Biotechnology, Synthetic Biology, and Genetic Circuit Design Module Lesson Plan

1 day

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Introduction

In this single module students will build upon their previous knowledge of basic molecular biology concepts with material from a wide range of biotechnology applications, including but not limited to: stem cell therapy, genetic manipulation and modification, genomic sequencing, and pharmacogenomics. This module is designed to give students a rigorous applications-based exercise in adapting biology for real-world needs, a critical feature for future leaders in medicine. Additionally, this module will cover basic aspects of synthetic biology, allowing students to explore and design novel genetic mechanisms for medicinal, environmental, or biological purposes. This module will prepare students to build their own genetic circuits, a key feature of the emerging synthetic biology movement, and a key mathematical/logical feature, intersection both biology and mathematics.

Day 1

1. Lecture 1: Biotechnology & Genomics (8:50-9:35)
2. Lecture 2: Introduction to Synthetic Biology & Circuit Design (9:40-10:25)
3. Activity: Building a Genetic Circuit (10:30 – 11:15)

Note: There are no rotations for this day planned.

For more detailed descriptions regarding the content of each lecture or lab please refer to the specified section in this manual. To find a list of the California State Science standards which are met through the course of this curriculum, please refer to the 'Appendix' section of this manual.

This manual contains detailed descriptions on the material that should be covered in the lectures, the protocol for the lab experiment, along with important questions to ask the high school students in order to keep them engaged.

Day 1

Lecture 1: Biotechnology & Genomics

This presentation is designed to give students a brief overview of the field of biotechnology: discussing both the basic foundations and scientific concepts behind *biotechnology*, and their perspective real world applications. This lecture will segue into an analysis of *human genomics*, a rapidly rising medical field that plays in the intersection between biotechnology, medicine, and fundamental engineering concepts. This presentation will give students both a fun and informative basis on which the rest of the module will be based on.

Note 1: This presentation includes extra information on stem cells. You don't need to go into great detail with stem cells. This information is simply here to clear up any misconceptions you may find in researching your topic. As always, let us know if you have any questions about what to include/not include.

Note 2: This presentation is intended to display the creative avenues that researchers and bioengineers have undertaken to harness the power of biology for technological or synthetic uses. As such, this talk should be intended on providing inspiration, excitement, and wonder at the power of biology, and puts you in a great position to talk about how students can become biologists or engage in research as high school students. Keep that in mind for your presentations!

1. **Required:**
    a. Introduce the field of biotechnology.
    b. Discuss genetic engineering, mention several examples.
    c. Talk about fluorescent proteins (GFP, YFP, RFP,…); mention Osamu Shimomura (Nobel Prize 2008).
        - What are the origins of fluorescent proteins? What are they useful for? How is research conducted using fluorescent proteins?
    d. Talk about the differences between *in vivo* and *in vitro.*
    e. **Stem Cells:**
        - What is a stem cell and where do they come from?
        - Discuss self-renewal and differentiation
            - Stem cells can either self-renew, or differentiate.
                a. Discuss potency here (omnipotent vs totipotent vs pluripotent vs multipotent vs unipotent).
        - Discuss the differences between embryonic stem cells and adult stem cells.
        - Briefly mention the ethics involved in embryonic stem cell research.
            - Stem cell lines are derived from leftover blastocysts from IVF treatment. These blastocysts are either discarded or frozen down.

At the request of the parents, they can also be donated to science for stem cell line derivation.

- Talk about iPS technology as a possible way to solve this issue and applications of iPS technology; mention Shinya Yamanaka (Nobel Prize 2012).
    - The main advantage of iPS technology is MHC matching. You can treat a patient using cells from the same patient therefore preventing any immune rejection. iPS also allows the creation of pluripotent lines without having to use blastocysts. iPS lines are not cheaper or easier to maintain.
- Find several examples of what stem cell treatment could do to treat various diseases.
    - Always remember to use the word POTENTIAL. Stem cell therapy is still many years away from being widely used in the clinic. This especially applies to regenerative medicine.
- Talk about regenerative medicine (growing organs from stem cells).
    - Growing organs always gets all the hype, but apart from that something that tends to be overlooked is that being able to culture the correct cell types is extremely beneficial for drug studies/screens.

The required topics should put you at around 10 minutes in your presentation, leaving the rest of the time for you to devote to other cool applications of biotechnology. *This is entirely up to your choice!* **I highly recommend a discussion about gene cloning**, the process by which molecular biologists can construct novel gene products and express them in various cell lines and organisms, leading to production of recombinant proteins and novel functions.

Some examples from the past that have incorporated the idea of gene cloning and its everyday applications:

- Genetically engineered food/organisms
- Synthetic Biology/DIY Bio
- Fuel-producing bacteria or fuel-consuming bacteria
- Biomimicry (this is not technically biotechnology, but it fits the presentation)
- Targeted cancer treatment using viruses.
- CRISPR/Cas9, RNA interference as genetic manipulation methods.
- **Specific examples of recent (within the past 5-10 years) breakthroughs at UCLA**

Lecture 2: Introduction to Synthetic Biology and Circuit Design

The presentation is designed to give students a primer of synthetic biology, an emerging life science field that deals with the development of novel genetic mechanisms and gene-based systems for biotechnological applications. In other words, synthetic biology uses the powers of biological tools that we have derived from the natural world, and uses the resulting tools for novel and creative applications for the betterment of society.

Specifically, this presentation will cover the basics between genes; what is needed for genetic synthesis, and how we can modulate and control the rate of gene product formation, namely through the design of genetic circuits.

1. Topic 1: Introduction to Synthetic Biology
    a. What is synthetic biology?
    b. Discuss critical features of genes involved in synthetic biology
        i. Be creative! Design presentations that discuss several applications of genetic parts for a synthetic biology application (i.e. biofuel synthesis, disease prevention, materials fabrication, etc.)

2. Topic 2: What's in a gene?
    a. Discuss critical features of a gene
        i. ATG start codon
        ii. STOP codon (we will not discuss terminator step looping for mRNA stop)
        iii. RBS (SD sequence)
        iv. Promoters/Enhancers
            1. Discuss inducible vs. constitutive promoters
        v. Repressors
            1. Discuss both the regulator region and the proteins involved.

3. Topic 3: How are genes regulated?
    a. Genes are not on all of the time, they are
        i. Transcriptionally regulated
        ii. Translationally regulated
    b. Discuss chemical induction of promoters/repression.
    c. Discuss positive feedback loops vs. negative feedback loops.

4. Topic 4: Applications of Gene Regulation
    a. Discuss genetic circuit design, toggle genes on and off.
    b. Discuss the lac operon, and the uses for genetic regulation
    c. Discuss biosensor, biological computing as mathematical models for gene regulation usage.

Activity: Designing a Gene Circuit

Please see attached worksheet.

Divide the students into groups of 2-3 and have them work on the worksheet together.

After about 15 minutes, have a few groups come to the front and discuss their final answer. Encourage them to come up, even if they are not sure of their answer, and be sure to guide them through the steps. Even if they got the problem correct, take the time to thoroughly explain all steps.

Background

When scientists want to create a bacterial chassis that can self regulate the production of two separate proteins, synthetic biologists design *genetic toggle switches* to regulate the production of said proteins. These toggle switches are basic components of genetic *circuit*, the application of electrical engineering toward biological genetic design. These circuits are designed to create a tunable and sensitive system for the activation or repression of genetic elements, all of which may play a variety of roles and applications. For example, genetic circuits can be used as tools for biosensing, allowing for bacteria to serve as a marker for disease, presence of waste, or as an alert system. Genetic circuits also allow for the development of regulating protein production that may otherwise by toxic to the bacterium, including the production of biofuels, critical antibiotics, etc. Today, you will be designing your own genetic toggle switch to regulate the colors of an *E. coli* cell!

Materials:

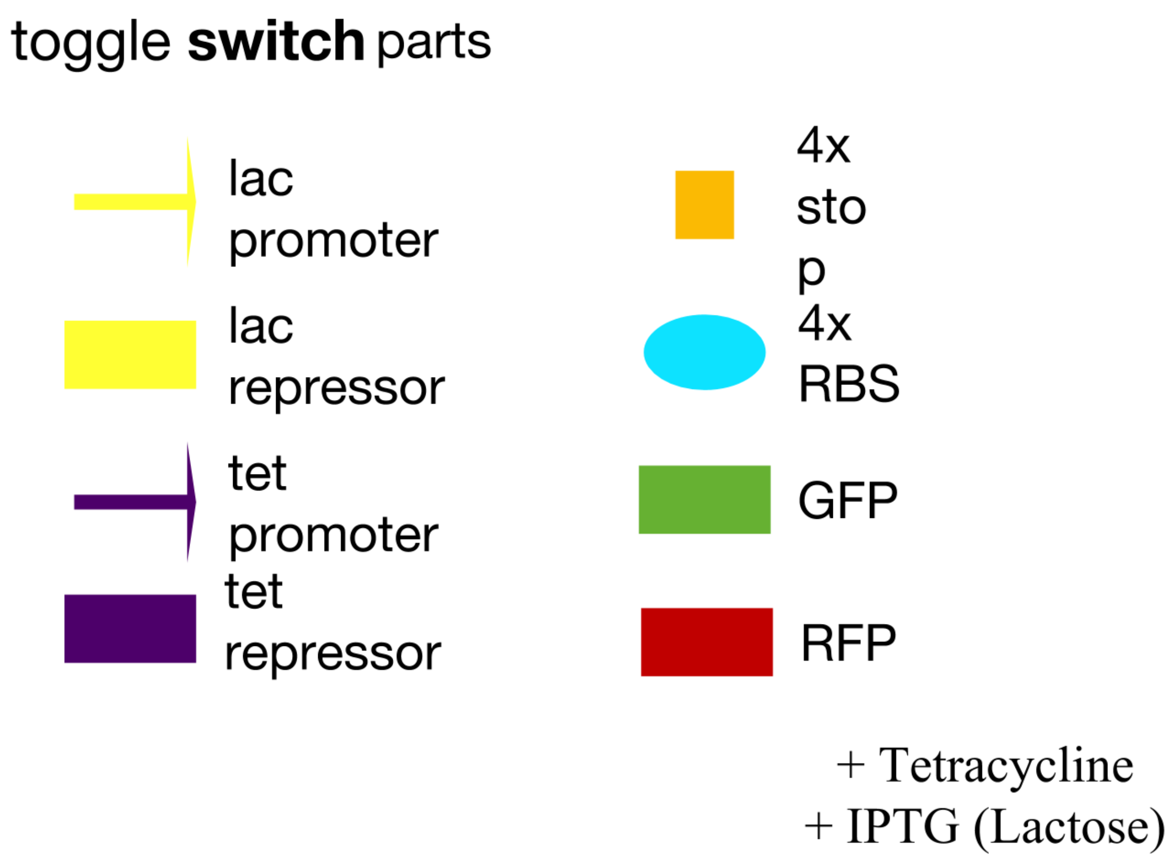
(1) Packet of Shapes
(2) Instructions Worksheet
(3) Sheet of Paper for Answers
(4) Pens

Goal:

(1) Design a transcriptional system where you can switch GFP on and off (and it will stay on or off) using lactose (IPTG) and tetracycline.
(2) Design a transcriptional system where you can alternate between expression of GFP (turning the cells green), and RFP (turning the cells red) using lactose (IPTG) and tetracycline.

Procedure:

(1) **Students will be given a packet of the following shapes and quantities. Each shape will represent a separate transcriptional part as follows:**



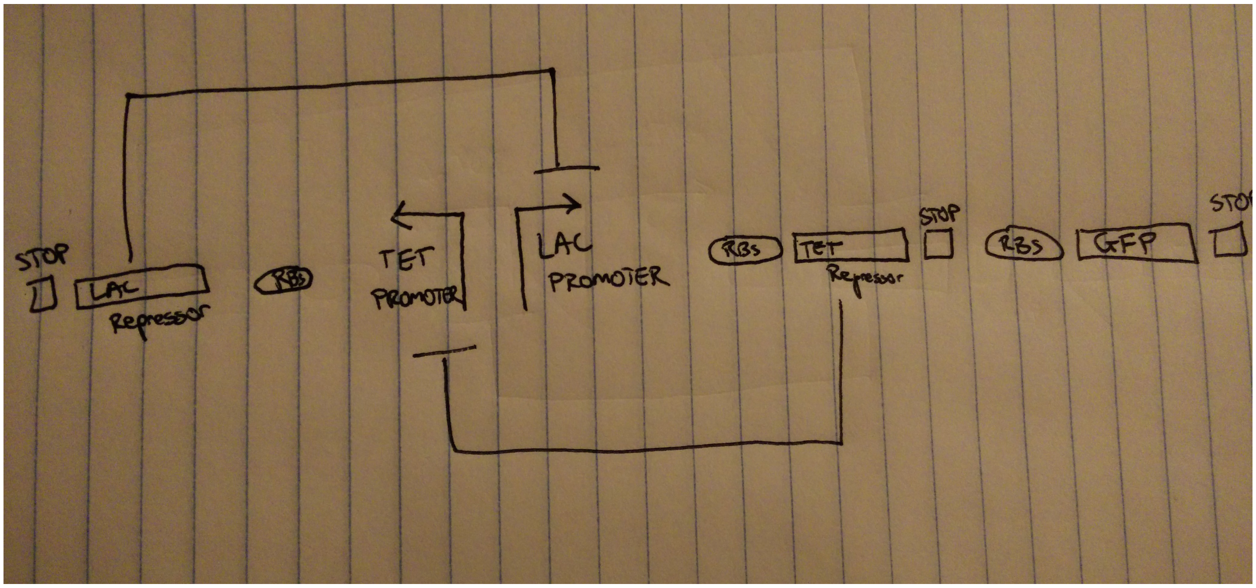
NOTE: NOT ALL PARTS MAY BE USED FOR PART ONE.

(2) Each group will have 10-15 minutes to design each of the genetic circuits. After the 15 minutes are finished, staff will discuss with each group their progress, and will correct any issues or concerns.

(3) Once every group has completed each task, two groups will be selected to come to the board and draw out each circuit, explaining as they draw the logic and rationale for (1) why the pieces are in their respective locations, and (2) how to the toggle switch will function.

Answer Key:

PART 1:



PART 2: