Building a 21st Century Bioeconomy

Fostering Economic and Physical Security Through Public-Private Partnerships and a National Network of Community Labs

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What is the Bioeconomy, How Big is it, and How Fast is it growing?

Biological production is a substantial economic and employment opportunity for the United States. While the U.S. economy already depends heavily on biology, primarily via production in the agricultural sector, new technologies will enable the biomanufacturing of large volumes of fuels, materials, and enzymes. I hereafter refer to the totality of biological production in the U.S. economy as the "bioeconomy".

According to the USDA Economic Research Service, the U.S. agricultural sector added $331 billion to the economy in 2009[1]. This figures is impressive, but revenues from biological technologies are rising rapidly and will soon surpass those from agriculture alone.

A recent estimate published by Biodesic put total U.S. revenues from genetically modified (GM) products at more than $300 billion annually[2]. While "biotechnology" is typically thought of as either drugs or crops, a more detailed look at the sector reveals instructive complexity. Biologics (biotech drugs) had sales of approximately $75 billion in the United States in 2010. GM crops brought in at least $100 billion in farm scale revenues and GM seeds added another $10 billion. Industrial biotechnology, including biofuels, industrial enzymes, bioplastics, and other materials, generated sales of $115 billion[3]. Revenues from GM crops and biologics are growing at approximately 10% annually, while revenues from industrial biotechnology are growing at 15–20% annually.

1 See "Table 29—Value Added to the U.S. Economy by the Agricultural Sector" http://www.ers.usda.gov/Publications/AgOutlook/AOTables/CurrentTables/aotab29.xls

2 Carlson, R., "Biodesic 2011 Bioeconomy Update", Aug 2011, DocID: 20110811_01 http://www.biodesic.com/library/Biodesic_2011_Bioeconomy_Update.pdf

3 For a discussion of the methodology used to derive these figures, and of the resulting uncertainties, please see Carlson (2011).

> 2010 U.S. revenues from genetically modified products were greater than $300 billion, or the equivalent of more than 2% of GDP.

The difference in growth rates is partly explained by the high cost of developing new biologics and new GM crops. The high costs, in turn, are partially explained by the regulatory barriers accompanying drugs, food, and the environmental release of novel organisms. In contrast, most industrial applications are unregulated because they are used for materials production and do not involve the environmental release of GM organisms. In other words, the largest and fastest-growing subsector of the bioeconomy is generally not subject to regulation.

The United States is on course to dramatically increase its reliance upon biological technologies for the production of food, drugs, materials, and fuels. The relative contribution of the different sectors to the total is worth considering. In the past, drugs dominated "biotech" revenues in the United States, but today this contribution accounts for less than half the total. As biological technologies mature, becoming more useful and prevalent across different sectors of the economy, industrial and agricultural applications will amount to an ever larger share of total revenues. But, in order to foster the necessary *amount* of innovation to supply new technologies domestically, we must foster the necessary *structure* for that innovation.

The U.S. Economy Begins in Garages

Start-ups and small organizations are at the heart of both innovation and job creation in the United States. A recent re-analysis of Census Bureau data published by the Kauffman Foundation determined that 100% of net job creation in the United States is due to start-up companies[4]. Companies in their

4 Kane, T., "The Importance of Startups in Job Creation and

Table 1: Important Innovations By Small U.S. Firms, 1900–2000

Air Conditioning	Geodesic Dome	Polaroid Camera
Air Passenger Service	Gyrocompass	Portable Computer
Airplane	Heart Valve	Prestressed Concrete
Articulated Tractor Chassis	Heat Sensor	Prefabricated Housing
Assembly Line	Helicopter	Pressure Sensitive Tape
Audio Tape Recorder	High Resolution CAT Scanner	Programmable Computer
Bakelite	High Resolution Digital X-Ray	Quick-Frozen Food
Biomagnetic Imaging	Human Growth Hormone	Reading Machine
Biosynthetic Insulin	Hydraulic Brake	Rotary Oil Drilling Bit
Catalytic Petroleum Cracking	Integrated Circuit	Safety Razor
Cellophane Artificial Skin	Kidney Stone Laser	Six-Axis Robot Arm
Computerized Blood Pressure Controller	Large Computer	Soft Contact Lens
Continuous Casting	Link Trainer	Solid Fuel Rocket Engine
Cotton Picker	Microprocessor	Stereoscopic Map Scanner
Defibrillator	Microscope	Strain Gauge
DNA Fingerprinting	NMR Scanner	Strobe Lights
Double-Knit Fabric	Optical Scanner	Supercomputer
Electronic Spreadsheet	Oral Contraceptives	Two-Armed Mobile Robot
Freewing Aircraft	Outboard Engine	Vacuum Tube
FM Radio	Overnight National Delivery	Variable Output Transformer
Front-End Loader	Pacemaker	Vascular Lesion Laser
	Personal Computer	Xerography
	Photo Typesetting	X-Ray
		X-Ray Telescope
		Zipper

Source: U.S. Small Business Administration

first year of business create an average of 5.7 jobs, for a total of 3 million new jobs per year nationwide, while "all other ages of firms are net job destroyers."[5]

Small firms are also responsible for an impressive array of innovations now driving the U.S. economy. Table 1 includes a list—literally A to Z—of important innovations provided by small firms during the 20th century[6]. Mature products based on these technologies are unlikely to be mass-produced in garages, but garage innovation played a critical role during their development.

Recommendation 1: An innovation and job creation blueprint for the bioeconomy must include fostering large numbers of start-up companies.

Job Destruction", July 2010, The Ewing Marion Kauffman Foundation.

5 ibid.

6 This particular list is from Baumol, W., "Small Firms: Why Market-Driven Innovation Can't Get Along without Them", U.S. Small Business Administration, 2005, p 183, from the original in U.S. Small Business Administration, Office of Advocacy, "The State of Small Business: A Report to the President", Government Printing Office, 1994.

Many of the technologies listed in Table 1 passed through garages as part of, or as a result of, dramatic reductions in cost. Those cost reductions further increased access, which consequently led to innovation that further reduced cost. Biotechnology has been experiencing exponential decreases in cost for several decades[7]. Prices fell precipitously during this period, though they remained sufficiently high to limit access to well-funded academics and relatively large or well-funded companies. Within just the last few years, costs in biotechnology have fallen to the point where a credit card with a modest spending limit is sufficient to outfit a capable laboratory with used equipment. As a result, garages are now beginning to shelter hobbyists, artists, and entrepreneurs interesting in building a new world using biology[8]. Given the history of U.S. innovation, we should expect that burgeoning garage innovation in biology (not just biotechnology) will provide seeds for a more pervasive and more valuable bioeconomy.

7 Carlson, R., "The Pace and Proliferation of Biological Technologies", *Biosecur Bioterror,* 2003;1(3):203-14; Carlson, R., *Biology is Technology*, Harvard University Press, Cambridge, MA 2010.

8 Ledford, H., "Garage biotech: Life hackers", *Nature* 467, 650-652 (2010).

Fostering Safe and Secure Garage Innovation in the Bioeconomy

Any honest appraisal of the broad proliferation of a powerful technology must acknowledge both opportunity and risk. As described above, there is a large economic opportunity in embracing innovation in biological technologies and historically this innovation has often been found in garages. Given that biological technologies might be used in ways that cause accidental or intentional harm, how might we encourage garage innovators in biotechnology to conform to practices that reduce risk?

Community labs now emerging across the country are an excellent opportunity for the U.S. government to engage budding biological innovators on multiple fronts. The National Bioeconomy Blueprint should include support for a greatly expanded network of community labs through public-private partnerships. The purpose of the network is multifold: 1) the network will provide infrastructure to support "garage style" start-up activity; 2) community labs will enable participants to share information and resources to accelerate their own progress; and 3) community labs will facilitate the ability of the U.S. government to engage the community in discussions that range from Grand Challenges to biosecurity.

> **Recommendation 2**: The National Bioeconomy Blueprint should include support for a network of community laboratories that would provide access to infrastructure, increase communication between innovators, and facilitate engagement with the U.S. government in regards to national security and national technology development goals.

It is already feasible to build a functional garage lab for as little as $500, assuming one has access to a garage or similar space[9]. However, R&D efforts aimed at commercialization are likely to require greater resources and will usually benefit from dedicated space. It is also generally far easier to work in a biology lab populated by people who may know tricks of the trade or be able to spot potential mistakes. Therefore, access to a larger community laboratory space could enable more innovation and communication among entrepreneurs building the bioeconomy.

A network of community labs would also provide an opportunity to improve security and reduce risk. Because biotechnology is already so widespread, it is likely that reducing risk will be more readily accomplished through building open networks that increase information transfer than by attempting to prohibit or control access to the technology[10]. Indeed, The National Strategy for Countering Biological Threats has identified broad access to biological technologies as a key component of physical and economic security; "The beneficial nature of life science research is reflected in the widespread manner in which it occurs. From cutting-edge academic institutes, to industrial research centers, to private laboratories in basements and garages, progress is increasingly driven by innovation and open access to the insights and materials needed to advance individual initiatives."[11] The National Strategy explicitly recognizes that as costs continue to fall, and as skill and access proliferate, we should expect important innovations to be generated in "basements and garages". Going beyond this recognition, the National Bioeconomy Blueprint should include strategies that actively engage innovators in a conversation around 1) the risks and benefits of biological technologies and 2) priorities for technology development in the service of national needs ranging from environmental monitoring of pathogens, to new human and animal diagnostics, to biofuel production technologies.

The FBI already has a program in place to facilitate communication between its agents, local law enforcement, and biotechnology innovators working in unconventional settings[12]. As a result of this process, innovators and artists are reassured that the FBI's primary interest is public safety and security, and the law enforcement community is introduced to the mindset and working environment common in garages and community labs. This ongoing conversation should serve as a foundation for extending the model of engagement beyond national security and law enforcement policy to become a pillar of national economic policy.

Supporting the Formation and Funding of Community Labs as a National Resource

Existing community labs have been set up in empty office spaces and mixed-use buildings

9 Brunstein, J., "The quest for the $500 home molecular biology laboratory", http://www.mlo-online.com/features/201112/tips-from-the-clinical-experts/the-quest-for-the-500-dollar-home-molecular-biology-laboratory.aspx

10 See Carlson (2003) and Carlson (2010).

11 "National Strategy for Countering Biological Threats", National Security Council, November 2009, http://www.whitehouse.gov/sites/default/files/National_Strategy_for_Countering_BioThreats.pdf

12 See Ledford (2008).

around the country. These facilities are supported by a combination of donations, membership fees, and revenues from courses that cover everything from ecology, to genetic engineering, to growing functional architectural elements out of mushrooms.

The funding requirements for these facilities are generally modest. They are typically set up as non-profit organizations, and are therefore eligible to receive grant support and donations of equipment. The National Bioeconomy Blueprint should forward guidelines that clearly identify the roles and responsibilities of community labs—and of members of those labs—that would enable qualifying labs to receive government grants of financial support, surplus equipment, and expired but still useful laboratory supplies.

> **Recommendation 3**: The National Bioeconomy Blueprint should contain guidelines that clearly identify the roles and responsibilities of community labs—and of members of those labs—that would enable qualifying labs to receive government grants of financial support, surplus equipment, and laboratory supplies.

An alternative approach to the direct funding of non-profit community labs might be grants to local governments to fulfill the same role. Local libraries are already examining ways to expand their offerings beyond books and internet access to hosting "Maker spaces" with 3D printers and computer controlled machine tools[13]. These efforts could be expanded to add or convert space in public libraries into community labs that promote the safe and secure learning and practice of skills related to biological technologies. This strategy would build upon the long relationship the public has with libraries as a resource at a time when many of those facilities are seeing less use due to electronic books.

In general, the National Bioeconomy Blueprint should make it easier for innovators to try ideas. Facilities within the community lab network would not need to be elaborate, perhaps only providing access to basic laboratory needs such as a sink, deionized water, freezers, and waste disposal, while leaving other expenditures to "members". Publicly funded community labs could still charge for classes or sublet space to start-ups. One component of a successful application for government support of funds or material might be a financial plan that leads to self-sufficiency. These facilities should not be viewed as "incubators" per se, or at least not as envisioned by venture capital firms and many state agencies. Community labs, as described here, should probably not aim to generate revenue. Policy makers should recognize that some subsidy may be acceptable in exchange for the public good of a safer network and greater overall innovation.

Conclusion

If the past is any guide, producing future biotech innovation will require the involvement of small businesses and entrepreneurs. Government policies intended to foster economic growth and job creation are therefore best focused on facilitating the founding of start-ups and their participation in domestic and global markets. One mechanism of connecting small business with consumers would be the continued expansion of the USDA Biopreferred Program to include a greater array of products, and to include certification of products that are the subject of large daily demand on "Main Street".

The National Bioeconomy Blueprint must include the contributions of small organizations. Defining standards and a national role for community labs, and then supporting those labs, will improve both economic and physical security.

More information is available at www.biodesic.com

13 Reeder, J., "Are Maker Spaces the Future of Public Libraries?", http://www.shareable.net/blog/the-future-of-public-libraries-maker-spaces, and Torronne, P., "Is It Time to Retool Public Libraries as TechShops?" *Make*, 28, 28, and http://blog.makezine.com/archive/2011/03/is-it-time-to-rebuild-retool-public-libraries-and-make-techshops.html

Microbrewing the Bioeconomy:

Innovation and Changing Scale in Industrial Production

Rob Carlson, Rik Wehbring

The future of the U.S. economy might be found in a pint of beer. The rise of craft brewing in the United States is a fascinating test case of distributed biological manufacturing emerging in a market dominated by large scale industrial production. Microbreweries today compete successfully in a commodity market with the largest of multinationals, suggesting that small scale biological manufacturing may be even more successful in higher margin markets. Over the coming decades advances in biotechnology will improve the feasibility and competitiveness of manufacturing firms of all sizes.

How Big is the Bioeconomy?

Biotechnology is often associated with just two markets: medicine and agriculture. Yet the role of biology in the economy is pervasive and there are many more markets and many more dollars at stake. For example, the biofuels industry is concerned not just with liquid fuels and agricultural feedstocks, but also with producing enzymes, metabolic pathways, and organisms that convert biomass to fuels. More broadly, industrial biotech uses biology to replace industrial processes in the manufacturing of the products of everyday life. Revenues from industrial biotech in the U.S. are already larger than medicinal or agricultural biotech and are growing roughly twice as fast. In 2010, total U.S. revenues from genetically modified (GM) drugs were roughly $75 billion, total revenues from the three largest GM crops were approximately $80 billion, while revenues from GM industrial biotechnology were about $100 billion.[1]

A low regulatory burden clearly contributes to the high growth rate of industrial biotechnology. Whereas new drugs or crops require years of testing, which increases both cost and time to market, new bioplastics, biofuels, or industrial enzymes face little or no regulatory barriers to the marketplace. The critical role of regulation can also be seen in the history of the brewing industry in the U.S. Understanding the interrelated roles of technology, regulation, and demand in brewing serves as an excellent starting point for thinking about the future of the bioeconomy.

Microbrewing the Bioeconomy

Fermentation is an example of a widely distributed biological technology used to produce everything from laundry enzymes, to vitamins, to beer. The evolution of brewing economics and technology in the United States provides an example of meeting market needs via distributed biological manufacturing.

Before Prohibition, the vast majority of beer produced in the U.S. was brewed by relatively small operations and distributed locally. Refrigeration was uncommon, as were motorized trucks, reducing the amount of beer that could be produced, stored, and shipped in large quantities without spoilage. During the years 1920–1933, the official count of breweries was forced to zero by government policy and enforcement.

After Prohibition, regulatory structures kept small businesses out of the brewing market. With the aid of refrigeration and transportation, large scale breweries proliferated. Subsequently, industry consolidation set in and the number of breweries in the United States shrank. In 1979, the passage of the Cranston Act allowed individuals to brew 100 gallons a

1 Carlson, Robert H. *Biology Is Technology: The Promise, Peril, and New Business of Engineering Life*. Harvard University Press; 2010.

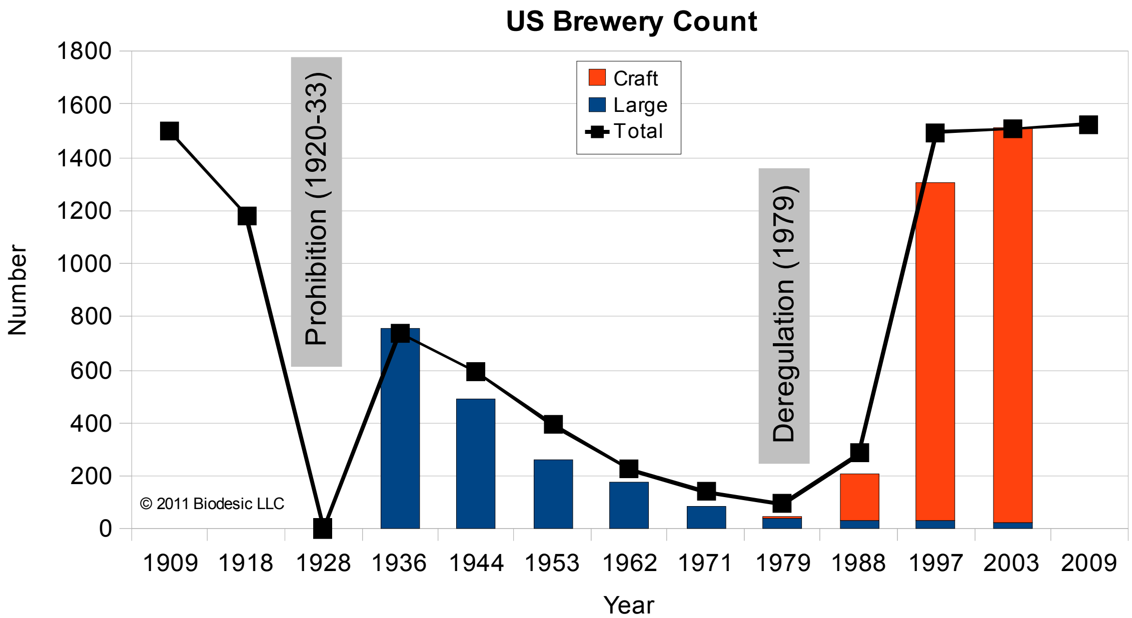

Figure 1: Historical Beer Production (Solid Line: Tremblay et al., Bars: Brewers Assoc.)

year for personal use. Contemporaneous changes to federal and state excise taxes enabled those individuals to sell their beer, and in fact granted small scale brewers a lower excise tax rate, thereby facilitating market entry for small brewers.[2] This deregulation reopened the market to craft brewers and the industry blossomed through organic growth and the preferences of consumers.

The growth in the United States of a new industrial sector shows that small scale, distributed production can compete against an installed large scale infrastructure base. According to the Brewers Association, as of the middle of 2009 there are about 1,500 craft brewers in the United States, about 20 large brewers, and about 20 "others", with brewpubs accounting for about 2/3 of the craft brewers (Figure 1).

> Conclusion 1: Emerging small scale, distributed production can compete against an installed large scale infrastructure base.

The definition of a "craft" brewer varies across the various interested organizations. From the Brewers Association: "An American Craft Brewer is small, independent, and traditional." "Small" here means less than 2 million barrels a year (at 31 gallons per barrel); "independent" means less than 25% owned by a non-craft brewer; "traditional" means either an all malt flagship beer or 50% of total volume in malt beer. There is a profusion of other requirements to qualify as a craft brewer, some of which depend on jurisdiction, and which are important for such practical concerns as calculating excise tax.

Beer generates retail revenues of about $100 billion in the United States (we estimate revenues to breweries at less than half this figure), and provides direct and indirect jobs totaling 1.9 million[3]. But craft brewers account for only a small fraction of the total volume of beer brewed in the United States; just three brewers now supply 50% of the world market and 80% of the U.S. market.[4] In 2007, only 5% of beer brewed in the United States was produced craft brewers, but they took in a disproportionate 9% of revenues. Crucially, this demonstrates not only the ability to survive in a commodity market, but also

2 Tremblay VJ, Iwasaki N, Tremblay CH. The Dynamics of Industry Concentration for U.S. Micro and Macro Brewers. *Rev Ind Organ*. 2005;26(3):307–324.

3 Beer Institute "Economic Impact". Available at: http://www.beerservesamerica.org/economic/default.aspx

4 Beer Institute "Craft Brewers Conference Statistical Update - April 2007" (PPT). Available at http://www.beerinstitute.org/statistics.asp?bid=220.

to outperform larger brewers by winning higher margins.[5]

> Conclusion 2: Small scale producers can command a premium in a commodity marketplace.

Labor & Innovation

Growing markets and high profit margins are important demand-side considerations. However, businesses are also concerned with supply-side considerations such as the availability of skilled labor and a steady flow of innovation to avoid commoditization. Home brewing had been rare in the United States prior to 1979, which points to an important feature of the market; namely, that the skill base for brewing was quite limited. Yet another effect of legalizing home brewing was that people could practice and build up their skills; they could develop new recipes and explore new business models.

The craft brewing movement developed a culture of innovation which extends to technology development. Homebrewers are now incorporating advances from the open source hardware and software communities into their projects. For example, the Brewtroller Project is an "open source community focused on developing and supporting control systems for brewing beer".[6] The hardware is based on the open source Arduino microcontroller and the associated community makes available schematics, parts lists, process code, and recipes. Notably, the goal of the software portion of the project is a program that "will walk through a series of stages (some optional) such as filling, preheat, dough-in, protein rest, acid rest, saccharifaction rest, mash out, sparge, boil and chill."[7] This is a complicated process that is presently directed toward producing the perfect pint. However, the instrument is complex enough to grow a wider variety of organisms than just yeast and to produce a wider variety of substances. The Brewtroller also reduces the skill level required to use fermentation enabling a greater number of individuals to brew beer, produce recombinant proteins, or in other ways join the bioeconomy.

Historical Lessons

In summary, the proliferation of distributed biological manufacturing that followed the legalization of craft brewing in the United States provides three general lessons relevant to considering investment in the future bioeconomy. First, it is clear that, given access to tools and skills, entrepreneurs can innovate and change markets even when those markets are dominated by large companies. Craft brewing emerged in the United States amidst an already established large scale, industrial infrastructure for producing and distributing beer. Second, small scale, distributed production can command a premium at the cash register. Third, the largest shift in the transformation of the U.S. brewing industry came about 10 years after deregulation (See Figure 1). Revolutionary change may have a long lead time, but the ensuing market transition can be quite sudden.

Structural Changes in the Marketplace

It is often said that greater efficiency is found in greater scale or, in other words, that economies of scale always favor large production facilities. This is true for many industrial activities, for example all throughout the petroleum industry, in which both thermodynamics and surface-to-volume considerations favor larger ships, larger storage tanks, and larger refineries. Consider also steel making, where one large blast furnace is more efficient than a hundred smaller smelters. This is an assertion that China unwittingly tested during the Great Leap Forward of the 1950's when peasants were directed to create backyard smelters and promptly cut down 10% of China's trees for fuel in just a few months, while producing only piles of useless low quality ore that still

5 Brewers Association. Brewers Association | Facts. Available at: http://www.brewersassociation.org/pages/business-tools/craft-brewing-statistics/facts [Accessed October 17, 2010].

6 *BrewTroller Project*. Available at: http://www.brewtroller.com/wiki/doku.php [Accessed October 17, 2010].

7 Parekh A. BrewTroller - Brewing Control System. *Hacked Gadgets*. 2009. Available at: http://hackedgadgets.com/2009/04/09/brewtroller-brewing-control-system/ [Accessed October 17, 2010].

litter the countryside.[8] In contrast, large organisms are relatively uncommon; the biosphere is dominated in both mass and number by small organisms. In other words, biological process rarely display the same returns to scale as industrial processes. Competing successfully may not require that companies the employ biological processes be large in order to succeed. Consequently, the bioeconomic marketplace may not be dominated by a few large producers. Instead, there may be numerous participants and a great diffusion of skills and knowledge.

Those participants will have access to an increasingly mature marketplace. Even a decade ago, to attempt a genetic experiment required a monolithic, vertically integrated, strategy. Producing a product based on a genetically modified organism required in-house expertise in a wide range of skills spanning biochemistry, molecular biology, and microbiology. Yet within the last few years every one of these specialized skills has become available for purchase as a service in a competitive marketplace. Specialization creates new niches where companies can thrive; it also facilitates proliferation and competition. It is now quite simple to find an interesting gene sequence in an online database, electronically submit this to a DNA foundry to be fabricated, and have the resulting molecule shipped to a protein expression house for manufacture and delivery to your doorstep. This protein could be used as a tool in house or could be immediately reshipped as a product. That the skill base for genetic modification has recently seen a rapid proliferation suggests we may soon see an economic disruption analogous to the transformation of the brewing industry. However, given the great breadth of application of genetic modification, the resulting disruption could lead to far greater change within our economy

Conclusion

The bioeconomy is much bigger than recombinant insulin or genetically modified corn. Increasingly, ordinary industries outside medicine or agriculture will be transformed through the adoption of biological technologies. Technological change always brings the possibility economic disruption and produces new winners or losers. One significant aspect of biotechnology is that the economies of scale are very different from those of previous technology revolutions, such as chemistry, and may favor smaller, distributed production rather than enormous centralized facilities. The historical example of microbrewing demonstrates that these ideas are not just theoretical, but very real. Intense small scale innovation, coupled with biotechnology, has allowed microbrewers to gain a share of the beer market and be more profitable than traditional macrobrewers. The transition to a bioeconomy is just beginning and the years of disruptive change are still ahead.

8 Economy EC. *The River Runs Black: The Environmental Challenge to China's Future*. illustrated edition. Cornell University Press; 2004.