SURF Proposal Info Session

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SURF PROPOSAL STARTER KIT

- SURF Proposal Starter Worksheet
- SURF Proposal Overview and Reviewer Questions
- Annotated Mock SURF Proposal
- PDF of Info Session Slides
- Writing Center Sign-Up Instructions

What are the purposes of a research proposal?

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THE SURF PROPOSAL IS...

- A chance to better understand and prepare for your SURF project
- A **persuasive** document demonstrating that your project is important and worthwhile, and that you are prepared to do the work you propose
- A demonstration of your ability to write and think clearly as a scientist

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- A **persuasive** document demonstrating that your project is important and worthwhile, and that you are prepared to do the work you propose
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...AND IS NOT

- A personal statement or job application letter
- A research paper or article
- A place to discuss your previous research experiences in other labs/groups or your qualifications for SURF

Writing a proposal isn't just about a final product; it's about developing the communication and critical thinking skills through the *process* that will help you as a professional!

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SURF proposals are a chance to practice the genre of grant/fellowship proposal writing

Research proposals **persuade** readers that the proposed project is worth funding (feasible and likely to produce something the funder wants)

Portrait of a funding agency reviewer…

- Tired (lots of proposals to read!)
- Has strict deadlines for reviews
- Aware of agency interests and research priorities
- Limited $$$$, lots of proposals
- General subject expert, may not know your research area in detail
- Wants to pick projects that will have a big impact

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WHO WILL READ YOUR PROPOSAL?

Mentor(s)

Knows your project inside and out.

Other faculty members

Experts in the field (and likely in the big question you are studying) but not the nitty gritty details of *your* project

What do readers look for in a proposal?

What your project is about and why

What you hope to achieve (specific aims, goals, objectives)

How you plan to answer the questions or achieve your goals + your plan is likely to succeed within the limitations of the project (time, money)

That YOU understand and are the expert on your project, and that you will have a valuable training experience!

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Overall: 1-3 page plan for your summer research

Title

Introduction to your project

Objectives/aims for the summer

Approach

Work plan

References

ANATOMY OF A SURF PROPOSAL

Where to begin?

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STEP 1: DO YOUR RESEARCH

The Writing:

- Talk to peers, mentors, or make an appointment with an HWC peer tutor or writing specialist to plan your proposal or discuss examples
- Read the SURF program application instructions closely!

The Science:

- Talk to mentors and lab members
- Explore the literature – use suggested reading as a starting point

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Gather information about your project:

- **What** is the goal or the question you want to answer?
- **Why** does the question matter? To the broader efforts in the lab? To the field? Society at large?
- **How** will you approach the question?
- **Where** might you face challenges or find opportunity to develop something new? Where can you draw on existing knowledge/progress?

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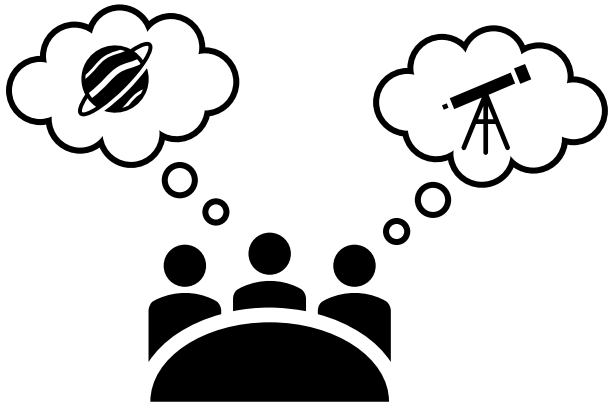
STEP 2: DEFINE YOUR RESEARCH STORY

A strong story will make your project feel memorable, logical & easy to understand AND will help you write a focused & cohesive proposal.

Research follows a problem-solution story

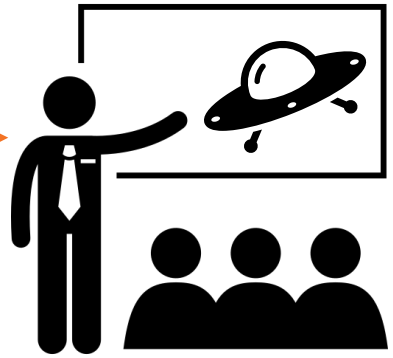


Research topic, what is known in field

Question, problem, task, gap in knowledge

Your methods – how you approach the problem

Getting results



Field has new knowledge!
New questions?
Future work?
Applications?

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Use an ABT statement to quickly capture your story

A	B	T
AND	**BUT**	**THEREFORE**
What you are studying and why it's interesting	The problem	What your proposal is all about: steps you'll take to solve the problem.

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Use an ABT statement to quickly capture your story

AND

And, also, in addition, currently, we know, recent work suggests...

BUT

But, yet, however, we don't know...

THEREFORE

Therefore, so, as a result, to solve the problem I propose to, to answer this question we...

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Use an ABT statement to quickly capture your story

Plant biologists know photorespiration occurs when oxygen binds to rubisco **AND** it greatly reduces photosynthetic efficiency

BUT we don't yet understand how rising temperatures and elevated CO2 levels will affect photorespiration in crop plants

THEREFORE, we conduct computer models and field trials that simulate future conditions in order to understand how plants will respond to different climate drivers

AND **BUT** **THEREFORE**

Tip: one problem, one angle = happy readers

It's tempting to talk about multiple questions your research answers, or to talk about why it's important at multiple levels or for different groups of people. But this can be confusing to your audience! Take the time to distill your message into one simple story.

Too many themes ☹

I'm interested in the topic because I'm curious about how bacteria interact in their communities, but it's also important for understanding antibiotic resistance and treating disease. My project also answers biochemical and biophysical questions about how the resistance proteins work.

Focused ☺

This research is important because it will tell us how bacteria resist an important class of antibiotics on the molecular level, allowing us to develop new drugs that can evade resistance.

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Tip: don't confuse your problem with your significance

Problem-solution narratives in research usually work on long- and short-term scales. For a successful proposal, specify the short-term goals that you will be able to achieve within the SURF timeframe...but connect them to the big picture goals of the lab/field – why your individual contribution matters.

Too ambitious! Too broad!

The goal of this project is to stop climate change by inventing a building material that is more environmentally friendly than any alternative.

Reasonable goal + long-term impact

We want to know if sustainably-produced materials A and B have the right physical properties for use in building construction. This work will help us develop more attractive alternatives for the environmentally unfriendly materials currently in use.

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Statement on the Use of Generative AI: The Student-Faculty Programs office believes that the effective communication of one's interests and research is a critical skill for undergraduates to develop. As you prepare your SFP application, research proposal or project plan, interim reports, and final report, you should consult with your mentor(s), or the SFP office, about policies related to the use of generative AI tools. ***Any usage that is not specifically permitted is not allowed.***

https://sfp.caltech.edu/undergraduate-research/programs/surf/application_information

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STEP 3: FROM ABT STATEMENT TO INTRODUCTION

What does your reader need to know about your topic to understand your plan (including context, problem, and solution) for your project?

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Plan your writing

Use our SURF Proposal Starter to help organize your thoughts and get your ideas on paper before you start writing!

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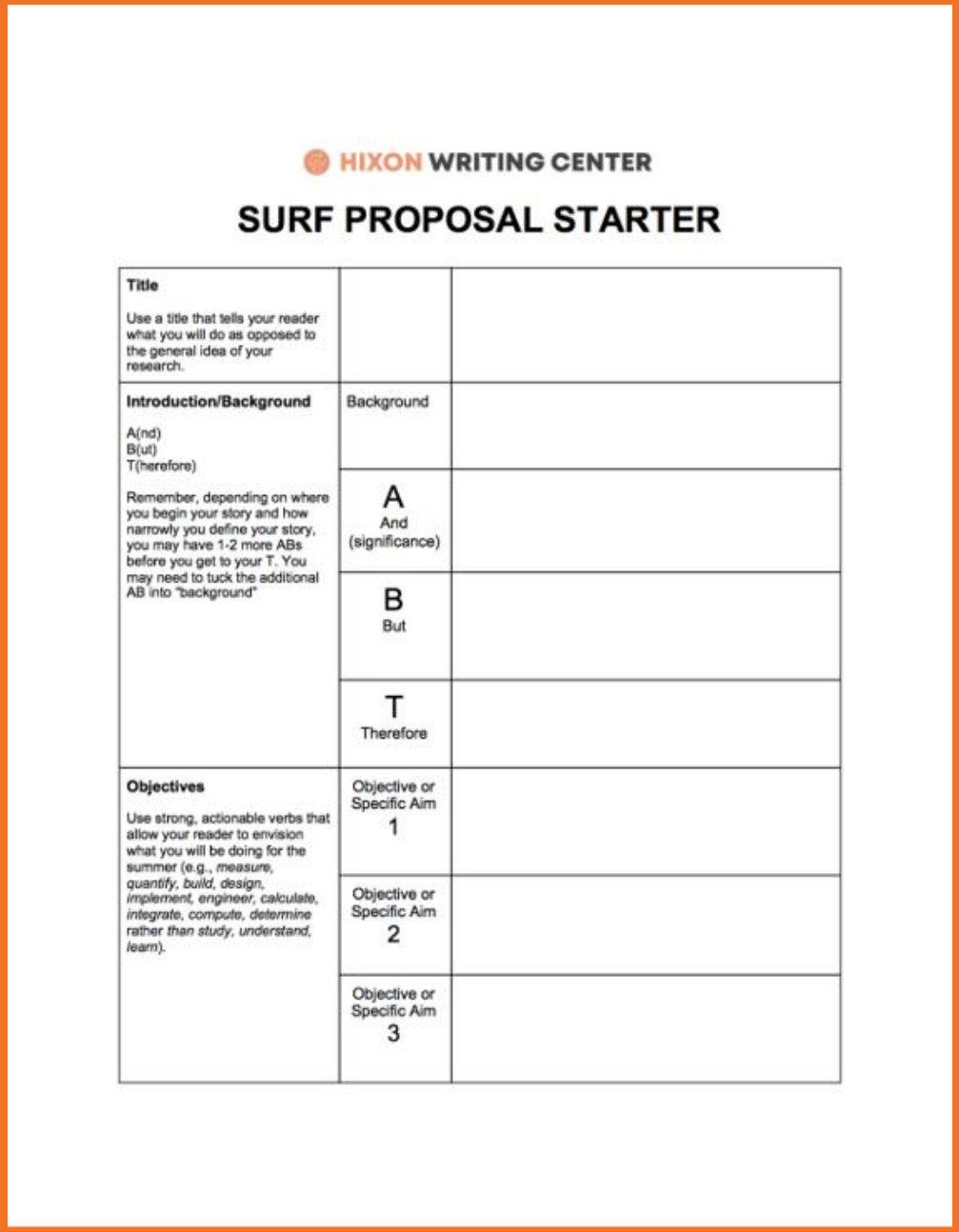

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SURF PROPOSAL STARTER

Title Use a title that tells your reader what you will do as opposed to the general idea of your research.		
Introduction/Background A(nd) B(ut) T(herefore) Remember, depending on where you begin your story and how narrowly you define your story, you may have 1-2 more ABs before you get to your T. You may need to tuck the additional AB into "background"	Background	
	A And (significance)	
	B But	
	T Therefore	
Objectives Use strong, actionable verbs that allow your reader to envision what you will be doing for the summer (e.g., *measure, quantify, build, design, implement, engineer, calculate, integrate, compute, determine* rather than *study, understand, learn*).	Objective or Specific Aim 1	
	Objective or Specific Aim 2	
	Objective or Specific Aim 3	

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Funnel your introduction to guide your reader from the problem to your solution

GENERAL → SPECIFIC

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A

B

T

To date, three genome-wide nucleosome maps in mammalian cells have been reported [5,6,7]. However, due to their low-resolution, these maps are inadequate for studying the dynamic features of nucleosome positioning. To dramatically improve the resolution and accuracy of nucleosome mapping for mammalian cells, we propose to extend the chemical mapping method into mouse cells and construct the first high-resolution nucleosome map in the mammalian genome.

Not only can your ABT be directly incorporated into your text, but the ABT formula of context + problem + solution can guide your structure of the entire introduction

What are nucleosomes and why do we care where they are located?

What we know about nucleosome positioning mostly comes from yeast, because it is difficult to map nucleosomes in larger, more complex genomes.

In my SURF, I will investigate if the recent chemical mapping technique is feasible for use in mammalian cells, making it possible to map nucleosomes in high resolution.

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A

B

T

Use your ABT to shape your introduction

Focus on context, problem, and solution as you zoom in on your research topic

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The basic structural unit of eukaryotic chromatin is the nucleosome, which is composed of 147 base pairs of genomic DNA spooled around an octameric histone core [1]. A majority of our genome is tightly bound by nucleosomes, which can occlude the underlying regulatory DNA sequences and limit their accessibility to regulatory factors that must act on them [2]. Consequently, where nucleosomes are positioned along DNA can determine the transcriptional output of the genome. However, the extent to which nucleosome positioning influences gene expression is unknown.

BROADEST: what are nucleosomes and why does it matter where they are located?

Genome-wide nucleosome positioning has been most widely studied in yeast. Recently, the ____ lab developed a novel chemical mapping method to determine nucleosome positions in budding yeast *S. cerevisiae* [3,4]. This mapping method relies on site-directed hydroxyl radical cleavage of nucleosomes carrying modified histones to determine the positions of nucleosomes in the genome. The resultant map defined nucleosome positions at single base pair resolution and revealed new aspects of *in vivo* nucleosome organization for the entire yeast genome that had not been observed using previous mapping technology. Though general features of nucleosome dynamics might be shared between yeast and mammals, the size and complexity of the mammalian genome present a challenge to accurately mapping its nucleosomes. Such mapping would pave the way for better understanding the role nucleosomes play in gene regulation in higher organisms.

BROAD: what do we already know about nucleosome positioning?

To date, three genome-wide nucleosome maps in mammalian cells have been reported [5,6,7]. However, due to their low-resolution, these maps are inadequate for studying the dynamic features of nucleosome positioning. To dramatically improve the resolution and accuracy of nucleosome mapping for mammalian cells, we prose to extend the chemical mapping method into mouse cells and construct the first high-resolution nucleosome map in the mammalian genome. In my proposed SURF project with the ___ lab, I plan to work with ___ to demonstrate the feasibility of chemical mapping in mouse embryonic stem (ES) cells.

NARROW: the specific problem and solution being proposed in this SURF proposal

The first single base pair resolution mouse nucleosome map will advance our understanding of the dynamic interplay between nucleosome positioning and gene expression in higher organisms. Specifically, my SURF project will establish a genetic toolkit and a chemical mapping method that will allow researchers to interrogate the epigenomic function of nucleosomes in mammals.

NARROWEST: how exactly the writer's work will move the field forward

The basic structural unit of eukaryotic chromatin is the nucleosome, which is composed of 147 base pairs of genomic DNA spooled around an octameric histone core [1]. A majority of our genome is tightly bound by nucleosomes, which can occlude the underlying regulatory DNA sequences and limit their accessibility to regulatory factors that must act on them [2]. Consequently, where nucleosomes are positioned along DNA can determine the transcriptional output of the genome. However, the extent to which nucleosome positioning influences gene expression is unknown.

Repeatedly introduces problems to reinforce need for work and big-picture goals and significance

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Highlights prior work which paves the way for the writer's proposal

To date, three genome-wide nucleosome maps in mammalian cells have been reported [5,6,7]. However, due to their low-resolution, these maps are inadequate for studying the dynamic features of nucleosome positioning. To dramatically improve the resolution and accuracy of nucleosome mapping for mammalian cells, we prose to extend the chemical mapping method into mouse cells and construct the first high-resolution nucleosome map in the mammalian genome. In my proposed SURF project with the ___ lab, I plan to work with ___ to demonstrate the feasibility of chemical mapping in mouse embryonic stem (ES) cells.

The first single base pair resolution mouse nucleosome map will advance our understanding of the dynamic interplay between nucleosome positioning and gene expression in higher organisms. Specifically, my SURF project will establish a genetic toolkit and a chemical mapping method that will allow researchers to interrogate the epigenomic function of nucleosomes in mammals.

Incorporates the ABT statement for their project directly in the text!

Describes how the results of the SURF project will enable progress toward the long-term goals in paragraph 1

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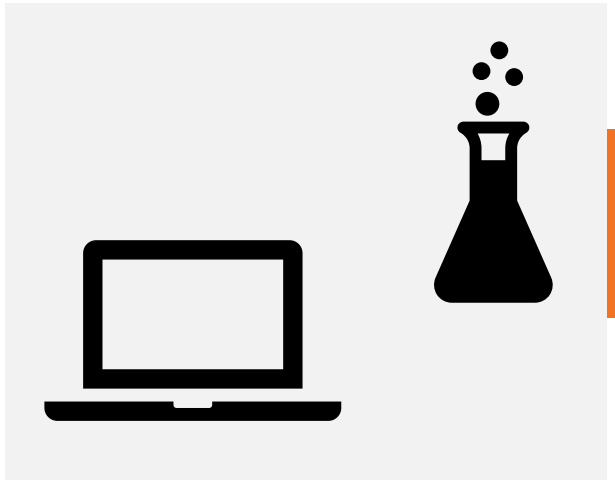
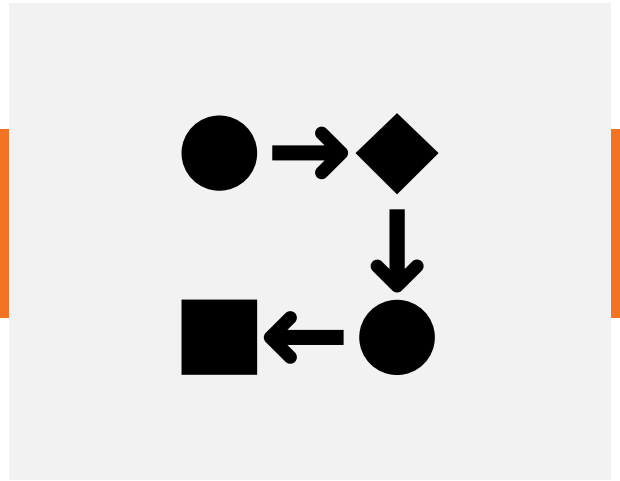
STEP 4: STATING YOUR OBJECTIVES/AIMS

Objectives = short statements describing what you will do to complete the project



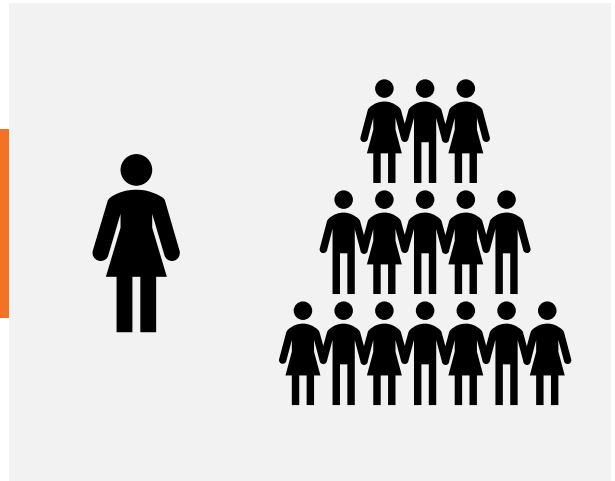
Techniques or approaches

Ex) using both a computational model + *in vitro* experiment



Subgoals or phases

Ex) you have to design a device, build it, and then test it



Checkpoints to assess progress

Ex) you will test and optimize a prototype, and then scale up

Objective Tips:

Objectives should be:

- **action-oriented**
  use descriptive verbs (measure, engineer, model vs do an experiment, study)
- **specific**
  give details of what you'll use and what you'll do
- **achievable**
  can be completed in the SURF timeline
- **aligned with your ABT**
  make sense as steps toward answering the question

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Big picture summary

The overall aim of this SURF project is to determine genome-wide nucleosome positions in mammalian cells at single base pair resolution. **The specific aims are to:**

Clearly stated goals including key methodological details

(1) Engineer mutant H4S47C mouse embryonic stem (ES) (AB2.2 cell line) for chemical mapping.
   a. The chemical mapping approach requires introducing a unique cysteine into histone H4 at position 47 (H4S47C) to covalently attach a sulfhydryl-reactive copper-chelating label. This label enables the chemical cleavage of DNA at the nucleosome center. The criteria for success is our ability to show H4S47C mouse ES cells have sufficient levels of H4S47C and are functionally equivalent to wild type cells.

(2) Establish and optimize the chemical mapping protocol for H4S47C mouse ES cells to demonstrate feasibility of chemically mapping nucleosomes in mammals.

Short summary includes criteria for success

   a. This protocol is based on the ___ lab's previously established protocol in yeast [4]. The success of this aim will be determined by our ability to (1) generate the desired cuts at nucleosome centers with limited non-specificity and (2) obtain sufficient amount of DNA for downstream analysis.

STEP 5: DESCRIBE YOUR APPROACH

What will you do in your 10 weeks of SURF to meet your objectives?

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Approach: Explain the reasoning behind the process

APPROACH

We will analyze the sequences of 13 mouse H4 genes, identify two common regions shared by all H4 genes in mouse, and design shRNA constructs to knockdown all H4 genes in the mouse genome. Concurrently, we will synthesize an RNAi-resistant H4S47C transgene vector that will express the H4S47C transgene in the mouse ES cells.

TO UNDERSTAND

METHODS

To construct mU6-driven H4-shRNA, the oligos will be phosphorylated, annealed, and ligated into a BbsI and XhoI digested *PB-mU6::PGK-Puro* vector: H4-Sh1 sense and H4-Sh1 antisense, H4-Sh2 and H4-Sh2, and H4-Sh3 sense and H4-Sh3 antisense to target all mouse H4 genes. To express H4S47C in the presence of H4-shRNA, we will synthesize a codon-modified, RNAi-resistant H4S47C cDNA expression vector *PB-CAG-H4S47C::PGK-Hygro*.

TO BORROW

PROTOCOL

I will construct mU6-driven H4-shRNA. First, I will set up the following reaction in a microcentrifuge tube on ice:

COMPONENT	20 µl REACTION
T4 DNA Ligase Buffer (10X)	2 µl
[illegible]	[illegible]
[illegible]	[illegible]
Nuclease-free water	to 20 µl
T4 DNA Ligase	1 µl

(T4 DNA Ligase should be added last. Note that the table shows a ligation using a molar ratio of 1:3 vector to insert for the indicated DNA sizes.)

TO REPLICATE

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WHAT are you going to do, and WHY?

Tip: persuasive writing requires more than methodology

You are building a case for your project – what would be convincing?

- What might be challenging? How will you overcome that challenge?
- What resources will you need? What is available to you and what will you have to make or acquire?
- Are you collaborating with anyone (in your lab, other labs, or working with institutional research facilities)? What support do you have?

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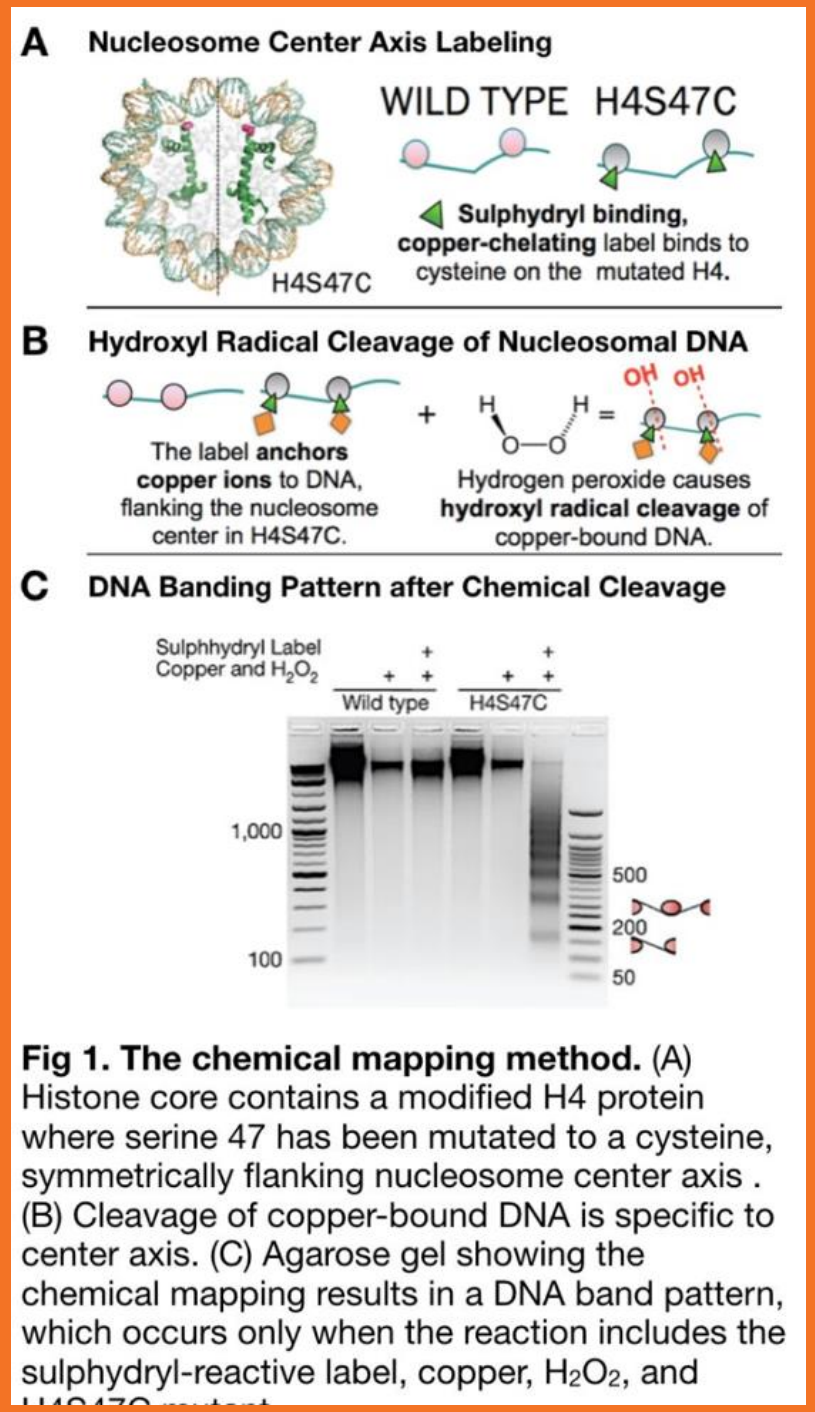

Fig 1. The chemical mapping method. (A) Histone core contains a modified H4 protein where serine 47 has been mutated to a cysteine, symmetrically flanking nucleosome center axis . (B) Cleavage of copper-bound DNA is specific to center axis. (C) Agarose gel showing the chemical mapping results in a DNA band pattern, which occurs only when the reaction includes the sulphydryl-reactive label, copper, H_2O_2, and

The chemical mapping strategy relies on the substitution of wild type histone H4 with H4S47C, in which serine 47 has been replaced with a cysteine [3,4]. The unique cysteine in H4S47C symmetrically flanks the nucleosome center axis and is in close proximity to the DNA backbone (Fig. 1A). Covalent linkage of a sulphhydryl binding copper-chelating label (phenanthroline-iodoacetamide)to the cysteine anchors a copper ion to the DNA at the same position – symmetric around the center axis (Fig. 1A). With the addition of hydrogen peroxide, the copper becomes a site of hydroxyl radical production, and a localized hydroxyl radical reaction cleaves the DNA precisely at the center (Fig. 1B). H4S47C-targeted nucleosome cleavage generates a characteristic DNA ladder in the presence of the copper chelator (Fig. 1C). Each step in the DNA ladder in the agarose gel represent the center-to-center distance between two adjacent nucleosomes.

Figures explain complicated concepts, first paragraph explains the key technique

Specific Aim 1: The first step in developing a chemical mapping strategy for mouse ES cells is to substitute multiple endogenous histone H4 with H4S47C. The mouse genome encodes 13 histone H4 genes, each of which encodes for identical H4 proteins. However, it is impossible to replace all 26 alleles of mouse H4 genes with the engineered H4S47C through gene targeting. Chemical mapping experiments in fission yeast *S. pombe*, however, showed that substitution of only two of the three H4 genes, with H4S47C produced comparable levels of chemical cleavage to the strain with all three H4 genes replaced [8]. Therefore, we will design a strategy to replace a majority of endogenous H4 proteins with mutant H4S47C by a combination of RNAi knockdown and cDNA expression.

To determine whether chemical mapping strategy is feasible in mouse ES cells, we will analyze the sequences of 13 mouse H4 genes, identify two common regions shared by all H4 genes in mouse, and design shRNA constructs to knockdown all H4 genes in the mouse genome (Fig. 2A, box). Concurrently, we will synthesize an RNAi-resistant H4S47C transgene vector that will express the H4S47C transgene in the mouse ES cells.

To test whether H4-shRNA constructs can efficiently target endogenous wild type H4 and not the synthetic H4S47C, we will transiently transfect each H4-shRNA with Flag-tagged-H4 and Flag-tagged-H4S47C into HEK 293T cells and test for loss of Flag-tagged-H4 protein expression by Western blot analysis. After confirming that our shRNA constructs are specific only for endogenous H4, we will use a PiggyBac transgenic approach to simultaneously express the H4-shRNA and the H4S47C into mouse ES cells (A. Fox, personal communication, Dec 30, 2013). After sequential drug selection with Hygromycin (for PB-CAG-H4S47C vector) and Puromycin (fo
cell clones (Fig. 2) and analyze the clones for fu

Clear topic sentences indicate the purpose of each activity

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Specific, active verbs sound authoritative and make the steps clear

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Names key materials and techniques to show they have a plan and make it easy to follow for the reader

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References other work to build a case for how their strategy will overcome a potential obstacle

STEP 6: MAKE A WORK PLAN

If you are performing multiple tasks sequentially:

Pre-SURF - Week 1 | (1) Design RNAi-resistant H4S47C transgene vector and shRNA constructs for H4 knockdown (2) Prepare and expand mouse ES cell cultures

Week 2 - 4 | Sequential drug selection with Hygromycin (for PB-CAG-H4S47C) and Puromycin (for U6-shRNA-H4) to establish stable ES cell clones.

Week 5 - 7 | Evaluate clones via functional assays: RT-PCR, Western blot, and growth curves to test for normal cell behavior and gene/protein expression in mutant ES cell clones.

Week 8 - 10 | Optimize chemical mapping protocol for mouse ES cells and purify nucleosomal DNA

Descriptions are organized, call back what was discussed in the approach, and clearly demonstrate how the work will be done in 10 weeks

STEP 6: MAKE A WORK PLAN

If you are performing multiple tasks in parallel:

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10
Task 1										
Task 2										
Task 3										
Task 4										

STEP 7: ORGANIZE YOUR REFERENCES

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Reference literature to support your ideas, definitions, and plans and to demonstrate your knowledge of the field/relevant literature

[1] K. Luger *et al.*,, Crystal structure of the nucleosome core particle at 2.8 A resolution. *Nature* 389, 251 (1997).

[2] T. J. Richmond, C. A. Davey, The structure of DNA in the nucleosome core. *Nature* 423, 145 (2003).

[3] A. Flaus, T. J. Richmond, Base-pair resolution mapping of nucleoso
hydroxy radicals. *Methods Enzymol* 304, 251 (1999).

[4] K. R. Brogaard *et al.*, A chemical approach to mapping nucleosome
Methods Enzymol 513, 315 (2012).

[5] D. E. Schones et al., Dynamic regulation of nucleosome positionin
887 (2008).

[6] A. Valouev et al., Determinants of nucleosome organization in prim
(2011).

[7] V. B. Teif et al., Genome-wide nucleosome positioning during embry
Struct Mol Biol 19, 1185 (2012).

[8] G. Moyle-Heyrman *et al.*, Chemical map of Schizosaccharomyces
features in nucleosome positioning. *Proc. Natl. Acad. Sci.* 110 (2013).

TIPS FOR REFERENCES

- Ask your mentors for suggestions of key papers in the field
- Choose a scientific citation style (*ACS*, *Nature, Science*)
- Be consistent
- Consider learning to use a citation management system (Zotero, Endnote, Mendeley)

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STEP 8: Revise, Revise, Revise

Reading Your Writing with Fresh Eyes

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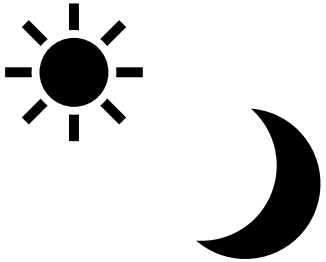
Let your writing sit for at least a day or two (or longer!) between writing and coming back to revise

Print your paper out and annotate the physical copy as you read. Alternatively change the font and/or layout

Read your writing out loud, or use a text-to-speech tool to hear it read to you to identify places that “don’t sound right”



Try rereading and revising at a different time of day or in a different location than when you usually write

Reading Your Writing with Fresh Eyes

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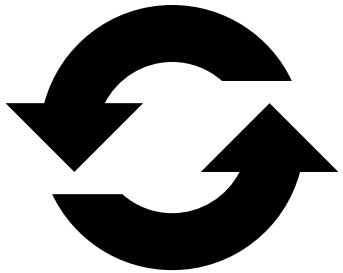
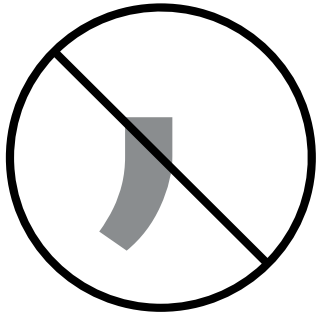


Don’t expect to fix everything on one readthrough – it’s about progress, not perfection



Save the small changes for the last pass – commas and word choice issues can wait until you are happy with the overall organization

Go into each revision round with a clear goal – you can’t focus on everything at once!

Get help with your SURF Proposal at the Hixon Writing Center

- One-to-one meetings with Writing Specialists or peer tutors
- Come at *any stage* of the writing process
- View samples of successful SURF proposals
- Virtual or in-person meetings
- Located 3rd floor Center for Student Services

How to Sign Up
Visit access.caltech.edu > Writing Center Scheduling > book open times

Any questions?

Or email us at:
writing@caltech.edu

—

Thank you for attending!

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Fill out form for Starter Kit!

What if I don't feel motivated to write my proposal?...

Read about others' writing methods or analyze a piece of writing you enjoy and try to reverse engineer it

Game-ify your writing with tools like Written Kitten, 4theWords, or Fighter's Block

Write in a group setting

Track your progress and reward yourself for milestones

Talk through your ideas out loud (or use a speech-to-text tool to transcribe them)

Find the right soundtrack for your writing

Find an accountability buddy – check on each other's progress, set goals, and discuss challenges

Create writing "rituals" to help keep you in a productive mindset: designating a space to write, having a special snack or beverage while you work, playing favorite music

Try writing at a different time of day – are certain tasks easier in the morning/at night?

Remove distractions – temporarily block social media or internet access, turn off wifi, or try handwriting or editing on a printed copy of your text

Set a timer and write until it goes off without worrying about quality – or challenge yourself with The Most Dangerous Writing App

Schedule blocks of time to write

End your writing session with the first sentence of the next paragraph to make it easy to pick up again

Stay on task with timers (try the pomodoro method) or focus apps that reward study time or limit access to distracting websites

Break down big projects into smaller sections

Change up your environment

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