A retrospective prospective perspective on agricultural biotechnology ten years on

Martina Newell McGloughlin
Date Received (in revised form): 4th August, 2006

Martina Newell McGloughlin
is Adjunct Professor in the Department of Plant Pathology at the University of California (UC), Davis and directs the UC Systemwide Biotechnology Research and Education Program (UCBREP), which covers all ten UC campuses and the three national Laboratories, Lawrence Livermore, Lawrence Berkeley and Los Alamos. UCBREP was founded by inaugural director, Nobel Laureate Paul Boyer. She is co-director of an NIH Training Grant in Biomolecular Technology, one of only four in California. Prior to this she was director of the UC System Life Sciences Informatics program and the local UC Davis Biotechnology Program. She helped contribute to the formation of the National Science Foundation of Ireland (SFI) and is now a member of its Board of Directors.

Abstract
Since the first biotech crop was commercialised in 1996, these crops have enjoyed a rapid adoption and are now grown commercially by 8.5 million farmers in 21 countries, an 11 per cent increase from 8.25 million in 17 countries in 2004. Research and development is being conducted in another 45. The billionth cumulative acre of biotech crops was grown in 2005. Notably, last year Iran grew its first crop of biotech rice, the first biotech planting of this important food crop globally. The Czech Republic planted biotech maize for the first time, bringing the total number of European Union (EU) countries growing biotech crops to five with Spain, Germany and the Czech Republic being joined by France and Portugal, which resumed planting biotech maize after four and five-year gaps, respectively. This could signal an important trend in the EU. Although North America leads in the research, more than half of the 63 countries engaged in biotech research, development and production are developing countries. The first generation of such crops focused largely on input agronomic traits, the next generation will focus more on value-added output traits. In the next decade, some studies estimate the global value of biotech crops will increase nearly five-fold to $210bn.
Journal of Commercial Biotechnology (2006) **13,** 20–27. doi:10.1057/palgrave.jcb.3050031

Keywords: *biotechnology, adoption, agronomic traits, output traits, co-existence*

INTRODUCTION

Innovation is essential for sustaining and enhancing agricultural productivity. This involves new, science-based products and processes that contribute reliable methods for improving quality, productivity and environmental sustainability. Biotechnology has introduced a new dimension to such innovation, offering efficient and cost effective means to produce a diverse array of novel, value-added products and tools. It has the potential to improve qualitative and quantitative aspects of food, feed, fibre, and biofuel production, reduce the dependency of agriculture on chemicals and fossil fuels, diminish over-cultivation and erosion, and lower the cost of raw materials, all in an environmentally sustainable manner. Commercialisation of the first generation of products of recombinant DNA technology was another facet in a long history of human intervention in nature for agricultural and food production purposes. As such, the same parameters of risk-based assessment should apply. Commercialisation of products must be undertaken within a regulatory framework that ensures adequate protection of the consumer,

Correspondence: Martina Newell McGloughlin DSc, Adjunct Professor, Department of Plant Pathology, 300 LSA, University of California Davis, CA 95616, USA
Tel: +1 530 752 8237
Fax: +1 530 752 4125
E-mail: mmmcgloughlin@biosci.ucdavis.edu
Web: http://ucbrep.info

the environment and alternate production systems while not stymieing innovation.

North America remains the epicentre of Research and Development on plant biotech, with the United States and Canada in the top five producing nations in terms of commercial biotech crop value: $2.0bn in Canada and $27.5bn in the United States primarily from soybeans, corn, cotton and canola. Thousands of field trials have been conducted in the two countries. In the United States, farmers continue to grow more biotech crops than any other country – 123 million acres or 55 per cent of the world's biotech area in 2005. That represents an increase of 5.4 million acres over 2004. Nearly 20 per cent or 23.6 million acres are now planted with multiple or stacked biotech traits. US farmers also planted the first triple-stacked variety in 2005 in about 1.24 million acres.[1] Field trials are continuing in other traits and crop varieties including research on fungal-resistant potatoes, peanuts, plums, bananas, rice, lettuce, salt-tolerant cucumbers, herbicide-tolerant peas, onions, tobacco and many others. Canada has produced, approved or field tested more field crops than any other country. The United States has approved in total 15 crops to date, including corn, cotton, canola, soybeans, chicory, cotton, flax, melon, papaya, potatoes, rice, squash, sugar beets, tobacco and tomatoes. In the next decade, some studies estimate that the global value of biotech crops will increase nearly five-fold to $210bn.[2]

Agricultural biotechnology has helped farmers around the world boost their productivity and grow crops in more ecologically healthy fields while allowing much more efficient use of resources. This technology allows reduced tillage, which cuts down on greenhouse gas emissions, water runoff, and machinery use and soil erosion. Meanwhile, the benefits experienced by larger-scale farmers in both industrialised nations and lesser developed countries are already considerable. Research by Brookes and Barfoot[3] in 2005 shows that in the first nine years of genetically modified (GM) crop cultivation:

- Global net farm income increased by $27bn (€23bn);
- The environmental footprint of farming was reduced by 14 per cent;
- This includes a reduction in carbon dioxide emissions in 2004 equivalent to taking nearly five million cars off the road for a year. Reduced-till agriculture – made much easier by the use of GM herbicide-tolerant crops – means healthier soil, with reduced erosion and far less carbon dioxide release; in general, cultivation is not a sustainable practice. It is energy intensive, and exposes soil to wind and water erosion. It allows rain to compact the soil, and increases the oxygen content of the soil, allowing organic matter to oxidise away. In turn, lower organic matter in the soil allows more compaction and more nutrient loss.
- Pesticide use fell by over 170,000 tonnes. In 2004 alone this was over 40,000 tonnes, equivalent to more than 30 per cent of total active ingredients used on European arable crops. Because less spraying means fewer tractor passes, this also contributes to lower CO2 emissions.
- Insect-resistant maize also has an additional health benefit; because fewer insect-damaged leaves and cobs result in much less infection by fungal moulds, there is also a marked reduction in the presence of naturally occurring toxins (called fumonisins) produced by these fungi, toxins that are known health risks to animals and that are associated with human health problems. The only 'natural' way to control for those fungi is the use of copper sulphate which has one of the highest toxic hazard ratings of acceptable pesticides and selects for antibiotic resistant bacteria in the soil.

This supports a 2002 study of biotech crops by the National Center for Food and Agricultural Policy (NCFAP), which found that 11 biotech crops planted in the United States produced an additional 5.3 billion pounds of food and fibre on the same acreage, improved farm income by $1.5bn and reduced pesticide use by 46.6 million pounds.[4] The NCFAP study found that Roundup Ready soybeans offered several advantages to farmers, including easier weed management, less injury to crops, no restrictions on crop rotations, increase in no till and cheaper costs. US farmers using Roundup Ready soybeans saved an estimated $753m in 2001 due to lower herbicide costs. The broad spectrum of weeds controlled by glyphosate means that soybean growers no longer need to make as many multiple applications with combinations of herbicides. All together, the 40 case studies of 27 biotech crops showed that plant biotechnology can help Americans reap an additional 14 billion pounds of food and fibre, improve farm income by $2.5bn and reduce pesticide use by 163 million pounds. In 2004, an additional NCFAP study demonstrated that US farmers who grew biotech crops garnered a 27 per cent increase in net farm income.[5] Increasing yields on existing acreage reduces the pressure to convert forests and protected land into farmland.

The Food and Agriculture Organization (FAO) of the United Nations in a report issued in May 2004 found that biotechnology and genetic engineering of crops hold great promise for agriculture in developing countries.[6] The report noted that more than 70 per cent of the world's poor still live in rural areas and depend directly on agriculture for their survival. Of the 8.5 million farmers in 21 countries who grew biotech crops in 2005, 7.6 (90 per cent) of those were in developing countries. Agricultural research of all forms holds an important key to meeting their needs, the FAO said, and added that biotechnology can speed up conventional breeding programmes and may offer solutions where conventional methods fail. That is good for growers, consumers and anybody who cares about the environment. For example, in China, use of genetically engineered cotton eliminated the use of 156 million pounds of pesticides in 2001, an amount approximately equal to all of the pesticides used annually in California. A 2005 paper from the Royal Society suggests that intensive high-yield farming on less land is better for wildlife than 'wildlife friendly' less efficient farming.[7] They provide convincing evidence that without yield increase land use will double by 2050 and that this effect will be especially significant in developing countries where, without greater productivity at least two of those nations, China and India, will need four times the land area to support their expanding populations. They show that in Latin America where increased productivity was achieved there was a significant decrease in deforestation and those producers with greater yield increase had lower land use.

While many are aware of the corn, cotton and soybean impacts, one of the non-marquee crops possibly best illustrates the power of this technology to provide solutions to seemingly insoluble problems. Papaya is a major tropical fruit crop in Hawaii and Asia. The production is, however, set back by the prevalence of the papaya ringspot virus (PRSV) for which there is no natural resistance. The PRSV-resistant papaya, based on RNA interference (RNAi) suppression of the coat protein expression, literally saved the $17m economy in Hawaii and is of significant importance in Taiwan and other south-east Asian countries. Coat protein-based resistance is a demonstration of what is known as post-transcriptional gene silencing (PTGS). While initially it was considered a strange phenomenon limited to petunias and a few other plant species, it is now one of the hottest topics in molecular biology. RNAi in animals and basal eukaryotes, quelling in fungi, and PTGS in plants are examples of a broad family of phenomena collectively called RNA silencing. This system has now been applied to other species. A five-year effort to combat plum pox virus disease through PTGS resistance is paid off. In 1990, United States Drug Administration/Agricultural Research Service (ARS) scientists began their efforts with a papaya ringspot virus coat protein gene obtained from Dennis Gonsalves.[8] This gene shows 70 per cent homology to the plum pox gene and has been used to control other viruses similarly related to papaya ringspot. Irrespective of the mechanism however, it is important that resistance based on a single gene is managed well and alternate control mechanisms are introduced to reduce pressure on the development of viral resistance. Other approaches include expression of the RNA replicating enzymes of the virus, expression of satellite RNA, replicating RNA molecules that are molecular parasites of the virus or the use of protease inhibitors to interfere with processing of the viral proteins.

Scientific, civic and religious opinion leaders from all over the world have expressed support for the value of this technology. Florence Wambugu of Kenya states that the great potential of biotechnology to increase agriculture in Africa lies in its 'packaged technology in the seed', which ensures technology benefits without changing local cultural practices. For example, over 120 million children worldwide are deficient in vitamin A. Potrykus[9] group has engineered rice to accumulate provitamin A (β-carotene). Incorporation of this trait into rice cultivars and widespread distribution of this 'packaged technology in the seed' could prevent 1 to 2 million deaths each year. Wambugu observes that in the past, many foreign donors funded high-input projects, which have not been sustainable because they have failed to address social and economic issues such as changes in cultural practice.[10] In concurrence with this, Ismail Serageldin, former chairman of the Consultative Group on International Agricultural Research (CGIAR) noted that, *a priori*, biotechnology could contribute to food security by helping to promote sustainable agriculture centred on smallholder farmers in developing countries. For example, 40 per cent of the worlds irrigated land is no longer arable because of salinity. To address this problem Zhang and Blumwald[11] have developed plants than can grow in soil that has 50 times the salt level of normal water. Similarly, a gene that produces citric acid in roots can protect plants from soils contaminated with aluminium.[12] Genes such as these can allow crops to be cultivated in hostile soils and temperatures increasing geographic range while reducing potential impact on fragile ecosystems.

The first generation of biotechnology crops focused largely on input agronomic traits, the next generation will focus more on value-added output traits. This will include identifying and isolating genes and metabolites that will make possible the enhancement of valuable traits, with some of the later compounds being produced in mass quantities for niche markets. Two of the more promising markets are nutraceuticals, or so-called 'functional foods', and plants developed as bioreactors (production factories) for the commercial level production of valuable proteins and compounds, a field known as plant molecular farming.[13] Functional foods are defined as any modified food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains. Scientific evidence is accumulating to support the role of phytochemicals and functional foods in the prevention and treatment of disease. Epidemiological research has shown a positive association between dietary intake of food components. Developing plants with improved quality traits involves overcoming a variety of technical challenges inherent to metabolic engineering programmes. Both traditional plant breeding and biotechnology techniques are needed to produce plants carrying the desired quality traits. Examples include improvement of nutritional quality at the macro- (protein, carbohydrates, lipids, fibre) and the micro-level (vitamins, minerals, phytochemicals) and amelioration of anti-nutrients, allergens and toxins. In addition to functional foods, rDNA technology allows the engineering of plants to address issues of animal nutrition and impact of animal effluent on the environment. A good example of this is the addition of transgenic phytase enzymes to crops to reduce the need to add phosphate to feed.[14,15] Most of the phosphate is added to counteract the non-bioavailability of phosphorus in phytic acid and the sequestering effect of phytic acid on uptake of divalent mineral ions such as iron and zinc. Unfortunately, excess phosphate is excreted, which can have serious environmental consequences as it leads to eutrophication of waterways with resultant microbial blooms causing fish kills in regions with intense pig and poultry farming.[14,15] In addition, in humans such mineral deficiencies due to phytate binding are estimated to afflict 2–3 billion people, primarily in the developing world. Several studies have shown that *Aspergillus*-derived phytases can be produced at high levels in a range of plants including cereals with clear-cut positive effects on phytate degradation, and phosphate and mineral bioavailability in animal-feeding trials.[16,17] It is thus conceivable that genetic engineering of staples for increased phytase expression could have potential for improving iron and zinc bioavailability, alleviating the need for supplementation in all monogastrics and consequent reduction in polluting runoff from non-ruminant animals. Continuing improvements in molecular and genomic technologies are contributing to the acceleration of such product development. One estimate states that foods that are used for functional purposes made up 10 per cent of the $503bn total US retail food market.

In addition to being a source of nutrition, plants have been a valuable wellspring of therapeutics for centuries. During the past decade, however, intensive research has focused on expanding this source through rDNA biotechnology and essentially using plants and animals as living factories for the commercial production of vaccines, therapeutics and other valuable products such as industrial enzymes and biosynthetic feedstocks. More pressingly, with the increasing costs to our pockets and the environment of our dependency on fossil fuels, biotechnology offers innovative means to improve plant material for biomass conversion and enzymes to do the converting.

US consumer attitudes also tend to be positive on the whole about agricultural biotechnology. A majority of them continue to be open to the benefits of food biotechnology, but less interested in the subject compared to other food issues, according to a survey conducted by the International Food Information Council (IFIC) in late 2005.[18] It is notable that consumers do not mention products of biotechnology as avoided foods on an unaided basis. In fact, in an IFIC survey conducted in 2005 a clear majority of consumers (62 per cent) expect food biotechnology to provide benefits for them and their families over the next five years, primarily in the form of better health/nutrition or improved food quality/taste/variety. They continue to indicate a willingness to purchase products of food biotechnology, particularly if biotechnology is used to reduce pesticides (64 per cent), or improve taste and freshness (50 per cent). Regarding the potential benefit of producing a more healthful oil, 41 per cent state that this would have a positive impact, while 38 per cent state that this would have no effect on their purchase intention. An overwhelming majority of consumers (76 per cent) state that there is no information that they would like to see added to food labels, consistent with findings since 2001 when the question was first asked on the survey. Although support for the current US Food and Drug Administration policy on labelling food biotechnology has decreased over the years, more than half (55 per cent) of consumers in 2005 say they support the policy, with more than a third expressing strong support. On an open-ended basis, only one per cent name biotechnology as a labelling issue.

On the other side of the spectrum, what of the context in which these crops are grown? Can all cropping systems co-exist in harmony? According to Brookes and Barfoot,[19] it is important to determine the relative importance of different crop production systems based on planted area, production and economic value to the region in question. The issue is what, if any, are the economic consequences of adventitious presence of material from one crop system within another based on the notion that farmers should be able to cultivate freely the crops of their choice using whichever production system works best in any given context (GM, conventional or organic). It is never a food or environmental safety issue but rather a production and marketing matter. The heart of the issue is assessing the likelihood of adventitious presence of material from one production system affecting another and the potential impacts. This requires consistency when dealing with adventitious presence of any unwanted material including, but most definitely not limited to, biotech-derived material. Adventitious presence is simply the unintended incidence of something other than the desired crop such as small quantities of weed seeds, seeds from other crops, dirt, insects or foreign material (eg stones). It is unrealistic to expect 100 per cent purity for any crops, or products derived there-from, so thresholds that are consistent across all materials should be set and should not discriminate (eg, thresholds for adventitious presence of biotech material should be the same as applied to thresholds for other unwanted material and vice versa). All measures should be proportionate, non-discriminatory and science-based.

The issue of economic liability provisions that compensate growers for adventitious presence of biotech material is often raised. Historically, worldwide the market has adequately addressed economic liability issues relating to the adventitious presence of unwanted material in any agricultural crop. For example, for certified seed the onus is on the producers, who require isolation from undesired pollination for the purity of their product, to insure such purity; this is not their neighbour's problem. By extension the onus is on growers of any specialty crops to take action to protect the purity of their crops since these are self-imposed standards for and by that market. Growers who have themselves chosen a more stringent standard than that established in European Union (EU) legislation should not expect their neighbours to bear the special management costs of meeting that self-imposed standard; to do so would reverse fundamental freedoms of economic activity and would establish a dangerous precedent. To allow specialty operators to formulate unrealistic standards for GM in their own produce would impose impossibly high standards on neighbours and would effectively impose a ban on the choice of other producers. Such growers usually are rewarded by higher prices and niche markets for taking such actions. Their neighbours enjoy no such advantage.

Existing legislation in North America and the EU is more than adequate to protect all grower and consumer interests but if new regulations were considered to address economic liability provisions for any negative economic consequences of adventitious presence of unwanted material, the same principle should apply to all farmers regardless of their chosen production methods. On equity grounds, biotech growers should have equal access to compensation for adventitious presence of material from conventional or organic crops (such as fungal contamination) as conventional and organic producers have from biotech growers. No one sector should be able to unfairly prohibit another – access and choice work both ways. All co-existence measures should be based on legal, practical and scientific realities and not on commercial or niche marketing objectives.

According to Brookes and Barfoot[19] biotech crops co-exist successfully with conventional and organic crops in North America (where, as noted, biotech crops account for the majority of acreage of important arable crops like soybeans, cotton and maize) and Spain. The market has developed practical, proportionate and workable co-existence measures without new regulations or indeed any government intervention. Where isolated instances of adventitious presence of biotech material have been found in conventional or organic crops, these have usually been caused by inadequate implementation of good co-existence practices (eg, inefficient segregation of crops in storage and transport, non-use of tested, certified seed). Under civil liability (ie tort damages) and for intellectual property infringement (except for the unauthorised StarLink), there have been no lawsuits brought by any parties for adventitious presence. Every case brought by a seed company for infringement has involved a claim that the farmer charged with infringement was an intentional infringer (ie adventitious presence was not the issue). And, to date, each of these cases was upheld by the courts. Indeed, all except one notable exception in North America have conceded to this claim.

Within the EU, provision has been made for a *de minimis* threshold for unavoidable presence of genetically modified organisms but no actual threshold has been set. Therefore, the default state of the 0.9 per cent on labelling and traceability is the one enforced. In the United States, organic products cannot be (legally) downgraded or the producer decertified by unintentional presence when all required measures and best practices are adhered to and no producer has been so impacted to date.

Going forward there are four major stanchions to the furtherance of co-existence and all of them are incumbent on cooperation.

1. Monitoring: Verify the models and predictions about cost, isolation standards, and generally learn how the farming community copes with the requirements for keeping the product streams separated.
2. Dialog: Strategy development takes place in a dialog between the scientific and technical community and all relevant stakeholders (Denmark).
3. Stewardship: Stewardship programmes should take into account the interests of both GM and non-GM farmers. Existing product stewardship programmes for non-GM crops in farming should be a starting point for developing stewardship schemes for GM crops.
4. Research: The scientific community should be encouraged to fill the knowledge gaps that have been identified. Projects are needed to validate models and guidelines, including long-term studies. Building up mechanistic, probabilistic and predictive models of gene flow, etc. Methods for restricting gene flow by eliminating the fertility of pollen or seeds (apomixis, cytoplasmic male sterility, plastid transformation, Genetic Use Restriction Technology, etc).

The World Trade Organization ruled on February 6, 2006 that a six-year European ban on genetically engineered crops violates international trade rules, although they will not be final until later this year. The three person panel issued its decision ruling in favour of the three countries, US, Canada and Argentina, on a large majority of the 25 crops under dispute in the case while issuing mixed rulings on a few crops. The panel also ruled in favour in challenging national bans on specific biotech crops issued by Austria, France, Germany, Greece, Italy and Luxembourg. The EU had argued that it did not have a moratorium but that it just took more time to weigh the possible risks to health and the environment posed by genetically engineered foods. It said it needed to take a 'precautionary' approach to regulation, which is different from what it called Washington's 'laissez-faire' stance.

The trade organisation panel appears not to have challenged Europe's regulatory process for biotech crops. Rather, it said Europe failed to follow its own procedures, resulting in undue delay of decisions. Interestingly, one of the most comprehensive assessments on the technology was conducted by EU scientists. An EU Commission Report[20] that summarised biosafety research of 400 scientific teams from all 15 EU countries conducted over 15 years stated that research on biotechnology-derived plants and derived products so far developed and marketed, following usual risk assessment procedures, has not shown any new risks to human health or the environment beyond the usual uncertainties of conventional plant breeding. Indeed, the use of more precise technology and the greater regulatory scrutiny probably make them even safer than conventional plants and foods. If there are unforeseen environmental effects – none have appeared as yet – these should be rapidly detected by existing monitoring systems. A declaration signed by over 3,500 international scientists including 25 Nobel Laureates reiterates this position.

While biotech research and development in Europe slowed significantly following the EU's 1998 *de facto* moratorium on approvals, which has since been lifted, Europe's stance on biotech crops cannot prevent biotech adoption in the rest of the world and especially Asia is forging ahead. According to a study by Runge and Ryan[2] as the EU becomes increasingly isolated, it will discourage its young scientists and technicians from pursuing European careers. They opine that if on the other hand, the EU engages biotech in an orderly regulatory framework harmonised with the rest of the world, it will encourage a more rapid international diffusion of the technology. More nations will join the top tiers of commercial production, and emerging nations will continue to expand the sector.

In the final analysis resources are finite, true sustainability can come only from an enlightened philosophy that promotes the development of resource-enhancing technologies. The only sure way to protect the planet's resources is not to settle into the complacency of maintaining the status quo but to engage in continual, constructive change based on scientific knowledge.

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