How to Read a Scientific Paper

You may read a scientific paper from the primary experimental research literature for many different reasons and the way in which you read it will be different for different purposes. What follows is a general strategy for critical reading that can be adapted depending on the purpose (e.g. writing a grant proposal, doing a journal club presentation, or just identifying a specific method you wish to use, etc). The underlying themes of this method are: (1) that critical reading of a scientific paper is very much a matter of first asking your own questions about the material and (2) that effective integration of information in the paper into your larger body of knowledge is facilitated by your drawing a picture/cartoon of the "new reality" which the work reveals.

STEP 1. LOOK AT THE PICTURES!! Yes, do this even before you have read any of the text. The "pictures" (i.e. Figures and Tables) contain the data (the "observables") upon which the paper was based. They are the focal point of the paper and while it is true that the text will help you understand them, you can learn a lot and, most importantly, put yourself in "Question Asking Mode" (a very useful state) by just diving in to the data first. Follow this strategy:

a. Make brief notes on what you do understand about each Figure. What was being measured? What technique was used to generate the data? Look it up on the web if you are not familiar with it. What were the independent variables, the dependent variables? What was actually observed by the investigators?

b. For anything (and everything) that you don't understand write an explicit question in the margin, e.g. "What technique made these bands appear on the gel?" or "Why does the mutant strain have the highest enzyme activity?" And, most importantly, MAKE YOUR BEST GUESS as to the answer to each question and write that down, too.

c. As you finish each Figure, make a guess about what methods you expect to see described in the Materials and Methods section. Write this down also. After going through each Figure in order using this strategy, move on to the Tables and do them the same way, in order, and also be sure to do this for supporting material online.

STEP 2. READ THROUGH. Now that you have the data in mind and are primed with your own questions, read the paper through from beginning to end and highlight:

a. every place where one of your earlier questions is answered;

b. every place where you don't understand something. In this case, form an explicit question. I.e don't just write "huh?" in the margin; write (e.g.) "Why does the buffer contain sodium dodecyl sulfate?" or " What does novobiocin do?"

STEP 3. CRITICAL ANALYSIS. Every scientific paper is a narrative of things that people thought and did. The formal structure of a modern paper (Title, Abstract, Materials and Methods, Results, Discussion, and References) obscures this very human process. Since humans have a natural ability to remember stories, examining the thought processes and the experimental methods that these humans used will help you to make sense of the paper and remember what contribution this work made to the larger field. Note that "critical" doesn't mean "negative"; you should also look for clever insights and elegant strategies employed by the researchers. Attend to the following points on your second read-through.

a. Significant Prior Knowledge/Current Ignorance. What specific information (from earlier work of their own or others) formed the basis for the experiments reported in this paper? An unusual observation? The behavior of certain mutants? A particular technical method? Often several such things will be important prior information underlying the work at hand. Most importantly, state in your own words what we still DO NOT KNOW in this particular area. These points will lead naturally to the next step.

b. **The Main Hypothesis and Its Alternatives.** Modern experimental science is "hypothesis driven". Every paper reports the experimental testing of at least one major hypothesis (a specific "guess" about

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what is actually going on in a given domain of nature). This "educated guess" may not appear explicitly in the Introduction; sometimes hypotheses appear in the Results and even, in poorly edited papers, in the Discussion. The hypothesis can be rephrased as a simple statement ("If X is true, then result Y should be observed under condition Z"). Ideally, the authors will state that several alternative hypotheses are under consideration and the work is designed to disprove one or more of them. Implicit in the major hypothesis is that "if X is not true, then a distinct result W will be observed under condition Z", but there can be other alternative hypotheses. State all hypotheses the authors are testing in this work.

c. **Assumptions (Explicit and Implicit).** Often the authors will tell you that they assumed something would (or would not) affect their experimental results. This is an explicit assumption. Be sure to note each one and decide if you agree. More subtle are the implicit (unstated) assumptions. These can be trivial (like assuming that Ohm's Law was working when they ran the electrophoresis) or non-trivial (like assuming that if they can't isolate plasmid DNA from a strain that means there are no plasmids in the strain). Identify implicit assumptions and state why you agree or disagree with them. NOTE: "Hypotheses" (things that are tested in the paper) are not the same as "assumptions" (things that are not tested in the paper); I expect you to distinguish these important terms in your critique.

d**. Tests of the Hypothesis(es).** Hypotheses are tested by the evidence acquired using experimental procedures, in other words, by the data. You've already looked at and wondered about the data in the Figures and Tables. Look at them again as you re-read the Materials & Methods and the Results sections. It is often useful to draw a cartoon to illustrate the experimental procedure used for a particular experiment. The appropriateness of the methods used is something you will learn more about as you progress in science, but you can begin to think about what a given method can (or cannot) tell you every time you read a paper. Your first goal here is to know exactly how each observation was made. Methods information can come from previous publications cited in this paper, from methods manuals such as the Current Protocols series (John Wiley, Inc) and increasingly from the web (e.g. Wikipedia). Also ask faculty and fellow students who use such methods in their research. Is this band on a gel really more intense than that one? Most importantly, do the authors provide statistical assessment of their data. Are there unequivocal answers to each question posed initially? Do the data really support one hypothesis or the other? The paper stands or falls on the answers to these questions. Don't assume that just because a paper was published that it is 100% correct. Lastly, read the Discussion where the authors interpret their observations. State in your own words the reasons for your agreement with them and for your doubts. What additional data you would like to have seen in the paper?

e. **Change in Reality.** The observations made by scientists and their interpretations of such observations define what we collectively call our "model of reality" in a given context. Each scientific paper changes reality, usually by just a little bit, sometimes by a lot. Considering the results reported in this paper, how is "reality" different in this area? What is it we now know that we didn't know before? Or what is it that we thought was true and we now know is not true? Is this a major "change in reality" for the field in question -or is it a minor change? Was it a major or minor change in terms of your view of reality? To clarify and contrast the old and the new reality, make a cartoon-like diagram or model of what was considered correct before this work was done and what is considered correct now that this work has been done. This model need not be elaborate, but it should emphasize the "pictorial" or "graphic" over the use of words. Sometimes the authors will have drawn a model for you; embellish it with your own additions. I strongly recommend doing this by hand with colored pens or pencils, not by PowerPoint. Simple freehand cartoons can teach you a lot about what you know -and don't know!

f. **The Next Step.** Even as prior knowledge/ignorance inspired the authors to perform the experiments in this paper, the observations they made here set the stage for the next experiments they and others will do. The end of this paper leaves you at the edge of their knowledge. What is the most important hypothesis they should now test in their next experiments? What alternatives does their new "model of reality" predict and how can they test them? Should they use an in vivo method or an in vitro method for such a test? Or both? What kind of mutants should they make and what phenotype would they have if the model is correct?