Tips for Preparing the Prelim Proposal by Jonathan Raper

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General points:

(1) Follow the formatting guidelines for organization, font, and total length without fail. This is your first experience in learning how research grants are put together and arbitrary and fixed constraints on presentation are the rule. Just as a range of thoughts and experiences can be expressed in the impossibly restrictive form of poetry called haiku, the style requirements in grant writing can (occasionally) provoke some remarkably elegant writing.

(2) Your proposal must be hypothesis driven and the hypothesis must be clearly stated early and repeatedly. You will find that with sufficient narrowing, pretty much any clear idea can be stated as a hypothesis. However, as a question gets narrowed further and further, it often appears less and less interesting. Your job in the proposal is to formulate a hypothesis that is narrow enough to answer, but which you can put into a context that makes it interesting. You should avoid including descriptive aims, even if they will be a necessary part of your thesis work.

You must propose experiments that address your hypothesis in a meaningful way. That means that one possible outcome of the experiments you propose is that your hypothesis is wrong! Avoid the common trap of trying to think of a way that every result is consistent with your preconceived notions. If your experiments cannot disprove your hypothesis, then you probably need to reformulate your hypothesis or think of better experiments. An ideal experiment is one in which all experimental outcomes can be interpreted. A more reachable standard is that for each experiment you propose, at least one plausible outcome is either predicted by your hypothesis or disproves it.

(3) More is not necessarily better. Two really definitive experiments are worth any larger number of fuzzy experiments. If you have a smaller number of experiments, you can do a better job of explaining what you will gain from them. Avoid trying to make a grand impression by packing your proposal with a large number of experiments.

(4) One important thing to keep in mind while writing and editing your document is that clarity and conciseness are essential. You will have spent months thinking about the ideas and experiments that you are describing, but your committee will be spending only an hour or two reading your document. To compress your months of thought into a one-hour discourse requires that your writing be logically precise. Many scholars believe that poor writing reflects confused thinking. Even if this is not always the case, confused thinking surely produces poor writing. Formulate your experiments in detail. Reformulate them as you and others identify weaknesses. Outline your arguments before you start writing. You will know that you are doing a good job when you identify and repair weaknesses in your arguments as you write.

Even a good argument will fail when poorly presented because your readers will be unable to follow your train of thought. Show drafts to your smartest friends. If they can't understand you, then you have somehow failed in your presentation. It is essential that you formulate good experiments, but it is not enough. You have to convince your readers that your ideas are sound.

What to do in each section of the research proposal:

Specific Aims

You have three objectives in this section. The first is to focus the reader's attention on the problem you are addressing, the second is to present the hypothesis you are going to test, and the third is to provide an outline of the experiments you are proposing that test your hypothesis. This is the hardest section to write since there is never enough room to include everything you want to say. You must pick only the most essential points and present them as concisely as possible.

The format is nearly invariant. You should write one or two paragraphs that dispose of the first two objectives, and then write one paragraph for each of your major experiments or experimental categories (Aims). The opening paragraph(s) is effectively a summary of your Background and Significance section plus a brief description of your hypothesis.

You may wish to formulate each of your Aims as a question, write a sentence that motivates the question, describe the experiment that will answer it, and then provide an example outcome and how it would be interpreted. For example (I am completely making this up to make my immediate point-this isn't a particularly good 'aim' since it is too descriptive):

> ***Aim 1. Are new neurons generated under normal conditions in the mature mouse retina?*** *Recent research has shown that progenitor cells in selected areas of the mature brain generate neurons throughout life. I will determine if this is true in the retina by administering BrdU to 6 month old mice, sacrificing them at 1 week intervals, sectioning their eyes, and determining if label accumulates within the nuclei of neurons identified with several independent immunohistochemical markers. I will conclude that progenitors contribute new neurons to the mature retina if BrdU is detected within neurons.*

Obviously you will need to leave out a lot of information about the thinking behind the experiment, the experimental design, the data you will collect, and how you will interpret it; but you should be able to get the basic idea across.

The whole 'Specific Aims Page' should be 1 page, no more. Between 25-33% of it should be devoted to the opening paragraph(s) and the rest to the individual aims.

Research Strategy

Significance. You have two objectives in writing this section. First, you need to provide the background information your readers will require to understand your project, and second,

you need to convince them that the questions you will be asking are interesting and important. This is effectively a review of the relevant literature that provides the motivation for your project. It should be aimed at an intelligent generalist, not an expert in your chosen subfield. Don't assume the reader knows anything other than the basics. Lead them from the general to the specific.

However, keep in mind that one or more of your readers may be an expert. It is therefore important that you demonstrate good scholarship in this section. Choose your references carefully. Be sure that you draw the appropriate conclusions from each. Use primary citations rather than reviews as much as possible. Use either the first paper, the best paper, or both for each citation of the primary literature. Try not to make general statements and then cite a list of papers. Papers worth citing are usually worth some sort of brief description. When significant papers conflict, at the very least, mention both sides. Sometimes you will be pointing out deficiencies or gaps in papers that you cite. Be fair, be polite, but above all be rigorous. You will be judged by the papers you pick and the conclusions that you draw from them. Finally, if you have written this section correctly, your readers will really want to know the answers to the questions you are addressing in your experiments.

There is an art to finishing up the Significance section in a way that provides a good transition into your experiments. You might end with a brief statement pointing out current gaps in knowledge that need to be filled. Coincidently, these will always be the very gaps that your experiments address!

Approaches. You should begin this section with a restatement of the hypothesis you are going to test. You are not limited to a single page as you were for the Specific Aims section, so here you can state your ideas more fully. While there are different ways one can present an aim, I suggest you use the following format:

Specific Aim #X. Restate the Aim exactly as written on the Specific Aims page.

Rationale. Explain the connection between your hypothesis and the experiments you propose. Give any specific background that motivates the aim. Describe the system you will be using and why you have chosen it. Be brief.

Experimental Approach and Analysis. Describe your experimental design in detail. If you are proposing more than one experiment, describe each experiment in a separate subsection. Describe all of the experimental conditions including the controls. Don't forget to define key reagents you will use in your experiments. Describe the methods in enough detail so that the reader can understand how you will do the experiment, but do not go overboard, this is not a methods section. Describe the relevant biological variable (including sex if applicable), how many replicate experiments you will perform, how the data that will be collected, how measurements will be performed, and identify the statistical procedures you will use to analyze your data. Explain how your controls will validate your experimental design.

Not everyone will have preliminary results, so this is optional. The committee does not expect you to have ample preliminary results, but if you do have results that support your hypothesis or experimental approach these data should be presented. If you include preliminary results in your proposal, its objective is very straightforward. It should describe any unpublished experiments that are essential for the reader to understand your proposal. Be sure to provide appropriate citations for data you present. Do not include any published figures; those results should be cited as background literature. And eschew all inessential findings since those would simply be a waste of space. In a real grant proposal, preliminary results show the reviewers that the applicant is able to do the experiments he or she proposes, and to present evidence that makes the hypotheses under consideration more plausible. Unlike most granting agencies, we will assume that you can master any established technique. Just the same, it is important that you understand the principles behind the techniques you will use and are prepared to answer questions about them during the oral exam.

Possible Results and Interpretations. In this subsection, it is important to consider a range of plausible outcomes. Most people have the unfortunate tendency to focus all their analysis on the results they expect to get. As a starting point you may want to explicitly consider the two most divergent outcomes that you can imagine and describe the conclusions that you would draw from each. Some experiments are more nuanced than this approach would allow but do your best to categorize at least some of the possible outcomes. Many real data sets are a sad shade of grey that will not fall into any of the neat categories you propose. Don't worry too much about that, just explain what kinds of data sets you could interpret and the conclusions you would draw from them.

Potential Problems and Alternative Approaches. So you think your experiment is perfect? Think again. Whenever you propose an experiment to a smart and knowledgeable person, they can always think of a hypothetical reason why it might not work. One colleague maintains that no experiments would ever be performed if sufficient thought were put into all the reasons why they might not work. Your job in this section is to identify potential problems before your reader does, and to propose alternative approaches to reach the same objectives. You need not go into significant detail about either the problems or your proposed solutions. Your committee will ask you about specific problems and your alternatives if they are interested. Don't try to destroy your own aim, show that you are aware of potential soft spots.

Finally, end this section with a summary of the experimental findings that would support your proposed hypothesis. Don't be shy about pointing out potential findings that would falsify your hypothesis. If you are really ambitious, you might even propose an alternative hypothesis if yours fails the experimental tests you have proposed. Occasionally your guess is wrong, and it pays to be ready if it is proven to be wrong!

Tips for the oral exam:
Have a reasonably brief oral description of your project prepared for your committee. Aim for about 5 minutes summarizing Background and Significance and about 10 minutes

summarizing your Research Approaches. You may have a one-page handout with complex figures. A PowerPoint presentation with a maximum of five slides is allowed. The content of the slides should be limited to simple diagrams and bullet points, as might be presented using a whiteboard, and should not contain primary data or complex figures. Concentrate on getting the main ideas across and avoid excessive detail. Don't expect to give this talk without interruption. You are likely to get an increasing barrage of questions as you go along. These questions can range from simple points of clarification, a request for a more comprehensive (or comprehensible) description of your line of thinking, detailed questions about your methods, or even questions that test your general knowledge in a broad area related to your proposal. Don't get rattled by the questions. Questions are good, they mean your committee is paying attention. Just the fact that so many questions are coming does not mean that you are making mistakes or that the committee is dissatisfied. If you get a chance, you can try to steer discussion towards the unfinished remainder of your prepared presentation, but if the faculty are disinclined to move on to the next experiment, answer their questions without worrying about completing your presentation. It is not uncommon for an exam to end before all of the experiments you proposed are discussed.\

Even though your prepared talk is likely to get interrupted, organize this talk carefully and practice it repeatedly with your peers and helpful postdocs. First practice the talk without interruption, but as you become more comfortable presenting the talk ask your listeners to play the part of examiners and interrupt you with questions. They'll have a lot of fun trying to identify weaknesses in your thinking. You will learn where you need to put a little extra thought and the spots where your presentation lacks clarity.

Your objectives during the oral exam are to convince the committee that you know what you are talking about, that you have picked a research topic that is interesting, and that you have identified a few good questions you can answer with well thought out experiments. You will need to be well prepared, confident, and poised. Try to stay as calm and 'professional' as possible. Listen to the questions and try to give brief, considered answers that are to the point. If you don't understand a question, ask for clarification before you try to answer it. If you don't know the answer, say so. If you have a good guess, say something like "I'm not sure, but maybe.." and then take a shot at it. Whatever you do, never babble on about things that seem related to a question hoping you'll say the right thing by accident.

Keep in mind that no matter how good your proposal is and how smart you are, there will always be imperfections that become apparent to you and your examiners during the course of the exam. Don't lose heart. (Warning, stupid sports analogy coming up!) It is like a tennis match, you can lose a point or even a whole set, and still come back to win the match. Stay in the game and do your best.