IPRO 302: Synthetic Biology: Engineering Novel Organisms
Project Plan

Background

The basis for this Project is a growing body of work in recent years in the development of new organisms, primarily using *Escherichia coli* as a base. To the best of our knowledge, no work of this type has yet been attempted within IIT to date. Our work will be building on the body of knowledge generated from the work of others in this field, and has as its central aim to extend the work into specific results that have not yet been achieved within any institution. Past successes in this field have included the generation of bacteria which flash a certain color, behave as a two state oscillator, or create simple logic gate functions.

Objectives

The overall aim of this project is to use the resources available within the IIT Department of Biological, Chemical, and Physical Sciences to first replicate and then expand on work done by various research groups in the field of Engineering Novel Organisms. We will be tailoring the methodology used in previous work to better fit the model of IIT's IPRO program, though we do not anticipate this having any impact on our ability to generate promising results, as the changes will be primarily administrative. Specifically, the Project aims to first either duplicate work previously done in creating a form of *Escherichia coli* which would flash a specific color with a predictable oscillation, or to conduct a parallel experiment using a different simple observable behavior or different base organism.

Once this initial work has progressed sufficiently, we will begin work on performing more elaborate experiments, which would entail creating a more arresting demonstration of this type of metabolic engineering, such as creating a system by which the behavior is coordinated amongst all cells in a population and so becomes macroscopically observable. If successful, this would represent the first time this particular goal has been achieved anywhere. This represents a long-term goal, spanning at least two semesters, as the work involved is quite complex, and there currently exist no proven data on synchronization. A secondary, though perhaps more realistic goal within the timeframe of a single semester, is the creation of more complex cellular functions than the simple two-state oscillator, such as multi-state oscillators. A parallel goal of the Project is the creation of a software modeling solution to help form logical hypotheses as to the interaction of certain combinations prior to actually creating them.

Expected Results

For the inaugural semester of this IPRO, the extent to which we can succeed is uncertain. We have no benchmarking information from previous work. However, it is likely that we will be able to create at least one organism in the laboratory and complete the design phase of the second set of organisms that can be the basis for work in the next semester. Within the modeling task, this semester should see the creation of a simple modeling solution for certain tasks, suitable primarily for the use of those fairly familiar with the Project. A design and initial work on a larger solution should also be completed, with a partially functional prototype prepared. This design will be carried into the next semester for completion.

Budget

An initial line item is posted in the PRS Database. These costs may need some updating in the future. Our foreseeable costs are all in the procurement of various genetic materials. The components needed for our first iteration of work appear to be, on first review, available within the IIT community, so our initial costs should be low. However, the creation of more complex organisms later may require additional compounds. An offset to this cost is the fact that as biological agents, these are generally renewable resources once purchased, so long as they are maintained correctly.

Scheduling and Milestones

The Project will be largely divided into three functions. The first function is the assessment of the direction of work i.e. the development of a framework concept describing what type of system we would like to create.

There is also the task of actually implementing this by actually creating the target system; this entails the actual lab work. Finally, a theoretical understanding via a computation and modeling environment will be developed to provide a development tool to link the concept with the implementation. Initially these two paths are largely independent; however, once the modeling is functional it will server to guide the lab work.

I. Conception

We should assess how we can improve upon the seminar work to produce a more interesting target. As a guide, improvements will include a more directly observable phenotype, more robust or complex behaviors, more practical systems capable of performing useful functions.

1. Procedural Decision

This phase is primarily concerned with the decision of using either bacteria or yeast. This will be based on equipment and materials available, as well as the relative difficulty of working in either medium. This phase should be very short, presumably within one week

2. Behavior Specification

This phase involved producing a specification lest that describes the novel type of behavior to be produced. For instance, the specification of the inspiration work would be

- produce a bacteria with an oscillating metabolite cycle
- have this oscillation observable by fluorescence

Possible improvements could add things like

- Synchronize this oscillation in a population of cells.

This phase will develop an initial target chosen for practicality that is achievable in a one or two semester IPRO environment, but is also an ongoing process by which new novel or improved products are described.

II. Lab work

The overall goal of this phase is to design and create at least one novel organism. Initially, we will begin to replicate the work already performed, and start construction of the “represillator”. Once the conception work has provided a more definite direction, these construction efforts may be modified.

1. Assessment and Inventory

The first step is to determine what components are needed. Of these, some are certainly available within the IIT community. Those that are not available will need to be acquired from elsewhere, else engineered around. This phase should be completed no later than 14 Sep 2004, excluding any wait time involved in ordering materials.

2. Detailed plan

This activity will entail developing a detailed plan to achieve the target system using various biotechnology protocols. We will develop a detailed list of supplies and equipment needed, and a project plan to describe the multi-step synthesis process.

3. Creation

This is where the true work of the Lab work begins. This phase will involve the creation of a 'simple' test organism, primarily as a proof of concept that we are able to do such work within the facilities here at IIT. Success at this phase should be considered success of the Project for one semester, as getting to this point represents considerable progress for a new project. It would be unrealistic at this point to suggest a timeframe for this phase, as any such prediction would be completely unfounded.

4. Assessment and Continuation

Presuming that Phase 3 is successful with any appreciable time left in the semester, this phase will determine the next step and begin design of a more complex organism. The specific scope of this phase will be determined based on the remaining time.

III. Modeling

The overall goal of the Modeling component is to create a solution for simulating

1. Assessment of Existing Solution

This phase will consist of analyzing existing mathematical modeling software, including, but not limited to, Mathematia, Matlab, and Maple. A determination will be made whether any of these will be sufficient for our purposes, or if a new solution must be created. This phase should be completed no later than 14 Sep 2004.

2. Design and Implementation

Having chosen the back-end for the modeling unit, design of this unit will be conducted. If the creation of a back-end is called for by the judgement in Phase 1, the creation of this back-end must be the priority. This phase will be the bulk of the work in the Modeling component, and as such any timeframe established at this point would be unreasonable.

3. Testing and Integration

This phase will consist of testing the simulation capabilities versus known results and creating a working hypothesis to accompany the work being done in the lab at the time. The secondary function of this phase will be to ensure that new components can be added to the system with ease, and that their behavior with respect to previously catalogued components can be extrapolated.

4. Polish and Scale

In this phase, the anticipated raw functionality will be incorporated into a Graphical User Interface, if this can be accomplished with the chosen back-end. The solution will be modified as needed to accommodate large-scale expansion of the component library. The ideal solution will have no hard limit to the number of components it can keep track of and model.

Individual Assignments

At this stage, only a rough division of labor has been established. To start we have appointed a Team Leader who is James Anderson. We have divided the team into two divisions known as the Cloning Group and the Modeling Group. The Cloning Group lead by Anthony Gaddini includes Phuong Bui, Sushanth Ramakrishna, Anthony Vu and Elizabeth Young. The Modeling Group lead by James Anderson includes Ahren Ceisel, Jason Fessel, Sheryl Lau, and Khiem Nguyen. The IPRO website will be maintained by Jason Fessel and Khiem Nguyen. As we have little experience to draw on for estimating the amount of time and work involved in many of the tasks specific to this project, any specific planning would be premature. As this information is rather important for both the progress of the Project and oversight by the IPRO office, specific tasking information will be available on the Project website as soon as it is established.