CONTENT *Crafting a scientific manuscript for publication can be a daunting task. Here two former editors attempt to demystify the manuscript writing and review process. This article contains tips on how to start writing, organize the writing process, create informative figures, select a journal, work with editors, and respond to referees' comments. The authors also offer hints on what »trendy« journals are looking for and what they avoid like the plague.*

Science nonfiction

Tips for writing a scientific manuscript

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• So, you've invested several years in learning to be a scientist. You've worked hard, produced provocative results – and you're ready to write a paper. This should be the easy bit, right?

Wrong. Maybe writing a paper isn't the hardest thing you have to do as a scientist, but manuscript drafting is one of several skills (for example, grant writing, lab management, how to be a good boss) that new prinicipal investigators (P.I.s) often find themselves having to learn on their own. And it's a crucial skill. You might be the best experimentalist in the world, but if you do a poor job of communicating your results your contribution to science will be undervalued.

Is this introduction making you feel worse? Are you now even more unwilling to sit down and write? Does the bench suddenly look amazingly friendly and inviting by comparison? In emphasizing the importance and difficulty of writing a first-rate paper, we are not trying to increase your anxiety level. Rather, we are attempting to make it clear that this skill, like any other, needs to be learnt. Don't expect to be able to draft your first paper in one sitting just because your supervisor or P.I. can. She's had a lot of practice. Do understand that this skill is a basic professional requirement – if you want to be a scientist, there is no way to get out of writing papers.

Take a deep breath. You can do it. Very few people find paper-writing easy at first; graduate students often reach the manuscript-writing stage years after the last time they had to produce a serious bit of text, and a research paper is very different from anything you've ever had to write before. So it's not surprising that it's hard. However, you can find comfort in the fact that nearly everyone gets dramatically better with practice.

Writing, like interpretation of results, is hard to teach except by example. We hope that your P.I. takes seriously his or her responsibility to help you learn to write. But because scientists are usually not trained to be professional writers or writing teachers, it may be hard for your advisors to articulate exactly what they think you should change about your style. This article, which was originally used in a course on the Practice of Science at the University of California in San Francisco (UCSF), CA, USA[***], may provide a different angle on the problem. In reading it, consider the source: one of us is an ex-editor of *Science*, and the other is an ex-editor of *Nature*. This may bias our perspective on occasion, but we've tried our best to offer widely applicable tips and information.

When to stop doing experiments and write

• When do you have what it takes to make a paper? The only way to answer this is to try to draft the manuscript. This process often exposes

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holes in your argument that cause you to go back to the bench and do more experiments. Thus the drafting of a manuscript is a useful exercise to undertake as soon as you think you know where your research is leading.

To draft a paper, begin by working out what the figures and tables will look like. Write a sentence or two about the conclusions each of the figures and tables is intended to convey. When the sentences look as if they tell a story, it's time to start writing.

Deciding what to leave out can be as important as deciding what to include. Fascinating little bits of information that are off the main point are distracting to reviewers and always cause trouble. At best, you have to revise the paper to leave them out; at worst, criticisms of the incidentals can be used to reject the paper even if the main points are unassailable. We realize (from personal experience) that it can be painful to slash these insightful asides from your manuscript, but the ability to do so is crucial.

Getting started

The art of writing is the art of applying the seat of the pants to the seat of the chair.
– Mary Heaton Vorse

• Most people put off starting to write until the last possible moment. There is something about a blank page that causes the mind to go just as blank. Train yourself out of this terrified-rabbit syndrome by writing early and often. Most people find it easier to edit something, however close to garbage it is, than to start from scratch.

Writing gets easier as you get used to doing it. Different scientist-writers have distinct rituals that help to shift them into »writing mode.« Some of these fetishes are temporal (reserving the same hours of each day for writing), others spatial (a sunny spot at the kitchen table or in a secluded corner of the library or a local coffee shop). You may decide to take walks or exercise before settling in front of the computer. However you do it, the important thing is to persist.

The text

To write simply is as difficult as to be good.
– W. Somerset Maugham

• First things first: you're writing a paper because you have something important to tell the scientific community. What is it? Before you start, decide on the one thing you want to get across in this paper. It's your bottom line, and it should be conveyed clearly in the manuscript. Repeat the bottom line over and over again – at the end of the abstract, in the introduction, in the results, and in the discussion.

Once you have figured out what you want to say, draft the *results* section of the paper. It's best to first lay out the figures that you need to make your point in a sequence that tells the story. Any result that isn't relevant to the bottom line should probably be deleted. If the result seems really important to you, yet is irrelevant to the bottom line, you probably need to rethink the bottom line.

It often works well to let the story unfold in the way it actually happened in the lab. Write down why you did the experiment and what the conclusions are. If it's not too late, get into the habit of doing this in your laboratory notebook as you go along. (It may seem impossible that you will ever forget why you did an experiment or the conclusions you drew from it, but when a series of experiments stretches over many years, motivations and inferences can get lost.) Unless your experiments were done for reasons that turned out to be irrelevant to what you actually found out, simply writing down what you did and why will be a good first draft of your results section.

After completing the results, list what *methods* were used to generate the results, then write down what you did to carry out the experiments. Simple. But if you're re-using a methods section from elsewhere (such as a student thesis) don't just cut and paste; check that all the methods described in the sections you pirate were indeed used in the current paper. You'd be surprised how many people forget to do this. And remember to define abbreviations that your audience might find unfamiliar (such as your pet name for the buffer you used).

What to include in the *discussion* is, in part, a matter of taste – and of where you plan to send the paper. We think that the discussion should do more than merely reiterate the results. It's your chance to put your findings in perspective, propose a model, outline a direction of investigation, and make the reader think. But be aware that if your speculations go too far beyond what you've actually shown in the paper, the referees will challenge you. Make sure that you clearly distinguish between what you've shown and what you imagine. (After all, you could be wrong.)

We've left the *introduction* until last because many people prefer to write it last, when they're clear about exactly what they have to introduce. The introduction should be written with a view to setting up the background for what the readers are about to learn (the bottom line) and why it matters. It should cover the aspects of the field that raised the question you addressed in this series of experiments. In an ideal world, you really did know about all these points before you started, and the experiments really were designed to elicit the answer you got. More often, the background evolved for you as you did the work. This doesn't matter as long as you can give a coherent reason for thinking that your question is interesting, and for having believed that the experiments you did would address it. To end the introduction, briefly summarize what the reader is going to learn and why it is important.

The figures

• Each figure should have one clear point or purpose. Describe it succinctly in the figure legend; usually you can use this point as the first line of the legend. Make sure that the figure is clearly labelled and that symbols are defined in the legend. Avoid complicated figures if you can. Consider whether different ways of pre-

senting the data would better serve the same purpose. For example, do you really need to show 20 binding curves, or would a table of 20 K_ds do just as well?

When constructing a figure with multiple parts, give some thought to the pattern the reader's eye will follow. In the Western world, we're used to reading left to right, then top to bottom. Therefore, showing a sequence of events that runs left to right then right to left and back again is usually not a good idea. Using different orders of presentation in different but related figures is also confusing for readers. Certain colours (e.g. bright red) attract more attention than others. Does your colour code correspond to the message of the figure (that is, does it highlight the key points)? If your figures are unusually complex, persuade a graphic designer at your institution to help you, or invest in a good book on how to design figures for scientific texts.

If you have intricate colour photographs, consider the quality of the photos in the journal you choose. For example, *Development* does lovely colour photos on high-quality paper, whereas *Nature* and *Science* use lower quality paper (not great for colour photos). Colour figures can be pricey: do you really need colour for your message to come across?

The thank-yous

• Carefully consider whom to name in the *acknowledgements*. It is much worse to forget someone who deserves to be acknowledged than to include someone who doesn't deserve it. Err on the side of inclusion.

General tips for clear writing

• You have a story to tell, and its logic is clear to you. The question is, how do you make that logic clear to the reader? Here are our tips:

(i) help the reader all you can with signposts. For example, it sometimes helps to start the paragraph with a question that indicates where you're going with the argument that follows. Subheadings can be very useful, if the journal allows them.

(ii) As well as the paper having a »bottom line«, each paragraph should have one. What are you trying to explain to the reader in this paragraph? What should they have learnt by the time they've finished reading it? It is because of the need for a paragraph to have a bottom line that many teachers advocate outlining an essay before you write it. Some people find it useful to list the points to be made in the order in which they should be made, and then to expand each point into a paragraph. For others, it's not necessary or helpful. But try it before you decide that you're one of the latter group.

(iii) Treat each paragraph as a thought. Starting a new paragraph indicates a new thought. It should be clear how the new thought follows from the previous thought. There should be a clear link (or transition) between the end of one paragraph and the beginning of the next, and the successive bottom lines of the paragraphs should follow a logical order. If you didn't originally outline your paper, summarize the finished paper in the form of an outline to check that the ideas in your paragraphs follow a logical progression.

(iv) Sentences within a paragraph need to be connected by an obvious flow of ideas. Keep sentences fairly short and to the point. Bear in mind that sentences in English tend to be considerably shorter than »good« sentences in German or French, for example. Trying to get too many ideas into one sentence (or one paragraph) will make it hard for the reader (or reviewer) to decipher your meaning. Remember, people are busy, and few of your readers will understand your system as well as you do. Points that you think are blindingly obvious may well not be to your reader.

(v) Check that phrases within the same sentence connect with each other and do so unambigously. When you use a pronoun like »it« or »they«, check that it's clear what the pronoun refers to. For example, »there are several differences between microtubules and actin filaments; first, they are larger« leaves the reader in confusion over whether »they« refers to the microtubules or the filaments.

(vi) If you provide several lines of evidence that all tend toward the same conclusion, don't simply say »1 is true, 2 is true, 3 is true. The conclusion is...« Help the readers to understand why you're giving them all these facts from the start, by pointing out how all the lines of evidence support one another: »1 is true, suggesting this conclusion. Similarly, 2 is true, and furthermore 3. Thus it seems clear that...«

(vii) Don't be afraid to say what you think is going on. But don't claim that a hypothesis is proven if it's not. »An obvious explanation is ... but many other explanations are possible« or »a plausible explanation is that...« are two ways to show the reader how you're making sense of the data without misleading them into thinking that you believe you've proved the hypothesis conclusively.

Ways to improve your text

• Most people explain things better when they're talking than when they're writing. In part this is because many people seem to think that scientific writing requires you to use complicated multi-syllable words, the passive voice, and intricate sentences. First, try writing the way you talk. Dictate into a tape-recorder if that helps. Most journals don't insist on the passive voice, and none of them require you to use five syllables where one will do (utilization instead of use, for example).

When you're writing your first draft don't worry about minor issues, such as using the same word over and over, ending a sentence with a preposition, and splitting infinitives. It's a *draft*; don't expect it to be perfect. You can always tidy up later. Most texts undergo several rounds of editing and revision before they are ready to be submitted to a journal. Worry about organization of the manuscript and how best to ensure that it makes sense. Worrying about style too early tends to lead to a loss of clarity or the dreaded writer's block.

Ask an intelligent colleague or two who are as far removed from your immediate scientific field as possible to read the draft and mark all the places where they get lost. Ask some other colleagues who know a lot about your field to scrutinize it for errors; you'll get entirely different comments from the two groups. Do consider every comment carefully, but don't feel that you have to accept every suggested change. Sometimes you can fix the problem in an entirely different way; occasionally the reader is plain wrong. Remember that sometimes the best way to fix a problem is to delete a sentence. Maybe it was off the point and shouldn't have been there in the first place; maybe that's why your readers are asking what exactly you mean.

Once you've produced a draft, put it aside for a week and do something else. Then read it again. You'll be surprised how much easier it is to spot the parts that are difficult to understand when you've been thinking about something else for a while.

Where to send the paper

• This is a decision you need to make early on, unless there are several journals in your field that all use the same format and have similar length requirements. In most cases it's not too difficult to narrow the choice to a couple of journals; think about who you want to see the paper and why, who is likely to be interested in it, and which journals publish papers on similar subjects, at similar levels of interest.

Usually you're looking for a quality journal with the right kind of audience that is not too painfully slow and whose editors and referees seem to make reasonably sensible decisions. Sometimes you're just looking for a journal that's respectable and won't give you a hard time (for example, if all you want to do is archive something that's not particularly interesting). The decision is hardest when you have what seems to you to be a really exciting paper. Should you try one of the »trendy« journals?

The pleasures and pitfalls of high-profile journals

• Publishing a paper in a high-profile journal can do you a lot of good. But it's a risky business. There is a huge element of luck in getting a paper accepted by a journal like *Nature* or *Science*. Both of those journals select about ten papers a week from over a hundred submissions. Even though up to 70 of those 100 submissions may fall short of the journal's criteria for interest or technical quality, there is still some level of subjectivity in which of the remaining 30 are selected. Sometimes a referee will show an inadequate level of enthusiasm, while giving no real criticism of the data; the referee might just have been having a bad day when he or she reviewed your manuscript, but your paper is rejected just the same. Another factor is that some papers are hard to write in a *Nature* or *Science* short format. If you really need to show six or more figures to make your story convincing, or if you need more than about 2,000 words to say what you absolutely have to say, you should probably give in gracefully and go elsewhere. Depending on your field, there may be equally high-profile journals (usually, alas, equally selective) that offer more space.

Because most papers submitted to *Nature* or *Science* are rejected, deciding to submit a paper there will, more often than not, cost you time – usually at least 1-2 months. Half the papers are rejected after two weeks, and you then have to rewrite in another format (another two weeks). The rest of the papers that are rejected are refereed first, which usually takes an extra 3-5 weeks.

If you submit to one of the trendy journals, do so in the full knowledge that your paper is quite likely to be rejected even if it's good, and you will then have to rewrite and submit elsewhere. Don't get suicidal when this happens. Nobel-prize-winning research has been rejected by these journals. If the paper's good, and it's published in a high-quality journal, it'll be recognized for the groundbreaking research it is.

Despite all we've said about the negatives, undoubtedly you'll want to run the gauntlet at some point in your career; so, what is it that *Nature* and *Science* are looking for?

It's easier to define what turns them off. Describing your results as additional confirmation for a well-accepted theory is a certain route to rejection, for example. The editors are primarily looking for papers that fall into one of the following categories:

(i) an advance whose implications cross disciplines, i.e. a result of »general interest«. For example, the discovery of cyclins and cyclin-dependent kinases was interesting to researchers in many fields, including cell-cycle regulation, DNA replication, transcription regulation, tumour suppressors and oncogenes, and so on;

(ii) a result that connects two previously unrelated areas of research;

(iii) a really big advance in a trendy field, even if it isn't all that relevant to anyone outside the field; or

(iv) supremely important methods, e.g. polymerase chain reaction (PCR), differential display.

Other criteria constantly change. For example, the editors will periodically decide that a particular subject is under-represented and accept papers in this area to show an interest. Or papers that use a pioneering technique such as gene knockouts may be given an easy time for a while, until the technique is no longer perceived as pioneering.

Dealing with editors

• It is important to realize that when it comes to editors, there are two distinct kinds of beasts: academic editors and professional editors. Some journals that use professional editors are *Cell, Current Biology, PLoS Biology, Nature,* and *Science*. These are also the journals that attempt to select papers that have a poorly defined characteristic called »general interest«, measured by the effect of the paper on the jaded palate of the professional editor. If you want to publish in one of these journals, make sure that the elements that make your paper »spicy« are obvious.

Professional editors probably will not be experts in your field. This has the disadvantage that these editors will rarely be able to make their own judgements about the quality of your work. Academic editors are much more likely to be knowledgeable about your field than professional editors, and will more often be able to supplement the referees' criticisms with their own or dismiss a referee's criticisms as irrelevant. But professional editors are, in the end, professionals: they spend all day, every day, reviewing and judging manuscripts, and they have access to a database of information on what has been accepted and rejected in the past and why. All of this influences the decision-making process. (And remember, when you call a professional editor to complain about how long it's taking for your manuscript to be reviewed, that she knows all about how long you take to review papers.)

Writing to editors

• When you submit a paper, or resubmit a revised paper, make the editor's life easier (and thus expedite the review process) by including a cover letter. This should concisely explain the major conclusions of the paper, as well as why and to what fields they are important. This is particularly important for »trendy« journals.

It is often helpful to list possible reviewers. But it is more important to list people that you absolutely, positively do not want to review your paper. Be reasonable. It is not acceptable to rule out all of the major players in your field. (*Science* once had an author request that »no one from Boston, San Francisco, or San Diego« review his paper!) Also let the editor know if you have concrete information about competition. For example, if you know that a related paper has been or is about to be submitted to another journal, tell your editor so that she can take steps to minimize your chances of being scooped.

The cover letter for a revised manuscript MUST include a point-by-point rebuttal of the issues raised by the referees. If you really want the editors to like you, send them a marked-up copy of the new version showing which bits have changed.

Referee selection and the review process

• Peer review is a crucial component of scientific research. Therefore, editors must carefully consider what kinds of scientists are needed to assess the quality of a given manuscript. Editors will almost always select at least two expert referees, usually with complementary expertises. Sometimes the editor will also select a referee with a broader perspective, who may be in a field that is only loosely connected to the one that is the subject of the manuscript. For example, let's say your paper is about discovering a transcription factor that (i) regulates development in flies and (ii) houses a helicase activity. The editor will certainly have the manuscript reviewed by a *Drosophila* developmental biologist and someone who understands helicases. However, the editor might also enlist the help of a developmental biologist who uses zebrafish as her model system, or a biochemist who studies other proteins that regulate transcription.

An important part of an editor's job is finding and calibrating new reviewers. Is the reviewer close enough to the field, without being so close as to be an almost-certain competitor? Are they generous enough to spend hours helping to improve a paper instead of writing one of their own? Will they look beyond the irritations of poor prose and minor mistakes and ask whether the main point of the paper is securely established, and important?

How (not) to deal with comments from reviewers

• Comments from referees fall into several classes. Most can be categorized as one of the following:

(i) valid criticisms that are easy to address;

(ii) valid criticisms that are hard to address;

(iii) invalid criticisms that you can easily show to be invalid;

(iv) invalid criticisms that seem valid unless you know an awful lot about the subject;

(v) matters of opinion, or

(vi) deliberate attempts to delay the paper for no good reason (fortunately rare).

Obvious pitfalls in dealing with the comment types listed above include:

(i) not addressing the easy valid criticisms because you've put too much work into this paper already. If it improves the paper and it's easy, just do it. That's what the review process is all about.

(ii) Complaining about the incompetence of the referee instead of addressing her comments, or rubbing the referee's nose in how stupid the invalid criticisms were. If a referee, carefully chosen to be expert in your field, had a problem with your paper, then 99% of the rest of the world will as well. Try to see where the misunderstanding came from, and be thankful for the opportunity to fix it before prime time.

(iii) Mistaking comment types iii-v for comment type vi;

(iv) Failing to realize that there really can be two opinions regarding the interpretation of your data.

The case of the valid criticism that will take a lot of work to fix is perhaps the hardest to deal with. Do you go away and do the work, taking a year and perhaps being scooped in the process, go to a less high-profile journal (and perhaps run into the same problem), or try to persuade the editor and referee to let you talk your way out of it? One argument you can use in this situation is that one paper doesn't have to solve the whole problem.

When responding in writing to a reviewer's comments, do respond to every point (even those you think are ridiculous or incorrect). In a letter to the editor, list these points, along with the changes you've made to address them (or the reasons you haven't addressed them). Point out which pages in the manuscript contain the changes you've made in response to the referees' comments.

In all dealings with reviewers and editors, you will do better than aver-

age if you work under the assumption that all editors and referees are, like you, serious, conscientious people who are doing their best for science and for the scientific community – even if the evidence *appears* to indicate otherwise. Be polite, however provoked. Editors and referees are conscientious people, and so they will probably forgive your rudeness. But why take the chance? Don't fire off a furious e-mail the moment that you receive the rejection letter. By all means write it and get it out of your system, but then throw it away and write a more measured response the next morning.

Our bottom line

• Take writing seriously, and work at it. Science is a community effort, and communicating your results promptly and clearly is part of your job as a professional scientist. Take reviewing seriously, too, from both ends. As an author, remember that a conscientious referee can save you from appalling errors. As a referee, remember to keep a sense of perspective; just because you've spent hours reviewing a paper doesn't mean that every single thing you found has to be fixed before publication. Finally, making an effort to work with your editor can help to facilitate the review and publication processes.

Good luck, and happy writing!