

Let's Experiment: A Guide for Scientists Working at the Bench



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Educator Guide

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Introduction

What is the purpose of this guide?

This guide is meant to demonstrate how iBiology's online course "Let's Experiment: A Guide for Scientists Working at the Bench" (LE) can be used in multiple settings to assist you when teaching experimental design. Here we will give you examples of how to use the whole course, as well as pieces of the course and materials associated with this course, to effectively teach important concepts and strategies behind experimental design, including aspects of rigor, reproducibility, and transparency as well as responsible conduct of research. We also provide a comprehensive list of course components and resources for your convenience.

Here are some examples of how the course can be useful in training your students or mentees:

- 1. To train new or inexperienced graduate students or undergraduates in the basics of experimental design, rigor and reproducibility as well as good record keeping techniques.
- To provide a set of standards for doing rigorous experimental biology research for all undergraduates, graduate students, postdocs and early career stage professors in your lab.
- 3. To help specific undergraduates, graduate students or postdocs who have been struggling with experimental design, rigor and reproducibility or record keeping improve their laboratory practices.
- 4. To give new or inexperienced undergraduates or graduate students an idea of what doing real science at the bench is like through our case studies and descriptions of experimental design and laboratory techniques.

Who is this guide for?

This guide is intended for educators and mentors who teach or train undergraduate and graduate students in life science research. Examples include:

- Scientific mentors at all levels, from principal investigators supervising research trainees in the lab to postdocs or graduate students training mentees on how to perform experiments at the bench.
- Faculty and administrators who are planning curricula around rigor, reproducibility, and transparency for their training programs.
- Faculty and administrators who are looking for content to supplement their responsible conduct of research curricula as part of their training program.
- Faculty and administrators who teach introductory research classes at either the undergraduate or graduate level.



Our Course

Course Description:

"Let's Experiment: A Guide for Scientists Working at the Bench" (LE) is a free 6-week online course designed to help guide participants through the process of planning and executing experiments in biology. The course was designed so that individual course students (undergraduates, graduate students, and/or postdocs) could take the course on their own, without it necessarily being part of official training at their institutions. However, integrating the course into training (either in part or whole) will allow for expanded peer learning and mentoring.

In the online course scientists from a variety of backgrounds give concrete steps and advice to help participants build a framework for how to design experiments. We use case studies to make the abstract more tangible. In science, there is often no simple right answer, and our course reflects the important nuances of research. Through the course, participants develop a general approach to experimental design and understand what they are getting into before they begin.

<u>Syllabus:</u> The course syllabus can be found <u>here</u>.

<u>Format:</u> The course is composed of videos, text, relevant journal articles, forum discussion questions, and open response assessments. The majority of the instructional materials are contained within the videos and text.

As participants go through the modules, they are prompted to apply what they are learning to their own research through a series of self-reflective exercises. The goal of these exercises is to probe their thinking as they design an experiment. Their responses from these exercises are accessible through a printable document titled "My Experimental Plan."

This course is self-paced so participants can register and access all course materials at their leisure. We estimate participants will spend 1 to 3 hours on the course per week. This includes time spent watching videos, reading text, doing assessments, and engaging in the forum.

Grading Policy (for self-paced course hosted on edX): This is a pass/fail course, and participants' grades are based solely on the completion of the open response assessments. They will receive an iBiology Courses Certificate if they complete at least 50% of the assessments. Assessment fields are defined as any text input box that appears under the "Assessment" heading within the course. Each required assessment is numbered (e.g., "Q1," "Q2,") to help them keep track as they take the course. Each assessment field has equal weight so there will be no difference in penalty for assessment fields they leave incomplete. That being said, we highly recommend that they endeavor to complete as many assessment fields as possible in order to get the most out of the course.



Course Goals:

Here is a high level description of what participants learn in this course:

- The elements of a well-designed experiment, including variables, controls, sample size and replication.
- An introduction to experimental variability, sample size estimation, data analysis, and p-values, and how to seek help when needed.
- Insights into their potential bias as an experimenter, how that affects reproducibility, and how to prevent it from impacting the design and execution of an experiment.
- Experimental tips and best practices on reagent authentication, keeping a good laboratory notebook, and getting an experiment to work.

Participant Takeaways:

Here is what participants will take away from this course:

- A detailed plan for their experiment(s) that they can discuss with a mentor (their "My Experimental Plan").
- A colorful flowchart for how to prioritize experiments.
- A handy lab notebook template.

At the end of this course participants will have a comprehensive understanding of how to think more effectively through the design of an experiment, and to be more rigorous and transparent in its execution.

Learning Objectives:

Module 1: An Introduction to Experimental Design

Lesson 1: Welcome to Let's Experiment!

At the end of this lesson, you will be able to...

- Summarize the course goals, as well as the key factors in designing and executing an
 experiment.
- Use the discussion forums to meet your course community, get advice and support, as well as share your knowledge.
- Establish and document what you hope to get out of the course.
- Describe the role the case studies will play in the course.
- Broadly summarize the science examined in each case study.

Lesson 2: The Experimental Setup

At the end of this lesson, you will be able to...



- Prioritize experiments based on different criteria such as feasibility, risk, and potential impact.
- Describe an experiment you wish to plan and evaluate in the assessments in this course.
- Articulate your research question and/or hypothesis.
- Describe potential outcomes you expect from the experiment, and how it will address your question/hypothesis.
- Understand the importance of using a model system that is appropriately matched to your research question.
- Delineate the strengths and weaknesses of a model system.
- Understand why the experimental technique and model systems in the case studies were implemented.
- Justify the use of a particular model system in your experiment.

Module 2: Key Elements of Experimental Design

Lesson 3: Variables & Controls

At the end of this lesson, you will be able to...

- Define the terms "independent variables," "dependent variables," "controlled variables," and "confounding variables."
- Explain why it is important to enumerate all the variables in an experiment.
- Identify the different types of variables in your experiment.
- Summarize the role of controls in experimental design.
- Define the terms "positive" and "negative controls."
- Describe the controls you plan to include in your experiment, and how they will help you analyze and interpret your results.
- Understand the utility of internal controls, and how they may not be present in every experiment.
- Explain any internal controls in your experiment, if applicable.

Lesson 4: Variation and the Need for Replication

At the end of this lesson, you will be able to...

- Understand that random variation, or noise, often arises from the inherent complexity of biological systems as well the vagaries of the technique.
- List possible sources of random variation or noise in your experimental system.
- Define biological replicates, technical replicates, and repeat/independent experiments.
- Articulate the importance of replication in helping you account for the variability in an experimental system.
- Outline a plan for repeating an entire experiment.
- Describe the type and number of replicates used in case study examples.
- Determine the type and number of replicates and repeat experiments for your own experiment.



- Articulate why you want to put some time and energy into estimating the "right" sample size for your experiment.
- Understand that to publish and get grants you will need to explain how and why you chose the sample size you did.
- Explain how doing a power calculation can help you identify an appropriate sample size for your experiment.
- Understand that there is no one easy formula for the power calculation. You need to choose the correct version based upon your specific experimental conditions.

Module 3: Account for Bias

Lesson 5: Rigorous Experimental Design

At the end of this lesson, you will be able to...

- Explain why rigor, reproducibility, and transparency are important mindsets and approaches to science that impact not only your own progress, but the progress of science as a whole.
- Describe how rigor and transparency will be incorporated into your experimental plan.
- Recognize that bias is inherent in everyone when performing experiments, and there are ways to minimize that bias through rigorous techniques.
- Describe at least one type of bias and how it might affect your research.
- Define randomization and blinding and how they prevent bias from influencing an experiment.
- Explain how you will employ randomization and/or blinding techniques in your experiment.

Lesson 6: An Unbiased Approach to Data Analysis

At the end of this lesson, you will be able to...

- Explain how determining your data analysis process before doing the experiment is a critical part of experimental design.
- Define qualitative and quantitative data types, and give examples of both.
- Describe how you will measure the data, how the data will be expressed (i.e., data type), and, if possible, the analytical method(s) you will use in your experiment.
- Understand that choosing the right statistical approach for an experiment depends the study design, sample size, and the type of data collected.
- Understand that identifying the appropriate statistical test to use and applying them correctly can be challenging, but critically important for rigor and reproducibility; seek help from statisticians and educational resources.
- Identify a statistician or statistics expert whom you will consult for your experimental design.
- Define preregistration and explain why it is useful.
- Debate the pros and cons for preregistering your experimental plan.



Lesson 7: A Side Note About P-Values

At the end of this lesson, you will be able to...

- Define p-value.
- Understand the a p-value is not the probability that your hypothesis is true.
- Understand that a low p-value (p<0.05) does not necessarily mean something is biologically meaningful.
- Describe ways that p-values can be misused in science.
- Define p-hacking and and describe a few ways in which it can manifest.

Module 4: Gear up to do the Experiment

Lesson 8: Tips & Best Practices

At the end of this lesson, you will be able to...

- Describe how to successfully approach a new experimental protocol.
- Explain the importance of validating and authenticating the key biological and chemical materials in your experiment.
- Summarize how you will validate and/or authenticate the materials you are using in your own experiment.
- Express the importance of good recordkeeping for your own science and for that of the scientific community.
- Assess the reproducibility of past entries in your lab notebook.
- Use appropriate recordkeeping checklists for reporting your own research.
- Employ good lab notebook practices with a comprehensive recordkeeping model.

Module 5: Getting the Experiment to Work

Lesson 9: Piloting and Troubleshooting

At the end of this lesson, you will be able to...

- Define pilot experiments and their utility in research.
- Describe what it means when an experiment "works."
- Apply a basic troubleshooting framework to use when the technical aspects of the experimental design are failing.
- Explain real examples of troubleshooting in experimental design.
- Describe any anticipated troubleshooting for your planned experiments.

Lesson 10: Optimizing and Experimental Next Steps

At the end of this lesson, you will be able to...

• Define experimental optimization.



- Apply basic optimization techniques to your own research.
- Explain real examples of optimization in experimental design.
- Articulate the concept of signal-to-noise.
- Explain why optimization is especially important when working with live animals or human subjects.
- Define and understand the importance of orthogonal approaches in doing science.
- Articulate the meta-framework for a research project.
- Apply the research meta-framework to your own work.

Course Outcomes:

When we first released the Let's Experiment online course in early 2019, we did so in a hosted format where there was a start/end date, and content was released weekly for a six-week period. During this hosted run, we were able to gather information regarding the learning gains that participants made throughout the course as well as changes in their attitudes toward science before and after they took the course.

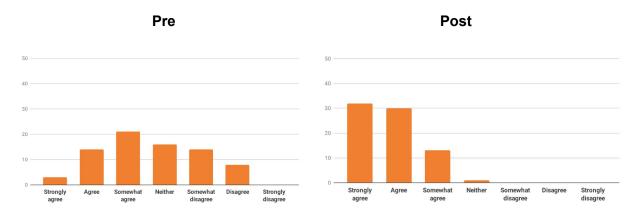
Participants made statistically significant learning improvements for 15 key competencies in experimental design.

To measure potential learning gains, we asked participants to report on their familiarity with key experimental design principles and practices before and after the course. For all 15 questions, participants made statistically significant learning improvements (N=77). Here is a sampling of those results:

When asked how much they agreed with the statement: "I know how to address and account for experimental bias," participants responded with the following distributions in the pre and post-course surveys:



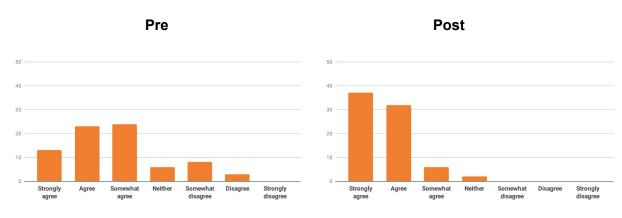
"I know how to address and account for experimental bias."



*N = 77. All assessments show statistically significant change. Statistical test: Two Tailed Wilcoxon Signed-Ranks Test (p<0.05)

When asked how much they agreed with the statement: "I know how to keep a thorough, rigorous and reproducible research notebook," participants responded with the following distributions in the pre and post-course surveys:

"I know how to keep a thorough, rigorous and reproducible research notebook."



*N = 77. All assessments show statistically significant change. Statistical test: Two Tailed Wilcoxon Signed-Ranks Test (p<0.05)

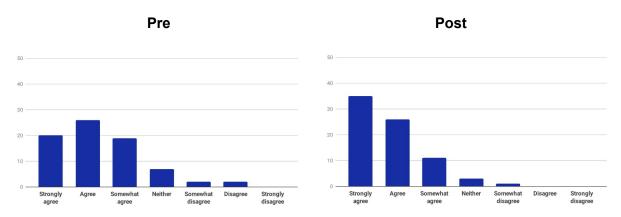
Participants identified more strongly with being a scientist.

To measure perceived changes in scientific identity, we also asked course participants if they agreed with certain statements regarding their feeling of belonging in science before and after taking the course. For all 5 questions (N=77), participants identified more strongly with being a scientist after taking the course. Here are two of those five questions:



When asked if they agreed with the statement: "I have come to think of myself as a scientist," participants responded with the following distributions:

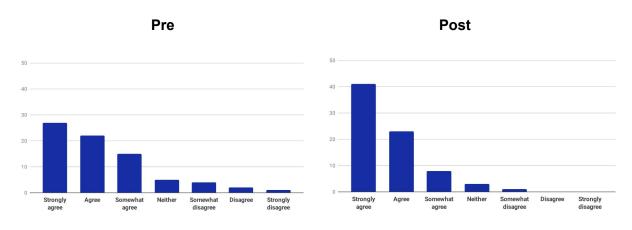
"I have come to think of myself as a scientist."



*N = 77. All assessments show statistically significant change. Statistical test: Two Tailed Wilcoxon Signed-Ranks Test (p<0.05)

When asked if they agreed with the statement: "I feel like I belong in the field of science", participants responded with the following distributions:

"I feel like I belong in the field of science."



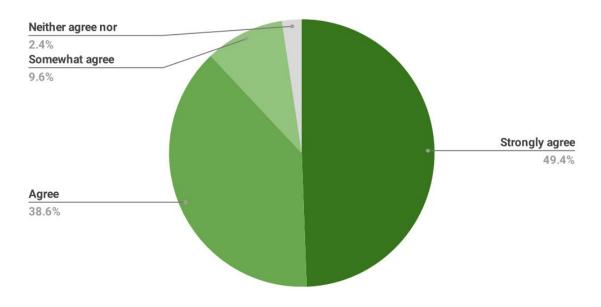
*N = 77. All assessments show statistically significant change. Statistical test: Two Tailed Wilcoxon Signed-Ranks Test (p<0.05)

These data demonstrate that, not only did surveyed participants make significant learning gains in the course as related to experimental design, but their experience in the course also increased their feeling of belonging in science.

Most participants were satisfied with the course and believed it better prepared them for their scientific endeavors.



When participants were asked in the post-course survey if they agreed with the statement: "I believe that participation in this course has better prepared me for my upcoming scientific endeavors," they responded with the following distribution:



*N=83

Finally, when asked about their overall satisfaction with the course, 65.5% responded that they were very satisfied and 29.7% responded that they were satisfied, demonstrating that **95.2% of all learners surveyed were at least satisfied with the course**.

We have an expanded set of preliminary data that you can peruse here. If you would like more information regarding our course outcomes, please feel free to contact us at courses@ibiology.com.

Where to Find Course Materials

The online version of this Educator Guide for "Let's Experiment" can be found at https://courses.ibiology.org/educator_resources/LE. This site provides access to all videos, video transcripts, infographics, assessments, discussion prompts, and templates used in the course. The videos can be downloaded in high and low resolution, with and without closed captioning. For convenience, we have also included this table of resources at the end of this document.



The self-paced version of the course can be found here on iBiology Course's platform: https://courses.ibiology.org/courses/course-v1:iBiology+LE+SP/about. We encourage all educators to log in and view the content of the course within the context of the online platform.

We have also created a YouTube playlist with all of the course videos, which can be found here: https://www.youtube.com/playlist?list=PL5zi65Byv2hiQMMRS9PCR2v8w5ZlKcc4o

Model Examples

In this section, we provide a small set of examples for how to use our course materials, either whole or in part, to teach different aspects of experimental design. We anticipate that there are many ways to use the course materials which are not covered here. And, we plan to expand this list as we develop more models or are given models from colleagues. (We love to hear how our work is being used and will consider including any models of those who are willing to share with us and the public.)

However you might use the content in person, we suggest using techniques that increase the interaction of students. Although the stand-alone course is a great resource for training needs, evidence exists (Garrison, D.R. & Kanuka, H. The Internet and Higher Education 7, 95-105 (2004), Means, B., Toyama, Y., Murphy, R. & Baki, M. Teachers College Record. 115, 1-47 (2013)) demonstrating that deeper learning occurs when online courses such as this one are paired with in-person discussions between peers and facilitators. The following are some evidence-based active learning techniques that you can use during your in-person sessions. In these techniques we provide some ideas of questions that can be asked of the participants, but we also recommend using the assessment and discussion questions from the course (see table of links and downloads).

- 1. Short writing sessions such as the "Minute Paper": During the discussion, ask participants to take out a blank sheet of paper and a pen. Then, state a topic or concept you would like them to think more deeply about or give context to. For example, "We have been discussing bias so far this week. List all the times that you have noticed any kind of bias in your research or have seen it in the research being conducted around you. You've got two minutes to make your list."
- 2. Whole-Group Discussion: Develop a list of questions that you would like participants to discuss as a whole group. These questions should be designed to stimulate conversation between participants or just get participants talking about the topics presented that week in the course. For example "What struck you as something new or exciting that you learned this week? Or "A template for keeping a thorough lab notebook was presented in the course this week. What similarities or differences did this template have to your current recordkeeping strategy?"



- 3. **Think-Pair-Share:** Present a question or concept that was discussed in the course that week and have participants reflect on it silently for a minute or two (they can write things down to organize their thoughts). Then have them pair up and compare their thoughts and synthesize a joint consensus on the question or concept.
- 4. Peer Review: Pick an assessment or two that participants worked on in the course that week and ask them to print it out and bring it to the discussion section. Then ask participants to pair up and exchange their printed assessments with their partner. Next, each student gives critical feedback, corrects mistakes in content and provides any other feedback that they feel might be useful for their partner's assessment for 5-10 min. Finally, they give their partner's assessment back to them, and each of them talks through the feedback they provided.
- 5. **Brainstorming:** Introduce a topic or problem discussed in the module you are discussing and ask for student input. Give participants a minute to write down their ideas. Then, ask for volunteers to present their ideas and record them on a chalkboard, whiteboard or digital screen and to talk through each idea presented with the whole group.
- 6. Case Studies: Use real-life stories from your lab or a colleague's lab (or the case studies from the course) to illustrate a certain concept, topic or question in the module you are discussing. Then ask participants to break into small groups and discuss how the story/stories you presented exemplify or differ from the concept, topic or question you are focusing on.
- 7. **Jigsaw Discussion:** You can take a general topic and divide it into smaller, interrelated pieces like a jigsaw puzzle. Then break the discussion section into groups in which each member of the group is assigned to read and become an expert on a different sub-topic. After each member has become an expert on their piece of the puzzle, they teach the other team members about that piece. For example, if the topic you are discussing is "Variables" and you have 4 people in the group, one person would take on "Dependent Variables," one would take on "Independent Variables," another would take on "Controlled Variables," and the last one would take on "Confounding Variables." Each would learn as much as they can about their assigned sub-topic in the time allotted and then they would come back together and teach the others in the group about what they learned about their type of variable.
- 8. Clarification Pauses: If giving a recap of what was covered in the module you are discussing this week, make sure to take small breaks in your recap to allow participants to think about what is being presented or remember when/how this topic was covered in the course. This is especially important when defining a key concept, presenting information that you believe will be central to this week's discussion or once you have stated an activity that you are planning to do during this week's session. Once you have paused, ask if anyone needs clarification.

For more information on how to design your teaching and how to incorporate the best evidence-based practices, we recommend the <u>Vanderbilt University Center for Teaching</u> and



their extensive list of <u>Teaching Guides</u>. We also recommend reviewing these <u>online courses</u> offered by the <u>Center for the Integration of Research, Teaching and Learning</u>.

Example: Using the whole LE course as part of an official training course

Many graduate programs have, or are building, one or more courses on foundational competencies essential to the mastery of a PhD. Many of these courses are a semester or quarter in length, and begin the first semester/quarter that students enter graduate training. This course work is often done at the same time as their laboratory rotations in possible mentors' labs.

The "Let's Experiment" course content can be an official addition to a formal course to ensure that important concepts are being applied by the students to their own research as they learn them. One of the key features of "Let's Experiment" is that all of the assessments in the course urge the student to use their own research (or research of interest) to answer them. (Note, we believe this blended model presented could help address NIGMS T32 training grant requirements for "Instruction in Methods for Enhancing Reproducibility" topics including "rigorous experimental design and data interpretation, consideration of relevant biological variables such as sex, authentication of key biological and/or chemical resources, data and material sharing, record keeping, and transparency in reporting." And that integrating in this way helps ensure that "instruction strategies are sufficiently well integrated into the overall curriculum" (see PAR-17-341).)

Integrating LE into an in-person course

The full LE course is typically done in about 6 weeks (5 weeks of content + 1 week of catching up/finishing up the assessments and talking to a mentor about the assessments). In this schedule, students typically do about 1-3 hours of work a week for LE. If your in-person course is less than 6 weeks long this model will be difficult, and we suggest using portions of the LE content as opposed to the whole course (see the example of the lab notebook, below).

To integrate the course we suggest comparing the "Let's Experiment" syllabus and learning objectives with your own course syllabus and learning objectives. Align the "Let's Experiment" course with the course plan for the in-person training course and determine the following:

- 1. When will students be required to start and end the "Let's Experiment" course?
 - a. Suggestion: Make the start and end of LE roughly match the beginning and end of the formal in-person course. This could mean progressing more slowly through LE than the typical online schedule.
- 2. Will the students do all the assessments in LE as homework?
 - a. Suggestion: Have the students complete all the assessments in the course to create a "My Experimental Plan" document. The assessments can be answered in the course platform and printed out from there. To complete the assessments the students could use:



- i. Their current or past rotation project experiments (recommended).
- ii. Experiments from their undergraduate research.
- iii. Experiments from their first-year fellowship proposals (often first year students are required to apply for fellowships like the NSF Graduate Research Fellowship).
- iv. Experiments from a paper or research that they find particularly compelling, or is being used in the in-person course or another course they are taking.
- 3. How will "Let's Experiment" be referenced and utilized in the in-person classes?
 - a. Suggestion: For each of the 5 content modules spend 30-45 minutes of in-class time referring to LE and doing LE-related activities. For example:
 - i. Choose a video from an LE module to show in class (~5 minutes).
 - Using an evidence-based teaching technique (see examples listed above), discuss the main points of the video and related concepts (10-20 minutes).
 - iii. Refer to one or two related assessment questions from LE. Have students work on them in class and then share with a classmate or the whole group (10-20 minutes).
- 4. How will students show that they have completed the LE course?
 - a. Suggestion: As part of their grade, they should hand in a completed "My Experimental Plan" document to the instructor. Each student's "My Experimental Plan" can be downloaded and printed from the iBiology Courses platform. Depending on the desires of the instructor, these experimental plans can be simply pass/fail (i.e., passing grade if the student has shown a real effort to address the assessments) or graded relative to the learning objectives of LE or the in-person course.
 - b. Students can also hand in the earned iBiology Courses certificate of completion for the LE course. However, note that a certificate is earned when LE students have completed 50% of the assessments in the course. You may wish for a more stringent completion percentage.
- 5. How will you assess whether the LE course content has worked for your learners?
 - a. Suggestion: In-person or online surveys can be a good way to assess efficacy. For more detailed information on evaluation, please contact us at <u>courses@ibiology.org</u> (we plan to add more to this section of the Educator Guide in the future). We also suggest investigating the <u>CIRTL Program Resource</u> <u>Collection</u> (free login required). For LE we have a number of metrics that we assess through online surveys, and here are several that we suggest:
 - i. Pre- and post- course knowledge gain assessments: ask questions preand post- course that refer to specific learning objectives or competencies in the course.
 - Overall course satisfaction.
 - iii. Perceived impact on preparation for scientific endeavors.



iv. A change in some action or behavior (e.g., use of the "My Experimental Plan" in their research, talking to their advisor about their plan, improved lab notebook recordkeeping..)

Determining these 5 elements will allow for the LE course to be effectively integrated into the in-person course and support the broader learning objectives of the overall graduate training. If this doesn't quite match your training program, you could also imagine using the LE course in the following ways:

- As pre-work for a workshop or training series on experimental design, rigor and reproducibility or record keeping.
- Schedule weekly (or bi-weekly) meetings/discussion sessions (or learning communities) with those who are taking the course in your lab, department or institution. During these meetings center the discussion that occurs around the material that was covered in a single module, i.e., discuss module 1 during the first week's meeting, module 2 during the second week, etc.

For a deeper dive of an example of how to use an online course in in-person training we suggest the following reference: <u>Bruff, D., Fisher, D., McEwen, K., & Smith, B. (2012). Wrapping a MOOC: Student perceptions of an experiment in blended learning. Journal of Online Learning and Teaching, 9(2).</u>

Example: Using LE as part of a rotation project

As we mentioned above, this course is a great resource for training graduate students who do not have much experience in designing or performing experiments and, therefore, can be used as a resource for training rotation students in your lab or program. Our course covers many of the techniques and activities that many rotation students are asked to learn or perform during their rotations (see <u>learning objectives</u> for full course topics).

We also strongly advocate for the laboratory mentor/supervisor to be an integral part of teaching experimental design. Because of this, we present here one model of formally integrating LE into one of the mandatory first year laboratory rotations (assuming that they are at least 6 weeks in length). (Note, we believe this model presented could help address NIGMS T32 training grant requirements for "Instruction in Methods for Enhancing Reproducibility" specifically "how all program faculty will reiterate and augment key elements of methods for enhancing reproducibility when trainees are performing research in their laboratories" (see <u>PAR-17-341</u>).)

The overall idea is to require the graduate student to go through the online LE course under the guidance of their rotation mentor, using their rotation project to answer the assessments. The graduate student and mentor would meet regularly (preferably weekly) to go over the LE assessments and course concepts.



Possible Meeting Structure: Weekly Meetings

Rotation student and research mentor (advisor and/or lab mentor) meet each week to iteratively develop an experimental plan for the rotation project.

Week	Meeting Goals	Student Instructions	Mentor Instructions
1	Determine the experiment(s) the student will work on during the rotation and subsequently use to develop "My Experimental Plan" in the course. (NOTE: this may take more than 1 meeting)	Come to this meeting with an understanding of the different research projects in the lab as well as your possible research interests. To prepare, talk to more senior individuals in the lab in order to learn more about the research projects and to get a reading list of key publications; read those key publications.	Ask the student what their research interests are and how they think those interests align with the different projects in your lab. Work together to identify a research project and a specific experiment.
2	Review, evaluate, and iterate Module 1 assessments. Review the experimental setup and identify where to find relevant protocols.	Before this meeting, complete Module 1 of Let's Experiment. Make sure to apply all assessments in Module 1 (and all future Module assessments) to your rotation project experiment. Bring your responses and any related questions to the meeting.	Ask the student if they have a model system in mind for their research question and then talk about the feasibility of using that model system in your lab for a rotation project. Evaluate student's understanding of the utility of the model system. Discuss/review the experimental setup and, if applicable, where to find relevant protocols.
3	Review, evaluate, and iterate Module 2 assessments.	Before this meeting, complete Module 2 of Let's Experiment and review the experimental setup again, making sure to have a firm grasp of the experiment. Bring your Module 2 responses and any related questions to the meeting.	Review core concepts in experimental design such as variables, controls, experimental variation, and experimental replicates. Make sure the student is applying these concepts appropriately to their rotation work. Can they explain what controls to use and why they are doing a certain number of replicates?
4	Review, evaluate, and	Before this meeting,	Discuss the important issues



	iterate Module 3 assessment	complete Module 3 of Let's Experiment. Bring your Module 3 responses and any related questions to the meeting.	of scientific rigor, reproducibility and transparency. Review the impact of bias on research. Can the student see where bias could enter their own work? Discuss the issue of p-values and p-hacking in science.
5	Review, evaluate, and iterate Modules 4 & 5 assessment	Before this meeting, complete Modules 4 & 5 of Let's Experiment and review the experimental protocol (if applicable). Bring your Module 4 & 5 responses, protocol notes, and any related questions into the meeting.	Review proper lab notebook recordkeeping and reagent authentication protocols for your lab. Discuss the experiments that the student is doing. Do they understand why they are doing certain steps in their protocol? Review troubleshooting, optimizing, and orthogonal approaches. Do they have ideas about how to move forward with their project?
6	Wrap-up and evaluation. This meeting is to allow both the student and mentor to discuss and evaluate how the experimental design training progressed through the rotation.	Before this meeting, finish any LE course assessments that haven't yet been finished and attend to any work that your mentor has asked to be addressed. Formulate an assessment of your strengths and weaknesses in relation to the concepts of the course.	Prior to the meeting jot down notes of the students strengths and weaknesses in relation to concepts covered in the course. Discuss your evaluation with the student, including a discussion of what the student believes are their strengths and weaknesses. Identify actions that the student can do to build and improve their skills.

We recognize that some projects move more quickly than others, and that some students are more advanced than others. We recommend that the mentor adjust and tweak the above schedule to reflect the realities of the scientific work, while at the same time ensuring that the student makes it through the concepts of the entire course.

We also know that not every laboratory advisor will be able to meet with the graduate student weekly. We recommend that there be an additional mentor identified (staff scientist, graduate student or postdoc in the lab) that can be readily available to join and continue the weekly meetings when the lab head is unavailable.



Assessing the curriculum:

We recommend that both the mentor and student assess the utility and fit of the LE curriculum when it is used. For a more detailed information on evaluation, please contact us courses@ibiology.org (we plan to add more to this section of the Educator Guide in the future). We also suggest investigating the CIRTL Program Resource Collection (free login required). For LE we have a number of metrics that we assess through online surveys, and here are several that we suggest:

- 6. Pre- and post- course knowledge gain assessments: ask questions pre- and postcourse that refer to specific learning objectives in the course.
- 7. Overall course satisfaction.
- 8. Perceived impact on preparation for scientific endeavors.
- A change in some action or behavior (e.g., better design of controls, improved ability to describe the importance of individual protocol steps, improved lab notebook recordkeeping..)

Example: Lab notebooks, using part of the course

Many institutions and educators might not need the full LE course for their training curricula, having fully developed courses already, or wanting, instead, something more customized for their trainees. As such, they might be interested in using parts of the LE course to bring a variety of formats and contexts into their curriculum, or to address a particular concept that hadn't been integrated into their instruction yet.

Here we present a model of using a small part of the LE course, the lab notebook and good recordkeeping units, as the basis of a workshop that could be a one-off workshop or integrated into a course or workshop series. The workshop template we provide could be adapted to other topics that we cover in the course.

Workshop Template

In Module 4, we present good recordkeeping practices and why it's important, not just for the benefit of the scientific enterprise, but also for the benefit of the individual scientist. We also provide a detailed notebook <u>template</u> that satisfies all the NIH guidelines on good recordkeeping, which include:

- Who did it (the person making the record)
- What you did
- When you did it (clearly stating month, date and year)
- Why you did it
- What project the research was part of
- How you did it (including the methodology)



- What materials were used
- The findings
- Your interpretation
- The next step

To use in a classroom situation we suggest you review the relevant section on good recordkeeping in Module 4 and translate it into an in-person seminar/class with facilitated group discussion. Below is one example of how this section could be translated into a 1-1.5-hour workshop for life science trainees.

A Workshop on Strategies for Keeping a Reproducible Lab Notebook

Class format: In-person workshop, 60-90 minutes depending on how you structure it.

Learning Objectives

In this workshop, participants will learn to:

- Express the importance of good recordkeeping for the benefit of their own research endeavors and for that of the scientific community.
- Assess the reproducibility of past entries in their lab notebooks.
- Use appropriate recordkeeping checklists for reporting their own research.
- Employ good lab notebook practices with a comprehensive recordkeeping model.

Workshop Outline

- Before the workshop
 - Ask students to bring to the workshop their lab notebooks, with entries from at least a few months ago. For the individuals who don't have access to their own lab notebooks or forget to bring their notebooks to the workshop, provide a sample notebook entry that seems realistic but doesn't clearly follow many of the best practices in keeping a good lab notebook (draft one yourself or ask someone you know to volunteer their notebook entry with the understanding you will remove any identifying information).
- Introduction (~10-15 min)
 - At the start of class, have students do the "How Reproducible is Your Notebook?" pre-assessment in Module 4: "Open up your lab notebook to a random day in the past (say 6 months, if it goes back that far). Read over what you have written."
 - Group discussion: Ask students "If you had to redo that day's experiment using only what is written in your lab notebook, could you? Are there things you wish you had included? What would you change about your recordkeeping now that you have thought about it?"
- Why keeping a good lab notebook is important (~15 min)



- Watch "Pay Attention and Write it Down" from Module 4 (refer to "<u>Table for Links</u> and Downloads" for links to the video)
- Group discussion: Ask students "Why is keeping a good lab notebook important?
 Can you share any additional reasons that may not have been covered in the video?" As students offer reasons, write them down on the board.
- Add any additional reasons the students may not have addressed to the discussion.
- Review best practices for keeping a lab notebook (~15 min)
 - Introduce the different types of lab notebooks (bound vs. digital), as well as their respective strengths/limitations.
 - Review general best practices for good recordkeeping (see the checklist of best practices offered in Module 4 as well as those included in the resources cited in Module 4). Incorporate guidelines that are relevant to the type of research, notebook (bound vs. digital), and institution!
 - Share a list resources for good recordkeeping offered in Module 4, where students can get more detailed information.
- Case study for good recordkeeping (~15-30 min)
 - o Share Neil's <u>lab notebook template</u> before playing the video.
 - Watch "Case Study: Neil's Approach to Recordkeeping"in Module 4 (refer to "Table for Links and Downloads" for links to the video).
 - Group discussion: Ask students "What do you think about Neil's process? Will you change how you keep your records after seeing this model?"
 - As the discussion winds down, ask students "Do you have a favorite way to keep your lab notebook? Please share with the group any tips and tricks you have learned about keeping a good lab notebook that Neil may not have captured."
 - OPTIONAL In-class activity or homework: "Take a recent experiment you have done and write up the experiment (in your notebook or elsewhere) using Neil's notebook model."
- Conclusion: What have you learned and what will you do differently? (3 min)
 - Ask students to "Write down three things you learned in this workshop." Then, ask them to "Write down what will you implement from this workshop into your research endeavors."
- Evaluation: Have students hand in a copy of their "What have you learned and what will you do differently" work from the conclusion (could be through electronic means). Examine the responses and assess whether the students overall achieved the learning objectives from the workshop. Also, reflect on the discussion portions of the workshop, did the students grasp the important concepts and seem able to apply them? You can also ask further evaluation of the students in a simple survey they hand in (or do online) in which you can ask about how helpful they found the resources, their satisfaction in the workshop, or pre- and post- knowledge gains around specific learning objectives and competencies.



Resources for lab notebook/recordkeeping (from Module 4)

- NIH: Guidelines for SCIENTIFIC RECORD KEEPING in the Intramural Research Program at the NIH (PDF)
- NIH: Keeping a Lab Notebook (PDF)
- Enhancing the QUAlity and Transparency Of health Research (EQUATOR) Network:
 Reporting guidelines for many study types.
- The ARRIVE Guidelines Checklist | Animal Research: Reporting In Vivo Experiments
- The CONSORT guidelines for randomized controlled trials.
- Transparent Reporting for Reproducible Science

Notes for facilitators

- Depending on class size, duration of the workshop, and your own interests, you may
 want to substitute "think-pair-share" or some other kind of evidence-based teaching
 strategy for the whole group discussions.
- Tailor the "best practices for keeping a lab notebook" content of this workshop to the
 needs of your audience. For example, you will want to thoroughly review the reporting
 guidelines for human subjects research if you are teaching to an audience of clinical
 scientists. Also, don't forget to include guidelines that are specific to your institution or
 program.

Review of "Neil's Approach to Recordkeeping"

For your reference, here is a detailed outline of Neil's process for taking notes at the bench and then transcribing them into a digital notebook. This process uses the <u>lab notebook template</u> for its written structure and is included in the case study video referenced above:

- Before you even start an experiment, review the protocol that you're going to follow step by step while you execute it. You should keep this protocol at the bench with you at all times.
- 2. Then as you are following those steps and collecting data, keep a paper-bound notebook with you to record the data being generated, any notes you might have as well as observations about the protocol or the experiment itself.
- 3. Once you have completed the experiment, take your paper notebook and transcribe it into digital form following the template outlined in the attachment above. Include any pictures of drawings or tables you made in your paper notebook.
- 4. The background section of the digital notebook helps document your explicitly stated experimental question, your hypothesis and your expected results. This will help you and



- others who might read your notebook in the future see what your underlying thought process was behind why you did things the way you did.
- Next is the experimental design section which is basically a bulleted list of what you did at the bench from beginning to end including the dates on which you performed each step.
- 6. Next comes the results and observations section in which you should dump all of the data that you collected from your experiment. This would include all of the observations from your handwritten notes, spreadsheets, explanatory figures, and any pictures you might have drawn or taken.
- 7. Finally comes the conclusions and future directions section. The conclusions section includes any conclusions you were able to draw from the data, what new information were you able to glean, what meaning were you able to extract from the data? In the future directions section you should answer the question "Based on what I observed in this experiment, what should I do next?" Does this experiment need to be repeated? Did your results demonstrate any modifications that you need to make to the current experimental protocol? Did this data inspire you to do any new experiments that you had not considered previously?
- 8. Using this template helps you keep all of your experimental protocols and notes within a common and defined structure so if you are ever going back through your notes you know where everything is.
- 9. This not only helps you keep a permanent record of what you did but allows you to work through what you did one last time and think about potential changes for the future.



Complete List of References, Recommended Readings, and Resources in Let's Experiment

References (by order of appearance in the course):

- 1. Prachi Avasthi blog post "On Prioritizing Experiments"
- 2. Richmond, A., Su, Y. (2018) "Mouse xenograft models vs GEM models for human cancer therapeutics." Dis Model Mech. 1(2-3): 78–82.
- 3. Consideration of Relevant Biological Variables in NIH Grant Applications
- 4. Kaplan, R., Chambers, D., Glasgow, R. (2014) Big data and effect size: a cautionary note on the potential for bias Clin Transl Sci. 7(4): 342–346
- 5. Enhancing Reproducibility through Rigor and Transparency (NIH)
- 6. STAR Methods Guides for Authors
- Ioannidis, J. P.A. (2014) How to make more published research true. PLoS Med. 11 (10), e1001747
- 8. Statistical power and underpowered statistics
- 9. Sample Size Calculations
- 10. How to Calculate Sample Size and Why
- 11. Introduction to Power Analysis
- 12. Designing an Experiment, Power Analysis
- 13. The Experimental Design Assistant EDA
- 14. NIH: Principles and Guidelines for Reporting Preclinical Research
- 15. NIH: Enhancing Reproducibility through Rigor and Transparency
- 16. Biophysical Journal: Guidelines for the Reproducibility of Biophysics Research
- 17. <u>The Extent and Consequences of P-Hacking in Science, Head et al., 2015, PLoS Biol</u> 13(3): e1002106.
- 18. Center for Open Science (Preregistration)
- 19. Register your study as a new publication option
- 20. BMC Biology becomes the first specialist biology journal to offer Registered Reports
- 21. The ASA's Statement on p-Values: Context, Process, and Purpose
- 22. Origin of the 5% P-value Threshold
- 23. Science Isn't Broken
- 24. Common misconceptions about data analysis and statistics
- 25. The Economics of Reproducibility in Preclinical Research
- 26. The ghosts of HeLa: How cell line misidentification contaminates the scientific literature
- 27. <u>Authentication of Key Biological and/or Chemical Resources in NIH Grant Applications</u> (NIH's Mike Lauer blog post)
- 28. Reproducibility crisis: Blame it on the antibodies



- 29. <u>Karahara et al (2012) Demonstration of osmotically dependent promotion of aerenhcyma</u> formation at different levels in the primary roots of rice using a 'sandwich' method and X-ray computed tomography
- 30. Western Blot (The Human Protein Atlas)
- 31. Principles of Dot Blots
- 32. <u>National Centre for the Replacement, Refinement, and Reduction of Animals in Research "The 3Rs"</u>
- 33. Ethics of animal research in human disease remediation, its institutional teaching; and alternatives to animal experimentation
- 34. Animals, Research, and Alternatives: Measuring Progress 50 Years Later
- 35. UCI's Ethical Guidelines, Federal Regulations and State Statutes
- 36. UCI's Activities that Require IRB Review
- 37. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2147348/

Recommended Readings:

- 1. Ana's Case Study Paper:
 - a. Ruiz-Saenz, A. et al. (2018) "HER2 Amplification in Tumors Activates PI3K/Akt Signaling Independent of HER3." Cancer Research. 78(13), pp 3645-3658
- 2. Neil's Case Study Paper:
 - a. Bao et al. (2014) "Plant roots use a patterning mechanism to position lateral root branches toward available water." PNAS, 11(25), pp 9319-9324
 - b. Neil's detailed protocol for the agar sandwich: Robbins & Dinneny (2016), "A Method to Analyze Local and Systemic Effects of Environmental Stimuli on Root Development in Plants" DOI: 10.21769/BioProtoc.1923
- 3. Using animals in research:
 - a. <u>Drugs That Work In Mice Often Fail When Tried In People</u>
 - b. Of Mice and Not Men: Differences between Mouse and Human Immunology
 - c. NC3Rs/BBSRC/Defra/MRC/NERC/Wellcome Trust (2017) "Responsibility in the use of animals in bioscience research: expectations of the major research councils and charitable funding bodies". London: NC3Rs
 - d. Experimental Design: Top Four Strategies for Reproducible Mouse Research
- 4. Confounding variables:
 - a. <u>"Confounding Variables" in John H. MacDonald's Handbook of Biological Statistics.</u>
- 5. Replicates and Repeats:
 - a. Replicates and repeats—what is the difference and is it significant?
- 6. Experimenter Bias:
 - a. How scientists fool themselves and how they can stop
- 7. Randomizing your samples:



- a. An overview of randomization techniques: An unbiased assessment of outcome in clinical research
- b. Workplace Wellness Programs Don't Work Well. Why Some Studies Show Otherwise.
- 8. General Statistics:
 - a. Choosing Statistical Tests, du Prel et al., Dtsch Arztebl Int. 2010 May; 107(19): 343–348.
 - b. P Value and the Theory of Hypothesis Testing: An Explanation for New Researchers
 - c. <u>Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations</u>
 - d. Confidence Interval or P-Value?
 - e. Using Effect Size—or Why the P Value Is Not Enough
 - f. P Values (from StatsDirect)
 - g. What a nerdy debate about p-values shows about science and how to fix it
 - h. In Defense of P Values
- 9. Mentoring:
 - a. Getting the Mentoring You Need

Recommended External Resources:

These are external resources mentioned in the course as helpful tools for experimental design.

- 1. Resources for choosing a model system:
 - a. Yeast
 - b. E. coli
 - c. Mouse
 - d. Zebrafish
 - e. Nematodes
 - f. Fruit flies
- 2. Finding statistical help:
 - a. https://statistics.berkeley.edu/consulting
 - b. https://statistics.stanford.edu/resources/consulting
 - c. https://stat.utexas.edu/consulting/free-consulting
 - d. https://www.uidaho.edu/sci/stat/about/scc/
 - e. Cross Validated
 - f. Reddit r/AskStatistics
- 3. Other resources on Statistics:
 - a. Ten Quick Tips for Getting the Most Scientific Value Out of Numerical Data,
 - b. The Handbook of Biological Statistics by John MacDonald:
 - c. Modern Statistics for Modern Biology,
 - d. StatXFinder: web-based tool for researchers to help them select statistical



- e. <u>StatXFinder: a web-based self-directed tool that provides appropriate statistical</u> test selection for biomedical researchers in their scientific studies.
- f. Research Gate
- g. <u>Promoting Awareness and Knowledge to Enhance Scientific Rigor in Neuroscience.</u>
- h. Principles, Statistical and Computational Tools for Reproducible Data Science.
- i. The BD2K Guide to the Fundamentals of Data Science Series.
- j. The Many Forms of P-Hacking
- 4. Data representation:
 - a. <u>Ten Simple Rules for Better Figures</u>, Rougier et al., PLoS Comput Biol. 2014 Sep; 10(9): e1003833.
 - b. <u>Beyond Bar and Line Graphs: Time for a New Data Presentation Paradigm</u>, Weissgerber et al., PLoS Biol. 2015 Apr; 13(4): e1002128.
 - c. <u>Tips on Effective Use of Tables and Figures in Research (article)</u>
 - d. <u>Visual Strategies, A Practical Guide to Graphics for Scientists and Engineers,</u> Frankel & DePace (Book)
 - e. The Visual Display of Quantitative Information, Tufte (Book)
- 5. Cell line/reagent authentication:
 - a. Antibody validation
 - b. Standards for Cell Line Authentication and Beyond
 - c. <u>Cell Line Authentication Publication Requirements</u>
- 6. Lab notebook/record keeping:
 - a. NIH: Guidelines for SCIENTIFIC RECORD KEEPING in the Intramural Research Program at the NIH (PDF)
 - b. NIH: Keeping a Lab Notebook (PDF)
 - c. <u>Enhancing the QUAlity and Transparency Of health Research (EQUATOR)</u>
 Network: Reporting quidelines for many study types.
 - d. <u>The ARRIVE Guidelines Checklist | Animal Research: Reporting In Vivo Experiments</u>
 - e. The CONSORT guidelines for randomized controlled trials.
 - f. <u>Transparent Reporting for Reproducible Science</u>
- 7. Troubleshooting:
 - a. How to deal with a failed experiment
 - b. <u>How Science Really Happens (video from the Planning Your Scientific Journey course)</u>
- 8. Optimizing western blots:
 - a. OpenWetWare
 - b. Biocompare
- 9. Dose response curves:
 - a. Pharmacology Education Project
 - b. Int J Nanomedicine. 2013; 8: 4277-4



Table of Links and Downloads

Legend



Resources List

			Video			
Туре	Title	View	Download	Download w/ Subtitles	Transcript Text	Resource
Module	e 0: (Introduction)					
	Course Trailer	View				
	Term Sheet					_pdf
Module	e 1: An Introduction to Experiment	tal Desig	n			
	The Art and Practice of Experimental Design	View	High Low	High Low	Transcript	
	Case Study: Neil's Investigation of Root Growth	View	High Low	High Low	Transcript	
	Case Study: Ana's Investigation into Mechanisms of Breast Cancer	View	High Low	High Low	Transcript	
	What experiment to do next?	<u>View</u>	High Low	High Low	Transcript	
	Flowchart: What Experiment To Do Next?					.pdf
	Flowchart: What Experiment To Do Next? (White background)					.pdf



H	Case Study: Neil's Experiment	View	High Low	High Low	Transcript	
(Neil's Experimental Setup					.png
	Case Study: Ana's Experiment	View	High Low	High Low	Transcript	
(Ana's Experimental Setup					.png
	Choosing a Model System	View	High Low	High Low	Transcript	
	Case Study: Neil's Model System	View	High Low	High Low	Transcript	
(Case Study: Ana's Model System					.png
?	Assessment questions for Module 1	ssessment questions for Module 1				
	Discussion questions for Module 1					
Modul	e 2: Key Elements of Experimental	Design				
H	Keeping Track of All the Variables	View	High Low	High Low	Transcript	
	What Are Your Controls?	View	High Low	High Low	Transcript	
	Case Study: Neil's Internal Controls	View	High Low	High Low	Transcript	
	What is Variation or Noise?	View	High Low	High Low	Transcript	
H	Variation Between Samples	View	High Low	High Low	Transcript	
	How to Think About Replication	View	High Low	High Low	Transcript	
(Ana's Replicates					.png



<u>View</u>

High Low

High Low

Transcript

?

The Importance of Sample Size

Assessment questions for Module 2

	Discussion questions for Module 2						
Modul	Module 3: Account for Bias						
H	Be Rigorous and Transparent	View	High Low	High Low	Transcript		
	Case Study: Neil's Initial Bias	View	High Low	High Low	Transcript		
	Don't Be Wed to Your Hypothesis	View	High Low	High Low	Transcript		
	Be Aware of Measurement Bias and Blind Yourself	View	High Low	High Low	Transcript		
	Think About Your Data and How to Analyze It	<u>View</u>	High Low	High Low	Transcript		
	Clarifying the P-Value	<u>View</u>	High Low	High Low	Transcript		
?	Assessment questions for Module 3						
	Discussion questions for Module 3						
Modul	e 4: Gear Up to Do the Experiment						
H	Familiarize yourself with the protocol	View	High Low	High Low	Transcript		
	Pay Attention and Write It Down	View	High Low	High Low	Transcript		
	Case Study: Neil's Approach to Recordkeeping	View	High Low	High Low	Transcript		
G	Neil's Lab Notebook Template (Google doc)						
?	Assessment questions for Module 4						
	Discussion questions for Module 4						



Modul	ule 5: Getting the Experiment to Work					
	Pilot Your Experiment	View	High Low	High Low	Transcript	
	Getting an Experiment to Work	View	High Low	High Low	Transcript	
G	Troubleshooting Framework (Google doc)					
H	Case Study: Neil's Problem with Gravity	View	High Low	High Low	Transcript	
H	Case Study: Ana's 100 Clones	<u>View</u>	High Low	High Low	Transcript	
H	Optimize Your Experiment	View	High Low	High Low	Transcript	
	Circulto Naine Crambia					
	Signal to Noise Graphic					.png
G	Figure: Dose Response Curve Source: Int J Nanomedicine, 2013; 8: 4277–4290.					.png
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(Figure: Dose Response Curve Source: Int J Nanomedicine. 2013; 8: 4277–4290.	<u>View</u>	High Low	High Low	Transcript Transcript	
¢	Figure: Dose Response Curve Source: Int J Nanomedicine. 2013; 8: 4277–4290. Decreasing Noise Case Study: Ana's Variability in Tumor				·	
	Figure: Dose Response Curve Source: Int J Nanomedicine. 2013; 8: 4277–4290. Decreasing Noise Case Study: Ana's Variability in Tumor Growth Validate Your Results Through	View	High Low	High Low	Transcript	

