Summarizing

Topics: abstracts, specific aims, making things shorter, titles

ABSTRACTS

Key points:

- Purpose
  - Cited as many times as possible
  - Published in highest possible impact journal
- What purpose means you should include (in addition to results)
  - Important problem your work addresses
  - How your work relates to the problem
  - The research question
- Can assemble parts from paper, then:
  - Revise to make it easier to follow
  - Make it shorter—see last section

An obvious function of an abstract is to provide the reader with enough information to allow him or her to decide whether to read the whole paper. Thus, the abstract acts as a sort of advertisement for the paper; in order to determine what information to include, we must consider who you want to read the paper. Most likely, you want everyone doing research related to yours to read your paper. These readers may then use your findings to interpret their results and thus cite your work in their papers, increasing your impact. Another person you want to read the paper (and whose concerns many overlook since they assume this person will always read it) is the editor of the journal to which you submit. If you submit to a high-impact, broad audience journal[*], the editor likely does not have time to read every paper submitted, so the abstract must convince him or her to consider your paper for review.

In order to determine what information would convince your desired audience to read the paper, we'll start with the bare minimum of content. The part that an abstract obviously must include is the results—the payoff for all your hard work and what determines the potential impact of your paper. Let's see whether a results-only abstract would serve the functions we have determined:

Abstract example 1 version 1: no rationale

We explored how competitive interactions between microbes affect the acquisition of virulence characteristics. During model murine nasal colonization, *Haemophilus influenzae* outcompetes another member of the local flora, *Streptococcus pneumoniae*, by recruiting neutrophils and stimulating the killing of complement-opsonized pneumococci. For *S. pneumoniae*, resistance to opsonophagocytic killing is determined by its polysaccharide

[*] This isn't to imply that you should only follow the guidelines in this lesson if your paper is for a high-impact journal. Including everything explained to be necessary for that goal would improve any abstract; further, writing all your abstracts this way will make it easier to do when you do have *Nature*-worthy results.

capsule. Although there are many capsule types among different *S. pneumoniae* isolates that allow for efficient colonization, virulent pneumococci express capsules that confer resistance to opsonophagocytic clearance. Modeling of interspecies interaction predicted that these more virulent *S. pneumoniae* will prevail during competition with *H. influenzae*, even if production of a capsule is otherwise costly. Experimental colonization studies confirmed that competition increased survival of the more virulent *S. pneumoniae* type. Modified from Lysenko ES et al., "Within-host competition drives selection for the capsule virulence determinant of *S. Pneumoniae*," *Curr Biol* June 2010.

This abstract would interest an editor of a journal on infectious microbes, not the editor of a journal like *Current Biology*. In order to interest an editor of such a journal (or the highest-impact journal appropriate for your work), the abstract must explain why your paper belongs in it—why your results are important. How does your work relate to the big picture—why does it matter to science or human health? One way to address this is to state the problem your work addresses; another is to say what they mean for the broader field—their implications. Including both would best show why editors and other scientists should care, especially if the implications are clear and direct. Since the important problem is at the beginning of the story, they're especially effective—they can grab a reader's attention with the importance of your work.

Include the important problem

Since we know these parts are key to the goals of an abstract, let's add the important problem and implications to the example:

Abstract example 1 version 2: problem unconnected to results

Many opportunistic pathogens, such as *S. pneumoniae*, have evolved virulence determinants and express pathogenic behavior, though damage or death of their host offers no obvious selective advantage to microbial growth or transmission. We explored how competitive interactions between microbes affect the acquisition of virulence characteristics. During model murine nasal colonization… Experimental colonization studies confirmed that competition increased survival of the more virulent *S. pneumoniae* type. Our findings demonstrate that competition between microbes during their commensal state may underlie selection for characteristics that allow invasive disease.

Now we see that this work addresses a question of broad scientific interest—how can a feature that offers no obvious survival advantage evolve? However, it's unclear why the researchers chose to study competition to get at this problem; this version leaves out the connection between the problem and the results. Without that, whether this paper actually offers an answer to the problem is ambiguous, so we don't know whether it really is as high impact as the problem. We need another step in the authors' logic: Many pathogens initiate interactions with their host on mucosal surfaces and must compete with other members of the microflora for the same niche. This allows us to specify the way in which we would expect competition to affect virulence: Here we explore whether competitive interactions between microbes promote the acquisition of virulence characteristics. Now we have a clear logical progression—not only do we see the connection between the experiments and the problem, but we can see the story.

Include the research question

We've shown that explaining why you did the work is important for conveying its significance and telling a story, but is it enough? Let's consider an abstract with only these elements, from a paper considered in previous lessons:

> **Abstract example 2**: no question
> Tumor cells display progressive changes in metabolism that correlate with malignancy, including development of a lipogenic phenotype. How stored fats are liberated and remodeled to support cancer pathogenesis, however, remains unknown. Here, we show that the enzyme monoacylglycerol lipase (MAGL) is highly expressed in aggressive human cancer cells and primary tumors, where it regulates a fatty acid network enriched in oncogenic signaling lipids that promotes migration, invasion, survival, and in vivo tumor growth…
> From Nomura DK et al., "Monoacylglycerol Lipase Regulates a Fatty Acid Network that Promotes Cancer Pathogenesis," *Cell* Jan 2010.

This abstract leaves unclear whether the authors suspected that MAGL was involved in malignant lipogenesis, or whether this study is the first to suggest that—whether the science is hypothesis-driven or exploratory. This question is important not only for truly understanding what the authors did, but also for determining the significance of the work. If evidence existed to suggest that MAGL had something to do with metabolic changes in aggressive cancer, this paper would be less important than if it identified this enzyme's role. The key piece that would answer this question is what the authors were trying to find out when they started the work—their research question. The reader could find this in the rest of the paper, but editors of high impact journals, which receive huge numbers of submissions, may not have time to do so. Therefore, including this step could appreciably affect a paper's fate.

Abstract as assemblage of parts

From these examples, we can extrapolate the general importance of telling the whole story. In an abstract, this generally requires the most important pieces of the important sections (introduction, results, and discussion). The key parts of the introduction are the problem, how you got from the problem to the question, and the question; those in the results are, of course, what you did and what you found; and the discussion's highlights are the conclusion and, if it's significant, the implication for health or future research. The lessons on "Explaining rationale" and "Putting results in context" cover how to formulate these pieces. Describing the experiments and their results should be a straightforward task, but we'll look at how to do so succinctly later in the lesson. You can construct an abstract by taking these sentences from the already-written paper and pasting them together (or you could write it from scratch, using a similar question and conclusion to those in the paper). Of course, such a collage-style abstract may not automatically read smoothly—it will likely need some revision for coherence (see lessons 12 and 13, "Revising for reader ease"). Further, it will likely be longer than the journal allows, so you'll need to make it shorter (see the third part of this lesson). Consider how different the competition abstract is from the assemblage of parts from the paper:

Abstract example 3: cut-and-paste

One of the most basic and important evolutionary questions posed about pathogens is why they harm the very sources of their livelihoods, their hosts. Though theoretical models frequently assume that traits contributing to virulence provide a net selective advantage to the pathogen, such advantages are difficult to identify for many pathogens, including *S. pneumoniae*. *S. pneumoniae* must compete with *Haemophilus influenzae* for the same niche, and *H. influenzae* directs host immune responses towards *S. pneumoniae*. Thus, we asked whether competitive interactions between microbes promote the acquisition of virulence characteristics. To address this, we analyzed a simple model for the within-host dynamics of two strains of pneumococcus (virulent and susceptible) together with *H. influenzae*. The virulent form has an increasing advantage over the susceptible form as the density and/or immunomanipulative behavior of *H. influenzae* increases, because it can resist the inflammatory response generated by *H.* Further, in vivo, immunomodulation by *H. influenzae* can dictate the relative capsule-type-dependent fitness of pneumococcal strains. We therefore suggest that events during within-host competition may underlie the benefit of virulence determinants that either induce or protect against the host's inflammatory responses.

In this version, "virulence" appears in the second sentence without an explanation of how it relates to the first, which might lose a reader not familiar with the term. The published version connects virulence to pathogenic behavior in the first sentence, avoiding this problem. Further, here, the statements of the results are too detailed, and it's hard to see how they address the question. The authors' decision to frame everything in terms of competition unifies the final version of the abstract. From this example, we can draw some lessons about coherence in abstracts: *define terms before using them, and frame results and conclusions so that they clearly correspond to the question*.

SPECIFIC AIMS

Key points:

- Purpose—get proposal funded
    - Must explain rationale—aims also serves as introduction
    - Rationale includes problem, unknown, and overall goal
- What purpose means you should include in addition to these:
    - How your work relates to the problem
        - Explain as thoroughly as possible
        - Will take up considerable proportion of aims page
    - Innovation

We can use the same approach to determine what a specific aims page should include. Its purpose is to persuade study section members, including many who will not read the rest of your proposal, that your project should be funded. As discussed in "Explaining rationale," one of the keys for this is explaining how your work relates to a significant problem to which the funding agency is devoted. The key parts of this explanation covered in the previous lesson are the problem, the unknown, and the overall goal. Here's an example (modified) opening of a specific aims that includes well-written statements of these:

Specific aims example part 1: goal unconnected to problem

Eukaryotic innate immune systems act as effective barriers to infection by microorganisms. Plants have numerous pattern recognition receptors (PRRs) that can recognize specific virulence proteins specifically present in pathogens (known as Avr proteins). *Pseudomonas syringae* uses type III protein secretion systems to inject effector proteins into host eukaryotic cells, where they suppress innate immunity. We have shown that a primary role for many *Pseudomonas syringae* type III effectors is to suppress innate immunity. However, the enzymatic activities and the mechanisms that type III effectors use to suppress innate immunity are not well understood.

The objective of this application is to identify targets of the *P. syringae* type III effector HopU1, a mono-ADP-ribosyltransferase (ADP-RT), and to determine its roles in bacterial pathogenesis. Our preliminary data shows that HopU1 binds to the *Arabidopsis* RNA-binding protein GRP7, which plays a role in innate immunity. *We hypothesize that HopU1's targets are components of innate immunity.*

Modified from Alfano JR, "Suppression of innate immunity by an ADP-ribosyltransferase type III effector," SF424 application, 2007. Available at: http://funding.niaid.nih.gov/ncn/grants/app/Alfano-AI069146-01.pdf

The authors suggest that the proposal has to do with eukaryotic innate immunity in general, while they study the interaction of a specific protein from a certain type of bacteria with a single plant species. To convince study section members of the relevance of this project to human health (it was submitted to NIAID), the specific aims should explain more thoroughly how these are related—how similar is innate immunity in plants to that in humans? Do bacteria that infect humans use similar mechanisms to suppress host responses? How important are type III effectors to the pathogenicity of *P. syringae*? How important is HopU1 among the type III effectors? Would all of these effectors bind to the same targets? The authors might have assumed that their proposal would be assigned to someone who studied immunity in *Arabidopsis*, but the specific aims must convince the whole study section to fund the research. Thus, this explanation is more important than what the authors spend most of their space on (see part 2—re-stating their hypotheses and describing their qualifications to do the research), so it's okay if it takes up a large portion of the specific aims

→ *Explain the relationship of your project to the funding institution's goals*

Include innovation

Assuming you can accomplish this, what else does the study section need to see what the proposal is about and deem it worthy of funding? You're probably eager to tell them about the experiments you've planned, since you've spent so much time and effort choosing and refining them. However, those reviewing your proposal are less interested in the details of what you will do than you might think: they will assume while reading the Specific Aims that the experiments you've chosen are appropriate to the aims and technically feasible (and in any case, they can suggest that you drop some and add others). What the study section cares about is whether the research is high impact; you've partially addressed that by showing its relationship to an important problem, but they'll also want to be sure that your results will be novel—if they're unsurprising, the research isn't really worth doing. This presents a bit of a catch-22,

since you also need to have a plausible hypothesis, but that's why getting proposals funded requires preliminary data. You might think that the novelty of your results would be apparent from the fact that your research goal addresses an unknown, but there are varying degrees of "unknown," and the more evidence of excitement about your work you can give, the more convinced the reviewers will be. You might also think that stating the Aims will give the reviewers enough idea of novelty since they'll include your expected results (your hypotheses). However, that assumes that they know enough about your field to know how these results compare to what's known, and they may not—study sections tend to include reviewers from diverse areas, and they won't have the time to search the literature. Stating directly what makes your research innovative, as in the (unaltered) remainder of the Aims considered above, will help make a case for the impact of your work:

Specific aims example part 2: states (some) innovation

We are prepared to undertake the proposed research because we have extensive experience in manipulating type III systems, and we were among the first to report that certain type III effectors suppress innate immunity. In addition, our preliminary identification of HopU1's substrates has positioned us well to perform the experiments described in this application. Our research team includes experts in the following areas: type III secretion systems, proteomics and mass spectrometry, Affymetrix microarrays, plant glycine-rich RNA-binding proteins, and animal pathogen ADP-RTs. This qualified group of investigators will insure that our discoveries are linked to basic concepts of pathogenesis and immunity in both plants and animals.

The Specific Aims of this application are as follows:

1. **Determine the molecular consequence of ADP-ribosylation on the function of *At*GRP7 and elucidate the role this protein plays in innate immunity.** Our *working hypothesis* of this aim is that *At*GRP7 binds to immunity-related RNAs to enhance the innate immune response and that ADP-ribosylation by HopU1 disrupts its function.

2. **Identify additional substrates of HopU1 and verify their involvement in innate immunity.** Our *working hypothesis* is that the plant targets for the HopU1 ADP-RTs will be important components of plant innate immunity.

3. **Analyze the affect that HopU1 has on host-microbe interactions.** Our *working hypothesis* of this aim is that HopU1 type III effector suppresses innate immunity. This is based on our preliminary data and in this aim we will determine to what extent this occurs with *HopU1*.

The proposed research is innovative because, to date, ADP-RTs have not been implicated in the suppression of innate immune surveillance systems. Moreover, RNA-binding proteins have not been described as substrates for ADP-RTs and, therefore, represent novel substrates for this important group of bacterial toxins. Collectively, we expect the outcomes of these experiments will greatly add to our understanding of the activities and roles of type III effectors, particularly in how they suppress innate immunity in eukaryotes.

The authors directly state what's innovative about their proposed research at the end of the aims: implicating ADP-RTs in suppressing innate immunity and identifying new ADP-RT substrates. This helps explain what's new since the unknown only concerns type III effectors. However, they could have given even more evidence for how their work will

be an advance for science, such as how these expected findings would open up new areas of inquiry. Two types of innovation isn't necessarily too few for any proposal, but this one would benefit from further focus on that topic since it currently dwells on the past—the investigators' previous discoveries and expertise. This argument is less important than the impact of the research, and doesn't necessarily need to be addressed in the aims since the biosketches and preliminary data would show their qualifications to do the work.

→ *Focus on the <u>proposed</u> research, not what you've already done*

Nonetheless, this specific aims focuses on the big picture—bacterial pathogenesis and innate immunity in eukaryotes—by relating both the authors' expertise and the expected contribution to scientific knowledge to these topics. The lack of detail about their experiments helps to keep the aims centered on the goals and hypotheses rather than devolving into a list of methods. Naming each experiment is unnecessary here anyway, since a reviewer could probably figure out how you would achieve each aim from the information given (for example, AtGRP7 is an RNA-binding protein, so assessing function would involve measuring how well it binds RNA).

→ *Focus on the big picture*

This example isn't meant to say that you can't discuss experiments in the Specific Aims—if you have the space, it would help reviewers assess the impact of the results. Describing the experiments might even help convince reviewers that your work is innovative if you use approaches that they wouldn't expect from the aims. In that case, you should not only say what you will do, but explain how it's different from conventional methods and why it works better for your project than other possible methods.

→ *Include methods if they're innovative*

HOW TO SHORTEN SUMMARIES

Key points:

- Omit nonessential parts
- Combine sentences
    - Method (subject) + result (completer)
- Make sentences more direct
    - Make the action the verb
    - See lesson 14 for further details

So far, we've covered how to draft an abstract and a Specific Aims, but there's still the obvious matter of space—or rather, the lack of it. The draft you've generated from this guide is probably much longer than is allowed by the journal or funding agency. You've got to cut it down, but how? Shorten the summary in a way that serves its purpose—consider which parts of it are most important to achieving that purpose and focus on condensing or omitting the less essential parts first. The parts that are likely least important for getting published or funded are the details of the research—the methods and minor results. If the method is obvious from the aim or the result, you don't need

to describe what you did. Similarly, not every result is essential to the conclusion, so you may need to leave some of them out. To decide which to keep, rank them by how exciting or necessary to support the conclusion they are and keep as many as will fit. For example, in the paper whose abstract we analyzed earlier, there were three results from the in vivo colonization experiments. The authors omitted one, that the virulent strain survives co-colonization with *H. influenzae* while the susceptible one doesn't, because it's not essential to the conclusions—it was a step towards the experiment they did include, where both strains compete. They omitted the other, that the ability of *H. influenzae* to reduce the susceptible strain's survival requires phagocytosis by neutrophils, because it confirmed a previous finding—it wasn't exciting.

→ *Omit non-essential parts*

Combine sentences and make them more direct

Even after you omit some nonessential information, your summary might still be long. The only things left to do to shorten the draft now are to combine sentences and to shorten individual sentences. You may be able to combine a piece of background information with the statement of the unknown, or a method with the result it yielded. In such a sentence, the method becomes the subject and the verb the completer; for example, "We mathematically modeled interspecies interaction of virulent and susceptible strains of *S. pneumoniae* with *H. influenzae.* In the model, the virulent strain prevails, even if production of a capsule is otherwise costly," becomes: "Modeling of interspecies interaction predicts that these more virulent *S. pneumoniae* will prevail during competition with *H. influenzae*, even if production of a capsule is otherwise costly." To shorten sentences, the most effective approach is to make them more direct by using the verb to convey the action—this will eliminate verbs that don't do anything in the sentence (see "Revising for sentence clarity"). For example, in the sentence "There are well-documented seasonal variations in 25-hydroxyvitamin D (vitamin D) concentrations and documented correlations between those concentrations and latitudes of residence*,"* the verb "are" doesn't do anything—the action is "correlation." If we make that the verb: "25-hydroxyvitamin D (vitamin D) concentrations vary seasonally and with latitude of residence,*"* the sentence not only becomes about half as long (12 words instead of 21), we also make the topic, vitamin D concentrations, the subject (instead of "there," which doesn't do anything either).

→ *Combine method and its result into one sentence*

TITLES

Now that we know a little about how to make sentences direct, we can discuss the one sentence in the paper that should be as direct as possible—the title, the ultimate summary. The purpose of a title is simply to tell you what the paper or proposal is about, which you could do by indicating the topic—something like "An ADP-ribosyltransferase type III effector and innate immunity." However, not all of those words tell you something—"and" is just filler, and we could say more in the sentence. Further, a list of topics sounds rather flat and unexciting, and a title should attract editors' and reviewers' attention—you need a verb. A verb will let you state the result

or expected result of your work: “An ADP-ribosyltransferase type III effector suppresses innate immunity.” This is the most powerful thing you could say about the work in a single sentence—it’s the most effective use of the title. However, just because we’ve stated the (expected) result doesn’t mean we’ve got the best possible title. The structure of the title matters—whatever’s at the beginning is what the paper or proposal is about, and maybe we don’t want it to be about “an ADP-ribosyltransferase type III effector.” That’s awfully specific, so not many people would likely care about it, but “innate immunity” is a big concept. Putting that at the beginning makes the title even stronger: “Innate immunity is suppressed by an ADP-ribosyltransferase type III effector.”

→ *State your conclusion directly in the title*