Conference Report

Four perspectives on business model evolution in synthetic biology

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INTRODUCTION

Back in 2010 in these same pages, managing editor, Yali Friedman asked: Is the biotechnology industry ready for a new business model?[1]

Historically, the industry had three models, the fully integrated life science company (or FILCO), the platform company, and the hybrid. The FILCO model is best characterized by Amgen and Genentech, early biotech pioneers that built large vertically integrated companies.

The platform company developed a technology platform–a tool, equipment, or software—licensed it out or sold it. This business model is similar to technology platform companies, where a firm develops a technology that can be sold to other research and development firms or is split up and sold off piecemeal, ultimately generating more total value. In the 2010 OECD Workshop on the Outlook of Industrial Biotechnology, platform companies were also categorized as service providers.

The hybrid model combined product development with a technology platform that could be sold or licensed to others. This model was especially popular in the years leading up to and after 2000, and could be best characterized by Human Genome Sciences and Millennium.

Since biotechnology is a young industry, funding sources change, and corporate interest wax and wane, new business models emerge without necessarily replacing the older ones. Most recently, the biotechnology industry is beginning to, according to Ryan Bethencourt of Berkeley Biolabs, "benefit from a digitization of biology, the maker movement, quantified self, grinders/transhumanists, crowdsourcing… a resurgence in local production technologies like 3D printers… biotech equipment at 1/10th to 1/1000th the cost"[2] and cheap outsourcing.

Is the business of biotechnology on the verge of radical disruption? To find out, we interviewed the CEOs of three synthetic biology companies and a futurist in biological technologies to find out.

Tim Fell: Synthace is an applied synthetic biology company focused on making valuable chemicals and biologics cheaper and faster than existing companies. We create and capture value by being more efficient and decreasing the cost of goods.

At the moment, we are making known molecules and we're not doing research into novel chemicals. That will come in the future.

Jamie Bacher: Pareto Biotechnologies utilizes a specific polyketide pathway and related technologies to develop new designer molecules. Our first products will be high-value chemicals. As the technology develops we are looking to other areas as well.

Omri Amirav Drory: Genome Compiler is focused on developing software for the engineering of biology. People can use our design software on our website to design, build and test biologically engineered products. People can buy their DNA and bioinformatics directly from the software. Our model is designed to bring products to market faster.

1 Friedman, Yali. "Time for a New Business Model?" Journal of Commercial Biotechnology (2010) **16,** 1-2. doi:10.1057/jcb.2009.33

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2 Bethencourt, Ryan. Biotech's Cambrian Era. BioCoder, Fall 2013. Accessed at http://programming.oreilly.com/2013/10/biotechs-cambrian-era.html

Andrew Hessel: Autodesk has a long history of offering stand-alone 3D design software running on desktops or servers. Over the past ten years, the company moved many of its products to the cloud. Today, we offer a wide variety of powerful design tools and applications that are available online, via an Internet browser. We support the idea that software should be easy to connect to, easy to use and are actively working to democratize technology. Now, we're using that approach in the development of software tools for biotechnology and nanotechnology.

JOCB: Could you describe your current business model?

Tim Fell: Synthace is primarily pursuing a licensing model where we engineer microorganisms and bioprocesses to produce a specific chemical. We develop those strains within partnerships where our partners will either use and/or sell the products they produce. Our ideal partner brings scale-up expertise and a route to market, but also shares their intimate knowledge of the specialty chemical industry because without such information it can be a challenge to understand the pain in the marketplace and which products to target.

Jamie Bacher: We have a technology—a platform—that's very broad. We will use our technology to develop valuable products with partners, that they can quickly move to market, then leverage the technology development that goes into those products to fuel additional technology developments and additional products. Where a lot of other companies backed into this strategy, we are going forward with it.

I think of the model as an expanded Elon Musk model because he not only founded Tesla but Space-X. The Tesla model was to sell a high-end roadster to a very small market then to use that funding to develop a family sedan that you can sell to everyone. The model allowed for rapid feedback from the marketplace and is a model that is more analogous to a software or web development company using lean principles.

The parallel for biotechnology is that we sell high-valued products like flavors, fragrances, or cosmetics and use the funding from those to develop and refine a technology platform. Pareto is going after high-value products first, where we can do 20 percent of the technology development and get 80 percent of the output value. The Musk model is to then leverage that into commodity chemicals (the family sedan) or into therapeutics (the rocket).

Omri Amirav Drory: We are a startup, so our business model will likely change. Right now, our core business is focused on developing the software on our website. People have access to it as a software-as-a-service (SaaS) and customers can pay for the full software package. They can just pay as they go or they can pay only for features that they want. In addition we offer a marketplace where people can share and buy DNA and other services.

JOCB: What are some challenges faced by synthetic biology companies?

Tim Fell: There seems to be a revolution brewing as we start to further professionalize, standardize and digitize the biotechnology industry. Biotechnology's biggest challenge is that it is still very artisanal. We are now further along in bringing engineering principles to the field, in being able to create more complex bio-organisms faster, and in scaling up production, but there is still much work to do. This type of transition occurred in most other industries a long time ago, biotechnology has taken bizarrely longer.

Jamie Bacher: For companies that are young and small like Pareto, one challenge is how much you outsource versus how many people you hire since that will have a real effect on your company culture. Having been at several startups, I understand that culture is hugely important and not to be underestimated. It's something every company has to figure out for themselves. In other words, at what point are you trading off efficiency for culture building, at what point are you trading efficiency for building in-house capabilities that in the long run might not be that important for you?

Omri Amirav Drory: The biggest challenge is market maturity. Genetic engineering is not a new market. In the U.S., it's estimated at $350 billion with PWC conservatively estimating the global biotechnology market will be $1.2 trillion by 2020. Synthetic biology or the use of synthetic DNA very much depends on the price of DNA, which has been decreasing rapidly. Today, the price of DNA synthesis is around 25 to 30 cents per base pair. In the next year or two, we will see an infection point where people will move from traditional PCR-based cloning towards the use of digital tools and synthetic DNA. They will outsource most DNA synthesis and construction. People will do more designing and testing, and less construction.

Andrew Hessel: The rate-limiting step for biotechnology is manual work at the lab bench and software tools that accurately connect to bench research. At Autodesk, the Bio/Nano/ Programmable Matter group is developing

powerful software tools that can take big data as an input and also directly connect to robust printing tools. Today, 3D printing tools are available for a variety of materials including living cells and even DNA. As laboratory hardware and software become more integrated, the rate-limiting step will disappear quickly.

JOCB: What are some emerging opportunities or innovative ideas in the synthetic biology industry?

Andrew Hessel: The one that I love sharing is Glowing Plant. It is not that expensive to make the genes that will make something glow. Doing that work in the plants has gotten easier. The founders of Glowing Plant wanted to make an ornamental glowing plant and found the existing regulations allowed it. They didn't have much money, so they ran a Kickstarter campaign. Kickstarter served as a focus group for them and not only showed there was a market for glowing plants, but helped them raise almost a half million dollars.

Omri Amirav Drory: We started the Glowing Plant project that raised half a million dollars on Kickstarter in 2013. One of our European users, a DIY hacker wanted to make a glowing plant and built different designs on our platform. He didn't press the "Buy" option on the web site because he didn't have the money to pay the few thousand dollars for the DNA. We thought why not do that because it's feasible and done dynamically. The science isn't new.

The experience shows you don't have to be in academia or in industry to start a biotechnology company. You can be a couple of kids from California, build it online, crowdsource the funding, then built it. I met Anthony Evan, the project lead at Singularity University. Kyle Taylor, the Chief Scientific Officer, studied plant biology in Stanford. Genome Compiler gave the two of them a lot of support. The result caught the imagination of a lot of people and caused a lot of uproar. Now, they are trying to commercialize the technology. Genome Compiler has other, similar projects in the pipeline.

JOCB: What business models do you see emerging?

Andrew Hessel: There are a few. Glowing Plant is one of the best examples to date in the startup space. I see another model emerging for cancer. We know today that once you've been diagnosed with cancer it never really goes away. The oncologists take their best shot, and then the waiting game begins.

A more logical way, particularly with early detection, might be to treat cancer continuously, starting by killing the weakest cells and just keep knocking them back, the way you might prune a tree or a bush. Managed this way, cancer might never reach a point where it crashes major organ systems. This would require customized medicines, programmable for each cancer, that are easy to update if the cancer develops resistance. Computer-generated synthetic oncolytic (cancer-busting) viruses are one possibility.

A treatment model that provides a steady stream of targeted drugs personalized to individuals and their cancer is like Netflix, a subscription business, where you subscribe to a process rather than just purchase one single drug.

Another business model is more familiar: advertising. About seven or eight years ago, I pointed out that if you put genetic code (such as "ATGGCATA…" and so on) into a Google search, you got no result whatsoever. That surprised me. Why didn't it tell me if it matched a known gene, genome, or marker?

I expect that as more people get their genome and microbiome sequenced, Google and other groups will match my results to products or services linked to that information. The mix of bacteria in my mouth might determine which toothpaste I might want to buy, or my skin type the soap or shampoo. I expect to see this type of genetic marketing to begin appearing very soon.