Applied Biotechnology

Sudhir U. Meshram
G.B. Shinde

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APPLIED BIOTECHNOLOGY

Editors
Sudhir U. Meshram
Director
Rajiv Gandhi Biotechnology Centre
R.T. M. Nagpur University, LIT Premises,
Nagpur, India

Professor & Head
P.G. Department of Microbiology
R.T.M. Nagpur University, LIT Premises,
Nagpur, India

G. B. Shinde
Professor
P.G. Department of Biochemistry
R.T.M. Nagpur University, L.I.T. Premises,
Nagpur, India

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Preface

Biotechnology is the fountainhead technology of the new millennium and if properly harnessed, its potential for improving the lives of millions is limitless. Biotechnology is making rapid strides in the field of research and development. It is, therefore, imperative that a developing nation like ours keeps pace with these advancements.

This book vividly brings out the complexities, intricacies and constraints in developing and adopting appropriate sustainable technologies in the applied fields of Agriculture, Environment, Biomedical and Animal Genetic Engineering, Immunology, etc. It covers Biosensors, Bioremediation, Biofertilizers, Fermentation, Immunization, DNA Transportation, Biopesticides, Sustainable strategies, Agriculture, Animal and Health Sectors, etc. It will be of great use not only to teachers and students of Biotechnology and Life Sciences but also to farm scientists, extension managers, policy makers and administrators alike.

The readers, through this book, will explore new avenues to alleviate the human and other biospheric sufferings because of poverty, ignorance, mismanagement and diseases particularly in developing countries.

Editors

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1

Biotech—Advancing Towards Another Revolution

PROF. SUDHIR U. MESHRAM

With the advent of molecular cellular biology, powerful tools and means to play with natural DNA have become available. These techniques are being improved at a rapid pace making recombinant DNA technology almost a new avatar of biology, an avatar that can touch the lives of billions of people positively. Originally, the term "Biotechnology" simply meant consciously manipulating and using processes of life for the benefit of humankind. But gradually the scope of the definition has become so enormous that all the new discoveries in any area of biology are accredited to biotechnology. The newer field of nanotechnology too is part of this new, all inclusive definition of biotechnology. The advent of nanotechnology and a galloping progress in understanding the fundamentals of life processes and devising of newer, more sophisticated technologies have resulted in an unsurpassed boom in the field that we are currently witnessing. It is now the general feeling that biotechnological innovations are poised to sweep the entire globe influencing every aspect of human ecospheric life.

While biotechnology touches virtually every aspect of human life today, one can try and divide the impact of biotechnology on human beings into the following categories:

- The medicinal field which includes development of new targeted drugs, development of new diagnostic and preventive technologies, gene therapy, exploitation of plants and microbes as vehicles and factories for producing drugs and, in general, development of technologies that make human health better.
- Development of transgenic traits in plants that make them produce more and sustain adverse climatic conditions such as drought, salinity,

Director: Rajiv Gandhi Biotechnology Centre
Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur

aridity etc. Evolution of biofertilizers and biopesticides that reduce our dependence on counterproductive chemical moieties is also another cherished goal that impacts us. The question of higher food production is also included in this category.

- Addressing the question of environmentally sustainable technologies that will allow us to carry on with our activities with least damage to the environment or, conversely, allow us to restore the environmental conditions to their earlier, pristine nature. Included in this category is the development of alternative sources of energy since it is the exploitation of fossil fuels mainly that is responsible for the state in which the environment is today.
- Bioinformatics which includes management of data created by galloping genomics and proteomics studies and *in silico* development of drugs and enzyme inhibition studies.

The above categorization is not watertight since each field impacts the other field. However, such categorization has become necessary so as to summarize and classify the numerous developments that have taken place in the field of biotechnology in the last decade or so.

Impact of Biotechnology in the Medicinal Field

A veritable boom: This is one field that has undergone a complete paradigm shift in the last 5 years. With the completion of the human genome project, we no longer think and address the problems of health in the classical manner. Consequently, the developments in this field have been fast and reorienting. But while there is euphoria about these developments, there are great challenges also before us.

The 20th century saw the golden age for the discovery and synthesis of chemical entities, drugs and medicines. The present century seems to bring in an era of drugs from biomaterials, particularly from biotechnology. Modern biotechnology is aimed to make or modify products using interdisciplinary techniques and approaches, with a commercial outlook. The pharmaceutical industry has become perhaps the greatest beneficiary of the advancement of biotechnology.

Biotechnology for healthcare applications is expected to go through a paradigm shift following the sequencing of the human genome that was announced in 2001. In the long run, as per Levinson, this is expected to result in “individualized medicine” “the ability to deliver therapeutics on an individual basis through molecular phenotyping of disease sub-types and to predict both patients' therapeutic and side effect response to drugs”. However, in the short term, the sequencing of the genome may not reduce drug development time and drug development is expected to continue to be a research and science-intensive process. What is, however, clear is that the effective use of information such as that contained in gene sequences and in the emerging field of proteomics have changed the nature of biotechnology. Biotech companies are therefore looking for people with skill sets in information science and technology related disciplines as well.

The biotechnology industry is getting more globalized with companies from all over the world joining the race. Though the core work of the human genome sequencing project was done in the US and the UK, the availability of genome sequences and software tools on the Internet has made it possible for scientists anywhere in the world to participate in contemporary research. However, for such reasons as the availability of finance, the size of the market, government funding for research projects, and the intellectual property rights regime, the United States is expected to continue to be at the centre of the biotechnology industry for the foreseeable future. For example, the budget of the National Institute of Health of the United States alone was about $27 billion in 2003 with the life sciences research budget of the whole of the European Union being less than half of this (Cooke, 2002). Compare this with what Biocon India has to say. As per Biocon India, quoted in "The Economist", Sept. 2001, the biotechnology market in India is estimated at US $2325m at the end of 2005 in various sectors such as Animal and Healthcare product (vaccines, antibiotics and other ($925m); Agricultural products, i.e., high yielding and genetically modified seeds and other ($850m); Industrial products, i.e., enzymes, amino acids, organic acids, yeast products ($550m)). In view of this, the globalization of biotech companies in the US is mainly in terms of pushing their products into other markets and limited research collaborations where very specialized pockets of expertise exist (NSF-Workshop : R.T. Krishnan *et al*. 2003).

The biotechnology industry is booming. The United States biotech sector generated revenues of US $ 25 billion in 2001 from 1,379 companies. There is a boom in development of new drug molecules. From 1995 to 2000, nearly three times as many biotech drugs were approved than in the previous 13 years combined (Morrison and Giovannetti, 2001, quoting the Biotechnology Industry Organization). In 2001, there were 117 biotechnology drug products and vaccines approved by the U.S. FDA, and of these three-fourths were approved in the preceding 6 years; another 350 biotech drug products and vaccines were in advanced clinical trials at that time (Biotechnology Industry Organization, 2001). Before 1995, the number of biotechnology patents granted in the United States had not crossed 4,000 per year but in 1998 it touched 9,000 (Biotechnology Industry Organization, 2001, quoting U.S. Patent and Trademark Office). The number of biotechnology drugs and vaccine approvals never exceeded 7 per year till 1994, but was as many as 32 in 2000.

The challenges before the industry : While the industry booms and the developments of new drugs are coming up at a faster rate, there are enormous challenges too. The field continues to be highly R&D intensive with R&D expenses exceeding 50% of revenues (Biotechnology Industry Organization, 2001). This in itself is a great challenge. Furthermore, though an increasing number of product candidates are reaching the final stages of clinical validation, developing biotech drugs remains an expensive proposition with the cost associated with bringing a drug to market estimated at $500 million (Levinson, 2001). Biotech-based medicinal products involving the use of genetically modified organisms are subject to a wide range of regulations concerning stringent quality and safety requirements. The process must be reproducible and economical too. Such crucial issues need to be dealt with from the early research stage of R&D and need inputs from the engineering disciplines and the industry itself as far as commercialization is concerned.

The United States biotech industry raised considerable amounts of funding in the boom time of 2000 and 2001 and now faces the challenge of delivering on the confidence placed in it by investors. Manpower shortages may constrain these companies more than shortages of funding. There may thus be immigration opportunities for qualified technology personnel from other countries. European countries may also face manpower shortages and are expected to overcome these by being more flexible on immigration (Crocker and Creighton, 2001, www.bio.org). However, immigration may worsen the problem for countries like India which are already facing a talent crunch.

Recent developments in research and future directions : There is a flurry of activity and one can say that a thousand flowers are blooming. Developments have been so numerous that it is virtually impossible to present a summary. Still, let's cast a look at the more momentous directions in research.

Techniques have been developed to produce rare and medicinally valuable molecules, to change hereditary traits of plants and animals, to diagnose diseases and cure them either through biotechnologically derived proteins and polypeptides forming a new class of potential drugs, or through immunodiagnostically designed vaccines. In this way, biotechnology has had a great impact in the field of health. Indira Krishnan, Hewlett Chief (Centre for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, USA), while talking on application of biotechnology to medical diagnostics and blood donor testing, made a presentation that included illustrations of the successful use of biotechnology in improving HIV/AIDS prevention through early diagnosis. In the technical session (NSF Workshop-2003) on Medical Biotechnology, C. B. Sanjeevi (Karolinska Institute, Sweden) spoke on

'KIR haplotypes' and their association with susceptibility in patients with type-1 diabetes mellitus.

An important area in plant molecular biology is the development of plant vaccines against diseases in humans and animals, including domestic pets. Development of hepatitis B vaccine (HBV) in tobacco is one example of this new technology.

Plants have formed the basis for traditional medicinal systems and today approximately 80 per cent of the world's population relies on traditional plant-based medicines for primary healthcare. The essential values of some plants have long been established, but a large number of them remain unexplored as yet. Conservation of depleting medicinal plant resource is therefore of serious concern. Prakasha Rao mentioned some of the methods of *in situ* and *ex situ* conservation strategies, modern methods of cryopreservation of seeds/materials, issues involved in cultivation of medicinal plants, including plant improvement, agro-technologies, post-harvesting methods, preliminary value-addition, cropping systems, quality and economics in great detail.

Plant biopharming is the production of pharmaceutical proteins in genetically engineered plants. This involves growing and harvesting genetically modified crops with the object of producing pharmaceuticals. The idea is to use such crops as biological factories to generate drugs, which are difficult or expensive to produce. The advantages include the low cost of producing raw material on field scale, rapid scaling up of production and safety of plant products as they are non-hosts for human pathogens. The pharmaceutical-crops that have been grown in US field trials are corn, tobacco, rice, alfalfa, potato, safflower, soya bean, sugarcane, and tomato. The production strategies target production and storage of the engineered product in seeds, which naturally accumulate high concentrations of proteins and oils and are easy to store and transport. Some of the recombinant proteins that are produced in transgenic plants include hirudin in canola, collagen, hepatitis B surface antigen, rabies vaccine, and erythroprotein in tobacco, and antibodies in tobacco and soybean. Major concerns in the production of recombinant proteins in GM plants are differences in glycosylation gene silencing and have to be addressed in future. An increasing number of transgenic plant-derived proteins are entering clinical testing. The initial success of these programs suggests an important role for low cost and large-scale production technologies.

The advent of recombinant DNA techniques has provided new tools for vaccine research. Specific antigens are selected on the basis of the immunological data from patients, and their corresponding genes have been cloned so that the antigens can be produced at large scale. The approach has its own limitations including the fact that immunogenic proteins are not necessarily protective antigens or, even if protective, the antigens cannot be used in vaccine formulations because of sequence variability, difficulty in expression and/or purification, high production costs, etc. (Biotech News, Vol. 1(2) 2006).

The use of biomarkers in medicine lies in their ability to detect disease and support diagnostic and therapeutic decisions. Research over the past few years on the molecular basis of disease has led to the identification of several new biomarkers that have great potential in everyday clinical practice. Currently used biomarkers include proteins, transcript profiles, single nucleotide polymorphisms and small molecules. Disease specific biomarkers are being developed for cancer, central nervous system, inflammatory diseases, etc. In the future, biomarkers identification by 'clinical proteomics' will play an increasingly important role in all phases of drug development, including regulatory review. Pharmacogenomic approaches, including those based on differential expression of gene/ protein arrays, will provide panels of relevant biomarkers that can be expected to transform the drug development process.

Impact of Biotechnology on Agriculture and Food Production

Challenges and expectations from biotechnology: Plant biotechnology is expected and predicted to have direct impact on improving health, primarily by making more food available to meet basic dietary needs and also by making better foods that are high in vitamins and have other healthy traits. In the developing world, where 840 million people are chronically malnourished, the challenge often is just getting people enough calories. Biotech crops can ward off insect pests and viruses that could have far reaching impact in helping farmers in Southern Africa and Asia. Such are the lofty expectations from biotechnology. To come true to these expectations, we need a second green revolution, no less.

Need for a second green revolution: The world needs a second Green Revolution to feed its ever growing population, as stated by UN Food Agency. A cumulative international effort is required to feed the world as its population soars from the current six billion to nine billion, the agency Director General Jacquest Diouf stated. While addressing the World Affairs Council of Northern California in San Francisco, Diouf stressed on the need for preserving the natural resources and environment while increasing the food production. The earlier Green Revolution relied on the lavish use of inputs such as water, chemical fertilizers and pesticides. Diouf suggested an additional requirement to grow an extra one billion metric tonnes of cereals a year by 2050. For this, the cultivators need a base of land and water in many of the world's regions. The present environment is increasingly deteriorating the land by global warming and climatic changes. The indiscriminate use of chemical fertilizers and pesticides adds to this deterioration. So, the need of the hour is spelt out clearly: to increase the food production without worsening the environment.

There are diverse ways in which biotechnology is addressing these problems. These are:

- Develop new plant varieties which give higher yield of food per ha.
- Increase the content of nutrients in the plants.
- Increase the shelf-life of food so that one saves on the losses due to spoilage and thus indirectly adds to the amount of food available.
- Develop more effective biofertilizers and biopesticides to save the environment and soil from degradation and again indirectly adds to the food store.
- To spread awareness among the farmers about the newer objectives and the ways available to achieve them.

Recent advances relating to the above points: While speaking on 'Recent advances in plant biotechnology for human welfare', G. Madhava Reddy stated that plant molecular biology techniques like isolation of specific genes, synthesis of chimeric genes, etc., have been used for developing transgenic for more than 250 traits in more than 1000 plant varieties. As examples, he cited the case of transgenic tomatoes possessing qualities such as delayed ripening, high lycopene content, and also potatoes modified with high starch content, under commercial cultivation. Ultimately, gene manipulation through biotechnology provides an unlimited opportunity to solve problems of hunger, food security, diseases and also environmental pollution amongst the growing population in developing countries like India.

A gene that produces a plant hormone that counteracts ageing and keeps fruits and vegetables fresh longer was recently discovered at the University of Leeds in the United Kingdom. Researchers currently are investigating practical applications for the commercial food marketplace that would help lengthening the shelf-life of fruits and vegetables and ensure that they reach consumers.

As important as plant biotechnology is the production of more food for a growing population, researchers are also developing healthier foods that can improve human health. Scientists today can use biotechnology to improve food by introducing health-enhancing traits, it otherwise would not have. Field tests are underway on a cancer-fighting tomato with three times more lycopene—an antioxidant that protects human tissue and could help prevent breast and prostate cancers as well as heart disease. In India, mustard seeds have been improved so as to contain more beta carotene. These could help alleviate vitamin A deficiencies. Several research teams are working to improve rice by putting more nutrition into each grain. Enhanced Golden Rice may help reduce childhood blindness, while new iron-rich rice could have a truly global impact. One in three people worldwide does not get enough of the nutrient. Researchers working with cassava, a staple food in many poorer parts of the world, have boosted protein levels by 35 to 45 per cent and increased the levels of essential amino acids. Other members joining the group of functional food include vitamin E-enriched corn and canola oil, soybeans with higher levels of healthy monounsaturated fats, and vitamin A-enriched rice.

Various biotechnological tools are utilized in improving the fertility of soil especially N and P content, through nitrogen fixing and phosphorus solubilizing bacteria thereby reducing the requirement of inorganic source of these nutrients resulting in economizing the crop production. Though efforts have been made successfully in popularizing these bacterial inoculants as biofertilizers, little has been done in improving their bioefficacy in the soil. Application of beneficial bacteria, fungi and actinomycetes as biocontrol agent against fungal phytopathogens is an emerging eco-friendly alternative to chemical pesticides. Soil reaction, deficiency and toxicity of nutrient elements and their balance in the soil are few important factors that determine their efficiency.

The biopesticidal genes from *Bacillus thuringiensis* (Bt) have been transferred into pigeonpea (*Cajanus cajan*), brinjal (*Solanum melanogena*), tomato, potato, rice, sorghum, cauliflower, cabbage, mustard and chickpea (*Cicer arietinum*), and are at different stages of testing. Several groups are working on the manipulation of fatty acid content in oil crops, or improving protein content in rice and potato by transgenic methods, or on delaying fruit ripening in tomato and banana using antisense technology. Although most of the transgenic varieties have yet to be cultivated on a commercial scale, hopefully these efforts would produce various transgenic plant varieties and provide them at affordable costs to the farmers, helping to prevent private sector monopolies. Many plant genetic engineering efforts to develop fungal resistance involve PR (pathogenesis-related) protein genes. Among the PR proteins, chitinase (PR-3) and beta-1, 3-glucanase (PR-2) are efficient in the lysis of chitin and glucan polymers in the fungal cell wall.

The possibility to transfer genes across almost all taxonomic borders by molecular techniques has expanded the potential resources available to plant breeders enormously. The need of the hour is that the differences between transgenic and non-transgenic crops should become irrelevant when the focus of plant breeding is on achieving maximal production in a sustainable way to feed the growing human population. Dubbed 'the Green Phoenix', transgenic plant technology offers both challenges and opportunities for growth and development of mankind. This technology should be used to complement the traditional methods for enhancing productivity and quality, rather than replace the conventional methods.

To adopt this technology, GM crops and their products, awareness has to be created among the farming and consumer communities regarding their benefits and effects on human life by the scientific communities and national leaders.

The aesthetics of food is almost as important as the food itself. In food plaza, colour of food is one of the most vital elements in determining acceptance, besides making it attractive, and appetizing. Historically, natural or "biocolours" were used extensively till the end of 19th century, when synthetic colours called 'coaltar dyes' were developed and acquired a widespread acceptability. Unfortunately, many of these have proved themselves to be allergens, or worse, to be carcinogens. Biocolours like anthrocyanins, betalaines, carotenoids, chlorophylls, xanthophylls, etc. occur widely in nature. Among these, carotenoids are responsible for many of the brilliant red, orange and yellow colours of edible fruits (ripe mango, orange, papaya), and vegetables (agathi, amaranth, colocasia leaves, carrot and mushroom). Carotenoids have vitamin A activity and are associated with an array of biological functions like antioxidant, anti-cancer, modulation of detoxifying enzyme, enhancing immune system, all requiring intestinal uptake. Thus, the use of biocolour is of immense significance from health point of view. Due to the hazardous nature of synthetic dyes, there is an increased commercial interest in using microorganisms as a colour source. Fungal systems are considered to be the best alternative, as they can grow and produce colour within a short period of time in a limited space. Many of the plant sources are also useful for biocolour production.

Farmers have been educated mostly on the use of biofertilizers and biopesticides, but they have not been enlightened on the soil management to reap the maximum benefit of these biofertilizers. In this regard, the govt. policies require effective implementation by means of scientific local dialects communication by providing know-how and regular training programme among rural and tribal farming community, thus improving the national production and their socio-economic condition as well.

Rajiv Gandhi Biotechnology Centre has been instrumental in addressing some of the issues raised above in Central India. It has developed nano-probiotics, biofertilizers and biopesticides and has popularized them at the rural level. The centre has also done yeoman's service in spreading awareness among farmers about the manner in which they can harness biotechnology in addressing the need for better farming.

Biotechnology and its Impact on Environment

An indiscriminate fossil fuel consumption, a lack of desire to develop alternative energy sources due to reasons mainly economic and/or political, lack of sophisticated models that predicted global warming till comparatively recently, use of CFC chemicals, initially due to ignorance and later wantonly, an uneducated and uninformed rampant use of fertilizers and chemical pesticides, wanton destruction of animals and plants for economic or supposedly aesthetic reasons are all reasons for the environmental degradation that we see today and that threatens to uproot whole populations from their traditional homes and play havoc with the food supply of the globe. Biotechnology is supposed to address these momentous problems. Let us try and believe that it is not too late in the day and that biotechnology may just be able to address these cantankerous issues.

Biodiversity is key to environment protection. The tiger in India faces extinction mainly because its visceral parts are of medicinal use in traditional Chinese medicine and its skin is of ornamental use. The cheetah is on the verge of extinction in Africa mainly owing to a limited genetic pool and problems that have arisen in that pool. Many other animals, small and big, are in danger of extinction. So is the fate of plants. To clear the land for building activities, for organized farming or merely for timber has created the condition whereby we will lose plants and many undiscovered medicinal molecules with them. Biotechnology is trying to address these problems by addressing and correcting the gene pools of the cheetah, improving the reproductive traits of the tigers and, by protecting the germplasm of plants and by devising ever new micropropagation techniques and by various other methods. We are also trying to save the eagles by establishing that diclofenac sodium, a drug used in cattle, is responsible for their plight and then banning this drug. According to IUCN: "The major proximate causes of species extinction are habitat loss and degradation".

The primary causes of habitat loss are agricultural activities, mining, fishing, logging and harvesting and development of human settlements, industry and associated infrastructure. The pressure on the land and rivers lead to the loss of habitat and prey base. Another important reason for the loss of species is poaching. The global market for animal products stands at an alarming $2.5 billion. In the past decade, poaching has emerged as an organized crime and has become virtually impossible to control. Unlike the mega species, the smaller ones are victim of their low-priority conservation status. No census is done on them. The major roadblock seems to be the lack of funding. According to a World Resource Report, the planet is on the verge of an episode of major species extinction. This phenomenon, during which a significant portion of global flora and fauna were wiped out, has happened five times over the last half-billion years (Naturalli, Vol. 1, No. 1 2005).

The United Nations Environment Protection agency (UNEP) believes that ecotourism can cause the loss of the very biodiversity, thus, leading to loss of tourism potential. Tourists often unknowingly cause enormous disruption, and even destruction of ecosystems by destroying the species (insects, wild and cultivated plants, etc.) that are not native to a local environment. The destruction and disturbance caused by the tourism industry, especially over the last few decades, when access to remote areas improved greatly, has led to questions being asked about its sustainability.

India is always regarded as a land of diversity. According to the Govt. of India's Ministry of Tourism, out of India's three million square kilometres of forest cover, 1,50,000 sq km is protected. Generating the data using different techniques, principally using polymerase chain reaction (PCR) and analysis through the computational tools, provide a more reliable and appropriate approach to ascertain microbial biodiversity too. With the advent of genomics tools, the microbial diversity could be applied in various environment management options in changing environmental conditions due to pollution.

Industrial processes are also responsible for air pollution as well as soil and water pollution. Leather industry uses huge amount of chromium during tanning of skin and hides, and pentachlorophenol (PCP) as biocide for preservation of leather. Effluent contaminated by chromium and chlorinated phenols are difficult for remediation because of the mixed nature of the contaminants. These compounds are toxic and recalcitrant; they persist for long in the environment and cause adverse effects to flora and fauna. Bioleaching is emerging as a potential tool to decontaminate soils affected by heavy metals. The present approach assesses the efficiency of bioleaching to decontaminate heavy metal laden soil employing *Acidithiobacillus thiooxidans*.

Application of microbial biotechnology is expected to go a long way in helping us to restore the environmental quality of wasteland too, and some measure of success has been achieved in this field. On account of disturbed ecology, disturbed soil conditions and climatic extremes, these sites have been rendered practically denuded of organic matter and poor in supply of essential plant nutrients, in effect, rendering them inhospitable for plant growth. Therefore, the development of wastelands also needs a biotechnological package, which can improve such sites and bring back the ecological balance as an alternative measure for arable production unit. The major arable crop production unit is already on the verge of extinction. With the use of proper soil amendments, the wasteland sites can be developed to become amenable for producing the biomass as a source of energy.

Another development that can improve the economics of waste and barren lands is the emergence of the so-called biofuels. Extracted from Jatropha, Mahua, Neem, Karanjee and a host of other plant seeds, these biofuels are supposed to be the answers for the coming energy crunch as well as being seen as environmentally less polluting. Many of these plants can grow on barren lands and thus will, in near future, improve the economic status of many of the farmers owning such lands.

Alternative and renewable energy sources have become even more important today with the rising prices of crude sources. An anaerobic bio-hydrogenation revealed by M. Sivakumar from cattle excrement biomass is receiving recent attention as one of the new sources of energy production, because wastewater and other biomass can be used as raw material and hydrogen gas can be continuously produced in an anaerobic fermenter.

Development of better biofertilizers and biopesticides as stated above, coupled with education of farmers about the use of these new technology products, will go a long way in returning the soil to its productive nature of the past and reduce pollution. It may also go a long way in restoring microbial diversity as well as biodiversity of the bigger animals and plants.

Bioinformatics: Dawn of a New Industry

Bioinformatics started as a mere application of computer technology for the management of biological information. The need for bioinformatics capabilities has been precipitated by the explosion of genomic information resulting from the Human Genome Project and other attempts at genomic sequencing. However, since this humble beginning, bioinformatics has gone on to become much more than just a database management application. Today bioinformatics is important *in silico* studies leading to targeted drug development and enzyme inhibition studies. The expectation is that in recent future all drugs will be designed first *in silico* and only then tested out in the laboratories.

Bioinformatics has emerged, in recent years, as an industry in its own right. As stated above, it is much more than just a tool to aid gene and protein sequence analysis in the post-genomic era. Bioinformatics companies provide the computational tools and databases that made genomic research possible. A 2000 estimate of the bioinformatics industry puts its size at $300 million generated by 50 companies, evenly divided between data suppliers and IT/tool providers. This was expected to rise to about $1.5-2.0 billion by 2005 (Reed, 2000). In addition to companies that focus on bioinformatics, IT and IT service companies like Sun Microsystems, IBM and Agilent Technologies have entered the arena of research and bioinformatics solution providers. Most large pharmaceutical and biotech companies have already made major investments in bioinformatics infrastructure and entered contractual arrangements with tools and products suppliers and/or developed substantial in-house capabilities (Reed 2000:8). New vendors can hope to obtain business from these companies only if they have some very distinctive new tool to offer. Due to considerations related to protection