CAMB 695: Scientific Writing

2011 Course Readings

Reading for Week 2:
  Five Principles of Clear Scientific Writing
  Re-writing Exercises
  General Guidelines about Verb Tense
  Gopen & Swan (attached)

Reading for Week 3:
  Parts of a Grant Proposal
  How to write Significance & Innovation (grants); Introduction (papers)

Reading for Week 4:
  How to write Preliminary Data, Figures & Tables (grants), Results Section (papers)

Reading for Week 5:
  How to write Specific Aims

Reading for Week 6:
  How to write Approach (grants), Discussion (papers)

Reading for Week 7:
  How to write an Abstract (for grants and papers, respectively)
Five Principles of Clear Scientific Writing

When scientists use dense language to describe their work, the story gets murky and no clear message emerges. In this course, we will show you how to assemble the parts of a research proposal into a comprehensible story that has a clear message.

1. **Get to the subject quickly and follow the subject as soon as possible with its verb.**

   Gopen and Swan pp 551-552 “Subject-Verb Separation”

   (Additional material: Williams *Style: The Basics* Chapter 8 “Shape” pp 94-97)

   - **Get to the subject quickly**
     - Avoid long, abstract subjects – noun clusters
       In English, one noun is commonly used to modify another noun, e.g. blood flow, lung function, ion concentration. But adding more nouns to an existing noun pair (a noun cluster) creates long, abstract subjects and is confusing. To untangle a noun cluster, start at the end of the cluster and add words to indicate how the nouns relate to each other.

       - **Example:** Early childhood thought disorder misdiagnosis often results from unfamiliarity with recent research describing such conditions.
       - **Problem:** Confusing noun cluster, abstract subject
       - **Revision:** Physicians misdiagnose disordered thought in young children because they are unfamiliar with recent research describing such conditions.

     - Avoid lots of introductory words - “throat clearing”
       Readers have a problem with sentences that open with long introductory phrases and clauses, because, as they read them, they have to keep in mind that the subject and verb of the main clause are still to come.

       - **Exercise:** In most cases, because of the efficacy of the recently available treatment regimens, physicians are able to diagnose and successfully treat PCP.

   - **Get past the subject and to its verb quickly** – avoid subject-verb separation
     Readers expect the grammatical subject to be followed almost immediately by its verb. Anything of length that separates the subject and verb is read as an interruption. An interruption after the subject forces the reader to hold his mental breath until he reaches the verb. Without the verb, the reader does not know what the subject is doing, or what the sentence is about.

     - **Example:** The smallest of the URF’s (URFA6L), a 207-nucleotide reading frame overlapping out of phase the NH2-terminal portion of the adenosinetriphosphotase (ATPase) subunit 6 gene has been identified as the animal equivalent of the recently discovered yeast H+-ATPase subunit 8 gene.
     - **Problem:** 23 words separate the subject “the smallest” and the verb “has been identified.”
Revision A: The smallest of the URF’s is URFA6L, a 207-nucleotide reading frame which overlaps, out of phase, the NH₂-terminal portion of the adenosinetriphosphotase (ATPase) subunit 6 gene. URFA6L is the animal equivalent of the recently discovered yeast H⁺-ATPase subunit 8 gene. This revision incorporates the interrupting material into the sentence structure.

Revision B: The smallest of the URF’s (URFA6L) is the animal equivalent of the recently discovered yeast H⁺-ATPase subunit 8 gene. This revision deletes the interrupting material and also eliminates the unnecessary phrase “has been identified.”

- **Exercise:** Some scientists, because they write in a style that is impersonal and objective, do not communicate easily with laypeople.

2. **Put the action in the verb.**

   Gopen & Swan pp 557 “Locating the Action”

   (Additional material: Williams *Style: The Basics* Chapter 3 “Actions” pp 27-38)

   - Readers expect that the action of a sentence will be articulated by its verb. If the action of the sentence is expressed by the verb, the sentence is direct and easy to understand. If the action is not expressed as a verb, it is usually lodged in a noun made out of a verb. We call such a noun a *nominalization*.

     - **Examples:**

       | verb | nominalization |
       |------|---------------|
       | prolong | prolongation |
       | inhibit | inhibition   |
       | measure | measurement  |
       | evaluate | evaluation  |
       | remove  | removal      |
       | exist   | existence    |

   - Nominalizations are not bad in and of themselves, only in the way they are (mis)used. The thing is to know which nominalizations to keep and which to turn into verbs.

   - Turn a nominalization into a verb when it expresses the action of the sentence.

     - **Example:** Removal of potassium perchlorate was achieved by centrifugation of the supernatant liquid at 1400xg for 10 min.

       - **Revision A:** Potassium perchlorate was *removed* by centrifugation of the supernatant liquid at 1400xg for 10 min.

       - **Revision B:** Centrifugation of the supernatant liquid at 1400xg for 10 min *removed* potassium perchlorate.

       - **Revision C:** We *removed* potassium perchlorate by centrifuging the supernatant liquid at 1400xg for 10 min.

     - **Exercise:** Our lack of data prevented evaluation of the role of the D1 receptor in the locomotor stimulant effects of cocaine.
Keep a nominalization when it does the following:
- Refers to the previous sentence
  - Example: When added to the nuclear extract, the egg extract inhibited transcription generally. This inhibition could be alleviated in part by supplementing the mixture with RNA pol III.
- Replaces an awkward “The fact that”
  - Example: The fact that the Zip2 protein localized to discrete foci on meiotic chromosomes suggested that...
  vs
  Localization of the Zip2 protein to discrete foci on meiotic chromosomes suggested that...
  (However, an alternative would be “Zip2 protein localized to discrete foci on meiotic chromosomes, suggesting that …”)
- Names what would be the object of the verb
  - Example: We accepted what they found.
  vs
  We accepted their findings.

3. **Put information where the reader expects it.**
- There are two moments in the reading process which occur over and over again and are very important to both writer and reader: They are the beginnings and the ends of sentences.
  - We’ll label the ends of sentences the “Stress Position.”
  - We’ll label the beginnings of sentences the “Topic Position.”

**The Stress Position – save the best for last**
Gopen and Swan pp 552-554 “The Stress Position”
(Additional material: Williams *Style: The Basics* Chapter 6 “Emphasis” pp 66-71, 74-78)
- Readers naturally assign emphasis to the words at the end of a sentence, the “Stress Position.”
- Use the stress position of a sentence to introduce long, complex, or otherwise difficult-to-process material, particularly unfamiliar technical terms and “NEW” information.
  - Example: The role of calcium blocker drugs in the control of cardiac irregularity can be seen through an understanding of the role of calcium in the activation of muscle groups.
  
  Problem: New, complex terms are at the beginning of the sentence.
  
  Revision: If we understand how calcium influences the contraction of muscles, we can see how cardiac irregularity is controlled by the family of drugs called “calcium blockers.”

- Exercise: A determination of involvement of lipid-linked saccarides in the assembly of the oligosaccharide chains of ovalbumin in vivo was the principal aim of this study. *In vitro* and *in vivo* studies utilizing oviduct
membrane preparations and oviduct slices and the antibiotic tunicamycin were undertaken to accomplish this.

- Use the stress position to place emphasis on words that you feel deserve it.
  - **Example:** compare (a) and (b)
    - (a) Overall, although this proposal is scientifically sound, the preliminary results are not persuasive.
    - (b) Although the preliminary results are not persuasive, overall this proposal is scientifically sound.
  
  While neither of those statements would be considered a rave review, version (a) will probably make the scientist less happy than version (b). In (a), the bad news occupies the stress position; in (b), the good news occupies the stress position.

- **Exercise #1:** The data offered to prove ESP are too weak for the most part.

- **Exercise #2:** Mucosal and vascular permeability altered by a toxin elaborated by the vibrio is a current hypothesis to explain this kind of severe condition.

**The Topic Position – first things first**

- The topic position extends through the first few words of a sentence up to and including the grammatical subject. It stops short of the verb.

- Use the topic position to introduce “whose story” a sentence is going to be. Readers expect a sentence to be a story about whoever shows up first.
  - **Example:** Compare (a) and (b) and (c)
    - (a) In the 1970s a few scientists in the United States and Europe began to find a way through disorder. They were mathematicians, physicists, biologists, chemists, all seeking connections between different kinds of irregularity.
    - (b) Finding a way through disorder was accomplished in the 1970s by American and European scientists. This goal was accomplished by a variety of scientists all seeking connections between different kinds of irregularity.
    - (c) The United States and Europe made it a priority in the 1970s that their scientists should find a way through disorder. These two countries funded mathematicians, physicists, biologists, and chemists, to find connections between different kinds of irregularity.

In each of these examples, by changing the occupant of the topic positions, we’ve changed the answer to “whose story is this?” In (a) the
answer is “a few scientists,” in (b) it is “finding a way through disorder,” in (c) it is “the U.S. and Europe.”

- **Exercise**: Rewrite the following sentence. Make the story about “plants.”
  Richly fertilized plains and river valley are places where plants grow most richly, but also at the edges of perpetual snow in high mountains.

- Use the topic position to communicate “OLD” information that forges a logical backward link to the previous sentence. The term “old information” refers to any material that has already appeared in the particular piece of text. Often it will have appeared in the sentence immediately preceding; sometimes it will have appeared farther back within the paragraph. When a piece of old information appears at the beginning of a sentence it gives the reader context.
  - **Example**: In both (a) and (b), old information in the topic position of the second sentence provides a backward-link to the first sentence.
    (a) Meteorologists look cheerful and confident when they report normal weather, but tense and crisis-ridden when they warn us about *hurricanes*. *These storms* cannot be predicted with any sense of surety, despite the great leaps forward we have made in meteorology.
    (b) *Hurricanes* fascinate and haunt us, acting like irrational characters in a high-intensity, reality TV drama. *Hurricanes* cannot be predicted with any sense of surety, despite the great leaps forward we have made in meteorology.

- **Exercise**: A is a B-class GTPase. C-type kinases phosphorylate some B-class GTPases.

  - **Two Ways to Depict Reader Expectations about Sentence Structure**

  In terms of a diagrammed sentence

<table>
<thead>
<tr>
<th>Topic Position</th>
<th>Stress Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Old, simple, backward-linking information</td>
<td>New, complex, emphasis-worthy information</td>
</tr>
<tr>
<td>Subject</td>
<td>Verb</td>
</tr>
<tr>
<td>Person, thing or concept whose story it is</td>
<td>Action, What is going on</td>
</tr>
</tbody>
</table>
In terms of the progress readers expect as they travel through a sentence

<table>
<thead>
<tr>
<th>Time</th>
<th>Question a reader expects to have answered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right away</td>
<td>How does this link backward to what I’ve just read?</td>
</tr>
<tr>
<td>ASAP</td>
<td>Whose story is this? (=the grammatical subject)</td>
</tr>
<tr>
<td>Immediately thereafter</td>
<td>What’s going on? (=the verb)</td>
</tr>
<tr>
<td>Then, at leisure</td>
<td>How will this thought develop?</td>
</tr>
<tr>
<td>At the end</td>
<td>What is the most important piece of information here?</td>
</tr>
</tbody>
</table>

4. **Write cohesive sentences and coherent paragraphs.**
   Gopen and Swan pp 556-557 “Perceiving Logical Gaps”
   (Additional material: Williams *Style: The Basics* Chapter 5 “Cohesion and Coherence” pp 59-60)

   o **Cohesion: a sense of flow from sentence to sentence**
     - We judge sentences to be cohesive, or connected, when the first few words in a sentence lean backward (provide OLD information), and the last few words lean forward (provide NEW information).

     - This information flow in a sentence can be depicted as OLD $\rightarrow$ NEW.
       - Put old, familiar information in the topic position of a sentence.
       - Put new or complex information in the stress position. The information in the stress position often becomes the “whose story,” or the old information in the topic position of the next sentence.

     - **Example:** Some astonishing questions about the nature of the universe have been raised by scientists studying black holes in space. The collapse of a dead star into a point perhaps no larger than a marble creates a black hole. So much matter compressed into so little volume changes the fabric of space around it in puzzling ways.
     - **Problem:** The information flow from sentence to sentence is not old $\rightarrow$ new.
     - **Revision:** Some astonishing questions about the nature of the universe have been raised by scientists studying black holes in space. A black hole is created by the collapse of a dead star into a point perhaps no larger than a marble. So much matter compressed into so little volume changes the fabric of space around it in puzzling ways.

   o **Coherence: a sense of the whole point of a paragraph**
     - We judge a passage to be coherent when three features are present:
       - The opening sentence prepares us for the themes of the passage by emphasizing them in its stress position.
       - Individual sentences follow the old $\rightarrow$ new principle, connecting to the sentence before and after (see Cohesion, above)
       - The words beginning each sentence in the passage cumulatively constitute a limited and related set of words (a “topic string”) that tell us what the passage is about.
Example: Compare (a) and (b).

(a) Since the discovery that one factor of its development might be genetic, great strides in the early and accurate diagnosis of Alzheimer’s disease have been made in recent years. Senility in an older patient who seemed to be losing touch with reality was often confused with Alzheimer’s. Genetic clues have become the basis of newer and more reliable tests in the last few years. The risk of human tragedy of another kind, though, has resulted from the increasing accuracy of these tests: predictions about susceptibility to Alzheimer’s have become possible, long before the appearance of any overt symptoms. An apparently healthy person could be devastated by such an early diagnosis.

(b) In recent years, researchers have made great strides in the early and accurate diagnosis of Alzheimer’s disease. However, these improved diagnoses have raised new concerns about how to inform those most at risk. Previously, when a physician examined an older patient who seemed out of touch with reality, she had to guess whether that person had Alzheimer’s or was senile. Now, physicians can utilize new and more reliable tests focusing on genetic clues. Yet, in the accuracy of these new tests lies the risk of another kind of human tragedy: while physicians may be able to predict Alzheimer’s long before its overt appearance, such an early diagnosis could psychologically devastate an otherwise healthy person.

Version (a) feels unfocused and unorganized, while version (b) feels cohesive and coherent. Why?

In version (b) we revised the passage to make the topics more related – the topic string now focuses on researchers/physicians and testing. Also, in (b) we revised the first sentence so that its end stressed those words expressing the themes that the rest of passage develops.

Exercise: 1. EGFR forms dimers and higher order oligomers with itself and other members of the ErbB family (ErbB2/HER2, Erbb3/HER3, and ErbB4) via a primary dimerization domain, as well as several secondary receptor–receptor contact points. 2. The 170 kD Epidermal Growth Factor Receptor (EGFR, also known as ErbB1), is one of four members of the ErbB/HER family of transmembrane tyrosine kinase growth factor receptors. 3. Binding of naturally occurring extracellular ligands (e.g., amphiregulin, epiregulin, HB-EGF) to the extracellular ligand-binding domain (domain III) of EGFR induces conformational shifts that permit homo- and hetero-dimerization events between EGFR molecules and its family members. 4. EGFR autophosphorylation activates multiple key signal transduction cascades that are mitogenic, antiapoptotic, angiogenic and pro-invasive. 5. Multimer formation promotes tyrosine autophosphorylation of the EGFR intracellular domain; the resultant open configuration of the kinase domain enhances access by ATP and substrate and creates binding sites for signaling molecules. 6. The EGFR kinase is also active at a low level when the protein is in the unliganded state; the degree of activity varies by cell type, glycosylation state and environment.
5. **Make the words mean what you want them to say.**
   - Often, the words do not mean what you want them to say because they are not written in parallel form. If parallel ideas are not written in parallel form, the logical relation of the ideas (similarity, alternatives, contrast, comparison) is obscured.

   - **Example #1:** DNase I nicking interference patterns correspond precisely to methylation interference patterns with both 10 bp sequences.
     - **Problem:** Makes it sound like both patterns are 10 bp long.
     - **Revision:** Interference patterns induced by DNase I nicking correspond precisely to interference patterns induced by methylation for both of the 10 bp sequences.

   - **Example #2:** These results are similar to previous studies.
     - **Problem:** Comparison of unlike things
     - **Revision A:** These results are similar to the results of previous studies.
     - **Revision B:** These results are similar to those of previous studies.

   - **Example #3:** Like poliovirus, interaction of coxsackievirus with its receptor triggers release of its viral RNA.
     - **Problem:** Interaction is not like poliovirus
     - **Revision A:** Like the interaction of poliovirus with the poliovirus receptor, the interaction of coxsackievirus with its receptor triggers release of the viral RNA.
     - **Revision B:** Like poliovirus, coxsackievirus interacts with its receptor to trigger release of its viral RNA.

   - **Exercise #1:** Activation-controlled relaxation in these membrane-deprived cells resembled intact myocardium from frogs.

   - **Exercise #2:** In the transgenic animals, expression of beta-galactosidase was limited to pharyngeal muscle, a pattern identical to that observed in wild-type animals.
A few comments on ACTIVE versus PASSIVE voice:

**Active is preferred …**
For direct writing, we prefer "active" rather than "passive" verbs, especially if we can avoid nominalization. Here are three examples:

   Passive-nominalized:
   An investigation WAS CONDUCTED into why so few interviews of minority applicants WERE DONE.

   Active-nominalized:
   We CONDUCTED an investigation into why the employment office DID so few interviews of minority applicants.

   Active-verbal:
   We INVESTIGATED why the employment office INTERVIEWED so few minority candidates.

… but passive is OK

**Passive can be useful!**
Passive can help shift a long and complex bundle of information from the beginning to the end of a sentence. In the sciences, the passive contributes to an objective point of view.

   We must decide whether to focus on A or B. The weight given to two factors, X and Y, will influence this decision.

   We must decide whether to focus on A or B. This decision will be influenced by two factors, X and Y.
IN-CLASS RE-WRITING EXERCISES

For each of the five “blinded” re-writing exercises below do the following:

(1) Identify the writing principle that is ignored in the sentence(s)
(2) Re-write the sentence(s) so that it follows that principle

**Exercise #1:** Prolongation of life for uremic patients has been made possible by improved conservative treatment and hemodialysis.

**Exercise #2:** A disease that progresses with few or no symptoms to indicate its gravity is an “insidious” disease, under this definition. Asbestosis, neoplasia, mesothelioma, and bronchogenic carcinoma are all examples of insidious diseases. Asbestos insulation installers who have inhaled asbestos fibers over a period of many years regularly contract these diseases.

**Exercise #3:** Laboratory animals are not susceptible to these diseases, so research on them is hampered.

**Exercise #4:** Propranolol had variable effects on the hypoxemia-induced changes in regional blood flow. In the cerebrum, the increase in blood flow caused by hypoxemia was not significantly altered by propranolol. However, in other organs and in the peripheral circulation, propranolol caused a more severe decrease in blood flow than did hypoxemia alone.

**Exercise #5:** The molecular events determining the developmental lineage of the gonadotrope in the anterior pituitary, utilizing approaches in transgenic mice including ectopic expression of regulatory proteins, will be investigated.
GENERAL GUIDELINES ABOUT VERB TENSE USAGE

Use present tense to describe established findings that have passed peer review and are regarded as fact.

“Resting CD4+T cells are the best-defined reservoir of HIV-1 infection.”
“Establishment of the intricate nervous system of vertebrate animals requires the specification of diverse neuronal cell types.”
“Translation initiation of some viral and cellular mRNAs occurs by ribosome binding to an internal ribosome entry site.”

Use present tense for the question.

“We hypothesized that cigarette smoking by young men causes abnormal metabolism of plasma cholesterol.”
“We asked whether these fragments arise from the same point of cleavage as the naturally occurring fragments of B-100 and B-74.”
“To determine whether four different asthma drugs inhibit the late asthmatic reaction, we…”

Use past tense for methods.

“We dehydrated the pellets and cleared them with propylene oxide.”
“After 30 sec, we centrifuged the samples.”
“To prepare surface layers for EM, we resuspended the pellets in…”

Use past tense to describe the experiments done.

“We assessed these variables in 24 sensitized subjects divided into 4 groups of 6 subjects each.”
“We used kallikrein to digest LDL from human plasma and compared the resulting fragments with B-74.”
“Subjects in each group received one drug for 7 days according to a double-blind, placebo-controlled study.”

Use past tense to describe the results obtained.

“Slow-release theophylline partially inhibited the increase in FEV1 but had no effect on airway responsiveness to methacholine.”
“Sham nucleus tractus solitarius lesions and lesions lateral to the nucleus produced no changes.”
“Pulmonary lymph flow doubled within 2 hr.”

Use present tense for the answer.

“These results indicate that ceh-22 and nkh2.5 perform similar functions.”
“These experiments demonstrate that lesions of the NTS alter PA pressures.”
“Thus, only the high-dose inhaled steroid beclomethasone inhibits late asthmatic reactions.”

Use hypothetical verbs for implications or speculations.

“These results suggest that the identified EGases may facilitate intracellular migration through plant roots by partially degrading the cell wall.”
“We propose that Zip2 promotes the initiation of chromosome synapsis.”
“Our findings could partly explain the high incidence of coronary artery disease in older male smokers.”

Use future tense for future, planned, or proposed work.

“We will identify the steps involved in coxsackievirus B uncoating during entry into polarized epithelial cells.”

“The temporal production of SarA will be assessed by Western blot of S. aureus whole cell extracts with an affinity-purified anti-SarA antibody.”

“I will use heat shock-inducible transgenic zebrafish to determine when BMP signaling is required to specify lim1+ INs.”
HOMEWORK/READING for Week 3 - PARTS OF A GRANT PROPOSAL AND HOW TO WRITE SIGNIFICANCE & INNOVATION (GRANTS); INTRODUCTION (PAPERS)

PARTS OF A GRANT PROPOSAL

The preliminary exam tests your ability to formulate a research proposal and to construct a sound experimental approach to accomplish the proposal's specific aims. Your preliminary exam proposal should be scholarly and original. Your prelim proposal will not mirror exactly the current NIH grant format (which was recently revised), but many of the principles will be the same. The research plan of the NIH format focuses on: Significance, Innovation, and Approach. The other two scored criteria are Investigator and Environment.

- **Project Summary/Abstract (No longer than 30 lines of text using the required font and margin specifications):** Give a clear, succinct summary of the proposed work that can stand alone when separated from the rest of the application.
- **Specific Aims (1 page):** State the specific purposes of the research proposal and the hypothesis to be tested.
- **Research Strategy (12 pages)**
  - **Significance and Innovation:** Give a brief overview of the significant background to the proposal. Convey the importance of your proposed research by relating the specific aims to broader, long term objectives.
  - **Approach:** Describe the research design and methods that will be used to accomplish the specific aims. Discuss the expected outcome and interpretation of results. Explore potential experimental difficulties together with alternative approaches that could achieve the desired aims.
  - **Preliminary Studies (for New Applications) or Progress Report (for Renewal Applications) are included within the above sections (these are required in NIH grants, but NOT in your preliminary exam):** Present the observations that led you to the hypothesis for your proposal and explain any significant changes and new directions if this is a renewal application.

For both your preliminary exam and an NIH grant, attention to organization and clarity, in addition to the science, is essential. The proposal cannot be just a list of experiments-- the underlying scientific thought must be evident. The proposal must be written so that it is clear and convincing even to someone who is not familiar with the field. Use the page limitations wisely and present only important and relevant information.

To learn more about the preliminary exam requirements and to read prior proposals:
http://www.med.upenn.edu/camb/handbook/Prelim.shtml
http://www.med.upenn.edu/camb/user_docs/PrelimSample1a.pdf
http://www.med.upenn.edu/camb/user_docs/PrelimSample2.pdf

You can also read an annotated example of a well-written NIH grant application:

**How to write SIGNIFICANCE AND INNOVATION: Selling your proposal**

Formats for research proposals are as varied as the many granting agencies that solicit them.
Also, proposal formats for a given donor organization can be expected to evolve over time. An example of this is the recent change in the Research Strategy format of individual research grant applications to the National Institutes of Health (NIH “R01s”). This new format emphasizes significance and biomedical impact over methodological or technical detail and mandates clarity, conciseness and brevity by decreasing the page limitation for this section from 24 to 12. Such variety notwithstanding, virtually all scientific proposal formats call on you to make a case for the work you propose by placing it in the context of general biomedical needs and/or specific gaps in scientific knowledge that you propose to fill.

The current format for this section of an NIH grant proposal calls for dividing the narrative into two sub-sections: Significance and Innovation. The instructions for these sections from NIH Form PHS 398 are quoted verbatim below. Please use this format for your Week 3 writing assignment.

“(a) Significance

• Explain the importance of the problem or critical barrier to progress in the field that the proposed project addresses.
• Explain how the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more broad fields.
• Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved.

(b) Innovation

• Explain how the application challenges and seeks to shift current research or clinical practice paradigms.
• Describe any novel theoretical concepts, approaches or methodologies, instrumentation or intervention(s) to be developed or used, and any advantage over existing methodologies, instrumentation or intervention(s).
• Explain any refinements, improvements, or new applications of theoretical concepts, approaches or methodologies, instrumentation or interventions.”

How to write INTRODUCTION: Putting your paper in context

The essential elements of a good Introduction to a paper, as presented in Chapter 10 of Day and Gastell’s How to Write and Publish a Scientific Paper, overlap to a degree with the Background or Significance/Innovation section of a grant application in that they include

1) a clear and concise presentation of the character and extent of the problem under investigation,
2) a brief, focused and, above all, relevant literature review, sufficient to orient the reader to the current state of the art in the area under investigation as well as the open questions addressed in the paper and
3) a brief statement of the major methodology used in the paper and, if appropriate, the rationale for its selection.
Because a paper reports results and interpretations from experiments already conducted, two additional elements of a well-written Introduction depart from the Background or Significance/Innovation of a proposal. These are:

4) the principal results of the study and
5) the principal conclusions based on the results.

While elements 1-3 should be included in any Introduction, journals differ in their requirement results and conclusions in the Introduction section and some prohibit their inclusion. It is wise to consult the instructions for authors in the target journal on this point prior to writing the Introduction to your paper.

Of all the five essential elements discussed by Day and Gastell, the first, a statement of the problem with a level of clarity and directness that captures the reader’s attention, is the most crucial. At its best, this statement is said to provide the “hook” that stimulates the reader to want to read further. Wordiness or ambiguity in this statement serves to discourage readers, making it a chore to finish reading the paper, and potentially causing them to lose interest altogether. The other feature of a well-written Introduction is that the problems and questions it articulates will ultimately be resolved in the Discussion.
PRELIMINARY DATA (grants)

Your preliminary exam proposal will not include preliminary data, but NIH grants require preliminary data. The information below is also applicable to the Results sections of scientific papers.

The function of the Preliminary Data section of a grant proposal is two-fold: (1) to discuss the observations that led you to the hypothesis for your proposal, (2) to direct the reviewers to figures or tables that present supporting data. It is important to present data that are relevant to each of the Aims. Experiments presented as preliminary data do not have to meet all the standards used in evaluating data for publication.

Figures and Tables

A figure or table, like text, needs careful editing and revision. Present the most important data in figures and tables where the data are highly visible and easy to read. The point should be evident independent of the results text or the legend. Show the figure to a colleague (preferably someone in another lab) to see if she can explain it without the legend. If not, revise.

When Writing/Revising Results Sections

- Look closely at the figures.
  - What is each figure about? What is the figure’s point or message?
  - Is it easy to discern? Is it heavily dependent on the figure legend, or does the figure tell a story that the legend identifies more specifically?
- Look over the sequence of the figures.
  - Is there a story to the data?
  - How is the story of the figures structured?
- Read the text of the results section.
  - What is its story? How is it structured and organized?
  - How is it related to the story told by the figures?
- Evaluate the story.
  - Is this a good piece of science? Is it interesting, significant, logical?
  - What aspects are compelling? Strongest?
  - Where did you hesitate? Find problems? Disagree?

The Results Text

The results text narrates the story that the figures tell visually. Ideally, you should start planning your paper as soon as you get your first results. Remember that results are different from data. Data are facts, often numbers, obtained from experiments and observations. Results are statements that interpret the data. Keep data to a minimum in the results text. Data can rarely stand alone; the results (=the meaning of the data) must be stated.
Organization of the results text. A helpful way to organize the results text is as a repeating four-part pattern. The four-part pattern is QERA: (Q) Question, overview of the (E) Experiments, (R) Results, (A) Answer to the question. Ideally, each repeat of the pattern is a separate paragraph.

The results text should state the meaning of the data. The purpose of the results section is to make the point clear. To make the point clear, state the result first, and then present the data, or, better, cite a figure or table that contains the data in ( ) at the end of the sentence.

Example: In the 20 control subjects, the mean resting blood pressure was 85 + 5 (SD) mmHg. In comparison, in the 30 tennis players, the mean resting blood pressure was 94 + 3 mmHg.

Problem: Data but no Result. Are the data similar? Different? What is the point?
Revision: The mean resting blood pressure was 10% higher in the 30 tennis players than in the 20 control subjects (Fig. 3). In the revision, the statement “was 10% higher” states the result and gives a clearer idea of the magnitude of the difference than do the data alone. The figure containing the supporting data is cited in ( ) at the end of the sentence.

Subordinate figure legends and table titles. Do not repeat a figure legend or a table title as a topic sentence. Do not direct traffic “Figure 1 shows…” Cite figures and tables in ( ) after results statements.

Example: A summary of renal function data is presented in Fig 2. Continuous positive airway pressure (7.5 cm H2O) in newborn goats decreased urine flow, sodium excretion, and the glomerular filtration rate.

Problem: The topic sentence is essentially a figure legend. For a more powerful topic sentence, omit the figure legend, state the results, and cite the figure in ( ) at the end of the sentence.
Revision: Continuous positive airway pressure (7.5 cm H2O) in newborn goats decreased urine flow, sodium excretion, and the glomerular filtration rate (Fig. 2).

Subordinate methods. Do not use a methods statement as a topic sentence.

Example: We administered propranolol during normal ventilation. This beta-blocker decreased phospholipid (Fig. 1).

Problem: The topic sentence is a methods statement. The next sentence is the results statement.
Revision: When propranolol was administered during normal ventilation, phospholipid decreased (Fig. 1).

Sample Results Text
In this paper, investigators asked whether the nematode gene ceh-22 and the zebrafish gene nкс2.5 perform similar functions. They examined the ability of the zebrafish gene nкс2.5 to substitute for the nematode gene ceh-22 in transgenic C. elegans.

Zebrafish Nкx2.5 Can Activate Myo-2 Expression When Expressed In C. Elegans Body Wall Muscle.
To determine whether \textit{nkx2.5} can function similarly to \textit{ceh-22}, we expressed \textit{n} in \textit{C. elegans} body wall muscle and examined expression of the endogenous \textit{myo-2} gene by antibody staining. The rationale for this approach was as follows. In wild-type \textit{C. elegans}, \textit{ceh-22} is expressed exclusively in pharyngeal muscle, where it activates expression of the pharyngeal muscle-specific myosin heavy chain gene \textit{myo-2} (14). However, ectopic expression of \textit{ceh-22} in body wall muscle can activate expression of \textit{myo-2} (15). Because \textit{myo-2} is normally never expressed in body wall muscle, this ectopic expression assay provides a sensitive test for \textit{ceh-22} function. \textbf{E}We generated two transgenic lines expressing an \textit{nkx2.5} cDNA under the control of the control of the \textit{unc-4} body wall muscle-specific promoter. \textbf{R}In both lines, we detected \textit{myo-2} expression in the body wall muscles (Fig. 1A and B). \textbf{A}These results show that \textit{nkx2.5} can function like \textit{ceh-22} to induce \textit{myo-2} expression.

We next asked whether Nkx2.5 directly interacts with the same sequences recognized by CEH-22. \textbf{E}To answer this question, we examined expression of a reporter gene under the control of multimerized CEH-22 binding sites. CEH-22 binds a region within the \textit{myo-2} enhancer termed the \textit{B} sub-element (14). In wild-type animals, a \textit{lacZ} reporter under control of a synthetic enhancer consisting of four copies of a 28-bp \textit{B} sub-element oligonucleotide is expressed specifically in pharyngeal muscle; only occasional expression is observed outside the pharynx (Table 1;14). \textbf{E}In a transgenic strain bearing the \textit{unc-54::nkx2.5} expression construct, \textbf{R}we found a significant increase in the number of animals expressing beta-galactosidase in body wall muscle (from 2.5 to 16.5%) (Table 1; Fig. 1C). To rule out the possibility that Nkx2.5 was indirectly increasing expression of \textit{myo-2} or the \textit{B} sub-element reporter by activating ectopic expression of the \textit{ceh-22} gene, we examined expression of a \textit{ceh-22::lacZ} fusion in animals bearing the \textit{unc-54::nkx2.5} transgene. Expression of beta-galactosidase was limited to pharyngeal muscle in the transgenic animals (Table 1); this pattern was identical to that observed in wild-type animals (14). \textbf{A}Thus, Nkx2.5, like CEH-22, activates transcription by interacting directly with the \textit{B} sub-element of the \textit{myo-2} enhancer.

\textbf{Nkx2.5 Can Substitute for \textit{ceh-22} During Normal Pharyngeal Development.} \textbf{B}In addition to its role in \textit{myo-2} activation, CEH-22 likely regulates other genes required for pharyngeal development. \textbf{B}Indeed, a \textit{ceh-22} mutant exhibits profound contractile and morphological defects in the pharynx, despite expressing \textit{myo-2} nearly as well as wild-type (15). \textbf{Q}To examine the extent to which Nkx2.5 and CEH-22 are functionally equivalent, we asked if expression of \textit{nkx2.5} in pharyngeal muscle can rescue a \textit{ceh-22} mutant.

\textbf{Strong points of this sample results text:}

\begin{itemize}
  \item Follows the organizational pattern \textbf{QERA}
    \begin{itemize}
      \item Each repeat of the pattern (each paragraph) moves the story line forward by adding more evidence that \textit{nkx2.5} functions like \textit{ceh-22}.
      \item Within each paragraph, additional information makes the story line clearer.
        \begin{itemize}
          \item in paragraphs 1 and 2, rationale for the design of the experiment
          \item in paragraph 2, the purpose and result of the control experiment
          \item in paragraph 3, background leading to the next question
        \end{itemize}
    \end{itemize}
  \item States the result first and cites the figure/table that contains the supporting data in ( ) at the end of the sentence.
\end{itemize}
Homework/ Reading for Week 5 – HOW TO WRITE SPECIFIC AIMS

SPECIFIC AIMS

The Specific Aims page is the most important page of the grant. The Specific Aims should clearly lay out the problem you are addressing, the hypotheses you are testing, and the experimental steps you will take. The Research Design and Methods section of the proposal will expand on how you propose to accomplish the Aims. Reviewers will read the Specific Aims quite carefully; if they don't like what you propose, don't understand it, or think your goals are unrealistic, they may be prejudiced against you as they read on. The Specific Aims page also serves as a summary page of your grant for the reviewer; they'll return to that page often to remind them of the major goals of your proposal.

The first 1-2 paragraphs of the Specific Aims page should explain the scientific problem and its importance. The Aims follow and are usually listed as hypotheses that you will test or positive statements of what you intend to do. Preferably every Aim you propose will provide important information whether or not the experiments turn out the way you expect. That is not always possible. However, no Aim should depend on another Aim. The proposal should be structured so that a negative result in Aim I doesn't make it impossible to proceed to Aim II or III.

When writing the Specific Aims for your preliminary exam, keep in mind that the work should be able to be accomplished in 2 years. For people who are new to grant writing or are applying for their first R01, a common mistake is to outline a career rather than a piece of work that can reasonably be accomplished in 3-5 years. This is often criticized by reviewers as overly ambitious. If you have too many great ideas to fit in one grant, mention them as something you want to do in the future, once you've accomplished the Aims of the present proposal.

Sample Specific Aims from Preliminary Exams

#1) from http://www.med.upenn.edu/camb/user_docs/PrelimSample1a.pdf
Title: Recognition of nonstop mRNA by Ski7p
Specific Aims:

- mRNA stability plays a critical role in controlling the expression of proteins. Along with normal mRNA decay, surveillance mechanisms dependent on translation have evolved to ensure the quality of the mRNA produced and prevent the mis-expression of possibly deleterious proteins. The removal of mRNA containing a premature stop codon occurs through the well studied pathway of nonsense mediated decay (NMD). Recently, a mechanism has been described for the removal of transcripts that lack a termination codon. Nonstop mRNA decay (NSD) has been shown to occur through a separate, distinct pathway from that of NMD. While normal mRNA are removed through deadenylation, decapping and 5’ to 3’ degradation, nonstop messages appear to be degraded through a secondary pathway of 3’ to 5’ decay via the exosome and Ski complex. Another related protein, Ski7, has also been shown to be required for nonstop mRNA decay. Ski7p is an ERF3/EF1-α homologue and putative GTPase that is normally required for removal of viral and other polyA- messages. The Ski7p N-terminus is required for the association with the Ski complex and exosome and presumably plays a critical role in coupling this degradation machinery to the aberrant mRNA. Because this is a newly discovered phenomenon, many questions still remain, especially about the role that Ski7p plays
in recognizing the nonstop messages and targeting them for degradation. The experiments described herein will attempt to elucidate the characteristics of nonstop messages, that target them for this rapid degradation, and further clarify the role of Ski7p in the nonstop-mediated mRNA decay pathway.

**Specific Aim 1: Elucidate the role of the polyA tail and polyA binding protein in the recognition of nonstop mRNA.**

To identify what characteristics are necessary to identify an mRNA as nonstop, *in vitro* transcribed luciferase mRNA constructs will be created. Stop codons will be placed at the beginning, middle, and end of the polyA tail, and the effects on mRNA stability and NSD recognition will be assessed in WT and NSD mutant yeast. Using other constructs and engineered yeast mutants, the fate of polyA- mRNA and the role of polyA binding protein (Pab1p) will also be assessed. The results of these assays should help elucidate exactly what constitutes an mRNA that is recognized and degraded via the nonstop pathway.

**Specific Aim 2: Determine if the C-terminus of Ski7p is necessary/sufficient to recognize a NSD ribosome.**

Because the C-terminus of Ski7p is only necessary for NSD, and not viral mRNA recognition, it is likely to play a specific role in NSD. To test this idea, serial C-terminal truncations along with internal deletions will be constructed to determine the minimal sequence necessary for NSD. Also, a FLAG-tagged C-terminus will be expressed in yeast, along with a nonstop mRNA. The construct will be immunoprecipitated and assayed for interactions with the ribosome or other proteins in the presence and absence of nonstop mRNA, or with the mRNA constructs designed in Aim 1.

**Specific Aim 3: Determine the importance of Ski7p GTPase activity to NSD.**

Ski7p is also a putative GTPase, but this has never been formally shown. Using standard assays (GTP binding, GTP/GDP hydrolysis/exchange) it will be determined if Ski7p contains GTPase function. Known mutations that disrupt GTPase activity of other closely related translational factors will be used to determine if this activity is required for NSD. The contribution of this activity will also be assessed in relation to recognition of nonstop mRNA or interaction with ribosomes, exosome and/or the Ski complex.

**Strong points of Specific Aims sample #1:**
- Starts with background for the informed non-expert, writing at about the level of *Scientific American*.
- Puts less technical information first.
- Scope of research is limited to three specific aims listed in bold and followed by a brief description of how each aim will be accomplished.
- The aims are the steps designed to prove the hypothesis.
higher eukaryotes. In addition to its role in post-transcriptional mRNA degradation, the RNAi machinery has been implicated in silencing at the transcriptional level in multiple organisms. Recently, it was demonstrated that deletion of *Schizosaccharomyces pombe* RNAi machinery proteins causes a defect in heterochromatic silencing at centromeres. The heterochromatin defect is accompanied by the accumulation of complementary RNA transcripts from the centromeric regions, further implicating the RNAi machinery in proper silencing of these regions.

While the recent studies in *S. pombe* provide strong evidence for a link between RNAi and heterochromatic silencing, little is known about how the RNAi machinery operates in this process. I propose to further elucidate the mechanism through which the RNAi machinery establishes a heterochromatic state at *S. pombe* centromeres. I will identify and characterize new components involved in RNAi-mediated centromeric silencing, and determine whether dsRNA processing by the RNAi machinery occurs in the nucleus or cytoplasm. In addition, I will test the hypothesis that the centromeric small interfering RNAs (siRNAs) produced by the RNAi machinery interact directly with silencing factors by analyzing the RNA-binding activity of centromeric silencing proteins.

**Specific Aim #1:** To identify new components involved in RNAi-mediated centromeric silencing. Genetic screens to isolate suppressors of the RNAi-mutant silencing defect will identify additional factors required for RNAi-mediated heterochromatin formation. Once identified, the role of these factors in the silencing pathway will be assessed.

**Specific Aim #2:** To characterize the components and sub-cellular localization of RNAi machinery complexes. Analysis of the composition and sub-cellular localization of RNAi machinery complexes will determine if processing of centromeric dsRNA is a nuclear event. Complex purification will also identify novel components of the machinery, which will then be characterized to determine their function.

**Specific Aim #3:** To assess the RNA binding activities of silencing factors involved in heterochromatin formation at centromeres. It is proposed that centromeric silencing factors can bind to siRNA, thereby linking the processes of RNAi and heterochromatin formation. I will test this hypothesis by assessing the RNA-binding activity of these proteins *in vitro* and *in vivo*.

**Strong points of Specific Aims sample #2:**
- Starts with the background for the informed non-expert
- Points out a gap in knowledge that will be addressed in the proposal “While the recent studies...little is known…”
- Steps that student plans to take are signaled by “I will identify…,” “…and characterize,” “I will test…”
- Scope of research is limited to three specific aims, followed by a brief description of how each aim will be accomplished.
- Could have used bullets or numbered lists to give additional guideposts to reviewers
- Indents, spaces, and bold type add readability.
- Its importance
- Hypotheses you are testing
- Steps by which you plan to go about it
- Aims don’t depend on each other

**Writing**
- Subject early
- Verb nearby
- Good use of topic and stress positions
- Nominalizations --> verbs
- Concise, cohesive sentences
- Coherent paragraphs

**White space**
HOW TO WRITE “APPROACH” (FORMERLY, “RESEARCH DESIGN AND METHODS”) for grants.

In this section, explain how you will accomplish your Specific Aims and convince the reviewers that you will be able to do what you propose. It is not enough just to describe the experiments—you need to state why they are being performed, why you have chosen the specific approach, which methods will be employed, what results are possible, how the data will be interpreted, what problems you anticipate, and how you will deal with them.

Many people write the Approach section for each Aim in a standard format with the following subheadings:

Specific Aim #1. Restate the Aim exactly as written on the Specific Aims page.  
Rationale. Explain why your proposed studies are important and how they will advance the field.  
Research Design and Methods. Describe the specific experiments, including methods, that you will perform in this Aim. Subdivide this section to clearly communicate the order of the experiments and how they relate to the Aim.  
Possible Results and Interpretations. Discuss the different results that are possible and how you would interpret their significance. For example: If we find X, then this supports our hypothesis that … If we find Y, then this does not support our hypothesis, but would be a very exciting result because…  
Potential Problems and Alternative Approaches. Are there potential pitfalls to the experiments you proposed? If a pitfall arises, what alternative method could you use? It is important to convince the reviewer that you have thought deeply about your experiments and have already considered and addressed alternatives for the obvious pitfalls.

If your proposed experiments involve techniques that are new to your lab, your proposal will be strengthened by letters from consultants or collaborators who will provide any help you need. If specific reagents are needed, be sure to document how you will obtain them.

HOW TO WRITE THE DISCUSSION (Papers)

A well-written Discussion puts the findings of the paper in the proper context, directing and guiding the reader through the implications of the study. The Discussion should not merely recapitulate or summarize the results but should extend the findings, making conclusions and examining the significance of these results to the field. Do not attempt to hide obvious limitations of the study but address these in the text; smart reviewers will have picked up on these already. The results and conclusions should also be compared and contrasted with previously published work; if these differ from published work, speculate on the reasons for these differences.

One should be bold in stating the importance of the conclusions but must also be careful not to overstate the significance or to misinterpret the meaning of the results. An example of
this comes from the story of the biologist who trained a flea, from “How to Write and Publish a Scientific Paper” by Robert Day and Barbara Gastel:

"After training the flea for many months, the biologist was able to get a response to certain commands. The most gratifying of the experiments was the one in which the professor would shout the command “Jump,” and the flea would leap into the air each time the command was given. The professor was about to submit this remarkable feat to posterity via a scientific journal but he - in the manner of the true scientist - decided to take his experiments one step further. He sought to determine to location of the receptor organ involved. In one experiment, he removed the legs of the flea, one at a time. The flea obligingly continued to jump upon command, but as each successive leg was removed, its jumps became less spectacular. Finally, with the removal of its last leg, the flea remained motionless. Time after time the command failed to get the usual response. The professor decided that at last he could publish his findings. He set pen to paper and described in meticulous detail the experiments executed over the preceding months. His conclusion was one intended to startle the scientific world: When the legs of a flea are removed, the flea can no longer hear.”

Day and Gastel also point out, “Much as the Methods and Results should correspond to each other, the Introduction and Discussion should function as a pair...Be sure the Discussion answers what the Introduction asked.” Finally, the Discussion should end with a brief but strong summary of the overall significance of the paper. In other words, as Anderson and Thistle said in 1947, “good writing, like good music, has a fitting climax.”
**Reading for Week 7 – HOW TO WRITE AN ABSTRACT (Grants and Papers)**

**HOW TO WRITE AN ABSTRACT**

**Abstract for a Grant Proposal**
The abstract should explain your proposal - what you want to do, why it is important, and how you plan to do it. In your abstract, state your hypothesis, specific aims, objectives, and why they are important and innovative. Make your abstract a clear, succinct summary of your project. It also must have two to three sentences written in lay language that describe your project's potential contribution to public health.

When writing the abstract, ask yourself
- Is it a succinct description of all major aspects of the proposed project?
- Did I state my hypothesis?
- Does my abstract describe my objectives and specific aims?
- Does it state the importance of the research and how it is innovative?
- Does it outline the methods I will use to accomplish my goals?
- Did I keep the language easy to understand for a broad audience?

**Sample Grant Abstract**
(from http://funding.niaid.nih.gov/researchfunding/grant/pages/titleabs.aspx)

**[Significance]** The integrin alpha 4 beta 1 (VLA-4) contributes to the etiology of common autoimmune disorders, including multiple sclerosis, inflammatory bowel disease, and systemic lupus erythematosus. Although VLA-4 is widely viewed as contributing to T cell function by directing cell trafficking and by enhancing cell adhesion, VLA-4 potently costimulates T cell activation. The mechanisms underlying this costimulation are not well understood and may play a significant role in the etiology of human immune disorders. Our long-range goal is to understand how to manipulate the costimulatory functions of VLA-4 in order to regulate T cell activation in vivo. Our immediate objective is to determine how VLA-4 modulates T cell responses to antigen. Here, we present preliminary data characterizing a previously unknown effect of VLA-4 ligation on the movement of signaling complexes induced by the TCR. Our specific hypothesis is that structures containing SLP-76 and ADAP are required for the transmission of tension-dependent costimulatory signals initiated upon VLA-4 ligation.

**[Innovation]** The rationale for the proposed work is that it will provide an enhanced understanding of the fundamental mechanisms that enable the integration of the signaling pathways downstream of the TCR and VLA-4.

**[Specific Aims]** Three aims will examine how ADAP contributes to T cell costimulation and how cytoskeletal tension contributes to VLA-4 dependent costimulatory signals:
1) How does ADAP contribute to the assembly and translocation of SLP-76 microclusters?
2) How does costimulation depend on the VLA-4-dependent immobilization of microclusters?
3) How does cytoskeletal tension contribute to T cell costimulation by VLA-4?

**[Reemphasis of the proposal's innovation]** These studies explore a novel effect of VLA-4 ligation, the lateral immobilization of TCR-induced complexes, and use it as a tool to dissect the
pathways involved in costimulation by VLA-4. We expect these studies to define the mechanisms by which VLA-4 ligation costimulates T cell activation. This will have a positive impact on our understanding of autoimmune disease and will assist in the identification of unique intracellular targets for drug development. This work will also generate insights into the systems linking cell shape to cell growth and proliferation, providing useful insights into cancer.

This grant abstract:
- Describes the protein to be studied
- States the significance (including with regard to health) early in the abstract.
- Addresses the long-term goal.
- Addresses the innovation of this proposal.
- States hypothesis and specific reasons for hypothesis.
- Describes three specific aims, using numbers to guide the reader.
- Includes additional information after the specific aims, reemphasizing the proposal’s significance and innovation.
- Is a succinct summary of the project.

Abstract for a Scientific Paper
The abstract should provide an overview of the paper by presenting highlights from each section. The abstract should concisely state the question (Q) that is being asked, the experiments (E) that were done, the results (R) that were obtained, and the answer (A) to the question. In addition to these 4 basic parts, QERA, the abstract may begin with 1-2 sentences of background (B) information to orient the reader, and may end with a sentence stating an implication (I) based on the answer, giving the abstract the form BQERAI.

Sample Paper Abstracts
#1)
B Development of pharyngeal muscle in nematodes and heart muscle in vertebrates and insects involves the related homeobox genes ceh-22, nkh2.5, and tinman, respectively. Q To determine whether the nematode gene ceh-22 and the vertebrate gene nkh2.5 perform similar functions, E we examined the activity of the zebrafish nkh2.5 gene in transgenic Caenorhabditis elegans. R1 We found that ectopic expression of nkh2.5 in C. elegans body wall muscle directly activated expression both of the endogenous myo-2 gene, a ceh-22 target normally expressed only in pharyngeal muscle, and of a synthetic reporter construct controlled by a multimerized CEH-22 binding site. R2 nkh2.5 also efficiently prevented ceh-22 growth defects when expressed in pharyngeal muscle. A These results indicate that ceh-22 and nkh2.5 perform similar functions. I Further, these results suggest that an evolutionary conserved mechanism underlies pharyngeal development in nematodes and heart development in vertebrates and insects.

This abstract has all of the standard elements in the right order:
- B Background
- Q Question
- E Experiments
- R Results
- A Answer
- I Implication
During mitosis, the mitotic spindle, a bipolar structure composed of microtubules (MTs) and associated motor proteins, segregates sister chromatids to daughter cells. Initially some MTs emanating from one centrosome attach to the kinetochore at the centromere of one of the duplicated chromosomes. This attachment allows rapid poleward movement of the bound chromosome. Subsequent attachment of the sister kinetochore to MTs growing from the other centrosome results in the bi-orientation of the chromosome, in which interactions between kinetochores and the plus ends of MTs are formed and stabilized. These processes ensure alignment of chromosomes during metaphase and their correct segregation during anaphase. Although many proteins constituting the kinetochore have been identified and extensively studied, the signalling responsible for MT capture and stabilization is unclear. Small GTPases of the Rho family regulate cell morphogenesis by organizing the actin cytoskeleton and regulating MT alignment and stabilization. We now show that one member of this family, Cdc42, and its effector, mDia3, regulate MT attachment to kinetochores.

This abstract deviates from the standard form of an abstract:
- Too much background
- Buried question
- Background again after the buried question
- No description of the experiments that were performed
- No statement of the results
- The answer is not parallel to the (buried) question

**TIMELINE**

It is helpful to the reviewers to provide a timeline for your experiments. A timeline entails listing each grant year and what you expect to accomplish in that year. While not required for your preliminary exam, a timeline is a useful exercise, because it makes you think realistically about the time needed to perform and analyze your experiments.

**REFERENCES**

You should be familiar with the references that you cite and the references should indeed contain the information that you reference. In NIH grants, references are not subject to the page limit. It is best not to be stingy with references.

**CREDITS**

This is based substantially upon the syllabus for 2007 CAMB 695, which was directed by Erica Golemis.

Here are her acknowledgements:

In preparing the 2007 CAMB 695 syllabus, we drew principles and examples of clear and unclear writing from several excellent sources of information. Those sources are: Style: The Basics of Clarity and Grace and Style: Ten Lessons in Clarity and Grace by Joseph Williams, “The Science of Scientific Writing” by George Gopen and Judith Swan, American Scientist.
In addition, for the 2011 edition, Drs. Katz and Lok acknowledge *How to Write and Publish a Scientific Paper* by Robert A. Day and Barbara Gastel. The passages on active and passive voice were prepared by Hillary Nelson.