I have very broad research experience, in chemistry, aerospace, computer science, and more. However, there is a unifying theme: I build tools for addressing new questions in biology. Along the way, I have taken on high-risk, technically challenging pilot projects; some of them failed, but I got better quickly. These experiences have prepared me to succeed in the highly interdisciplinary fields of systems biology and synthetic biology.

HIGH SCHOOL RESEARCH: VEDERAS LAB *(Chemistry - University of Alberta)*

After my junior year of high school, I was given a chance to do summer research in medicinal chemistry. I would be helping a postdoc synthesize possible inhibitors for a SARS virus protease. Specifically, I was to make a known compound as starting material - from a protocol published in the 1890s. There seemed to be good reason this compound had never been heard from again; I got all sorts of colorful muck, but none of it was the right muck. As I combed through century-old journal articles looking for clues, I saw their ignorance as well as my own, and understood that this was part of what it meant to do real science. Some of the compounds I pulled from the muck showed some activity; they went into a publication, and I was made 4th author.

UNDERGRADUATE RESEARCH: MARS GRAVITY BIOSATELLITE *(MIT)*

During my first three semesters of college, I worked for a student-run group developing small animal habitats for unmanned research satellites. The goal was to advance space life sciences by enabling cheaper data collection. I worked on an automated system that preserved urine samples for post-flight analysis, refining the design and overseeing a six-week ground trial. Because the design teams were spread across three continents, I wrote several white papers documenting my findings. I also presented at a NASA design review and gave a conference poster. Along the way, I helped give space workshops for young Scouts and supervised a high school intern.

UNDERGRADUATE RESEARCH: ENDY LAB *(Bioengineering - MIT)*

As my research skills matured, I joined the Endy lab to pursue a long-held interest in synthetic biology. I would be attempting to optimize DNA coding sequences to resist mutation. Because exogenous genetic parts often slow growth, mutants can take over a bacterial culture in a matter of hours. Stable parts would help address this problem. I searched the literature for sequence-specific factors and put together a pilot version of the optimization code. However, the available sources suggested that any improvement would be small. With my agreement, the project was dropped.

UNDERGRADUATE RESEARCH: KNIGHT LAB *(Computer Science - MIT)*

I joined one of Prof. Endy's collaborators, studying the mycoplasma *M. florum*, which has perhaps the smallest genome of any non-pathogenic organism. This trait makes it useful for systems biology. Prof. Knight hoped to put its genome (800kb) into yeast as a synthetic chromosome, so it could be manipulated more easily. No one in the lab had worked with yeast before. Using protocol books, I taught myself how to prepare and transform intact chromosome-scale DNA.

Fortunately, an easier plan emerged. A graduate student was able to transform *M. florum* with a resistance marker, raising the possibility of editing its genome in situ. This is routinely done in *E. coli* with lambda RED, phage-derived recombinases which promote integration of foreign DNA into the genome. Distant relatives of this phage infect mycoplasma. Using published genomic data from the *M. florum* clade, I was able to identify several "fossil" phage sequences and reconstruct the original RED-analogue genes. I then helped train the student who continued this project.

RESEARCH ASSISTANT: CODON DEVICES *(Startup - Cambridge, MA)*

My professional work began here, as an intern in Process Development. The company wanted to use microarrays as an oligonucleotide source for DNA synthesis. My job was to optimize each step of the protocol, then put it into production. I had never used high-throughput automation

before, but I had the manuals, and full access to the production facility after the night shift. I often watched the sun rise over the industrial park as I programmed robots and tested protocols. I got the process working months ahead of schedule, and also found ways to make it cheaper.

My boss asked me to investigate microarray strategies for repetitive or GC-rich sequences, which fail in standard PCR assembly. In production, these sequences were diverted to a ligation-based assembly process. Unfortunately, as my boss explained, the process didn't work. It generated so many errors that finding the correct product required dozens of clones. Worse, the process had been down for months; the oligo vendor changed its brand of 96-well plate and nothing had worked since. Intrigued, I persuaded the production team to give me the protocol. It was standard kinase/ligase treatment, but with very high levels of enzymes.

Following a hunch, I checked the assembly design software, and quickly spotted the problem. The software chopped its target sequences into short ligation fragments, complementary oligo pairs with single-stranded ends. The fragments had recessed 5' ends - a hindered substrate, which the kinase virtually ignores. The 5' ends would be phosphorylated only if the oligos were poorly annealed or had defects causing "float" at the ends; since ligase requires a 5' phosphate, only defective fragments were assembling. This explained the reliability issues and high error rate. With accessible 5' overhangs, the process worked smoothly, removing a major bottleneck.

Codon Devices broke a hiring freeze to keep me when I graduated. They had shifted their focus to synthetic biology design services, launching several ambitious projects in metabolic engineering. The Product Development group, a fresh PhD and myself, handled the biology R&D; I also provided data analysis and automation support. Seven months later, the money ran out.

RESEARCH ASSISTANT: FISHER LAB *(Dermatology - Massachusetts General Hospital)*

Since June 2009, I have been a technician in a melanoma research group. I was hired initially to prepare cell cultures and order supplies. However, soon after I arrived, they fired the sysadmin; he broke the department's server on his way out. My PI had several terabytes of data on that server, most of it not backed up. Fortunately, both the previous technician and I had grown up around computers. We recovered the data and rebuilt the various IT services that were on the server. I then handled computer support for six months until a new sysadmin could be hired. During this time, I set up a proper off-site backup system and showed users how to sync to it automatically.

When the department launched a new core facility for drug screening, I was asked to participate. I have been working on a screen of melanocyte growth in a skin analogue, optimizing assay conditions and developing custom image-based analysis methods to track the rare melanocytes in each sample. I have also written a program to classify tumor sections based on immunostaining intensity, and will soon write another to quantify fluorescence colocalization.

My training has given me the confidence to take on anything - and the skills to back it up. In graduate school, I will refine these skills as I train to become an independent researcher.

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