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# Synthetic Biology Annual Investment Report

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www.synbiobeta.com

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# Executive summary

Synthetic biology startups are attracting venture funding in record amounts, with $1.9 billion making 2018 the largest year ever – and that's only counting deals closed by early August. Even with more almost five months left in 2018, this represents 73% growth over 2017. As in the last four years, half or more of the funding went to later-stage (more mature) companies. The exceptional year of 2017 saw a drop in funding amount, but a sharp rise in the number of companies funded (56, compared to 48 in the previous year). Thus we see mature synbio companies continuing on an expansion trajectory, while a new wave of early-stage startups promises continued growth and innovation in the future.

# Methodology

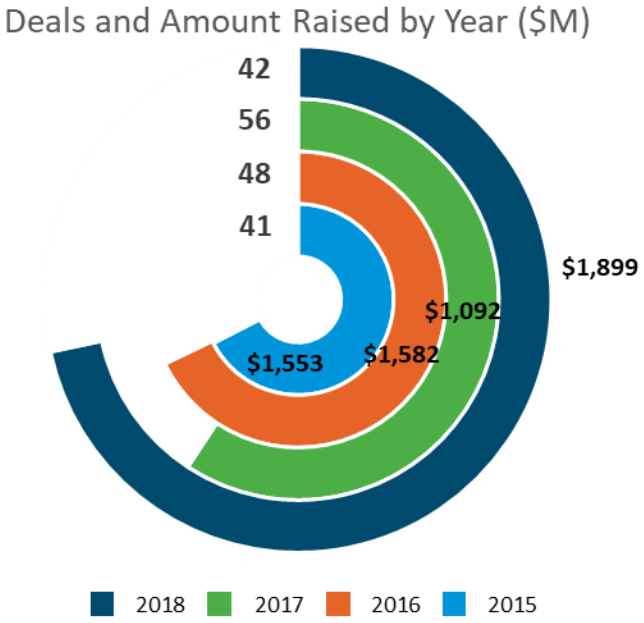
This study of venture funding activity seeks to understand investment trends into synthetic biology startups, the reasons behind them, and both prognosis and recommendations for the future. It was conducted by SynbioBeta, Silicon Valley Bank (SVB), and InnovationLab,[1] and covers the years of 2015-2018 (2018 through 8/7/2018). Using data from PitchBook, media and press releases, company interviews, and SVB proprietary data, we found 187 deals in 115 companies for a total of $6.1 billion dollars, supplied by 501 investors. Unless otherwise specified, we divided the analysis into Early stage (Seed, Series A, and Series B) investments and Late stage (Series C and later).

# Findings

Synthetic biology startups are attracting venture funding in record amounts, with $1.9 billion making 2018 the largest year ever – and that's only counting deals closed by early August. Even with more almost five months left in 2018, this represents 73% growth over 2017. In total, synbio venture investment for the nearly four-year period totaled $6.1 billion, with early-stage investments accounting for $1.96 billion (32%) and late-stage $3.5 billion (57%).[2] Year-on-year growth was volatile, with flat (+2%), plunging (-31%) and soaring (+73%) changes in investment amount.

[1] None of the companies that conducted the analysis are investors in the space. However, all of them do business with startups, investors, or both. John Cumbers is a seed fund investor through DCVC/Data Collective.
[2] An additional $665 million (11% of total) was not specified as to stage.

Figure 1: Deals and amount raised, by year




# Trends by Year

In all of the last four years, half or more of the funding went to later-stage (more mature) companies. 2018 is already the biggest year on record, with $1.4 billion in late-stage investments. The exceptional year of 2017 saw a drop in funding put into both early and late-stage companies - despite a sharp 26% rise in the total number of companies funded (56, compared to 48 in the previous year).

It's well-worth noting that any analysis of synthetic biology investment trends will be greatly influenced by two factors: large deals, especially in biopharma and later-stage rounds; and the definition of synthetic biology used to choose the companies included. In this case, Moderna Therapeutics had an outsized impact. Without the inclusion of Moderna, the data is closer to steady year over year (2015: 40 deals $1,103, 2016: 47 deals $1,108, 2017: 56 $1,092, and 2018: 40 deals $1,274). Synthetic biology companies don't always move together as a more conventional asset class – say, oil stocks – would do, so it's critical to understand each individual company as well as the field as a whole.

What does a deeper dive into Moderna reveal? The company makes biotherapeutics, specifically messenger RNA (mRNA) to treat a wide variety of conditions. We consider it more specifically as a synthetic biology company for two reasons:

1. they use in vitro transcription, not in vivo, to synthesize the mRNA
2. they use a non-naturally occurring nucleoside (initially 1-methylpseudouridine, now a new undisclosed one) to help their mRNA dodge the immune system

In-vitro transcription means that the mRNA is synthesized outside of living cells. This cell-free manufacturing can greatly boost both flexibility and output efficiency, meaning that the process is easier to change and easier to scale up, and is commonplace among synthetic biology companies.[3] Using a non-natural nucleoside is also a more common practice in the synthetic biology field, compared to conventional biopharma that tends to use naturally-occurring ones.[4] Edge cases like Moderna thus help explain how investors should think about synthetic biology as a category and about individual firms.

Figure 2: Amount Raised By Series and Year

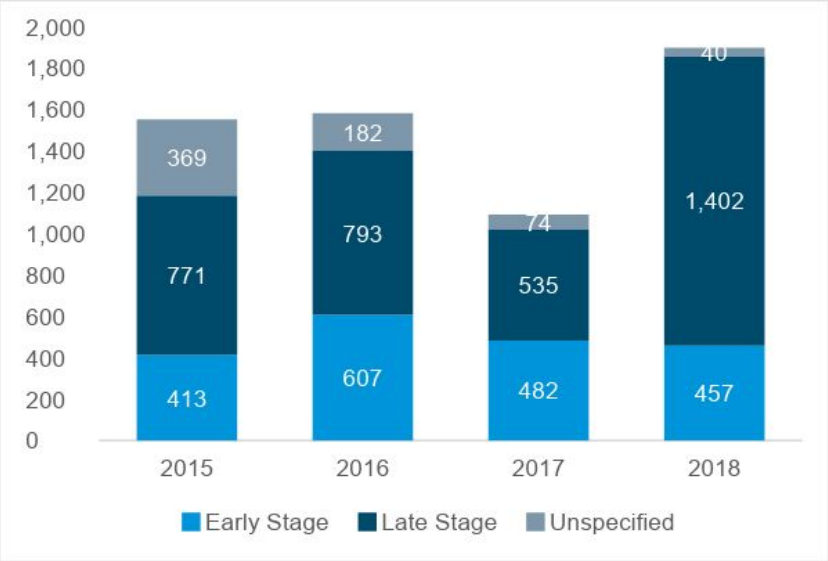
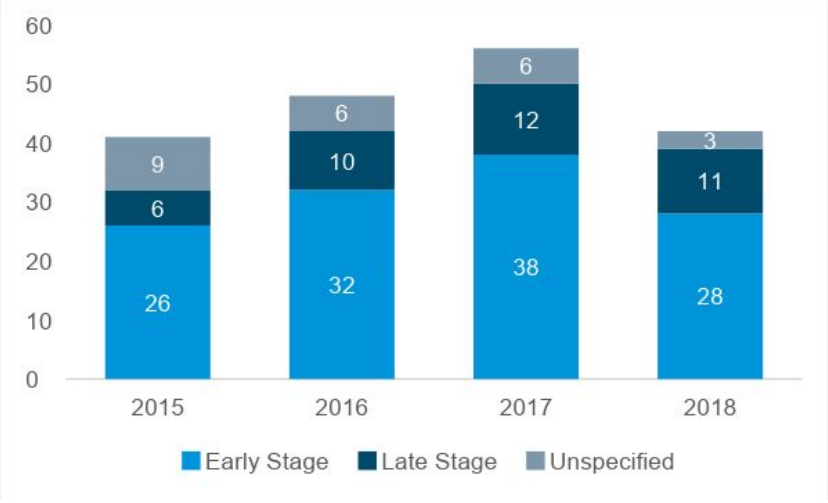



Figure 3: Number of deals by stage and year




[3] See for example https://www.sciencedirect.com/science/article/pii/S2405805X1730008X
[4] See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3152792/

# Post-Money Valuation is unpredictably volatile

An analysis of the post-money valuations over time shows abrupt changes in every segment, but especially at the high end. The highest-valued companies saw valuations exceed $18 billion in 2018, more than 10 times 2017's level, due to deals like Moderna raising $125 million at a post-money valuation of $18 billion. Yet 2017 was artificially low, with top valuations just one-third of 2016's $4.8 billion, as a larger number of new companies brought average investment numbers down.

Figure 4: Valuations (in $ million) of Quartiles, Top, Median, and Lowest synthetic biology firms

| Quartile | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|
| High | $3,000 | $4,749 | $1,375 | $18,125 |
| Q3 | $100 | $149 | $97 | $373 |
| Median | $56 | $50 | $48 | $79 |
| Q1 | $25 | $18 | $18 | $35 |
| Low | $3 | $5 | $6 | $10 |
| *n=* | *27* | *34* | *38* | *22* |

# Startups

Venture funds are only meant to sustain a company for a relatively short period, and about half of the companies in this four-year study raised money more than one time. Three companies (BiOWiSH Technologies, Ginkgo Bioworks, and Moderna Therapeutics) saw four deals, while thirteen companies saw three deals, 37 saw two, and 62 companies only had one transaction. The companies that saw four deals illustrate the wide range of industries synthetic biology addresses, as well as the span of company sizes from small to large:

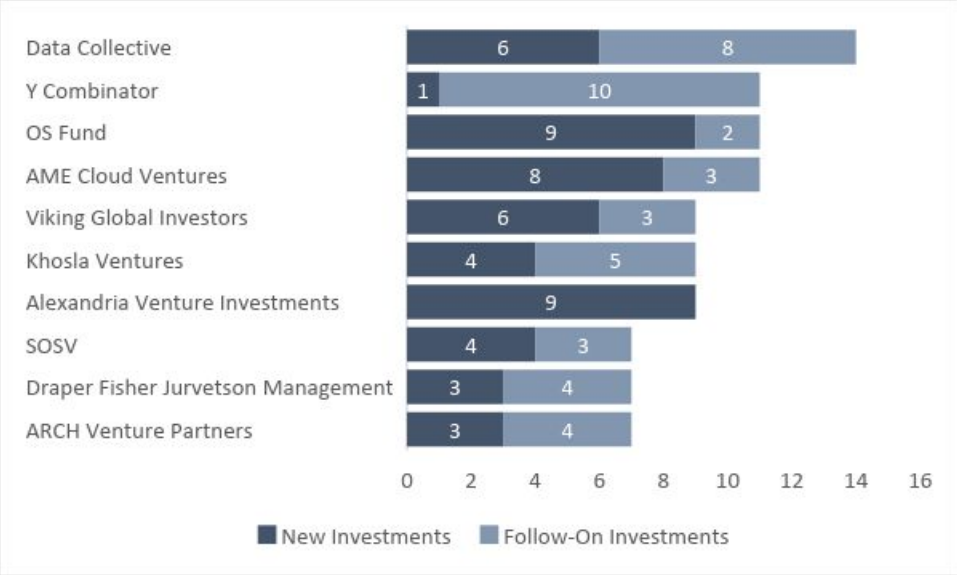
- **BiOWiSH Technologies** is developing microorganisms for applications like environmental management (treating eutrophic pools), agri-business (hydroponics), and consumer products (food production). The company has raised $27.2 million to date, including two rounds in 2017.
- **Ginkgo Bioworks** is an organism engineering company that has raised $429 million in venture investment. While not a direct equity investor in Gingko, the company has a strong relationship with German chemicals manufacturing giant Bayer; together, the two have a $100 million joint venture Joyn that is developing agricultural biotechnology.
- **Moderna Therapeutics** (as noted above) is developing new drugs based on messenger RNA (mRNA) to treat indications as different as infectious diseases and cancer. Its

investors include collaborators like Merck and AstraZeneca, and since its founding in 2011, they have put more than $1.6 billion into the company.

# Investors

There are just over 500 investors funding synbio startups, but ten of them (ARCH Venture Partners, Draper Fisher Jurvetson, SOSV, Alexandria Venture Investments, Khosla Ventures, Viking Global Investors, AME Cloud Ventures, OS Fund, Y Combinator, and Data Collective) are the most active, collectively participating in 95 of the 187 deals. The most new investments (9 each) came from OS Fund and Alexandria, while Y Combinator was most active in follow-on investments, making 10 deals.

Figure 5: Top investors (by number of deals) in synthetic biology firms




# Analysis

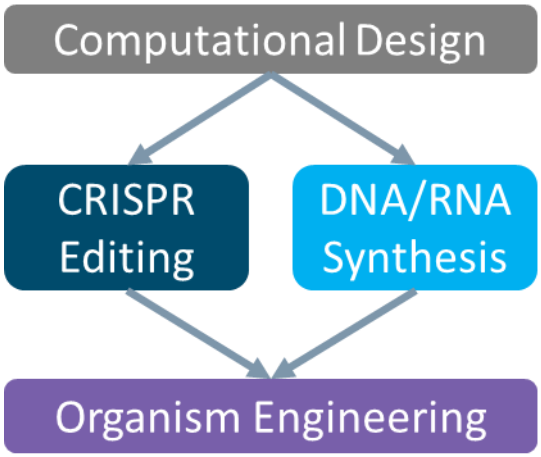
Looking at the huge $1.4 billion return to late-stage investment in 2018, we see mature synbio companies continuing on an expansion trajectory. At the same time, the large number of early-stage companies being funded in 2017 represents a new wave of early-stage startups that promises continued growth and innovation in the future. How should investors think about synthetic biology as a class – not just looking at individual stars like Moderna, but what drives success for Moderna and the field as a whole? Why do synthetic biology startups need each other to succeed?

Key to both established and new startups' success are the new tools driving synthetic biology's core. While many companies are focused on applications like Moderna is, large-scale synthetic biology is being simplified by innovations like CRISPR editing and machine learning.

Application-centric investment built around genome engineering is leveraging these groundbreaking technologies, much in the same way that all of information technology – from videoconferencing to autonomous vehicles – leverages advances in silicon chips or fiber optic networks. If Moderna is developing end-use applications (like, say, Facebook or Netflix), the infrastructural equivalents of Intel and Cisco in synthetic biology are companies like Zymergen, Twist Bioscience, and Gingko Bioworks, each of which has gained well over $100 million in investment. Of these tool developers, there are four main segments we examined:

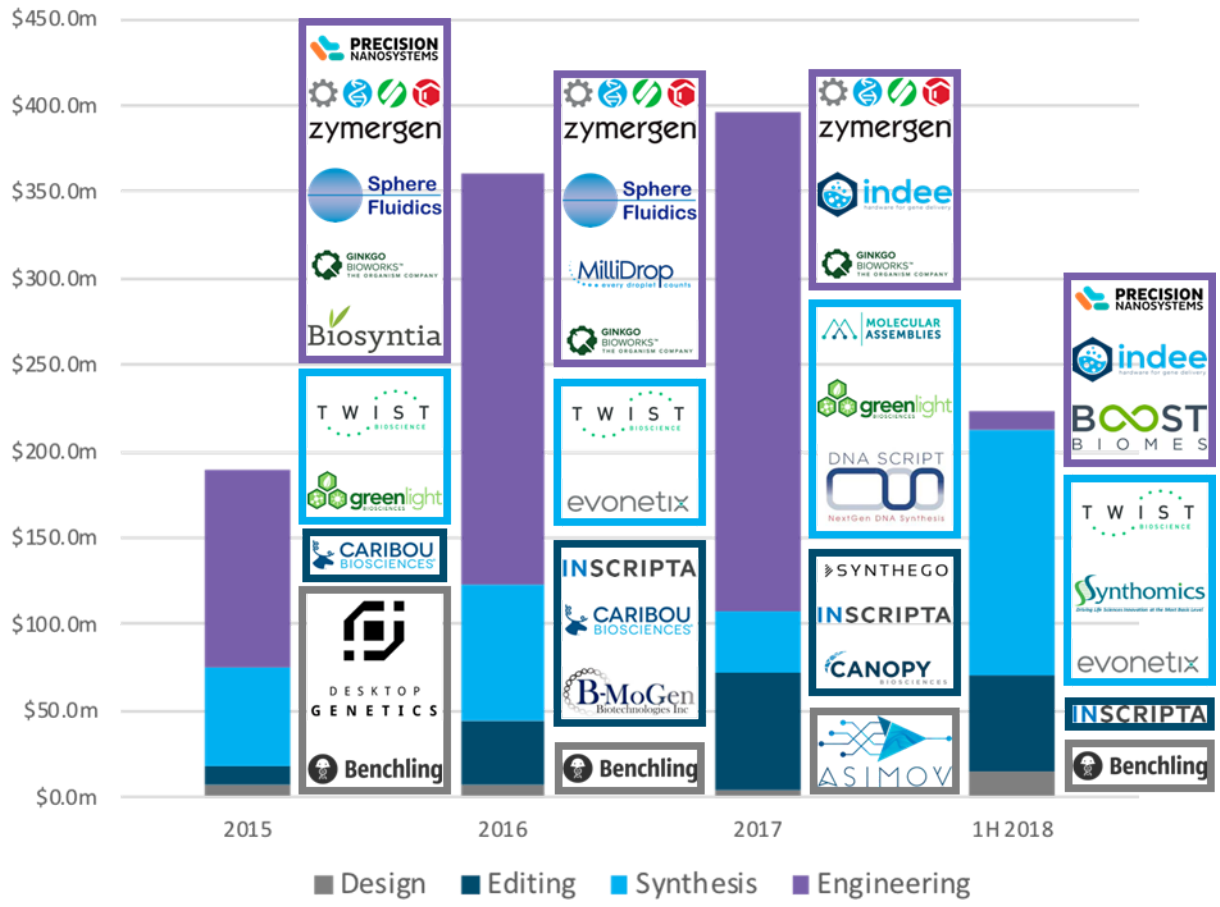
- **Computational Design.** Computational design technologies provide data-backed suggestions for optimizing experiments. For example, Arzeda which uses advanced computation to engineer enzymes for producing industrial chemicals and crop traits, raised $15.2 million in 2017.
- **CRISPR Editing.** CRISPR editing technologies simplify gene modifications. CRISPR pioneers Caribou Biosciences raised $30 million in 2016, in a Series B round than included Novartis, Mission Bay Capital, and 5 Prime Ventures.
- **DNA/RNA Synthesis.** DNA/RNA synthesis technologies create DNA/RNA without cells. In 2018, for example, Twist raised $125 million and Evonetix raised $12.4 million.
- **Organism Engineering.** Organism engineering technologies introduce DNA/RNA or editing tools into cells or organisms. For example, Pivot raised $16 million in 2016; Ginkgo (mentioned earlier) raised $275 million in 2017.

Figure 6: Key subsegments of synthetic biology tool developers




Focusing on these four tools developers, our analysis of investment by subsector showed that investment has been rising steadily since 2015, to nearly $400 million last year (which it is set to surpass in 2018). The figure below shows overall funding amounts in each segment, along with logos of some of the leading companies in each field.

Figure 7: Amounts raised by year by synthetic biology tool development firms




# A Revolution in DNA/RNA Synthesis

Drilling deeper into the DNA/RNA Synthesis space, we see different technical breakthroughs leading to better, faster genetic engineering – which advances the field as a whole. Like DNA sequencing before it, exponential advances in the cost and speed of synthesizing DNA are following "Carlson Curves" – the genetic equivalent of Moore's Law. As with semiconductors, the improvements in core technology benefits not just the companies *making* the technology, but the ones *using* it as well. The breakthroughs (and companies achieving them) generally fall into hardware advances and biochemistry advances.

Hardware advances are new devices, structures, and materials that improve the process of synthesizing DNA and RNA. The benefits that brings has boosted investment in companies like:

- **Twist Bioscience**, was one of the first to make high-throughput DNA/RNA synthesis possible with semiconductor-based technology. It has raised $259 million since the

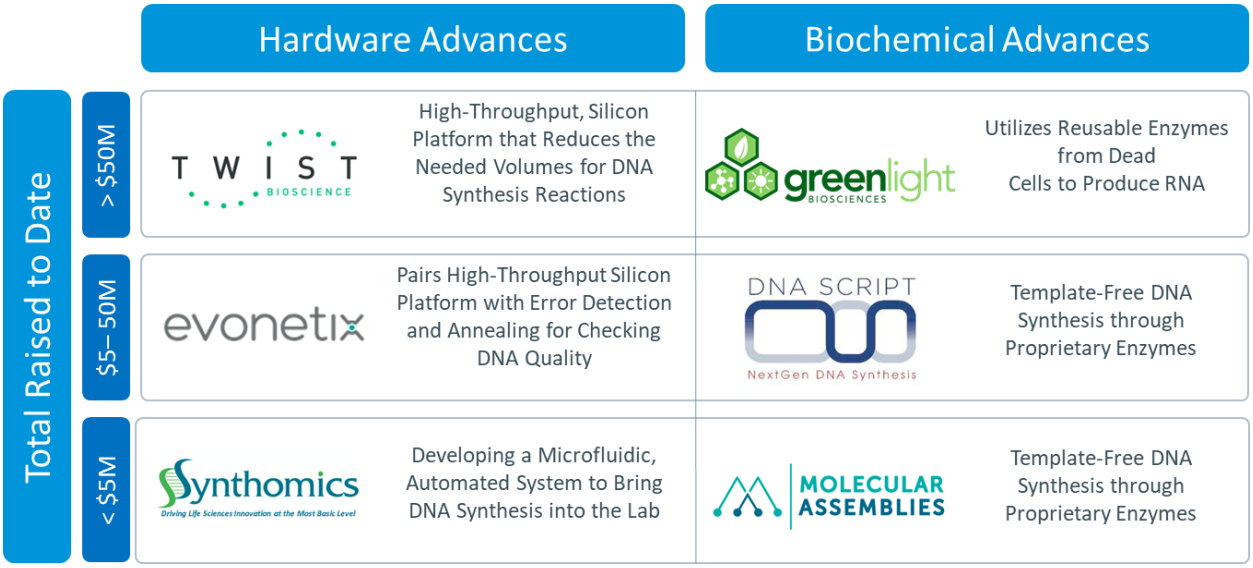
company's founding in 2013, and counts data storage (using DNA like a hard drive for archival storage) among its applications, with Microsoft as a key partner.

- **Evonetix**, also uses semiconductor technology for synthesizing DNA, integrating multiple reaction sites on the chip surface to control synthesis, and then error-checking the synthesized DNA. The company raised $12.3 million in its 2018 A round – a very healthy amount for a company just entering the field.
- **Synthomics**, which aims to bring synthesis capabilities into labs by automating the entire process in a microfluidics-based device, raised $4.6 million in 2018.

Biochemical advances are more about the use of novel enzymes to avoid error-prone synthesis steps. Some examples include:

- **Greenlight Biosciences**, which utilizes reusable enzymes from dead cells to produce RNA, raised $18 million in a 2017 series D, from investors that included Syngenta.
- **DNA Script**, a French startup which creates template-free DNA synthesis through proprietary enzymes, raised $13.1 million in 2017.
- **Molecular Assemblies**, which synthesizes template-free DNA with proprietary enzymes, raised $6.5M in 2018, following on a $2.3 million seed round in 2016.

Figure 8: Hardware and biochemical advances in synthetic biology startups



# Recommendations

- **Be mindful of the distinctions between applications and tools in assessing synbio investment.** As our analysis showed, there are many companies like Moderna using synthetic biology for a particular application. Those companies' valuations should be based in a traditional way, looking at their progress towards a market, the size of that market, the share they can capture, and the price/cost performance they can achieve. That's a very different proposition than the companies making the tools that enable synthetic biology. Twist, Caribou, and Synthace are literally creating markets that did not exist before. That carries greater risks, and potentially greater rewards, but above all it obliges investors to understand their technology and not just the end market.
- **Look to invest in next-gen applications and tools companies in 2019 and 2020.** The large group of 56 companies that raised capital in 2017, includes early-stage firms that will need more to advance to their next stage, which should happen in the next two to three years. For example, eGenesis' $38 million Series A in 2017 sounds large, but the company's ambitious goal (using gene editing to make pig organs amenable to human transplantation) will certainly require more support. On the tools side, Synthace closed a Series A round of £7.3 million ($9.6 million) is developing software to help automate gene design and production.
- **Corporations should continue to enter the space, both as investors and collaborators.** Synthetic biology is already having an impact on industries beyond pharma and fuels – chemical manufacturing, food and beverage, consumer products, and agriculture are up next. Large global companies in these fields should be actively engaging with synbio startups in order to keep pace with the technological shift – or even lead it. Gingko's collaboration with Bayer on agriculture is one example, but the company is also working on breakthroughs in flavors and fragrances used in consumer products like toothpaste and deodorant. Ecovative and Bolt Threads are working on novel performance materials (based on mycelium and spider silk, respectively) that are being used in buildings and apparel.