**Bi 8 Outline: Dissecting primary research papers**

Ellen Rothenberg, Jan 6-8, 2016

1. What scientific papers are trying to accomplish
   1. A FOCUSED GOAL
   2. Why this goal?
      1. Context
      2. ***Posing the question***
   3. Use of validated method
      1. References to previous successes
      2. Technical details
      3. Needs to be consulted recursively because results depend on this
   4. Results
      1. Clear experimental design and rationale
      2. Clear ability to distinguish between one answer and another
      3. Exclusion of alternatives (recursive, convergent)
   5. Corollary: if this is right, then…
      1. Testing the corollary
      2. Extends scope
      3. Further tests falsification
   6. Stating the impact on the field
      1. Immediate consequences: immediate question resolved
      2. What this opens up for the future
2. Kinds of papers
   1. Structure papers
      1. Question is to solve the structure already implicated in a given function
      2. Result is hard to get but usually very clear
      3. Lots of prior evidence is often available to validate
      4. Sometimes, added tests: effect on function if you change structure
      5. Details reveal the WHY rather than the WHAT
   2. Discovery papers
      1. What is the molecule/ family of molecules that carries out a particular function?
      2. Search strategy (can be very creative)
      3. Arguments for specificity and power of search strategy
      4. Evidence for identity
      5. (Also see network/pathway linkage papers)
   3. Network/pathway linkage papers
      1. Is X (X, Y, Z) required for process A? Is it required to mediate the response of P to signal Q?
      2. Molecules identified in advance but relationship is not
      3. Crucial point is to carry out perturbation to determine how process A is affected when X is added abnormally or taken away
      4. Tests: is X CORRELATED WITH function?
      5. Tests: is X NECESSARY for function?
      6. Tests: is X SUFFICIENT for function?
      7. What other conditions modify the role of X in process A?
3. Taking apart the paper
   1. Reading the paper in the right order
      1. Abstract
      2. Introduction
      3. Figures
      4. Discussion
      5. Results
      6. Methods
      7. Then go back again in written order
   2. What an abstract tries to do
      1. Distill message
      2. Set up falsifiable claims
   3. Introduction: crucial for background and for focusing the issue
      1. Why is this work interesting?
      2. What is already known about the system?
      3. What is the most important, powerful question that can be asked about the system that is within the authors’ power to resolve?
   4. Figures: for the experienced, defines scope and methodology
      1. The “guts” of the paper
      2. Need knowledge of the methods and what they can accomplish
      3. Figures show what is and isn’t addressed
      4. Implicit logic of figure order
      5. Quality of data: are differences convincing?
      6. Statistically repeatable, statistically different?
   5. Discussion: what the authors think their work has shown
      1. Some claims are more important (for broader understanding) than others: these should be highlighted
      2. Some claims are more convincing than others (good authors will mention the weak ones in a way that distinguishes them from strong ones)
      3. Not every question can be solved with tools available to authors
      4. Results can be specific to one setup: a long standing puzzle solved, or an example of a new mechanism not proven to exist before
      5. Results can be general to change view of an entire process
      6. Elements of both are in many papers
   6. Results: now you follow the actual logic and the caveats that the authors note to go from the introduction to the conclusions
      1. Experimental design: skim first to look at overall logic, then read experiment by experiment
      2. What are the authors measuring? Are they attempting to detect the presence/amount of something in a mixture or to purify something?
      3. What are the samples? Is purity a problem for interpreting results?
      4. What are the controls? Do the authors think of all the things that could affect what they are detecting in their experiments?
      5. Do the implications of the first experiments get tested further in the following experiments?
      6. Often, successive experiments go deeper and deeper into the molecular mechanism that is involved in the process (discovery and pathway papers)
      7. Must be read recursively with Materials and Methods: are the methods the right ones to measure effects that the authors are trying to study? How do the methods and available controls limit the confidence of conclusions?
      8. Often, papers do not always tie things up in neat little bows – they resolve some things and open doors toward the exploration of other things
   7. Methods: often abbreviated, but the key to the reliability of the results
      1. Often heavily based on previous publications
      2. Often, the ideal method to solve a question will not exist at the time that work is done… importance of result spurs development of better methods
      3. How well do the authors use techniques that ARE available? How honestly do they explain the limits of what they can conclude?
4. “Sociological context”
   1. Types of journals
   2. Peer review system
   3. What gets through
   4. Impact of length limits
   5. Impact of “impact factors”
5. Scientific papers: flagstones on a path
   1. Science is alive, constantly moving forward
   2. An innovative paper is rarely the last word on a subject
   3. High impact is often low innovation
   4. It is easy to conclude trivial things with extreme certainty
   5. Conceptual advance often requires stepwise logic of experiments leading from certainty into implications that may be less certain
   6. Strength of support for early going on “solid ground” is key to strength of bridge into “terra incognita”