

Biotechnology overview

Applications and forecasts

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Abstract This paper describes the field of biotechnology and likely advances in health care, agricultural and other applications in industry, environmental science and energy over the next 15 years. The intent is to give those without a background in the life sciences a perspective of the broad scope of biotechnology. The forecasts at the end of each section illustrate some advances as well as some of the benefits and risks to society that might occur during the next 15 years.

Introduction

This overview describes the field of biotechnology and likely advances in health care, agricultural and other applications over the next 15 years. The intent is to give those without a background in the life sciences a perspective of the broad scope of biotechnology without too much technical detail. The forecasts at the end of each section illustrate some advances that might occur during the next 15 years to stimulate thinking about the impact they would have on society.

Many consider biotechnology to be the next revolution following right on the heels of the "information age", and believe it will profoundly affect all aspects of society. The speed of development and application of biotechnology will make the impact even more dramatic.

General overview of biotechnology

Biotechnology represents the convergence of biology, computer science, chemistry, physics, and engineering. These component technologies work in synergy, and they are each advancing rapidly. On the one hand nature is very complex and does not give up her secrets easily, while on the other hand the field of biotechnology is progressing much faster than we can imagine, leaving social institutions scrambling to prepare for the consequences. The inflection point of rapid change may be very close. Some experts argue that perhaps as early as 2005 we will see a profound

acceleration of knowledge and proliferation of new products and services because of biotechnology (Oliver, 2000).

Genomics involves the identification of an organism's genes, understanding how the genes work, and devising ways to manipulate the genetic process for various purposes, including treating illness.

Basic principles

Most living things are made of cells (viruses are an exception). Simple things like bacteria and yeast consist of a single, self-sufficient cell, whereas plants, animals, and humans are made of many different types of cells with specific tasks. In spite of the great diversity of living things, all cells contain essentially the same kinds of molecules.

Living cells contain genetic material that provides instructions for performing cellular tasks and making new cells. This information is passed from parents to offspring and determines the nature of the organism. The genetic material is contained in chromosomes in the cell nucleus. Chromosomes are made of unique strands of a chemical structure called DNA (deoxyribonucleic acid). DNA is actually a string of genes, each of which carries instructions for making specific proteins and coordinating their activities. Each protein has a unique identity and specific functions such as catalysing (facilitating) chemical reactions or being part of a structural component of the cell.

Many of the differences between people are caused by alterations in DNA that change the way important proteins are made. Most of these alterations involve a single base pair (smallest DNA building block) and are called SNPS (single nucleotide polymorphisms, pronounced "snips"). SNPS occur maybe once per thousand of the estimated three billion



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bases in the human genome, and the majority do not cause physical changes. However, some of these variations lead to unique responses to medications or to disease. Researchers are comparing the DNA of those with a particular disease to the general population to identify SNPS that may play a role. Discovering the genetic variations that cause diseases will permit genetic testing of individuals to forecast their risk of developing diseases in the future. Gene therapies will someday be available to replace the abnormal gene to prevent some diseases from occurring or to treat them.

Mapping of the human genome, the entire system of genes, has been completed in a preliminary sense, and work is now being done to understand how genes affect health and disease. A rapidly growing area of research is proteomics, the study of the proteins produced by the organism, in order to understand how each protein works. This is being done “top-down” by discovering the protein created by each gene and “bottom-up” by starting with a function or disease and finding the causal proteins. Each protein’s unique three-dimensional shape causes its effects. Efforts are underway to determine and catalogue the shape and function of each protein, a very difficult task that some experts estimate will take at least ten years. This knowledge will be used to determine targets of opportunity in disease pathways and then to engineer specific drug therapies to interact with the target to either prevent or cure the ailment. Pharmacogenomics is the study of an individual’s unique response to a medication. This knowledge can be used to develop tests to select the safest and most effective drug for a particular person, and also to develop custom drugs for subsets of the population with similar genetic characteristics.

Because genes are the blueprints for specific proteins that provide the unique characteristics of an organism, much of the work in agricultural and industrial biotechnology is directed to understanding these relationships so that new characteristics can be bioengineered into useful species of bacteria, plants or animals. For instance, transgenic plants have genes inserted from other organisms to improve qualities such as resistance to disease, increased yield, or improved fruit size and flavour. Another example is the utilization of recombinant DNA technology to create a bacterium that produces human insulin for manufacture into a drug for diabetics.

Underpinning the biotechnology revolution is a host of innovative technologies for testing and knowledge processing. Biosensor technology is a synergy of chemistry, informatics, biology, and engineering. Biosensors are used for gene identification, biological function, and disease diagnosis. Automated machines can test thousands of samples at once, and high-speed computers are used to make sense out of all the data produced. Bioinformatics broadly defined is the use of computers to manage biological information, but usually refers to “computational molecular biology”. The rapid accumulation of genomics information along with better knowledge of organ function in

health and illness will be used in computer programs to simulate biologic processes of “virtual organs”, permitting the discovery and development of drugs *in silico*. This capability will eliminate many animal experiments and be used to predict product effectiveness and risk before final clinical trials are designed and performed.

Health care biotechnology

Overview

The primary purpose of biotechnology applied to health care is to find ways to diagnose, monitor, prevent, and treat diseases. A few intend to use genomics to improve the gene pool, eliminating familial diseases, selecting traits for offspring, and even creating a superior species. Although some of these goals are beginning to be achieved, the major focus of biotechnology research at present is discovery – first, how do the genes and the proteins they code operate in biochemical pathways for healthy functioning organisms and what can go wrong to lead to disease? This includes the questions of “biochemical individuality” or why our genes, for example, lead to different degrees of metabolising a medication and hence differences in its safety or efficacy. This knowledge is being applied to design innovative therapies. The result is that the practice of medicine could fundamentally change to become comprehensive and integrated, highly individualized, and focused more on prevention rather than simply the treatment of established diseases. Some of the promising aspects of health care biotechnology are as follows.

Biosensors

Biosensor devices are among the fastest developing of the biotechnology related technologies. Diagnostic tests such as home blood glucose tests have been around for a long time, but now advances in computer technology, physics, biochemistry, genomics and engineering are merging to create a wide variety of new devices. For example, the DNA chip is the marriage of semiconductor technology and molecular genetics, allowing the analysis of tens of thousands of genes simultaneously on one small chip. It can detect mutations in disease-causing genes, diagnose infectious diseases or map sections of one’s genome at a time. Laboratories are being built on silicone computer chips that are very small and can be mass-produced. These devices can be embedded in jewellery, watches, or clothing to monitor individuals, as well as being used to monitor indoor or outdoor environments for health threats. It is possible, and could become widespread, for the data to be automatically communicated and collected by individuals, their physicians, and public health departments.

Currently diagnosis is often delayed and treatment not given in time because individuals miss early warning signs. Biotechnology applications using unobtrusive biosensors could constantly monitor health status, storing the information for the individual and presenting key feedback information, say on the bathroom mirror, and sending relevant data to the

individual's health care providers. As expert systems in home software develop, they will "coach" the individual toward healthy living and effective medication use.

Possible forecasts include:

- By 2002 biosensors thinner than a hair placed under the skin will monitor blood sugar for diabetics.
- By 2004 personal "digital medical assistants" will monitor an individual's health status through sensors, coach healthy behaviours, provide information and advice, and be connected to the health system for professional support.
- By 2005 a gene chip is available that includes markers for all human genes and test for over 100,000 genetic conditions (Enriquez, 2000). Health care providers will use it in selected applications.
- By 2010 this capacity will be inexpensive enough to be widely used by health care systems, and to some degree by individuals doing their own self-care.
- By 2013 biomarkers will be used for most individuals with cancer or thought to be at risk of getting cancer to monitor early development, determine subtype of tumour and preferred treatment, and monitor response to therapy, as well as to estimate prognosis.

Pharmacogenomics and personalized medicine

Pharmacogenomics is the science of developing customized and personalized medicine based on genetic variations in the drug response of individuals. For instance, the cytochrome P450 system of liver enzymes is responsible for a major portion of human drug metabolism. People with certain genotypes are poor metabolisers of more than 50 drugs used in clinical practice for cardiovascular diseases and psychiatric disorders. Recently Genelex Corporation, a US DNA testing firm, offered DNA prescription drug reaction profile test kits online to the general public to assist their doctors in prescribing medications[1]. This knowledge can be very important in preventing adverse drug reactions and selecting medications that will be effective for that individual. Accumulated genetic data will be used to discover the genetic variations of subgroups of people that influence disease and affect metabolism. This will lead to more effective prescribing of drugs and ultimately to targeted, customized drugs designed for these specific subgroups, rather than "one size fits all" drugs currently in use. Pharmacogenomics will contribute to personalized medicine unique to each patient.

Possible forecasts include:

- By 2005 many new and older drugs will be prescribed after a screening of the patient's genetic profile to better estimate likely efficacy and safety. A screening kit will be part of new drug prescriptions.
- By 2010 drugs designed for specific genotypes and phenotypes start appearing on the market. Pharmacogenomics has accelerated the discovery and development process, and more focused trials lead to faster regulatory approval. There is a fundamental

change in pharmaceutical economics as the blockbuster drug era comes to an end.

- By 2015 pharmacogenomic tools will reduce cost of drug development and approval by a third, and cut the time from discovery to regulatory approval by almost a half.

Predictive medicine

Genes, environment and behaviour are principal factors in health and disease. Biotechnology will contribute to the understanding of the specific predisposing causes and the factors that affect the course of diseases. As disease aetiology is unravelled, genetic, environmental and behavioural screening tests will progressively improve in predicting the probability for developing specific diseases in the future. With this knowledge steps can be taken to try to prevent the disease from occurring through lifestyle modification, genetic modification and specific preventive therapies. Another option is early treatment to cure or control the ailment.

Predictive medicine poses several challenges. Medical personnel will have to develop counselling expertise to appropriately explain these possibilities and guide patients. Many people probably will not want to know their future risk, especially if the disease is currently incurable, such as Alzheimer's disease. To date, the medical professions are not very successful in getting patients to modify their lifestyle to prevent or ameliorate disease. Biotechnology assisted forecasting may support more effective behaviour change (or for some make it more difficult). Health care has the opportunity, with predictive medicine, to shift toward deliberate and personalized prevention.

Possible forecasts include:

- By 2005 biomarkers indicate the likely presence of several cancers, classify their defining molecular characteristics, and indicate which therapies should be beneficial to the particular type of tumour.
- By 2010 comprehensive genetic, behavioural and environmental screening will be capable of forecasting degree of predisposition for most major chronic diseases.
- By 2010 comprehensive legislation in Europe and North America will have defined the protections against discrimination based on predictive medicine.

New cures for disease

Biotechnology is discovering the underlying molecular pathways for disease and identifying thousands of new targets of opportunity for specific therapies to intervene. "Rational drug design" utilizes three-dimensional modelling of cell receptor sites to design drugs with the optimal shape to produce effective therapeutic results. Biotechnology will add to the options for delivering medications. In addition to pills and injections, pharmaceuticals could be part of our food, soap or cosmetics, or administered via micromachined implants (*Technology Review*, 1999).

There is the possibility that biotechnology will lead to the cure of a chronic disease as early as 2015. A few examples of advances are:

- *Gene therapy* is the correction of a heritable disease by the addition of a functional gene. Although this can be done through “germ-line therapy”, ethical concerns currently only allow “somatic cell gene therapy” which will not alter the genes of offspring. To be a candidate for gene therapy the biochemistry of the disorder must be well understood, a cloned functional gene must be available, there must be a means of transferring the new gene into a tissue where it will be beneficial, and the gene must self-propagate into more cells to keep the process going, without generating harmful side effects – all big challenges! Currently there are a few human trials using viral vectors to introduce the gene. Results have been mixed, as it is hard to get enough of the gene inserted into cells and properly expressed to create the desired effect. It will probably be several years before gene therapy is perfected, but when this occurs the therapy will be beneficial for inherited diseases like cystic fibrosis and haemophilia, and possibly for other diseases such as certain cancers.
- *Vaccines* stimulate the body to build immunity to a pathogen or even specific cancer cells. Biotechnology is uncovering new ways to create more effective vaccines, such as DNA vaccines, that will stimulate both humeral and cellular immunity. DNA vaccines for AIDS, malaria, hepatitis B and some cancers are now in clinical trials and may be available in five to ten years. Work is also being done on transgenic plants that express surface proteins for pathogens. Some day genetically altered foods such as bananas, tomatoes, potatoes, or alfalfa sprouts may be used to stimulate immunity generally or to specific pathogens.
- *Monoclonal vaccines*. The antibody is ideal for drug therapy because of its specificity and ability to carry out distinct functions. Biotechnology techniques permit the production of large numbers of exact (monoclonal) “human” antibodies that can do their job without being rejected. They are incorporated into diagnostics to do such things as distinguish cancer from normal cells or to diagnose infectious diseases. Monoclonal medicines are available for treating breast cancer, non-Hodgkin’s lymphoma and myeloid leukaemia. Under development are monoclonal antibodies that link to a toxin or radioactive material to more effectively destroy cancer cells. Another approach is to bind with vascular endothelial growth factor to prevent blood vessels from growing into tumours, thereby limiting the growth of cancers. Monoclonal antibody trials are also under way to treat asthma, psoriasis and other diseases.
- *Genetically modified organisms*. Bacteria can produce essentially any protein if they have the right gene blueprints. Applying this concept, genetically modified bacteria, plants and animals are producing specifically designed substances that are harvested and converted into pharmaceutical products.

Possible forecasts include:

- By 2010 gene therapy will be commonly used to treat a few genetic diseases.
- By 2013 the first preventive vaccine for a specific cancer will be introduced.
- By 2014 genomics-based drugs will make up 50 per cent of all new drugs. Many of them are designed to specifically target a subset of the population of a particular genotype. Medical therapy is personalized.
- By 2015 molecular nanotechnology will be used for lab fabrication, manipulation and manufacture of molecular compounds such as bioengineered medications. Nanotechnology will allow compounds to be “built from the ground up”, producing more precise formulations and making production more efficient.
- By 2015 the first major chronic disease will be prevented at the molecular level by a novel, genetically engineered drug.

Stem cells

Unlike most cells of an organism which are specialized for a certain tissue and function, stem cells are undifferentiated and have the potential of becoming many kinds of cells. Stem cells from embryos are the first cells of life and go on to create the many tissues and organs of the body. Neonatal cord blood of newborns is another source of stem cells. There are also adult stem cells in the bone marrow and possibly throughout the body, which have the potential of becoming such things as blood, heart muscle, cartilage and possibly even nerve cells. Embryonic stem cells are felt to be more versatile, but because they come from discarded human embryos with resultant ethical and political controversies that restrict research, most effort is currently directed to adult stem cell research. Great Britain is the only country with a specific law permitting scientists to clone human embryos for the purpose of creating stem cells (not for reproductive human cloning).

There are several promising animal studies using stem cells. In mice, transplanted bone-marrow-derived stem cells have been shown to migrate into the brain and develop into brain cells. After an induced heart attack, pigs injected with adult stem cells had significantly improved survival rates, and the stem cells were shown to promote repair of cardiac muscle. Goats with osteoarthritis repair the cartilage of a damaged joint if it is injected with stem cells. It appears that stem cells somehow promote healing, even if the cells themselves might not turn into functional tissue. Also there is evidence that stem cells do not evoke an immune response of rejection so they would not have to come from the patient. A small number of human trials using stem cells are already underway and others will start soon. It is possible that some day stem cell therapies may be used for Parkinson’s disease, stroke, heart attack, diabetes, liver disease, osteoarthritis and other chronic diseases. In the more distant future stem cells might be used to build an entire organ through a process of “tissue engineering”.

Possible forecasts include:

- By 2010 stem cells will benefit patients with Parkinson's disease by maturing into cells that produce dopamine, a neurotransmitter missing in the disease.
- By 2015 heart disease will be treated via growth of functional tissue using stem cells (Anton *et al.*, 2001). Cryopreserved universal stem cells are on hand in emergency rooms for early treatment of heart attack victims (Hall, 2001).

Cloning

Clones are genes, cells or entire organisms derived from a single common ancestor, and therefore, are genetically identical. Cloning of genes and cells is a common laboratory procedure to create many copies essential for biomedical research, such as the production of monoclonal antibodies. The first cloning of animals occurred in 1952 using frog eggs, and the technology has steadily progressed so now there are several cloned animal species. The potential for human cloning is approaching. *The Sunday Times* (2001) reported "Monkey test breakthrough brings human clones closer", and worldwide media on 26 November 2001 reported the claim that Advanced Cell Technology of Worcester, Massachusetts, cloned the first human embryo (Regalado *et al.*, 2001). Several groups around the world have announced their intention to clone babies in the near future (*Scientific American*, 2001). However, these early reports also describe how technically difficult it is at present to clone higher organisms.

Potential uses for animal and human cloning related to health are:

- Creating large number of transgenic animals for the production of human medicines such as special proteins in the milk that are therapeutic.
- Rapid production of large animals carrying genetic defects that mimic human illnesses such as cystic fibrosis for medical research and maybe to make cell-based therapies. (Lab mice often do not work because they have very different genes.)
- Production of genetically modified animals with organs that are suitable for transplantation into humans.
- Human therapeutic cloning is used to clone the genes of an individual to create a very early embryo of maybe 100 cells that are then harvested as embryonic stem cells. Besides being a way to obtain stem cell lines for medical research, they could be utilized to grow replacement tissues or some day organs genetically unique to that individual so that rejection would not be a problem. To repair a problem due to a genetic defect, such as replacing the islet cells of the pancreas to produce insulin in a diabetic, the genetic defect in the stem cells would have to be repaired before they could create healthy islet cells.
- Human reproductive cloning, which aims to implant the cloned embryo into a woman's uterus leading to the birth of a cloned baby.

- Human reproductive cloning where the parents chose to have defective genes replaced before the embryo is implanted to prevent the child and subsequent offspring from inheriting a genetic disease.

Possible forecasts include:

- By 2005 a team of scientists somewhere in the world will probably announce the birth of the first cloned human baby (Green, 1999).
- By 2005 therapeutic cloning under strict controls for the production of embryonic stem cells will be accepted by most European countries and USA.

Agriculture and food biotechnology forecasts

Overview

Humankind began domesticating animals and plants at least 10,000 years ago and has been modifying species ever since. The first systemic attempt to produce an insect-resistant plant in Europe occurred in the eighteenth century with the grafting of grapevine stems onto resistant American rootstocks to defeat the aphid. Significant advances occurred in the last century when, in the 1960s, the selective breeding of hybrid rice and wheat led to vastly increased worldwide yields. In 1973 researchers developed techniques to move genes from one organism to another, and in the 1990s genetically engineered plants reached the market. Many argue that agricultural biotechnology holds great promise if its safety can be demonstrated to the public's satisfaction and people are willing to purchase genetically modified (GM) products.

Benefits

Some experts believe that agricultural biotechnology has the potential for producing many benefits:

- The International Food Policy Research Institute forecasts world demand for rice, wheat and maize will increase 40 per cent by 2020 (Mann, 1999). The only way to increase production with limited land and water is through biotechnology. GM crops can be designed for poor quality land with limited water and with resistance to natural pests (that to date severely reduce the yield of native crops in developing countries).
- Increased productivity – faster growth of livestock and plants, drought tolerance, disease resistance, increased milk production.
- Alternatives to chemicals – biofertilizers to help plants absorb phosphorus into their roots, pest resistant plants, biovaccines for animals.
- Improved animal feed – probiotics to create favourable gastrointestinal bacteria for more efficient feed conversion, reduced protein requirements, decreased environmental impact, improved milk composition.
- Improved foods – better flavour and texture, larger fruit, delayed spoilage and advanced shelf life, increased nutritional value (such as meats with lower fats, rice with

- increased vitamin A), and modification to remove allergens affecting humans.
- Advanced diagnostics to prevent food-borne pathogens in raw materials and finished products.
- Foods with enhanced medical properties such as probiotic and nutritional supplements.
- Animals as bioreactors to produce high volumes of precise drugs at low cost.
- Environmental benefits – reduced chemicals, soil conservation, more efficient management of wastes, environmental cleanup, and biodegradable products.
- Genomics information can be utilized to add biodiversity by adding desired new traits, making more varieties for a given situation.

Risks

However, because agricultural biotechnology is so new and advancing so rapidly there are concerns about potential ecological risks and ethical issues raised by a wide range of sources:

(1) Environmental concerns

- Will genes giving crops tolerance to herbicides spread by cross-pollination to nearby weeds, creating “superweeds” resistant to herbicides that overrun farmland?
- Could plants with added natural antibiotics lead to antibiotic resistant pathogens?
- What happens when insects, weeds and other pests develop resistance to the GM crop?
- Might plants with a built-in genetic pesticide harm other creatures such as birds or butterflies?
- Will GM crops (or their cross-pollinated wild cousins) invade other habitats and threaten native species?
- Will reliance on a few GM crops reduce biodiversity and make the entire crop more vulnerable?

(2) Health concerns

- Will some people develop an allergic reaction or other adverse effect from a GM food?
- Could transgenics permit a pathogen to vault the species barrier into a new realm, where it could be harmful to mankind?

(3) Consumer benefits

- Are GM foods more nutritious and beneficial or just easier to grow, transport, and market?
- Should GM foods be labelled so the consumer can decide? With complex supply and production networks when is something a GM food?

(4) Social and economic impacts

- Is the purpose of agricultural biotechnology evolutionary success or just economic and professional success? Is industry taking the time and effort to assure biosafety?
- Are some governments pushing worldwide deployment too fast and shielding the public too much?

- Are advances in biotechnology outpacing the scientific understanding of its risks and the development of a coherent regulatory apparatus to supervise its use?
 - Will there be incentives and public funding for BioAg corporations to create seeds for developing countries where they might be very useful and provide these in ways that support sustainability?
 - How can intellectual property protection be redesigned so seeds are affordable to farmers in poor developing countries?
 - If terminator genes were incorporated in crop varieties, it would prevent farmers in poor regions from using seeds from this year’s crop to plant next year’s. They would have to buy new seed from the manufacturer every year. Should terminator genes be prohibited for crops targeted to developing countries? (Terminator genes can also protect the environment by giving farmers control.)
 - Is the precautionary principle the proper way to proceed?
 - What is the liability? What are the limits of liability for manufacturers, farmers, and grocery marketers for harm that may result from GMOs?
 - In developing countries where malnutrition and famine are widespread and basic subsistence requires 70 per cent of a person’s income, should the development of genetically modified crops be aggressively pursued?
- #### (5) Moral and ethical issues
- Is it proper to own life forms through patents? Should a corporation own the patent when the genetic source material comes from a developing nation or the traditional land of indigenous people?
 - What about global equity? How is beneficial technology shared with the developing world where the consequences of not having access are severe but the populace cannot afford the royalties?
 - Science now has the ability to manipulate and redirect the course of evolution by altering the “stuff of life”. Are we “playing God”? If so, how can science work with commerce and society in a way that respects this great responsibility?
 - Will Jewish or Islamic dietary codes allow vegetables with a pork gene?
 - Do vegetarians have the right to know if plant food products have any animal genes?
 - Will biotechnology require any additional animal welfare protections or rights?
 - What are society’s obligations on biotechnology for supporting a sustainable planet?

Answers are likely for some of these issues, but they may take some time to develop. How do we deal with the uncertainties that will remain for many of these questions?

Genetically modified foods

Genetically modified (GM) food comes from plants which have had genes from other species inserted to improve their qualities, for example, for better yield or improved characteristics. The first GM food, the FlavrSavr tomato (delayed ripening for longer freshness) was approved in the USA in 1994. In 1997 the first weed and insect-resistant biotech crops became available in the USA. By 1998 over 4,500 genetically altered plant varieties had been tested in America with about 50 approved for unlimited use (Mann, 1999). Worldwide, farmers planted 44.2 million hectares of transgenic crops in 2000, a 25-fold increase since 1996 and an 11 per cent increase from the year before. A total of 13 nations are growing these crops with America (68 per cent), Argentina (23 per cent), and Canada (7 per cent) producing the majority (Brown, 2001). The common crops are corn, soybeans, cotton and canola with potatoes, squash, melons and tomatoes and others grown in small amounts. In spite of the overall increase, Canada dropped hectareage by 25 per cent in 2000, and transgenic corn production dropped by 2 million hectares in the USA as the result of farmer uncertainty about market acceptance and reduced profitability (Stikeman, 2001). To date China is the only developing nation to have engineered its own GM crop, insect resistant cotton.

In 2000 the first plant genome, a mustard plant, was sequenced. This is an important milestone for it will allow the analysis of biochemical processes that can be applied to most plants. The next initiative is The 2010 Project, a £350 million multinational collaboration, to determine the proteins expressed by every gene in the mustard plant, each protein's job within the cell, and their biochemistry. The ultimate goal is to have enough understanding to create a computer simulation of a "virtual plant" that will depict every cellular function of the life cycle of the mustard plant. This knowledge would allow improvements in plants by modifying their own genes rather than transplanting genes of foreign species such as bacteria (Moffat, 2000).

Draft forecasts intended to stimulate thinking about the scope and rate of growth include:

- By 2004 genetically modified elm trees resistant to the Dutch elm disease fungus are introduced.
- By 2006 the first "green" genetically modified plants are developed containing altered genes from the original plant, rather than foreign genes, to achieve desired traits.
- By 2010 sales of genetically modified crops reach £17 billion, globally (Minerd, 2000).
- By 2011 a computer model "virtual plant" that simulates the common plant molecular functions is used to understand plant physiology and select genetic modifications for favourable traits.

Animal biotechnology

Biotechnology plays an important role in livestock management. Enzymes, probiotics and bioengineered feed plants are used to improve digestion. Special vaccines called

immunopharmaceuticals stimulate the immune system, and can also be designed to render animals sterile without surgical castration. Specific amino acids to stimulate natural growth hormones and the discovery of a cattle "obese gene" may someday grow animals with optimal muscle mass and fat levels. Researchers are working on transgenic sheep that would produce their own essential amino acids, eliminating the need for supplements. Monoclonal antibody technology is used for diagnostics for animal diseases and to treat animal cancers. DNA testing will be able to track the sale of caviar and whale meat from endangered species almost anywhere on the world market. DNA typing has been used in wildlife management to determine how closely species are related to one another and whether endangered species are threatened by excessive inbreeding.

Genetically modified bacteria with human genes do not always produce the protein that is functionally active in humans. However, transgenic animals can often produce those proteins and convert them into the active, medically useful form. Milk from genetically engineered animals can produce a large amount of human clotting factors, hormones, interleukin-2 for cancer therapy and monoclonal antibodies. The proteins are isolated, purified and converted into medicinals without harm to the animals. Although much research is being done with transgenic animals for produce, none are currently licensed for human food.

In the 1980s scientists cloned a sheep embryo. Dolly, the sheep cloned in 1997, is unique because mature cells from an adult sheep were used. Many animal types have been cloned. Although the US Food and Drug Administration's position is that neither cloned animals or their offspring should enter the human food chain, cloning firms have been delivering cloned animals to customers. Some Japanese supermarkets openly sell beef from cloned cows (*Wall Street Journal*, 2001). A study sponsored by a leading cloning company in the USA found cloned cattle that grow to adulthood to be normal on examination and by immune system testing, and to be able to give birth to healthy calves (*Wall Street Journal*, 2001).

There are a number of potential applications:

- Animals cloned for medical research are genetically identical, thereby reducing variability factors.
- Cloning is a more effective means of generating large numbers of transgenic animals to produce pharmaceutical products.
- Animals cloned with certain human genes would not be rejected when used for human organ transplants (xenotransplantation).
- Once a transgenic animal is perfected, cloning could reproduce a large number quickly with consistent quality to be used to create "founder flocks" which could then be allowed to breed naturally.

Possible forecasts include:

- By 2002, cloned transgenic lab animals with genes causing human cancer will be used in cancer research.

- By 2005, with technical refinements eliminating almost all abnormalities and deaths, cloning will be accepted for livestock.
- By 2006 milk containing vaccines produced by a transgenic cow will be approved for human use.
- By 2013 transgenic pig organs that significantly reduce human rejection are used for heart, liver and kidney transplants.

Aquaculture (fish farming)

Aquaculture is a global industry and now accounts for more than 27 per cent of all fish consumed worldwide (Goldburg, 2000). Aquaculture is growing 11 per cent a year and is now the dominant source of shrimp, salmon, catfish, carp and other species (Brown *et al.*, 2001). More than 20 kinds of fish have been genetically engineered for scientific study and commercial production. Fish genes have been introduced into different species to speed growth, increase cold tolerance, improve disease resistance and alter flesh quality. For example, transgenic Atlantic salmon can grow up to 600 per cent faster than native fish. To date no transgenic fish have been approved for use as human food in the USA, but companies are close to requesting approval.

There are concerns about using transgenic fish commercially. Some are likely to escape rearing facilities and threaten native fish and aquatic ecosystems by out competing natives for food or spawning sites. Genes for freezing tolerance might expand the geographic range. As transgenic fish often grow larger, they have the advantage of attracting mates, but the genetic changes tend to reduce their offspring's ability to survive, so the wild population could shrink to extinction.

Concerns over public acceptance of transgenic fish are leading researchers to use genomics technologies to facilitate natural breeding methods. They are looking at the traits of natural species and developing genetic maps with markers to help select traits for targeted breeding efforts to rapidly develop fish with improved growth, feeding efficiency, and so on.

Forecasts include:

- By 2002 a transgenic fish will be approved for commercial production as human food.
- 2010 world aquacultural output (fish farming) will exceed beef production (Brown *et al.*, 2001)
- By 2025, 50 percent of the world's fishery protein will be produced through aquaculture (Manci, 2000).

Other uses of biotechnology

Overview

Biotechnology can be applied to assessing the wellbeing of ecosystems, transforming pollutants into benign substances, generating biodegradable materials from renewable sources, conversion of waste into energy, and developing environmentally safe manufacturing and disposal processes. Over the next 15 years researchers will strive to understand genetics, industrial processes, and material characteristics

at the molecular level to find ways to enhance these capabilities.

Environmental biotechnology – cleaning and protecting the environment

Environmental biotechnology is the use of living organisms in a wide variety of ways to treat hazardous wastes and prevent pollution. For instance, certain bacteria have enzymes allowing them to feed on toxic materials, thereby transforming or degrading the toxins into harmless materials that are recycled. Some plants remove large amounts of toxic or radioactive metals from soil or water by incorporating them into plant tissues where they pose no harm (unless the plant is eaten). Algae produce secretions that bind metals so they are in effect removed from the food chain.

Bioremediation can clean unwanted substances from soil, water, air, and materials from industrial processing.

Draft forecasts intended to stimulate thinking about scope and rate of growth include:

- By 2003 the market for bioremediation of the estimated 200,000 hectares of contaminated land in the UK is estimated to increase 28 per cent above 1999 (CLARRC, 2002).
- By 2004 biosensors will be available to monitor bioremediation *in situ* in many currently inaccessible locations, such as the degradation of pollutants deep in the ground, and may be applied to many pollutants now difficult to measure.
- By 2006 there will be early use of genetically modified microorganisms designed to remove difficult-to-degrade materials.
- By 2010 the global environmental technology industry is worth more than £1 trillion, of which 20 per cent is bioremediation[2].

Industrial biotechnology

Biotechnology can reduce the environmental impact of manufacturing. Industrial processes traditionally rely on noxious chemicals such as acids and alkali, require high temperature and large amounts of energy, and generate hazardous wastes. Biotechnology can create a gentler manufacturing environment while at the same time improving efficiency and cost-effectiveness. Another important component of the "green" shift is the use of genetically modified raw materials such as plant polymers as a replacement for petroleum-derived polymers in the production of plastics. Biotechnology will be a major factor in "industrial sustainability" by reducing pollution levels and consumption of resources, including power. It is predicted that biotechnology will transform the industrial sector just as it is in the process of changing the pharmaceutical sector.

Possible forecasts here include:

- By 2005 a wide range of bioengineered microorganisms will be available as cost-effective biocatalysts targeted to specific industrial needs. An example is the

production of the essential amino acid lysine from sugar for cattle feed.

- By 2010 environmental concerns and consumer pressure will rapidly accelerate the transition to environmentally sustainable biomanufacturing in the chemical, textile, paper and food industries.
- By 2015 the biobased economy will have begun with agricultural operations providing significant sources of energy and natural resources, and biotechnology serving as the underpinning of many manufacturing processes.

Biomaterials

Plants and animals have always been used as a source of materials for all kinds of products besides food. Now advances in biotechnology and materials are leading to new substances that possess unique properties and genetic modifications so that living organisms produce them. For instance, transferring specific genes into canola causes it to “grow” substances for plastic parts for car engines, detergents, soaps, cosmetics, greases, lubricants, chocolates, fabric softeners, candles, and drugs to fight infections, including AIDS. The first medicine produced by a genetically engineered bacterium was for human insulin and was approved in 1982. The number of organically created materials will grow rapidly over the next 15 years as technology allows custom designed materials with improved characteristics to be produced in a cost-effective and environmentally friendly way.

Possible forecasts here include:

- By 2005 biodegradable plastics will be created by bacterial action on potato wastes from plants producing potato chips. Edible plastics will be used for fast food plates, cups and packaging. After use they can be eaten, utilized in animal feed or put in the compost pile.

Fuel sources

A variety of fuels can be made from biomass resources or by using bioengineered microorganisms to produce fuel from natural resources. Ethanol is made from fermenting wheat, corn or pulp sludge, and biodiesel fuel is made from canola oil. Fuels can also be made from woody plants, forestry residues, and solid and industrial wastes. All these are renewable resources that produce fewer air pollutants overall than standard oil products. Photobiological processes use the natural photosynthetic activity of bacteria and green algae to produce hydrogen from water and sunlight.

Possible forecasts here include:

- By 2010 biofuel will represent over 5 per cent of automotive fuel in Europe.
- By 2015 commercial production of hydrogen from water using genetically engineered algae will be used for fuel cells generating electricity. ■

Notes

- 1 Health and DNA (Homepage of Genelex Corporation), available at: www.healthanddna.com/drugreactiontest.html (accessed 29 April 2002).
- 2 Overview (Homepage of Contaminated Land Assessment and Remediation Research Centre (CLARRC)), available at: www.clarrc.ed.ac.uk/link/overview.html (accessed 29 April 2002).

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