Advice for writing your first NIH R01s

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This document is an amalgamation of advice I've received directly from other scientists, guidance I have read and found useful, and some of my own thoughts. In particular, Craig Montell provided excellent comments on an earlier draft, and his inputs, both practical and inspirational, have been incorporated.

At its best, **grant writing is a tremendously creative and productive scientific exercise.** You begin with ideas: hypotheses you want to test or topics you wish to explore. The ideas may be vague at first, or quite specific, but you will discover more about your ideas as you write them down. You will test your ideas as you articulate them, examine them, and ultimately defend or find flaws in them. You will sharpen your ideas, place them on rigorous foundations, and craft a perfect grant. The process is rewarding by itself, aside from the funding. But we definitely want you to get the funding.

Starting point

Logistics: For your first R01, start six months out to give yourself time to get preliminary data. Start writing two months before the deadline, and have a full draft a month before the deadline so that you can get feedback. Once you are more experienced, a month can be sufficient to write an R01.

Identify your idea: What do you want to do? Test a hypothesis? Explore an area? Develop a tool? Characterize a process?

Develop your idea: This is where you get deep into the science. Some people like to start by drafting a Specific Aims page. Other people prefer to write the Aims *last*, and instead start with the Research Strategy section and see how the ideas develop around planned experiments. Starting with the Significance section can work too, to focus attention on a specific problem and devise a project for maximum impact. Where you start depends on your preferences and the type of project. Find what works for you. Whichever route you take, the emphasis needs to be on rigor. The project needs to be solid and well thought out. You will read papers and reach out to colleagues for questions and scientific discussions. During this process you will identify two things: (1) a set of experiments you will do, and (2) what the deliverables are. A deliverable is a resolution to the problem or an answer to the question. There might also be additional benefits, e.g., a definitive characterization of something, which had to be done to answer the question.

Crafting your narrative

Once your idea takes shape, you need to be sure that you can communicate it effectively to others. For this, you need to **craft your narrative**. This is the packaging for the project and will guide how you talk about it with other people, and how you write the grant. You have to do this to help people understand why your grant should be funded.

First**,** you **explain a problem or question and make the audience care about it**. It needs to be clear and compelling. If you're working on curing a disease, then this is easy, but you still have to be specific. If you want to study something more esoteric, or if you're doing exploratory work (a.k.a. "discovery science" or "fishing expeditions", rather than hypothesis-driven) you will have to figure out how you're going to make people care about it.

Second, once you have your audience on board and they are concerned about the problem or question, then you **cast yourself as the hero**. Why are you the best person in the world to answer this question or solve this problem? Do you have special skills, tools, insights? Are you making a new connection between two distant topics? You need to nail this part, and a lot of people skip it.

Finally, after doing those two things, *only now* you can **tell us what you're going to do**. You can't jump to this part. For many projects, those first two things won't change much as the grant develops. By contrast, how you organize the research plan into Specific Aims can change a lot. Along the way, **do not lose the reviewer.** Don't drown them in jargon, meandering prose, or technical minutiae that can make them lose faith in their grasp of your project. It should be easy to relate each experiment back to the problem you are trying to solve or the question you are trying to answer. It should be easy for the reader to see how the components of the project address the goal and contribute to the deliverables. Still, you need to spell it out for us anyways, and **remind the reader what we get from your project**.

Process

Okay, **now you have an idea** and you can get to work writing an R01.
Here are the next steps:

0. ***Optional* Targeting**. Usually you will respond to the Parent R01 Request for Applications (RFA), a catch-all RFA for R01s. However, if there is a special RFA that fits your idea, you can apply to that. If you are applying to the Parent R01 RFA, then you might want to look for a program where your grant might fit. A program, in this context, is a group of grants under the stewardship of a single Program Officer (PO) at NIH. Use *NIH Reporter* to see what study sections are funding PIs you are familiar with. See who the Program Officer is for those grants. You can email that PO and ask if your idea might be appropriate for their program. Some (but not all) POs can be very helpful and even provide guidance on how to navigate through the Study Section that will review your grant. However, this step is optional. If you choose to respond to a specific RFA or want your grant to go to a specific Study Section, you can fill out the *PHS Assignment Request* and attach that to your grant when you send it in.
1. **Draft the whole grant.**
    a. **Remember your audience:** the reviewers. They don't have time to do this review. Make everything neat and tidy. Make it easy for them to find the information they will need to fill out their review form. Examine the review criteria (in the RFA) so that you can review your own grant before they do (see note below), and you can ensure the information they need is there and easy to find. If available, download the reviewer form so you exactly what the reviewers will be filling in.
    b. **Give them the information they need.** Do not assume that they have read your papers. If you need to, reproduce a key figure or two from your recent paper(s) in the grant (properly acknowledged, of course). Do not expect the reviewer to look stuff up to review your grant. Reviewers do that all the time of course, but it's dangerous. If I start reading papers in your field, I might find things that plant questions in my mind (*Is this novel enough? Is the preliminary data solid enough? This other paper I just found makes me question the entire premise of the project.*). Ideally, all the information I need is right there in the grant. You can use a little bit of bold text or italics (not too much, just a little) to draw attention to phrases or sentences that you hope the reviewers will lift and use in their review, especially in the *Significance* and *Innovation* sections.
    c. **Use figures to illustrate what you write.** Use lots of figures, maybe 10-20, if you can fit them in. Small, simple figures work well because there is one take home message to digest per figure and you can make sure that it appears right next to the words that refer to it. Don't make the reviewer search around for figures or figure references. Avoid small text (even on scale bars or axis labels) because it will annoy or frustrate reviewers if features of the figure are hard to read. Every figure needs a caption too. Ideally there will be at least one figure on every page of the Research Strategy. Sometimes it can be effective to have a figure or diagram on the Specific Aims page, especially if there is some multi-part pathway you need them to quickly understand. However, the majority of grants do not need a figure on the Specific Aims page, so don't try to force it if it isn't needed.
    d. **Inspire the reviewer to champion your grant.** Reviewers are often at least slightly biased for the applicant at first, especially if the grant looks neatly prepared. Your job is to keep the reviewer happy and make them feel like *(i)* they understand the grant, *(ii)* it's important work, and *(iii)* they can defend the grant to others in the room. If the reviewer is unsure about what you're doing in Aim 2, then they're going to hesitate about sticking their neck out for you and scoring it well. Keep the grant easy to understand for people

outside of your immediate field. Look at the recent rosters for the study section you're targeting (it's public information, and available on the NIH web site). That old person who is only adjacent to your field, what if they get assigned the grant? Make sure they can be happy with it.

e. **Demonstrate mastery.** Although you need to keep it easy to understand, you also need to make sure you have enough detail to satisfy experts (include some gritty details for the aficionados), while still ticking all of the boxes: rationale for experiments, alternative approaches, potential pitfalls, interpretation of results-- reviewers love to ding people for leaving one of those components out.

2. **Recruit** someone to read the whole grant. Targeting is less critical for that, but still try to find someone in your general area. Good reviewers are hard to find because everyone is so busy, and it is time-consuming to do it thoroughly. If you find someone that goes through your grants with a fine-tooth comb and offers constructive feedback, reward them handsomely, return the favor, and consider marrying them.
3. **Revise** according to that feedback. Be open to extensive revisions. Also, reviewers often give contradictory advice. You make the call on what advice to take.
4. **Submit** the grant.

Reviewers score five things

There are five components that are scored individually, and the reviewers have to write something for each one (even though the *Overall Impact* is the only score that matters, and is not an average of the component scores).

Significance: Make it clear that your project has a strong premise. The reviewer should be nodding along with you when they read your *Significance* section. Meet them on common ground, and then make your case. Your tools are, in descending order of power: (i) strong preliminary data, (ii) references from the literature, and (iii) sound logic. Give them everything they need and lead them along. The reviewer should be thinking, "Wow! What they're saying makes a lot of sense. This needs to be done. It's absolutely urgent!" They should already be cheering for you. The *Specific Aims* page got them interested, but the *Significance* section really nailed it, and they want this work to get done.

Investigator(s): Tell them why you're the hero. Fortunately, your CV is already very strong, so no worries. But you do need to clearly state somewhere why you're the best person on the planet to do this work. You do this in the *Biosketch.* Reviewers will look at that when they fill out the *Investigator* portion of the review, and the Personal Statement section of the *Biosketch* should be customized for the project and make it clear why you're the best person for this work, or at least highly qualified. If it fits, echo the same points about how you're a great fit for the project in the *Research Strategy* section, and maybe even the *Specific Aims*. Be objective. Find a way to highlight your strengths and qualifications, without using qualitative statements. The reviewers prefer to write objective things in their review. You can strengthen the score even more in this section if you have strong collaborators, even if they're not in the budget and just write letters of support.

Innovation: Tell them why your project is fresh and new. Have 1 – 4 bullet points for innovative aspects of the project. If you're applying new technology, then of course highlight that here. If it's something no one's done before, great. And if it's just state-of-the-art, that's good too. However, *Innovation* isn't just technology. Sometimes the old ways are perfectly fine. Conceptual innovation is often more exciting to read about. It's nice when a grant has both technical and conceptual points of innovation.

Approach: This is what you have the most control over, and the score received here has the highest correlation with the Overall Impact score. This is where people pick apart the actual experiments, and look for weak points in logic, potential pitfalls that the applicant hasn't addressed, and so forth. Make sure that the reviewer understands what you're going to do, what the data could look like, and how it will be interpreted. Try to anticipate criticisms, acknowledge them, and address them. The way that it's addressed doesn't have to be bulletproof. Nothing ever is. But it's better to acknowledge it and address it at least partially, rather than let a reviewer think that they picked up on a weakness that you didn't see. That said, don't write defensively. Don't argue with an imaginary reviewer. Be positive, objective, thoughtful, and open-minded. Use section titles like "Results & Interpretation" and "Potential Pitfalls" to guide the reviewer and help them keep track of the discussion. You don't have to use those exact titles or organization. Just know that you need the reviewer to have a clear idea of what you are going to do, what the data will look like, and what it can tell you.

Institution: Assure them that your institution is a wonderful place to do this work. This part doesn't typically affect the *Overall Impact* much, but it is good to address it effectively. In the *Facilities* section, you can highlight the collaborators you have at your institution, the seminar speakers (list some recent ones that are relevant to your field), and list key resources around the campus. Some reviewers may be unfamiliar with your field at your institution, or have an outdated impression from a visit years ago. Highlight some impressive facts and figures (total funding to campus, Nobel prize winners, etc.). Mention graduate programs you get good PhD students from. Just make the case that your institution is well resourced and has a rich intellectual community that you benefit from.

Writing mechanics

- **The goal is to make it easy to read.** This is not a creative writing exercise. No one wants to wade through clever wordplay, ingenious turns of phrase, or spellbinding flourishes of purple prose. Get to the point, clearly, using as few words as possible.
- **Avoid extra words**. If you tend to be wordy, then get the ideas down first and then hack away at the extra words. Some common replacements:
    - due to the fact that → because
    - in close proximity → near
    - successfully complete → complete
    - has a requirement for → requires
- **Write assertively.**
    - Notice when you're using the passive voice and see if it would sound better in the active voice. Use *"can"* instead of *"may"* or *"might"*. The statement *"Exercise may cause heart attacks."* Is weak because it invites the reader to think that it might not. It's equivocal. Instead write, *"Exercise can cause heart attacks."* This sounds assertive and is objectively true if it happens even once. I got this piece of advice from a colleague, and it seems silly, but it can help.
    - Don't write *"accumulating evidence shows that…"* or "*it has been proven that…"* or *"it is widely accepted that…"*. Just don't. Just delete it and add a reference and move on. You don't want to invite the reviewer to wonder how strong the evidence is for some bit of background for your grant.
- **Use short sentences.** Not all of your sentences need to be short. Use a balance. If it is all long sentences, then it can be hard to read. Break up long sentences into easier-to-follow short sentences.

- **Use parallelism.** When possible, structure sentences and even paragraphs, the same way. The sentence "*A binds to B in condition K, but in condition L it is C that A binds to."* is grammatically correct, but it is easier to parse if written *"In condition K, A binds to B; but in condition L, A binds to C."*
- **Don't use too many acronyms.** A few can be okay, and some are very routine in the field, but be aware of how many acronyms you're using and try to minimize it. No one ever complained about a grant that had too few acronyms in it.
- **Put the thesaurus away.** Don't worry about reusing the same word over and over again. It's easy to follow. If you call the same thing by four different names, it can confuse the reviewer. And if you confuse the reviewer, you're in trouble.
- **Put the new information at the end of the sentence.** Consider the statements: *"We coat the board with a protective layer. Then a knife is used to cut the layer into segments."* It's okay, but it's faster to read if you write, *"We coat the board with a protective layer. Then the protective layer is cut into segments with a knife."* The old thing, the protective layer, comes at the beginning of the second sentence. It's the old thing. We know about it already. It gives us a reference point to work from. Then the new information comes at the end of the sentence. It's a subtle thing, but it makes parsing writing faster.
- **Write plainly.** Don't be too formal. Imagine that you're talking to a friendly colleague and sharing this cool idea you have. Use the wording you would use in that context.
- **Aims that start with "Determine whether…" or "Test the hypothesis that…"** are often good. Binary, yes/no results. Clear, easy to understand. And of course, the results will tell you more than just a yes-or-no answer.
- **Have a hypothesis somewhere.** It might not be the guiding star for your whole project, but it is often helpful to articulate a hypothesis somewhere in your grant. If a reviewer searches for the term "hypothesis" and finds nothing, they might dismiss the grant with a cheap criticism like, "This work lacks a hypothesis."
- **Exploratory research can be reformulated as hypothesis-driven.** For example, say you want to look for a protein that modulates X. You can write, "We hypothesize that an ABC screen can identify a protein that modulates X."
- **Experiments that can yield uninterpretable results are bad.** Ideally the results will be informative however they turn out.
- **Dependent aims are bad.** Sometimes it is unavoidable, but when you can, ensure that the Aims can be pursued independently. This is a cheap criticism that reviewers will be ready to pounce on, even if it's a great project. So be aware of it, and avoid leaving yourself vulnerable to it. Dependent sub-aims are often okay.
- **Small effects dampen enthusiasm.** Even the preliminary data is rock solid with statistical power and significance, if the reviewers have to squint to see the effects, they might lose enthusiasm for the project.
- **Read Gopen and Swan.** George D. Gopen and Judith A. Swan wrote *"The Science of Scientific Writing."* It is a nice, short piece that addresses some common problems with technical scientific writing.
- **Break any of these rules.** Feel free to break these rules. For example, use the passive voice when describing a portion of the methods if it sounds awkward to use the active voice. But know that you are doing so and have a good reason for doing so.

Additional notes

- Don't submit until **you** are happy with it. You can't control the idiosyncrasies of peer review. What you can control is how happy **you** are with your grant. Submit **perfect** grants.
- Grant reviewers do not always get it right. No matter what, even if it's triaged (i.e., not discussed or scored) you still get feedback. Address the feedback, revise and re-submit. You will get funded, but we don't know when. Take none of the rejection personally. Keep an even keel.
- When you're in a lull or have a bit of writer's block, work on the other parts of the application (Vertebrate Animals, Facilities, updated Biosketch, etc.). You don't want to rush through those at the end. They're not critical, but if you rush through them, you might make some silly mistakes. And if you're very careful on some of those parts (e.g., impress them with the facilities you have in your lab, or with a fastidious Vertebrate Animals section), that can bias reviewers in your favor. It's a turn-off to see brief, sloppy work, or outdated information in those sections.
- If you might be doing something a bit outside of your track record, get some strong colleagues to write letters of support for you. This isn't essential, and if it isn't a good fit for your grant, don't worry about it. However, if there's a method or technique, or a behavioral assay that is a bit challenging, or if you're working on a system that you don't have a track record in, it can be helpful to get a letter of support form an expert. Even if they get zero dollars from the grant, it inspires confidence because reviewers see that you have a support network of experts, and are willing to reach out for help to get things done.
- When you're an early-stage investigator (ESI) and/or a new investigator (NI) it's still good to have preliminary data, to underpin your grant's premise, and/or to show that you can make the measurements you're proposing to make. For the latter, a figure from a paper you've already published (properly cited) is fine.
- You can recycle grants to other mechanisms, e.g., a New Innovators to a conventional R01. Or an R21 into a private foundation grant. This is the craft you learn when "churning" grants. Recycle text.
- Train yourself to get things done with a minimum of fuss. We all love obsessing about things. It's part of the fun of being a scientist. You will need to block out time in your schedule for thinking, planning, and writing. Figure out what enables you to work fast. Quantify and track your productivity (e.g., words written per hour, or pages edited per hour). Many writers like to wake up early in the morning and write. Notice what distracts you. If a newer computer or nicer chair helps productivity, it's a wise and practical investment.
- Program yourself to enjoy the process. It can be an enriching intellectual exercise, organizing thoughts and refining your thinking.