What You Learn in Graduate School (in my lab)

Iris Lindberg, 2010

Graduate school is an apprenticeship during which a student learns the practice of science through the performance of specific projects. The projects themselves are less important than the experience of handling them, although infinite projects – those that are extremely labor-intensive and technically impossible unless a miracle takes place- are not well-suited for thesis projects. You will often have several types of projects running concurrently. One kind will most likely be a bread-and-butter type of project guaranteed to result in a thesis chapter (but perhaps with less than earthshaking results). Another may be a collaborative effort with another person in the lab who has primary responsibility for the project. A third kind will often be a succession of short "what-if" types of experiments, most of which will fail, but one or more of which will succeed and turn into a real project. These are called high-risk, high-reward types of projects - and the trick is to know when to pull the plug.

Through execution of these three very different types of projects, you should come out with the following set of skills:

KNOW HOW TO CARRY OUT AN EXPERIMENT

1. You will be able to independently **design an experiment**. This includes going to the literature to find a method and adapting it to your needs. (You also need to develop an ever-growing network of friends with different technical expertise that you will draw upon during your scientific career). While you will at first discuss all experimental design with your major advisor, by the end of your graduate tenure you will independently design all of your experiments. Your experiments will start with the results of others but go further, will test **new** hypotheses.

Designing an experiment also includes knowing what **positive controls and negative controls** are necessary to include right at the start. You will also know **how many replicates** to use, based upon previous results of yours and of others in the field. You will be able to carry out all of the math-related operations, such as calculating molar concentrations and figuring dilutions, that are necessary for experimental design.

You will know how to **use estimation to aid your experiments:** for example, you will estimate and calculate how much of a reactant you would need to add in order to be able to see a signal significantly over background.

Lastly you will know how to **record the design** of the experiment in a manner that will be clear to you later when you try to write methods up, and to others when they go through your notebook.

2. You will be able to independently **execute an experiment**. This is where the concept of "good hands" comes into play. People with good hands know what steps must be executed painstakingly, and with what steps short cuts can be taken. There are two elements here - **experience in general biochemical techniques and good common sense**. Only the first can be taught. People who do not have the second should generally not engage in bench research; there are many other types of science.

Execution of an experiment also includes **knowing when to ask for more help**. There is nothing worse than losing your valuable time. Your P.I. and your colleagues in the lab will generally always be happy to answer your questions, provided they are there when you need to ask them- i.e. plan daytime execution of new experiments! (It's better to ask senior lab colleagues rather than your P.I. the really simple questions!)

Lastly, you will have learned to **think about the output style at the beginning**, for example, loading a gel so it is very easy to interpret the results in a published photo. (All experiments should be carried out as if they were for publication. They may be!) You will know that **all** information pertaining to the experiment should be recorded, no matter how small a detail.

3. You can independently **analyze the results** of your experiments. This includes knowing how to use the software and what its limits and advantages are; and knowing when you really need statistical analysis, and how to use it. You will know how to graphically **present the results** in a manner that best shows the result that you think is most important -without exaggerating its significance. You will use **estimation** to expedite your analysis: for example, from looking at a stained gel you can approximately estimate your protein yield.

Indeed, you will **never over-interpret your data**. Instead, you will be your own worst critic. Only you are on the front lines of an experiment; so, only you can see how you could have gotten your results from an artifact rather than through the application of your experimental variable. You will know when and how to spot these possibilities and how to redesign subsequent experiments to be able to address these potential problems.

You will be able to **troubleshoot problems** based on your extensive experience at the bench; for example, you will be able to pinpoint sources of irreproducibility and devise mechanisms to deal with them.

You will be able to present your results in light of what others have found and will know immediately when your data conflict (and, you will often be able to come up with possible reasons for the conflict). You will **know the literature** better than anyone- except your competitors.

4. **Your lab notebook** will record the progress and findings of your experiment in clear, succinct statements. It will not be a random collection of data, but **will emphasize the presentation of the hypothesis and the results** in a manner accessible to a total stranger in ten years (and this has indeed happened!)

5. You will have a **repertoire of basic biochemical techniques**; but further, you will understand **basic principles of biochemical experimentation**, such as making sure the unknowns fall in the middle of the standard curve; treating the sample and standards identically; knowing how to label your samples/films during use and storage for minimal possibility of a mix-up. **You will date everything that you do.** In general, you will know how to go about your experiments in the most efficient and expedient way.

6. You will know how to **use all standard biochemistry equipment**, such as centrifuges, balances, pH meters, PCR machines, protein/DNA gel electrophoresis equipment; and you will be able to figure out how to use a piece of equipment new to you. You will always first obtain the necessary information that can guide you (either from the manual, the company, or the web) rather than risk damage. You will constantly **assess when a piece of equipment is performing optimally** and either optimize it yourself or arrange to have it fixed by others if suboptimal performance is detected.

7. You will know **how to organize your time** efficiently. This means that while something is spinning, you will be labeling tubes or designing primers or reading the literature for a paper you are planning. You will use weekends to speed overnight steps (starting cultures, etc), if not to do carry out actual experiments. You will have learned to run multiple projects running concurrently by using an organized (and ambitious!) list of all tasks/experiments to be carried out that for all projects. Efficient use of time will most likely have saved you up to a year in your graduate studies.

8. You will be **expert in independently locating information**. This will include protein and nucleotide databases; journal sources; web sources; technical information from companies; the extensive collection of books and manuals in the laboratory; and your network of colleagues.

KNOW HOW TO HANDLE A PROJECT

1. After you complete an experiment, as a senior graduate student you will immediately see what experiments naturally come next. (Generally, you will either need to repeat the experiment to confirm; to refine your hypothesis in a new experiment; to change gears and test an altered hypothesis; or to pull the plug on the line of research altogether.) You may often need to use a different line of experimentation to confirm your hypothesis another way, which will greatly support your idea. You may need to spend time with your results and the literature to see whether your line of work is profitable. If it is, then you will be able **to plan out a series of experiments** that center around your hypothesis that will eventually form the nucleus of your paper.

2. If you are unable to uphold your hypothesis through different lines of experimentation, or if you cannot consistently get a result that upholds your hypothesis by repeating an experiment, then you will know that it is time to pull the plug on the hypothesis and you will do it quickly and without regret for the time you spent. On the other hand (rarely) the question is so important that this is the time to develop a new method to answer the question, which will require considerable additional effort. You will know how to tell the difference between these two scenarios, i.e. **perform continuous cost-benefit analyses**. Initially, it will be your advisor that tells you when to quit; later, you will make these decisions yourself.

3. Eventually **you will develop your own project ideas** yourself (in the last year of graduate school). Because you are a student you will need to pass them by your advisor for approval, but in your last years, you should be more knowledgeable and more proficient than he/she is in your area of research, and should be able to come up with good new ideas for projects. Your ideas will represent not just what is <u>possible</u> to do, but also what is most <u>important</u> to do; you should not be afraid to tackle the most important questions in your field.

KNOW HOW TO WRITE AND EVALUATE A PAPER

1. You will know **how to format a paper** so that it contains:
   a. an outline that summarizes the major findings in the broad context of the work.
   b. an introduction that orients the reader as to why the work is important.
   c. a methods section that enables the reader to actually repeat the experiments.
   d. a results section that succinctly describes each major finding, and groups them appropriately in figures. Every statement in the results will be supported incontrovertibly by the data in the paper.
   e. a discussion that does not repeat the results but rather takes each major finding presented in the results and discusses it in the context of how it relates to previous and future work, with comprehensive and appropriate literature citation.
   f. figures that are easy to read and logically presented, and can be reduced severely without loss of legibility.
   g. absolutely no mistakes of any kind-either typos, omissions, inconsistencies in the data, redundancies, or errors in referencing.

2. You will be able to write a **rebuttal letter** to the journal editor that explains how you have responded to each point in the review.

3. You will be able to **critique your own papers**, those of other lab members, and those of others in the field. Your critiques will essentially reflect the standards that you would expect of your own work. You will be able to judge the quality of data not just in your own field, but also in others.

KNOW HOW TO GIVE A GOOD TALK AND POSTER

1. You will be able to **present a talk for your lab group** that summarizes your recent work. This will involve: a) presenting a hypothesis that you are trying to confirm or refute; b) discussing the methods you used; c) presenting the graphed data; and d) interpreting the data in terms of your hypothesis. You will then discuss how your results fit into the literature, and present your ideas for future experimentation, either along this line of research, or whatever else you plan to do.

2. Through involvement in the **Work-In-Progress seminar series**, you will be able to present a 50-minute seminar to a group outside your field. This will generally follow the same format as above, but will include a much larger introductory segment so that the group can understand why your work is important. You will have learned how to make your talk interesting (posing questions and answering them; presenting a limited amount of information). You will know how to design slides and use PowerPoint.

3. You will be able to present your findings in poster format. Most advisors encourage (and support) all students who have data to **attend one yearly national meeting**. Through these yearly poster presentations they learn how to present a poster that is nicely formatted and easy to follow. It is not unusual for this poster text to evolve into the actual nucleus of the subsequent paper. You may also elect to participate in LSUHSC's Research Day forum.

KNOW HOW TO WRITE A GRANT

You will have acquired experience in **presenting your ideas** through the following exercises:

1. You will have seen at least four years' worth of your advisor's grants as examples; you may also have attended a seminar on grant writing.

2. If you are a US resident or citizen, you will have applied for your own funding, and will have written a short proposal on the work you expected to do for your thesis.

3. You will have **written grant proposals for your qualifying and preliminary exams** that are NIH-format proposals lacking the budget items.

BE ABLE TO WORK WITH OTHERS

1. Through four to five years interacting with others you will have learned how to be **a good laboratory citizen**. You will spontaneously contribute your effort to clean up general lab areas or to make commonly used stocks. You will respect the work of others by replacing all reagents you finish and not sequestering any reagents or common equipment in your area.

2. You will have had **experience as a supervisor** in directing undergraduate students. In our Department laboratories often have at least one undergraduate "helper" in the lab; upon occasion, these students will perform actual experiments under your direction. You will have learned how to teach these students beginning laboratory procedures, and how to direct people so they perform well and are not discontent (for example, people like to be able to plan ahead; having a slave is nice for the master, but not for the slave).

3. You will know how to **work in a research team** as a primary member (i.e. the first author position) and as a secondary member (contributing work for a paper ultimately first-authored by others. (Upon occasion this will require going through a departed lab member's lab notebook, which is when you will learn how important it is to be totally clear in your record-keeping.) This also often happens via collaborations with other laboratories, i.e. when one laboratory contributes data to a study originated by another. In addition to supplying data, you are then asked for the methods, data interpretation, and appropriate literature citations for use in papers; all must be accurate.

DEVELOP GOOD ETHICAL PRACTICES

You will **always use original- this means your own- language** in any written work that you submit for publication or for your courses. You will repeat experiments until you know that even when judged by the harshest criteria, the **findings will be reproducible**, and the conclusions will be valid. You will prefer to develop original lines of research rather than directly copying those that you know that others are already engaged in. You will **review the work of colleagues without bias,** and will voluntarily eliminate yourself as a reviewer if you are in direct competition. Your **treatment of animals will always be humane**. You will **handle radioactivity and toxic materials in a responsible manner**, both for your own health and for that of your colleagues.

When you know all of the above- congratulations, YOU ARE A POST-DOC!