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The Global Roots of Innovation in Plant Biotechnology

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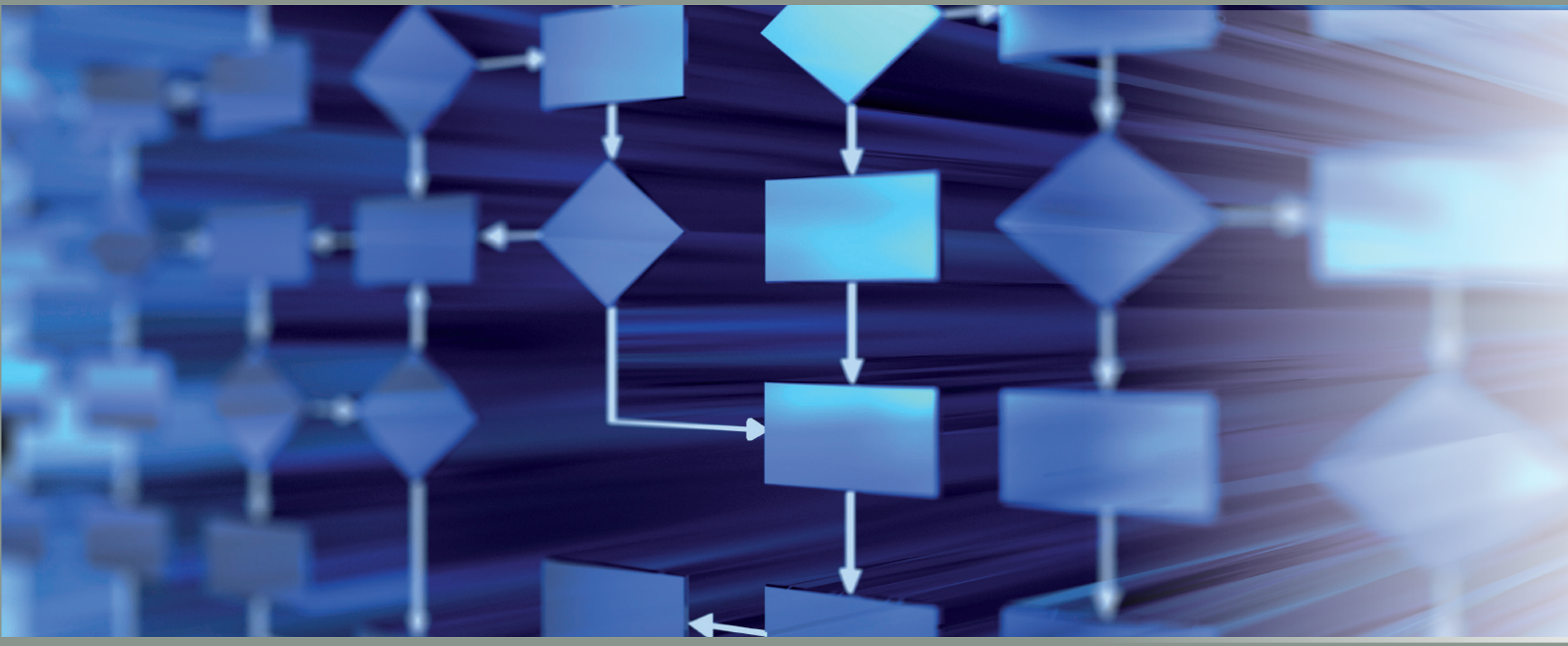

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Abstract

Innovation in agricultural biotechnology has the potential to increase agricultural productivity and quality, ultimately raising incomes for farmers across the world. Advances in the field have produced crops that are resistant to certain diseases, that result in higher yield than before, that can grow in extreme soil conditions, such as in arid and salty environments and even those that are infused with nutrients. Moreover, the technology has been hailed as a potential solution to addressing global issues of hunger and poverty. It therefore follows that innovation in this field finds strong support from the public sector as well as the private sector. This paper traces the evolution of the global innovation landscape of plant biotechnology over the past couple of decades. Drawing on information contained in patent documents and scientific publications, it identifies the sources of innovation in the field, where they are located and demonstrates how these innovative centers connect to one another. There are three important findings. First, the global innovation network of agricultural biotechnology showcases a prime example of how innovation activities spread to many parts of the world. Second, while there are more countries participating in the innovation network, most of these innovation centers are concentrated in the urban areas and away from the rural where most of the transgenic crops are harvested. Third, the increasing need for collaboration between the private and public sectors to bring the invention to the market may have effect on how the returns to innovation are appropriated.

JEL codes: O34, O38, Q16, R12

Keywords: *Innovation, government policy, agriculture, genetic engineering, geography of innovation*

Disclaimer

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All errors remain our own.

1. Introduction

The last few decades have seen an unprecedented level of technological advances in the field agriculture. Modern farming, especially in the industrialized economies, use sophisticated technologies and devices to make farming more productive, efficient, sustainable and environmentally friendly. Investments in infrastructure that collect large amounts of information from sensors, aerial images, drones and GPS technology have transformed farming. At the molecular level, developments in biotechnology has helped produce crops with desirable traits, such as those that are resistant to certain diseases and even those that are able to tolerate arid and salty environments. It is therefore not surprising that modern farmers must have some understanding of science, engineering, and business.

Biotechnology is changing the agriculture industry. Technically speaking, biotechnology refers to "any technological application that uses biological systems, living organism, or derivatives thereof, to make or modify products or processes for specific use."[1] When applied to agriculture, it can refer to the different methods of working with biological systems and life sciences. It can also refer to the implementation of advanced molecular and cellular technologies and techniques. In both the broader and narrower sense of its application, agricultural biotechnology relies on the discoveries and research tools of a relatively new field of science to improve the productivity and increase the outputs of an industry that has been in existence since prehistoric times.

The objective of this chapter is to illustrate the workings of the global innovation network (GIN) of agricultural biotechnology—with a focus on plant biotechnology—as a case study. It first chronicles the events that shape the industry's global innovation landscape. Using two complementary measures of innovative activities—patent documents and scientific publications—this chapter identifies the location of innovative activities in the industry. It shows how more countries are innovating in the industry than before. It also points to how the spread of innovation concentrates within innovation clusters in different parts of the world.

Several features of agricultural biotechnology make it a unique case study. First, agricultural biotechnology has the potential to address food security issues in many parts of the world. It thus has support from various national, international and not-for-profit organizations to promote its diffusion globally. However, insufficient levels of absorptive and innovative capacities, including inadequate resources to commercialize the inventions in many emerging economies has necessitated collaboration with the private sector.

Second, the increasing need for collaboration between the private and public sectors imply some changes to the use of Intellectual Property (IP) protection. On the one hand, private sector firms rely heavily on the IP system to appropriate their returns on investment. On the other, public sector research institutions in many emerging economies tend to shy away from the IP system, focusing instead on ensuring that the knowledge can be easily shared. Collaboration between the two sectors – either to help with commercialization (for the research institutions) or as sources for diverse pool of germplasm (for the private sector) – leads to a probable hybrid approach to IP use.

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[1] The United Nations *Convention on Biodiversity* (CBD). The CBD definition differs slightly from the Biotechnology Innovation Organization (BIO), a major industry association of the biotechnology industry. BIO defines biotechnology as "technology based on biology – harnessing cellular and biomolecular processes to develop technologies and products that help improve our lives and the health of our planet (https://www.bio.org/what-biotechnology)."

Third, the public perception of innovation in agricultural biotechnology is still evolving, and this has a strong impact on the policies, rules and regulations governing the industry. Governments, influenced by the competing concerns expressed by civil society, agribusiness stakeholders, and farm groups, approach the latest technological advances offered by the industry in varying degrees of caution. This, in turn, reflect the different policies, rules and regulations across regions. Accordingly, the industry's players adapt their innovation and business strategies to these changes.

This chapter is organized in the following manner. The next section highlights how four transformative events have shaped of the plant biotechnology innovation landscape. The third section takes a closer look at the geographical spread of agricultural biotechnology innovation worldwide. It attempts to show where and how innovation has dispersed to certain regions of the world. It also provides explanation of how this dissemination took place. The penultimate section discusses how despite the spread of agricultural biotechnology to different parts of the world, that there is a rising concentration of innovators in the industry. It further shows this concentration is influenced by the policies, rules and regulations governing the field. The final section concludes with suggestions for further research.

2. The evolving landscape of plant biotechnology

Biotechnology is the latest breakthrough innovation to disrupt the agriculture industry (G. Graff, Heiman, Yarkin, and Zilberman, 2003). It affects all main sectors of the industry, from crop farming to animal livestock and even to agricultural commodity processing (see Box 1).

Box 1: Biotechnology methods and applications are in all major sectors of agriculture

Plants

- *Plant breeding and seeds:* development of new varieties and traits through hybridization, outcrossing, mutation, genetic engineering and genome editing, tissue culture, grafting and cloning of plants
- *Soil health and fertility*: biofertilizers, culturing and use of microbes for soil amendment, plant growth
- *Pest control and pesticides*: biocontrol strategies, biopesticides, breeding and genetic engineering of pest resistance traits in both crops and livestock, mutation and genetic engineering of herbicide tolerance traits in crops

Animals

- *Animal breeding and genetics*: traditional and advanced animal breeding techniques, artificial insemination, in vitro fertilization, embryo transfer, and other animal reproduction technologies as well as cloning and stem cell technologies
- *Animal health*: biologics and vaccines, biological approaches to diagnose, prevent and treat disease
- *Animal nutrition*: feed processing technologies, and feed supplements, as well as breeding and genetic engineering of crop traits for feed quality

Biofuel production: fermentation and other biorefining processes, as well as breeding and genetic engineering of crop traits for biofuel feedstock

Agricultural commodity processing: biological applications in milling, separation, ingredient formulation, fermentation

Table 1: Selected discovery or scientific breakthroughs in agricultural biotechnology field

Year	Discovery/scientific breakthrough	Affiliation
1866	Mendel postulated a set of rules to explain the inheritance of biological characteristics in living organisms.	St. Thomas's Abbey, Brno, Czech Republic
1907	Erwin Smith identified *Agrobacterium tumefaciens* cases crown gall tumors in plants	Bureau of Plant Industry, U.S. Department of Agriculture, Washington, D.C. USA
1911	Ernst Berliner isolated *Bacillus thuringensis (Bt)* bacteria that kills feeding caterpillars of the Mediterranean flour moth	Research Institute for Cereal Processing, Berlin, Germany
1927	Hermann Joseph Muller demonstrated that mutagenesis results from exposure to x-rays	University of Texas, Austin, USA
1928	Frederik Griffith demonstrated transformation of hereditary traits in bacteria	Pathological Laboratory, Ministry of Health, United Kingdom
1943	Oswald Avery, Colin MacLeod, and Maclyn McCarty demonstrated that DNA is the material responsible for genetic heredity	The Rockefeller Institute for Medical Research, New York, USA
1953	James Watson, Francis Crick, Maurice Wilkins and Rosalind Franklin discovered the double-helix structure of DNA.	Medical Research Council, Cavendish Laboratory, Cambridge, and Kings College, London, United Kingdom
1961	Marshall Nirenberg and Heinrich Matthaei deciphered the genetic code	National Institutes of Health, Bethesda, Maryland, USA
1974	Stanley Cohen and Herbert Boyer developed a technique - rDNA - that would splice together strands of DNA from more than one organism, paving the way for genetic engineering	Stanford University and University of California, San Francisco, California, USA
1977	DNA sequencing methods were independently devised by Walter Gilbert with graduate student Allan Maxam, and Frederick Sanger	Harvard University, Cambridge, Massachusetts, USA, and Cambridge University, England, United Kingdom
1981	George Willems and Robbert Schilperoort genetically engineered first plant (tobacco) using Agrobacterium	University of Leiden, Leiden, Netherlands
2000	Complete sequencing of *Arabidopsis thaliana* genome published in 2000, as part of the Aradibopsis Genome Initiative	Consortium of universities as well as public research institutions in the United States of America, Japan and Europe
2012	A new genome editing technique, CRISPR-Cas9, is developed	University of California, Berkeley, California, USA; University of Vienna, Austria; Massachusetts Institute of Technology and Harvard University, Cambridge, Massachusetts, USA; and Vilnius University, Lithuania

Source: Based on Babinard, 2001; Hermans, Löffler, and Stern, 2008; Swaminathan, 2012; The Arabidopsis Genome Initiative, 2000.

The origin of agricultural biotechnology can be traced back to 1866 when Gregor Mendel postulated the fundamental laws of inheritance using pea plants in an abbey in the Czech Republic. He laid the groundwork for the rise of scientific breeding and genetic engineering, the genesis of agricultural biotechnology. Subsequent breakthroughs and discoveries in the 1920s and 1930s on methods of chromosome and gene mutation, followed by the discovery of the double helix structure of deoxyribonucleic acid (DNA) in 1953, at Cambridge and London in Great Britain, led to an explosion of research in genetics, genes, genetic variation and heredity in organisms. **Table 1** lists a few breakthrough discoveries as well as innovations that form the basis of biotechnology methods and their application in agriculture.

It was not until the development of recombinant deoxyribonucleic acid (rDNA) technologies in bacteria at Stanford University and University of California, San Francisco, in California, USA, that the basic approach to working with DNA at the molecular level was subsequently taken up in microbes and then, only after further breakthroughs, in plants and animals (Table 1). The commercial application of biotechnology tools and techniques was first advanced in the field of medicine in the mid-1970s. Agricultural applications began just a few years later.[2] This was primarily because initial developments in molecular biology were mainly in medical schools and universities that were not involved in agricultural research. The Land Grant universities in the U.S.–supported by the federal government to promote development in the field of agriculture, among others–did not initially play an important role in the development of biotechnology because the experts as well as sources of funding were in medicine, and not agriculture (Kenny, 1988). As the use of biotechnology in medicine and human health became more established, scientists began to apply biotechnology to veterinary science for animal health and to plant breeding.

By the 1980s, the USPTO granted patents on genetically engineered (GE) plants (Carrer, Barbosa, and Ramiro, 2010). Towards the end of the decade, field trials of transgenic plants were underway in Australia, Canada, some European countries and the U.S. These events coincided with the rise in the number of agricultural biotechnology specialized start-ups established during the 1980s and 1990s. China began commercially farming the first transgenic crop, pest-resistant tobacco, in 1988. But, by the mid-1990s, farmers in China stopped growing these varieties, as many tobacco producing companies were concerned with using the technology (Tao and Shudong, 2003).

Figure 1 illustrates the potential commercial viability of agricultural biotechnology as inventors filed for protection on their inventions in many more jurisdictions from 1980s onward, measured by the difference between total number of patent filings (red line) and the first filings (blue line). Advances in plant biotechnology in mid-1980s forced government regulators and the public to question when and how to ensure that these purposefully transformed crops would not adversely affect human health and the environment.

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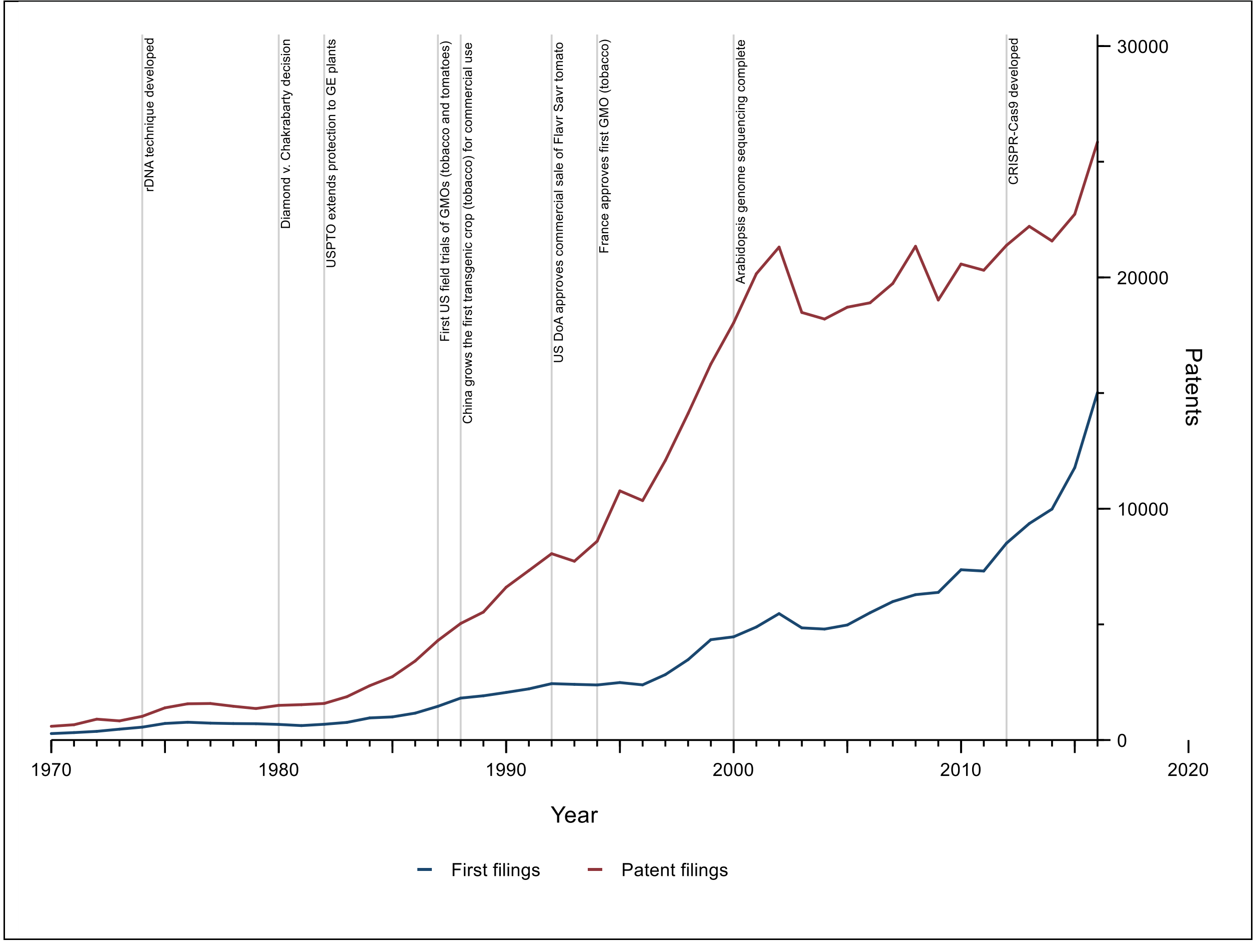
[2] The first licensed drug using rDNA technology was human insulin drug, produced by Genetech and licensed to Eli Lilly and Company (Johnson, 1983).

Figure 1: The rise of genetic engineering in 1980 coincides the increase in the number of subsequent patent filings worldwide

Total patent filings of plant biotechnology, 1970–2017



Source: WIPO based on PATSTAT and PCT data.

2.1. How policies, rules and regulations shaped the industry

Policies, rules and regulations implemented during the uptake of agricultural biotechnology have fundamentally shaped its innovation landscape. These include government support of basic science, availability of intellectual property (IP) as an appropriation mechanism, as well as regulations on the use of the resulting innovations.

Intellectual property (IP) policies

Most jurisdictions do not allow for the patentability of things that exists in nature, including biological organisms. However, the lines of what can be patented or not became blurred in light of new technological advances in biotechnology.[3]

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[3] Other forms of IP protection on plants are plant varieties and plant patents (specific to the United States). However, these two IP instruments are outside the scope of this paper and thus not addressed here.

In the United States (U.S), two changes related to IP policy in the 1980s played pivotal roles in shaping the agricultural biotechnology industry. They led to the increasing reliance on IP to appropriate returns to investing in this innovation (Barton and Berger, 1970). The first was the passing of the Bayh-Dole Act in 1980, that streamlined rules for the patenting by universities of research results funded by taxpayers. The second was the extension of patent protection to genetically modified organisms. The landmark case decided by the U.S. Supreme Court, *Diamond v. Chakrabarty,* paved the way for genetically modified organisms to be patented (Brennan, 1980). By 1985, the USPTO extended patent protection to genetically engineered plants. Europe and the rest of the world soon followed suit.

The appending of an IP-specific agreement, called TRIPS, to the treaty establishing the multilateral global trading system of the World Trade Organization, implied that many of the developing countries would potentially have to allow for the patentability of genetically engineered organisms. However, several emerging economies, such as Brazil, restrict the patenting of certain plant biotechnology inventions, especially those that relate to seeds or plant varieties. Instead, the private sector in Brazil rely on *sui generis* rights, such as breeders' rights, to protect their innovations. Some file for patents on the development process or complementary assets that lead to crop biotechnology inventions (Figueiredo, Vasconcellos, Prado, and Grossi-de-Sa, 2019).

One of the concerns with patenting in agricultural biotechnology is similar to concerns expressed on biotechnology overall (Barton, 2000). That is the granting of exclusive rights on research tools, which is argued may dampen follow-on innovation. Specific to agricultural biotechnology, patents would make it difficult for poorer economies to benefit from research that could alleviate poverty and address world hunger problems. In addition, critics have pointed out that most of the patents granted in the area have been overly broad and are likely to infringe on other proprietary technology, resulting in a relatively high rates of litigation in the industry.

Policies and regulations to protect consumers and safeguard the environment

Europe has a relatively long history with agricultural biotechnology, almost similar to the U.S. Some of the important breakthroughs were discovered on the continent (see **Table 1**). Moreover, in the early 1990s, Belgium, France and the United Kingdom (U.K.) were three of the top five countries that accounted for nearly 95 percent of transgenic crops released since 1986 (Brenner and Komen, 1994). However by the end of the decade, the continent's sentiment on transgenic crops changed. Between 1993 and 2003, the European Commission (Commission) as well as five of its Member States imposed a *de facto moratorium* on the approval of genetically engineered organisms.[4] From 2003 onward, the Commission put into place several regulations and directives on genetically modified organisms (GMO).[5] During the moratorium, the Commission differentiated plants whose genes have been edited via conventional breeding methods and those via that have been genetically edited using biotechnology tools (see **Box 2**). The measures established specific requirements to conducting field tests and planting of transgenic crops on the continent, importation and use of transgenic crops, as well as labelling of GMO products.

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[4] See WTO dispute settlement case DS291: European Communities — Measures Affecting the Approval and Marketing of Biotech Products. https://www.wto.org/english/tratop_e/dispu_e/cases_e/ds291_e.htm

[5] For the list of regulations and directive on GMOs see https://ec.europa.eu/food/plant/gmo/legislation_en.

Box 2: Centuries of plant genetic improvement

Genetic improvement of crops has been taking place for centuries. The techniques used to select and propagate crop varieties with desirable traits – known as cultivars – for cultivation can generally be divided into three categories: traditional, conventional and modern. All three methods are in use today, in varying degrees.

Traditional methods of gene editing, which began circa 10,000 BC, involved the domestication of crops from the natural biological diversity. These crops differed from their wild predecessors through the propagation of careful selection of specific plant materials, which were cultivated for human consumption and use.

Gregor Mendel's postulation on the law of genetic inheritance in 1863 underpins the science of conventional breeding. Conventional breeding of new crop varieties and traits involved the sexually reproduction of two compatible crop varieties that would produce a mutated offspring with the desired biological traits.[6] Oftentimes this method of genetic manipulation would require many crosses to get to the right combination of genes that would produce the desired crop. It also necessitated sexual compatibility of the crops.

Today, new crop varieties could be achieved by altering the DNA of the plant through use of biotechnology. This modern crop breeding technique relies on the understanding of the plant's make-up – genomics – and makes changes to the plant's DNA using different methods of genetic engineering.

There are two ways to introduce desired traits into plants and they differ according to plant type. Dicots, or broad leaved-crops such as cotton, soybean and tomato, rely on the transformation brought about by a bacterium known as *Agrobacterium tumefaciens*. In nature, the bacterium infects plants,inserting some of its own DNA directly into the DNA of the plant. By modifying the bacterium to exclude its unwanted traits and include the gene of interest, a crop may be transformed through bacterial infection. The cells containing the new gene subsequently can be identified and grown using plant cell culture technology into a whole plant that now contains the new transgene incorporated into its DNA.

Monocots, or grass species such as maize, wheat, and rice, are transformed by physically shooting small tungsten balls coated with an external DNA into the plant's genome. Some of the DNA comes off of the balls and is incorporated into the DNA of the recipient plant. Those cells can also be identified and grown into a whole plant that contains the foreign DNA.

The differences between the traditional and conventional breeding, on one hand, and its modern counterpart, on the other, boils down to the control over the breeding process.
The outcomes of plants bred through the traditional and conventional methods are often unpredictable. Breeders choose the parents with the desired traits to cross but the progeny may not carry the genotype with the desired traits or display it, the phenotype. Moreover, the breeder may only choose traits of plants to cross that are sexually compatible.

Modern breeding techniques such as the use of genetic engineering, on the other hand, allows for targeted transfer of desirable crop traits, the transgene, to breed new transgenic plants in an efficient and fast manner. These transgenic crops are also known as genetically modified organisms (GMOs). First, it simplifies the breeding process by bypassing the need

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[6] Other traditional ways include hybridization as well as grafting.

for sexual compatibility of the plants with desired traits, and allows for selection of desirable traits from any living organism. The desired traits can come from the same species or cross-species; it can even come from a modification of the expression of the plant's own genes. Second, the targeting the desired gene, tracking it and inserting it into a crop's DNA ensures its clean breed of the crop, and excludes the potential of unwanted, ancillary traits are often a by-product of traditional and conventional breeding. Moreover, there is a faster turnaround in the development of new crop varieties in modern breeding techniques than its predecessors.

Source: FAO (2004), and Persley and Doyle (1999).

Several explanations have been put forward for this change towards transgenic crops. Graff and Zilberman (2007) argue that Europe's strong agrochemical businesses enjoyed a comparative advantage in chemistry and wanted to prevent their competitors from eroding their market share using biotechnology. Others proposed that EU farmers saw the measured approach to approving genetically engineered plants as an opportunity to prevent agricultural commodities from the rest of the world from entering their market (Sheldon, 2004). Regardless of the motives, the EU regulations – including its most recent decision on the equivalence of transgenic crops produced using *CRIPSR-Cas9* techniques with conventional GMOs – have arguably had a chilling effect on the research and development of agricultural biotechnology on the continent.

Figure 2 shows the share of agricultural biotechnology patenting over total patent filings for the U.S. and several European countries.[7] From 1980s, the share of patents filed in the industry has been increasing at a faster rate than the average filings for both the U.S. as well as EU-28 countries. However, from 1995 onward there is a widening gap between the patent filing growth rates in the U.S. and EU-28. It is difficult to say conclusively if this is due to Europe's *de facto moratorium* without further research. But since 1998 the EU-28 countries have been filing at relatively slower rate than the total patent filing rate.

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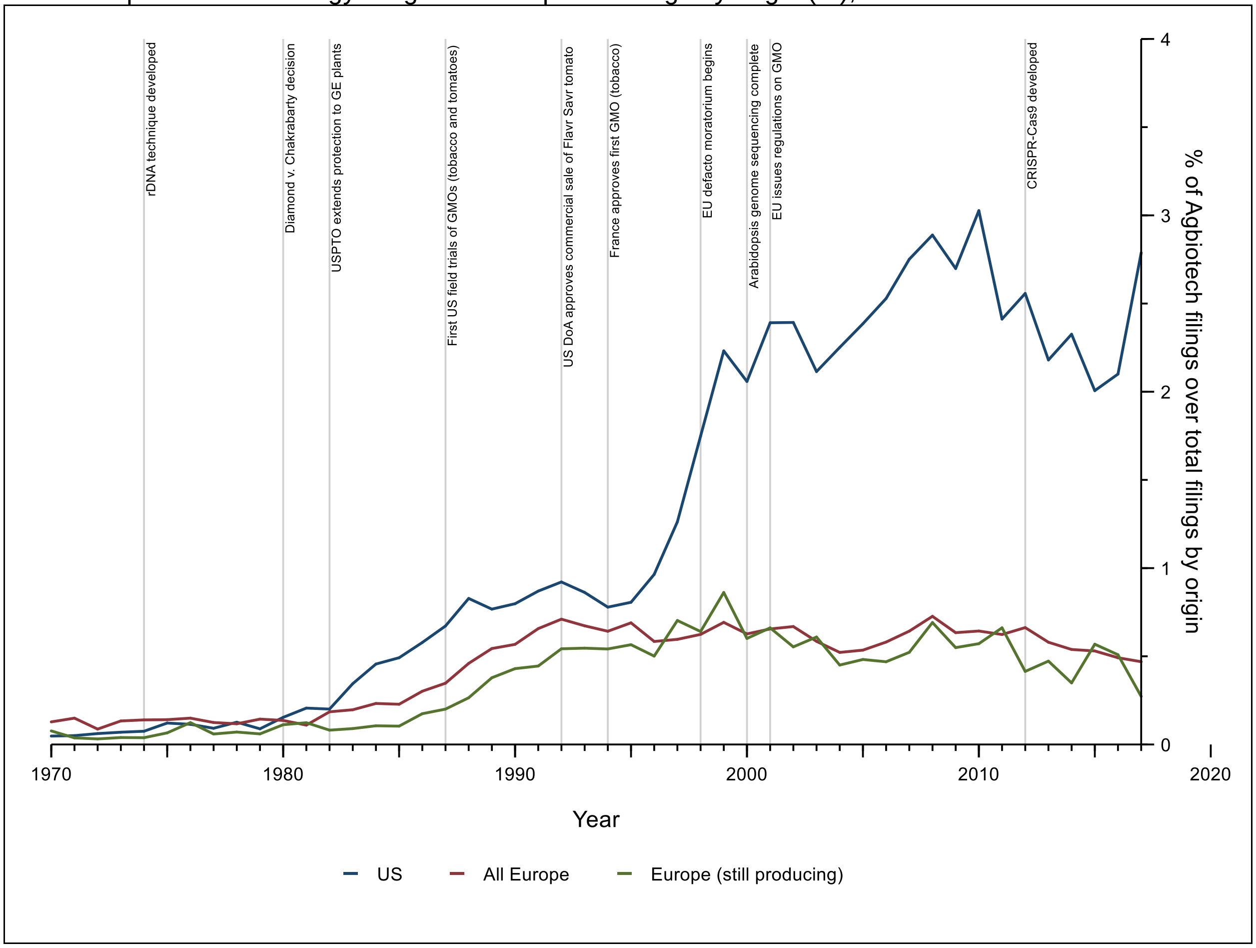
[7] The European countries included in the figure are: EU-28 (except for missing data from Malta, Bulgaria and Poland). Portugal, Spain and the U.K. are included in the list of countries in Europe still farming transgenic crops.

Figure 2: A gap between patents filed by US applicants versus those from EU-countries began in the mid-1990s

Share of plant biotechnology filing over total patent filings by origin (%), 1970–2016



Source: WIPO based on PATSTAT and PCT data.

Industry reports have recorded how the continent’s stance on transgenic crops affected the business strategies of companies in the industry. A recent study conducted by the USDA Foreign Agricultural Service reports that many European companies have shifted their R&D outside of Europe, relocating to places such as the U.S.. While public institutions as well as universities in Europe continue to conduct basic research in the field of plant genetics, the likelihood of research outputs to reach the EU markets is small. In addition, the report notes that many European biotechnology firms have shifted their focus away from agricultural and towards medical or industrial applications (USDA Foreign Agricultural Service, 2018). Another report cites that one of the major European multinational companies in the industry, BASF, discontinued the development and marketing of transgenic crops for the EU in 2012 (ISAA, 2017).

2.2. How emerging economies shift the innovation landscape

While many of the main advances in biotechnology occurred in the U.S. and some in European countries, China was the first country to plant transgenic crop in its farming system in 1988. The emerging economies, led by China, India and Brazil, are increasingly innovating in

agricultural biotechnology. From 1990 to 2013, China's public sector agricultural R&D spending grew by nearly ten-fold, from USD 1 billion to USD 9 billion (Clancy, Fuglie, and Heisey, 2016). At the same time India's spending tripled, from less than USD 1 billion to almost USD 3 billion, and Brazil's almost doubled, from less than USD 2 billion to almost USD 3 billion. Public sector spending in the U.S., by contrast, grew from about USD 4 billion in 1990 only moderately, then declined from 2003 to 2013, and returned its initial level of USD 4 billion by 2015.
Today, China's public agricultural R&D spending exceeds that of the U.S. by two-fold.

China's rise as an agricultural biotechnology powerhouse

From the investments of emerging economies, China is fast becoming one of the lead innovators in the agricultural biotechnology industry. Both trends from patent filing as well as scientific publication, 1998-2017, confirm China's rising influence in the field. As in many emerging economies, and during the early nascent years of genetic engineering the U.S., majority of the innovation in agricultural biotechnology in China was conducted by the public sector, namely universities and public research institutions (Huang, Hu, Wang, Keeley, and Zepeda, 2002).

China has a relatively strong innovation capacity in agricultural biotechnology, partly due to the strong political and financial backing from its government since 1980s.[8] The only genetically modified organism currently farmed in the world that has been developed by an emerging economy comes from China. In 1991, the Biotechnology Research Center of the China Academy of Agricultural Sciences (CAAS) in Shenzhen initiated a major research program to develop cotton variety that would address the problem of the cotton bollworm, a major pest for cotton grown in warm climate (Pray and Huang, 2003). By 1995, the crop was approved for testing in field tests and by 1997, the transgenic cotton was approved for commercial use.[9]

Other emerging economies

Similar to China, for many developing economies most of the biotechnological research was and is conducted by institutions supported by public funds. However, unlike China, many of them do not have adequate capacities or financial resources to conduct research in the field (Fukuda-Parr, 2006; Komen and Persley, 1993; Persley, 2000). For these emerging economies, national agricultural research centers (NARS) as well as international agricultural research centers (IARCs) play important and pivotal roles in the research and in advancing agricultural biotechnology to address these countries' concerns (see subsection 3.2). Brazil and India, however, are exceptions to this case. In both Brazil and India, strong research capacities from their public research institutions have contributed to the advances of agricultural biotechnology in their respective regions (FAO, 2004; Figueiredo et al., 2019).

2.3. The geographic sources of plant biotechnology innovation

Majority of the innovation in plant biotechnology come from the three global centers of innovation, namely the U.S., European countries, and East Asian countries. While the beginnings of agricultural biotechnology may have begun in universities and public research institutions, most of the commercialization is conducted by companies in the private sector.

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[8] Ibid.

[9] The transgenic crop is *Bacillus thuringiensis* (Bt) cotton.

Table 2 show the different applicant type that contribute to plant biotechnology in the top six patenting countries. It provides the average share of patent applications filed by individuals, companies, universities and public research institutions for every ten years since 1980. In most cases, the majority of innovations from the top five countries in agricultural biotechnology come from the private sector, except for China.

Table 2: Private sector accounts for most patent filings in the world

Comparison of applicant type breakdown by top six patent filing countries

Share of inventions by companies

Country	1980s	1990s	2000s	2010s
China	25.0	9.6	10.6	27.9
Germany	47.3	50.4	76.6	73.4
Japan	56.9	69.9	58.1	51.9
South Korea	50.4	34.1	31.8	22.5
Switzerland	70.2	89.1	93.9	95.1
U.S.	63.0	62.5	73.3	77.8

Share of inventions by universities and public institutions

Country	1980s	1990s	2000s	2010s
China	39.0	32.7	48.3	42.6
Germany	10.4	17.2	9.9	12.6
Japan	3.1	5.3	24.1	22.1
South Korea	5.8	6.3	23.3	32.0
Switzerland	1.0	1.3	3.9	3.7
U.S.	25.2	30.8	20.9	16.6

Share of inventions by private individuals

Country	1980s	1990s	2000s	2010s
China	25.8	43.8	29.1	16.6
Germany	30.7	18.9	9.7	10.8
Japan	15.4	13.6	13.8	17.1
South Korea	32.4	49.5	33.9	28.6
Switzerland	27.6	8.6	2.1	0.6
U.S.	8.8	4.4	5.1	5.1

Source: WIPO based on PATSTAT and PCT data.

Note: Share of unknown applicant type ranges from 1 to 25% on average, with China at the higher end due to incomplete data.

In the U.S., many important agricultural biotechnology innovations which came from publicly funded science labs were commercialized through start-ups and contracts based on join research partnership between research labs and private companies.[10] Early startups such as Cetus (Agracetus), Agrigenetis, Calgene, Advanced Genetic Systems, Molecular Genetics in the U.S. were pioneers in applying biotechnology to the field of agriculture. Two factors facilitated this transfer of technology from university lab to the private sector. First, the Bayh-Dole legislation passed in 1980, allowing for research outputs funded with public money to

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[10] The most important agricultural biotechnology innovations originated in universities, were transferred to start-up companies, and were then absorbed by global corporations (Kenny, 1988).

rely on IP rights as a means for appropriating the returns to investment. And secondly, universities had established technology-transfer offices with the aim of applying the research results from labs to the real world.[11]

In Europe, major chemical and pharmaceutical companies explored the commercialization of inventions from agricultural biotechnology. Companies such as Syngenta (Anglo-Swiss) and Bayer and BASF (German) shifted their R&D have invested to some extent in biotechnology. The shift in R&D strategy was in part in response to the growing awareness of environmental and regulatory issues related to using chemical fertilizers in farms, and the incentive to generate high-value agricultural products (Babinard, 2001). Many of the large multinational companies consolidated their in-house R&D efforts in rDNA. In addition, many have expanded their research scope to include both medical as well as the agricultural applications of biotechnology.[12]

In a similar vein, Japan’s foray into biotechnology came from large existing companies with diverse backgrounds such as tobacco (Japan Tobacco), technology (Mitsubishi), pesticides (Sumitomo), brewing (Suntory and Kirin), and pharmaceutical (Mitsui Toatsu) industries in the early 1980s. However, unlike Europe, these Japanese companies relied on joint ventures with companies from the U.S. to build their technology base; one count set the number of strategic alliances for biotechnology at 375 (GRAIN, 2019).

China also relied on joint ventures to help commercialize research outputs. For example, in order to commercialize the *Bt* cotton developed in the 1990s, the Chinese firm Heibei Provincial Seed company entered into a joint venture with two American companies, Monsanto and Delta and Pineland. The transgenic cotton was available to Chinese farmers in 1997 (Huang et al., 2002).

3. The global innovation landscape of plant biotechnology

The global innovation landscape of agricultural biotechnology is spread relatively well across the globe. In addition to the three main corridors of innovation in the U.S., Europe, and East Asian countries, namely Japan and South Korea, the agricultural biotechnology international clusters appear across different regions including India, Israel and China in Asia, Australia in Oceania, and Argentina and Mexico in Latin America and the Caribbean.

Figure 3 maps the international clusters of agricultural biotechnology across the world. It shows the most inventive regions producing agricultural biotechnology innovation based on the number of scientific publications as well as patented inventions (see **Box 3** on how the clusters are determined).

International clusters of agricultural biotechnology (in green) appear to coincide with the metropolitan cities of the world. These clusters are comparable across countries and regions. The national clusters (in mustard) are regions within a country where there inventive activities related to agricultural biotechnology take place.

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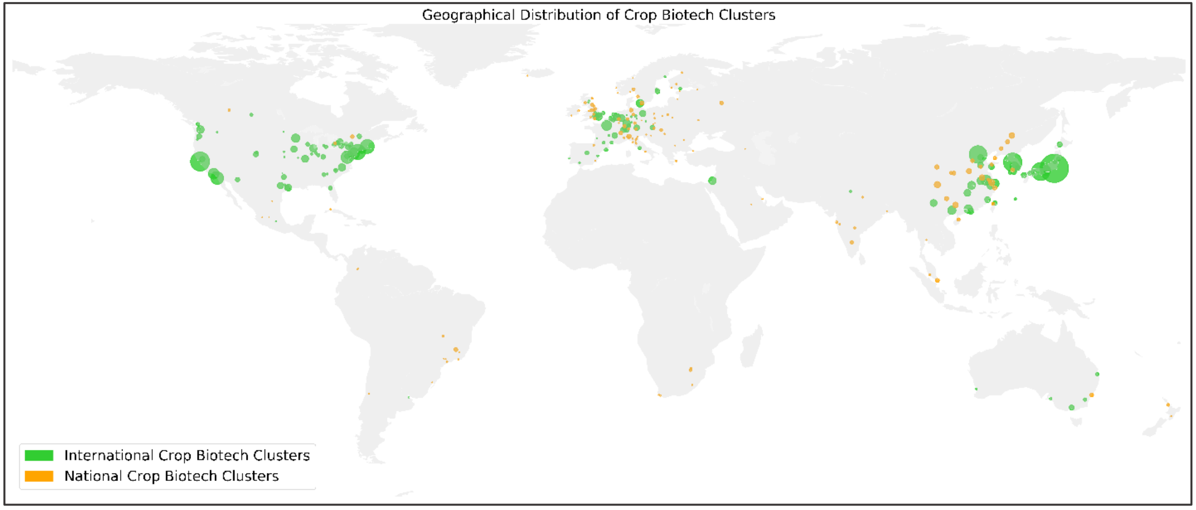
[11] The first biotechnology start-up based on rDNA technology in the United States was Genetech, Inc.

[12] For example, Sandoz (pharmaceutical company) and Ciba (chemical) merged in 1996 to form Novartis to focus on life sciences in the pharmaceutical and agrochemical field. In 1999, Novartis became a “pure Healthcare company.” See Babinard, 2001; Doyle and Persley, 1998; Persley, 1990.

Figure 3: Agricultural biotechnology clusters are spread across the globe

Geographical distribution of plant biotechnology clusters, 1970-2017



Source: WIPO based on PATSTAT, PCT and Web of Science data.

Box 3: Identifying the international and national clusters of agricultural biotechnology

Identifying international and national clusters of agricultural biotechnology involves at least three steps.

Step 1: Identify agricultural biotechnology patents and scientific publications

Patents: use combination of IPC/CPC codes and keywords to arrive at crop-specific agricultural biotechnology (see annex for complete list). The categories for crop patents include: (i) crops genetic improvement, (ii) pest control in crops, and (iii) soil fertility.

Scientific publications: use a combination of well-known top journals in agricultural biotechnology and combined with relevant agricultural biotechnology-specific keywords (see annex for details).

Step 2: Geo-coding the addresses of inventors and authors

The addresses of patented invention inventors and scientific publication authors related to agricultural biotechnology are geocoded and mapped. Inventors' resident addresses as listed in the patented documents are used, while for scientific publications, the authors' addresses are usually not disclosed. Instead, the location of the authors' affiliations are employed.

Step 3: Differentiating between national and international clusters

Once the location of both patented inventions and scientific publications are mapped out, two different thresholds are used. For international clusters, foreign-oriented patent families only are considered, in combination with scientific publications. For national clusters, both singletons – patent families for which a patent application is made only in the same country as the applicant's residency – and foreign-oriented patents along with the scientific publications are used. Moreover, international clusters are based on a global threshold combining the foreign-oriented patents and scientific publications, while national clusters are only based on a country specific threshold. Only the international clusters are comparable across countries.

3.1. Where innovation has spread

Both the international as well as national clusters of agricultural biotechnology show a relatively quick diffusion of innovation across countries since the 1980s. Farmers in the U.S. and Canada started using transgenic crops in 1998. Around the same time, countries such as Argentina, Australia and China started growing transgenic crops as well (Barry and Horsch, 2000).

Figure 4 show the global innovation landscape of agricultural biotechnology for every ten years since 1990. It shows the evolution of the innovative regions in the industry across the three decades and illustrates how patenting and publication tend to mirror one another. The figure also shows how some regions lean more towards more patenting, while others towards scientific publications. The U.S., for example, seem to lean towards patenting while most developing countries toward scientific publications.

More disaggregate regional analysis, on patents and scientific publications separately, show similarities and differences between agricultural biotechnology inventions as measured by patent documents against those measured by scientific publications. The top five countries inventing in agricultural biotechnology field are the U.S., Germany, Switzerland, China, Japan and South Korea. The top five countries publishing in same field are the U.S., China, Germany, Japan, France and Spain.

Figure 4: Relatively wide distribution of agricultural biotechnology innovation since 1998

Distribution of plant biotechnology clusters by patent filings and scientific publications, 1998-2007 (top) and 2008-2017 (bottom)

Source: WIPO based on PATSTAT, PCT and Web of Science data.

Note: Size of bubbles correspond to the relative volume of patent and scientific publications, respectively, per time period.

This difference is to be expected for several reasons. First, patenting of agricultural biotechnology inventions are subject to different patentability criteria across different jurisdictions. Hence, using patenting as the sole indicator of agricultural biotechnology would miss the important research work carried out by scientists in countries where patenting possibilities may be narrower.

Second, while both patented inventions and scientific publications are complements in measuring innovative activities, there are some important differences. For example, inventions disclosed under patenting requirements may be closer to the commercialization stage than research outputs published in scientific publications (Griliches, 1990). Moreover, majority of the inventions in the U.S. are by the private sector, which tend to rely on patents, while Chinese patents tend to consist of higher share of universities and public institutions as sources of innovation (see **Table 2**).
In addition, studies examining patent-publication links show that the dates associated with scientific publications tend to lag after patent applications; this is partly to ensure that the invention novelty would not be invalidated by the publication date.

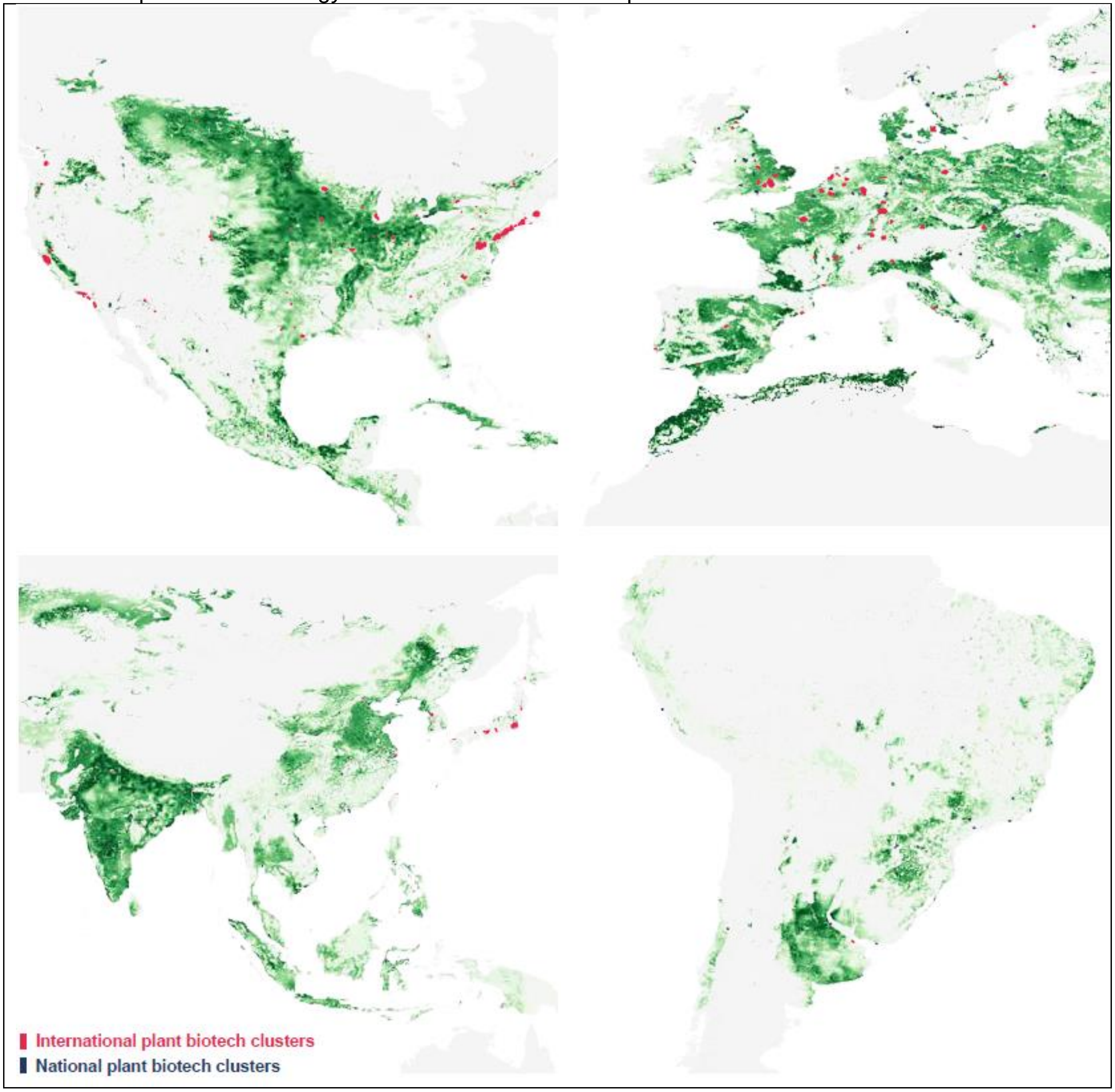
Nevertheless, there are notable insights from the global mapping of agricultural biotechnology's international clusters. Most significantly, there is an urban-rural divide between the location of agricultural biotechnology innovation and agricultural production (Samad and Graff, 2020).

Figure 5 maps the international agricultural biotechnology clusters (in red) against the crop areas of the world (in blue) for three regions: North America, Europe and Asia. Most of the international agricultural biotechnology clusters tend to be in urban areas, such as San Francisco/San Jose, Boston, and New York City. This clustering within urban areas is observed in biotechnology generally, due to strong agglomeration forces that allow researchers as well as companies to benefit from knowledge production, knowledge spillovers, and specialized inputs necessary for the industry (Hermans et al., 2008).

Some agricultural biotechnology clusters that are adjacent to major crop areas, represented by the green shades on the maps in Figure 5. The location of these clusters is not an accident. Most of these clusters are located in major important agriculture-related universities, that is, Land Grant Colleges, in the U.S. In emerging economies, however, the location of these clusters adjacent to crop areas seem to coincide with the presence of IARCs and NARS in the region.

Figure 5: Where innovation takes place is far from the farming fields

Location of plant biotechnology innovation centers and croplands



Source: WIPO based on PATSTAT, PCT and Web of Science data. Crop land data from Ramankutty *et al.* (2008).
Note: Green areas represent croplands and pastures circa 2000.

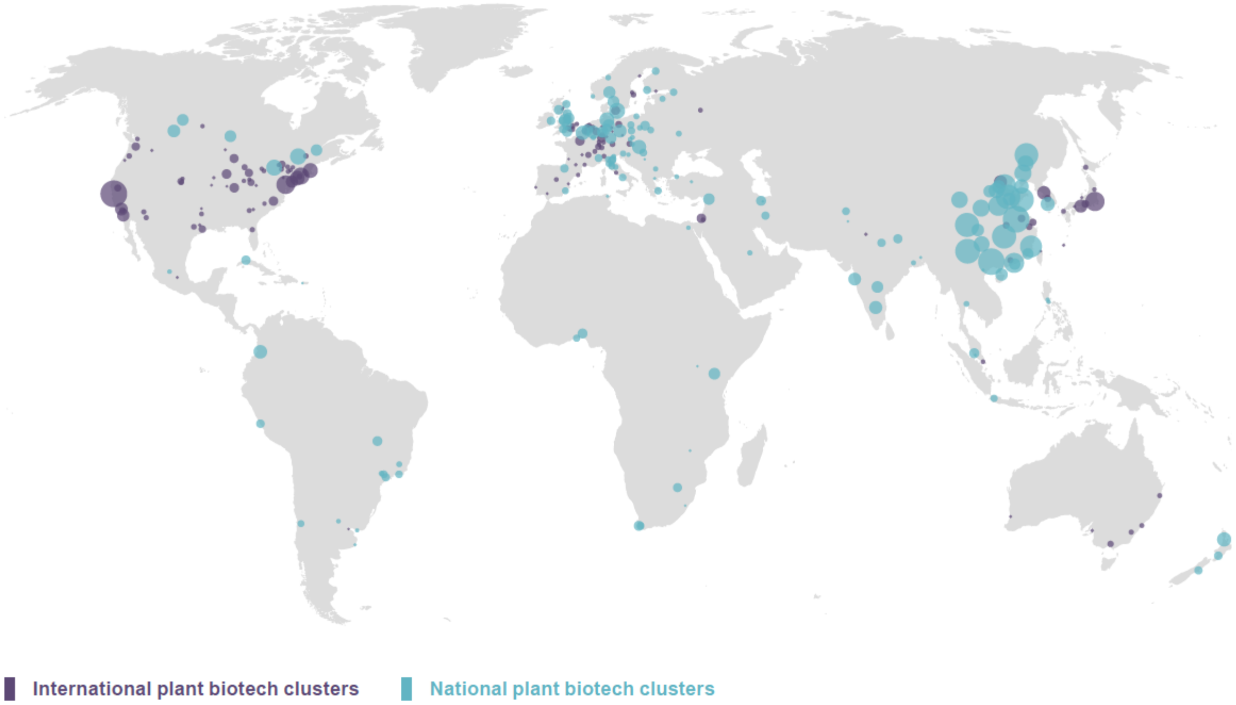
Moreover, the international clusters of agricultural biotechnology tend to be adjacent to major innovative regions, especially in the U.S., Europe, and Japan.

Figure 6 plots the location of these international clusters alongside the global innovation hotspots (GIH) and global specialized clusters (GSC). For these three regions, these co-location mirrors the biotechnology clusters, lending further support to the strong agglomeration forces of innovative regions.

Where the location of international clusters differ from the GIH as well as GSC are due to the location of large public institutions, such as universities or NARCs, that support agricultural research work.

Figure 6: Innovative activities tend to cluster, particularly in metropolitan areas

Worldwide distribution of innovation, comparison of GIH, SNCs and international plant biotech clusters



Source: WIPO based on PATSTAT, PCT and Web of Science data.

Hence, the second insight is the importance of research facilities in rural areas. The few international clusters that are adjacent to agricultural production areas are likely due to the presence of large research institutions located in those regions. For example, the international clusters of Mexico, Argentina, and India are close to their respective NARC's locations. Moreover, the presence of these agricultural institutions are likely to create a regional ecosystem that are conducive to start-ups as well as R&D facilities of companies in the industry. Samad and Graff (2020) show that the single most important determinant of the number of inventions to come from a given region is the number of inventions that have come from that region in the past. This relationship represents the sticky nature of fixed investments in regional knowledge infrastructure and human capital, as well as the localized nature of knowledge spillovers.

In addition, universities and public institutions continue to play an important role in advancing the knowledge in agricultural biotechnology. For example, the latest development in the field is the potential brought about by *CRISPR-Cas9*, which was co-developed by scientists at the University of California, Berkeley, California, Umea University, Sweden and University of Vienna, Austria.

Both **Table 2** in subsection 2.2 and **Figure 9** in subsection 4.1 show how collaboration with universities and public research institutions continue to be relevant in the field of agricultural biotechnology.

3.2. How and why innovation spreads

The spread of innovation in agricultural biotechnology industry to other regions can be attributed to two factors. First, the commercialization efforts of agricultural biotechnology companies to bring their products to the market require field trials before the transgenic crops enter the farming systems. These field trials are often conducted in several farms with different regional agro-ecological conditions. This implies that the transgenic crops have to be customized to the local conditions, including the need to adapt it to the combinations of soil, landform and climatic characteristics to the region. Most of the transgenic crops in emerging countries during the late 1990s were locally adapted germplasms of their North American counterparts (Barry and Horsch, 2000).

Second, global movement and international support to eradicate world hunger has translated into various multinational, regional and even national initiatives to promote robust and sustainable agricultural programs.

How innovation spreads downstream: from lab to field

Research institutions or private companies that intend to commercialize their inventions have several developmental stages to undergo. In many cases – both in the cases of the high-income and emerging economies – the transformation from lab research work to the field tests and later large-scale farming are usually done by the private sector (Barry and Horsch, 2000; Fukuda-Parr, 2006).[13]

Before introducing the new transgenic plant into the farming system, the plant biotechnology firms must obtain approval under at least three regulatory processes from the respective local authorities. These include: (i) approvals to conduct field test, (ii) approvals to farm for commercial purposes, and (iii) approval to sell and market to consumers.

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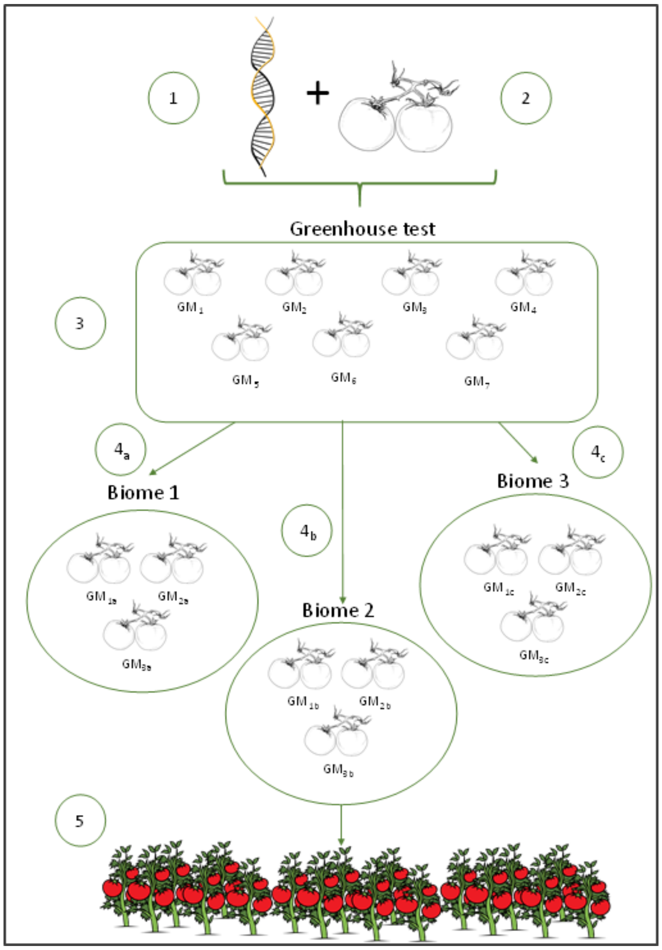
[13] Fukuda-Parr (2006) details how the top four transgenic crops – soybean, cotton, canola and maize – farmed globally is a reflection of the private investments from the private sector operating in the seeds industry in “economically important crops” relevant to the United States market.

Box 4: Example of transgenic crop process from lab to field



Box 4 provides a simplified illustration of how a transgenic plant progresses from the research lab to the farming system using the Flavr Savr tomato—which was briefly commercialized in the mid 1990s—as an example. In general, a research lab – either in the university, public institution, private company or any combinations thereof – would transform existing plant lines by inserting the promising gene(s) and producing an initial transgenic line with several permutations of the initial plant (steps 1 and 2). This line would be tested in a greenhouse and if they survive, would be fit for field tests (step 3). In many countries approval from the competent authorities are needed before the field test are carried out (step 4). The field tests are usually conducted in different regions to adapt to its agro-ecological conditions.[14] This is usually done through cross-breeding the region's cultivars with the new transgenic crop using the conventional method (step 5). If the field tests are successful, the owner of the transgenic crop would need to apply for the approval to use the crop in breeding programs.

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[14] See Chapter 2 of FAO (1996) for further details on agro-ecological conditions.

In the case of Flavr Savr tomato, researchers at Calgene, an American start-up company, generated nearly 50 independent transformation events for line selection of every tomato plant variety transformed (step 3) in the late 1980s (Bruening and Lyons, 2000). From these transgenic lines, more than ten field experimental field trials were conducted in Mexico, and the U.S., namely California and Florida (step 4). By 1994, the U.S. Food and Drug Administration gave its approval for the sale of the first transgenic food in the U.S. Due to high production and distribution costs, Calgene was acquired by Monsanto (now Bayer) in 1994.

How efforts to provide knowledge as a public good help diffuse innovation worldwide

Formal agricultural research centers and universities specializing in agricultural science play a pivotal role in the research as well as diffusion of innovations in agricultural biotechnology.

First, discoveries in the field were mainly generated by scientists and researchers in universities as well as public research institutions; this is similar to many examples of breakthrough innovations.[15] Backed by government funding as well as the mandate to improve agronomics, advance genetic improvements in crops and agricultural innovation in general, most of these institutions conduct important basic and applied research that may lead to field application. Moreover, many of the fundamental advances in molecular biology and genetics were by the publicly funded institutions.

Second, collaborations between scientists across different research centers facilitate the diffusion of the knowledge. In the U.S., the broad network of agricultural research institutions built in the rural regions of the country through the Land-Grant colleges as well as agricultural experiment stations help facilitate this knowledge diffusion (Samad and Graff, 2020). Moreover in 1839, the Agriculture Division of the Patent Office (now known as the U.S. Department of Agriculture (USDA) was established to collect and disseminate research and innovation related to agriculture to the public (Wright, 2012).

In many emerging economies, one such link is through the network of IARCs, for example the Consultative Group for International Agricultural Research (CGIAR). The CGIAR consists of 15 independent, non-profit research centers focused on innovation in agricultural - including the two research centers that have played important roles in the Green Revolution - the International Maize and Wheat Improvement Center (CIMMYT) in Mexico City, Mexico and the International Rice Research Institute (IRRI) in Los Baños, the Philippines. This network provides a unique research infrastructure. It has shaped the historical evolution of innovation in agricultural biotechnology, particularly in crop genetic development. IARCs such as this one plays the role of nodes in the global innovation network connecting agricultural scientists and breeders across many NARS, including agricultural research universities in the world.

Besides sharing researchers, one way that IARCs help diffuse the agricultural biotechnologies into emerging economies is by licensing-in proprietary technologies held from private companies (Barton and Berger, 1970). A technology may be purchased by the IARC from a firm at an agreed cost. The firm may be paid by funds raised by donor countries, or is rewarded through good public relations. The collaboration from the IARC and the private firm would be made available royalty-free to developing economies or on reasonable royalty terms.

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[15] See Zilberman *et al.* (1997) on case studies of sequential patterns with which new technologies are developed, scaled up and commercialized. They show that start-ups and universities were more likely to carry out the research phase while major corporations would carry out the latter stages of product innovation development. See also WIPO (2015).

The second collaboration is through joint research collaboration. The private firm may collaborate with the NARS or IARC with commitment of commercial exclusivity on the resulting technology in the developed markets. Developing economies would be entitled to the resulting technology at a preferential rate. Crucial in these two collaborative frameworks is that there is market discrimination between the high income, developed economies and their developing counterparts.

4. The concentrating innovation network

The specific characteristics of the agriculture industry may explain the spatial distribution of innovative activities seen in **Figure 3**. First, solving food scarcity and food security issues are global objectives set by many national governments and international institutions (FAO, 2004; Serageldin and Persley, 2000). Hence, governments, intergovernmental agencies as well as non-for-profit organizations tend to support the research, diffusion and use of agriculture-related innovation that may address these problems (Bijman and Tait, 2002). Second, the nature of agriculture-related innovation inherently implies a very specific need to adapt the innovation to different regional agro-ecological conditions. As noted in subsection 3.2, many commercialization efforts require additional R&D investments to adapt the innovation to the different regions, necessitating some knowledge transfer between the owner of the innovation and the researchers in the targeted farming regions. Moreover, recent studies have underlined the importance of accessing the germplasms and cultivars from different regions to further advance the reach of innovations in agricultural biotechnology (Byerlee and Fischer, 2002; FAO, 2004).

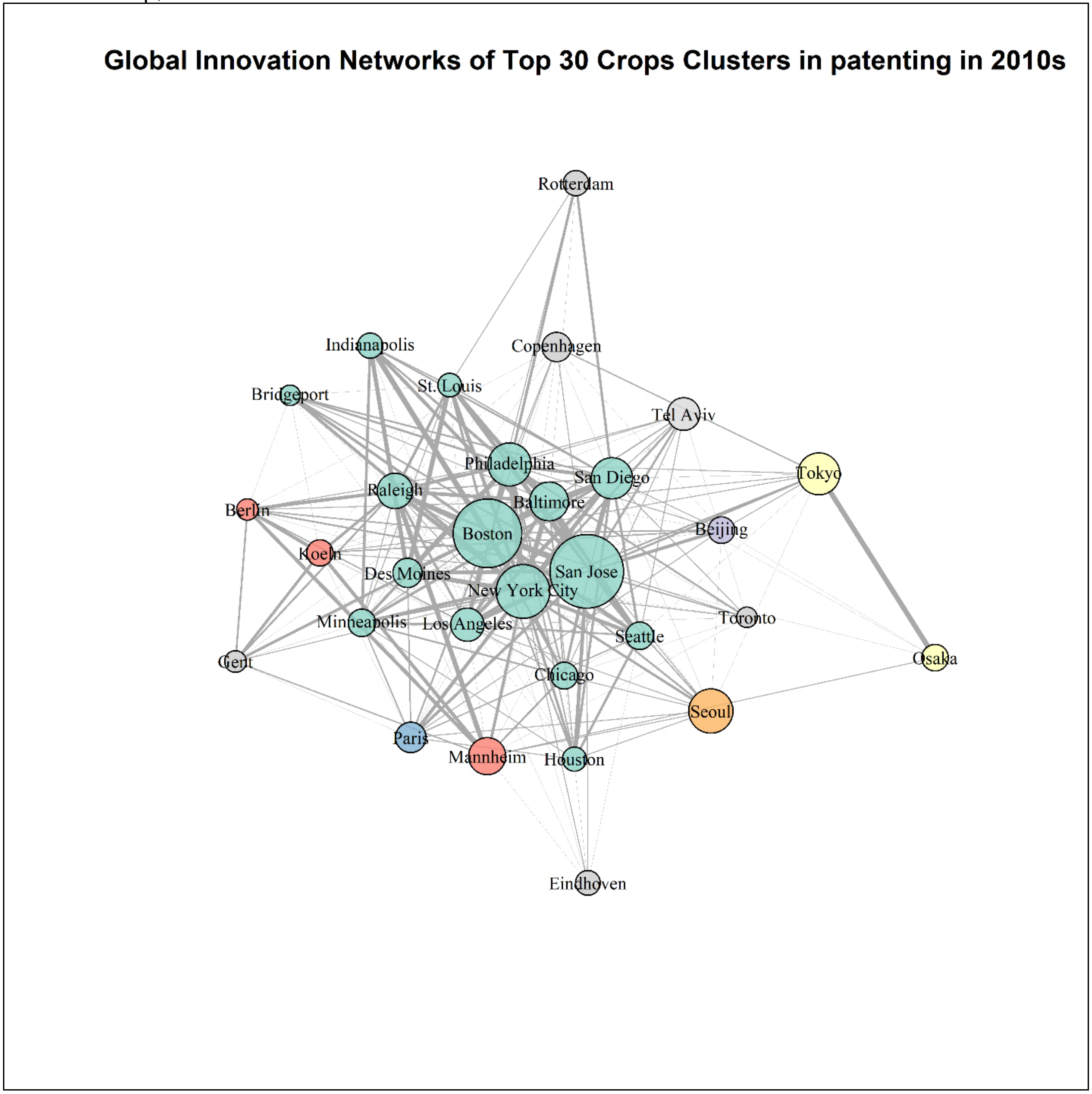
In spite of this spread, there is a concentration of who innovates in agricultural biotechnology. This concentration reflects: (i) where the sources of innovation are and their linkages to one another, (ii) the policies and regulations that govern the research and commercialization, and (iii) the resulting effect from the interaction of innovation, IP policies and specific regulations of this industry.

4.1. How are the nodes connecting?

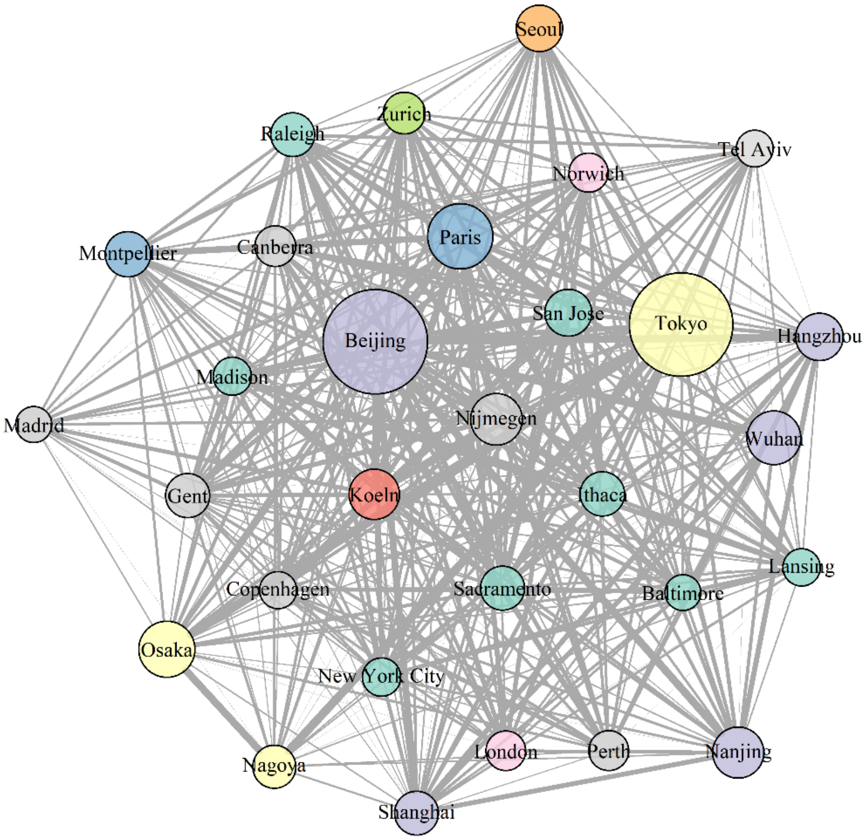
The main innovation clusters in agricultural biotechnology are found in the leading countries that invest in agricultural R&D. Figure 7 provide rough illustrations of how the top 30 international clusters connect to one another, based on patented inventions (top) and scientific publications (bottom) for 2010-2017. These clusters link to one another based on co-inventorship and co-authorships across regions. The sizes of the bubbles in the figure represent the volume of patented inventions (or scientific publications) in that particular cluster, while the thickness of the lines represent the frequency of the interactions between them.

Figure 7: More openness in scientific publications than patenting?

Differences in linkages between international agbiotech clusters when comparing co-inventorship and co-authorship, 2010-2017



Network of Top 30 Crops Clusters in scientific publications in 2010s



Source: WIPO (2019) based on PATSTAT, PCT and Web of Science data.

International clusters based on patented inventions highlight the fact that that the U.S., Canada, Australia, countries in Europe, particularly Germany, France, Netherlands, Denmark, and the U.K., and countries in East Asia (Japan, South Korea, and China) are home to most of the innovation for agricultural biotechnology. Moreover, like in the case of biotechnology, distance is not necessarily the main criterion for connecting. For example, inventors in the two largest international clusters, San Jose and New York City (nearly 4,724 km apart), interact more frequently than San Jose with San Diego (approximately 739 km apart). Inventors in Rotterdam, the Netherlands, co-invent more frequently with inventors in San Diego than with their compatriots in Eindhoven.

The picture of plant biotechnology international clusters based on scientific publications confirms the homes of the international clusters as in the case for patenting. However, the size of the clusters and their interactions with one another are more diverse and denser. The two biggest clusters based on scientific publications are Beijing and Tokyo. Here, the U.S. does not figure as prominently as it does in the case of patenting.

Nevertheless, the U.S. has by far the most number of international clusters based on both measures of innovation: 16 clusters using patents as a measure and seven using scientific publications. It is followed by Germany with three international clusters as measured by patents, and China with six international clusters as measured by scientific publications.

Both measures of internationally comparable agricultural biotechnology clusters point to the U.S. as the country with important clusters of agricultural biotechnology.

Importance of access to specialized researchers

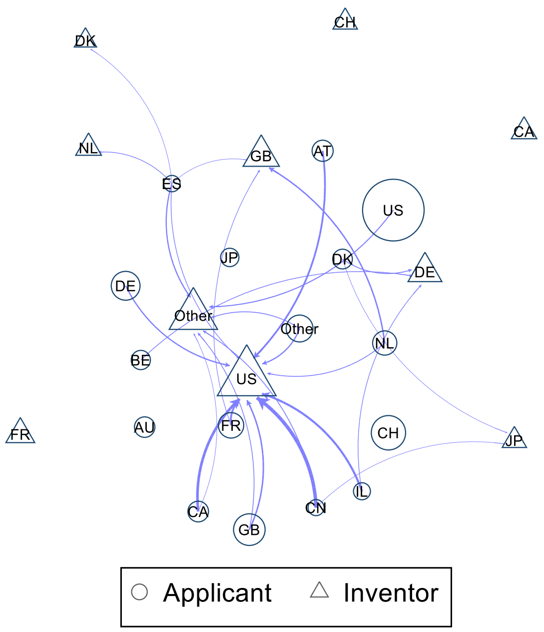
One of the reason that explains the U.S.' importance in the international clusters of plant biotechnology is due to its specialized inventors. When looking at where most of the inventors reside, especially when the inventors' residence are different from the applicants', show an overwhelming centrality of the U.S. as the location to find agricultural biotechnology researchers.

Figure 8 illustrates the location of researchers in agricultural biotechnology by exploiting the different locations of the applicant (circle) and the inventor (represented by the triangle shape) of a particular patent. The top figure provides the links between applicant-inventor pair in the years 1970-1999, while the bottom paints the picture for the years 2000-2016. The lines connecting the applicant to the inventor is a proxy for the strength of the relationship, as measured by the share of applicant-inventor mix above the ten percent threshold of the total number of co-applications. For example, after the year 2000, at least ten percent of all co-applications from Switzerland are of the US-inventor-Swiss-applicant combination.

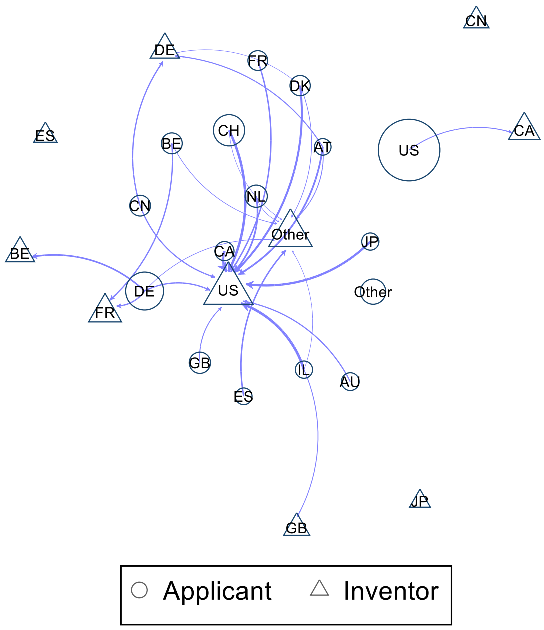
In both scenarios, many patent applicants residing outside the U.S. search for American researchers and scientists. One of the reasons why American scientists and researchers are highly sought after can be partially explained by the fact that many of the importance discoveries relating to agricultural biotechnology came from American universities and public institutions. The second explanation is the first-mover advantage of private companies in the U.S. that had invested strategically in the exploration of commercial applications of biotechnology in plants. Therefore, the result of these combined factors weighted the innovation network in agricultural biotechnology towards the U.S., relative to the background of biological research in agriculture that was more widely distributed globally

Figure 8: Specialized researchers in agricultural biotechnology tend to come from the U.S.

Comparison of top 10% applicant–inventor ties of foreign-oriented patents, 1970–1999 (top) and 2000–2017 (bottom)



Agbiotech, offshoring co-application network, period (<2000)
Share of innovation offshoring by applicant-inventor partner (Foreign-oriented families, no applicant-inventors)
Bubble=total patents, Arrow=% of total int. co-applications, only >10% shown)
Path:N:\OrgESD\Shared\IES\data\Mapping_WIPR15\Agbiotech\charts\chart_3.10\ch_3.10.0, created on 23 Aug 2019, 17:19:51.



Agbiotech, offshoring co-application network, period (>=2000)
Share of innovation offshoring by applicant-inventor partner (Foreign-oriented families, no applicant-inventors)
Bubble=total patents, Arrow=% of total int. co-applications, only >10% shown)
Path:N:\OrgESD\Shared\IES\data\Mapping_WIPR15\Agbiotech\charts\chart_3.10\ch_3.10.1, created on 23 Aug 2019, 17:19:57.

Source: WIPO based on PATSTAT and PCT data.

4.2. Why the concentration?

Reliance on scientists and researchers in the main innovating countries of the U.S., Europe and the East Asian economies underscore the concentration of innovation in the hands of a few innovating firms.

The particularities of the agricultural biotechnology industry may help explain the concentration (Zilberman, Yarkin, and Heiman, 1997). First, the high fixed costs of commercializing transgenic plants require large financial resources. Many public research institutions as well as start-up companies do not necessarily have this capacity.

Second, the high fixed costs also necessitates an increasing reliance on IP rights to appropriate the returns to investment. Accumulated proprietary technologies in plant biotechnology can be barrier to innovating in the field, similar to the case in the semiconductor industry. Hence, firms that collaborate are less likely to infringe on one another's IP. For example, Monsanto, BASF, Dow, Bayer, DuPont, Syngenta cross-licensed one another's IP rights on transgenic crops (Howard, 2015).

It is therefore not surprising that there are high instances of collaborations between rival firms, or even between the public-private sectors, to work around the need to access the proprietary knowledge. Alternatively, some large multinational firms have acquired and merged with their rivals to buy-in and access their complementary assets (Bijman and Tait, 2002; Fulton and Giannakas, 2001; 1997).

Third, adapting the main transgenic plant to regional agro-ecological conditions entail access to very specialized knowledge of the region and its cultivars. Accessing this knowledge entails collaboration with various NARCs as well as their pool of researchers. The NARCs tend to be located close to the farming sites.

From rivals to collaborators: how innovation is concentrating in the hands of a few

The story of why there is a concentration of innovation is due to the importance of access to complementary assets, genetic materials and costs of bringing the product to the market.
In particular, the consolidation of the agricultural biotechnology industry over the past few decades is a reflection of these factors.

When biotechnology first started to be applied to agriculture in the 1980s, the market was dominated by small, university-based start-ups. However, from 1990s onward, many of these start-ups were being acquired by large multinational companies. One study estimated that nearly 90 percent of all research and development agreements on agricultural biotechnology were between start-ups and large MNEs.[16]

At the same time, firms in the seed, chemical and fertilizer industries experienced significant market concentration since the 1970s. The consolidation of this market is both at the vertical integration as well as at horizontal levels, both within the U.S., Europe and Japan but also in emerging economies.

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[16] Kalaitzandonakes and Bjornson (1997) calculated the number of mergers, acquisitions and strategic alliances between start-ups and MNEs at 167 between 1981-1985, and 801 mergers between 1991-1996.

By 2001, 30 separate firms in the seeds and agrochemical industries whittled down to six – Monsanto, DuPont, Syngenta, Bayer, Dow and BASF.

Today, four agrochemical companies account for almost 60 percent of the agricultural biotechnology market. They consists of four major agrochemical-seed groups: Bayer Crop Science (Germany), Corteva Agriscience (U.S.), Syngenta (Switzerland) and BASF (Germany). Some of the notable mergers and acquisitions by a few of these large agrochemical companies include: Bayer Crop Science purchase of Aventis Crop Science in 2002, and Monsanto in 2018; and DuPont's acquisition of the seed company Pioneer Hi-Bred in 1999 and merger with Dow, first announced in 2015.

Table 3 lists selected alliances, including mergers and acquisitions, in the plant biotechnology field. It shows how the industry has become more concentrated since the 1990s.

Table 3: Selected alliances in the plant biotechnology industry, 1996-2017

Company[a]	Company[b]	Agricultural chemicals	Biotechnology	Seeds
Bayer [Germany] purchases Monsanto [U.S.] (2016)	Monstanto [U.S.] (merged with Pharmacia March, 2000; spun off entirely August, 2002)		Agracetus [U.S.] (1995)	DeKalb [U.S.] (1996)
			Calgene [U.S.] (1996)	Asgrow [U.S.] (1997)
			Ecogen [U.S.] (2003)	Holden's Foundation Seeds [U.S.] (1997)
			Joint venture with Millennium Pharmaceuticals [U.S.] (1998)	Cargill International Seeds, Plant Breeding International [U.S.] (1998)
			Paradigm Genetics [U.S.] (2000), name changed to Icoria (2004)	Delta and Pineland [U.S.] (alliance, 1994; bought 2007)
				Sensako [South Africa] (2002); Carnia [South Africa] (2002); later merged under DaKalb brand
				Seminis [U.S.] (2005)
				Emergent Genetics [U.S.] (2005)
				Acquired De Ruiter [Netherlands] (2008); and Peotec Seeds S.r.l. [Italy] (2008) via Seminis
	Bayer (Bought Aventis Crop Sciences, 2001) [Germany]	Hoechst [chemical, Germany] merged with Schering [pharmaceutical, Germany] to create Hoechst Schering AgrEvo (1994) [Dusseldorf, Germany]	Plant Genetics Systems (PGS) (acquired by AgrEvo in 1996; became part of Monsanto in 2002) [Belgium]	Nunhems [Netherlands], Vanderhave [Netherlands], Plant Genetic Systems [Belgium], Pioneer Vegetable Genetics, Sunseeds (1997) [U.S.]

		Hoechst (Agrevo) and Rhône-Poulenc [pharmaceutical, France] merged (and their agrochemicals division became) to Aventis CropScience (1999);	PlanTech [Japan] (1999)	Nunza (vegetables), Proagro (India) and two Brazilian seed companies (1999)
		Bayer buys Aventis CropSciences in August 2002	Lion Biosciences (11.3%, 1999)	Fibermax (joint venture with Cotton Seed Inc. of Australia, 2000)
			Limagrain (purchased the Canadian seeds activity; 2001) [France]	
ChemChina [China] purchases Syngenta [Switzerland] (2017)	Syngenta [Switzerland]	Ciba-Geigy and Sandoz merged to form Novartis [Switzerland] (1996)	Zeneca Ag. [U.K.] bought Moden International N.V. [Netherlands] (1997)	Merger between Northrup-King and Ciba Seeds brings together SandG Seeds, Hilleshog and Rogers Seed Co. under one umbrella (1997)
		Novartis [Switzerland] buys Merck's pesticide business for USD 910 million (1997)	Alliance with Japan Tobacco [Japan] on rice (1999)	ICI (Imperial Chemical Industries, pharmaceuticals and agrochemcials) [U.K.] splits into Zeneca (inclduing ICI seeds) and ICI PLC (1993)
		Merger of Novartis agriculture division [Switzerland] and AstraZeneca's Ag. Chemicals [U.K.] to form Syngenta [Switzerland] (1999)	Alliance with Diversa [U.S.] (2003)	Garst [U.S.] reborn as a Zeneca company (1996)
			Zeneca [pharmaceutical, U.K.] buys PSA Genetics (via Garst subsidiary, 1999)	Zeneca [U.K.] via Garst [U.S.] buys Agripro Seeds [U.S.] (1998), Gutwein Seeds (2000)
Corteva Agriscience [U.S.] spinoff created in (2019), result of DuPont and Dow merger (2015)	Dow Chemicals [U.S.]; Dow AgroSciences [US]	Dow purchases Eli Lilly's [U.S.] 40% share of Dow Elanco for USD 900 million (1997)	Mycogen (1996) [U.S.]	Mycogen buys Agrigenetics [U.S.] (1992)
		Rohm and Hass Ag. Chem [U.S.] (2001)	Ribozyme Pharmaceuticals Inc. [U.S.] (1999)	United AgriSeeds [U.S.] becomes part of Mycogen (1996)
			Contract with Proteome Systems Limited [Australia] (1999)	Joint venture of Mycogen [U.S.] with Boswell [U.S.] on cotton seed to form Phytogen (1998)

				Joint venture with Danisco Seeds [Denmark] (1999)
				Agreement with Illinois Foundation Seed [U.S.] (1999)
				Cargill Hybrid Seeds [U.S.] (2000)
	DuPont [U.S.]		Alliances with Human Genome Sciences [U.S.] (1996)	Pioneer [U.S.] (1997, 20%)
			Alliance with Curagen [U.S.] (1997)	Hybrinova [France] (1999)
			Purchased Verdia from Maxygen [U.S.] for USD 65 million (2004)	
BASF [Germany]		Bought corn herbicide business from Sandoz [Switzerland] (1996)	Joint venture with Institute of Plant Genetics and Crop Plant Research [Germany] to create SunGene [Germany] (1998)	Bought 40% of Savlöf Weibell [Sweden] (1999)
		American Cyanamid [U.S.], crop protection subsidiary from American Home Products for USD 3.8 billion (2000)	Joint venture with Max Planck Institute [Germany] and Metanomics [Germany] (1997)	

Source: Updated, based on Pray and Nassem (2003).
Notes:
[a] *The corporate entities as they currently exist.*
[b] *The corporate entities as they had existed up to their latest merger, acquisition or takeover.*

Importance of collaborating in plant biotechnology

Large multinational companies from chemical and seeds industries commercialized and cultivated all of the major transgenic crops, bred through genetic modifications, in the early years (Fukuda-Parr, 2006). The only exception was *Bt* cotton, which was developed by the Chinese public research institution (see section 2.2). However, *Bt* cotton was commercialized based on a joint venture with the private sector.

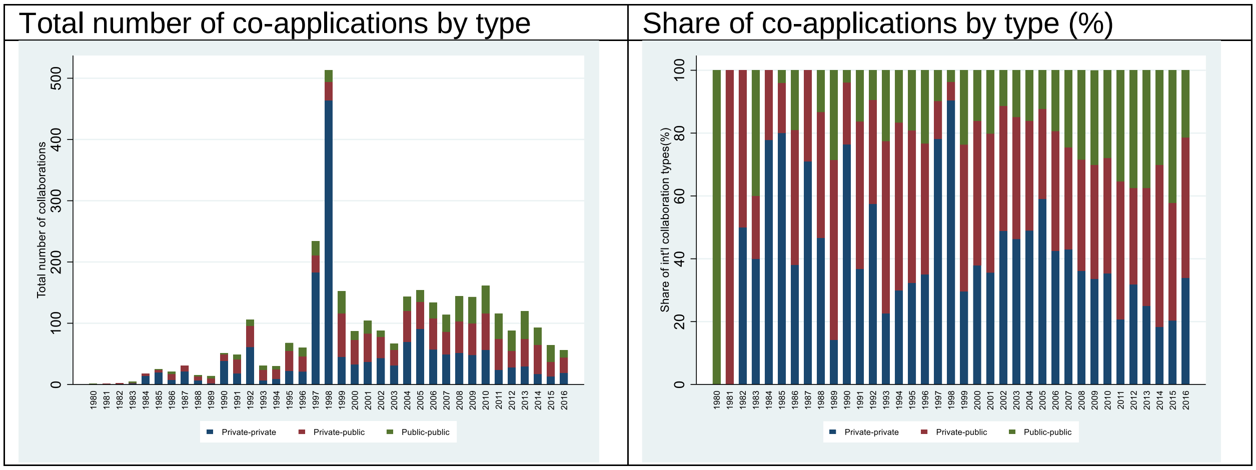
The need for access to complementary assets in innovating in agricultural biotechnology necessitates collaboration between the innovators. First, commercialization of research work from the universities, or public research institutions in emerging economies, may require further assistance from the private sector. This was the case for the Chinese *Bt* cotton and continues to be the case for many of the joint research projects between university research labs and private companies.

In many emerging economies, there are many instances of collaboration between the NARC and large multinational companies to develop transgenic crops adapted to the region (Byerlee and Fischer, 2002). In particular, these public institutions may need access to the proprietary biotechnological research tools to conduct their research work, and thus would need the collaboration of the IP owners to do so. One such example is a collaboration between the International Potato Center in Peru (CIP) with Plant Genetic Systems, a Belgian firm (Pinstrup-Andersen and Cohen, 2003).[17]

The collaboration can also be initiated by the private sector. For example, these large life sciences firms may need access to the pool of germplasms in the various IARCs and NARS for further innovation. For example, CGIAR has a collection of germplasm, in which it has committed to keep in the public domain. Access to this pool of germplasm would help in cultivating various different versions of the transgenic crops for use in many parts of the world.

Figure 9 plots the number of international co-applications by types of applicant collaborations (left) and its share (right). On average, 18 percent of all patent filings have co-applicants. The trend shows that there is an increase in the number of patents filed with at least one public-sector applicant type since 1998. By 2005, public-type collaborations overtake the private-private type.

Figure 9: Innovation by the private sector is the main driver of agricultural biotechnology innovation



Source: WIPO based on PATSTAT and PCT.

5. Conclusion and further research

The global innovation network of agricultural biotechnology showcases a prime example of how innovation activities spread to many parts of the world. Large multinational companies are the main source of patented innovations in the field. Their commercialization efforts tend to spread this innovation overseas. In addition, the presence of publicly-funded international agricultural research centers (IARC) and national agricultural research services (NARS) in many emerging economies have also facilitated the spread of innovation to these locations.

But this spread tends to concentrate within existing innovative regions. Several factors explain this uneven spread. The first is the strong agglomeration forces of innovative regions, similar to the case of the biotechnology industry more broadly. Second, innovation in plant biotechnology is strongly tied to co-locating close to universities that produce high quality research in the field.

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[17] PGS was acquired by Bayer Crop Science in 2002.

These universities tend to be located in urban areas. On the other hand, public research institutions such as the NARC and IARC conduct important research work on agricultural biotechnology. They tend to be located adjacent to the farming areas of the world.
This urban-rural divide is typical of the agricultural biotechnology case.

An additional layer to the concentration of innovation is the consolidation of competition in the agricultural biotechnology industry. While innovations in agricultural biotechnology are diffusing to different parts of the world, the number of market participants in the industry is becoming more concentrated. Many private startup companies specializing in agricultural biotechnology that were established in the 1980s – when the industry was nascent – were later merged or acquired by large multinational companies. Such equity exits by startups are a common feature of technology startups. But, as barriers to entry to agricultural markets increased, the initial set of startup agricultural biotechnology companies were not replaced by new startups at the same rate they were being acquired by the corporate incumbents during the 1990s and early 2000s.

This consolidation of the agricultural biotechnology innovation in the hands of few has not necessarily translated into a reduction of innovative activities in this field (Fuglie, King, Heisey, and Schimmelpfennig, 2012; OECD, 2018).[18] Moreover, the increase in public spending into research and development (R&D) in emerging economies may offset the consolidation in the private sector. However, it is not clear if the increase in public agricultural R&D and concomitant rise in academic and public research sector outputs (in emerging economies) is also followed by an increase in private R&D spending and innovation. Some argue that these public investments are crowding out the private ones (Hu, Liang, Pray, Huang, and Jin, 2011).

Developments that may affect the GIN of agricultural biotechnology

Two new developments in agricultural biotechnology are currently underway and could transform the current GIN.

A relatively recent breakthrough innovation in molecular biology is opening new research avenues and hence applications for plant biotechnology. The adaptation of *CRISPR-Cas9* – an RNA-enzyme system from bacteria – as a tool for genome editing is likely to reinvigorate research on genetic improvement of crops as well as livestock.[19]

The next step for genomic science is the application of sensors and artificial intelligence to systematize the quantification of organism phenotypes, physical traits, enabling much more powerful and precise connections to be drawn between genotype, genetic traits, and phenotype than was previously possible. New technological opportunities for the genetic improvement of crops, as well as livestock, are now possible with the combined abilities to “read,” “write,” and “edit” nucleotide sequences.

CRISPS-Cas9 has also the potential to democratize innovation in agricultural biotechnology, as the use of this technology becomes more affordable (Mahfouz, Piatek, and Stewart, 2014; Shwartz, 2018). In combination with the rise of emerging economies who are also innovating in agricultural biotechnology field, this latest advance in molecular biology could result in a further

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[18] The OECD (2018, p. 104) reviewed the empirical literature on concentration in the seed industry and impact on innovation. The study concludes that there is little evidence for the adverse impact of concentration on innovation based on historical data.

[19] “CRISPR” stands for clustered regularly interspaced short palindromic repeats while “Cas9” refers to CRISPR-associated protein 9.

spread of the technology. This could result in a more even distribution of the global innovation network, with clusters all over the world making important contributions that will enhance future food security in a more efficient and sustainable manner.

The second development that may change the current GIN status is CGIAR’s stance on using IP rights as a way to incentivize collaboration with private companies (CGIAR, 2006, 2013). As mentioned in subsection 4.2, there seems to be an increasing need to address IP issues, especially for collaborations between the private sector and IARCs and NARS. The importance for private companies for IP rights as an incentive for innovating in stark contrast with the IARCs stance on keeping their research work open and free for the public are at odds with one another. Various relatively ad hoc arrangements have been set in place. For example, the CGIAR center may have a license to use the proprietary research tool for research purposes but cannot distribute the resulting products. Or in the case of the collaboration between CIP and PGS, CIP may not use the resulting research product in certain countries but can do so in others (Pinstrup-Andersen and Cohen, 2003).

CGIAR’s recent shift in their stance on IP may lead to better participation by the emerging economies in the GIN of agricultural biotechnology.

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Appendix

Identifying plant biotechnology inventions

The plant biotechnology map is based on a combination of patent and scientific publications. The patent data used in this report are from the European Patent Office's (EPO) Worldwide Patent Statistical Database (PATSTAT, April 2019) and WIPO's Patent Cooperation Treaty (PCT) collections, which are available from 1970 until 2017 (with some truncation in the later years). The scientific publication data used in this report comes from records published from 1998 to 2017 in the Science Citation Index Expanded (SCIE) of the Web of Science (WOS), the citation database operated by the Clarivate Analytics company.

Innovation in the industry were identified and extracted using combination of patent classifications, scientific journals and keywords. These are detailed as follows.

The following IPC and CPC symbols were used to determine the patents on each crop biotech category and the union of these constitute the total of crop biotech patents:

- **Crop genetic improvement:** A01H1*; A01H3*; A01H4*; A01H5*; A01H6*; A01H7*; A01H17*; C12N5/04*; C12N5/14*; C12N15/05*; C12N15/29*; C12N15/79*; C12N15/82*; C12N15/83*; C12N15/84*; (C07K14/415* but not A61K*).
- **Pest control in crops:** A01N63*; A01N65*; C12N15/31*; C12N/32*; (C07K14/325* but not A61K*).
- **Soil fertility:** C05F*.
- **Climate change:** Y02A40/146; Y02A40/162; Y0240/164.

The scientific publications were extracted from top plant biotechnology scientific journals and from the conjunction of top scientific journals for agriculture biotechnology and keywords. These are:

(1) All articles from the following top plant biotechnology journals: *Agri Gene*; *Crop Science*; *Euphytica*; *Genetics, Selection, and Evolution*; *Journal of Experimental Botany*; *Journal of Plant Physiology*; *New Phytologist*; *Physiologia Plantarum*; *Plant and Cell Physiology*; *Plant Cell*; *Plant Cell and Environment*; *Plant Cell Reports*; *Plant Journal*; *Plant Molecular Biology*; *Plant Physiology*; *Plant Physiology and Biochemistry*; *Plant Science*; *Planta.*

(2) Top agriculture biotechnology scientific journals and keywords:

- **Top agriculture biotechnology scientific journals:** *Biochemical and Biophysical Research Communications*; *Cell*; *Journal of Biological Chemistry*; *Journal of Biology*; *Journal of Cell Biology*; *Journal of Molecular Biology*; *Journal of the American Medical Association*; *Molecular and Cellular Biology*; *Nature*; *Nature Biotechnology*; *New England Journal of Medicine*; *PlosBio*; *Proceedings of the National Academy of Sciences of the USA*; *Science*; *The EMBO Journal*; *Theoretical and Applied Genetics.*

- **Keywords:** *abscisic acid*; *ACC oxidase*; *ACC synthase*; *aerenchyma*; *agrobacterium rhizogenes*; *agrobacterium tumefaciens*; *agrobacterium*; *alfalfa*; *ammonium*; *anther culture*; *anthocyanins*; *apoplast*; *arabidopsis*; *arbuscular mycorrhiza**; *auxin*; *bacterial blight*; *banana*; *barley*; *beta vulgaris*; *rachypodium distachyon*; *brassica*; *bread wheat*; *breeding*; *breeding value*; *C-4 photosynthesis*; *canola*; *capsicum annuum*; *carrot*; *cassava*; *chickpea*; *chinese cabbage*; *chlorophyll a fluorescence*; *chloroplast DNA*; *citrus*; *coffea arabica*; *cold tolerance*; *common bean*; *conifer**; *cotton*; *crossbreeding*; *cucumis melo*; *cucumis sativus*; *cytokinins*; *cytoplasmic male sterility*; *daucus carota*; *defoliation*; *distillers grains*; *doubled*; *downy mildew*; *drought resistance*; *ectomycorrhizal*; *eucalyptus*; *flaxseed*; *forage*; *fructan*; *fruit development*; *fruit quality*; *fruit ripening*; *fusarium*; *fusarium graminearum*; *fusarium head blight*; *garlic*; *genome*; *genotype × environment interaction*; *genotype*; *germplasm*; *gibberellins*; *glycine max*; *gossypium hirsutum*; *grain*; *grain filling*; *grain yield*; *grapevine*; *hairy root*; *haploid*; *hevea brasiliensis*; *high*; *hordeum vulgare*; *hypersensitive response*; *kiwifruit*; *leaf anatomy*; *leaf growth*; *leaf rust*; *legume*; *linseed*; *lolium perenne*; *lycopersicon esculentum*; *maize*; *male sterility*; *marker*; *medicago truncatula*; *methyl jasmonate*; *micropropagation*; *mycorrhiza**; *nicotiana tabacum*; *nitrogen fixation*; *orchid*; *oryza*; *oryza sativa*; *osmotic adjustment*; *osmotic potential*; *pea*; *peach*; *pectin*; *pepper*; *perennial ryegrass*; *phaseolus vulgaris*; *phenotyping*; *phloem transport*; *physcomitrella patens*; *phytic acid*; *phytotoxicity*; *picea abies*; *pinus*; *pinus pinaster*; *pinus taeda*; *pisum*; *plant breeding*; *plant defence*; *plant regeneration*; *plant transformation*; *pollen development*; *pollen germination*; *pollen tube*; *potato*; *prunus persica*; *QTL**; *QTL analysis*; *QTL mapping*; *QTLs*; *quantitative trait loc**; *rapeseed*; *resveratrol*; *RFLP*; *rice*; *root elongation*; *root exudates*; *rubisco activase*; *rye*; *sap flow*; *seed*; *self-incompatibility*; *shoot regeneration*; *solanum lycopersicum*; *solanum tuberosum*; *somaclonal variation*; *somatic embryogenesis*; *sorghum*; *soybean*; *spinacia oleracea*; *stomatal conductance*; *strawberry*; *sucrose synthase*; *sugar beet*; *sugarcane*; *sunflower*; *suppression subtractive hybridization*; *tall fescue*; *thlaspi caerulescens*; *tomato*; *transgenic plant**; *transgenic rice*; *transgenic tobacco*; *tritic**; *triticum aestivum*; *vicia faba*; *vitis vinifera*; *water potential*; *water use efficiency*; *wheat*; *winter wheat*; *xylem sap*; *zea may*.*

Table A. 1: Top 30 clusters based on patent filings

Rank	1980-1989		1990-1999		2000-2009		2010-2016	
	City	Country	City	Country	City	Country	City	Country
1	Tokyo	Japan	San Jose	USA	New Haven	USA	San Jose	USA
2	Paris	France	Baltimore	USA	San Jose	USA	Boston	USA
3	San Jose	USA	New York City	USA	Boston	USA	New York City	USA
4	Osaka	Japan	Boston	USA	New York City	USA	Seoul	Rep. of Korea
5	New York City	USA	San Diego	USA	Tokyo	Japan	Tokyo	Japan
6	San Diego	USA	Tokyo	Japan	San Diego	USA	San Diego	USA
7	Boston	USA	Los Angeles	USA	Philadelphia	USA	Philadelphia	USA
8	Baltimore	USA	Minneapolis	USA	Jerusalem	Israel	Mannheim	Germany
9	Budapest	Hungary	Philadelphia	USA	Mannheim	Germany	Paris	France
10	London	UK	Paris	France	Baltimore	USA	Baltimore	USA
11	New Haven	USA	Osaka	Japan	Copenhagen	Denmark	Los Angeles	USA
12	Philadelphia	USA	Toronto	Canada	Seoul	Rep. of Korea	Beijing	China
13	Vienna	Austria	Copenhagen	Denmark	Los Angeles	USA	Osaka	Japan
14	Basel	Switzerland	Frederick	USA	Paris	France	Jerusalem	Israel
15	Seattle	USA	Buffalo	USA	Osaka	Japan	Copenhagen	Denmark
16	Raleigh	USA	New Haven	USA	Chicago	USA	Eindhoven	Netherlands
17	Copenhagen	Denmark	Cologne	Germany	Cologne	Germany	Chicago	USA
18	Strasbourg	France	Thornton	USA	Raleigh	USA	Minneapolis	USA
19	Los Angeles	USA	Lyon	France	Minneapolis	USA	Seattle	USA
20	Cologne	Germany	Seattle	USA	Berlin	Germany	Cologne	Germany
21	Reading	UK	Jerusalem	Israel	Seattle	USA	Houston	USA
22	Milan	Italy	Vienna	Austria	Eindhoven	Netherlands	Raleigh	USA
23	Jerusalem	Israel	Austin	USA	Melbourne	Australia	Toronto	Canada
24	Lyon	France	Raleigh	USA	Thornton	USA	Shenzhen	China
25	Iwakuni	Japan	London	UK	St. Louis	USA	New Haven	USA
26	Toronto	Canada	Chicago	USA	Houston	USA	Anaheim	USA
27	Oxford	UK	Des Moines	USA	Basel	Switzerland	London	UK
28	Brussels	Belgium	Alief	USA	Anaheim	USA	Berlin	Germany
29	Chicago	USA	Basel	Switzerland	Munich	Germany	Stockholm	Sweden
30	Braunschweig	Germany	Reading	UK	Vienna	Austria	Shanghai	China

Table A. 2: Top 30 clusters based on scientific publications

Rank	1998-1999		2000-2009		2010-2017	
	City	Country	City	Country	City	Country
1	Tokyo	Japan	Tokyo	Japan	Beijing	China
2	Paris	France	Osaka	Japan	Tokyo	Japan
3	Osaka	Japan	Nagoya	Japan	Paris	France
4	Nijmegen	Netherlands	Beijing	China	Osaka	Japan
5	Norwich	UK	Paris	France	Wuhan	China
6	San Jose	USA	Nijmegen	Netherlands	Nijmegen	Netherlands
7	Nagoya	Japan	San Jose	USA	Nanjing	China
8	Raleigh	USA	Raleigh	USA	Cologne	Germany
9	Sacramento	USA	Norwich	UK	Hangzhou	China
10	Cologne	Germany	Cologne	Germany	San Jose	USA
11	Pullman	USA	Sacramento	USA	Seoul	Rep. of Korea
12	Canberra	Australia	Seoul	Rep. of Korea	Montpellier	France
13	New York City	USA	Canberra	Australia	Ithaca	USA
14	Madison	USA	Ithaca	USA	Ghent	Belgium
15	Baltimore	USA	Sapporo	Japan	Sacramento	USA
16	Ithaca	USA	Montpellier	France	Raleigh	USA
17	Lansing	USA	Lansing	USA	Shanghai	China
18	Cupar	UK	Sendai	Japan	Nagoya	Japan
19	Copenhagen	Denmark	Madison	USA	Zurich	Switzerland
20	Zurich	Switzerland	New York City	USA	Canberra	Australia
21	Montpellier	France	London	UK	Perth	Australia
22	Tel Aviv	Israel	Baltimore	USA	London	UK
23	Minneapolis	USA	Minneapolis	USA	Norwich	UK
24	Gainesville	USA	Champaign	USA	New York City	USA
25	Wuerzburg	Germany	Lafayette	USA	Madison	USA
26	State College	USA	Pullman	USA	Lansing	USA
27	Ghent	Belgium	Zurich	Switzerland	Copenhagen	Denmark
28	College Station	USA	Kurashiki	Japan	Tel Aviv	Israel
29	San Diego	USA	Gainesville	USA	Madrid	Spain
30	Hoym	Germany	Perth	Australia	Baltimore	USA