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ABE591 Principles of Systems & Synthetic Biology

HOMEWORK #1 **Due: Tuesday, September 4, 2018 at end of class (1:15 PM)**

1. Cells induce metabolic pathways as needed to conserve resources. A canonical example of this is lactose metabolism, controlled by the *lac* operon. Here, genes for lactose uptake and metabolism are induced in the presence of its substrate, lactose. However, this signal is overridden by the presence of glucose in a process known as *catabolite repression* where the presence of glucose and lactose will inhibit lactose metabolism.
    a. Draw a truth table describing this phenomenon that encompasses the outputs of all possible inputs (**4 points**)
    b. Draw and name a logic gate that describes catabolite repression (**1 point**)

2. Using 2 arbitrary inputs and a single output
    a. **<u>Draw a gene circuit</u>** that functions as a **N-IMPLY** gate (**8 points**)
    b. Describe in words how the circuit would function (**2 points**)

3. Draw and describe the promoter architecture of a hybrid promoter that integrates lactose and tetracycline to complete an **AND** operation. Assume that *lacI* only needs one operator site for efficient binding, while *tetR* needs 2 operators roughly 6 nts apart for efficient binding. Be sure to indicate the positions relative to the -10 and -35 sites. (**5 points**)

4. DIYBio hopes to democratize science by making synthetic biology accessible to the public to complete in their own garage. One such project has been to engineer yoghurt microbes that detect the presence of toxins in the starter milk (https://bit.ly/2ccYtR7). In a brief 1 pg. essay, prepare a response regarding how responsible such an activity is including the following:
    a. Discuss potential risks of this project according to each of the criteria described in class (e.g. 'dual use', socioeconomic, etc – all criteria may or may not apply equally) (**5 points**)
    b. Describe the unique perspective of potential stakeholders, and discuss how the risks identified above impact them. (**5 points**)
    c. Based on your arguments, propose a **technical solution** (e.g. kill switch, etc) that could be incorporated in a more responsible design to minimize the risks discussed above (all risks may not be possibly addressed by design) (**2 points**)

5. **Design Project**
    a. Identify teammates (**1 point**)
    b. Identify problem to be tackled (**1 point**)
    c. Scope the systems needed for project [i.e. what major functions do they need to complete, input/output, calculations/logical integrations that are needed] (**1 point**)

See next page for details

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Group Design Project

In lieu of a final exam, you will demonstrate mastery of the course content in a single team design project due at the end of the semester similar to the iGEM competition (http://igem.org). For the term project, you are asked to **design and analyze a novel biological system or to analyze an existing biological system (synthetic or natural) in depth in a novel way**. The Design Project will be completed in groups of 3-4. You are free to pick the topic of your choice (see the end for suggestions) and to choose your group members. However, you are encouraged to select systems that allow you to demonstrate the full breadth of skills acquired in the class (DESIGN, BUILD, TEST, LEARN). You may also benefit from the experience of your teammates by forming appropriately interdisciplinary teams (i.e. no teams of exclusive undergrads or ABE majors). A list of possible project ideas to spark creativity is provided at the end of this prompt.

Deliverables

You will be evaluated on a ~ **10+-page technical report** (may include additional appendices) and a **20 min presentation** that will be weighted equally. The report should include:

- A 1-2 page problem description/motivation
- A 1-2 page solution/system design including specific parts
- A 2-3 page model description justifying part selection (equations, parameters, assumptions, dynamic performance, Matlab code/BioCAD simulations. May include dynamic analyses of performance e.g. stability analysis, vector fields, etc)
- A 1-2 page construction plan and pros/cons of techniques selected (including primers, sequence maps, etc)
- A 1-2 page proposed analytical pipeline
- A 1-2 page discussion of how results may refine solution design/provide additional biological insight
- A 1-2 page discussion of ethics (e.g. biocontainment risks, public perception, ethics of solution)

There will be opportunities for teams to receive feedback at various stages of their project through homework assignments.

Hint: To guarantee feasibility of design and analysis, you are encouraged to limit your proposed systems to no more than 12 elements (regulatory elements like repressor-operator pairs, miRNA-target pairs, reporter proteins etc.).

Due Dates

- ~biweekly homework check-ins to provide project feedback
- December 4 – Presentations and final write up

Grading

The term project comprises 30% of the course grade. This 30% is broken down as such:

Technical Report	**15%**
Problem Description	1
Solution/Insight	2
Design: Model	4
Build: Assembly	2
Test: Analytical pipeline	1
Learn: how results refine design	2
Design: Ethics	2
Format	1

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Presentation	**15%**
Clarity of content	4
Organization/Structure	4
Response to questions	4
Biological insight/design rules discovered	3
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Grades will be assigned on the basis of:

- clarity of content
- motivation for the project
- originality of the proposed circuit or method of analysis
- careful definition of the project scope
- feasibility of the project
- description of the approach to analysis
  - e.g. stability analysis, comprehensive study of the parameter space
- relevance of model to project
- level of model detail, thoroughness
- clarity of statements of any assumptions and the appropriateness of the justifications made for the assumptions

There will also be a peer evaluation to determine how the points will be distributed to individuals. If your team agrees that you only did half as much work as they did, your score will not be more than 50% of the grade according to the rubric above. Similarly, there may be bonuses for teammates that went above and beyond the call of duty as noted by their peers.

Potential Project Ideas

You are encouraged to pursue original ideas of interest to you (e.g. from your research) but may consult igem.org or the list below for inspiration. Be sure to select a project that allows you to ***fully*** demonstrate your newly developed skills, while not plagiarizing from existing projects.

- Sensor for pathogens in food supply (e.g. http://2017.igem.org/Team:TUDelft, http://2017.igem.org/Team:Munich)
- Creating stable microbial communities (e.g. http://2016.igem.org/Team:Imperial_College)
- Wastewater treatment (e.g. http://2017.igem.org/Team:TAS_Taipei)
- Design a bacterial cell that is capable of both self-renewal and differentiation during cell division: one daughter cell remains in a self-renewable, differentiable state while the other daughter cell terminally differentiates.
- Create a cell that can count
- Create the simplest biological circuit that can take three environmental inputs and turn on eight different response systems.
- Create a cell that produces a biofuel whose pathway includes a toxic intermediate
- Design a biological system with a form of simple associative learning.
- Design a bacterium that can circulate safely in blood, recognize arterial plaque, and degrade it. Ensure that it can survive long enough to have an effect yet can be cleared from the circulatory system on demand.
- Simulation of a phosphorylation-only toggle switch, ring oscillator or a relaxation oscillator design.
- Design a predator-prey ecosystem or a rock-paper-scissors type oscillating ecosystem.
- Design and simulation of a cell division counter.
- Design a synthetic system that is robust to mutations (as long as they are below a certain threshold). If the number of mutations exceeds the threshold, then the mutations result in cell death.