2013 Stanford-Brown iGEM presents:

# Accelerating iGEM Through Strategic Construct Synthesis: An Economic Evaluation

In this paper, the 2013 Stanford-Brown iGEM team will argue for a new framework surrounding gene construct development. This paper's target audience is sufficiently funded teams that have a well-developed program but seek to achieve more each summer.

## The Proposal

1. An iGEM team has their project ready 1-2 months before their lab work starts.
    a. Example: Labwork starts sometime in June. The team has their project ready before May. This means they have to order their DNA by end of April at the latest.
2. If using novel parts, the team has a company *de novo* (from scratch) synthesize one construct for each novel part, filling in the rest of the construct with existing parts.
    a. Example: The team is investigating a new promoter. The team orders a construct containing their new promoter, an existing RBS, a fluorescent protein, and an existing terminator.
3. The team orders the synthesis of any other constructs they might use in a genetic system (if the constructs are not already in The Registry).
    a. Example: The team wants to use a repressible/inducible promoter system, so they order 4 constructs that they can later mix and match to make the system they want.
4. Upon starting lab work, the team immediately tests the functionality of their constructs, characterizing any novel parts in the process.
5. The team uses PCR to brick novel parts out of their construct plasmid.
6. For malfunctioning constructs, the team redesigns by swapping out parts, mutating parts, or adding in small alterations like repressors or localization signals.
7. With working constructs, the team assembles systems of constructs to provide unique functionality.

## Notes/Advantages

1. There will be a unique cut site between each part, allowing complete modularity and interchangeability of parts.
2. Teams will *start* the summer with potentially working constructs they can test. They will get around a 3 week head start, which is significant considering the summer is only ~12 weeks of lab time.
3. For Biobricking, it is easier/faster to PCR out of a plasmid than out of genomic DNA.
4. Your novel part will be immediately Biobrick-compatible, as you can have it synthesized with any internal cut sites removed.
5. You can easily get rid of GC-rich sequences, repetitive sequences, or sequences that are difficult to clone or PCR.
6. If your DNA is prokaryotic, you can chain genes (e.g. Promoter, RBS, Gene 1, RBS Gene 2, RBS, Gene 3, Terminator).

## Assumptions

1. Assume $0.20 / bp
2. Assume $50 shipping & handling
3. Assume DNA synthesis companies can subclone into a viable expression vector for your construct with no extra cost.
4. Assume DNA gets to you before start of lab summer work
5. Asssume $10/hr wage if any wage at all (some groups don't have student stipends).
6. Assume half of each student's time in lab is spent actively working on a specific project flow
7. Assume average team size of 10 lab workers
8. Assume team is working on 4 constructs at a time. This is 2.5 students per construct.
9. Assume constructs take 3 weeks to complete (from novel part inception to construct completion/verification)
10. Assume the average construct is 1500 bp
11. Having the construct in pSB1C3 doesn't matter. This only matters for biobricking.
12. Assume DNA synthesis company will fail to synthesize 10% of orders due to complexity/lethality/other.
13. Assume 4-part construct (promoter, RBS, coding region, terminator) with prefix and suffix
14. Assume you would need 4 GBlocks to assemble a 1500 bp construct with 3A Assembly
15. Assume you either get to the lab and are faced with (A) 4 gBlocks that need to be assembled and ligated into a backbone to make a workable construct or (B) a workable construct already in a backbone
16. Assume $100 per student per week in lab costs
    a. Gloves, enzymes, pipette tips, buffers, agar(ose), markers, primers, sequencing, plates, kits, etc.
17. Assume each team needs 5 constructs

## Calculations

1. Ordering a full 1500 bp construct vs. doing it all in-lab vs. ordering 4 gBlocks and compiling
    a. Full DNA Synthesis
        i. 1500 bp * $0.20/bp = $300 for synthesis
        ii. Shipping = $50
        iii. Cost = $350 per construct
        iv. Failure cost = 10% of $350 = $35
        v. **Total cost = $385 per construct**
        vi. Total lag time until working construct: 0 weeks (assuming DNA synthesis complete before summer)
    b. All in-lab
        i. $10/hr/student * 20 hr/wk * 3 weeks = $600 in work costs (per student)
        ii. $100/wk/student * 3 weeks = $300 in materials costs (per student)
        iii. $900/student for 3 weeks of work
        iv. 3 constructs at a time for 6 team members is 2 students per construct
        v. $900/student * 2.5 students/construct = **$2250 per construct**

vi. Assuming work costs are a sunk costs, the marginal cost per construct is the materials cost, which is $100/wk/student * 2.5 students * 3 weeks = **$750 per construct**
vii. Note: the materials cost alone is approximately the same price as the DNA synthesis cost
viii. Total lag time until working construct: 3 weeks

c. 4 gBlocks and 2 sets of 3A Assembly
i. $100/gBlock * 0.50 (iGEM discount) * 4 gBlocks = $200
ii. Shipping = $50
iii. Assuming half the time of normal assembly…
iv. 1.5 weeks of work for 2.5 students = $750 in work costs, $300 in materials costs
v. Total cost = **$1300 per construct**
vi. Assuming work costs are sunk costs, **the marginal cost is $550 per construct**
vii. Total lag time until working construct: 1.5 weeks

The choice between these three work-flows is obvious if the goal to achieve as much as possible and win the competition in the most economic way possible. A team should go with choice (a), which – even if human-work-costs aren't taken into account – is $165 cheaper than the next cheapest option. In other words, the marginal cost per construct is the cheapest when ordered whole from a DNA synthesis company. This makes sense, as the companies have achieved economies of scale and have much lower marginal costs than the average synbio lab.

However, not all treat iGEM purely as a competition. To many, the 3 weeks and $2250 required to make a construct in lab are not wasted. One could easily argue that if learning is the goal, this time and money could be spent either compiling new constructs or working with already completed constructs. It makes little difference if the goal is learning synthetic biology, not winning the competition. The lab is paying for 12 weeks-worth of materials no matter what, so any DNA synthesis orders – though a cheaper option for the build-phase of development – will make the summer more expensive as a whole. This comes from the fact that the leftover materials for the extra 3 weeks will not be turned in for a refund, but rather spent to take the project even further. Labs are hiring 10 students to learn as much as they can in 12 weeks, so why spend extra money when the students will learn the same skills either way? When faced with the previous two economic vantage points (cheaper per construct but more expensive for the summer), many labs will decide that they're doing just fine and won't change their methods.

This is understandable, but I want the reader to consider one point: If you spend a little money now to do better in the competition, you will receive more funding in later years. This will allow you to further expand the synthetic biology community. Thus, in addition to quicker, more cost-effective building of constructs, *de novo* DNA synthesis also offers a way to reach more students in later years and spread the teachings of synthetic biology to a larger audience. This last point makes our suggested pathway an extremely enticing option for the majority of existing iGEM teams. We hope the reader takes our calculations and assertions into account when planning their team for next year.