

Title: Something old, something new: teaching the BMB lab

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Abstract. Lab courses are a significant component of biochemistry and molecular biology (BMB) education. In teaching the labs, we combine established techniques with novel approaches. Lab formats have also moved from traditional cookbook style labs to guided inquiry to course-based undergraduate research experiences (CUREs), where faculty bring their own research interests into the course setting with a larger number of students in a much more restricted time frame. This presentation is designed to explore some of these ideas and challenge the reader to introduce research opportunities to all students, not just the smaller group of students in your research lab.

There is a shift in educational culture to bring more open-ended opportunities into teaching labs [1]. This can be seen in recent publications about course-based undergraduate research in many areas of biology and chemistry [2–8]. Many instructors have been doing this in BMB lab courses for years. Some things remain the same, but some things change. We still ask students to keep notebooks, but electronic notebooks [9–11] are increasing in popularity. We begin with traditional methods (protein expression and purification, enzyme kinetics, SDS-PAGE and western blotting), then introduce newer approaches (PCR, site-directed mutagenesis, RNAi, CRISPR, computational and statistical methods). Few BMB lab instructors use textbooks, though new experiments may be introduced from the dozens published every year in the “laboratory exercise” category in this journal. Courses may even be redesigned to incorporate new instruments (MALDI-TOF, LC-MS) that have been purchased from grants or capital equipment funding.

One of the major shifts is a change in our perspective as instructors. Students are required to demonstrate critical thinking in their lab reports, but now the exercises are designed with learning goals, objectives, and rubrics that reflect Bloom’s taxonomy [12,13]. Different approaches to teaching laboratory courses are associated with specific terms. *Cookbook* or verification methods are tried and true experiments with a detailed procedure and known results. *Guided inquiry* labs provide the students with a more open ended approach to protocols and to the discovery process [14]. More recently, the term CURE (Course-based Undergraduate Research Experience) has been used to describe inquiry type labs that share five characteristics [15]:

1. Scientific Practice: students design experiments, create hypotheses, collect and analyze data, and draw conclusions.

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2. Discovery: neither the teacher nor the students know the expected outcomes.
3. Relevance: the experiments have the potential for impact on current scientific and social issues.
4. Collaboration: students work in teams.
5. Iteration: new discoveries build on the past and point to the future.

There are many well-known and widely adopted CUREs that intersect with biochemistry and molecular biology labs, including SEA-PHAGES [16], the Genome Consortium for Active Teaching [17], and the Small World Initiative [18]. A recent article by Bell et al. suggested the need for CUREs that focus on protein biochemistry [19]. Two such CUREs were mentioned at the IUBMB Education Conference 2019: the Malate Dehydrogenase CURE Community (<http://home.sandiego.edu/~josephprovost/MCC.html>) and BASIL [20], a project involving the author and faculty members on fourteen campuses.

BASIL (Biochemistry Authentic Scientific Inquiry Lab) is a CURE where students focus on predicting protein function [20], using *in silico* (sequence alignment, structure alignment, and docking) and *in vitro* approaches (protein expression, purification, quantitation, SDS-PAGE, enzyme activity and kinetics) to explore individual protein structures (Figure 1). Some methods are well established, but even simple methods have potential pitfalls. For example, most of these protein structures have been generated by the Structural Genomics Initiative [21] and are available in the DNAsu plasmid

repository [22] in carefully constructed vectors that generate proteins containing his-tags that can be easily purified using metal ion affinity chromatography. However, some of the vectors also express an accessory protein (e.g., maltose binding protein) to improve solubility. These accessory proteins sometimes interfere with the role of the his-tag in chromatography. In that case, students must study the plasmids to find out why their initial purification attempt did not work, then design a modified method to obtain their purified proteins. With the *in silico* methods, the student teams must

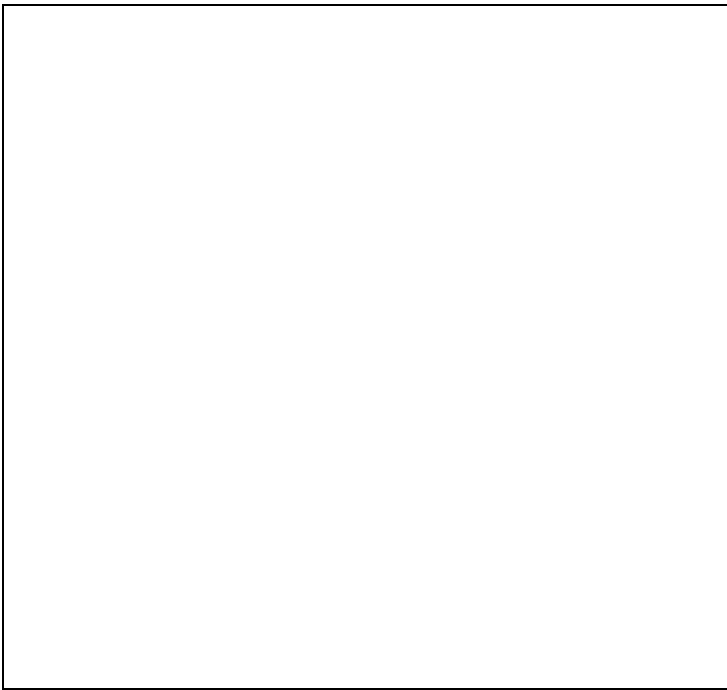


Figure 1. The *in silico* and *in vitro* path for protein function prediction in the BASIL Curriculum (used with permission [20]).

integrate results from the five different experimental modules to predict the function of a protein. For some structures, the results converge nicely, but in most cases the students must explore more deeply.

In addition to the five characteristics listed above, the exploration of the unknown in CURE-type labs also contain the real possibility of failure. An experiment simply may not work as designed. Then the students have to regroup, learn not to take it personally and design a new approach that will lead them down a different path.

Interest in CURE-type labs is growing. In fact, the 2020 Biennial Conference on Chemical Education at Oregon State University has four different symposia related to CUREs. In one sense, the CUREs that are being created are simply formalizing something many of us have been doing all along – adding our research projects to the teaching labs because they are so exciting and have the potential for broad impact. Moving forward, these CUREs may provide an opportunity to introduce students to more computational approaches for data analysis, beyond spreadsheets and calculators. Skills in scripting and coding in an environment like Jupyter Notebook [23] will empower them to apply computational and statistical approaches to large data sets they may generate.

As stated above, the purpose of this manuscript is to challenge instructors to change their BMB lab courses to incorporate more active inquiry. To conclude, here some questions to frame that challenge:

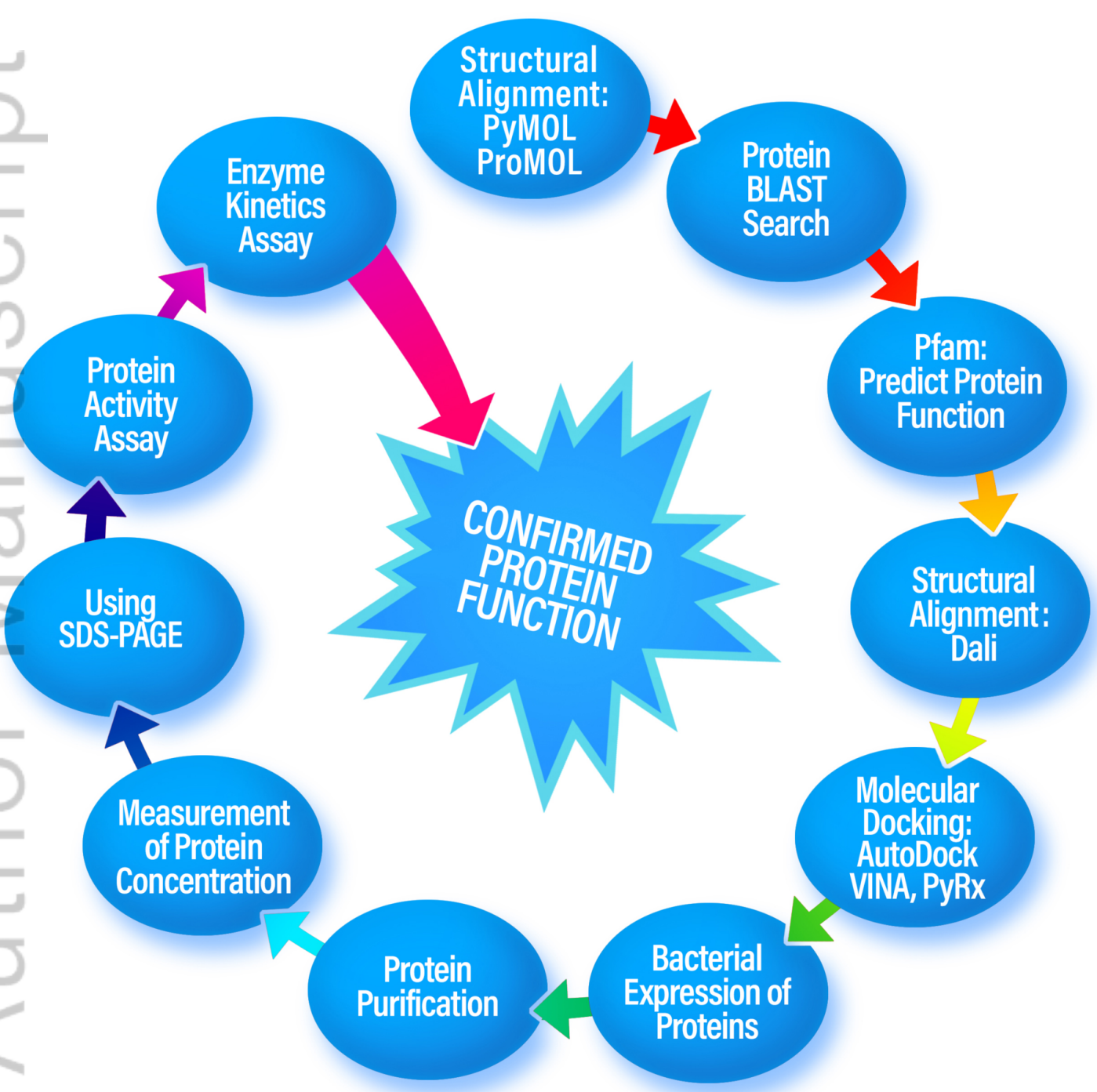
- What are your current practices?
- What would you like to change?
- What personal, institutional or social obstacles stand in your way?
- What is your first bold step?

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