Platform: Biophysics Education

1441-Plat
Centralized facilities improve biomedical researchers' access to cryoEM technology
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Cryo-electron microscopy (cryoEM) has roots in techniques developed nearly half a century ago, but recent technological advances have broadened its utility and enabled the reliable generation of atomic models of macromolecular complexes. CryoEM experiments are routinely utilized in structural science publications and new instrumentation is being installed in many research institutions resulting in a requirement to understand the best practices used within the field. The NIH Common Fund established the Transformative High-Resolution Cryo-Electron Microscopy program to provide access to this technology and support the development of cryoEM training curricula to promote a competent cryoEM workforce. The National Center for CryoEM Access and Training (NCCAT) is one of these NIH-sponsored service centers. NCCAT is housed at the New York Structural Biology Center and is strategically co-located with resources that broaden its outreach and enable users to travel onsite to participate in our local cryoEM community. This environment allows access to state-of-the-art equipment for the generation and analysis of high-resolution data. A unique opportunity at NCCAT is our intensive immersion program, where a trainee ''embeds'' by spending significant time at our facility. This program mentors scientists to become independent cryoEM researchers and helps create a support network of cryoEM practitioners across the nation. Our educational modules focus on everything from how to use the national cryoEM service centers, a media-rich curriculum to augment users' own hands-on training, and earning cryoEM merit badges that serve as proficiency certifications. Taken together, national service centers with centralized resources have emerged to support the expansion of cryoEM technology by increasing the nationwide accessibility of cryoEM throughout the biomedical research community.

1442-Plat
Deep-learning applications in the automated image analysis of giant unilamellar vesicles
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Recent progress in the field of machine learning allowed scientists to develop software to analyze a great amount of image data efficiently. Trained artificial neural networks can segment, analyze, and classify the target objects in complex images. Face recognition technology in our cell phones is an everyday experience now. We have been developing automated image analysis software to analyze lipid vesicle images efficiently. Giant unilamellar vesicles (GUV), characterized by a diameter greater than 1 μm are routinely used for reconstitution studies. They are used to study a wide range of physiological activities involving lipid membranes. One of the great advantages of the GUV system is that they can be readily imaged, and studied by optical microscopy due to their size much greater than the resolution of visible light's diffraction limit. Fluorescence microscopy image analysis can reveal the protein-lipid interaction, phase separation on the membranes, and mechanical deformation of the membranes. Such analysis typically involves the manual analysis by researchers to identify the target vesicles to analyze and perform quantitative analysis. Our approach to introducing deep-learning can automate the process to help researchers to analyze a great amount of vesicle image data efficiently. Our work shows that with some training, scientists can introduce the deep-learning as a module for their image analysis for various purposes. We discuss the progress in the field of software analysis of vesicle images and show our example works of deep learning applications. Deep-learning assisted identification, and classification of vesicle states and their connection with quantitative analysis will be shown. We suggest practical ways to implement it for various purposes of image analysis. We envision such modules can be potentially introduced in the classroom to teach future scientists to learn machine learning applications in biophysics.

1443-Plat
Teaching molecular interactions and coupling in binding reactions
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Students beginning their study of biochemistry or biophysics at the undergraduate level are often overwhelmed by the complexity of the systems and the nomenclature. By comparison, chemical systems appear simple to them, as students can more easily relate to introductory chemistry courses, where the molecules are smaller and bind yet smaller ions. This allows students to write the structure of the entire molecule on a piece of paper and see exactly to which functional groups an ion, such as a proton (H^+) in the simplest case, binds. Yet concepts that are fundamental in biochemical macromolecules, namely proteins, can perfectly well be taught at the undergraduate level, and probably be more easily understood, by using simpler, strictly chemical examples, which are already familiar to the students. For example, the concepts of interacting binding sites, which are at the root of cooperativity in protein binding reactions and conformational changes, are already present in simple molecules such as EDTA. In this paper, we show how to accomplish this goal by treating the binding of protons to EDTA in a very conceptual way, using the idea of the partition function and intramolecular interactions, rather than a formal algebraic approach. By doing so, the concepts of interacting sites appear naturally, in a small molecule where their origin can be easily ascribed—in this case, mainly to electrostatic interactions. Equipped with this understanding and this approach, students will be able to tackle more complicated biophysical systems, where the molecules are larger but the concepts are the same.

1444-Plat
Learning biological physics via modeling and simulation: A course for science and bioengineering undergraduates
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Undergraduate physical-science curricula are heavily mathematicized, despite research showing that learning should begin with qualitative phenomena of broad current interest. Meanwhile, undergraduate life-science curricula are often rooted in descriptive approaches, despite the fact that much current research involves quantitative modeling. I'll describe an alternative, an intermediate-level course now embodied in the 2022 edition of the textbook *Physical Models of Living Systems.* The course is the foundation of Penn's biophysics undergraduate major, as well as a response to rapidly growing interest among students in a broad range of science and engineering majors. Students acquire several research skills that are often not addressed in traditional undergraduate courses. The combination of experimental data, modeling, and physical reasoning used in this course represents a new mode of ''how to learn'' for many of our students. These basic skills are presented in the context of case studies from cell biology, including virus dynamics in single patients, and in populations; bacterial genetics and evolution of drug resistance; statistical inference, with applications to superresolution microscopy and cryo-EM; mechanobiology, for example, catching bonding in immune cell receptors; and cellular control circuits. Outcomes include student reports of improved ability to gain research positions as undergraduates, and greater effectiveness in such positions, as well as students enrolling in more challenging later courses than they would otherwise have chosen. [NSF EF-0928048; CMMI-1548571; PHY-1607611.]

1445-Plat
The BASIL cure: Using structure to predict function in protein biochemistry
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We have developed an undergraduate biochemistry lab curriculum based on authentic inquiry. This course-based undergraduate research experience (CURE) allows a large number of students to gain skills often learned only in the traditional one-on-one mentor-student research model by bringing a research project into the undergraduate teaching lab. The Biochemistry Authentic Scientific Inquiry Lab (BASIL) uses a combined computational and wet lab approach to study proteins of known structure but unknown function. Over 3800 structures in the Protein Data Bank (PDB) have unknown

function. Students following the BASIL curriculum use a combination of sequence and structure alignment tools to study these structures with the goal of identifying possible enzymes. They then use molecular docking to predict what model substrates fit near a proposed active site. Students can produce the target enzymes in the lab using standard wet-lab biochemistry techniques for expression and purification, and they then perform kinetic assays with model substrates selected from their docking studies. We have successfully used this curriculum in biochemistry lab courses for majors and non-majors. The curriculum is modular and can be used as a whole or individual parts may be incorporated into an existing course - either lecture or lab. Curriculum materials are available free-of-charge at basilbiochem.org. We are currently investigating how this curriculum can be used in a variety of academic settings, and we welcome new collaborators. We can offer synchronous support via virtual meetings and asynchronous support via Slack. This project is supported in part by NSF IUSE 2141908.

1446-Plat
MSFP: Undergraduate 'collaborate from home' research in macromolecular structure and function
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When the COVID-19 crisis shut down most undergraduate research opportunities, we developed an online, remote, computer-based Research Experiences for Undergraduates on the topic of Macromolecular Structure and Function that was funded by the USA National Science Foundation. The REU provided a mentored research experience and training in professional skills to assist the participants in pursuing a degree and future career in STEM. This fully virtual project involved faculty at four geographically-distributed institutions specializing in diverse but complementary approaches to study macromolecular structure and function. Importantly, its online ''collaborate-from-home'' format made it accessible to students during the pandemic to participate fully in the research, professional development, and other activities of the program. This project can also serve as an example for future remote, online projects that would especially be helpful for students who might not have access to these kinds of programs at their universities, might not be able to travel to a university for a summer program, have physical challenges that make it difficult for them to work at a lab bench, or students whose research opportunities are limited due to political unrest. We think our experiences with our MSFP REU program would provide helpful information for members of the BPS to set up similar programs to serve additional students.

1447-Plat
Assessments as research education tools in an undergraduate cell biology course
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A layered assessment strategy in an undergraduate cell biology course facilitated student understanding of how scientific knowledge was discovered in addition to measuring student learning. First, students were assigned a semester-long project to maintain a ''journal'' of 16-18 experimental techniques, such as fluorescence microscopy or cryo-electron microscopy. Some techniques were required for everyone, and other techniques could be selected by students based on their interest. In addition to writing about how the technique works, students were asked to find articles where scientists had used those techniques and describe the experiment and findings in the paper. Additionally, interactive lectures, group work during class time, and homework were necessary components to support student learning. Assessments asked students to apply what they learned about experimental techniques to specific processes or features in a cell, based on material covered in that unit. Each assessment included three components: individual take-home questions, individual multiple-choice questions, and a group component. The group component presented students with a scenario, asked them to propose a hypothesis, experimental approaches to test their hypothesis, and predict what the results would show if their hypothesis was correct. This strategy ensures students learn vocabulary and concepts and connect experimental techniques to their understanding of cellular structure and function and how that knowledge was discovered. The benefits of adjusting the overall course structure and to using this assessment strategy are many. Students reported learning even during the assessment, and the emphasis on group work required all students to be prepared while asking them to collaborate and communicate effectively as if they were scientists in a group working on a particular question.

1448-Plat
Implementation of specifications grading in an upper-division chemical biology course
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This work represents the first known full implementation of specifications grading to an upper-division chemical biology course. Due to the comparatively fast-paced developments in relevant knowledge in this discipline, the overarching goal of this course design was to prepare students to interpret and communicate about current research. In the past, a conventional points-based assessment method was inadequate to ensure satisfactory standards were consistently met on the comprehensive written assignments intended to prepare students to translate knowledge to meet real-world expectations in future careers. Specifications grading was chosen because the core tenet requires students to demonstrate learning objectives, with no exceptions, to achieve a passing grade and adequately complete more content of increased cognitive complexity to achieve a higher grade. This strict adherence to demonstrated skills is balanced, however, through opportunities for rework or flexibility in assignment deadlines are also provided through the use of tokens, enabling students to incorporate feedback and revisit challenging concepts in a productive way. Implementation strategies such as rubric criteria, overall grade determination matrix, and token opportunities will be presented in detail. Student comprehension and demonstrated skills qualitatively improved, final grade distributions were not negatively affected, and evaluation of the results of a verified survey on growth mindset and self-efficacy over the duration of the course showed slight positive trends. Instructors noticed that discussions with students were more focused on course concepts and feedback while overall grading time was reduced. University-administered student feedback revealed some reduction in anxiety as well as increased confidence in managing time and course material. Recommendations provided on how to continue to improve the overall teaching and learning experience for both instructors and students in future iterations will support specifications grading being broadly achievable in other biophysical classroom settings.

Platform: Membrane Protein Dynamics II

1449-Plat
Investigation of G-protein specificity and biased agonism at the beta-2 adrenergic receptor (β2AR)
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The beta-2-adrenergic receptor (β2AR) is a prototypical G-protein coupled receptor (GPCR). In cardiomyocytes, β2AR couples to the G-protein subtypes Gs and Gi to regulate cardiac function. We used this system to investigate the molecular determinants of biased agonism and G-protein specificity. We developed a Gi-biased agonist, LM189, that we used to obtain the Cryo-EM structure of the β2AR-Gi complex. Spectroscopic investigations by electron paramagnetic resonance spectroscopy (EPR) and single-molecule FRET (smFRET) show that distinct intermediate states, differentially stabilized by balanced and biased ligands, contribute to G-protein specificity. Understanding the basis of specificity and bias is important to design safer drugs that target GPCRs with reduced side effects.

1450-Plat
Protein-protein interactions at the tight junctions interface
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The epithelial and endothelial tissues are the physiological barriers against chemical and biological insurgents by constituting the tight junctions. Tight junctions are specialized adhesion constructs formed by the assembly of claudin family proteins. Membrane-embedded claudin proteins are the functional determinants of the tight junctions. In the paracellular space between two adjacent cells, claudins form size and charge selective pores that impede the free diffusion of these solutes. The vital role of tight junctions in various tissue barriers such as the blood-brain barrier, renal barrier, and gut barrier are currently active research fields, yet a complete molecular understanding of the tight junctions is elusive. Here we have employed multiscale molecular dynamics simulations to gain insight into the underpinnings of claudin assembly at tight junctions. From these simulations, a clear picture of how the membrane milieu