Outline of Talk

- General Writing Advice
- Writing a Biomedical Research Paper
- Resources
General Writing Advice

• Write with precision
• Simplify - avoid jargon
• Quantify
• Avoid figurative language
• Be concise
• Use the active voice
• Choose the right level of detail
• One paragraph = One thought
• Provide logical connections
• Rewrite with feedback
Word and Phrasing choice

Often several words may convey similar meaning, but usually only one word is most appropriate in a given context. Here's an example:

"population density is positively correlated with SARS transmission rate"

"population density is positively related to SARS transmission rate"
## Simplify

<table>
<thead>
<tr>
<th>Complex</th>
<th>Simple</th>
</tr>
</thead>
<tbody>
<tr>
<td>efficacious</td>
<td>effective</td>
</tr>
<tr>
<td>utilize</td>
<td>use</td>
</tr>
<tr>
<td>elucidate</td>
<td>explain</td>
</tr>
<tr>
<td>proximal</td>
<td>close</td>
</tr>
</tbody>
</table>
Quantify

Whenever possible, use quantitative rather than qualitative descriptions.
"development rate in the 30°C temperature treatment was 10% faster than development rate in the 20°C temperature treatment" vs
"development rate was fastest in the higher temperature treatment."
Avoid Figurative language

"experimental subjects were assaulted with a wall of sound"

vs

"experimental subjects were presented with 20 second pulses of conspecific mating calls."
Sentence structure

• Make the topic the subject.
• Put the action in the verb. (“An increase in heart rate occurred” becomes “Heart rate increased.”)
• Avoid long noun clusters.
• Talk about one thing at a time.
• Be precise and simple
• Use parallel constructions. (“It was both a long talk and very tedious” becomes “The talk was both long and tedious.”)
• Keep related words (e.g., subject and verb) together.
• Use the active voice. (“There were a great number of dead leaves lying on the ground” becomes “Dead leaves covered the ground.”)
Paragraph structure

- One paragraph = one thought.
- A summary of this thought is the first (or last) sentence.
- Elaborate in a logical order (pro then con; most to least important evidence; chronological).
- Continuity requires reasoning.
Level of Detail

Include as much detail as is necessary, but exclude extraneous information. The reader should be able to easily follow your logic without being distracted by irrelevant facts and descriptions.
How do most authors write (a children’s story, a poem, a newspaper column)?

• By modeling something in their “genre” they consider well-written
• By thinking about their audience
• Let’s apply this thinking to a biomedical research paper…
There are two very distinct audiences for your paper

- The Scientist in Your Field
  - Methods
  - Data (figures, tables, etc.)
  - Legends

- The Outsider (scientists, editors, others)
  - The “body” of the paper (introduction, results, discussion)

Each piece needs individually to tell your story in a way that is best suited to the appropriate audience.
Order of preparation

- Authors and their order
- Data
- Methods
- Results
- Introduction
- Discussion
- Acknowledgments
- References
- Abstract and Title
Authorship: ICMJE guidelines

• Authorship credit should be based on
  – 1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data;
  – 2) drafting the article or revising it critically for important intellectual content; and
  – 3) final approval of the version to be published.

Authors should meet conditions 1, 2, and 3.
What did you learn?

Data

• Include all data necessary to the conclusions you stated in the title and abstract, including controls
• Do not include data that are irrelevant to those conclusions
• BUT DO NOT EXCLUDE DATA THAT CONTRADICT YOUR CONCLUSIONS!!
Data

• Organize your data into discrete pieces that each make a specific point
  – The titles of the legends associated with each piece provide the outline for your results section of your paper
  – The order can be chronological (how the research unfolded) or in order of importance
  – The figures/tables should be self-explanatory so an expert in the field can know what you have done (though not at the level of detail of the Methods), what the controls were, how many times you have done the experiment, and so on. Don’t force them to go looking for that information in other parts of the paper
  – Do not hesitate to use as models well-presented papers that present results comparable to yours
Data Presentation

• Tables
• Graphs
• Images
Graphs vs Tables

- If exact numbers need to be presented, use a Table
- If the data show pronounced trends, making an interesting picture, use a Graph
Example where Table is appropriate

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Enzyme</th>
<th>$K_m$</th>
<th>$k_{cat}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>[S] = dTTP</td>
<td>HIV-1 RT</td>
<td>$3.5 \pm 0.6$</td>
<td>$3.5 \pm 0.4$</td>
</tr>
<tr>
<td></td>
<td>HIV-2 RT</td>
<td>$11.9 \pm 1.0$</td>
<td>$1.0 \pm 0.03$</td>
</tr>
<tr>
<td>[S] = AZTTP</td>
<td>HIV-1 RT</td>
<td>$0.17 \pm 0.03$</td>
<td>$3.5 \pm 0.23$</td>
</tr>
<tr>
<td></td>
<td>HIV-2 RT</td>
<td>$0.75 \pm 0.21$</td>
<td>$1.6 \pm 0.24$</td>
</tr>
</tbody>
</table>

Template/primer was incubated with various concentrations of substrate ([S]; µM dTTP or AZTTP) and the amount of product (IP; nM primer + 1) produced in a 1-min reaction time was determined using a Phospholimager. $K_m$ is in µM dTTP or AZTTP. $k_{cat}$ is the turnover number and is defined as $V_{max}$ (the maximum velocity of the reaction; expressed as nM primer + 1 generated in 1 min) divided by $[E_{total}]$, which in this assay is 3.0 nM RT. The turnover number indicates the nM of product (primer + 1) produced by each nM of active site (for RT, this equals 1) in 1 min (nM P nM RT $^{-1}$ min $^{-1}$). The assay was done three separate times for each enzyme and each substrate and the results averaged.

DOI: 10.1371/journal.ppat.0020010.t001

**Summary of the Single Nucleotide Incorporation Kinetics Assay**
Effect of streptomycin, isoniazid, or combination on *Mycobacterium tuberculosis*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percentage of Negative cultures at (x) weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>5</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>8</td>
</tr>
<tr>
<td>Both</td>
<td>30</td>
</tr>
</tbody>
</table>
Percentage of negative cultures upon antibiotic treatment

- Streptomycin
- Isoniazid
- Both

Time (weeks)
Figure Legends

• Figure title should summarize the point of the entire figure
• Panels titles could be used, and indicate sub-points
• Legends should provide enough detail that reader doesn’t have to look elsewhere in the paper to figure out what you’ve done and what you’ve learned
Figure 2. BREs Repress 48S Initiation Complex Formation

(A) BREs mediate involvement of repressed mRNA into unusually heavy RNP complexes. Radioactively labeled FLAG BRE (A–C) or FLAG BREmut (D) mRNA was incubated in the Drosophila ovary cell-free translation system in the presence of cap analog m7GpppG and either competitor BRE RNA (red line), nonspecific RNA (blue line), or H2O (green line). After incubation, the translation mixture was loaded on a 15%–35% sucrose density gradient, centrifuged, and fractions collected. The radioactivity in each fraction was measured and is represented as a percentage of total recovered counts plotted against the fraction number. The absorbance of each fraction at 260 nm was also measured to reveal the position of monoribosome peak (black dashed line).

(B) BREs repress 48S complex formation. The assay was performed as in (A) but with addition of GMP-PNP.

(C) BREs repress translation at initiation. The assay was performed as in (A) but with addition of cycloheximide.

(D) FLAG BREmut mRNA is not involved in silencing particles. Assay performed as in (A) but with FLAG BREmut mRNA.
Figures : Size for Print

More than likely, your figures will be reduced to fit the column width of the journal, so it’s a good idea to create figures as near to that size as possible. Be sure your fonts are neither too big nor too small and the visual information is readable at that size—and don’t forget to embed the fonts. Also, consider how your figures will look as a group, and size the elements relative to one another. For example, make sure stains have the same dimensions from one figure to the next.
Supplemental Information

- No longer limited to the types of information that can be provided in print
  - Can now provide underlying data for other researchers to mine
  - Can now show video sequences, electrocardiograms, etc.
Figure manipulation policy (from JCB)

No specific feature within an image may be enhanced, obscured, moved, removed, or introduced...All digital images in manuscripts accepted for publication will be scrutinized by our production department for any indication of improper manipulation. Questions raised by the production department will be referred to the Editors, who will request the original data from the authors for comparison to the prepared figures. If the original data cannot be produced, the acceptance of the manuscript may be revoked. Cases of deliberate misrepresentation of data will result in revocation of acceptance, and will be reported to the corresponding author's home institution or funding agency.
Fraudulent Manipulation Examples

- Adding a band:
Fraudulent Manipulation Examples

- Deleting a band:
Materials

• Include the exact technical specifications and quantities and source or method of preparation; avoid the use of trade names unless a particular brand is critical

• Accurately identify all experimental animals, plants, and microorganisms by genus, species, and strain designations

• If human subjects are used, the criteria for selection must be described, and an “informed consent” statement should be added to your manuscript
Methods

• Usual order is chronological (in the order of the data), but group related methods together
• Headings should parallel those in the figures when possible
• Be precise (you are creating a recipe to be followed)
• You can cite other methods, if you follow them, but be sure the cited method is easily accessible
• How do your approaches compare to the “state of the art”? Do you need to defend why you’re using your particular approach?
Results: State them clearly and objectively

• The results provide an overall description of the methods and data. It explains clearly and plainly (without the level of detail required to reproduce the results) what was done and what you learned. Use past tense.
• The organization of the Results matches the organization of the Data
• Lead each paragraph with the experimental aim and primary result. Then elaborate.
• Describe why you are moving from one experiment to another.
• Do not speculate within the results, unless that speculation drives the next part of the paper
“Herskowitz Rules”

• The amount of time you spend describing an individual result should be proportional to the importance of that result to the paper
  – Major results get a lot of space, and a lot of data to support them
  – Tangential results are mentioned tangentially if at all

• Save your speculation for the discussion, and only allow yourself one layer of speculation (don’t build a house of cards)
How to know whether the Results section “got it right”

• Check the organization and see if it matches that of the figures – does everything build towards an “answer”? Are you satisfied that the experiments lead to the conclusions, and the answer?

• Follow the Herskowitz Rules, eliminating speculation and making sure the appropriate amount of space is allotted to each result

• Check paragraph organization, leading with research design, then elaborating

• Replace words and phrases as necessary to make the language precise and simple
The Introduction: Defining the question

• Your research taught you something
• The Introduction convinces the reader this knowledge is worth having
Placing Work in Context

Introduction

Question

Experimental Design

(Answer)
How to know whether an Introduction “got it right”

• First, identify the question being addressed
• Second, look for how the background being provided is relevant to the question. Delete anything that isn’t relevant.
• Third, look to see if the authors have explained why the question is important
• Fourth, look for the experimental approach (and its justification)
• Finally, is the answer to the question stated?
Discussion: a chance to say what you think instead of what you know

- Do not simply repeat everything you’ve done and learned, but start by reiterating the main point of the paper (i.e., the answer to the question you posed in the introduction)
- THEN:
  - How does this fit with other reported studies and expectations?
  - Why is this important?
  - What are the caveats?
  - What interesting questions does this raise?
Don’t Be Afraid to Speculate

• Speculation can provide context, which nonspecialists need in order to understand where the work is leading. But follow Herskowitz Rule #2, and allow yourself only one level of speculation.

• If you think your discovery might (in the future) prove to be the explanation for mystery X, don’t make the reader figure out the identity of mystery X. State it explicitly.

• Make all links. A link that is glaringly obvious to you will not occur to many of your readers.
Acknowledge your limitations

• Your conclusions should be directly supported by the data that you present. Avoid making sweeping conclusions that rest on assumptions that have not been substantiated by your or others' research. For example, if you discover a correlation between fur thickness and basal metabolic rate in rats and mice you would not necessarily conclude that fur thickness and basal metabolic rate are correlated in all mammals. You might draw this conclusion, however, if you cited evidence that correlations between fur thickness and basal metabolic rate are also found in twenty other mammalian species. Assess the generality of the available data before you commit to an overly general conclusion.
“Because the Data and Safety Monitoring Board recommended to stop the trial after the intermediate analysis, it was not possible to follow all the participants as initially planned, and, as a consequence, only those participants recruited at the beginning had a full follow-up. This potential bias was taken into account by adjusting the analysis for the recruitment period; such an adjustment cannot fully account for the confounding effect associated with partial follow-up. When restricting the analysis to those participants who had a full follow-up, the intervention had an effect that was similar in size and significance, suggesting that this potential bias had a negligible impact…

Another limitation concerns the timescale of this study. Participants were followed up for a short period of time, and, therefore, this study did not explore the long-term protective effect of MC.”

How to know whether the Discussion “got it right”

• Did it simply reiterate the results or did it go beyond the results to discuss their impact?
• Did it acknowledge limitations and conflicts with other data, or open questions?
• Did it indicate where the work might head and how this might impact other fields or the more general questions within the field?
References

• Built over the course of the paper
• Check the list to make sure you’ve included
  – Papers that come to conflicting conclusions
  – Papers from your competitors
  – Papers that were published during the course of your work
  – (Reviewers will be looking)
Give Credit to Others

• Research builds on the work of others. Make sure to acknowledge this.
• Give proper credit for
  – Ideas
  – Results
  – Methods
  – Equipment
  – Experimental Help
  – Funding

Wherever it is appropriate to do so (Introduction, Results, Discussion, Acknowledgments)
Titles and Abstracts

• Written last
• Read first
Abstract

• Need to provide
  – Relevant background
  – Major Methodology
  – Major Conclusion
  – Significance

Many will just stop reading after the Abstract, so make sure the main points are clear
Background
Cellular localization of severe acute respiratory syndrome coronavirus (SARS-CoV) in the lungs of patients with SARS is important in confirming the etiological association of the virus with disease as well as in understanding the pathogenesis of the disease. To our knowledge, there have been no comprehensive studies investigating viral infection at the cellular level in humans.

Methods and Findings
We collected the largest series of fatal cases of SARS with autopsy material to date by merging the pathological material from two regions involved in the 2003 worldwide SARS outbreak in Hong Kong, China, and Toronto, Canada. We developed a monoclonal antibody against the SARS-CoV nucleoprotein and used it together with in situ hybridization (ISH) to analyze the autopsy lung tissues of 32 patients with SARS from Hong Kong and Toronto. We compared the results of these assays with the pulmonary pathologies and the clinical course of illness for each patient. SARS-CoV nucleoprotein and RNA were detected by immunohistochemistry and ISH, respectively, primarily in alveolar pneumocytes and, less frequently, in macrophages. Such localization was detected in four of the seven patients who died within two weeks of illness onset, and in none of the 25 patients who died later than two weeks after symptom onset.

Conclusions
The pulmonary alveolar epithelium is the chief target of SARS-CoV, with macrophages infected subsequently. Viral replication appears to be limited to the first two weeks after symptom onset, with little evidence of continued widespread replication after this period. If antiviral therapy is considered for future treatment, it should be focused on this two-week period of acute clinical disease.

EphrinB2 was recently discovered as a functional receptor for Nipah virus (NiV), a lethal emerging paramyxovirus. Ephrins constitute a class of homologous ligands for the Eph class of receptor tyrosine kinases and exhibit overlapping expression patterns. Thus, we examined whether other ephrins might serve as alternative receptors for NiV. Here, we show that of all known ephrins (ephrinA1–A5 and ephrinB1–B3), only the soluble Fc-fusion proteins of ephrinB3, in addition to ephrinB2, bound to soluble NiV attachment protein G (NiV-G). Soluble NiV-G bound to cell surface ephrinB3 and B2 with subnanomolar affinities (Kd = 0.58 nM and 0.06 nM for ephrinB3 and B2, respectively). Surface plasmon resonance analysis indicated that the relatively lower affinity of NiV-G for ephrinB3 was largely due to a faster off-rate (Koff = 1.94 × 10−3 s−1 versus 1.06 × 10−4 s−1 for ephrinB3 and B2, respectively). EphrinB3 was sufficient to allow for viral entry of both pseudotype and live NiV. Soluble ephrinB2 and B3 were able to compete for NiV-envelope-mediated viral entry on both ephrinB2- and B3-expressing cells, suggesting that NiV-G interacts with both ephrinB2 and B3 via an overlapping site. Mutational analysis indicated that the Leu–Trp residues in the solvent exposed G–H loop of ephrinB2 and B3 were critical determinants of NiV binding and entry. Indeed, replacement of the Tyr–Met residues in the homologous positions in ephrinB1 with Leu–Trp conferred NiV receptor activity to ephrinB1. Thus, ephrinB3 is a bona fide alternate receptor for NiV entry, and two residues in the G–H loop of the ephrin B-class ligands are critical determinants of NiV receptor activity.

Title

- State what you have learned clearly without overstatement
- Make sure this matches your abstract and text of the paper
• Inositol hexakisphosphate and Gle1 activate the DEAD-box protein Dbp5 for nuclear mRNA export.

• Crosstalk between peroxisome proliferator-activated receptor delta and VEGF stimulates cancer progression.

• Bradykinin B2 Receptor Does Not Contribute to Blood Pressure Lowering During AT1 Receptor Blockade.

• p120-catenin and p190RhoGAP regulate cell-cell adhesion by coordinating antagonism between Rac and Rho.
Zebrafish trilobite identifies new roles for Strabismus in gastrulation and neuronal movements.

Contribution of endothelial nitric oxide to blood pressure in humans.

Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer.
Avoid Novelty Claims

• Unless you’ve read every paper out there, you don’t really know if you’re the first to discover something. If you were surprised by a result, you might declare it unanticipated, or going against common dogma, but not unprecedented…

• Appropriately qualified, there are certain “firsts” you do know…
A Novel Coronavirus Associated with Severe Acute Respiratory Syndrome

None of the previously described respiratory pathogens were consistently identified. However, a novel coronavirus was isolated from patients who met the case definition of SARS.

(assumption is that the dataset of previously described respiratory pathogens is complete)
Revising

• Set aside the paper for several days.
• Look for logical gaps and inconsistencies.
• Cut ruthlessly. Use simple, direct constructions.
• Have others read the paper and give written comments.
Cut, Cut, Cut

• Shorter sentences are clearer.
• Shorter paragraphs are clearer.
• Shorter papers are clearer.
• Is it worth creating a 20-page masterpiece if no-one will read it?
Randy Schekman: *The Role of an Editor: A Delicate Balancing Act*
Vivian Siegel and Zena Werb: *How to Read and Respond to a Journal Rejection Letter*
William Wells: *Me Write Pretty One Day: How to Write a Good Scientific Paper*
Liana Holmberg: *What Happened to My Figures?!*

Writing Studio

www.vanderbilt.edu/writing/index.php
QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

medschool.mc.vanderbilt.edu/editors_club/
Thank you.

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