The role of DNA technologies in crop breeding

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ABSTRACT

DNA technologies are bringing together, in life science companies, genetic understanding of biological systems which will support the production of new agricultural and medical products. In crop breeding these technologies potentially extend the range of both the biodiversity that can be accessed and the traits that can be delivered. Some varieties bred using DNA technologies will require more screening and regulation, depending on the trait involved, than conventionally bred varieties. The first such varieties are being taken up by farmers very rapidly in many parts of the world.

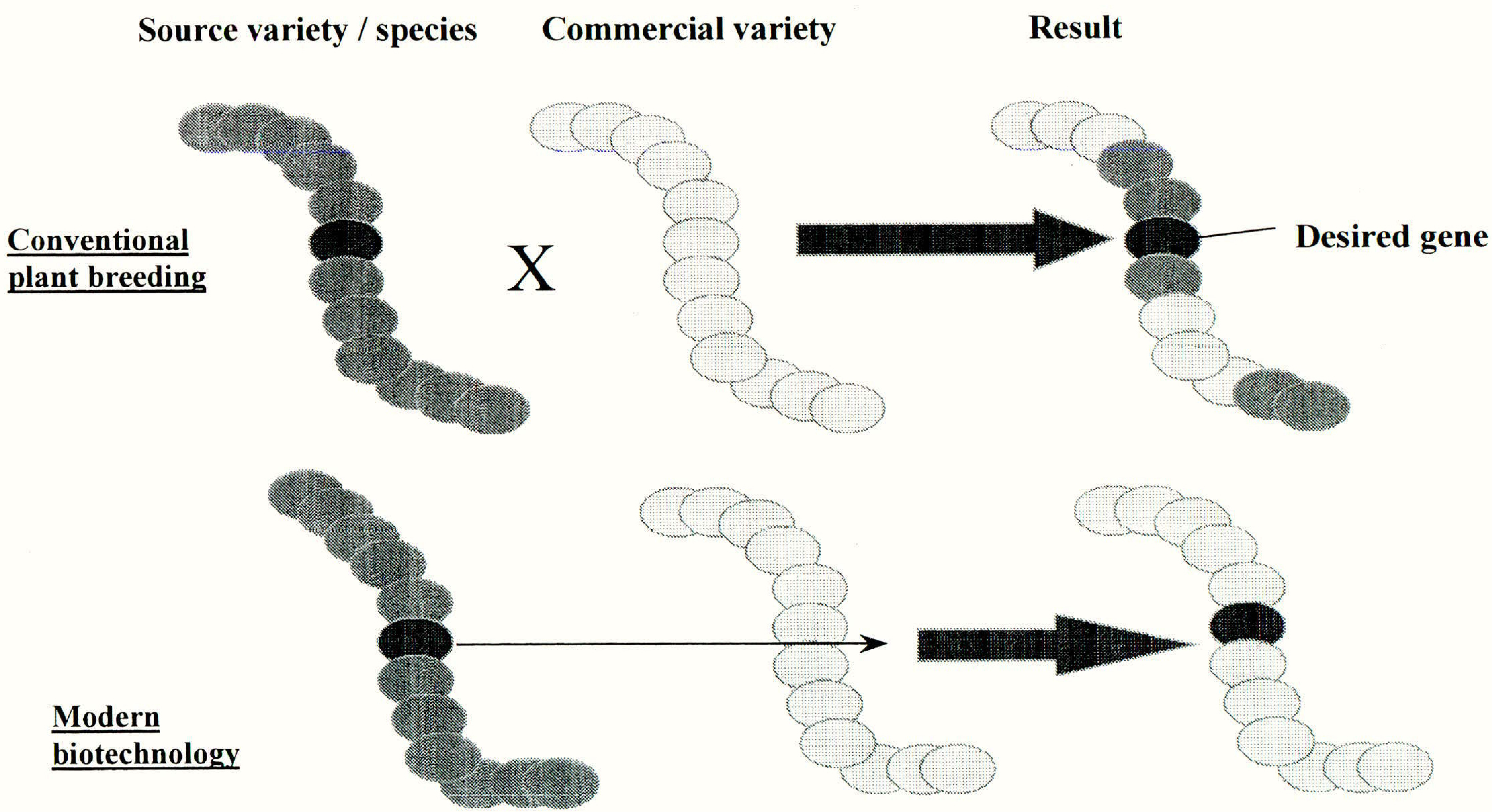
BACKGROUND

Conventional crop breeding, as carried out historically by farmers and, from the early part of this century, also by increasingly science based plant breeders, is predominantly a process of visual selection among a range of phenotypes produced by artificial cross-pollination. Its purpose is to offer to society new biological options, in the form of varieties, which are then taken up or not depending on society's assessment of their usefulness relative to the varieties already available. Usefulness is never easily quantified because it encompasses profitability, reliability, fitness for purpose, safety and adaptation to site and current husbandry. Conventional commercial plant breeders finance themselves, investing income from seed sales and, with inbred crops also royalties, in long-term, incremental improvements in both crop performance and selection techniques.

PLANT BREEDING

The DNA technologies, popularly referred to as Genetic Engineering or Genetic Modification, allow scientists to influence heredity at the molecular level. They form the basis of both Genomics and Plant Transformation, two new possibilities for crop breeders. Genomics provides ways in which all genes, not only those of large phenotypic effect, can be mapped and selected and Plant Transformation allows genes to be built into constructs which can be moved rapidly across species barriers. Structural Genomics is the process of finding out where all the genes are and has led to the remarkable discovery of the co-linearity or synteny, that is the conservation of gene order on chromasomes, that exists across different species within crop plant families. Functional Genomics is the process of finding out what individual genes control at the biochemical level and is leading to a greater understanding of many new and potentially economically important traits. An understanding of, and capacity in, Genomics gives the breeder the ability to track the genes controlling comparable traits in different species. If the crop breeder also has capacity in plant transformation he has the potential to combine the genes for a trait from different species and thus to exploit a much wider range of crop biodiversity than before. Conventional crop breeding is limited by its dependence on sexual compatibility and genes of large effect. Crop breeding using DNA technologies avoids these limitations and, since defined genetic constructs are used, also offers increased precision and speed (Figure 1).

Figure 1 Difference between conventional breeding and genetic engineering



It is useful to consider two questions when comparing conventional breeding with genetic modification. 1) Are they different because the juxtaposition of genes from distinct species might lead to dangerous novel gene interactions? and 2) Is this possibility exacerbated by the fact that, at the moment, the site of insertion of a construct into the chromosomes of the host in plant transformation is not predictable? These apprehensions are understandable enough in society at large which still has a predominantly creationist view of the origins of life. Evolutionary biology, however, shows that there is a great conservation of gene structure and function across the whole range of life. Thus gene mixing outside the species gene-pool may not be as inherently 'unnatural' as some people fear. A certain amount of experience has already been obtained. In the development of the bread wheat, *T.aestivum*, three distinct species of goat grass have amalgamated naturally and, in the last 30 years cytological techniques have resulted in the insertion of pieces of alien chromasome, and in the case of Triticale plants the whole Rye geneome, into wheat. In both wheat and barley many chromasomal translocations are known in which blocks of genes are moved about the geome and hence acquired different gene juxtapositions. All of this resulted in combinations of trait expression, none of which were dangerous, but very few of which were useful and stable.

In conventional crossing programmes, particularly back-crossing programmes, the acquisition of a desired gene is usually associated with undesirable ones which have to be selected out. This takes time and involves the discarding of very large numbers of lines which the breeder would not risk his reputation on by taking to the marketing stage. The same is and will be true of genetic modification. The combination of genes from very widely different species, animals and plants for example, will need to be studied with greater effort, until a body of experience is built up, than would combinations of well understood genes. Because the site of insertion of any construct in plant transformation is unpredictable many individual transformant plants will have to be made so that only those with optimal performance, stability and safety can be selected before marketing is considered. Variety production, whether conducted conventionally or with DNA techniques, will remain a numbers game in which only a very few lines, which have survived extensive screening tests, ever reach the market.

DNA TECHNOLOGY AND THE PLANT BREEDING INDUSTRY

The costs of conventional breeding are already so high that it has to be conducted, if it is to be profitable, on a climatic region basis rather than in individual countries. Thus during the past fifteen years governments in the developed world have withdrawn from funding crop breeding to be replaced by multinational seed companies. These in turn have tended to become aligned with agrochemical companies in order to exploit synergies in marketing to growers. We have now reached the stage where a number of global life science companies (Dupont, Monsanto, Novartis and most recently Aventis) are beginning to be formed, from the combination of pharmaceutical, seed and agrochemical companies, where the high cost of investment in genomics and plant and animal transformation can be spread across a greater number of products.

In the last three years these life science companies have launched the first wave of GM crops. These have genetically modified agronomic traits and are designed to help growers do more with less. But these will very soon be followed by a second wave which will have genetically modified quality traits and, eventually, by a third wave where the genetic modification will turn the plants into sustainable biofactories producing specific molecules. Thus the target is a whole range of value-added traits or specialty crops. Not all of these will be involved in the food chain and, indeed, not all of them will be offered widely to growers if only limited areas of specialist, identity preserved, production are required to meet demand.

REGULATION

The crop breeders inside life science seed companies want to utilise DNA technologies because they give, in a commercially highly competitive market, more efficient means to the end of offering new biological options. But, as we all know, society, particularly in Europe, is not yet convinced that it wants to take up these particular options. Public apprehensions centre around either the fear that by blurring the dividing lines between species we may be doing something that is unnatural or the fear that the new technologies are being introduced too fast with inadequate regulation by over-powerful multinational companies. Society at large, understandably, has difficulty in coming to terms with any new technology but particularly with a technology that affect its food. In Europe it is an irony of history that DNA technology is being introduced with more legal regulation in place than any previous technology just at a time when the BSE disaster has wrecked public confidence in regulation.

Regulation of GMOs in Europe is based on new, purpose designed legislation concerned predominantly with human and environmental safety. In contrast, in the rest of the world that has GMO regulation this has come about by the adaptation of pre-existing legislation. The European system is admirably thorough but it takes longer in Europe than in the rest of the world, not only to get applications approved, but also to get changes made to the application process. Despite this, European regulation of GMOs is evolving. On the one hand, as experience is accumulated, fast track product, as opposed to process, based systems of approval are being introduced. At the same time, however, an element of ethical consideration is being recommended for example by the recent UK House of Lords report.

Obtaining society's approval to use GMOs by passing the regulatory hurdles is, however, not the end of the need for rules concerning modified crops. Experience in other parts of the world has shown that the advantageous effects of a GM trait may not only affect the performance of the variety into which it is placed but may also influence what happens in subsequent crops in the rotation. A possible UK example of this may come to pass when Roundup Ready sugar beet are grown in rotation with non-herbicide resistant potatoes. It is probable that in this situation volunteer potatoes will be better controlled by glyphosate than by the more expensive, less environmentally benign, herbicide regimes currently used. The agricultural divisions of Life Science companies see themselves, from now on, not as providers of either varieties or agrochemicals, but as providers of sustainable solutions to farming problems.

INTELLECTUAL PROPERTY

For several hundred years western societies have encouraged new technology by granting intellectual property rights. These are a deal done between national governments and inventors whereby, in exchange for the inventor declaring details of an invention according to strict rules, society grants the inventor exclusive rights to the commercial development of the invention for a fixed time period after which the invention becomes freely available to all. World Trade Organisation rules currently require participating countries to move towards the intellectual property protection of plants and plant varieties.

Plant varieties can by protected in 37 countries using Plant Variety Rights based on the international conventions of UPOV, the **U**nion for the **P**rotection **O**f new **V**arieties. Plant Variety Rights have been extensively used, particularly for inbreed crops in Europe, since the mid 1960's. In fewer countries some plant varieties and novel gene constructs, which control particular traits involved in plant transformation, can be protected by patents.

The level of protection given by Plant Variety Rights and by patents differs in that with Rights the holder cannot prevent other breeders from using his protected variety as a parent in crosses aimed at the selection of further varieties but with patents he can. Thus on the face of it, particularly if patents with broad claims are granted, the holders of patents are in a powerful position and this possibility causes at least part of the disquiet that some members of the public feel about multinational companies. However it must be remembered that patents, unlike Plant Variety Rights, are expensive to both obtain and to defend from challenge. Also, given the great genetic complexity especially of many second and third wave traits, competitor inventors will always find ways of developing their own similar but not identical patents. Thus with sensible adjustment of the laws the consumer will continue to be offered choices. As long as this happens then, if innovation is to continue, society should see to it that a potential investor in life science activities can choose a level of intellectual property protection that is appropriate to the level of risk taken in making the investment.

CULTURAL GUIDANCE AND UPTAKE OF GM CROPS

It is important to ensure that understanding of the best husbandry practice relevant to a particular sustainable solution is rapidly and widely disseminated to farmers growing GM crops. This can be encouraged in two ways as is already happening in the USA. First when a farmer there signs up to buy GM seed he not only agrees to pay a technology charge but is also instructed in and agrees to carry out particular husbandry procedures. Secondly the supply chain also agrees on methods of labelling seed and produce and controlling their exchange so that the crop can be passed along the food chain with all concerned knowing what they are handling. Last summer in the UK, an organisation called SCIMAC (The **S**upply **C**hain **I**nitiative on **M**odified **A**gricultural **C**rops) (Figure 2), which consists of the Trade Associations associated with crop production, was formed and is already proposing 1) Terms of Inter-Professional Agreements, 2) Administration of Independent Audit and 3) The Ensurance of Compliance.

Figure 2 Who is SCIMAC?

SCIMAC membership includes:

- Farmers Union (NFU)
- British Society of Plant Breeders (BSPB)
- British Agrochemicals Association (BAA)
- United Kingdom Agricultural Supply Trade Association (UKASTA)
- British Sugar Beet Seed Producers Association (BSBSPA)

Launched publicly in June 1998

The importance of a meeting concerned with gene flow within and between species lies not only in that it will provide information relevant to the evolution of regulatory requirements but, probably more importantly in the long run, it will help to specify best practice on farms. The use of the phrase 'in the long run' implies that we have time to work out the systems before we grow the crops. Unfortunately, in practice, because of the speed with which GM crops are being taken up around the world, we will have to do both simultaneously.

THE PACE OF CHANGE

To emphasise this, figures indicating for GM crops the diversity of traits, the speed of development, the areas grown and their potential value are presented below:

It took Monsanto sixteen years from initiating its own research to getting its first GM product onto commercial farms in 1996. The first field releases to the environment of GM crop material began in 1987. By 1998 there were ten Monsanto GM products available. (Figure 3)

Figure 3 Monsanto's Biotechnology Timeline

Started R&D efforts in corporate R&D	1980
First engineered plants	1983
Programme transferred to commercial unit	1985
First field tests	1987
Demonstrated commercial performance	1993
First Regulatory submissions	1993
First Commercial approval	1995
First Commercial products introduced	1996
10 products available in the marketplace	1998

Figure 4 Extent of field tests of GM crops

- More than 25,000 field tests globally
- In 45 Countries
- With 60 different crops
- Most frequent categories 1987-1998

Herbicide Tolerant	29.0%
Insect Resistant	24.1%
Product Quality	21.3%
Viral Resistant	10.1%
Fungal Resistant	4.1%
Agronomic Properties	4.1%
Other	7.3%

(USDA Field Releases Permits Issued and Notifications Acknowledged)

Between 1987 and 1998 there have been more than 25.000 field tests in 45 Countries with GM material in sixty different crops. The most frequent trait categories have been herbicide resistance and insect resistance. (Figure 4)

In 1998 Monsanto's share of the area planted was over 50 million acres. This involved five crops, soyabean, maize, cotton, oilseed rape and potatoes and seven countries. (Figure 5).

Figure 5 Total 1998 Plantings of Commercialised Monsanto Biotechnology Crops
(acres in thousands)
* = First year of commercialisation

Region / Product	U S A	CANADA	CHINA	MEXICO	ARGENTINA 1998-99	AUSTRALIA 1998-99	SOUTH AFRICA 1998-99
Roundup Ready Soybeans	25,000+	100			10,000		
Bollgard/Ingard Cotton (B.t)	5,000+ (45% of cotton)		130*	100	20*	200	30*
Roundup Ready Cotton							
Bollgard/R R Cotton Stacked Gene				2			
Roundup Ready Corn	950*						
YieldGard Corn (B.t)	10,000+	300+			42*		
Roundup Ready/YieldGard Corn Stacked	30*						
Roundup Ready Canola		Well over 1,000					
NewLeaf Potatoes (B.t)	50	10					
Laurate Canola (oil modification)	50+						
BXN Cotton (herbicide-resistant)	1,000						
Approximate TOTALS	42,000+	1,400+	130	100+	10,000+	200	30

This very rapid uptake of varieties derived using genetic modification technology has come about because farmers want these varieties. Some understanding of why can be shown by the cost benefit experience of on-farm use of Monsanto GM crops in 1997 given in Figure 6. In each of five different crops a yield benefit over previous practice was clearly demonstrated. This translated into appreciable additional value potential which, in turn, produced high levels of farmer satisfaction and repurchase intention.

Figure 6 Monsanto cost benefit experience of on-farm use of GM Crops in 1997

Crop	Yield Benefit %	Value Potential $/acre	Farmer Satisfaction %	Repurchase Intention %
Roundup Ready Soyabeans	5	12-20	90	90
Yield Gard Bt Maize	8	20-35	90	80+
Bollgard Bt Cotton	10	35-70	80	70+
Roundup Ready Cotton	5-6	8-20	90	95
New Leaf Potatoes	5	40-100	85	90

The setting of the technology charge at approximately half the expected additional value potential ensures that the farmer and technology provider roughly share the financial benefit. This wider picture of the uptake of GM crops is in stark contrast to the often parochial and introspective debate that is going on in Europe. In our search for understanding of the environmental biology of GM crops we must not lose sight of the fact that, after a very large number of tests covering an eleven year period, most non-Europeans agree with our House of Lords' conclusion that the benefits are considerable and the technology has the potential to create and sustain revenue and jobs. This is reinforced by estimates of the value of the plant biotechnology industry by 2005 (Figure 7). This shows, as I suggested earlier, that the predominance of Herbicide Tolerance will fade as novel quality characteristics come on stream.

The most likely GM crop developments in the UK, and their estimated time of introduction, are listed in Figure 8. Beet and oilseed rape varieties are going to reach the market before wheat and potatoes. This means that our first commercialised GM crops, unlike the maize and soyabean of the USA, are precisely those where a knowledge of gene flow is going to be important and where we will not have the potential to learn from extensive experience from outside Europe.

Figure 7. Future development of the Biotechnology Industry by 2005, the Plant Biotechnology Industry will generate revenues of over $6 Billion

$ Billion	Year	
Annual industry revenues from	2000	2005
Herbicide Tolerance	0.8	1.1
Other Agronomic Characters	0.8	2.1
Quality Characters	0.6	3.4

Figure 8 Biotech development projects and possible timelines for the UK

Roundup Tolerant crops

Fodder beet	spring	2000
W OSR	Aut	2000
Sugar beet	spring	2001
Fodder maize	spring	2002

Hi-Laurate Spr OSR spring 2002?

Beyond 2002

Fusarium-resistant wheat
Virus resistant potatoes
Blight resistant potatoes
Septoria resistant wheat
Other speciality oils in OSR

A long term perspective on Ag-biotech

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ABSTRACT

The prediction of the future direction of the Ag-biotech industry is fraught with difficulties, yet it is a valuable exercise. Such assessments of the impact of biotech on a global scale needs to concentrate on direct effects including, an evaluation of societal needs as well the requirements for food, feed, raw material and energy production. The world has to move towards a sustainable food production system that is capable of feeding an increasing population on less land. There are two targets for biotechnology, input and output traits. The former mainly concern those that affect plant nutrition and adaptation to biotic and abiotic stresses. The target is to increase yields with reduced external inputs. Herbicide and insecticide resistant crops are already being grown and there has been some progress with fungus resistance. Future advances will concentrate on abiotic stress factors such as drought, heat and salt tolerance. The 'holy grail' of developing nitrogen-fixing cereals is being explored but will take time as it is a complex system. Anticipated advances in the acquisition of 'output' traits are, in the short term, the modifications of the starch, protein, oil and sugar contents of plants. In the longer term the development of 'functional' foods (*eg*. enriched with vitamins), 'cured' foods (*eg*. removal of allergenic factors) is predicted, along with modifications that affect food digestibility. Future advances in genomics will deliver an increasing range of genes with potential to develop totally new biochemical pathways in plants.

INTRODUCTION

Futurology is a very inexact science. That makes it quite safe to make long term prognoses on technology development. It also threatens to make the exercise seem futile.

Does it make sense to try to look 30-40 years ahead in a sector where most of the products coming to the market were not even conceived 10 years ago? Worse, most of the **technologies** needed to make those products did not exist ten years ago! Worse still, even among the technologies we work with today, there are lurking those that will transform the sector, and we are likely to miss them in any attempt to pick among the key new developments of today, those that will transform our lives in a decade or two.

We would be in good company in such a case. Alvin Toffler, arguably the most famous futurologist in the world, totally failed to see the coming of the Internet in a book he wrote on communications and power in 1989!

And yet, it is important to do this type of exercise. It is the only way we have to take stock of what we have achieved in the sector, and it forces us to reflect not on what will be (which is impossible indeed), but on what may be in different scenarios. This is precisely what this paper sets out to do.

Talking about the impact of biotech on a global scale only makes sense if the following premises are taken into account:

Be modest : concentrate on direct impacts.

- Identify areas of activity where biotech can have a direct impact.
- Evaluate societal needs in the broadest sense, as they are likely to be affected by demography, the environment, the economy, and emerging policies on sustainability and on health protection.
- Concentrate on the needs in food and feed production, industrial raw material production and energy production. Assess these needs in quantitative and qualitative terms.
- Assume that in the long run, key components of society such as food security are demand driven.

Within this framework, it does become possible to identify areas of activity in which biotechnology is likely to deliver a significant contribution. It is indeed likely that when a difficult problem related to agricultural production emerges that does not have a satisfactory solution through other technologies, then biotechnology will be asked to address it, and is likely to come up with a solution. In other words, what we will look at is the evolution of demand for the technology, not the evolution of its supply.

So what do we expect agriculture to achieve in the next 3-5 decades ? The nineties have been a decade of intensive reflection on the ways in which humankind has provided for its basic needs. Out of it comes a broad consensus that every major step forward in the future will have to be subjected to the « sustainability test ». In other words : does it have the potential to contribute to a more sustainable world ?

The modalities, and indeed what constitutes sustainable technology are still far from clear. There are large groups in society that have a fundamental problem with the association between high technology, cutting edge science and sustainability. In the long run though, knowledge driven society will come to terms with using technology to promote sustainability, not opposing it as a matter of principle (or as a matter of fear).

The challenge before agriculture between now and 2050 is to feed at least 3 billion more people on less land, while reducing a number of non-sustainable inputs. In addition, agriculture is also expected to allow space for the introduction of new crops (and the transformation of existing ones) and for the production of a much more diversified range of raw materials for a wider variety of industries. These are only the « material » objectives.

On top of that comes a much broader array of socio-economic and cultural considerations. These tend to be dismissed or marginalised in technical discussions, even though it is by now clear that technological innovation without an appraisal of its societal impact is likely to be less effective at least, and can even lead to the possible death of the innovation.

This neglect of the non-technical aspects of agricultural innovation has led to a gigantic backlash, to the point where technical elements are becoming absent from decision making. A good example is provided by the EU policy for agriculture (Agenda 2000). This so-called strategic document on EU Common Agriculture Policy does not even address innovation and technology as relevant!

TARGETS FOR AG-BIOTECH AT PRESENT AND IN THE FUTURE

Today, the biotechnologies considered most relevant for the next decades are those associated with IPM, those associated with seed technologies and those associated with the genetic make-up of the crop (and its associated micro-organisms). The industry most likes to divide the application fields in input traits and output traits.

Input traits

Input traits include those that affect plant nutrition and the adaptation of crops to biotic and abiotic stresses. These traits generate value by providing yield increases, or crop security, or replacement of other inputs. The value chain is short. Seed companies develop the product, and the farmer gets the immediate benefit.

Whatever the present controversies over consumer benefit from the first generation of GMO crops (almost all of which contain modifications of input traits), the most important impact of GM crops over the next decades may still be at this level. The reason is simple: over a 30-50 year perspective, increasing yield with reduced external inputs remains the biggest challenge for agriculture world-wide. The agricultural production glut of this decade is achieved at the cost of unsustainable levels of fertiliser, pesticide and energy inputs, and it uses categories of land for production that should not be farmed. It also uses unsustainable amounts of water.

All these factors have to be gradually corrected to make them sustainable, and this has to be done while increasing world basic food production by a minimum of 30 million tonnes per year. It looks like a challenge that will require every bit of human ingenuity and innovation available. It cannot be stressed enough that this remains the real challenge for world agriculture. It requires long term commitment from governments, academia and industry to keep developing the necessary tools: insights, knowledge, technology, products and policies.

Instead of this, we find that governments are gradually reducing their commitments for training and research, and ignoring the need for production increases in their policies. In fact, the flavour of the day in policy making is production decrease, and extensification. That is not a major long-term problem, as long as it remains reversible. The agricultural sector is sufficiently technically competent to introduce new production technologies for higher yield in a very short time. However, if R&D is slowed down, and if overly restrictive legislation covering new technologies is put in place, that effectively makes it much more difficult to reverse the trend when (not if) the present food glut changes to become a shortage. A food shortage due to short-term policies such as pricing and set-aside programmes is conjunctural, and easily reversed. A shortage due to an empty R&D pipeline is structural, and likely to lead to much longer periods of tight food supply.

Can genetic engineering deliver on the input traits? For biotic stresses, the answer is by now a clear yes. For abiotic stresses and for nutrition, it is too early to tell, but the answer should be there within the next few years.

Insect and herbicide resistant crops are by now fully integrated in agriculture, at least technically. This does not mean that there is nothing more to be done. We have not even started looking at how to integrate these traits in IPM schemes, although they could transform our capabilities there. We also are still all working with Bt crystal proteins. Given what is in the R&D pipeline now, it is most likely that within 20 years, we will look back on Bt as the Stone Age of insect control. 20 years may look like a long time, but let us keep in mind that even PCs needed more than 20 years to get where they are now.

Although technological feasibility has been demonstrated by now for fungus resistance, it is probably going to take another decade before we see widespread adoption of the technology. For this set of traits, breeders are going to be confronted with a new challenge : how to integrate in the most synergistic way « conventional » and « engineered » disease resistance genes in a finished variety. The same goes for nematode resistance, one of the key long-term objectives of crop genetic engineers.

Major advances can still be made in resistance to unfavourable weather conditions : drought, water logging, cold, heat. It is not clear at this moment whether these improvements will come mainly from genetic engineering or from genomics though. The improvements required here are often of a quantitative nature, and there tends to be a lot of genetic diversity available within the gene pool of each species for such traits.

There has been recent and quite spectacular progress in salt tolerance and in resistance to Aluminium toxicity. Both traits are of particular significance for tropical agriculture, and could well transform farming in parts of the developing world.

One of the holy grails for biotechnology has been, since day 1, the idea of developing nitrogen-fixing cereals. In fact, much of the early investment in the technology was « sold » on that promise. By now we know it is not going to be simple of course. However, our understanding of gene function and plant physiology is moving very fast indeed. Possibly the most interesting route will ultimately prove to be the one by which we create cereal plants that attract nitrogen-fixing micro-organisms, and feed them. In any event, this is not likely to happen in the next couple of decades (at least at the commercial level).

In the meantime though, our rapidly expanding knowledge of what goes on at the interface between plant roots and the community of micro-organisms that live on (and in) them, is slowly beginning to yield clues on how to direct these interactions more to the advantage of the farmer.

Output traits

It is generally believed that most of the potential added value of transgenic crops lies in the modification of traits that change the composition of the end product. The changes already achieved or in advanced research stage include dramatic composition changes of starches, proteins and oils in the final crop. Less widely publicised are changes in sugar composition (e.g. fructo-furanose producing sugar beet), changes in baking quality (wheat with altered gluten profiles), and changes in malting quality of barley. Into the same category belong traits such as long shelf life of fruits (and less known: flowers).

These products only present a very primitive first generation. At best they give a glimpse of how our understanding of the quality determinants of food and other agricultural products allows us to modify crops further to our advantage.

The next generation of products will certainly include two types of food products: functional foods, in which specific health promoting substances have been enriched (e.g. vitamins and specific types of fibres), and « cured » foods, in which toxic or allergenic components have been eliminated. Depending on the manufacturing costs, plants may also become more frequent bioreactors for the production of proteins with pharmaceutical applications. In this field they face stiff competition from milk produced proteins though.

In the long run, we should expect to see further improvements especially in factors that influence digestibility of food, especially in crops that are grown predominantly for animal feed. One of the most effective ways to increase available food and feed with reduced environmental impact is to ensure that the food is entirely available for the animal to metabolise. Early efforts include the same compositional changes of the macro-components mentioned above, but research now has moved on to the elimination of the numerous anti-nutritional factors that most plants contain, and to the addition of factors that improve the availability of nutrients. An elegant example of the latter is the expression of phytase in plants. Phytase increases the availability of phosphorus in diets by solubilising polyphosphates. The enzyme is used with considerable success as a feed additive, and now companies are moving on to expressing it in the storage organs of crops.

The elimination of anti-nutritional factors often brings its own problems though. Many of them are in fact defence mechanisms of the plant, especially against insects, but also often against fungi. So stripping the crop of these factors can leave them wide open to pest and disease attack. The future will probably see many projects where a native anti-nutritional factor is eliminated, and another gene inserted for the replacement of its defence function but without the side effects.

Even though the use of plants as sources of drugs is widely overestimated as a consequence of the politically correct reference to « natural products », plants do remain interesting targets for the pharmaceutical industry as bioreactors for the synthesis of raw materials or intermediates of drugs. Several crops have for decades been the preferred sources of oestrogen hormone intermediates, but now it becomes possible to take a species that produces an intermediate, and sometimes add new genes for further reaction steps. A vivid example of this process is on the market, albeit in a totally different field: it is the blue carnation. In this plant, enzymes that can metabolise the pigments that are responsible for the red colours of carnation have been added. The source of the genes was delphinium, which can naturally do the next biosynthesis steps.

The rapid advances in genomics are delivering a rapidly increasing store of genes for all kinds of metabolic steps, and it should not take more than another decade before we see many uses of this resource in the development of entire new biosynthetic pathways in plants.