Teaching Cell Biology: Changing the Paradigm

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Abstract: The paper presents a brief summary of methods of presenting laboratory information. It suggests that approaching lab problems in a way science is actually done requires a combination of methods structured into a problem-oriented learning experience. This begins with the instructor and/or students identifying problems, and the students working together in groups to solve the problem. Information pertinent to the problem is gathered from the web, visiting scientists, and the instructor. All projects are published on the web with each student having a home page. The specific example of a problem presented is the relationship of a glyoxysome to the chloroplast and the steps involved in solving it.

Keywords: cell biology, chloroplast, glyoxysome, imaging, microscopy, problem-oriented learning, world-wide-web.

Traditional science laboratories have served many pedagogic functions. Some are used for reinforcing materials covered in lecture or the text. They are simply adjunct resources for the presentation of additional facts. The lab is typically content oriented and is known familiarly as a "cookbook" procedure. The labs are time and place dependent, but cost efficient and effective for their purpose. They are also useful for large enrollment classes since they require little or no alteration between multiple sections of lab. Nearly everyone who has had a "classical" botany or zoology lab or unfortunately, most general biology labs, has experienced this approach.

Alternatively, laboratories can be inquiry based, research based or problem-oriented. Inquiry labs attempt to balance content with concept and are more open-ended. The student is directed to ask a series of questions or is given a series of questions to answer. The answers and/or outcomes are unknown to the student, but known to the instructor. Good lab design leads the student to the "correct" conclusions generally pre-determined by the instructor. This lab approach remains time and place dependent but attempts to engage the student in a more personal approach. Early attempts at computer assisted instruction were based on reducing the time and place dependency of this model, with the added advantage of individual processing by the student. A highly effective model of inquiry based learning was the BSCS program of the 1960's. The literature abounds with computer modeling and simulations.

Research labs take the inquiry one step further and ask questions that do not have pre-determined answers. This model engages students in "real science" where the outcome is unknown, at least in all of its details. Learning is highly individual and usually requires the development of sophisticated laboratory skills. It also requires more instructor time and expertise. Consequently, projects usually reflect the research interest of the instructor and the facilities of the institution. This is an expensive approach to lab. It requires considerable time and materials and is based on the older apprentice model of education. It is usually reserved for the best of the majors and is rarely used in lower division courses with large numbers of students. It is difficult to schedule (protocols don't always fit neatly into one or two hour blocks), and is highly dependent on place. Often, research projects require a significant investment in facilities and support staff and most projects are done within the facilities of the faculty supervisor.

The latest vogue in science education is problem-oriented learning. This is a modification of a research plan and involves new problems for the student, but not necessarily for the instructor. Labs are learner focused, cooperative team efforts, with a high level of "ownership." All knowledge is contextual and students learn only what they need to solve a problem. Case studies are often employed for starting points and the outcome is flexible but usually able to be controlled. The instructor's role is to choose appropriate case studies and attempt to steer the process in a particular direction (often to ensure content coverage). This approach to lab requires extensive library holdings and often-sophisticated facilities. It is also more demanding of instructor time in the role of facilitator.

So, which is best. For us, the answer is a combination of all of the above with a focus on how real problems are solved in science. None of the strategies mentioned above are appropriate to the way science is actually done. Each approach highlights only one aspect of solving a problem. For most
laboratory scientists, the process of solving a problem is likely to begin with the recognition of an interesting question or topic. Sometimes this can be assigned by others, but more likely, it is a phenomenon that grabs our attention and one for which we don't have adequate easy answers.

Once the problem is formulated, the next step is invariably checking the literature. The equivalent today would be to run it through a search engine on your browser. One need to know what has been reported before one can ask intelligent questions. Next, or perhaps simultaneously, the problem is discussed with local or regional experts. Having gained enough knowledge from the literature about the topic, we feel easier about approaching our peers. If the experts don't have a satisfactory solution, our interests may get piqued even more and then the fun begins. We decide to find a solution through experimentation. There is a problem or question that no one seems to have an acceptable answer. We first design a protocol based on our experience and skill and often expand those skills as it becomes necessary. Take, for example, a problem dealing with genetic variability. It could easily lead us to learn new techniques of molecular biology (PCR, restriction mapping, sequencing), while leading us away from the familiar and comfortable (microscopy, histology, karyotypes). We discover that while every technique has merit to someone, only a few will be relevant to a given problem. And some are more relevant than others. If we are going to answer a problem, we learn the techniques that are required. Alternatively, one learns a technique and then never asks questions that can not be answered with that technique.

The typical cell biology lab teaches techniques. Some will be used at a later date, most will not. Even twenty years ago, questions of genetic code would have been quite limited by the techniques available for RNA/DNA studies, when compared to modern procedures. Who would have thought those fluorescent probes would be as readily available as they are today? It should not surprise us that many of the hot techniques of today will be rather passe twenty years from now. In my day, we used a lot of colored pencils and drew every structure visible in the light microscope. Today, we are making digital videos of the movement of SNRPs within a nucleus, and publishing it on the Internet.

Consequently, it is time to evaluate, once again, our laboratory approach to cell biology. Instead of a traditional syllabus of 12-14 weeks with each week devoted to a different technique, the focus of the lab should be a project aimed at the solution of a problem. Rather than begin the sequence with "How to use a microscope," we should lay out a number of case studies, appropriate problems, or better still, use the first weeks to focus on teaching our students how to spot a significant problem that can be addressed. This is best done by utilizing group projects that require constant interaction and focus. Each group must be able to state the problem with sufficient clarity that all members of the group understand what is being asked and find their role within the solution.

In my course, we have done away with lectures, canned labs, written exams and even the textbook. This may sound like the instructor has it pretty easy, but it is not so. Working with up to 15 students in groups of 3 or 4, we meet once a week for a three hour session. In the early part of the semester, the group focuses on basic techniques of cell imaging (the focus of the course), and more importantly on the identification of appropriate problems. All of the students have completed a basic course in cell and molecular biology, so they are familiar with the terms and concepts of modern cell biology. They are asked to use their old texts, the library, the Internet or any source they can imagine and to return by the second week with some spark of a topic in cell imaging that excites them. Each student presents her/his "idea" to the entire group and the group critiques each idea. The main role of the instructor is to elicit the ideas, help to refine them and keep them on track. It is also important that the problems are stated in terms that are approachable in the limited time of a semester and with the equipment and facilities at hand. For example, a student may wish to complete the genome sequence for Arabidopsis. With coaching and discussion, that may be whittled to using FISH to study the location and regulation of a single gene. That gene should be one for which there is a commercial source of an appropriate oligonucleotide for the hybridization.

At this point, students begin to group themselves around the basic ideas and some are accepted as appropriate while others are left open for further work. Then the groups must decide what is it that they need to know before proceeding. In our example above, the students would have to determine what FISH is (fluorescent in situ hybridization) and how it applies to visualizing the action of a gene. There is no better way to determine this then using the web. Simple searches of "genome and localization" will yield a host of appropriate papers and abstracts, some of which will refer to visualizing the process. Then, the students ask for a review of FISH. If it is appropriate the instructor may choose to give a 20 minute or 3 hour lecture, or better, ask an expert to give a seminar to the group, or visit a laboratory where it is being performed. In other circumstances the students will do a review of the procedure and report it to the group. The important part is that FISH is introduced as a means of solving a question and not as an isolated technique. If they do not need to use FISH, it may never be covered in the course. The protocols are selected on the basis of the stated problems and often come from on-line sources (c.f. http://www.gac.edu/ cellab/).
Since this is a course on advanced cell imaging techniques, there are some basics. All aspects of microscopy are covered to some extent, usually by careful selection of the projects. Standard light, dark field and phase microscopy, photomicrography, and fluorescence are covered. If appropriate, TEM, SEM and AFM might be covered, at least in principle. All students are introduced to digital and analog techniques of image recording, including the use of scanners, darkroom techniques and file formats. All projects must utilize some form of image processing and analysis. The specifics are left to the students, but in our experience, Adobe Photoshop® and/or Corel Photopaint® work well for most image manipulations. These are PC based programs, but students opt for similar programs for Macintosh or even UNIX based programs. Metamorph® is used for advanced work (including 3D deconvolution) although NIH Image® and/or Sigma Scan® are also employed. Digital video and morphing are introduced and 3D reconstruction is accomplished with Spyglass Slicer® (now NOeSYS®). All projects are eventually published on the web and each student creates a home page. There are now so many programs for this that the students invariably lead the way. As a start they are introduced to the UNIX system on campus and learn to FTP and Pico edit from the start.

Now for the best part. Most of the images needed are available on the web. It is not necessary for a student to know how to do FISH if the images they need can be obtained from elsewhere. They should understand what the procedure is, but do not need to be skilled at performance of a protocol. For undergraduate projects, there is an almost unlimited resource of images available on the net. Normally, our projects are focused on protocols that can be performed by students, but they know from the start that it is the analysis that is important. For example, one of last year’s projects involved the reconstruction of a chloroplast. The project centered on the relationship of a glyoxysome to the chloroplast when it was noted that published images were always 2D TEMs. Without realizing what a formidable task lay ahead, the students chose to obtain serial sections of a chloroplast, digitize the images, stack them and reconstruct a rotatable image (hopefully in relation to microbodies in the cytoplasm). This was not a trivial undertaking, since cutting serial sections requires quite a lot of skill. Fortified with the enthusiasm of ignorance but excited about the ultimate image the students forged ahead. What they found was a citation that gave a series of 2D images of a sectioned plant cell. When photocopied and faxed images proved too blurry, they contacted the author by email, explained their project and obtained a set of original photomicrographs (by snail mail). The author was not up to the task of creating the digital images and was surprised by the students’ request for images that they could receive by FTP. The project was completed with the supplied images, even though the students, as a back-up, had fixed and embedded plant materials and learned to use a TEM. The images merely saved them many hours of sectioning and allowed them to put their time into the 3D reconstruction. As for the relation to the glyoxysome, the students learned that it was not as easy a solution as they had originally thought. They have a new respect for the published work of others.

The basic procedure is:

- Find a topic that excites the student curiosity
- Search the literature (web browsers, search engines) and refine the problem
- Obtain published images (FTP or download from the net)
- Digitize and enhance images (threshold, erase unwanted material)
- Image Analysis (counts, area, cross-section diameter, etc.)
- Morph or 3D reconstruction
- Plan and execute presentation on home page or as Authorware® presentation.

Our focus is on an image as data. It matters how the image was obtained, but the real work begins with the image. The production of a visual answer to a problem of interest to the student leads to retention of more content than one would imagine. The students become creative with their work and are justly proud of their accomplishment. Equally important, they learn to work with a team toward a set deadline (upon which their entire grade depends). They do not waste time going over cookbook protocols and techniques they may never use. Finally, they come to realize that they can either master any technique if there is a need for it or find someone who is a master to cooperate.

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