

The public–private structure of intellectual property ownership in agricultural biotechnology

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New findings indicate that there may be benefits from more collaborative models of intellectual property management in the public sector.

Historically, investments in crop research and plant breeding have resulted in substantial public benefits worldwide¹. Because the benefits came largely in the form of improved crop varieties released publicly and requiring only small additional investments for local adaptation, production and marketing, the small potential for private returns historically left crop research and development (R&D) largely to public-sector research institutions². However, over the past two decades the application of molecular genetic approaches to crop R&D have dramatically changed this landscape. The economics of R&D in agricultural biotechnology have been similar to those of R&D in agrochemicals or pharmaceuticals, with universities specializing in basic research but lacking the resources or expertise needed for commercialization of products resulting from the new technologies, something which requires substantial investments in product development and biosafety testing.

With the emergence of stronger intellectual property (IP) rights in biological innovations, beginning with the 1980 decision in

Diamond v. Chakrabarty over patenting microorganisms and later extended to plants and animals³, biotechnology startups and established seed and agrochemical companies initiated intensive research efforts, taking a leading role in the development, production and marketing of new biotechnology-based crop varieties.

The Bayh-Dole Act of 1980, which allowed universities to patent results of research financed by federal monies, and the subsequent proliferation of public-sector offices of technology transfer created new opportunities and outlets for the results of the public sector's molecular biology R&D efforts. Through the patenting of their inventions, public-sector research institutions could transfer rights over a technology to established commercial partners or to new entrepreneurial startups, which could then finance further development of the technology⁴. In plant molecular biology the result has been a proliferation of patenting by both private- and public-sector institutions.

The proliferation of IP rights among multiple owners in agricultural biotechnology appears to have affected the rate and direction of innovation⁵, a result of the so-called intellectual 'anticommons' as has been observed in biomedical research⁶. Concerns have been raised that the confidential terms of license agreements and the multiplicity of patent owners in core technology areas lead to incomplete information about property rights. Negotiations, paperwork and licensing fees make for high transaction costs in obtaining R&D inputs. Because of strategic access considerations, IP right owners may refuse to license enabling technology tools, even for developments outside their own product scope. Any or all of these factors may hinder the efforts of any one IP owner

to obtain the permissions from all of the other owners necessary to fully enable the development of their own technology or product. The potential for hold-ups in crop R&D was exemplified in the development of β -carotene-enriched rice by public-sector researchers who used at least 40 patented or proprietary methods and materials belonging to a dozen or more different IP owners in the gene transfer process⁷.

In this article, we examine the structure of assignment of IP in agricultural biotechnology to assess (i) the impacts of strengthening IP rights and the Bayh-Dole Act in this sector, (ii) the concentration of IP in both the private and public sectors and (iii) the technological breadth and strength of the public sector's contribution. These results provide a basis for considering broader questions of science policy in agriculture, public-sector IP policies and the design of more effective IP management strategies to maximize the exploitation of patented technologies in this rapidly innovating industry.

The growth of agricultural biotechnology's intellectual assets

The annual count of applications filed and patents granted at the United States Patent and Trademark Office (USPTO; Alexandria, VA, USA), the European Patent Office (EPO; Munich, Germany), the Japanese Patent Office (JPO; Tokyo, Japan) and the international Patent Cooperation Treaty (PCT) for agricultural plant biotechnologies has grown exponentially beginning in the early 1980s (Fig. 1). As data on European and Japanese documents include both patent applications and issued patents, in any case where a patent had issued, we removed the corresponding application from the collection. Thus, for each invention there could be up to

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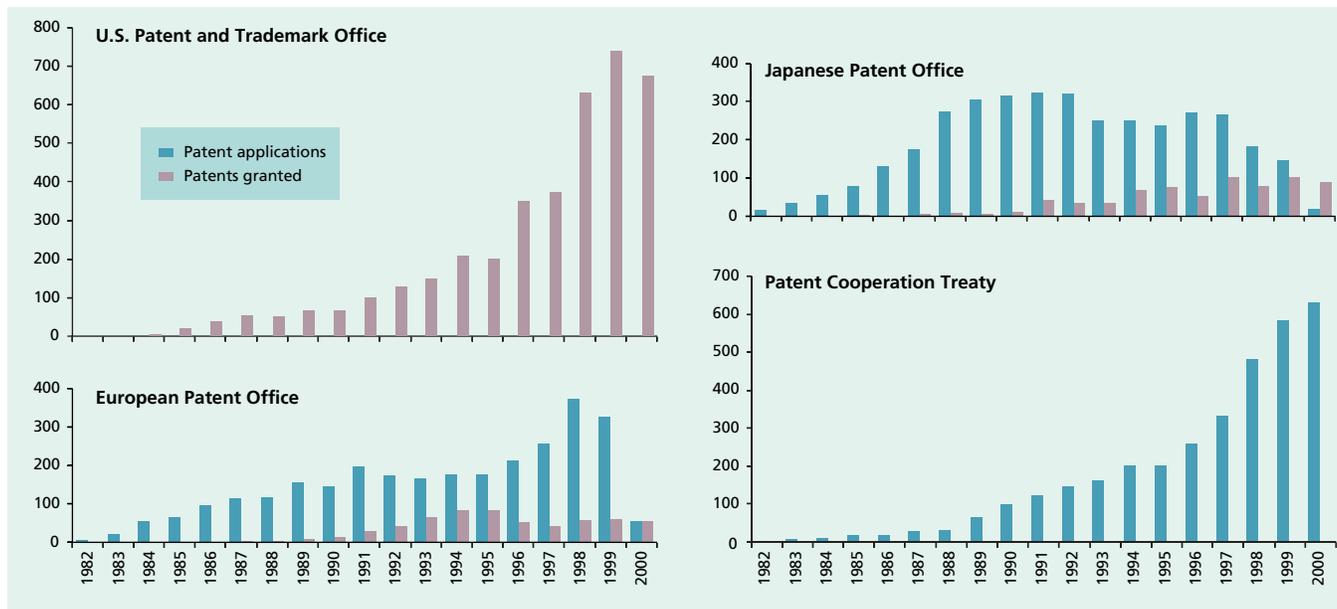


Figure 1 Annual trends in plant biotechnology IP 1982–2000, from a comprehensive dataset of 14,393 US, European, Japanese and PCT documents filed between August 1, 1982 and August 1, 2001. From patent data maintained by MicroPatent, rigorous queries based on a combination of international patent classification (IPC) codes and technology-related search terms were used to develop this large collection of IP documents in the field of plant biology. US patents are shown here by date of grant. European and Japanese applications published (but not yet granted) are shown by date of filing, whereas patents granted are shown by date of grant. Published PCT applications are shown by date of filing. The application data for the European and Japanese offices show truncation in recent years because of the standard 1.5-year delay of publication after filing.

four documents—one document per patent office (USPTO, EPO, JPO and PCT)—in the final collection.

The sustained rates of growth through 2000 indicate that agricultural biotechnology as a field has still not reached maturity. Early in the technology life cycle, before 1993, even though patent application rates were substantial in Europe and Japan, more patents were actually being issued in the United States. (Because patent applications were not published in the United States, we cannot know what the rate of applications looked like there.) After about 1995, patent grants in the United States increased dramatically, whereas both patent applications and grants stagnated in Europe and Japan. The recent drop in applications for Europe and Japan largely reflects a truncation of the data; patent applications in Europe and Japan take 18 months to publish. Throughout the two decades of the technology's history, the multicountry applications filed through the PCT show most clearly the smooth exponential growth that underlies the variations observed among the three major patent offices.

Identification of patent assignees and their 'parent entities'

To assess inventorship of technologies, we have identified the 'assignee-at-issue' for each

IP document. This information is recorded in the patent data and indicates which organization was assigned the IP rights when the patent authority issued the patent. We examined and adjusted the information to give a uniform version and spelling of each organization's name. Subsequently, we aggregated all documents assigned to smaller entities known to be wholly owned by larger entities under the names of their respective parent entities. An example of our aggregation for Syngenta (Basel, Switzerland) illustrates this process (Fig. 2).

These assignee data, however, do not indicate whether a document has remained in force or whether the property rights have been transferred from the original assignee to one or more other organizations through licensing, sale or other transactions. Licensing may be quite common in the public sector, where the primary purpose of obtaining patents is to enable technology transfer transactions to commercial entities. Such licensing of rights may be complete, giving exclusive control of the technology to a single licensee; partial, transferring exclusive rights for limited fields of use, particular applications, or geographies; or nonexclusive, sharing rights among one or more licensees. Licensing transactions are not typically recorded in patent office data and are often confidential.

We have classified each parent entity by organizational type: commercial firm, individual inventor, academic or government organization or patent management company. Document counts (applications plus patents) divided according to these organizational types are listed for each of the major patent offices (Table 1).

On the basis of US PTO summary statistics, we calculate that, overall, 2.7% of US patents granted from 1981 to 2001 came from public-sector (academic and government) organizations (Fig. 3a). This contrasts markedly with the distribution found in agricultural biotech, where one out of every four US patents (24%) came from a public-sector organization. A similar proportion of European filings (Table 1) came from the public sector (25%); but, interestingly, a smaller proportion of Japanese filings (14%) and a greater proportion of PCT filings (33%) did so. In general, the contribution of public-sector R&D to patenting in agricultural biotechnology is an order of magnitude greater than the contribution of public-sector R&D to patenting across all industry sectors.

The patent position of the public sector relative to the leading firms in the private sector is illustrated in Figure 3b. Monsanto (St. Louis, MO, USA) and DuPont (Wilmington, DE, USA) hold the largest cor-

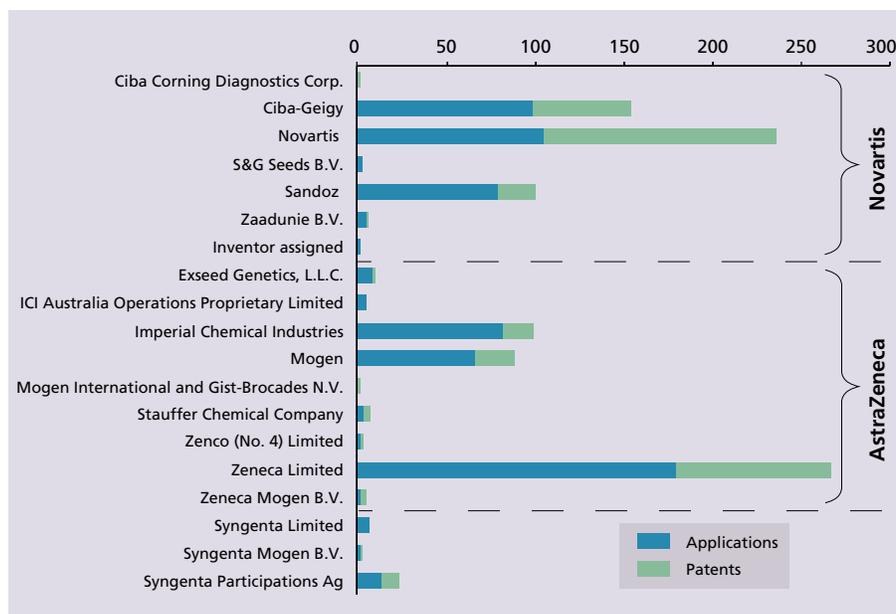


Figure 2 The IP portfolio of Syngenta as a 'parent entity' consists of earlier applications and patents assigned to the holdings of Novartis and AstraZeneca, whose agricultural assets were merged to create Syngenta, plus a few recent filings under the Syngenta name.

porate portfolios, with 14% and 13% of the industry's count of US patents respectively, followed by Syngenta with 7%, Bayer (Leverkusen, Germany) with 4% (with the acquisition of Aventis) and Dow (Indianapolis, IN, USA) with 3%. The 'rest of private sector' portion of 33% is scattered among other corporations, smaller businesses, still-independent biotechnology startups and individual inventors. No other organization holds more than 2% of US patents in agricultural biotech. This includes the very largest public-sector organizations, such as the University of California (Oakland, CA, USA) with 1.7% of the total and the US Department of Agriculture (USDA; Washington, DC, USA) with 1.2% (Fig. 3c). In a simple valuation analysis of the US patents in the dataset—based on how many citations each received from other US patents⁸—we estimate that the public-sector portfolio represents about 22% of the total value of the industry's IP assets. For comparison, the most valuable corporate portfolio is that of Monsanto, estimated by the same method to be about 19%.

Jointly assigned documents and public-private research collaboration

There has been considerable discussion of the potential for public-private research collaboration in agriculture⁹. Jointly assigned IP documents generally indicate inventions that have resulted from collaboration

between researchers employed at different organizations. A relatively small fraction (6.3%) of the total documents in the agricultural biotechnology dataset is jointly assigned to more than one organization (Table 2). This is similar to the rate of joint assignment of 7% observed among all US biotechnology patents but is high compared with the average rate of only 1.4% observed across all industries¹⁰.

To explore the extent to which these collaborations span across the public-private divide, we characterized each jointly assigned invention in this dataset as 'private-private',

'public-private' or 'public-public', reflecting the inclusion of public- and/or private-sector assignees in the document's assignee list. Of these categories, cross-sector public-private collaborations make up 2.8% of the total documents in the dataset (Table 2). Out of all documents in the dataset (singly and jointly assigned) with a private-sector assignee, only 6.3% are jointly assigned. In contrast, out of all documents in the dataset (singly and jointly assigned) with a public-sector assignee, 18.8% are jointly assigned. Thus, public-sector researchers have been approximately threefold more likely than their private-sector counterparts to jointly invent new technologies through collaborative R&D relationships. Furthermore, out of all jointly assigned documents involving a private-sector assignee, 60% represent collaborations with public-sector organizations, and, conversely, out of all jointly assigned documents involving a public-sector assignee, 63% represent collaborations with private-sector firms. Thus, from the perspective of both sectors, the majority of collaborations undertaken are cross-sector public-private relationships.

The technological composition of the public-sector 'portfolio'

Collectively, the universities and government institutions of the public sector have created a set of IP that is larger in number and estimated value than even the largest of the individual corporate portfolios. However, these public-sector holdings remain highly fragmented across many organizations, and no single institution owns a package of technologies sufficient to enable the development of a novel transgenic plant variety. It is also important to distinguish between

Table 1 Numbers of US, European, Japanese and PCT documents (published applications and granted patents) assigned by type of inventing organization

| Organization | USPTO | EPO | JPO | PCT | Total |
|-----------------------------|--------------|--------------|--------------|--------------|---------------|
| <i>Private sector</i> | | | | | |
| Commercial firms | 3,192 | 2,092 | 2,909 | 2,169 | 10,362 |
| Independent inventors | 34 | 37 | 120 | 73 | 264 |
| <i>Subtotal</i> | <i>3,226</i> | <i>2,129</i> | <i>3,029</i> | <i>2,242</i> | <i>10,626</i> |
| <i>Public sector</i> | | | | | |
| Academic | 806 | 468 | 176 | 819 | 2,269 |
| Government | 194 | 200 | 322 | 273 | 989 |
| Patent management companies | 25 | 49 | 16 | 62 | 152 |
| <i>Subtotal</i> | <i>1,025</i> | <i>717</i> | <i>514</i> | <i>1,154</i> | <i>3,410</i> |
| <i>Undetermined</i> | <i>68</i> | <i>65</i> | <i>142</i> | <i>83</i> | <i>358</i> |
| <i>Total</i> | <i>4,319</i> | <i>2,911</i> | <i>3,685</i> | <i>3,479</i> | <i>14,394</i> |

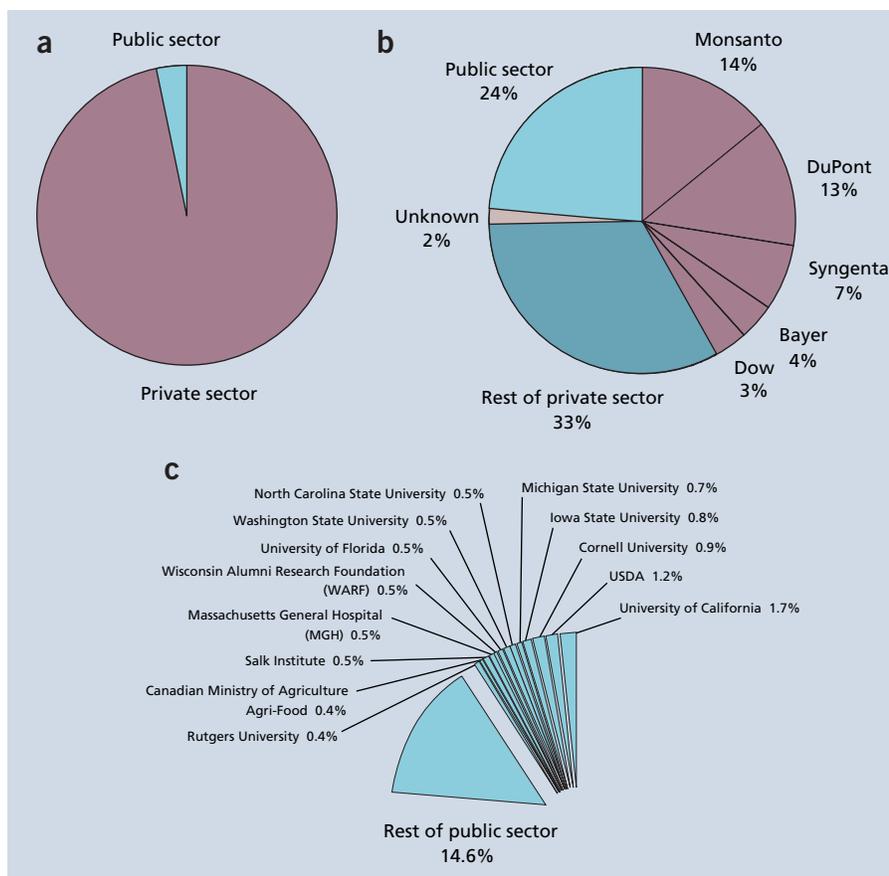


Figure 3 Distribution of assignment of US patents granted from 1982 to 2001. (a) All US patents. (b) US agricultural biotechnology patents. (c) Public-sector US agricultural biotechnology patents.

‘enabling’ technologies representing the research tools needed to create transgenic crops and the ‘trait’ technologies providing the genetic basis for new functionalities. Public-sector research has contributed substantially to both. Early plant biotechnology research in the public sector led to the development of core enabling technologies, but public-sector research increasingly has focused on functional genomics and today contributes more to discovery of new trait technologies.

To assess the breadth of the public-sector IP estate, we have examined to what extent public-sector inventions can be used to

assemble a platform of enabling technologies and gene-trait technologies sufficient to develop new transgenic varieties of organisms. This analysis is intended to evaluate the complementary R&D productivity of public sector IP assets in a qualitative sense and also to indicate several key technology areas in which the public-sector portfolio may be deficient. It is important to note that this is an assessment for R&D planning only and does not provide a legal analysis of freedom to operate, an exercise that would require much closer scrutiny of patent claims and licensing status of each piece of the public-sector IP cited. Many of the public-sector

patents referenced below are already committed on an exclusive basis to third parties and are therefore not available to contribute to a hypothetical technology platform.

Enabling technologies

Public-sector IP describing enabling technology falls into three main categories: transformation methods, selectable markers and constitutive promoters. In the first category, the development of most transgenic varieties relies on either *Agrobacterium tumefaciens*-mediated or biolistic-mediated gene transfer methods^{11,12}. Fundamental methods related to both processes of gene transfer into plant cells were invented in the public sector^{13,14}. However, a key patent for *Agrobacterium* was licensed exclusively to Ciba-Geigy (now Syngenta), and the biolistic technology was licensed exclusively to DuPont for most fields of use. In addition, public-sector R&D organizations have patented a number of improvements for transformation methods, including vectors, species-specific protocols, and new strategies to remove selectable markers and other ‘foreign’ DNA from the plant to be commercialized^{15–18}. These provide important improvements to basic transformation methods but are likely to be dominated by the broad patent claims for *Agrobacterium*-mediated or biolistic-mediated gene transfer. Thus, fundamental methods of gene transfer to plant cells were invented in the public sector and, in hindsight, had the IP rights been reserved for public-sector applications, would have provided an important component of a public-sector ‘tool box’ of enabling technologies. Instead, many of them were committed on exclusive terms to commercial licensees.

In the second category, the most commonly used selectable marker genes include the *nptII* and *hpt* genes that confer antibiotic resistance as a basis to select for cell transformation. Several other selectable markers conferring herbicide resistance or allowing positive selection based on novel carbon utilization pathways provide important alternatives to the antibiotic-based selection

| | Assigned to a single organization | | | | Jointly assigned to collaborating organizations | | | | Total |
|------------------------|-----------------------------------|--------|-----------|--------------|-------------------------------------------------|----------------|---------------|-------------|--------|
| | Private | Public | Uncertain | Total single | Private-private | Public-private | Public-public | Total joint | |
| Number of IP documents | 10,227 | 2,915 | 344 | 13,486 | 266 | 401 | 240 | 907 | 14,393 |
| Percentage of total | 71.1% | 20.0% | 2.4% | 93.7% | 1.8% | 2.8% | 1.7% | 6.3% | 100.0% |

strategies^{19,20}. Broad patents cover all of these selectable markers^{21–23}. Selection strategies appear not to have been the topic of public-sector research programs and there are no clear examples of selectable markers for use in plant transformation that are either in the public domain or patented by public-sector entities. However, active programs exist to develop new positive selection strategies, and one can contemplate a number of additional selection strategies that rely on conferral of resistance to biotic or abiotic stresses or the introduction of unique biochemical pathways. Thus, there is potential to invent new selectable markers for plant transformation.

A final category of enabling technology under research is constitutive promoters—genetic regulatory elements required to drive the expression of selectable marker genes and specific transgenes. Selectable marker genes are typically driven by high-level constitutive promoters, with the most common constructs using the cauliflower mosaic virus (CaMV) 35S promoter derived from a viral genome and owned by Monsanto²⁴. Many alternative promoters that confer constitutive gene expression were developed in public-sector organizations and are either in the public domain or can be licensed for nominal fees. These alternatives include a dicot ubiquitin promoter²⁵, a figwort mosaic virus (FMV) 34S promoter²⁶, mannopine/octopine synthase²⁷ or the FMV and peanut chlorotic streak caulimovirus full-length transcript (FLt) promoters^{28,29}. The FMV 34S promoter has been used to drive constitutive gene expression and is reported to be essentially equivalent to the CaMV 35S promoter^{30,31}, but has not been widely distributed to the public-sector research community. Each of these promoters provides a strategy for driving constitutive transgene expression using public-sector-derived components.

Trait technologies

We have also identified three major categories for public-sector IP on technology and inventions that influence plant traits: tissue- and developmental-specific promoters, targeting sequences and sequences conferring novel traits.

Although many genes can be expressed under the control of constitutive promoters, it is typically desirable to target expression to plant organs or tissues to minimize nonspecific effects of the introduced gene. For example, seed-specific promoters^{32,33} have been patented with claims directed toward their use to drive expression of heterologous genes in developing seeds. Public-sector

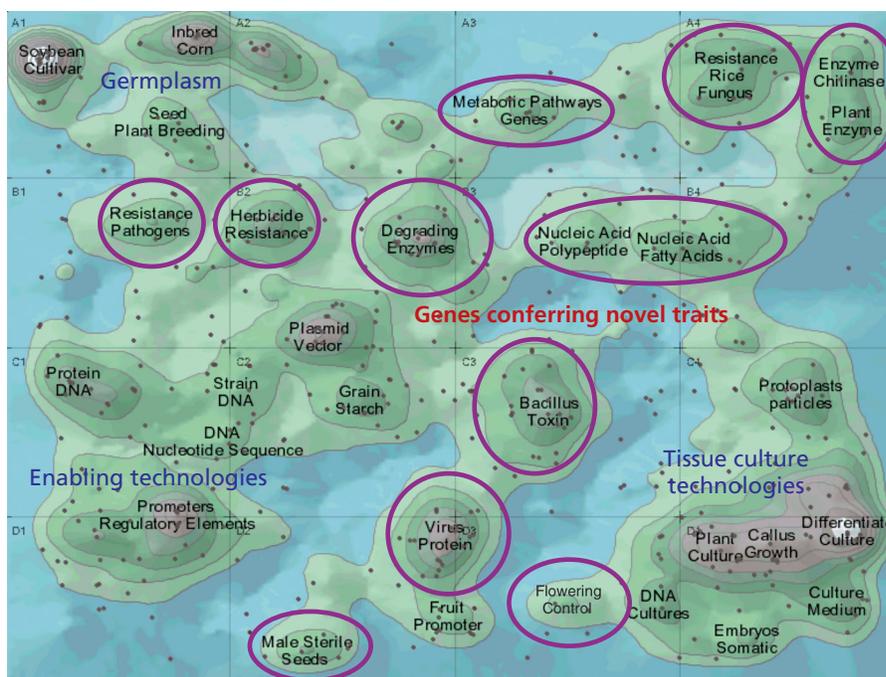


Figure 4 IP documents are ‘topographically’ mapped from the full agricultural biotechnology dataset of 14,393 documents using ThemeScape software from MicroPatent. Algorithms create an internally consistent categorization of the documents by clustering them into ‘mountains’ on the basis of the similarity of the technical language contained in the text. The distance, in any direction, between two documents on the map indicates their thematic proximity. Thus, brown and green ‘higher-altitude’ regions on the map represent high densities of closely related documents; blue ‘lower-altitude’ regions represent low densities with few or no closely related documents. Prominent categories of genetic trait technologies, circled in purple, are distinguished from other general topics, including germplasm, enabling technologies and tissue culture technologies.

institutions have also patented a relatively large number of tissue- and/or developmental-specific promoters. Examples include the root-specific CaMV 35S fragment A promoter³⁴, a root cortex-specific promoter³⁵, the Pyk10 root-specific promoter³⁶, an epidermal cell-specific Blec promoter³⁷ and a vascular tissue-specific promoter from rice tungro bacilliform virus³⁸. It is also likely that a large number of tissue- and developmental-specific promoters have been characterized and placed in the public domain through publication.

In addition to specificity in tissue-level transgene expression, a second category of IP demonstrates that it is also often important to direct the targeting of the new protein to a specific subcellular location. For example, because β -carotene is produced in the plastids, the development of β -carotene-enriched rice used a transit peptide derived from the small subunit of ribulose-1,5-bisphosphate carboxylase (Rubisco) to target proteins to this subcellular compartment. This and other transit peptides have been the topic of intense study, and several companies have patented their use to direct proteins

into plastids^{39,40}. However, several early publications from public-sector research organizations described alternative transit peptides that were not subsequently patented and thus should be accessible in the public domain⁴¹.

Both the private and public sectors have been active in identifying and patenting genes that confer novel plant traits (the third category), but their relative levels of activity are not uniform across all categories of traits. For example, in the case of β -carotene-enriched rice, patents with claims to genes in the carotenoid biosynthetic pathway (e.g., phytoene synthase and lycopene cyclase) appear to be held predominantly by private-sector companies, although a short list of patents is assigned to public-sector entities describing genes and strategies to increase biosynthesis of carotenoids^{48–51}.

To examine the range of patented genetic traits that may be available from public-sector sources, we identified 10 distinct categories of genetic trait technologies from a global clustering of the 14,393 agricultural biotechnology IP documents created using a text analysis and mapping tool that recog-

Table 3 Numbers of IP documents and percentages assigned to public- and private-sector organizations, by cluster of genetic trait technology (Fig. 3)

| Technology theme-based cluster | Number of documents (%) | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|---------------|
| | Private sector | Public sector |
| <i>Plant enzymes</i> Highly dominated by Japanese patents and highly focused on enzymes such as chitinases, xylanases, glucuronidase lipases, and alkali and acid proteases | 291 (92%) | 25 (8%) |
| <i>Bacillus toxin</i> Centered on the theme of insect resistance and bioinsecticides, particularly <i>Bt</i> genes and toxins | 497 (90%) | 57 (10%) |
| <i>Industrially important enzymes</i> Microbial and industrial enzymes and detergent agents; many claiming expression in plants | 229 (89%) | 29 (11%) |
| <i>Metabolic pathways, genes, enzymes</i> Primarily transcription and biosynthetic enzymes and the genes encoding them | 198 (86%) | 32 (14%) |
| <i>Disease resistance in rice</i> Predominantly Japanese documents; largely plant genes, centered on rice and resistance to fungal disease | 206 (77%) | 61 (23%) |
| <i>Male-sterile seeds</i> Production of hybrid seed, strongly emphasizing the use of genetically engineered male sterility to prevent self-pollination in the hybrid parent lines | 133 (75%) | 44 (25%) |
| <i>Viral proteins</i> Viral gene promoters and expression systems, plant virus resistance, and antisense gene suppression (including applications in fruit-ripening quality traits) | 378 (71%) | 153 (29%) |
| <i>Herbicide resistance</i> Genes, enzymes, compositions and methods for plant herbicide resistance and, to a lesser extent, for insect pathogen and disease resistance | 194 (69%) | 88 (31%) |
| <i>Product-quality traits</i> Various crop-product quality traits including protein (amino acid), oil (fatty acid), carbohydrate (sugar) and vitamin content; fruit ripening; and plant stress resistance | 291 (65%) | 157 (35%) |
| <i>Flowering control</i> Includes control of plant flowering for ornamental and agronomic purposes | 48 (58%) | 35 (42%) |
| <i>Pathogen resistance</i> Centered on the theme of plant disease resistance, with associated pathogen and stress resistances | 53 (44%) | 67 (56%) |

Categories are listed in order of increasing public-sector involvement.

nizes patterns of topic word usage to quantify degrees of textual similarity between documents and clusters them accordingly (Fig. 4). The percentage of IP documents assigned to public-sector researchers in each of these ten trait technology categories is listed (Table 3). Although the public sector holds only 10% of the patents for *Bacillus thuringiensis* (*Bt*) and other insect-resistance traits, at the other end of the spectrum, a few technology categories, such as flowering (42%) and pathogen resistance (56%) are relatively dominated by the public sector.

These results suggest that the public sector has invented across a wide range of key technologies important for the production of transgenic plants with novel traits. Of the major classes of technologies examined, including transformation methods, selectable markers, promoters, transit peptides and trait genes, public-sector organizations

have patented or published viable substitute technologies in every area except selectable markers.

Conclusions

In agricultural biotech, the public sector plays an important role in fundamental research and represents a substantial source of IP, to a degree perhaps unique among industry sectors. Yet, there are important quantitative and qualitative distinctions between the public- and private-sector IP portfolios that have emerged over the past 20 years.

Internationally, the public sector has generated 24% of the IP in agricultural biotechnology (ranging from 14% among Japanese patents to 33% among PCT filings). The largest public-sector patent holders are the University of California system and the USDA, with 1.7% and 1.2%, respectively.

The private sector accounts for 74% of the IP in this sector, much of it aggregated into a few very large IP portfolios at major corporations, the top five of which control 41% in the United States. This percentage is likely to be an underestimate, as a portion of the public-sector portfolio has also been licensed to companies in the private sector. The rest of the private sector, including independent biotechnology startups, holds 33% of agricultural biotechnology IP.

Although much has been written about the possibilities for public-private collaborations in agricultural biotechnology research, the results here indicate that only a relatively small proportion (2.8%) of patents in this area have been jointly invented by collaborating private and public-sector researchers. Overall, public-sector researchers have been more than threefold as likely as private-sector researchers to enter into collaborations.

Yet, from the perspectives of both sectors, the majority of collaborations are cross-sector public-private arrangements.

Case study and cluster analysis of IP documents illustrates a degree of qualitative distinction between the public- and private-sector IP portfolios. The private sector has, for example, dominant positions in IP related to hydrolase enzymes useful in industrial applications and in the insecticidal *Bt* toxin genes, whereas the public sector appears to have had greater activity focused in plant developmental processes, such as flowering control and in disease and stress resistance. It is likely that this type of specialization will continue in the future as public funding for research emphasizes the discovery of a wide spectrum of previously unknown gene functions and private research focuses on application-driven research in a narrower range of established product lines.

These results hold implications for those concerned about possible IP constraints on public-sector innovation in agricultural biotech. A major challenge for management of public-sector IP is the high degree of fragmentation of technology ownership across numerous institutions, especially in light of the need for multiple technology components to provide freedom to operate in transgenic crops. Based in part on some of the economic principles of an 'IP clearinghouse'⁵², a model of public-sector collaboration, including data sharing and patent pooling, has recently been suggested that could directly address this issue⁵³. On the basis of our analysis here, it seems that the technologies patented by the public sector might indeed be able to provide a platform of technologies sufficient to enable the development of new transgenic varieties and cultivars. Such a strategy may be particularly important in the future for sharing access to key enabling technologies, to enable innovators to develop and deploy the trait technology projects of the public sector.

1. Evenson, R.E. & Gollin, D. (eds.). *Crop Variety Improvement and Its Effect on Productivity: The Impact of International Research* (CAB International, Wallingford, UK, 2002).
2. Alston, J.M., Pardey, P.G. & Taylor, M.J. (eds.). *Agricultural Science Policy: Changing Global Agendas* (Johns Hopkins University Press, Baltimore, 2001).
3. Goss, P.J. Guiding the hand that feeds: toward socially optimal appropriability in agricultural biotechnology innovation. *Californian Law Rev.* **84**, 1395–1436 (1996).
4. Graff, G., Heiman, A. & Zilberman, D. University research and offices of technology transfer. *Californian Mgt. Rev.* **45**, 88–115 (2002).
5. Wright, B.D. Public germplasm development at a crossroads: biotechnology and intellectual property. *Californian Agric.* **52**, 8–13 (1998).
6. Heller, M.A. & Eisenberg, R.S. Can patents deter innovation? The anticommens in biomedical research. *Science* **280**, 698–701 (1998).
7. Kryder, R.D., Kowalski, S.P., & Krattiger, A.F. The Intellectual and Technical Property Components of Pro-vitamin A Rice (GoldenRice): A Preliminary Freedom-to-operate Review (Brief No. 20, ISSAA: Ithaca, New York, USA, 2000).
8. Hall, B.H., Jaffe, A.B. & Trajtenberg, M. The NBER patent citations data file: lessons, insights, and methodological tools. *National Bureau of Economic Research, Working Paper 8498* (National Bureau of Economic Research, Cambridge, Massachusetts, USA, 2001).
9. Fuglie, K.O. & Schimmelpfennig, D.E. (eds.). *Public-Private Collaboration in Agricultural Research: New Institutional Arrangements and Economic Implications* (Iowa State University Press, Ames, Iowa, USA, 2000).
10. Hicks, D. & Narin, F. Strategic research alliances and 360 degree bibliometric indicators in *Strategic Research Partnerships. National Science Foundation Workshop Proceedings, NSF 01-336* (Jankowski, J., Link, A. & Vonortas, N., eds.) 133–145 (National Science Foundation, Washington, DC, USA, 2001).
11. Herrera-Estrella, L., Depicker, A., Van Montagu, M. & Schell, J. Expression of chimeric genes transferred into plant cells using a Ti plasmid-derived vector. *Nature* **303**, 209–211 (1983).
12. Klein, T.M., Wolf, E.D., Wu, R. & Sanford, J.C. High velocity microprojectiles for delivering nucleic acids into living cells. *Nature* **327**, 70–73 (1987).
13. Barton, K.A., Binns, A.N., Chilton, M.-D.M. & Matzke, A.J.M. Regeneration of plants containing genetically engineered T-DNA. US Patent 6,051,757 (2000).
14. Sanford, J.C., Wolf, E.D. & Allen, N.K. Method for transporting substances into living cells and tissues and apparatus therefore. US Patent 5,036,006 (1991).
15. Hoekema, A., Hooykaas, P.J.J. & Schilperoord, R.A. Process for introducing foreign DNA into the genome of plants. US Patent 5,149,645 (1992).
16. Hamilton, C.M. Binary BAC vector. US Patent 5,733,744 (1998).
17. Yoder, J.I. & Lassner, M. Biologically safe plant transformation system. US Patent 5,792,924 (1998).
18. Roa-Rodriguez, C. Nottenburg, C. *Agrobacterium-mediated transformation* (CAMBIA IP Resource, Canberra, Australia, 2001). <http://www.cambiaip.org/>
19. Yoder, J.I. & Goldsborough, A.P. Transformation systems for generating marker-free transgenic plants. *Biotechnology* **12**, 263–267 (1994).
20. Roa-Rodriguez, C & Nottenburg, C. Antibiotic resistance genes and their uses in genetic transformation (CAMBIA IP Resource, Canberra, Australia, 2003). <http://www.cambiaip.org/>
21. Rogers, S.G. & Fraley, R.T. Chimeric genes suitable for expression in plant cells. US Patent 6,174,724 (2001).
22. Santerre, R.F. & Rao, R.N. Recombinant DNA cloning vectors and the eukaryotic and prokaryotic transformants thereof. US Patent 4,727,028 (1988).
23. Bojsen, K. *et al.* Mannose or xylose based positive selection. US Patent 5,767,378 (1998).
24. Odell, J.T., Nagy, F. & Chua, N.-H. Identification of DNA sequences required for activity of a plant promoter: the CaMV 35S promoter. *Nature* **313**, 810–812 (1985).
25. Sun, C.-W. & Callis, J. Independent modulation of *Arabidopsis thaliana* polyubiquitin mRNAs in different organs and in response to environmental changes. *Plant J.* **11**, 1017–1027 (1997).
26. Comai, L., Sanger, M.P. & Daubert, S.D. Figwort mosaic promoter and uses. US Patent 6,051,753 (2000).
27. Gelvin, S.B., Hauptmann, R., Ni, M. & Cui, D. Chimeric regulatory regions and gene cassettes for expression of genes in plants. US Patent 5,955,646 (1999).
28. Maiti, I. & Shephard, R.J. Full-length transcript (FLT) promoter from figwort mosaic caulimovirus (FMV) and use to express chimeric genes in plant cells. US Patent 5,994,521 (1999).

29. Maiti, I. & Shephard, R.J. Promoter (FLT) for the full length transcript of peanut chlorotic streak caulimovirus (PCLSV) and expression of chimeric genes in plants. US Patent 5,850,019 (1998).
30. van der Fits, L. & Memelink, J. Comparison of the activities of CaMV 35S and FMV 34S promoter derivatives in *Catharanthus roseus* cells transiently and stably transformed by particle bombardment. *Plant Mol. Biol.* **33**, 943–946 (1997).
31. Romano, C.P., Cooper, M.L. & Klee, H.J. Uncoupling auxin and ethylene effects in transgenic tobacco and *Arabidopsis* plants. *Plant Cell* **5**, 181–189 (1993).
32. Blechl, A., Anderson, O., Somers, D.A., Torbert, K.A. & Rines, H.W. Glutenin genes and their uses. US Patent 5,914,450 (1999).
33. Harada, J.J., Lotan, T., Ohto, M.-A., Goldberg, R.B. & Fischer, R.L. Leafy cotyledon genes and their uses. US Patent 6,320,102 (2001).
34. Benfy, P.N. & Chua, N.-H. Plant promoters. US Patent 5,110,732 (1992).
35. Conkling, M.A., Mendu, N. & Song, W. Root cortex specific gene promoter. US Patent 5,837,876 (1998).
36. Grundler, F., Nitz, I. & Puzio, P. Root-specific promoter. PCT Application WO 01/44454 (2001).
37. Dobres, M.S. & Mandaci, S. Plant promoter useful for directing the expression of foreign proteins to the plant epidermis. US Patent 5,744,334 (1998).
38. Beachy, R. & Bhattacharyya, M. Plant promoter. US Patent 5,824,857 (1998).
39. Herrera-Estrella, L. *et al.* Chimaeric gene coding for a transit peptide and a heterologous peptide. US Patent 6,130,366 (2000).
40. Dehesh, K. Plastid transit peptide sequences for efficient plastid targeting. US Patent Application 20020178467 (2002).
41. Smeekens, S., Bauerle, C., Hageman, J., Keegstra, K. & Weisbeck, P. The role of the transit peptide in the routing of precursors toward different chloroplast compartments. *Cell* **46**, 365–375 (1986).
42. Komarnytsky, S., Borisjuk, N.V. Borisjuk, L.G. Alam, M. & Raskin, I. Production of recombinant proteins in tobacco guttation fluid. *Plant Physiol.* **124**, 927–934 (2000).
43. Bednarek, S.Y., Wilkins, T.A., Dombrowski, J.E. & Raikhel, N.V. A carboxyl-terminal propeptide is necessary for proper sorting of barley lectin to vacuoles of tobacco. *Plant Cell* **2**, 1145–1155 (1990).
44. Tague, B.W., Dickinson, C.D. & Chrispeels, M.J. A short domain of the plant vacuolar protein phytohemagglutinin targets invertase to the yeast vacuole. *Plant Cell* **2**, 533–546 (1989).
45. Kato, A., Hayashi, M., Kondo, M. & Nishimura, M. Targeting and processing of a chimeric protein with the N-terminal presequence of the precursor to the glyoxysomal citrate synthase. *Plant Cell* **8**, 1601–1611 (1996).
46. Volokita, M. The carboxy-terminal end of glycolate oxidase directs a foreign protein into tobacco leaf peroxisomes. *Plant J.* **1**, 361–366 (1991).
47. Hayashi, M., Aoki, M., Kato, A., Kondo, M. & Nishimura, M. Transport of chimeric proteins that contain a carboxy-terminal targeting signal into plant microbodies. *Plant J.* **10**, 225–234 (1996).
48. DellaPenna, D. & Cunningham, F.X. Marigold DNA encoding beta-cyclase. US Patent 6,232,530 (2001).
49. Hirschberg, J., Ronen, G. & Zamir, D. Tomato gene B polynucleotides coding for lycopene cyclase. US Patent 6,252,141 (2001).
50. Cunningham, F.X. & Sun, Z., Genes of carotenoid biosynthesis and metabolism and a system for screening such genes. US Patent 5,744,341 (1998).
51. Hirschberg, J., Cunningham, F.X. & Gant, E. Lycopene cyclase gene. US Patent 5,792,903 (1998).
52. Graff, G., Zilberman, D., An intellectual property clearinghouse for agricultural biotechnology. *Nature Biotechnology* **19**, 1179–1181 (2001).
53. Atkinson, R.C. *et al.* Public sector collaboration for agricultural IP management. *Science* **301**, 174–175 (2003).