TIPS FOR EFFECTIVE READING OF A SCIENTIFIC PAPER

Most scientific papers in biomedical sciences follow a standard pattern.

1. The title. A one-liner, should convey the main message of the paper.
2. The abstract summarizes the main points of the paper. It should have a few sentences to introduce the problem, followed by the main results and a conclusion. The abstract is meant to generate interest in the paper, also from scientists who are not directly familiar with the field.
3. **The introduction** will give an overview of present understanding of the field. Importantly, the introduction should state the problems and questions that the paper addresses.
4. The results section describes the experiments and some intermediary conclusions. The experiments and the data produced by the experiments are described along with figures and tables. These items, figures and tables form the meat of the paper and you should pay much attention to them. Increasingly, papers being published contain supplementary data, sometimes only published on-line.
5. **The discussion** puts the results in the context of the questions originally asked, and will come to new conclusions and add some speculation. Sometimes, the discussion contains a diagram of a "new model".
6. References to the literature, which allows you to check the background to the work as done previously.
7. Supplements

When going over a paper, many scientists read the abstract and quickly scan the remainder, or ignore the main text depending on their interest. But if you are new to a field and new to reading scientific papers, you should spend more time and read the paper in a different way. Start by reading the introduction, and ignore the abstract for the time being. After reading the introduction, give yourself some time to think about the problem. What is the issue, what is the question that is being addressed? How would you approach it? What kind of experiments would you design to answer the questions? Then read the results, and look at the data carefully. Try to understand how the experiments are done. Then read the discussion and conclusions before reading the model figure at the end. See whether you agree with the conclusions.

In general, read actively! Take your own notes instead of just highlighting on the paper copy.

THERE ARE ONLY A FEW EXPERIMENTS:

The following 3 types of experiments exist in all fields, and together provide the evidence needed to prove that A does B.

1) Association experiments (what components are at the right time, place, and concentration to be able to function in a particular process):

What components are present?
When are they expressed?
Where are they expressed ?
How big are they ?
What do they interact with?
How tightly do they bind?
How does abundance as found compare with concentrations needed for action?

2) "Necessary" experiments (various ways of eliminating a component from a system, and asking if that component is necessary for the system to function):

Surgically remove a possible causal agent
Look for and study a mutant that inactivates a possible causal agent.
Drip in pharmacological inhibitors.
Add monoclonals, or morpholinos, or antisense, or RNAi to knock down particular components
Adsorb out a population of cells, laser ablate

Fractionate an in vitro system (genetics with salt)

3) "Sufficient" experiments (various ways of adding a component to a system and asking whether that component is sufficient to trigger particular events)

Transplants, beads, and implants
Make transgenics.
Microinject cells or messages or proteins.
Move regulatory sequences from one gene to another.
Express genes at different times and places to check effects.
Add purified components together in an in vitro system .

THE SYSTEMS THAT WE UNDERSTAND THE BEST ARE THOSE WHERE IT HAS BEEN POSSIBLE TO USE BOTH GENETIC AND BIOCHEMICAL TECHNIIQUES:

Genetic approaches:	**Biochemical approaches**
Mutants.	Proteins and antibodies.
Hierarchies and pathways.	Radiolabeling, pulse-chase.
Suppressors.	Fractionation.
Enhancer traps.	Purification.
Knockouts.	Direct tests of interaction.
Transgenics.	Reconstitution
	Structural and mechanistic studies.

These approaches give complementary information.
Genetics needs biochemistry to explain what hierarchies are really doing in physical terms.
Biochemistry needs genetics to test function of identified components in living system.

For in vivo experiments:

Could you reinterpret as some animals or cells being sick in a nonspecific way?

Could the observed phenomenon be an Nth order effect?

Can you imagine a way of pulling the system apart using genetics? Using simpler in vitro systems?

For in vitro experiments

Have all components been defined?

Has carry over been eliminated?

What is signal to noise ratio?

Have all possible rate limiting steps been separately considered?

Can you see dose response?

How does in vitro level compare to in vivo? Are concentrations within physiological range?

How does in vitro rate compare to in vivo? Are they reasonable?

Can you change interpretation by assuming that different members of the population act differently than population as a whole?

Can you use genetics to verify importance of components in vivo?

For any genetic analysis:

More than one example of each complementation class?

Dominance been examined?

Null phenotype established?

Time of action established?

Place of action established?

Number of genes required known?

Order of genes known?

Nature of genes known?

What components may have been missed because of redundancy, pleiotropy, or maternal masking?

General:

What is the positive control? What is the negative control?

What can you tell for sure?

What is only correlation or consistency? Could correlation be reversed, with different cause and effect?

What other models can you make?

Could a positive effect really be an anti-negative, or a negative effect an anti-positive (activators vs. repressors of represssors)

What are the advantages of this system over others?

Is there a better system for the same phenomenon?

What was the key technical breakthrough? What is the main handicap to further progress?

Could techniques, materials, or conclusions have applications to other problems?

What would you do next with this system?