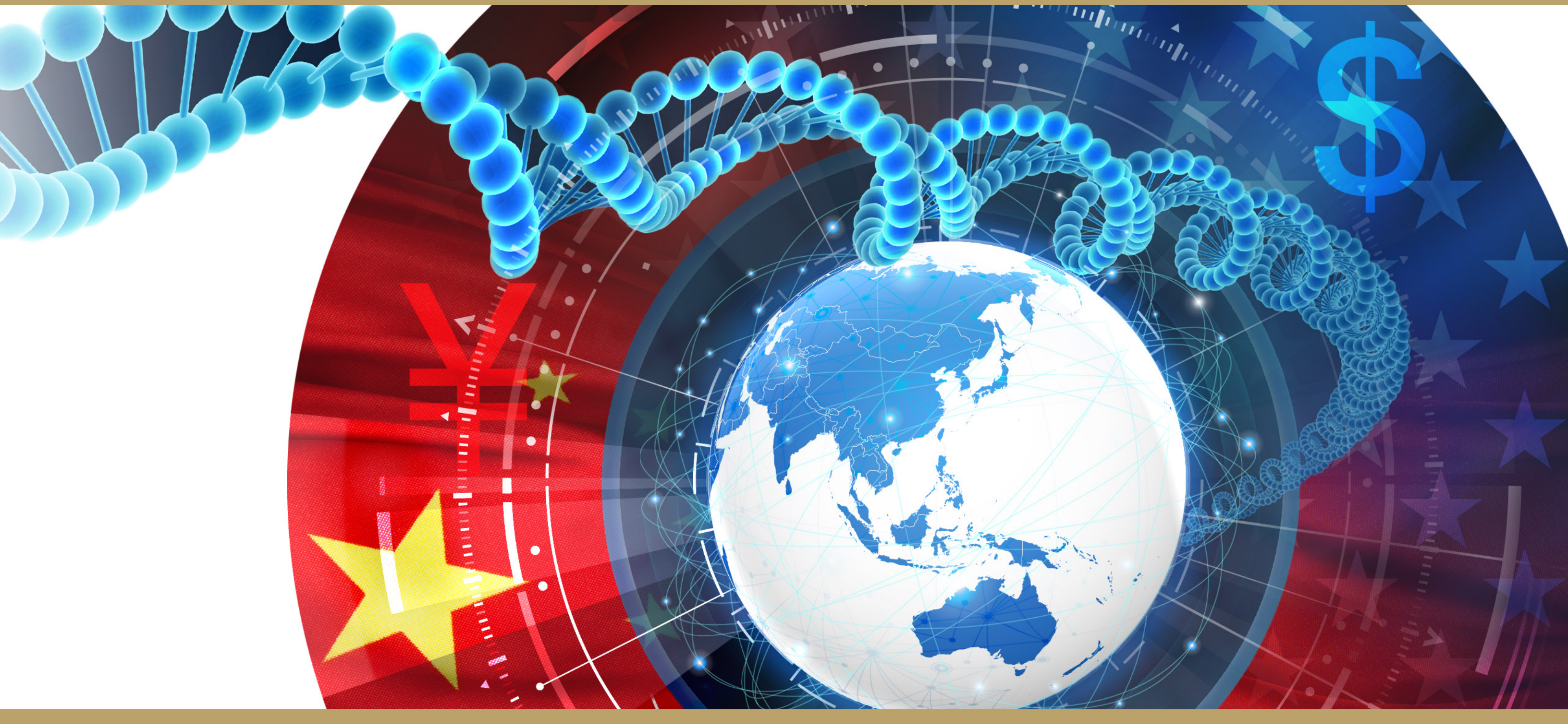
TWO WORLDS TWO BIOECONOMIES

The Impacts of Decoupling US–China Trade and Technology Transfer

National Security Report



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The views in this document reflect the opinions of the authors alone and do not represent any institutional position held by APL.

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Foreword

This paper is part of the "Measure Twice, Cut Once: Assessing Some China–US Technology Connections" research series sponsored by the Johns Hopkins University Applied Physics Laboratory.

As competition has intensified between the United States and China, actions to disengage their technology establishments from one another have also intensified. The two countries' systems for research and development, production, and sale of cutting-edge technologies have been substantially, though by no means uniformly, commingled. More recently, there have been concerted efforts by both nations' governments to reverse some or all of that commingling. Policymakers' priorities include perceived risks to national security, worry about economic disadvantage from proliferation, and concern about uses of technologies that intentionally or indifferently may harm civil liberties or the environment.

To explore the advisability and potential consequences of decoupling, the Johns Hopkins University Applied Physics Laboratory commissioned papers from experts in specific technology areas. In each of these areas, the authors have explored the feasibility and desirability of increased technological separation and offered their thoughts on a possible path forward. Other papers in this series include:

- *The History and Future of US–China Competition and Cooperation in Space* by Matthew Daniels
- *Symbiosis and Strife: Where Is the Sino–American Relationship Bound? An Introduction to the APL Series "Measure Twice, Cut Once: Assessing Some China–US Technology Connections"* by Richard Danzig and Lorand Laskai
- *An Entwined AI Future: Resistance Is Futile* by Christine Fox
- *Cutting off Our Nose to Spite Our Face: US Policy toward Huawei and China in Key Semiconductor Industry Inputs, Capital Equipment, and Electronic Design Automation Tools* by Douglas B. Fuller
- *The Telecommunications Industry in US–China Context: Evolving toward Near-Complete Bifurcation* by Paul Triolo
- *Addressing the China Challenge for American Universities* by Rory Truex
- *US–China STEM Talent "Decoupling": Background, Policy, and Impact* by Remco Zwetsloot

Summary

Biotechnology, the engineering and application of the science of biology to meet human goals, is critical to economic success in the twenty-first century. In the United States, revenues generated by biotechnology (principally drugs, crops, and chemicals) are already larger than 2 percent of gross domestic product and are growing approximately twice as fast as the economy as a whole. Individuals and news articles from China describe similarly sized biotechnology revenues there, but in both nations, the accuracy and precision of estimates is limited by the paucity of data.

Revenues to date have been achieved using first-generation technologies. Second-generation technologies will be more powerful and could supply up to 60 percent of physical inputs to the global economy, with a direct economic impact of $4 trillion a year. Chinese leaders have identified biotechnology in writings and in pronouncements as critical to their vision of China as a dominant global economic power. To that end, they are pursuing a long-term strategy of climbing up the value chain and using a familiar set of tactics that includes the following: financial support for industry champions, intellectual property licensing from abroad, infrastructure spending (laboratories, technology parks, academic research), as well as IT hacking and industrial espionage. By contrast, the United States has adopted a laissez-faire approach and has little strategy or policy regarding biotechnology.

The bioeconomies of the two nations may be similar in size but are configured differently. The United States relies on China for manufacturing (for example, 75 percent of active pharmaceutical ingredients), for services (for example, DNA sequencing), and for talented students who come to study and work at US universities. Meanwhile, China depends on external basic research to support a bioeconomy focused on commercialization of innovations created elsewhere. In the short term, decoupling would be painful for both countries. In the long term, it would be easier for the United States to replace manufacturing capacity and academic labor than it would be for China to find globally, or to replicate within China, a basic research and academic infrastructure that is the equivalent to that of the United States.

There are no absolute impediments that would prevent the United States from ultimately reducing interactions to near zero. Instead, decoupling decisions must revolve around the cost and the time they would require to implement. These decisions are currently impossible to make in an informed fashion, and we therefore make two recommendations: (1) the US government should measure the domestic bioeconomy, and the bioeconomies of its rivals, with greater granularity and accuracy, and (2) the US government should develop a framework and strategy for competing in biotechnology.

Biotechnology is at the center of a long-term contest for power between the United States and China. A technological edge in biological engineering and manufacturing will provide a substantive and lasting advantage that spans the full economy and the entire planet. The management of biotechnological trade and information flows in the near term will have consequences that will play out over decades.

Biological engineering should be viewed as critical infrastructure for the twenty-first century that will underlie and enable the entire economy. Biotechnology is already a substantial component of the economies of the United States and China, although analyses are hampered by the quantity and quality of information, and neither country officially tracks the contribution of biotechnology to their gross domestic product (GDP). After assembling data from a variety of sources, we conclude that in the United States, biotechnology revenues exceed those of better-measured sectors, such as semiconductors, mining, and utilities.[1] As detailed below, we estimate that US biotechnology revenues now exceed $400 billion, or 2 percent of GDP. Chinese biotechnology revenues are reported to be of a similar size. Our standard assumption is that product revenues are a useful proxy measure of technical capability, and thus the sum of these revenues could support the conclusion that the two countries are roughly equally matched today.

However, the existing technical capabilities and revenues should not be viewed as representative of the future. The extant economic impact has been quietly delivered using *first-generation* tools and methods based on the capability to modify and move genes from one organism to another. This impact will be dwarfed by changes to come. McKinsey & Company estimates that biological production could supply up to 60 percent of physical inputs across the global economy and that biotechnology could have a "direct economic impact of up to $4 trillion a year" for decades to come; the authors add, "The full potential could be far larger if we take into account potential knock-on effects, new applications yet to emerge, and additional scientific breakthroughs."[2] The assessment that biotechnology will further transform the global economy is based, in turn, on an assessment that biotechnology itself is undergoing a transformation.

First-generation biotechnology is now being superseded by the emergent capability to read and write DNA. This interconversion of biological and digital representations of DNA enables applying mature digital design methods to engineering biology. Digital transformation of biological engineering delivers quantifiably higher rates of progress. We illustrate the power of these technologies with several anecdotes that demonstrate the acceleration of commercial engineering efforts by more than an order of magnitude. Because scientific and technical progress compound on past progress, actors in this international arena, whether states or corporations, that demonstrate mastery of these emerging biotechnologies will benefit from compounding rates of technological change. Losing the lead is probably a one-time event, and whoever is not in the lead will be severely disadvantaged while constantly playing catch-up. This is the competitive space of the twenty-first century.

A technological lead in biotechnology not only impacts the health and well-being of populations but also provides an edge in developing and producing materials that serve as feedstocks for the rest of the economy. Advanced biological engineering using *second-generation* tools and methods has already delivered to market materials with novel properties that are useful in both civilian and military applications, where those new materials cannot plausibly be made via synthetic chemistry. Consequently, because of the breadth and depth of

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[1] Carlson, "Estimating the Biotech Sector's Contribution"; and US Bureau of Economic Analysis, "GDP-by-Industry."

[2] Chui et al., *Bio Revolution*.

its impact on the economy, biological engineering is now recognized as a strategically important technology by the governments of both the United States and China, and maintaining a technological lead in this area is critically important for both physical and economic security. The governments of the United States and China have both identified biological engineering as metaphorical high ground, and both are investing to secure it.

The government of China has explicitly described its intent to dominate the global stage in the twenty-first century through biotechnology and has been working to implement associated long-term strategic goals. While China has a multidecadal vision that has informed its strategy and has subsequently been implemented using various tactics, the United States has no similar long-term vision and has exhibited no coordinated response to Chinese actions. In this paper, we do not address this larger issue. Instead, we examine one particular strategy—decoupling—to lay the groundwork for further policy analysis. In particular, we describe the current environment (size and composition of US and Chinese revenues from biotechnology) and the interdependence of biotechnology in the two countries and then offer a first review of how some decoupling mechanisms might unfold. We also examine the strategic risk that decoupling may pose to each country in the context of accelerating, and compounding, learning rates in biological engineering.

The benefits of the present relationship appear to be asymmetric, as do the consequences of decoupling. Whereas the United States relies on China for some manufacturing and services, China currently depends heavily on access to US basic research in biotechnology; it would be easier for the United States to replace access to Chinese instrumentation and ingredients than for China to replace access to American basic research and education. More broadly, the biotechnological ties between the two economies span finance, trade, and the movement of people and ideas, each of which can be evaluated with respect to the impacts of decoupling.

We approach policy formulation and analysis with the expectation that they should be based on a firm understanding of the world as it is. However, we do not find that existing data is sufficient to support extensive specific recommendations. As a result, our brief recommendations are primarily directed at improving situational awareness to support more-detailed future analysis. Policy proposals derived from such analysis would also benefit from a clear strategic statement and a clear exposition of goals by national governments. Ultimately, this conversation has society-wide implications for how both the United States and China invest in education and domestic research and development (R&D) and for the extent to which each country benefits from those investments.

Biotechnology is recognized around the globe as a strategic technology. Countries that develop mastery of the relevant engineering and manufacturing capabilities will have distinct advantages over those that do not.

The emergence in 2020 of a global pandemic has starkly illuminated many elements of the relationship between the United States and China while also creating new points of contention. Companies and government agencies in both countries are engaged in aggressive competition to develop testing, countermeasures, and vaccines against a new pathogen that has crippled economies around the world. The intensity of this competition is serving to inflame existing political tensions and also to elevate concerns about the fragility of global supply chains, the risks of monopoly and sole-source manufacturing, the rise of digital intellectual property (IP) theft, and the suppression of facts and concomitant rise in propaganda. We use the pandemic as a case study to illustrate the themes of decoupling across these domains.

What Is "Biotechnology"?

Two significant challenges in quantifying the size of any nation's biotechnology industry are (1) confusion around the scope of technologies included in the definition and (2) conflation with the broader term "bioeconomy." We use biotechnology to refer to all engineered or genetically modified (GM) biological systems and revenues therefrom. This primarily encompasses pharmaceutical or other medical applications (also known as "biologics"), GM crops, and industrial applications such as chemical manufacturing accomplished via biological means. We use synthetic biology to refer to a component of biotechnology focused on bringing modern engineering concepts to biotechnology, a component that relies heavily on large, high-quality data sets, digitization, automation, and reading and writing DNA as well as, fundamentally, on the increasing fungibility of information and matter. We use the word bioeconomy to refer to a wider scope of products and activity, including fisheries, forestry, non-GM agriculture, and others.

The quality and quantity of data on biotechnology revenues is poor at best, leading to widespread misunderstanding about its economic importance. Biotechnology is generally underappreciated as a contributor to the US economy primarily because the relevant data is not collected by the government. Whereas the economic contribution of semiconductors was tracked by the Department of Commerce at least as early as 1958, when they made up less than 0.1 percent of GDP, as of 2020, there is still no official tracking of biotechnology.[3] As a result, its economic impact has crept up on us unawares. The same set of problems plague assessments of Chinese biotechnology revenues. For example, while it is difficult today for Western observers to ascertain exactly how many Chinese companies are operating in biotechnology, the Chinese government may have the same problem.[4] At a warm-up meeting for the 2011 Review Conference of the Biological Weapons Convention, one of us (Carlson) was told by a Chinese representative that the government "had no idea" how many biotechnology or synthetic biology companies existed in the country.

What Is at Stake?

If chemistry reigned as the science most powerfully shaping world affairs in the nineteenth century, in the twentieth century, physics took over that role. The development of quantum mechanics beginning in the 1920s led to nuclear weapons, which fundamentally changed military and diplomatic spheres. The same science also led to the understanding of semiconductors and a subsequent computer revolution beginning in the 1980s, serving as a foundation for technological and economic dominance. Now, after decades of effort, many of the techniques from these prior advances are being successfully applied to engineering biological systems, with the consequence that the molecular substrate of life on Earth is becoming a medium for innovation.

The science of the twenty-first century will be biology. The economic impact of biotechnology is already significant and will eventually span the entire range of human activity. Consequently, biotechnology is recognized around the globe as a strategic technology. Countries that develop mastery of the relevant engineering and manufacturing capabilities will have distinct advantages over those that do not.

Two decades into this century, biotechnology is already a significant contributor to the US economy. Biologically manufactured drugs now account for approximately 40 percent of new drug approvals and drug revenues in the United States.[5] The market penetrations of GM corn, soy,

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[3] Carlson, "Estimating the Biotech Sector's Contribution."

[4] "Next Biotech Superpower," *Nature Biotechnology*.

[5] Morrison, "Fresh from the Biotech Pipeline"; and Carlson, "Estimating the Biotech Sector's Contribution."

and cotton crops are each greater than 90 percent, which implies that GM crops are grown on more than 180 million acres of the 315 million acres of US farmland under active cultivation.[6] That is, at least 57 percent of total US cropland is now used to grow GM organisms. Approximately 20 percent of US chemical industry revenues are now generated by biotechnology, via products comprising fine chemicals, solvents, and plastics, thereby displacing petrochemicals from the market.[7] While it is difficult to forecast how large a share of the economy biotechnology will ultimately become, it is our view that, because of inherent scaling and energy efficiency advantages, anything that can be made using biotechnology eventually will be.[8]

This pervasive technology will be used to address urgent needs around the planet.[9] The global population is now some 7.8 billion people, and the United Nations projects a population of 9.7 billion people in 2050.[10] The consequent demand for food, health care, and materials will create an ever-larger pull for biological technologies. For example, because most arable land on the planet is already under cultivation in some way, feeding that global population is likely to come from continued improvements in yields due to genetic modification of crops and shifts in land use that are aided by engineered crops with novel traits, such as drought resistance and salt tolerance. In the United States, 17.9 percent of GDP is spent on health care, spending that yields paltry results as evidenced by the fact that the United States ranks twenty-sixth among the thirty-five Organisation for Economic Co-operation and Development (OECD) countries in life expectancy.[11] As the globe ages and more people are subject to afflictions of old age, such as cancer or Alzheimer's, halting disease through better use of biotechnology will become not just a moral imperative but an economic one. Finally, biology, as a technology, can be used to manufacture the crucial industrial items we require—plastics, building materials, chemicals, etc.—without inducing further climate change.

As we achieve greater control over engineered biological systems, the impact will expand across the economy. The change in capability will arise from the application of modern engineering techniques to biology, which will require large, high-quality data sets, computation for modeling, and extensive use of automation, all of which are inherently digital. In the long term, the fusion of the digital and the biological must be thought of as no less than enabling an entirely new capability to program matter at length scales spanning atoms to ecosystems.

The US Biotechnology Sector

We estimate that US revenues from biotechnology reached at least $388 billion in 2017, or approximately 2 percent of GDP (Figure 1).[12] Based on

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[6] USDA/NASS, "Farms and Farmland"; and ISAAA, "Global Status of Commercialized Biotech/GM Crops."

[7] Carlson, "Estimating the Biotech Sector's Contribution"; and Bioeconomy Capital, "Bioeconomy Dashboard."

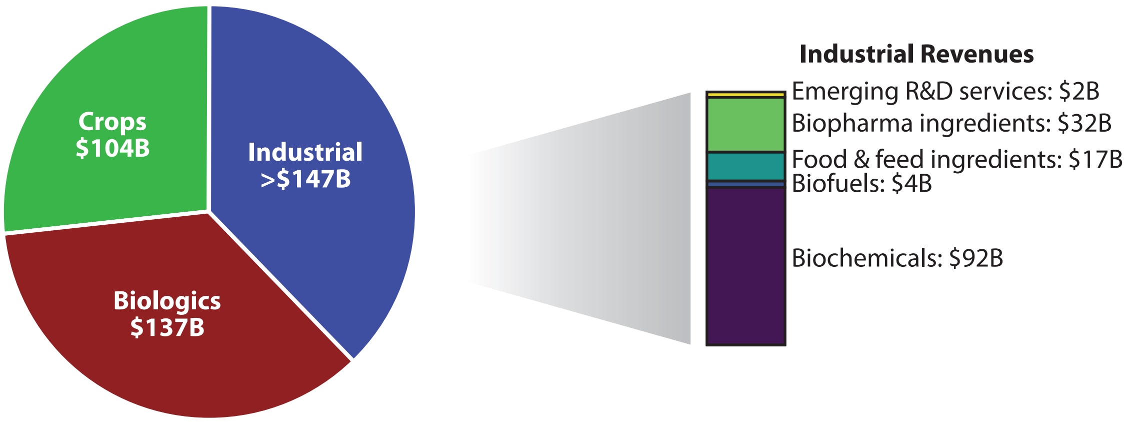
[8] Chui et al., *Bio Revolution*.

[9] Carlson, *Biology Is Technology*.

[10] United Nations, Department of Economic and Social Affairs, Population Dynamics, "World Population Prospects 2019."

[11] Statista, "U.S. Health Spending as Share of GDP 1960-2020" (figure of 17.9 percent is for 2017); and OECD, "Life Expectancy at Birth."

[12] Carlson, "Estimating the Biotech Sector's Contribution"; for updates, see the Bioeconomy Dashboard at https://www.bioeconomy.capital/bioeconomy-dashboard/. The primary challenge in estimating the size of any nation's biotechnology revenues, including those of the United States, is a paucity of data. No national governments collect or distribute data for biotechnology in the same manner as they to for other industries, leading to substantial uncertainty. To develop the US revenue picture presented here, we relied on third-party collation of biologics revenues received by public companies, a combination of industry and government surveys for GM crop revenues, and a combination of academic estimates and private marketing research for industrial biotechnology revenues. For a full description of methods, see Carlson, "Estimating the Biotech Sector's Contribution." Our estimates are intentionally



US biotechnology revenues in 2017 are estimated to be at least $388 billion, or 2 percent of GDP. *Sources:* Bioeconomy Capital, Agilent, and Carlson, “Estimating the Biotech Sector’s Contribution.” Data and methods are described on the Bioeconomy Dashboard website (https://bioeconomy.capital/bioeconomy-dashboard/).

Figure 1. Estimated 2017 US Biotechnology Revenues

differing product development costs and time lines (including regulatory approval), revenues from biotechnology naturally segregate into three different subsectors: biologics (drugs made using biological processes), GM crops, and industrial products (including materials, enzymes, and engineering tools).[13] For comparison, *worldwide* semiconductor revenues for 2017 were ~$400 billion,[14] approximately equal to US domestic biotechnology revenues alone.[15]

US biotech revenues are accelerating and have consistently grown at an average of 11 percent annually since 2001 (Figure 2). Extending the historical average aggregate growth of biotechnology through 2020 produces an estimate of approximately $530 billion in revenues this year.[16]

Two attributes of this summary illuminate the significance of biotechnology. We estimate that chemicals manufactured using biotechnology produced approximately $100 billion in domestic revenues in 2017 (Figure 1), the equivalent of one-fifth of total domestic chemicals revenues. When compared with the economy as a whole, it is clear that biotechnology is increasingly important both because of its absolute size and because it is an engine of growth. Generally, when the rest of the economy has slowed or contracted, biotechnology has remained stable and picked up the slack, contributing at least 7 percent of GDP growth during the recession that began in 2008.[17]

China’s Biotechnology Sector

At least thirty-two countries around the world have identified biological engineering as a strategic

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conservative to reflect uncertainties in the data. As an example of this uncertainty, a recent National Academy of Sciences report that used different data, and a different analytic methodology, concluded that existing US revenues are already between 5 and 7 percent of GDP (National Academy of Sciences, *Safeguarding the Bioeconomy*).

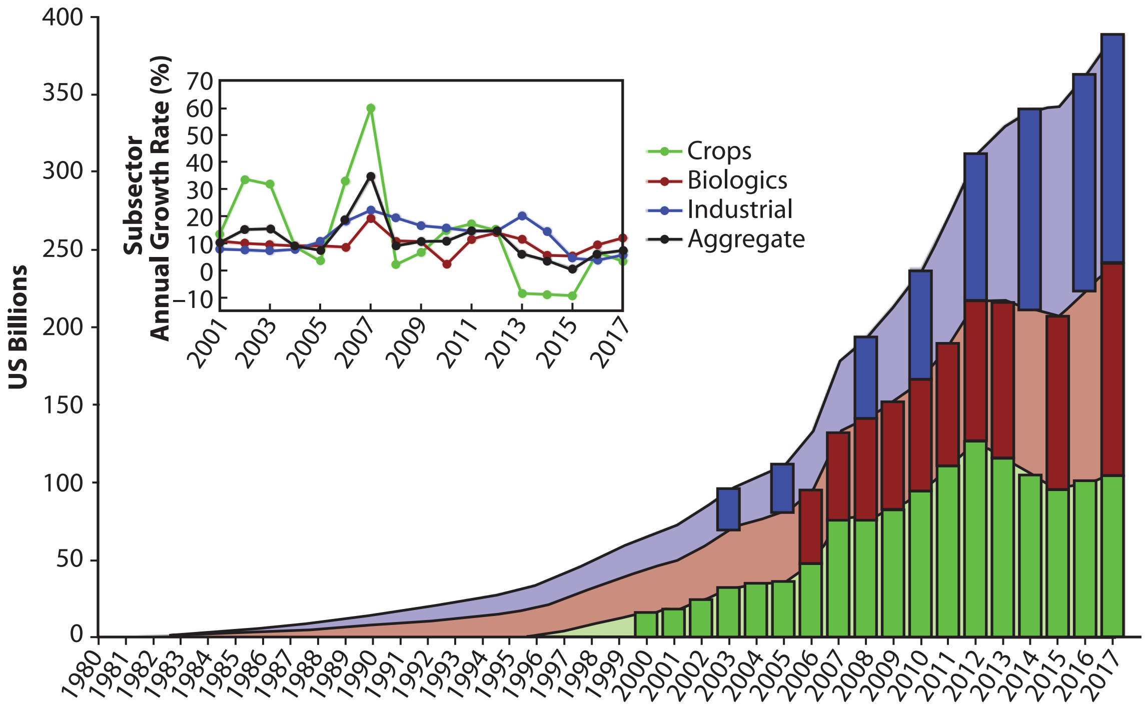
[13] Carlson, “Estimating the Biotech Sector’s Contribution”; and US Bureau of Economic Analysis, “GDP-by-Industry.”

[14] Semiconductor Industry Association, “Building America’s Innovation Economy.”

[15] Semiconductor Industry Association, “Building America’s Innovation Economy.”

[16] Carlson, “Estimating the Biotech Sector’s Contribution”; and Bioeconomy Capital, “Bioeconomy Dashboard.”

[17] See Figure 5 (retrieved May 22, 2020) in Bioeconomy Capital, “Bioeconomy Dashboard.”



Bars are data; shaded areas are a numerical interpolation. (Inset) Annual growth rates calculated from the interpolation.

Figure 2. Estimated US Biotech Revenues between 1980 and 2017

technology and are investing accordingly.[18] Many of these countries view domestic development of biotechnology and biomanufacturing as a less capital-intensive path to economic development than that pursued by the United States, Europe, and Japan in the twentieth century. China fits this pattern. A high-level Communist Party and Chinese Academy of Sciences (CAS) official stated this perspective clearly and unequivocally: "As Europe won in the 19th century using industry, and the United States won in the 20th using information technology, so China will win in the 21st using biology."[19] In 2006, Premier Wen Jiabao announced a plan to "catch up with the most advanced nations in biotechnology" while strengthening "independent" or "indigenous" innovation.[20] In 2008, he stated, "To solve the food problem, we have to rely on big science and technology measures, rely on biotechnology, rely on [genetic modification]."[21] The "food problem" to which the premier referred is a combination of a still-increasing population and a recent, precipitous decrease in arable land.[22] More recently, the Made in China 2025 initiative heralds significant increases in public support of biotechnology, and the Biotechnology Development Plan called for "20–30 leading new technologies to be developed by 2020, as well as 30–50 major strategic new products."[23] As of 2015, China's bioeconomy amounted to $700 billion, according to a CAS official.[24] It is unclear which revenues beyond biotechnology this statement references. The government

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[18] OECD, *Emerging Policy Issues*.

[19] Carlson, "Securing the Bioeconomy."

[20] Serger and Breidne, "China's Fifteen-Year Plan."

[21] Stone, "$3.5 Billion GM Crops Initiative."

[22] Carlson, *Causes and Consequences of Bioeconomic Proliferation*.

[23] Huggett, "'Innovation' Nation."

[24] Personal communication with Yin Li, deputy director-general, Bureau of International Cooperation, CAS (Berlin, 2018).

had a target of more than doubling this to $1.6 trillion by 2020.[25] As of 2018, the Chinese government had announced a goal of growing the domestic bioeconomy over the long term at 15 percent annually.[26] The 13th Five-Year Plan set a goal for biotechnology specifically to contribute 4 percent of GDP by 2020 (or ~$600 billion) and for 10–20 of its more than 100 life science parks to, together, generate an output of $1.5 billion annually.[27] These recent figures are consistent with assessments and projections we made in 2012.[28]

Private investment is supporting the government's push to expand its biotechnology industry, reportedly reaching $14.4 billion in 2019 compared with $10.4 billion in the United States.[29] Overall, these top-down and coarse-grained economic observations, derived from multiple sources, are consistent across at least a decade. And yet the details of this reported growth remain murky.

There is no central source of data for Chinese biotechnology revenues.

It is not currently possible to analyze biotechnology revenues in China with the same scrutiny applied to revenues in the United States. The combination of data scarcity and data quality create a challenging analytical environment, particularly for fine-grained, bottom-up tallies, and it is unclear how biotechnology in China might achieve the ~$600 billion revenue target for 2020. *This discrepancy may be due to some combination of mistranslation and lack of clarity or specificity in referring to biotechnology or to the broader bioeconomy, which we suspect is a persistent phenomenon*. It could also be that Chinese officials, either accidentally or intentionally, are misstating biotech revenues. In any event, there is no central source of data for Chinese biotechnology revenues. We describe below what little we can discern of China's revenues from biologics, GM crops, and industrial biotechnology.

Biologics

The Chinese market for biologics was recently estimated to be as large as $6 billion.[30] While nine of twenty-seven antibodies approved in China are reportedly manufactured domestically, total domestic manufacturing revenues are unknown and could still be minimal.[31] Significant investment in biologics development and production was ongoing even before the COVID-19 pandemic, though when that production will result in approved drugs with appreciable sales is uncertain.[32] To support the acceleration of development and approval of biologics that meet international standards, the domestic drug regulatory agency was renamed and restructured in 2015 as part of reforms aimed at achieving the "specific goals of improving the quality, speed and transparency of the drug review and approval process; eliminating the backlog of pending drug applications; and mirroring the gold-standard processes of regulators like the US Food and Drug Administration and the European Medicines Agency."[33]

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[25] Personal communication with Yin Li, deputy director-general of the Bureau of International Cooperation, CAS (Berlin, 2018).

[26] "China's Biotech Sector," *People's Daily.*

[27] "China's Biotech Sector," *People's Daily*; and Ellis, "Biotech Booms in China."

[28] Carlson, *Causes and Consequences of Bioeconomic Proliferation*.

[29] Cumbers, "China's Plan to Beat the U.S."

[30] Kazmierczak et al., *China's Biotechnology Development.*

[31] Langer, "Top Destination for Biologics Manufacturing."

[32] Mullard, "Chinese Biopharma."

[33] Huggett, " 'Innovation' Nation."

China has transitioned from being largely dependent on other countries for scientific innovation to being itself not just a contributor, but also a leader, in many fields. Meanwhile, the United States has enjoyed increased access to enthusiastic and capable Chinese students and has shifted a considerable fraction of its pharmaceutical and biotech reagent manufacturing to China in pursuit of lower costs.

GM Crops

While the acquisition of the seed company Syngenta by ChemChina in 2017 suggests a high-level shift in focus toward increasing the role of GM crops in the economy, current domestic sales of GM crops generate only marginal revenues. The total acreage of GM crops in China is minimal, amounting to only 1 percent of the total global planted area in 2017, and although GM cotton and GM papaya have high market penetration in China (95 percent and 90 percent, respectively), revenues from those crops are not significant.[34] Nevertheless, there is potential for substantial future revenues. The government recently approved 203 separate GM crop strains for both domestic cultivation and importation, with 201 of those having been domestically developed.[35] Yet this approval must be accompanied by licensing for specific planting events, only 73 of which have thus far been granted.[36]

Industrial Biotechnology

The uncertainty around China's revenues from industrial biotechnology is so large as to make any estimates mere guesses. Nevertheless, our personal experience in analyzing specific companies has revealed the existence of a substantial customer base in China that patronizes US bioengineering and strain optimization services. This is not a representative sample, but our impression is that China's industrial biotechnology revenues are potentially extensive.

In conclusion, it is difficult to square statements by central government and CAS officials about either extant or near-term aspirational biotechnology revenues with what little data exists about specific subsectors. If biotechnology is considered to be a critical component of physical and economic security in both the United States and China, then a proper security assessment will require a sustained commitment to gather much better data.

What Are the Ties between the Two Bioeconomies?

Over the last two decades, China has transitioned from being largely dependent on other countries for scientific innovation to being itself not just a contributor, but also a leader, in many fields. Meanwhile, the United States has enjoyed increased access to enthusiastic and capable Chinese students and has shifted a considerable fraction of its pharmaceutical and biotech reagent manufacturing to China in pursuit of lower costs. The US–China Economic and Security Review Commission has published a report that delves into the biotechnological ties between the two countries.[37]

For the sake of brevity and expediency, we categorize the interactions and dependencies between China and the United States into flows of capital, personnel, material, and information (which is

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[34] ISAAA, "Global Status of Commercialized Biotech/GM Crops."

[35] Huang, "China Paves Way."

[36] ISAAA, "GM Crop Events."

[37] Kazmierczak et al., *China's Biotechnology Development*.

further subdivided into scientific data, enabling technical knowledge, IP, and health-related data). A rigorous quantitative analysis of the relationship is not possible because of a paucity of data.

Capital

Inbound capital to China comes in three forms: direct investment, portfolio investment (e.g., venture capital [VC], private equity, hedge funds), and overseas listings of Chinese companies (for an estimated accounting, see Kazmierczak et al.[38]). Beyond access to funds, these transactions also provide access to Western operational and financial expertise.

Most of the outright IP purchase transactions in the United States were to secure access to medical device or pharmaceutical technology rather than biotechnology.

Outbound capital similarly participates in direct investment, portfolio investment, and equity purchases on public markets. Outbound VC in biotechnology was particularly active up through 2017, totaling $3.8 billion, with 131 of 153 investments located in the United States.[39] Acquisitions reportedly account for 67 percent of Chinese biotechnology investment in the United States, and VC accounts for 29 percent; consequently two-thirds of these investments resulted in transfer of control and IP.

Chinese companies have steadily increased spending on foreign IP licensing and acquisition, amounting to more than $28 billion in 2017. Most of the outright IP purchase transactions in the United States were to secure access to medical device or pharmaceutical technology rather than biotechnology.[40]

The fraction of Chinese investment in the United States targeted specifically at synthetic biology is difficult to assess. Kazmierczak et al.[41] catalog a variety of investments that could fall, all or in part, into the category of synthetic biology, amounting to more than 85 percent of total Chinese capital outflows. These include investments in genomics, cell and gene therapy, contract research, molecular diagnostics and precision medicine, research and discovery platforms and tools, bioproduction, and bioprocessing.

As of mid-2019, Chinese investment activity in the United States had fallen sharply from its peak, a decline widely attributed to the expansion of the purview of the Committee on Foreign Investment in the United States (CFIUS) to explicitly examine minority investments and biotechnology. (CFIUS examines potential inbound investments to the United States and may deny the transaction if there are concerns about national security or economic competitiveness. More stringent CFIUS review is one example of a US-enacted decoupling tactic that can be used to reduce financial and information flows.) Chinese VC flows into the United States fell by more than half from 2018 to 2019.[42] It is unclear what impacts the increased scrutiny by CFIUS will have on other sorts of transactions aimed at transferring IP to China, such as the direct licensing of patents.

Personnel

The strategy of sending Chinese students and scientists abroad for education and to participate in research, with the intent of bringing important skills and knowledge home upon their return, dates

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[38] Kazmierczak et al., *China's Biotechnology Development.*

[39] Kazmierczak et al., *China's Biotechnology Development.*

[40] Kazmierczak et al., *China's Biotechnology Development.*

[41] Kazmierczak et al., *China's Biotechnology Development.*

[42] Hancock and Kuchler, "Chinese VC Spending."

As of 2008, the United States imported approximately 75 percent of its active pharmaceutical ingredients from China.

back nearly three decades.[43] For much of this time, China used an informal system to permanently lure "sea turtles" (individuals who have left China to study or work overseas but have now "swum home") to return from overseas, while encouraging a large number of "seagulls" to transit multiple times between China, the United States, and Europe, maintaining collaborations around the world and serving as conduits for knowledge.[44] In 2008 this recruitment effort was formalized as the Thousand Talents Program. In the years since, the program has successfully recruited more than 7,000 scientists, native- and foreign-born, to spend at least part of every year in China, sometimes serving as directors of institutes carrying their names. However, in response to growing attention and criticism from Western governments, "China has asked officials to stop mentioning its premier programme to recruit the brightest tech talent from overseas."[45] Participation in the program now carries risks, as several scientists in the United States are now facing prosecution for obscuring their ties to China on grant disclosure forms.[46] Zwetsloot (who has authored another paper in the "Measure Twice, Cut Once" series) estimates that approximately 6,000 Chinese postgraduate scholars in the biological sciences worked in the United States in 2018.[47] China relies heavily on foreign institutions to train students. Approximately 122,000 Chinese students studied in the United States in 2018 across STEM disciplines, with approximately 10,000 of those directly studying biological sciences.[48]

We note a peculiarity of biology here. Lab protocols are complex and often involve a high degree of art embedded in the researcher. It is often the case that one laboratory cannot reproduce the work of another even when the first lab provides the starting materials and detailed instructions. For this reason, exchange of personnel has been the primary way to transfer the tacit knowledge present in one place to another, which is why movement of personnel between China and the United States is a larger concern for biotechnology than for other fields. However, as we explore below (see the Digital Transformation section), the shift away from depending on tacit knowledge and toward digital representations of laboratory protocols and manufacturing processes may reduce the importance of personnel in transferring knowledge between the two countries.

Material

The interdependence of China and the United States has grown particularly acute in the area of active pharmaceutical ingredients (APIs). As of 2008, the United States imported approximately 75 percent of its APIs from China, a large proportion of which were reportedly produced biologically via fermentation.[49] At least some of these fermented APIs were available only from Chinese manufacturers, which we identified in 2012 as a leading indicator of China's successful effort to use biological manufacturing as a foundation of its economy.[50]

By late 2019, the United States had reportedly grown even more dependent on outsourced

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[43] Hannas, Mulvenon, and Puglisi, *Chinese Industrial Espionage.*

[44] Carlson, *Causes and Consequences of Bioeconomic Proliferation.*

[45] Yang and Liu, "China Hushes up Scheme."

[46] Swenson, "Virginia Tech Professor"; Department of Justice, US Attorney's Office, Western District of Virginia, "Former Virginia Tech Professor"; and Barry, "U.S. Accuses Harvard Scientist."

[47] Zwetsloot, *US–China STEM Talent "Decoupling."*

[48] Zwetsloot, *US–China STEM Talent "Decoupling."*

[49] Tremblay, "Sourcing from China."

[50] Carlson, *Causes and Consequences of Bioeconomic Proliferation.*

manufacturing. China and India were producing 80 percent of APIs "used in drugs that end up in Americans' medicine cabinets," and the United States had become indirectly dependent on China through the finished drug manufacturing provided by India and Europe.[51] India relies on China for 70 percent of the APIs it uses as the world's largest exporter of generic drugs.[52] More specificity here is desirable, but unobtainable. Pharmaceutical companies treat the source of APIs as trade secrets, and they are not currently required to disclose that information to investors or to the US government. Consequently, the precise fraction of APIs imported by US companies from China is still unknown, an uncertainty that has led to proposed legislation in the US Senate to close this information gap.[53] Beyond APIs, China has now become the second largest exporter of finished small-molecule drugs and biologics.[54]

The United States currently imports almost half its personal protective medical equipment, including masks, goggles, and gloves, from China.

More broadly, biotechnology in the United States relies on poorly documented supply chains that permeate the economy. Reagents, personal protective equipment, materials and infrastructure used in the construction of laboratories and biomanufacturing facilities, laboratory instruments, and disposable plastic containers and pipette tips are all used in biotechnology. There is no systematic accounting of the relevant supply chains and no full understanding of the consequent risks.

While not part of the revenue-based analysis we use in assessing the size and capabilities of the biotechnology industry, this equipment nevertheless comprises critical components of the practice of research, development, and commercialization, particularly when a task requires maintaining sterility. The United States currently imports almost half its personal protective medical equipment, including masks, goggles, and gloves, from China.[55] As a metric for the growing dependence of the United States on China for instrumentation relevant to biotechnology, with nearly 40 percent of total shipments, China is now the largest exporter of medical devices into the United States as measured by "import lines," distinct regulated products within shipments through US customs.[56] Finally, while difficult to quantify, it is likely that US manufacturers of a wide range of laboratory instrumentation rely on mechanical and electrical components produced in China. The pandemic has cast a spotlight on some of these dependencies, but a thorough accounting of the industry to assess the impacts of decoupling would require an analysis of whence all the components that support the US biotechnology industry derive.

Information

Chinese scientists note with deserved pride the increasing sophistication of accomplishments in biotechnology over the years. Nearly two decades ago, Chinese scientists contributed a relatively small fraction of the total DNA sequenced by the human genome project. By 2020, as participants in a project to synthesize a yeast genome from scratch, Chinese scientists had contributed not only critical

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[51] Edney, "China's Role as Global Drug Hub"; and Findlay, Kuchler, and Neville, "Drugmakers Braced for Coronavirus Disruption."

[52] Findlay, Kuchler, and Neville, "Drugmakers Braced for Coronavirus Disruption."

[53] Findlay, Kuchler, and Neville, "Drugmakers Braced for Coronavirus Disruption"; and Williams, "US Lawmakers Push."

[54] *Hearing on Exploring the Growing U.S. Reliance*, Abdoo testimony.

[55] Williams, "US Lawmakers Push."

[56] *Hearing on Exploring the Growing U.S. Reliance*, Abdoo testimony.

technological improvements but also full synthesis and assembly of four of the sixteen chromosomes and significant portions of two other chromosomes.[57] Further, Chinese scientists have in recent years demonstrated foundational work in developing and deploying CRISPR as a tool for gene editing in plants and animals, including humans.[58] More than half of publicly available patent applications for uses of CRISPR were first filed by Chinese researchers.[59]

Despite this progress in building capacity for indigenous innovation, China's technology commercialization strategy depends heavily on importing information in the form of IP that is developed elsewhere. Only 16 percent of biotechnology patents granted in China between 2009 and 2018 were first filed in China, and only 1.25 percent of US biotechnology patents issued over that period were first filed in China.[60] Moreover, the quality of these patents has been assessed to be low, with fewer than 5 percent of Chinese patents filed by life science researchers judged to have commercial potential, as opposed to 50 percent in the United States.[61] Beyond the invention stage, innovation is often pursued through the licensing of patents and acquisition of early-stage companies.[62]

To develop the capacity for indigenous innovation, China is investing significant amounts in building academic research centers dedicated to synthetic biology.

Yet China's efforts to accumulate data, innovation, and IP are not always legal or ethical. China's explicitly articulated and executed strategy to acquire technology by any means necessary has been documented extensively elsewhere.[63] The looting of IP has so far been demonstrated in pharmaceuticals and hybrid and GM seeds.[64] While the scale and dollar value of this piracy may not yet rival those in other areas, it is evidence of intent. Wary of IP theft, Western companies have been slow to locate biomanufacturing facilities in China. As one example, in response to a Chinese government requirement for domestic manufacturing of even investigational new drug candidates, GE has begun to ship to China prefabricated biologics manufacturing facilities that can be run remotely.[65] These remotely operated manufacturing facilities are designed to allow important process IP and trade secrets to remain outside China, while cells and proteins are produced inside China. We note that this is a demonstration of the critical and emerging importance of process knowledge in biomanufacturing; that is, knowledge of how to economically manufacture objects is a requisite and large piece of value production. In this case, GE is enabling the encoding of process knowledge in the software used to manage the remotely operated facilities. This reduction of laboratory knowledge to code is an opportunity to control distributed manufacturing and thereby increase revenues. But it is also a risk as the code can be expropriated and reverse engineered to extract process knowledge intended to remain confidential.

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[57] Pretorius and Boeke, "Yeast 2.0."

[58] Cohen, "China Bets Big"; Cohen, "China's CRISPR Push"; and Wee, "Chinese Scientist."

[59] Cohen and Desai, "With Its CRISPR Revolution."

[60] Huggett, "'Innovation' Nation."

[61] Huggett, "'Innovation' Nation."

[62] Bradsher, "American Trade Secrets."

[63] Hannas, Mulvenon, and Puglisi, *Chinese Industrial Espionage*; and Joske, *Picking Flowers, Making Honey*.

[64] Temple University, "Combating Counterfeit Pharmaceuticals"; Wilber, "Saga of the Chinese Spies"; and Thompson, "Spies in the Field."

[65] Berry, "GE Ships Pre-built Plant." As of late 2019, GE Healthcare Life Sciences had shipped to international customers at least four of these "factory in a box" facilities, each of which consists of sixty-two shipping container–sized modules, two of which are located in China. See, e.g., GE Healthcare, "New KUBio Box," and Egan, "Depeche Module."

How Will Technological Progress Impact Decoupling?

Synthetic Biology

The vast majority of biotech revenue described above has been generated using technology developed between 1980 and 2000. Little, if any, of the current product mix in any of the three subsectors relies on synthetic biology. Until recently, synthetic biology was mostly an artisanal activity that was too immature and too expensive to be put to use in industrial R&D laboratories. Now, however, exponential increases in capabilities, and exponential decreases in costs, have put improved tools at the forefront of developing new drugs, new crops, and new chemical production pathways.[66]

The tools of synthetic biology have been embraced globally. As costs have fallen, Chinese companies have been quick to enter the market for related goods and services, including DNA sequencing (read) and DNA synthesis (write). China has previously developed a cost advantage for high-throughput sequencing services after purchasing a large number of instruments from Illumina that were manufactured in the United States. This move was enabled by a $1.5 billion government-backed loan to BGI, formerly the Beijing Genomics Institute.[67] The relationship between BGI and the People's Republic of China (PRC) remains very close. BGI stated in stock market filings that it has the goal of helping the Chinese Communist Party "seize the commanding heights of international biotechnology competition."[68] In the intervening years, sequencing centers have sprung up all around the United States and Europe, largely organized as academic user facilities, and are frequently described as intended to build local capacity, expertise, and economic competitiveness. Nevertheless, many scientific projects around the world continue to send samples to BGI for sequencing, despite the concern that in exchange for providing low-cost services, BGI is collecting massive amounts of genomic data on people, organisms, and environments. While we may debate the impact and risk associated with this activity, we should not mistake its intent as an explicit information-gathering exercise. In the words of Hank Wang, chief business officer of BGI Genomics Company, "We want all the data."[69] Data, however, is not by itself sufficient to build a biotech industry, and China is cognizant of its need to decrease reliance on tacit knowledge imported from abroad.

As part of its effort to develop the capacity for indigenous innovation, China is investing significant amounts in building academic research centers dedicated to synthetic biology. State and private coffers alike are being opened for the task: philanthropist Li Ka Shing last year donated $63 million to the Hong Kong University of Science and Technology for a synthetic biology institute.[70] These centers are, in some cases, intellectually anchored by prominent US academics working in synthetic biology whose careers, and knowledge base, have been developed using grants funded by US taxpayers.[71] China hopes to build its own solid domestic technological foundation for engineering biological systems using indigenous strengths developed via earlier investments in computation and automation. Ultimately, the goal of any such investment around the world is to facilitate the fusion of digital design and manipulation, via reading and writing DNA, with biological fabrication.

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[66] Carlson, *Biology Is Technology*; and Bioeconomy Capital, "Bioeconomy Dashboard."

[67] Fox and Kling, "Chinese Institute."

[68] Needham, "COVID Opens New Doors."

[69] Wang, talk given at SynBioBeta.

[70] Cumbers, "Trade Deal or Not."

[71] "American Fellow Jay Keasling," Chinese Academy of Sciences; and Bio-IT World Staff, "BGI Launches George Church Institute."

Digital Transformation

The same digital design and manufacturing techniques that underlie industries that produce iPhones, Teslas, and 787s are being applied to biological systems, with a consequent shift in capability that will open up entire new industries to biological innovation.[72] The engineering infrastructure used in the electronics, automotive, and aviation industries was developed alongside the products themselves and is therefore quite mature. These digital tools are now so sophisticated that they can be used to design and test complex objects in silico on a laptop, where the design file can then be used to drive automated manufacturing tools half a planet away. This so-called "design for manufacturing" infrastructure now supports much of the global economy. Biological engineering and manufacturing clearly do not yet have access to these same capabilities. But this contrast should emphasize the impending impact of introducing digital tools into biotechnology. Any policies implemented to decouple biotechnology today, even if successful, may well have different impacts on the world to come.

The market demand resulting from improvements in biological engineering will drive digital transformation across all life sciences companies, whether focused on health care, crops, or industrial products. We analyze digital transformation as delivering three solutions to provide infrastructure for reproducible, predictable, biological engineering:

(1) **Automation.** High-precision, networked laboratory robots can outperform humans in generating reproducible, high-throughput data. A common automation platform allows the data from the laboratory to be directly transferred to high-performance manufacturing.

(2) **Design for manufacturing.** Modern product development typically connects designers and automated manufacturing with a digital tool stack, but this infrastructure has so far eluded the life sciences industry. A biotechnology operating system is needed that can drive experiments, optimize production processes, and facilitate technology transfer; it would also serve to integrate basic product development with systems that manage customer-facing manufacturing and compliance.

(3) **Quality systems.** Life sciences companies need organization-wide standardization of tasks ranging from data gathering and annotation to root cause analysis, which together facilitate the use of modern process development and management tools. These tools can be applied to improving the reproducibility of basic research just as well as to identifying target patient populations in clinical trials.

The resulting collection of tools will enable the acquisition, curation, and processing of high-quality data sets that will have substantial scientific and commercial value. The electronic descriptions of experiments and production processes that drive automation will constitute implementable manufacturing algorithms precisely analogous to those used in the semiconductor, automotive, and aviation industries. The combination of these three solutions creates an opportunity to sell final products without transferring process knowledge, as in the example of the remotely operated drug manufacturing facilities discussed above. But it also creates new risks. The combination of databases and digital process descriptions is particularly vulnerable to digital theft (i.e., hacking), a method frequently used by China to acquire external innovation. Therefore, one consequence of the technological revolution inherent in the maturating of biological engineering is a requirement to better protect databases and electronic process specifications through improved digital security and through limitations on the legal acquisition of these digital resources via foreign investment.

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[72] Carlson, *Biology Is Technology*.

What Fraction of Existing Entanglements Could Be Decoupled if the United States So Chose?

While the United States has benefited from capital, personnel, manufacturing, and services obtained from China, none of these resources are irreplaceable; with domestic investment these could be established, or reestablished, either within the borders of the United States or distributed among other countries. Succinctly, there are no absolute impediments that would prevent the United States from ultimately reducing interactions to near zero. Instead, decoupling decisions must revolve around the cost and the time they would require to implement.

China has benefited from the same reciprocal exchange of resources from the United States. Yet, over time, China has followed an explicit strategy of developing indigenous vertical supply chains for a variety of manufactured items relevant to biotechnology and biomedicine—a necessary step for their decoupling from the rest of the world. However, China still depends heavily on external early-stage R&D to supply its commercialization pipeline. Consequently, China is likely to find it more difficult to reduce interactions toward zero. However, if blocked from being able to license technology or repatriate students and researchers, the PRC may concentrate further on digital theft.

Material

The building blocks of biology—carbon, oxygen, hydrogen, and nitrogen—are unusual for their very even and widespread distribution. Wherever there is existing organic matter, there is carbon; wherever there is water, there is hydrogen; and the atmosphere itself provides access to oxygen and nitrogen. Unlike other technologies, it is effectively impossible to monopolize the base materials needed for production.

In the short term, the most challenging resource for the United States to replace would be pharmaceutical ingredients and the components of laboratory and biomedical instrumentation. There is no doubt that the United States has more than enough expertise and capital to accomplish this goal. However, reshoring this manufacturing capacity would take time and probably require a long-term collaboration between industry and government.

A specific quantitative cost would require a thorough supply chain analysis of APIs and laboratory instrumentation, which is not currently possible given existing data.

Capital

While biotechnology represented only 2 percent of aggregate Chinese capital invested in the United States up to 2017, that investment almost doubled annually between 2012 and 2017.[73] Still, the 2017 total of $1.5 billion was only a small fraction of total biotechnology investment in the United States in 2017.[74] Total US VC investment across all technology sectors was $84.2 billion in 2017.[75] Thus, Chinese biotech capital represents, at 1.8 percent, a small fraction of overall investment, which could be reduced to zero if desired. If eliminated, the capital investment might be replaced by other investor sources (Europe, Middle East) or plausibly eliminated entirely with the effect that some start-ups, not necessarily biotech ones, would not get funding.

While the effect of CFIUS has apparently been a substantial decrease in Chinese investment activity in the United States, and while specific funding rounds were reportedly made more challenging by the decrease in Chinese activity, it is not clear that the reduction had any significant impact on the

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[73] Kazmierczak et al., *China's Biotechnology Development.*

[74] Kazmierczak et al., *China's Biotechnology Development.*

[75] Magistretti and Hensel, "VCs Invested the Most Capital."

More than half of the Chinese biotech investments in the United States were acquisitions, and more than half of the total was for strategic purposes, rather than simply by financial investors.

innovation economy. We have observed that some investment deals from companies in our own portfolio were slowed by the 50 percent drop in Chinese VC activity in 2019, yet those deals still eventually proceeded with other funding. It is our opinion that, if this source of funds were cut off completely, the US biotech industry could find sufficient investment capital elsewhere.

Notably, in 2017, more than half of the Chinese biotech investments in the United States were acquisitions, and more than half of the total was for strategic purposes, rather than simply by financial investors.[76] That is, more than half of acquisitions resulted in corporate control passing to Chinese companies along with the IP associated with the company. The dollar value of this activity, given that much of it involved private companies, is difficult to ascertain. Consequently, the impact of its reduction is difficult to assess. However, we note that significant capital was sitting on the sidelines of global markets even before the pandemic. A reduction in mergers and acquisitions (M&A) activity in the United States by Chinese companies should not affect the fate of the acquired companies, although a reduction in competition might result in lower acquisition prices.

Information

There is no obvious way to assess how much the United States depends on scientific work in China outside of scientific publications. Licensing and M&A activity in China by US companies is not tracked, so far as we are aware. Conversely, China depends heavily on access to US-produced innovation. Restricting access to this innovation would significantly impact Chinese industrialization in at least the short to medium term. However, restricting access would be problematic to achieve. Because of the way we conduct research in accordance with the Open Science Model, many ideas are going to be published in journals, and that spread cannot be curtailed without great difficulty. The United States could attempt to limit genomic data flows by restricting the use of Chinese suppliers for DNA sequencing and synthesis, a goal that might gain traction among commercial customers in the United States who are sensitized to the economic risks of sending sequence data abroad. But academic customers, who are frequently driven more by maximizing the use of small budgets than by protecting IP, may be more difficult to convince. The US government could also choose to implement contractual provisions in federal grants that restrict the use of Chinese service providers. Finally, the United States could choose to curtail information flows between the two countries by beefing up digital security. This step might include requirements that data analysis from experiments conducted in the United States not be performed on Chinese computers. As an example, many companies already maintain their own BLAST servers so that internal searches are not disclosed on the wider internet. This step would create perverse incentives that increase the motivation for electronic espionage, in turn requiring additional investment to secure domestic networks and computational resources.

Personnel

From a practical perspective, it is entirely possible to reduce the flow of personnel through reductions in visas issued. Indeed, the US government has recently announced that it will cancel the visas

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[76] Magistretti and Hensel, "VCs Invested the Most Capital."

of "thousands of Chinese graduate students and researchers in the United States who have direct ties to universities affiliated with the People's Liberation Army."[77] It is not unreasonable to speculate about whether this policy might be expanded beyond this student pool. Yet such action would not be consequence-free. One obvious impact could be that the United States finds itself with a probable shortage of graduate students and trained technical labor. US efforts in developing artificial intelligence have benefited significantly from a flow of Chinese talent, many of whom elect to stay in the United States long term, and eliminating that expert labor pool is judged to be a threat to continued US technological progress.[78]

If US visa and immigration policies are further restricted, we speculate that the supply of trained labor could be improved by increasing graduate student stipends to a level attractive to domestic talent that presently pursues other options, although this would require a shift in thinking at US funding institutions and in Congress about adequate compensation for labor. For a more in-depth analysis of decoupling the flow of personnel between the two countries, we refer the reader to Zwetsloot.[79]

Potential Tools and Mechanisms for Decoupling

Extensive private capital reserves could be incentivized to invest in US domestic manufacturing. One step toward this goal, already floated by Lawrence Kudlow, the current director of the US National Economic Council, is to allow companies to deduct 100 percent of capital spending incurred in relocating operations from China to the United States.[80] As an indication of the willingness of the US government to incentivize reshoring, it has been in talks with chipmakers to build new domestic manufacturing capacity.[81] TSMC is the first company to announce such plans.[82]

One possible goal of any policies aimed at recovery from COVID-19, as well as improving resilience in the face of inevitable future threats, could be to diversify and distribute manufacturing such that the United States benefits from independent supply chains that are more robust against disruptions of all kinds. Care should be taken in implementing any such policy because centralizing manufacturing in the United States might simply shift the locus of fragility. The obvious risk of such a shift is highlighted by a hypothetical future pandemic that first emerges domestically in the United States, potentially shutting down the manufacturing capacity that policymakers are presently working so hard to incentivize. Instead, a component of resilience planning might be to diversify manufacturing and supply chains across multiple countries and regions so as to limit vulnerability to disruption in any one country.

China's modernization strategy, first set out nearly three decades ago, is designed to rely heavily on external innovation to supply technology in prioritized areas of immediate economic interest. That dependence remains today.

Foreign direct investment and VC have historically played important roles in China's domestic biotechnology development, because those investors have served as both a source of capital and a

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[77] Wong and Barnes, "U.S. to Expel Chinese Graduate Students."

[78] Mozur and Metz, "U.S. Secret Weapon in A.I."; and "Global AI Talent Tracker," MacroPolo.

[79] Zwetsloot, *US–China STEM Talent "Decoupling."*

[80] Wingrove, "Kudlow Says U.S. Should Allow Firms."

[81] Singh, "Washington in Talks."

[82] Kharpal, "Apple Supplier TSMC."

source of operational and commercial expertise.[83] Consequently, restricting inbound flows of capital might serve to temporarily slow the growth of that enterprise going forward. However, one certain outcome of that action would be to focus and incentivize domestic Chinese investment in biotechnology. There is more than adequate domestic infrastructure and expertise in China to take on the task of solely indigenous innovation.

Restricting technology transfer constitutes an additional approach, but it, too, presents longer-term risks. China's modernization strategy, first set out nearly three decades ago, is designed to rely heavily on external innovation to supply technology in prioritized areas of immediate economic interest. That dependence remains today. Therefore, the US government could examine the feasibility of including contractual language in federal research grants that can be used to restrict the export of taxpayer-funded early-stage research and IP overseas. While it would be foolish to assume, or to plan, that China will remain dependent, that current dependence nevertheless is a strategic disadvantage in the present relationship with the United States. A close look at Chinese R&D brings this point home.

Chinese R&D

President Xi recently declared that "innovation is the primary driving force behind development; it is the strategic underpinning for building a modernized economy. We should aim for the frontiers of science and technology, strengthen basic research, and make major breakthroughs in pioneering basic research and groundbreaking and original innovations."[84] Premier Li Keqiang put this more stridently during a state visit by the president of the United States, reportedly stating that "China, having already developed its industrial and technological base, no longer needed the United States [and indicated] that the US role in the future global economy would merely be to provide China with raw materials, agricultural products, and energy to fuel its production of the world's cutting-edge industrial and consumer products."[85]

Li's statement appears to be overconfident. To be sure, China is now ranked second in gross domestic spending on R&D, having grown by a factor of more than thirty since 1991, and it may surpass such US spending in 2020.[86] This achievement is often described as a successful effort to recapitulate the development of a scientific and technical infrastructure equivalent to that of the United States. However, an examination of the structure of R&D funding in China reveals a strategy that is designed to support the importation of research performed in other countries for commercial exploitation by Chinese companies.

The primary long-term strategy for the United States to maintain its strategic lead, regardless of policies intended to effect decoupling, must be to increase its own domestic invention and innovation capabilities.

In fact, counter to Xi's declaration of intent, China's R&D funding has shifted over time toward a higher percentage of corporate rather than government sources.[87] Moreover, Chinese institutions of higher learning also perform a much smaller share of total R&D, as measured by percentage of domestic spending, than do similar institutions in countries such as Japan, Germany, and Finland.[88] Despite the increases in overall R&D spending, the

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[83] Kazmierczak et al., *China's Biotechnology Development.*

[84] Jinping, "Report at 19th CPC National Congress."

[85] McMaster, "How China Sees the World."

[86] China Power Team, "Is China a Global Leader?"

[87] China Power Team, "Is China a Global Leader?"

[88] China Power Team, "Is China a Global Leader?"

amount invested in basic research by China is below the global average for an economy of its size, while the amount invested in commercial development is higher than the global average. The disparity is the result of the explicit government strategy to import early early-stage ideas developed elsewhere and to focus on rapid commercialization.

One way to understand the implementation of this strategy is to view R&D through the functional definitions that differentiate invention from innovation.[89] In the economics literature, invention is typically defined as the combination of basic research and early early-stage development that leads to a scientific paper, a mechanical prototype or some other proof of concept, and, depending on the field of application, a patent. Innovation is defined as the development work necessary to turn that proof of concept or patent into a commercializable form (i.e., a product). Over the last two decades, China has increased the share of total R&D funding spent on innovation from 78 percent to 85 percent, whereas the United States and Japan have consistently spent approximately 63 percent over that time period.[90] In other words, China has consistently operated with an invention deficit that has now resulted in significant technical debt, which is revealed by the following contrast.

The design for manufacturing infrastructure for making silicon chips comprises software tools for circuit design and simulation and hardware tools for fabrication and testing. While Asian firms have come to dominate the integration of hardware tools into automated manufacturing lines, particularly for high-end chips, US firms have maintained dominance in software tools and in specialized test and measurement instrumentation. Newly imposed US restrictions on the use of advanced chipmaking software and hardware sold by US companies are described as threatening the survival of China's largest telecommunications company by making it difficult to obtain integrated circuits for its designs.[91] Industry experts argue that China is five to ten years behind the United States in developing design and modeling software, a lead that will be extremely difficult to surmount.[92] This turn of events suggests that limiting access to analogous data and digital tools might also be applied to preserving any lead the United States now has in commercializing innovations related to biological engineering. If the United States increased its pace of innovation at the same time, the compounding effects could lead to an overall capability gap that would be difficult for China to surpass.

Yet, in the longer term, any steps that the United States may take to decouple technologically from China may serve only to slow China's short-term progress in developing biotechnology according to its own strategy. It is unlikely that the United States could dominate all areas of biotechnology in the future, just as it does not dominate all areas of innovation today. Domestic investment in Chinese talent and innovation will inevitably produce world-leading biological technologies.

We reiterate that the primary long-term strategy for the United States to maintain its strategic lead, regardless of policies intended to effect decoupling, must be to increase its own domestic invention and innovation capabilities. In the words of Robert Zoellick, former president of the World Bank and US trade representative, "The best US response to China's innovation agenda is to strengthen our own capabilities and to draw the world's talent, ideas, entrepreneurs and venture capital to our shores. We will succeed by facing up to our own flaws, not by blaming others."[93]

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[89] Carlson, *Biology Is Technology*.

[90] China Power Team, "Is China a Global Leader?"

[91] Hille, "US 'Surgical' Attack on Huawei." Per Hille, "Huawei [says] new US sanctions put its survival at stake."

[92] See Douglas Fuller's paper on semiconductors (Fuller, *Cutting off Our Nose*).

[93] Politi, "Fears Rise."

To facilitate additional discussion and provide a proposed framework for further analysis, Table 1 compiles potential benefits and costs of decoupling to both countries. However, both countries may discover that events press decision-making faster than the policy process. The ongoing pandemic serves as an unexpected test of hypotheses about the impacts of decoupling.

Table 1. Summary of Benefits and Costs of Decoupling

Policy		Benefits	Costs
Restrict flows of students and researchers	United States	• Reduce tacit knowledge transfer and general IP leakage	• Academic labor shortage forces higher costs and/or reduced pace of science
	China	• Reduce "brain drain" to West, more researchers for indigenous innovation	• Loss of cutting-edge knowledge • Loss of personnel who know how to do basic research effectively
Restrict flows of materials, including reshoring some critical manufacturing	United States	• Guarantee domestic supply chain for critical R&D supplies such as personal protective equipment, reagents, and plastic labware • Large domestic industry represents a valuable tax base • Possible export markets if domestic production is economically competitive	• Capital expense to build new plants, train workers • Initially, and possibly ultimately, domestic reagents and APIs may be more expensive
	China		• Reduced markets as United States, and other nations, guarantee a minimum percentage of production outside Chinese control
Restrict flows of capital	United States	• Potentially increased investment in United States as global capital looks for new home	• Countervailing investment controls by China would cause US investors to lose access to fast-growing economy
	China		• Lose method for accessing IP by acquisition
Restrict transfer of early research and IP	United States	• Reduce flow of early-stage technology that can be used to support economic and military development	• Possible reduction in capital available for acquisitions and licensing • Need to police and enforce restrictions, including roundabout access via third countries
	China		• Forced to pursue technology elsewhere • Increased need for domestic investment in early-stage research capabilities
General decoupling policies	United States	• Stop supporting military/civil fusion • Reduced interactions and spheres of influence lead to reduced friction in bilateral relationship	• Prices for all manner of goods rise, general inflation, reduced access to material goods • Increased defensive costs to counter IP theft, including training, network hardening, CFIUS monitoring, etc.
	China	• Reduced interactions and spheres of influence lead to reduced friction in bilateral relationship	• China development stalls at middle-income status

Impacts of the 2020 Coronavirus Pandemic

In late 2019, a new zoonotic coronavirus emerged in China. Within just weeks of the virus first being reported by doctors in Wuhan, the virus had already spread globally. While the origins of the virus, as well as the specific timing of the initial spillover, are yet to be determined, the subsequent pandemic has become a political cudgel wielded by the governments of both China and the United States in efforts to assign blame and divert attention from perceived domestic missteps. The pandemic has also accelerated an examination of tensions between the two countries that have been developing for years.

In China, officials and the press have been demanding praise of President Xi from countries around the world in exchange for donations of medical and laboratory supplies, a tactic termed "Donation Diplomacy," while simultaneously denigrating the pandemic response outside China.[94] This stance has evoked rebukes from countries in Europe, as well as the European Union, and more than twenty African countries.[95] According to press reports, China's Ministry of State Security recently issued a report concluding that, as a result of the pandemic and China's handling of it, "global anti-China sentiment is at its highest since the 1989 Tiananmen Square crackdown."[96]

One already clear element of global debate is an assertion of the necessity of diversifying manufacturing away from China. In 2012, we pointed to the increasing centralization of manufacturing capacity in China as, first, a leading indicator of China's intent to dominate biotechnology and, second, a strategic weakness for the United States.[97] While most conversations over the last decade about offshoring and outsourcing have been focused on issues ranging across safety, trade policy, profits, and capital efficiency, the current crisis has now returned other concerns to the fore. The pandemic of 2020 has generated renewed attention on the current lack of US domestic standing manufacturing capacity to produce items critical to responding to biological threats, including drugs, personal protective equipment, and medical equipment such as ventilators. The US trade representative warned "overdependence on other countries as a source of cheap medical products and supplies has created a strategic vulnerability to our economy."[98] A senior Republican aide put it more bluntly, "If China cuts off our access to key medical ingredients, that would be devastating."[99] The pandemic appears to be accelerating the discussion and implementation of policy proposals to decouple manufacturing dependencies on China, both within the United States and beyond.

Japan has already allocated $2 billion to help companies relocate outside of China.[100] India is looking to take advantage of the current focus on diversification and risk mitigation; ten weeks into the pandemic, the government had announced $1.3 billion in incentives for domestic production of drugs.[101] In one step to reshore API production, the US government has funded the construction and operation of new "continuous manufacturing" capacity that relies on automation to reduce costs and lot sizes.[102] More broadly, US administration officials are proposing to allow deducting 100 percent of the costs of relocation for companies that shift production from China to the United States.[103] These proposals would address substantive supply chain risks that have been revealed by the current crisis. In addition to pandemic-related interruptions in the supply of personal protective equipment from China, preliminary results from the Resilient Drug Supply Project at the University of Minnesota suggest impending, and

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[94] Loh, "China Flew 31 Tonnes"; and Wong and Mozur, "China's 'Donation Diplomacy.' "

[95] Myers, "China's Aggressive Diplomacy"; and Tharoor, "It's Not Just Trump."

[96] "Internal Chinese Report," Reuters.

[97] Carlson, *Causes and Consequences of Bioeconomic Proliferation*.

[98] Williams, "US Lawmakers Push."

[99] Williams, "US Lawmakers Push."

[100] Reynolds and Urabe, "Japan to Fund Firms."

[101] Findlay, "India's Pharma and Chemicals Groups."

[102] Edney, "Trump Investing Millions"; and Lee, "Modernizing the Way Drugs Are Made."

[103] Wingrove, "Kudlow Says U.S. Should Allow Firms."

While a crude assessment of sector revenues may lead to the conclusion that the United States is presently in the lead technologically, the ongoing digital transformation of biological engineering will accelerate the progress of whoever successfully develops and implements these tools.

possibly imminent, shortages of 156 critical drugs in the United States due to the ongoing disruption of Chinese manufacturing and supply chains.[104] This potential fragility in US response capabilities extends to a vaccination campaign; whether the United States has the necessary manufacturing capacity for components of that campaign—such as adequate doses of the vaccine itself, syringes, vials used to distribute doses of vaccines, and even rubber stoppers for those vials—is already in doubt.[105] The uncertainty in supply extends even to raw materials such as polypropylene, rubber, and silicone. The existing and predicted shortages of equipment, drugs, and other supplies could be viewed as tests of the robustness of the supply chain. So far as we are aware, the forecast shortages of drugs supplied from China have not yet come to pass.

The COVID-19 pandemic is a proverbial lightning bolt, illuminating in an instant all aspects of the China–US relationship and creating a high-contrast view of ties and actions on both sides. While the US government has warned for decades about China's efforts to acquire basic research and IP, the Federal Bureau of Investigation is specifically citing increased espionage related to coronavirus research "because the scale has amped up at this moment of national crisis."[106] This crisis comes amid impending presidential and congressional elections in the United States, timing that exacerbates uncertainty about future policy responses even while the pandemic demands action on short time scales that reverberates across the entire biotechnology industry. Consequently, the trajectory of biotechnology and global trade has very likely been shifted away from whatever course was set just months ago, with repercussions that will play out over many years to come.

Finally, we note that decoupling from China at this juncture is likely to come with significant costs for all concerned. If and when humanity manages to control the specific virus causing the present pandemic, it will be because we elevate constructive cooperation above narrowly construed competition. That achievement will deliver us not into a "postpandemic" period, but rather into an interpandemic period. Humanity will face this sort of foe again, and our best hope for coping better the next time around is through cooperation.

Conclusion

China and the United States today each generate at least 2 percent of GDP from biotechnology. Both countries are looking for more. The combination of biological engineering and biomanufacturing constitutes a flexible and powerful technology platform, mastery of which is critical to the physical and economic security of both China and the United States, whether separated or cooperating, in the twenty-first century. While a crude assessment of sector revenues may lead to the conclusion that the United States is presently in the lead technologically, the ongoing digital transformation of biological engineering will accelerate the

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[104] University of Minnesota, "CIDRAP Finds Supply Chain Risks."

[105] Sheikh, "Find a Vaccine."

[106] Dilanian, Ainsley, and Kosnar, "Chinese Attempts to Hack Health Care, Drug Firms"; FBI, "Targeting of COVID-19 Research Organizations"; and Sanger and Perlroth, "U.S. to Accuse China of Trying to Hack Vaccine Data."

progress of whoever successfully develops and implements these tools. China has made surpassing US capabilities in biological engineering a central pillar of its twenty-first century industrial strategy, and the government is investing in a long-term program to accomplish that goal.

While "decoupling" has become a buzzword in the US policy circles over the last three years, it is also emerging from policy proposals in China. President Xi Jinping has placed increasing emphasis on increasing indigenous innovation, and his government in essence "seeks to ringfence the entire innovation ecosystem."[107] One question policymakers on both sides must consider is to what extent either country is in a position to sustain "ring-fenced" indigenous innovation, and in what areas, or whether that isolation will lead to stagnation. Moreover, we must also ask whether decoupling direct connections in biotechnology between the two economies would result in meaningful separation, or whether capital, trade, and information might still continue to flow between the countries via a third nation or global network. Any proposal to decouple the two economies should include metrics to measure the benefits, and costs, of implementation to ensure that the position and interests of the United States are indeed improved by such a move. For example, it would appear that China would be harmed in the short term by decoupling because China's commercialization efforts depend on importing early innovation, despite claims to the contrary. Yet the US lead in biotechnology is fragile and will wither without diligent effort.

We find that, while the United States appears to hold a lead over China, the United States is in danger of recapitulating in biotechnology those past practices in trade and IP transfer that have facilitated, in other domains, the acceleration of China's technological ambitions. The United States' laissez-faire approach to the market and to planning has its advantages but also its costs, where the latter now negatively impact physical and economic security. A hands-off attitude, coupled with a short-term focus and a complacency about China's intent to improve its capabilities, now puts the US lead at risk even as scientific exchange and trade are increasing. The current global pandemic has exacerbated the already elevated political tensions between the two countries and has put the relationship under strain and scrutiny. And yet this disruption can also be viewed as an opportunity to diagnose and address these issues.

A substantial component of the present trade and security disputes between the United States and China comprises claims and counterclaims around IP and trade secrets. The US position is that China acquires IP and process knowledge through unfair and illegal means, while the Chinese position is that the United States is attempting to "contain China's rise" through unfair and illegal means; "decoupling could be seen as 'strategic blackmail' for Washington to try to prevent China from growing stronger."[108] There is a significant difference, however, between the United States working to prevent industrial espionage and insisting on fair play on the one hand and intentionally containing indigenous technological innovation to suppress the development of China on the other.

We note that accusations of the United States targeting China specifically for containment ignore seven decades of post–World War II global outreach and scientific exchange sponsored by the United States through various branches of the United Nations, the OECD, and NATO. The Soviet Union was a participant in many of these forums, even while it was subject to restrictions on technology developed in the West during the years when it explicitly portrayed itself as a foe and actively sought to undermine US interests around the world. Beijing has recently reiterated that it sees

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[107] Foroohar, "Year in a Word."

[108] Kazmierczak et al., *China's Biotechnology Development*; and Wang, "Chinese Economists Warn Beijing."

its interests in opposition to those of Washington, while at the same time it continues to rely on research funded by American taxpayers to supply Chinese technological development. This tension creates a potential strategic vulnerability for China. Indeed, casting the US defense of the rule of law and of domestic IP development as a nefarious plot to restrict Chinese growth betrays a concern that the existing, explicit state strategy of importing external early-stage research to support domestic commercialization is at risk.

Recommendations

We should measure everything better. By necessity, the quantitative economic data presented here was gathered from disparate sources, of variable quality, over a period of more than a decade. There is no centralized source of economic data for biotechnology from any country, which hamstrings any effort to either assess strengths and weaknesses or evaluate costs and benefits of proposed policies.[109] The US government should institute mechanisms to measure its domestic bioeconomy and also those of rival states. Of particular utility would be high-quality data (or at least well-bounded estimates) describing (1) sector revenues, (2) sector employment, (3) relevant international trade, (4) capital flows, and (5) state and private investment in R&D. The ultimate goal of this measurement activity is to improve our situational awareness.

We should develop the strategy and framework for response. The United States has begun contesting Chinese actions—for example, by using CFIUS to reduce IP transfers—without necessarily developing a framework for understanding the contest, nor for choosing goals, nor for developing strategies and tactics to achieve those goals. Such a framework needs to acknowledge that China sees itself engaged in an existential struggle, even if we do not. Any strategy must be calibrated to a time line of decades, far longer than congressional or presidential terms, and must survive across administrations. It must also include specific tactical policy measures subject to near-term implementation. For example, we suggest that, at a minimum, the US government examine the feasibility of including contractual language in federal research grants that requires approval before the export of taxpayer-funded early-stage research and IP overseas.

Investing to develop and maintain the lead in advanced bioengineering and biomanufacturing will require concerted attention and effort. This is not a sprint to be won, but rather a long-term competition that will require continual effort; there is no finish line, and no time limit. But there is a looming, and exigent, deadline for organizing ourselves to compete. It is not an exaggeration to classify this race as an extension of the Great Game of international affairs, because that is precisely the way our global competitors describe it. We must be engaged for the long haul, and we must begin today.

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[109] Carlson, "Estimating the Biotech Sector's Contribution."

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