Overview

Design
Self-excising ribozymes

Modelling
UW 2010 Staphiscope

Human Practices
Marketing Plan: UW Staphiscope

Outreach
ESQ/Workshops
In-Vivo Protein Fusion Assembly Using Self-Excising Ribozymes
Background

Self-excising Group I Introns
Trans-esterification reactions
Fusion Proteins
Applications

Novel fusion proteins:
Antibody generation

DNA shuffling experiments:
Cry toxins
Experimental Design

Construction at the DNA Level

Functional protein GFP and self-excising elements in Staphylococcus viral phage twort ORF 142.2
Experimental Design

Construction at the RNA Level

- Post-transcriptional modification loops formed
- Loops facilitate splicing
- After splicing, fusion protein code remains
Fused protein expected to fluoresce once translated
Biobricks
Constructs pieced together using following submitted BioBricks
Controls

**Positive**
RFC 53 flanked by GFP 1 & 2

**Negative**
Intervening stop codon does not allow functional protein expression
Modelling
Modelling Fusion Protein Production

• Compute the number of possible fusion proteins
• $P_1 || P_2 || \ldots || P_N$
• $P_1 [P_2, P_3, \ldots P_{(N-1)}] P_N$
• $2^{(N-2)}$ possible fusion proteins
Extended 2010 Staphiscope

- Use is to detect staph rapidly in clinical settings (native Agr quorum sensing system)
- Wished to characterize the amplifier system independent of promoter
  * Would allow for choosing correct promoter based on desired sensitivity
Motivation & Goals

Extended 2010 UWaterloo Staphiscope project

- Amplifier parts characterized by Cambridge 2009
- Different promoter
- Empirical data to evaluate Hill parameters
- Calculate relative promoter units (RPU)

Expected to observe steady increase of fluorescence, eventually plateauing at steady state.
Method

- Assayed promoter activity*
- Cells grown until in exponential phase
- Untransformed cells to determine background absorbance and fluorescence
- Aimed to calculate steady state per cell GFP concentration
  - For both promoters
  - Promoter strength in RPU

*Measuring the Activity of Bio-Brick Promoters using an in-vivo reference standard (Kelly et al.)
Model

- araC represses for the pBAD promoter
- Same inducer-repressor ODE model as Cambridge in 2009
  - Promoter activity as hill function
- ODE model used to describe the transcription of GFP in each cell
- Promoter activity assay result shows RPU is given by (steady state assumption):

\[
RPU = \frac{S_{ss, cell, p}^{SS}}{S_{ss, cell, J23101}^{SS}} = \frac{(dF_{p}/dt)/ABS_{p}}{(dF_{J23101}/dt)/ABS_{J23101}}
\]
Results

- Results were anomalous: too unreliable to be conclusive
- Fluorescence curve obtained did not match predictions by the model
- Observed high initial fluorescence, then drop to lower steady-state value
- Untransformed cells used (BW27783) exhibited higher fluorescence than the transformed cells
Fluorescence time series for cells at 6.4 μM arabinose; depicts abnormality in untransformed cells
Discussion

- Possible presence of other compounds fluorescing in cells
- Untransformed cells appear to be expressing GFP
- Cell settling in bottom of well, and positioning of detector may have skewed readings
- Computational tools designed
Human Practices
Staphiscope

What are the inputs required to devise a marketing strategy:

- Competitive advantage
- Alleviate unfounded stigmas
- Pitch product to both a scientific/non-scientific community
- Utilize a knowledge transfer strategy
Competitive Analysis

BD GeneOhm™ StaphSR Genotype MRSA Brilliance Agar
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<th>FACTOR</th>
<th>STAPHISCOPE</th>
<th>BD GENEOHM STAPHSR</th>
<th>BRILLIANCE MRSA AGAR</th>
<th>GENOTYPE MRSA</th>
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In order for a synthetic biology technology to be competitively advantageous, it must excel in at least one of the following areas:
Avoid "not invented here" syndrome
Patent protection
Develop a commercialization plan
Achieving Public Acceptance

- Supported as part of the New and Emerging Science and Technology Programme
- Expert committee developed and presented a roadmap
- Attributes required in sustaining the field of synthetic biology
Achieving an interdisciplinary network through the development of a knowledge transfer strategy

The “Target Market”: Who do we want to educate?

1) Engineers
2) Industry Representatives
3) Non-governmental organizations
4) Non-scientific Community (ie. Hospital Staff)
5) Decision Makers
6) Natural & Social Scientists
7) Other Funding Agencies
Knowledge Transfer

1. Interdisciplinary Network
2. Sustainable Dialogue
3. Involving Stakeholders in the R&D Phase
4. Knowledge Brokering
5. Building Partnerships
Post-Regionals...

Commercialization Toolkit
Synthetic Biology Commercialization Roadmap
- From Ideation to Sustainability
- Building a collaborative network & utilizing existing business models

Knowledge Transfer Strategy
- From “Waterloo to the World”
- Pamphlets targeted to different stakeholders
Available on the University of Waterloo iGEM Wiki

Present our tools and templates to the stakeholders
- Measure the success of these tools: Have we achieved the concept of knowledge transfer?

Initiate a registry or portal that will store economic tools, templates and content that can be utilized by the synthetic biology community
- Business Proposal/Business Plan
- Budgeting
- Funding Strategies
- Communication Models
- Post-Mortem Analyses

The sustainability of science is achieved through leveraging these tools and analyzing all aspects of the technology’s life cycle.
Commercialization Toolkit

Synthetic Biology Commercialization Roadmap

• From Ideation to Sustainability
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Summary

Without a business framework, a scientific technology’s progression is limited.

The purpose of commercialization is to assess the technological and economic feasibility of a product. In this particular field, the term commercialization is defined from two different perspectives. The first stage of commercialization is educating all stakeholders impacted by the technology which will further help to develop a sustainable and paralleled stream of communication and knowledge transfer between the scientific and non-scientific community.

The second stage of commercialization involves the incorporation of the models, discussions and tools developed in the preliminary stages of the technology development process. This particular stage allows synthetic biologists to gain insight on the economics of their technology, achieve public acceptance and mitigate the stigmas that may arise if a knowledge transfer strategy did not exist. The following is a roadmap that simulates the prospective stages that a synthetic biology technology may undergo. With ample funding, active participation from all stakeholders & a continual level of knowledge transfer, a synthetic biology institution is able to attain a scientific milestone.
## Research & Development Phase

### Ideation

**Phase Description**
This is the stage in which the idea or concept is created. The idea or concept is generally inspired from a desire, need or opportunity recognized by various stakeholders. The purpose of the idea is to devise an improvement or advancement to what currently exists within an industry or relative market.

**What needs to be done?**
- Identify Opportunities
- Brainstorming

**Methods**
1. How do we gather information, collaborate & generate ideas?

**Who needs to be involved?**
1. Engineers
2. Synthetic Biologists
3. Companies that may participate in the use of synthetic biology
4. Members of Academia
5. Ethicists

### Technology Assessment

**Phase Description**
Once the idea is generated, its feasibility must be assessed. This stage is critical in that it defines how the technology is relevant to the impacted stakeholders, and does not only benefit the scientific community.

**What needs to be done?**
- Feasibility Assessment
- Ethics Assessment

**Methods**
1. How do we gather information, collaborate & generate ideas?
2. Roundtable Discussions, Workshops, "Whiteboard" Discussions, Survey, Conferences
3. How do we define the technologies that may evolve post-commercialization?
4. Roundtable Discussions, Workshops, "Whiteboard" Discussions, Survey, Conferences

**Who needs to be involved?**
1. Engineers
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4. Members of Academia
5. Ethicists

### Market Assessment

**Phase Description**
The intended goal during the technology assessment phase is to map out the inputs required to design the technology which is set out to be a relative improvement to what currently exists in the market. Stakeholders should then be able to define its competitive advantage and positioning within its respective market.

**What needs to be done?**
- Identifying Target Market
- Identifying Target Consumer within Target Market
- Define competitive advantage (i.e. What differentiates the technology from what currently exists?)
- Identify Financial Constraints

**Methods**
1. What business tools & models can be leveraged in order to make a competitive advantage?
2. SWOT & PEST Analysis
3. Roundtable Discussions
4. Survey to target market: What are their needs?

**Who needs to be involved?**
1. Engineers
2. Synthetic Biologists
3. Companies that may participate in the use of synthetic biology
4. Members of Academia
5. Knowledge Brokers
6. Business Intelligence Analysts
What is Synthetic Biology?

Connecting Biology and the Community

Synthetic biology is a field of study that combines the fields of science and engineering. It utilizes methodologies, applications and knowledge from the disciplines of mathematics, biology and engineering where Synthetic Biologists aim to develop and design biological systems that serve as an enhancement or improvement to what currently exists within nature.

This field of science will bring forth new technologies that will help to improve current applications within a range of different industries. Synthetic Biology has the capability to resolve several global issues that have currently left imprints of economic and social despair. Thus, the public's reception towards these technologies is a key driver in ensuring that this field is progressive and sustainable.

making life better, one part at a time

Examples of Bio-Systems that Evolved from Synthetic Biology

- Fungus that produces biodiesel
- Microbial platforms for space exploration
- Glucose sensors to benefit diabetes patients
- Anti-freeze proteins for de-icing solutions

Fundamental Units: BioBricks

Our DNA defines our individuality. The genetic code is comprised of a variation of parts that have a designated function that control the level of expression of a gene. Consider building a car with a Lego kit. In order for the Lego car to achieve its function, it requires various parts (ie. engine, wheels, other car parts etc.) Analogously, in order for a gene to be expressed and regulated, it also requires a variety of parts. Synthetic Biology refers to these biological parts as BioBricks. These can be interchanged to optimize the function of an existing gene or synthesize a completely new biological system with a function that is not found in nature. These biological systems are generally inserted into harmless bacterial cells that are able to proliferate and achieve this optimal response.

Let's go back to the Lego analogy. Suppose the car we created was too slow. We can take an engine piece from a car that is relatively more efficient. The fundamental concept of synthetic biology is to create and to store these BioBricks in a registry so that scientists are able to develop these interchangeable systems that can further be implemented in technologies that benefit humankind.
Present our tools and templates to the stakeholders

- Measure the success of these tools: Have we achieved the concept of knowledge transfer?

Initiate a registry or portal that will store economic tools, templates and content that can be utilized by the synthetic biology community

- Business Proposal/Business Plan
- Budgeting
- Funding Strategies
- Communication Models
- Post-Mortem Analyses

The sustainability of science is achieved through leveraging these tools and analyzing all aspects of the technology’s life cycle
Outreach
What we stand for..

- Better understanding of synbio
- Create informative opinions
- How does synbio affect the world?
Grade 12 Workshop

- More than 85 students
- Effect of synbio in biofuels/pharmaceuticals
- Hands-on activities
  - Enviro-pig
  - Design Your Own Pathway
- Possible career paths

Community brick submitted!
Building knowledge
Engineering Science Quest

- Grades 3-6
- More than 100 students

Grades 3-4
How clean are your hands?

DNA extraction
Grades 3-4
How clean are your hands?
Community brick submitted!
Grades 5-6
DNA extraction from cheek cells
Community

Alumni events
Open houses
Growth of current events
Movie night
Facebook/Twitter
Thank you to our sponsors...