version
- Put everything in the response letter (it may be the only thing they read!)
- Reproduce the responses even if multiple reviewers made the same point
  - reviewers may only read the part related to their own review
- Take a few days and sleep on it
- Use the appeal process sparingly
- Don't use the word "rebuttal" in the file or filename

Examples of Response Letters

UNIVERSITY OF CALIFORNIA, SAN DIEGO

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO

SANTA BARBARA • SANTA CRUZ

September 9, 2017

Dear Dr. Lee,

Thank you for your correspondence date February 1, 2017 related to our manuscript (ID: am-2017-001408) entitled "Organosilica nanoparticles with an intrinsic secondary amine: An efficient and reusable adsorbent for anionic small molecules", submitted for publication in *ACS Applied Materials & Interfaces*. We appreciate all the four reviewers' comments and your willingness to consider a re-submission.

We feel this paper would be a valuable addition to the journal because, to the best of our knowledge, there is no report detailing the use of organosilica nanoparticles (OSNP) with intrinsic amine for organic dye adsorption. Because the amine group is not only on the surface but also inside the silica frame, the OSNP retains the adsorption even after treated with basic solution.

We have thoughtfully reflected on the reviewers' comments and have performed additional experiments, analysis, and revisions to improve the manuscript and our conclusions. The experimental section and results and discussion have been reorganized. Most figures have been modified including six new figures in the supplementary. We also have performed many more experiments to better characterize this material and support our conclusions. Below, we detail these changes and specifically address each point raised by the reviewers. Reviewers original comments precede our response in bold. However, let me first outline the eight key new experiments.

A. Inductively coupled plasma analysis to determine the loss of OSNP during desorption of phenol red by NaOH.
B. CHN analysis to determine the amount of nitrogen/amine on the OSNP made with different fraction of bis(3-trimethoxysilyl-propyl)amine.
C. Solid-state ^{29}Si NMR spectra to evaluate the degree of condensation in the OSNP.
D. X-ray photoelectron spectroscopy analysis to determine the degree of protonation of OSNP at different pH values.
E. Dynamic light scattering to determine the zeta potential of OSNP treated with solutions from pH 1 to 13.
F. Adsorption of different dyes to determine the adsorption mechanism.
G. Short-term adsorption of phenol red at different dye concentrations to measure adsorption speed.
H. FT-IR experiments to confirm the template removal.

We think that these changes significantly improve this manuscript and now answer additional questions related to the nanomaterial properties, adsorption mechanisms, and tunable adsorption behavior. All changes to the original document are highlighted. We also include a clean version.

We hope that these changes make the manuscript suitable for immediate publication in your prestigious journal. We believe that this work now conforms to the primary function of *ACS Applied Materials & Interfaces* to publish the latest results in applied materials and interfacial processes that can be used for specific applications and is of great interest to the silica nanomaterial and environment communities.

Yours Sincerely,

Jesse V. Jokerst, Ph.D.
Assistant Professor
Department of NanoEngineering
University of California, San Diego
jjokerst@ucsd.edu

REVIEWER 1

Comments: The authors have synthesized organosilica nanoparticles (OSNPs) using the different ratios of bis(triethoxysilyl) ethane (BTSE) and bis(3-trimethoxysilyl- propyl) amine (TSPA). The nanoparticles have been successfully characterized using TEM and DLS spectra. The surface charge values and surface morphology/ porosity have been ascertained in terms of zeta potential and BET techniques. The as synthesized OSNPs are then used to selectively adsorb anionic dye (phenol red) from its mixture with a cationic dye (methylene blue). The maximum adsorption capacity of the OSNPs is found to be 175.44 mg/g that is claimed to be higher than 67 adsorbents among total of 77 reported adsorbents of its kind. The importance of adsorption parameters such as pH, time, dye concentration, adsorbent dosage, and ionic strength has been studied and optimal conditions have been found. The nanoparticles are found to be reusable for next 10 cycles which further strengthen their applicability. The manuscript lacks in certain ways and can be improved better. Hence it cannot be accepted to ACS Applied Materials & Interfaces with the current format. The below comments can be helpful to the authors to improve this manuscript.

We appreciate this referee for the helpful suggestions.

1. **Please add supplier details of methylene blue in chemicals section.**

   We regret not being more careful. We have added the supplier details of methylene blue and the new dyes we used in chemicals section. Page 3, Line 17, 19, and 20.

2. **The author has used the 1:10 and 10:1 ratio of dyes in selectivity experiments. They should also explain the reason for taking such extreme ratios.**

   The goal here was to study dye selectivity. Thus, we selected very extreme conditions to test selectivity. We have rewritten this section to explain our rationale. Page 11, Line 13-21.

From the Paper

EXPERIMENTAL SECTION

Chemicals.

Hexadecyltrimethylammonium bromide (CTAB, ≥99%), ammonium hydroxide (NH_4OH), bis(triethoxysilyl) ethane (BTSE), bis(3-trimethoxysilyl-propyl)amine (TSPA, 90%), dimethylhexadecylamine (DMHA), rhodamine B, sodium chloride, decane, and hydrochloric acid were purchased from Sigma Aldrich Inc. Phenol red was obtained from Acros Organics. Methylene blue and rose bengal disodium were purchased from the Fisher Scientific. Ethanol was purchased from VWR. Methanol was provided by Alfa Aesar. The water was Millipore grade with a resistivity larger than 18.2 MΩ·cm at room temperature (RT) unless specified otherwise.

were recorded using a Bruker AMX-600 spectrometer. X-ray photoelectron spectroscopy (XPS) analysis was performed using a Kratos Axis Ultra DLD instrument with monochromatic Al (Ka) radiation. The data was analyzed using Casa-XPS software, and two different components were fit to the N 1s signals, and the energy difference between these components was fixed at 1.8 eV[42]. An inductively coupled plasma optical emission spectrometer (ICP-OES, Optima 3000DV, Perkin Elmer) was used to quantify the loss of OSNP during the desorption treatment with base solution. All absorbance measurements used a SpectraMax M5 spectrophotometer from Molecular Devices.

Adsorption mechanism. 5 mg of OSNP with different compositions, zeta potential, and surface areas were added separately to 1 mL of 0.5 mg/ml (1.33 mM) phenol red. Upon mixing, the tubes were vortexed, reacted overnight, and then the supernatants were collected after centrifugation. For the dye investigation, 1.4 mg of OSNP made of 80% TSPA were added to 0.1 ml pH 7 or pH 13 solutions, and then 0.1 ml 0.2 mM of phenol red, rose Bengal, rhodamine B, and methylene blue were added to both solutions separately. The mixtures were then vortexed, reacted for 5 minutes, and centrifuged. For the refinement of dyes, phenol red (0.04 mM or 0.4 mM) and methylene blue (0.04 mM or 0.4 mM) were mixed at three molar ratios 10:1, 1:1, and 1:10. Then OSNP (80% TSPA) were added and allowed to adsorb dyes for 5 minutes before collection of supernatants.

Influence of crucial parameters. We used OSNP made of 80% TSPA to study the influence of crucial parameters. We first studied the effect of pH on the adsorption. 100 µL of solutions at different pH values were added to 100 µL of 0.5 mg/ml (1.33 mM) phenol red with vortexing. These solutions were then added to 100 µL of Millipore water containing 2 mg of OSNP with standing for 10 minutes before supernatant collection.

The effect of ionic strength was also investigated. NaCl solutions of different ionic strength were created and then mixed with 4 mg/ml (10.63 mM) phenol red at a ratio of 2:1. The mixtures were then added separately to 40 mg/ml OSNP solutions at a ratio of 3:1. The final mixtures were vortexed, stood for 30 minutes, and then the supernatant was collected. To study the effect of time, OSNP were added to phenol red solution at a ratio of 0.5 mg OSNP: 0.1 ml dye. The dye concentration varies from 0.015 mg/ml (0.04 mM) to 2 mg/ml (5.31 mM). The mixture was vortexed, allowed to react for XXX minutes, and then the supernatant was collected.

To study the effect of dye concentration, phenol red at 0 to 5 mg/ml (13.29 mM) were prepared, and then 2 mg of OSNP were added to 200 µL of each solution. The mixtures were vortexed, reacted for 30 minutes, and then the supernatant was collected for absorption spectroscopy.

We also studied the effect of adsorbent dosage. OSNP aqueous solutions at different concentrations were made, and 100 µL of each solution was then mixed with 100 µL of 5 mg/ml (13.29 mM) phenol red. These mixtures were vortexed and reacted for 30 minutes before supernatant collection for absorption spectroscopy.

After optimization of these adsorption parameters individually, we determined the experimental maximum adsorption capacity of OSNP at pH 3 in water with 1 hour of reaction; the dye concentration was 5 mg/ml (13.29 mM), and the OSNP dosage was 1 mg.

Final Steps

- If rejected, use the appeal process sparingly
  - wait at least one day before deciding to appeal

- If accepted, correct the proofs carefully
  - make your corrections before getting to the proof stage!
  - too many corrections will delay publication (“re-proofing”)
- After online posting, time to celebrate, share on social media
- Don’t read your own papers right after they’re published
- Small errors are inevitable; you will be forgiven for typos

Other Resources

- ACS video series “Publishing 101” (American Chemical Society YouTube channel)
  - Especially George Whitesides interview
    - https://www.youtube.com/watch?v=q3mrRH2aS98&list=PL6544210348021339
- Andrea Armani’s website (USC)
- *A PhD is Not Enough!: A Guide to Survival in Science* by Peter J. Feibelman
- Writing in general
  - *The Elements of Style* by Strunk and White
  - *The Sense of Style* by Steven Pinker

Questions?

Overall Philosophy on Writing.

- The best way to write is to use short, declarative sentences.

- Many people when reading text that is written find it enjoyable and more useful when that aforementioned text is compiled into sentences that are minimal in length and make points that are comprehensible in a facile manner by the reader.

Why do People Use Such Complicated Sentences?

- Lost in translation.
  - Differences in sentence construction versus English
- Want to impress their supervisor
- Want to impress themselves

Put the thesaurus away

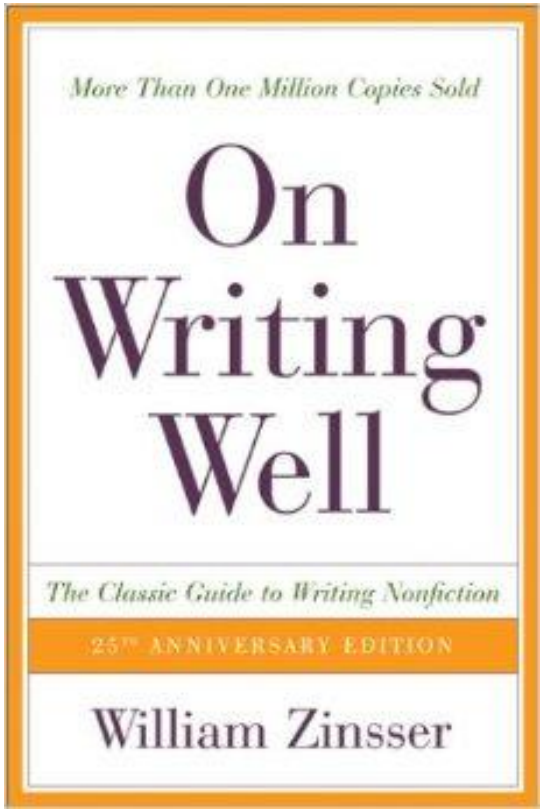
This novel code reduces processing time.

“Read above your level, and write below your level.”

–National Public Radio

Some Simple Rules

There are many “Rule Books”



2

Simplicity

Clutter is the disease of American writing. We are a society strangling in unnecessary words, circular constructions, pompous frills and meaningless jargon.

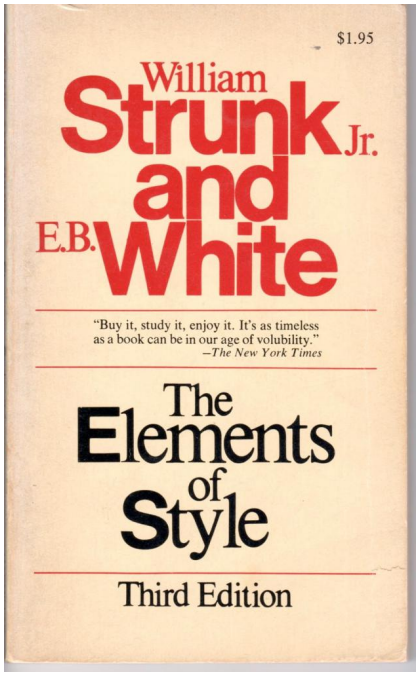
There are many “Rule Books”

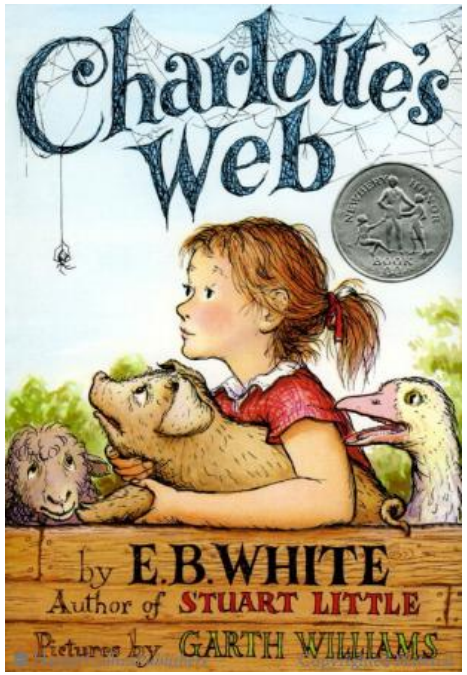
ADVANCED MATERIALS

Whitesides’ Group: Writing a Paper**

By *George M. Whitesides**

There are many “Rule Books”





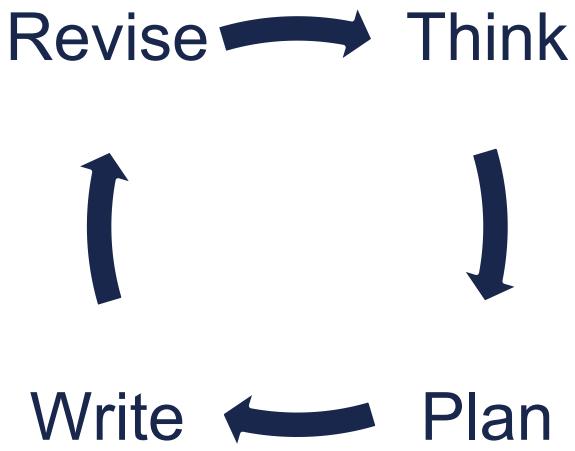
- Only 26 pages!
- $3.52 on Amazon
- Or washington.edu

  “strunk and white pdf”

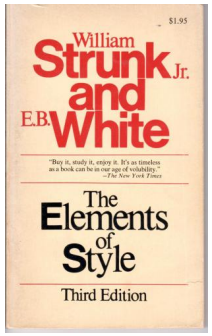
Here are some of my most important rules

0. Revise

1. Read
2. Plan
3. Write
4. Get feedback
5. Revise
6. Follow the rules
7. Revise



Rule 1: Use the Oxford Comma.



In a series of three or more terms with a single conjunction, use a comma after each term except the last.

Thus write,

red, white, and blue
honest, energetic, but headstrong
He opened the letter, read it, and made a note of its contents.

This is also the usage of the Government Printing Office and of the Oxford University Press.

For example . . .


Tails
Complimentary
EAT, RAY, LOVE
Rachael Ray finds inspiration in cooking her family and her dog
10 TIPS
TO KEEP YOUR PET HEALTHY AND HAPPY
TRAINED TO IMPROVE LIVES
A look at how service dogs aid people coping with health issues
Tails
Complimentary
EAT, RAY, LOVE
Rachael Ray finds inspiration in cooking, her family, and her dog
10 TIPS
TO KEEP YOUR PET HEALTHY AND HAPPY
TRAINED TO IMPROVE LIVES

Optional but strongly suggested . . .

We added the salts, HEPES and PBS.

We added the salts, HEPES, and PBS.

Rule 2: Use Subject-Verb-Object Design.

Subject: What does the action.

Verb: The action.

Object: What receives the action.

The software solved the equation.

Rule 2: Use Subject Verb Object Design.

Subject: What does the action.

Verb: The action.

Object: What receives the action.
Is affected by the action

(article) (noun) (verb) (article) (noun)

The software solved the equation.

(pronoun) (verb) (article) (noun) (prep.) (noun)

We solved the equation via software.

(verb) (prep.) (article) (noun) (verb) (noun)

Solving of the equation used software.

Example

Subject: What does the action.

Verb: The action.

Object: What receives the action.

Bad: To the flask, there was added 1.01 g of NaCl. (OVS)

Better: We added 1.01 g of NaCl to the flask. (SVO)

Better: NaCl (1.01 g) was added to the flask. (SVO)

Make the science the subject

Example

Subject: What does the action.

Verb: The action.

Object: What receives the action.
Is affected by the action

Bad: Sunlight is needed by photovoltaic systems.

Bad: Sunlight is needed by photovoltaic systems.

Good: Photovoltaic systems need sunlight.

Example

Subject: What does the action.

Verb: The action.

Object: What receives the action.
Is affected by the action

Bad: The load carrying capacity of the concrete is increased by pre-stressing.

Bad: The load carrying capacity of the concrete is increased by pre-stressing.

Good: Pre-stressing the concrete increases the load-carrying capacity.

Example

Subject: What does the action.

Verb: The action.

Object: What receives the action.

Tip: Only use one verb.

Bad: A reflection reduction of 40 to 22 percent is achieved by adding an anti-reflective coating to the silicon cell.

Bad: A reflection reduction of 40 to 22 percent is achieved by adding an anti-reflective coating to the silicon cell.

Good: The anti-reflective coating on the silicon cell reduces reflection from 40 to 22 percent.

Example

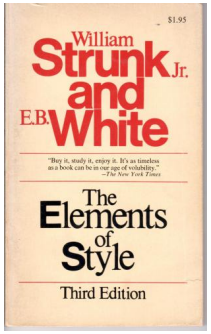
Bad: Using BHA and octanol as collectors at the pulp pH=7, the flotation recovery of cassiterite and concentration of collectors are summarized in Figure 2.

Bad: Using BHA and octanol as collectors at the pulp pH=7, the flotation recovery of cassiterite and concentration of collectors are summarized in Figure 2.

Better: Figure 2 summarizes the relationship between cassiterite flotation recovery and concentration of collectors when using BHA and octanol as collectors at pH=7.

“OK, that’s all well and good, but my sentences often have multiple subjects, objects, and verbs.”

Rule 3: Independent clauses



Place a comma before and or but introducing an independent clause.

OK, what's an independent clause? → A section of words that can "stand on its own".

The battery was charged and tested with the voltmeter. (DEPENDENT; NO COMMA)

The weight of the cars stressed the bridge, and the support columns buckled under the strain. (INDEPENDENT; ADD COMMA)

The code was computationally expensive and additional servers were used to complete the task.

The protein eluted from the column and was collected in a plastic container for downstream analysis.

What About Other Punctuation?

Semicolon (;):

- very independent clauses (but less than a period);
- no conjunction (and, or, but)

Semicolon: Examples

Ten patients were admitted with swine flu; two died within 48 hours.

The outcome data were entered into the database; all records were coded to preserve anonymity.

The fracture toughness testing was performed at room temperature with a testing rate of 0.5 mm/min using the Zwick 1446 universal testing machine; this same machine could also measure Young's modulus.

Other uses of semicolons

→To not start a sentence with a number.

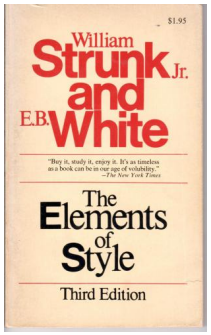
The cohort consisted of 79 subjects with Zika virus. 12 patients were under 55 years of age. (BAD)

The cohort consisted of 79 subjects with Zika virus. Twelve patients were under 55 years of age.

The cohort consisted of 79 subjects with Zika virus (12 patients were under 55 years of age).

The cohort consisted of 79 subjects with Zika virus; 12 patients were under 55 years of age.

Rule 4: Use the Active Voice



Use the active voice. The active voice is usually more direct and vigorous than the passive:

I shall always remember my first visit to Boston.

This is much better than

My first visit to Boston will always be remembered by me.

The latter sentence is less direct, less bold, and less concise. If the writer tries to make it more concise by omitting "by me,"

My first visit to Boston will always be remembered,

it becomes indefinite: is it the writer, or some person undisclosed, or the world at large, that will always remember this visit?

Use the Active Voice.

Jeb Bush: “Mistakes were made.”

Passive voice: Ok, who made the mistakes?

Active voice: George W. Bush made mistakes.

How do I know if it's active voice?

Ask yourself, "Who does what to whom?"

What's the "receiver"? And what's the "performer"?

Active: performer-verb-receiver

Passive: receiver-verb-performer

How do I know if it's active voice?

What's the "receiver"?

What's the "performer"?

Passive	Active
Plant seeds are dispersed by wind.	Wind disperses plant seeds.
The relationship was investigated by Smith et al.	Smith et al. investigated the relationship.
The results have been analyzed by us.	We have analyzed the results.

http://www.biomedicaleditor.com/active-voice.html

How do I Know if it is Active Voice?

Passive:
The activation of Ca++ channels is induced by the depletion of endoplasmic reticulum Ca++ stores.

What does what to whom?

Active:
Depleting Ca++ from the endoplasmic reticulum activates Ca++ channels.

KEY POINT: Make the science the subject

What's the "receiver"?

What's the "performer"?

Passive: The DNA was then subjected to qPCR analysis.

Active (Better): We subjected the DNA to qPCR analysis.

Active (Best): The qPCR analyzed the DNA.

Example

Passive:
By applying a high resolution, 90 degree bending magnet downstream of the laser electron interaction region, the spectrum of the electron beams could be observed.

Active:
We observed the spectrum of the electron beams by applying a high resolution, 90 degree bending magnet downstream of the laser electron interaction region.

But wait! You can't use "I" or "we"!

→ Not true.

"Use active voice when suitable, particularly when necessary for correct syntax (e.g., "To address this possibility, we constructed a λZap library ...)."

http://www.sciencemag.org/site/feature/contribinfo/prep/res/style.xhtml)

But wait! You can't use "I" or "we"!

Behavioral Ecology: "The first-person active voice is preferable to the impersonal passive voice."[4]

British Medical Journal: "Please write in a clear, direct, and active style....Write in the active [voice] and use the first person where necessary."[5]

The Journal of Neuroscience: "Overuse of the passive voice is a common problem in writing. Although the passive has its place—for example, in the Methods section—in many instances it makes the manuscript dull by failing to identify the author's role in the research....Use direct, active-voice sentences."[6]

The Journal of Trauma and Dissociation: "Use the active voice whenever possible: We will ask authors that rely heavily on use of the passive voice to re-write manuscripts in the active voice."[7]

Nature: "Nature journals like authors to write in the active voice ('we performed the experiment...') as experience has shown that readers find concepts and results to be conveyed more clearly if written directly."[8]

Ophthalmology: "Active voice is much preferred to passive voice, which should be used sparingly....Passive voice...does *not* relieve the author of direct responsibility for observations, opinions, or conclusions (e.g., 'The problem of blood flow was investigated...' vs. 'We investigated the problem of blood flow...')."[9]

Science: "Use active voice when suitable, particularly when necessary for correct syntax (e.g., 'To address this possibility, we constructed a lZap library ...,' not 'To address this possibility, a lZap library was constructed...')."[10]

http://www.biomedicaleditor.com/active-voice.html

Classic Mistake

Young writer – cautious writer – passive voice

Classic Example

equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

[1] Young, F. B., Gerrard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1920).
[2] Longuet-Higgins, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, **5**, 285 (1949).
[3] Von Arx, W. S., Woods Hole Papers in Phys. Oceanog. Meteor., **11** (3) (1950).
[4] Ekman, V. W., *Arkiv. Mat. Astron. Fysik. (Stockholm)*, **2** (11) (1905).

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

is a residue on each chain every 3·4 A. in the *z*-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 A. The distance of a phosphorus atom from the fibre axis is 10 A. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical *z*-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows : purine position

Rule #5: Always use the word “because”

Offender #1: As
Offender #2: Since

→ Avoid because they have a temporal connotation.

“I drank coffee as I drove to work.”

I drank coffee *because* I was driving to work? Maybe.

I drank coffee *while* I was driving to work? Maybe.

Rule #5: Always use the word “because”

The adsorption energy only increases by 0.020 eV as the cutoff varies from 4.8 to 5.3Å.

***because* the cutoff varies?**
***while* the cutoff varies?**
(*despite* the cutoff varying?)

Rule #5: Always use the word “because”

These will give your reader a mini-stroke:
“owing to the fact that”
“due to the observation that”
“in light of the occurrence of”

You wouldn’t tell your friends, “The police pulled me over owing to the fact that I was speeding.”
→ “The police pulled me over *because* I was speeding.”

REMEMBER: If it sounds insane when you read it out loud, then it is probably awful writing!

Rule #6: Minimize Clutter

"The secret of good writing is to strip every sentence to its cleanest components. Every word that serves no function, every long word that could be a short word, every adverb that carries the same meaning that's already in the verb, every passive construction that leaves the reader unsure of who is doing what—these are the thousand and one adulterants that weaken the strength of a sentence. And they usually occur in proportion to the education and rank."

--William Zinsser in *On Writing Well*, 1976

Great Example

Great Example

There are a variety of upcoming projects anticipated to be carried out by a number of different agencies that are intended to help improve mobility within the University City area, including the Caltrans North Coast Corridor Project, the Mid-Coast Corridor Project, and the UCSD Circulation Improvements.

Translation:

- **"We have no idea when this project will start or finish; don't even ask how much it will cost."**
- **"There are many other agencies that we will blame when things go wrong."**
- **"No one is accountable on this project."**

This is what Clutter Does

- Vague writing
- Passes the blame
- Useful when you aren't sure

Clutter Example

BAD: "This paper provides a review of the basic tenets of stem cell biology study design, using as examples studies that illustrate the methodologic challenges or that demonstrate successful solutions to the difficulties inherent in biological research."

- **Turned verb into noun**
- **Examples inherently illustrate and demonstrate**
- **Challenges and difficulties are the same thing**
- **"successful solutions" → as opposed to solutions that fail?**

BETTER: This paper reviews stem cell biology study design using examples that illustrate specific challenges and solutions.

Beware of Zombie Nouns

Zombie Noun: Taking a perfect verb and making it a noun

These findings imply that the rates of ascorbate radical production and its recycling via dehydroascorbate reductatse to replenish the ascorbate pool are equivalent at the lower irradiance, but not equivalent at higher irradiance with the rate of ascorbate radical production exceeding its recycling back to ascorbate.

These findings imply that, at low irradiation, ascorbate radicals are produced and recycled at the same rate, but at high irradiation, they are produced faster than they can be recycled back to ascorbate.

Minimize Clutter

The proposed method has the advantages of simplicity, low-cost and ease of operation, and allows for the determination of Sudan dyes in complex matrices with good accuracy and reproducibility.

The proposed method is a simple, affordable, accurate, reproducible, and easy way to measure Sudan dyes in complex matrices.

Minimize Clutter

The results concerning the accuracy and precision of the method have been shown in the Table 2 for three levels (LOQ, 5LOQ, 10LOQ) of salicylaldoxime.

Table 2 shows the accuracy and precision results for LOQ, 5LOQ, and 10LOQ salicylaldoxime.

Minimize Clutter

Wordy	Crisp
A majority of	Most
A number of	Many
Are of the same opinion	Agree
Less frequently occurring	Rare
All three of the	The three
Give rise to	Cause
Due to the fact that	Because
Have an effect on	Affect
Was found to be	Is
Provides an understanding of	Explains
Reduces the quantity of	Reduces
A total of ### samples	### samples
Taking into consideration	Consider
At the same time	Concurrently; simultaneously
were taken as evidence of	suggest

Minimize Clutter

Clutter	Why it is not needed	Simple
The measured data The observed data The obtained data	Versus the data you fabricated?	The data
The employed method	The method you didn't use?	The method
The stated hypothesis	The hypothesis you are keeping secret?	The hypothesis
The known facts	Unknown facts?	The facts
It is well known that X has been shown	Then why are you stating it; add a reference	X X
The XXX of interest	As opposed to the uninteresting one?	The XXX

Other Tips: Eliminate Negatives

Wordy	Crisp
Not harmful	Safe
Not important	Unimportant
Does not have	Lacks
Did not pay attention to	Ignored
Did not succeed	Failed

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AACR American Association for Cancer Research

AMERICAN SOCIETY FOR MICROBIOLOGY

ASN EST. 1928 American Society for Nutrition *Excellence in Nutrition Research and Practice*

Science AAAS

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