

Explaining rationale

Key points:

- Point of an introduction or specific aims is to motivate the rest of the document
- State the research question
 - In a paper, make it correspond to the conclusion
 - In a proposal, make it encompass all the aims
- Explain why you did/ will do the research
 - How it relates to an important problem
 - How it addresses something unknown about the problem
 - “Why” in a proposal should convey excitement
- Organize: problem → unknown → question

Have you ever sat down to write an introduction or specific aims section, only to realize that you don't know where to start? The task can be especially challenging if you try to write it first—the reason this lesson follows those on figures and results/ research strategy sections is that knowing what you're introducing is key to writing an appropriate introduction (if you have it clear in your head without writing the other parts, writing the sections in order may work). Even more important to composing a focused introduction is understanding its purpose. The purpose may seem self-explanatory—to introduce the results or proposed experiments by giving background information. However, that explanation of the purpose isn't particularly helpful, since it leaves unclear what background you should include. Should you organize historically, starting with the discovery of your protein or gene? Should you include background on your methods? Answering these questions is much easier when you consider what you look for when you read an introduction—you probably look for something more specific than “background.” Most people seem to look for why the authors did the study the paper explains: what are they trying to find out, and why is it worth doing?

Stating the question

The question of the purpose of your research is probably the easier one to address, and motivates the rest of the introduction. Because it's the motivator, like the thesis of a non-science paper, it helps to come up with it before you write the rest of the introduction, even though it comes near the end. By “motivator,” I mean that the research question is the point that the rest of the introduction leads to; keeping it in your head or posted in front of you as you draft will help keep the introduction focused. We've previously considered it in the “papers versus proposals” lesson, which explained that the question should be stated differently in each type of document: as a hypothesis in a proposal, and as a question or unknown in a paper. Though these ways of phrasing the purpose of the study are more open-ended than a hypothesis, the research question in a paper should not be vague or broad. Instead, it should be as specific as possible to the outcome of the research. This means that it may not be the same as the question you had when you started the project, but that's ok. A research paper does not have to be historically accurate, at least in terms of things that haven't been published. What's

more important is that the paper itself is consistent and tells a unified story, since that allows the reader to focus on evaluating the science.

→ *Compose the question of a paper by starting with the conclusion*

If you haven't yet composed the conclusion, try to come up with a sentence or two that is the most exciting, interesting thing you can say with **certainty** based on your results, and that you couldn't have said before you got your results. Now write the question that statement answers, using similar terms and point of view so that the reader can recognize that they correspond. This may seem like an overly simplistic, even boring, approach, but it ensures that your reader will not be disappointed by your results and that your question is as attention-grabbing as possible for your study. Stating an overly broad question or unknown at the beginning of the paper may lead the reader to believe that the results will solve it, even if you know that the broad question is a long-term goal, and the results in the paper are one step toward answering it. Conversely, limiting your question to something answered by a few of your experiments will fail to attract readers interested in the remaining ones, and will leave the reader lost when he or she gets to the part that doesn't address the question.

→ *Making the question correspond sets appropriate reader expectations*

The working-backwards approach also works for proposals, though in this case the overall statement is based on the specific aims. If you started with an overall goal and then broke it down into aims, all the better—your proposal will likely be even more unified. Nonetheless, it's worth evaluating the statement of the goal to make sure that study section or committee members will see how the aims will accomplish the goal. The statement of the purpose of the work should encompass all of the aims and make clear what the research will discover or find out. The research question is even more important in a proposal than in a paper, since in a proposal it is the strongest and most comprehensive statement (since it's so important, it's worth repeating in the research strategy section—in the significance part and/or to introduce each aim). As in any piece of writing, your reader should have an idea of what the whole thing is about, and it's much easier for the reader to identify it if you say it directly. Let's try generating a goal statement from a list of aims:

Example 1: how to compose an overall goal for a specific aims page

Aim 1: Test the hypothesis that *E. histolytica* has a phagocytosis receptor specific for the collagenous collectin tail.

Aim 2: Test the hypothesis that *E. histolytica* calreticulin stimulates phagocytosis by interaction with a host cell transmembrane signaling partner.

Aim 3: Identify the *E. histolytica* collectin receptor.

From Huston CD, SF 424 application in 2008, available at <http://funding.niaid.nih.gov/ncn/grants/app/default.htm>

To encompass all of these logical steps, we'll need a fairly general goal—something like “The goal of this project is to identify the *E. histolytica* phagocytosis receptor.” This statement omits many of the details in the aims, so we need to add more—we can combine all of the aims into an overall hypothesis: “We hypothesize that this receptor is calreticulin, which binds to the collagenous tail of collectins on host cells.” These two sentences directly identify what the authors aim to do, and clarify how the aims relate to one another.

→ *Either start with an overall goal or write a goal that covers all the aims*

Explaining why

Now that we know how to come up with the “what’s the point?” statement, we can move on to the “why bother to study this?” part. To establish that the question or goal is worth addressing, two criteria must be met: it must relate to an important problem, and it must concern something as yet unknown. Meeting the first of these criteria requires not only identifying a related problem but also explaining how the question or goal connects to it. This task is easier if you choose a narrow problem; for example, in the proposal considered above, the general problem is *E. histolytica* infection, but the specific aims does not simply mention how significantly this affects human health. The authors go on to explain that *E. histolytica* phagocytosis of host cells contributes to pathogenesis, which clearly relates to their research goal. The same principle would apply to explaining significance in an introduction to a paper—editors will be more likely to consider a paper of high impact if the research it explains directly addresses an important problem than if it only has some vague relationship to a disease or health issue.

→ *Define the important problem as narrowly as possible*

Explaining the second part of why you’re studying the question simply entails identifying what aspect of the problem is not yet known. That the research is on something not previously studied may seem obvious, but the unknown is still worth stating, since it directly identifies what’s novel about the project without using risky words like “novel” or “first,” and it’s also a necessary logical step from the problem to the question. The unknown may fall anywhere between the identification of the problem and the question, depending on how far the field has advanced. If the unknown is quite broad, it will come soon after the problem, as in the example proposal: “the molecular mechanisms underlying *E. histolytica* phagocytosis are virtually unknown.” This statement requires considerable explanation to get to the question—if so little is known about how phagocytosis happens, then on what will the authors base their expectations? If the unknown is more narrow, then most of the explanation will connect the problem to the unknown, and the question will follow soon after.

→ *State what’s unknown about the problem*

Explaining why in proposals and high-impact papers

This prescription for how to explain why you’re doing a research project may seem simple and even dry, but there’s a bit more to it, especially in the case of a specific aims page or an introduction to a paper submitted to a high-impact, competitive journal. To

get funding or to get published, these sections must get the reviewers or editor excited about the work in the document so that they will fight for it and argue that your document should be chosen over others. The simplest way to get a reader excited is to explain why you're excited (or why your mentor is excited)—why are you convinced that this project will lead to important results (or that your results are important)? You may have already explained this in your identification of the problem and the unknown, but you should be sure that it comes across—test it out on a few people who know what potential reviewers or editors would know, and revise as necessary to get them to understand your excitement. Another way to increase the chances that your work will be seen as high impact is to explain the significance in terms of the big picture, as the NIAID suggests. Write about how your work will “open up a new area of discovery or develop new approaches to major problems” (<http://funding.niaid.nih.gov/ncn/grants/cycle/part05.htm#a2>). These arguments would likely overlap those in the Significance and Innovation parts of the research strategy section of a proposal—these could elaborate on the rationale part of the specific aims, or the aims page could boil down the others.

Organizing an introduction

You may have noticed that the lesson so far hasn't discussed background information, though background seems to compose the majority of most introductions. The only background an introduction needs is the same as that in a specific aims page (with a few more details and including references)—enough to link the problem to the unknown and the unknown to the question. This approach generates a unified introduction, avoiding mini-reviews and awkward organization, such as the common “background on topic A, background on topic B” format. Starting with the problem also helps avoid starting so broadly that you say something your audience already knows, like “Inhibitory neurotransmission is essential to maintaining normal brain function,” which doesn't help the reader determine whether the paper is relevant to his research or whether it concerns something he considers important. Organizing logically also makes your introduction more effective—if you focus on convincing the reader that the work is worth doing, the paper will seem more interesting.

→ *Organize background to connect the problem to the question*

These guidelines may make more sense when applied to a real example. This introduction is somewhat unusual in its style, as it feels almost conversational, but is easy to understand and well-focused:

Example 2: Intriguing introduction

A large body of work has investigated the psychological and neurobiological mechanisms underlying the influence of emotion on memory (1–9). Yet, very little is known about the opposite relationship, namely, how memory impacts emotion.† One especially intriguing question is whether the sustained experience of emotion is dependent upon, versus independent of, intact declarative memory for the events that

initially caused the emotion. Consider the following real-life examples: the death of a close friend or family member, the fall of the twin towers, the end of a romantic relationship—these are all events capable of eliciting an intense and prolonged state of emotion such as sadness. In these previous examples, the experience of sadness and the memory for the sadness-inducing event are often inseparable, fused together within our stream of consciousness as we ruminate, regret, and repeatedly replay the event (10, 11). The tight fusion between emotion and memory is well known to those suffering from affective disorders. For example, individuals with depression or their negative affect, which in turn escalates and prolongs their emotional pain, and posttraumatic stress disorder show a striking tendency to ruminate about the causes of suffering (12–14). Thus, there are compelling reasons to predict that the persistence of emotional experience, such as sadness, is highly dependent on remembering the emotion-inducing event.

The dissociation between emotion and memory in patients with amnesia harkens back to 1911, when the Swiss neurologist Claparède concealed a pin between his fingers while greeting one of his amnesic patients with a handshake (18). The sharp pin surprised the patient and elicited a small amount of pain that quickly dissipated. Within minutes, the patient had forgotten the encounter. Yet, when Claparède tried to reintroduce himself shortly thereafter, the amnesic patient adamantly refused to shake his hand. When pressed to explain her reaction, the patient retorted, “Is there perhaps a pin hidden in your hand?” Claparède claims, however, that even with repeated questioning the patient could never explicitly remember that she, herself, had been stuck in the hand with a pin. Despite her impoverished memory for the devious handshake, Claparède's patient continued to demonstrate preserved avoidance learning. Similar forms of “nonconscious” emotional learning in amnesic patients have been shown using a variety of different tasks, including preserved conditioned responses during a fear conditioning paradigm (19), preserved learning of the advantageous strategy on a gambling task (20; but see refs. 21, 22), and preserved affective associations for different people using variations of a “Good Guy-Bad Guy” paradigm (23–25). Analogous results have also been obtained in patients with Alzheimer's disease (26–28) and even in rats with amnesia (29). A common theme in all of these previous experiments is the finding of preserved behavioral changes (as measured by avoidance responses, autonomic responses, or forced-choice preference judgments) in the face of impaired memory for the learning conditions. Moreover, the behavioral changes were only evident when the amnesic patients were re-exposed to the stimulus that was conditioned during the original learning trials. Beyond these behavioral changes, little is known about how the amnesic patients actually felt. Again, Claparède's patient provides a perfect example—it is unknown whether she still felt upset or nervous following the handshake even though she could not explicitly remember being pricked by a sharp pin. To the best of our knowledge, there have been no studies that have carefully and systematically tracked an amnesic patient's emotional experience in conjunction with their memory for the emotion-inducing event. Here, we report such a study, in which we examined whether the conscious experience of an emotion can persist once the emotion-inducing event is forgotten.

In the experiment, each amnesic patient (Am) underwent a sadness induction procedure, which entailed ... A detailed memory test for the film clips was current also

administered 5–10 min following. Immediately after the memory test, each patient's state of emotion was measured using a questionnaire. For comparison, emotion was measured immediately before induction (baseline), immediately after, and 20-30 min later. This procedure was also administered to a group of normal comparison (NC) participants without brain damage... By systematically tracking each amnesic patient's emotional experience before and after a memory test, the experiment opens up the possibility of uncovering a dissociation between the conscious awareness of an emotional state and the conscious recollection of that state's origin (30).
Feinstein JS et al., Sustained experience of emotion after loss of memory in patients with amnesia. *PNAS* April 2010. doi: 10.1073/pnas.0914054107

Analysis of example

Feinstein's introduction likely appears very different from the standard formula you've seen in most papers, but it still achieves the purpose of an introduction: it explains why the research is worth doing. Though the real-world examples of emotional memories and the details in the description of the previous experiment on an amnesic patient are outside the standard type of background, they serve the author's goals in the section—the examples help illustrate the importance of the research and the details help make the introduction more interesting as well as helping the reader understand how the previous research led to this study. Another reason the extensive detail works in this intro is that details are only given about the most important piece of background, so it doesn't make the section too long. A second difference from the standard is that the pieces are in a different order than that suggested in this lesson. Here, the question (how memory impacts emotion) arrives very early, before the problem (PTSD and depression) and the motivating observation (fear learning in an amnesic patient), then appears again at the end in another form. This inversion works because the question is understandable even to those outside the field—everyone knows what memory and emotion are, but this may not be true for the terms in your research question.

→ *Can deviate from formula if changes help explain why you did the work*

These deviations from the formula presented in this lesson are part of the reason this introduction appears here; another factor is how well it establishes the uncertainty of the outcome of the work in the paper. As discussed in lesson 1 (Papers vs proposals), papers must convince readers (especially editors) that the research in the paper was necessary to answer the question. This paper does that by including evidence for both possible outcomes. It suggests in the first paragraph that emotion may depend on the persistence of a memory based on the greater duration and clarity of memories associated with strong emotions (though this could have been stated more directly) and the apparent link between intrusive memories and psychiatric disorders. The authors provide support for the opposing outcome with previous research on fear and affective learning. (If this were a specific aims page, suggesting that the outcome is uncertain would not work well, since it could lead reviewers to doubt whether the authors knew enough about the field to make a prediction.)

→ *Set up a controversy in an introduction (not in specific aims)*

In other ways, the example meets the guidelines set in this lesson exactly. For example, it identifies what's unknown, and does so very specifically: "there have been no studies that have carefully and systematically tracked an amnesic patient's emotional experience in conjunction with their memory for the emotion-inducing event." This statement corresponds closely to what the authors do here, which helps to match the reader's expectations to the content of the paper. In addition, the section follows the unknown with a statement of the question that corresponds closely to the conclusion in the abstract, which states, "a feeling of emotion can endure beyond the conscious recollection for the events that initially triggered the emotion." This question makes clear exactly what the authors seek to determine and suggests how they might go about doing so.

The specificity of the question makes the detailed explanation of the setup of the experiment unnecessary. Mentioning the method at the end of the introduction would be appropriate if it weren't clear from the question how the authors might answer it and if the description were brief and simple. In this case, however, it's out of place and makes it seem as though the authors don't know that it belongs in another section (the results, if it were summarized, or the methods).

→ *Mention methods only briefly*