

BioBuilding: Synthetic Biology for Teachers: Biodesign

Biology by Design



Teacher Considerations

Using the bacterial photography system as inspiration, this assignment asks the students (individually or in groups) to use their imagination as they propose a design for a genetic system. The emphasis is on the decisions made by engineers during the planning of the design process and not on the genetics. The students are asked to consider existing technologies, risk, reward, and testing. Of course, they are expected to imagine a genetic system that will make a significant contribution to life on earth. You can worry about its feasibility later.

You may also find this design assignment useful for an iGEM team as it develops an idea for a project. Although the assignment itself is written for an individual student, it can be adapted for a group. The brainstorming exercises below lend themselves quite well to a group process, such as is needed within an iGEM team.

Some good resources for teaching this activity are listed at the bottom of this page. You may wish to assign these readings or videos before trying the assignment as a class.

When the students have completed this assignment, be sure they re-visit the BioBuilder website to share their design ideas and see some of the designs of others. They can do this at the ["Submit Your Data"](#) link.

Guiding your students



TEACHERS: This assignment is open-ended and can be adapted in many ways by you and your students. However, it might be helpful to take them through some exercises to help them to think about biological engineering design. These five questions, and the associated material, can help the students focus on a problem and begin designing a solution.

Brainstorming

Question 1: What does an engineered system look like, on paper and in reality?



TEACHERS: This material is matched to the content in the bacterial photography

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system lesson in [\(Lab 3\)](#)

Question 2: What will your focus area be?



TEACHERS: A word doc of this table may be found [here](#). You may want to divide groups of students into teams of 4 or 5 people to work on these projects together.

This table will help you pick broad areas on which to begin your design project.

Area	Challenge
Food or Energy	People need to eat. Planes, trains and automobiles need to eat too. Can biotechnology be responsibly used to produce food or energy without causing widespread shortages of either, and without harming the environment that future generations will inherit?
Environment	The quality of the air, water, and land on Earth and other heavenly bodies, limits the happiness of humans and other creatures. Can biotechnology be used to help clean the air, provide fresh drinking water, restore or enhance soil quality, <u>terraform</u> a near-earth asteroid, or protect, preserve or enhance natural biological diversity?
Health or Medicine	Many health and medical problems might be best addressed by improved biological technologies. What can synthetic biology do?
Manufacturing	Have you ever heard of nanotechnology? Well, biology is a nontechnology that already exists, and that actually works. The ribosome is a programmable <u>nano</u> -assembler embedded within a reproducing machine. Forget grey goo, we've got green goo, and it has already taken over the planet! Thus, could we responsibly use biology to manufacture useful products, from <u>nanoscale</u> (atoms) to the <u>decascale</u> (buildings and bridges)? What can biology <u>be</u> programmed to manufacture?
New Application Area	We're guessing that you have great ideas that nobody has ever thought about, or if they have they forgot to tell somebody else. Can you imagine an entirely new application area for biological technology? Go for it. We'll celebrate you in front of the class.
Foundational Advance	Modern biotechnology dates back to the invention of recombinant DNA technology, which lets people cut and paste pre-existing fragments of genetic material. That was only 35 years ago. In other words, biotechnology is a young adult, just entering its prime years. One thing that desperately needs doing is to develop improved tools and technologies that help to make the entire process of engineering biology easier. What foundational advance can you contribute that will take everybody's work forward?

Question 3: What particular problem do you want to address?



TEACHERS: the students can think very broadly about topics of particular interest to them. Some will be more suitable than others for a biotechnology solution but keeping a big, running list of ideas is more helpful than judging them as they are raised. If the students are working in teams, this can be an important chance for strong team dynamics to establish.

Having chosen a general area for your work, now think about any topics in that area you find especially interesting. These could be motivated by an article you've read, a

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personal experience, a research project you know about. You might want to have a couple of possibilities as you go forward. Remember: this is a brainstorming session. It's a time to keep all ideas that come to mind and then refine or combine them later.

Question 4: Can you imagine a biotechnology to address this problem?



TEACHERS: the hardest part here is thinking in somewhat concrete terms. A lot of ideas seem far-fetched but then a little research will show that nature has, in fact, provided the kind of circuitry or response that students are looking for. Luckily, they don't have to actually build this system that they are designing, and so just the investigation into what's interesting and what's possible is rewarding.

Now let your imagination kick in for a solution to the problems you've brainstormed

- Bacteria too smelly? Make them smell like bananas.
- Composting too slow? Make a living additive to accelerate the process.
- Need to fight cavities? Make a yogurt that sticks to your teeth and heals them.

You get the idea.

You get the idea. Remember that your assignment requires that you think big but stay away from science fiction.

Question 5: How will you narrow down your choices?



TEACHERS: this is the place where some projects may become clear front runners and others may fall by the wayside, especially if, after a little bit of additional reading, students find that the system they'd like to build already exists in some form. Rather than see this as a defeat, they should be encouraged to see this as demonstrating clear thinking and realistic designs.

You should now have a list of ideas and possible solutions. Deciding between them can be daunting. It might help to compare all your favorite ideas along these five lines:

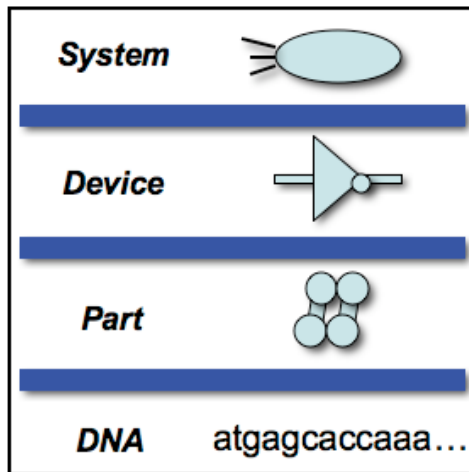
- What precisely is the problem or opportunity you are focusing on?
- How clear are you on an approach to make a dent in the problem?
- What if your project is fully successful? How big a difference could it make? What concerns will it raise?
- What other technologies can be used/have been used to address this area?
- What don't you know? How big are the gaps in what you know? How much is completely unknown or unknowable?

Going Further



TEACHERS: You may want your students to take the design assignment further by breaking down the systems they design into devices and then, perhaps, the devices into parts. This will be particularly helpful for an iGEM team.

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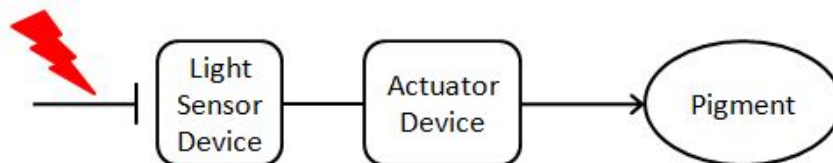


Systems to Devices



TEACHERS: a review of abstraction and why it's useful will help frame the engineering that the students are trying here. There is an animation about abstraction [here](#).

Think back to the bacterial photography system. We drew the system as two boxes, each with input and output arrows. One box had the "sensor," which detected the presence or the absence of the light (via the Cph8 protein). The other box was the "actuator," the parts needed to produce the pigment (by controlling β -Galactosidase production). In simple terms, the system requires two genetic devices. A block diagram might look like this:



To further specify your system, try to think about what devices are needed. This is best accomplished by thinking in terms of inputs and outputs. To get started, work through some practice problems.

Practice problem I: Bacterial Buoy

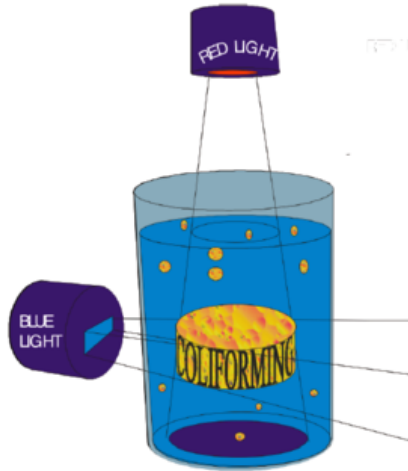


TEACHERS: this relatively straightforward example should include simple device names like: "red light detector," "blue light detector," and "floatation device" and perhaps "clumping device" if the students want the cells to stick together once they detect both kinds of light. There is some ambiguity in when the clumping vs floating occurs in this system...and that's OK to point out!

The 2007 iGEM Melbourne team wanted to build a 3D, floating mass of bacteria that

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adhered to one another when the cells detected both blue and red light. In other words: at the intersection of an incoming red light beam and blue light beam, a solution of bacteria would clump and remain suspended in its growth media.



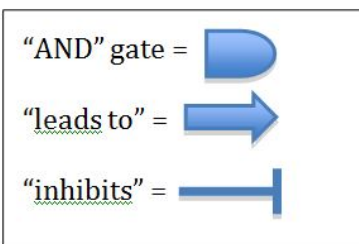
As a class we'll watch the first 5 minutes of the Melbourne team's [iGEM presentation](#). Next you should work out a high level overview of this system's behavior. Make a list of cellular inputs and outputs then write a block diagram that connects them. In other words: What inputs will the cell have to sense? What two ways will the cell respond? Don't worry about getting the clump to disassemble when the lights are off. Just think about what the cells need to do to make the clump and make it float. **Importantly:** don't get bogged down by what really exists. If you need a "floatation" device, you can have one.

Practice problem II: Polkadorks



TEACHERS: this dynamic example is more complicated but can usefully illustrate how "devices" can be slapped together to describe a system. Here too you can emphasize that there's no single right answer. The goal is to have the students discuss the behavior they want in terms of devices with names like: "coin flipper," "green signal generator," "green signal detector" "swimming generator" etc.

Let's try a more dynamic system. The 2004 IAP team wanted their engineered cells to "form, diffuse, and form again in random areas on the plate. Our system should thus form time-varying patterns based on local random time-varying symmetry breaking." Check out the Polkadorks [animation](#). Then make a list the devices needed to implement such a system (for example "coin flipper" to generate the random decision to turn red) then connect the devices with arrows to indicate the logical information flow pattern.



Your Challenge:

Now think about your system. What devices would you need to create it? Again, don't get bogged down by what already exists, but do keep it realistic. You are engineers. You may be able to make whatever device you need. So, if you need a "floatation device" or a "garlic smelling device", go ahead.

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Devices to Parts

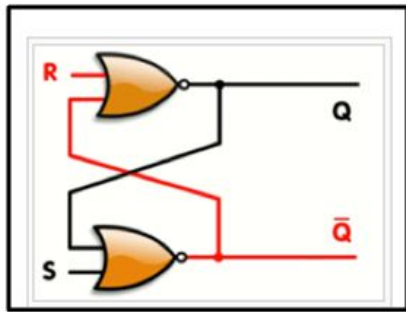


TEACHERS: understanding how to specify devices in terms of parts will require a reasonably sophisticated appreciation of how gene expression is controlled. You can review bacterial gene expression in advance of assigning this exercise by asking the students to watch [this](#) animation.

"Parts" are the individual components that make up a device. A simple device, for instance the one that encodes β -galactosidase, would need a promoter, ribosome binding site (rbs), open reading frame (ORF)—in this case the lacZ gene—and possibly a terminator sequences. Easy enough.

Sometimes devices are more complex assemblies of parts. Remember the "NOT" gate that described the bacterial photography system? That is a logic gate made from a transcription factor.

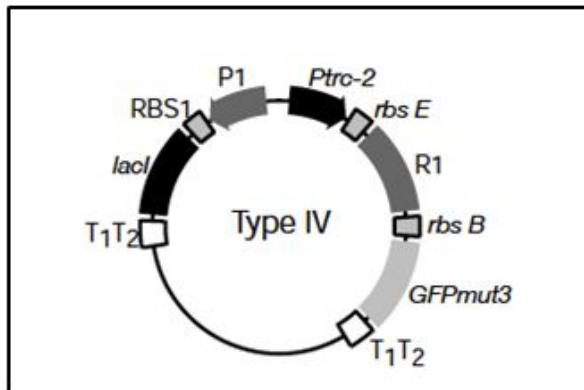
As an exercise, consider another kind of logic gate. This one comes from electronics and is called a "latch." It's made by cross-wiring two "NOR" gates. The gate is sometimes also called a "flip-flop" or "toggle" since it switches and holds between two states. Even if the initial input is removed, the circuit holds the output, until the other input is provided.



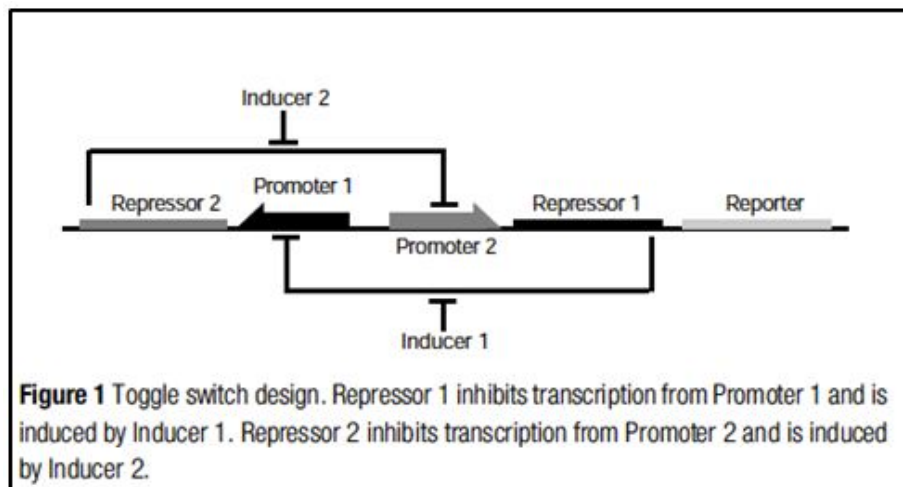
In a landmark paper, this kind of electronic circuit was recapitulated with genetic parts by Jim Collins at Boston University (T S Gardner, C R Cantor and J J Collins. [Nature 403\(6767\):339-42 \(2000\) PMID 10659857](#)).

Looking at the diagram of the plasmid below, we can see the parts that make up this switch: Starting at the top, we see an arrow pointing to the left. This is promoter 1. It is followed by a RBS and the lacI ORF, this is repressor R-2. Starting again at the top, we see promoter 2 (Ptrc-2) followed by a RBS, the repressor R1 ORF and the rbs and orf for a GFP (green fluorescent protein) reporter.

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So, how do these parts function as a toggle switch? As we can see in the second diagram:



If promoter P-2 is on, then it will turn on the reporter gene and the cell will glow green. But it will also turn on expression of repressor R-1. This will shut down promoter P-1 which will therefore not enable the repressor R-2 to be expressed. So, the cell will continue to glow green until P-1 is induced. Once P-1 is on, it will turn on R-2 which will repress P-1. Now the cell will not make the GFP reporter and will not glow green. And, since P-2 is repressed, no R-1 will be made and the cell will stay in the dark. Got that? Well, in order to prove you understand something, you need to be able to explain it.

So, now you try it: List each of the components and what its role is in the toggle device. Then, using the diagrams and your list, write an explanation of how these parts work in combination in the toggle device. Finally, explain the system to your lab partner or a stuffed animal.

Your Challenge: Think about the devices that make up your system. Then, think about the parts that are needed in each device. For each device list its parts. Don't worry if these parts actually exist. However, you **should** be specific where possible. For example, if you need a promoter that is induced by high salt concentration, write

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that you need a promoter that is induced by high salt concentration. We can search the Registry for one later...

Resources (just a sample)

Here are some background readings and videos that teach about synthetic biology, its goals and projects. You may wish to provide your students with these resources.

[Decoding Synthetic Biology \(YouTube\)](#)

[What is synthetic biology? \(pdf\)](#)

[A Life of Its Own \(pdf\)](#)

[Our Synthetic Futures](#)

[Handmade Biology](#)

[Synthetic Biology: Tools to Design, Build, and Optimize Cellular Processes](#)

[Video on design and synthetic biology by James King \(Hastings Center\)](#)

[Explanation of the Engineering Design Process](#)

[Design criteria](#)

[Teacher's Domain video and essay on the Engineering Design Process](#)

You may wish to see the type of projects that college synthetic biology students have designed as part of the [iGEM Competition](#). Please keep in mind that these projects put a much greater emphasis on the actual design of the genetic system than is intended by this assignment.

- plus some links to older articles:

[How to Make Life](#)

[Life Reinvented](#)

Assessment

Grading Rubrics

Design Assignment Rubrics and Scoresheets ([pdf](#))

Survey

To help us improve the labs, you can

1. send the students [here](#), where they can upload their data.
2. "join a discussion" from the [BioBuilder homepage](#)
3. email us: "info AT biobuilder DOT org"

Thanks!

Feedback

We're always looking to hear back from you if you've thought about this unit, tried it, or stumbled across it and want to know more. Please email us through [BioBuilder](#), info AT biobuilder DOT org.