# An assessment of the current Indian scene in biotechnology

*G. Padmanaban*

*Biotechnology holds great promise, and is sure to make an impact in India in the nineties. The role of the government's Department of Biotechnology in focusing attention and resources on crucial problems and in supporting basic research is laudable.*

When INSAT 1D or *Agni* streaks the sky, it is dramatic and visible. When a cow or a buffalo gives birth to a calf through embryo-transfer technology or when an immunodiagnostic kit for detection of filariasis is released or even when bamboo is made to flower through tissue-culture technique, the impact is less dramatic despite the efforts made to highlight the success. Biotechnology is a silent revolution and has the potential to touch millions of people. As an industry, it will be user-friendly, and, therefore, countries all over the world are striving to achieve something in the area, although, as expected, the US and Japan are leaders in the field.

## Old vs new biotechnology

The potential applications of biotechnology have been discussed and written about to an extent of almost becoming stale. Therefore there is no need to catalogue the endless possibilities but only to appreciate the realities on the ground. It is well recognized that biotechnology is not a new field but an age-old practice. However, with the advent of recombinant-DNA (r-DNA) technology, immunochemical technology and plant as well as animal tissue-culture methods, biotechnology has assumed a totally new relevance and significance. Controversies between old and new in biotechnology have died down elsewhere and the West is forging ahead. Even controversies hit us with a generation gap! In fact, biotechnology is more relevant to a country like India than it is to the West. With the establishment of Welfare States, where conventional infectious diseases have been banished, where food grains are overproduced, and where milk is run down the drain, the West has to search for priorities Of course, AIDS, cancer and a few other systemic diseases dominate the scene. The ultimate aim is also to capture the Third World markets, at the same time preventing imports of items, be they spices or cocoa. It is a different matter if this encourages the Third World to produce more cocaine and marijuana. In India, with the tremendous pressure of population, problems of sanitation and drinking water, the premium on cultivable land and the vagaries of the monsoon, fuel shortage and forest denudation, we have no dearth of priorities. We have almost reached saturation point in terms of production of foodgrains, and new strategies are needed Many of our vaccine-production units are old and out of date, and often vaccines from such units have psychological rather than immunological potency! Regreening of denuded forests will require millions of saplings in a short time Should we be arguing as to what is old and what is new? Should we not blend the two and get going?

## Achievements

Biotechnology as an approach has received attention in the country during the last seven or eight years, and a focus in the last three or four years. This is too short a time to see a visible product or a process that has made an impact. Nevertheless, products and processes have become realities and are not line drawings on paper any more. An enormous attempt at creating the scientific infrastructure, in terms of both physical facilities and trained manpower, is taking place and I am confident that the impact of all these efforts would be felt in the nineties. I shall list some of the realities very briefly so that a critical assessment can follow.

1. Collaborative efforts between different agencies have led to the successful birth of buffalo calves through embryo-transfer technology and success has been reported even with split embryos.
2. Commercial tie-ups have been developed for the production of diagnostic kits for filaria, early pregnancy, typhoid fever and amoebic liver abscess. Commercial kits for the detection of a variety of diseases, such as malaria, tuberculosis, leprosy and brucellosis, are on the anvil. DNA fingerprinting for identification of individuals is feasible in India.
3. Plant tissue-culture methods have been used to produce elite, disease-free cardamom plants for commercial exploitation.
4. An animal birth-control product has been developed for commercial use.
5. A yeast strain capable of producing 12–14% ethanol has been isolated and commercial feasibility established.
6. Field evaluation programmes for testing a couple of male and female birth-control vaccines and a couple of whole organism-based leprosy vaccines, propagation of palm trees from elite seeds, and bamboo and eucalyptus from tissue culture; and establishment of prawn culture are under way.
7. An oral polio vaccine unit with Soviet collaboration and a viral vaccine unit with French collaboration are under establishment.
8. Identified research projects relating to specific crops, production of recombinant insulin, drug targeting, biofertilizer and biopesticide production, process optimization, etc. have been funded.
9. National research infrastructural facilities for the supply of raw materials such as microbial strains, animal cell

lines, etc. as well as centres in specialized areas such as genetic engineering and bioinformatics have been established.

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10. Well-organized manpower-training programmes, including master's degree courses, postdoctoral training in India and abroad, technician-training courses and workshops in specialized techniques are under way.

## A critical analysis of the achievements

The programme summarized would read like the condensed version of the progress report of the Department of Biotechnology (DBT) of the Government of India! It is true that the entire programme in the country is planned by the department (first as the National Biotechnology Board in the Department of Science and Technology (DST) and subsequently as a full-fledged department). I am not sure that such an organized programme covering various facets of biotechnology has been orchestrated by any governmental agency in any country. For a government outfit, DBT has been extraordinarily active, vibrant and forward-looking. The planning has involved a large number of scientists in the country. I am fully aware that motives may be attributed to me for the unstinted praise given to a government set-up! But I stand by my statement. However, there are questions, at both philosophical and pragmatic levels.

## Why a department for biotechnology?

Unlike atomic energy or space applications, which in a developing country like India have to be necessarily programmed by the government, biotechnology is not only a much cheaper technology but lends itself to be decentralized, disseminated very widely, and to become a major activity in the private sector. However, the peculiar situation is that, in developing countries, there is actually a confusion in the perception of what this technology can deliver. An average industrialist is curious but is not able to mentally prepare a balance sheet for his investment in this technology. It is hi-tech and knowledge—but not labour-intensive. It is an industry where the industrialist has to be in constant dialogue with the scientist. Having missed the Industrial Revolution, there has to be a sense of urgency that if India does not move fast it will miss the biotech revolution as well. In the twentyfirst century the West may dictate what hybrid seeds we should sow, or what brand of r-DNA-based insulin we should use, or even what brand of detergent we should use to remove laundry stains. I do think that it is a wise move on the part of the government to have given a separate identity to the field and established DBT. I would eventually like to see it performing a catalytic role of motivating the scientists on the one hand and bringing in the users on the other.

## How modern or new is Indian biotechnology?

From almost a zero level in the early eighties, we now have at least two dozen laboratories where good recombinant-DNA expertise is available. At the technology level, the successful demonstration of embryo transfer in animals; development of antigen-/antibody-/DNA-based diagnostics, RFLP analysis and DNA-fingerprint analysis; and the cloning of a variety of genes attest to a high level of competence in modern biotechnology. But the fact remains that many programmes are organizational efforts at coordination rather than implementation of hi-tech knowledge. This effort should not be minimized in importance, since the results will be seen to be reaching the people. But at the same time, I do not see even a single r-DNA-based protein product on the anvil for commercial production. This definitely is not due to lack of expertise, but due to lack of commitment and application. I do not think that this can be achieved in the university sector in India in the present context. A group should be commissioned in well-endowed national laboratories with consultants from the university sector, if necessary, to get a couple of protein products up to the pilot-plant scale in three or four years. Insulin, growth hormone and some blood proteins are very relevant to our country's medical needs. The group has necessarily to include experts in downstream processing as well. Success in this area is very necessary for the projection of modern biotechnology in India.

## Basic research and manpower training

There is need for intense basic research in several areas of life sciences that are of relevance to modern biotechnology. A few specific technological approaches required are:

1. Expression of proteins in a wide variety of expression systems
2. Production of mutant proteins using site-specific mutagenesis
3. X-ray and computer-graphic analysis of crystalline proteins
4. Exploitation of polymerase chain reaction technique
5. Wide use of transgenic animal and plant systems
6. Plant-protoplast transformation and regeneration.

It is needless to emphasize the importance of basic phenomena-oriented research. Expertise must also be developed in downstream processing. DST has played a major role in supporting relevant basic research. It would be appropriate if DBT and DST got together and evolved a common strategy to sustain basic life-science research in the country.

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Despite early scepticism, biotechnology students are doing extremely well. The training programmes have been very useful. The worry is that these students find greener pastures elsewhere.

I am not unduly worried. With a little imaginative planning we can also get them back from abroad, provided political decisions do not derail social structure. I would even like to suggest that other agencies, such as Atomic Energy and Space, should run or adopt programmes in chemical and physical sciences at the masters level through the University Grants Commission (UGC). This is one way of introducing high-quality masters programmes in the country, without eating into the poverty of UGC.

## Why should technology be imported?

Was there any need to sign up agreements for imported technologies to manufacture oral polio vaccine and other viral vaccines? The government set up a target that 85% of children should be vaccinated against diphtheria, tetanus, tuberculosis, polio and measles, and 100% of pregnant women against tetanus by 1994. This is a tall order, since the country's production falls quite short of the requirement. But in the matter of the health of our population tall-order targets have of course to be achieved. The imported technologies should not only help to make good the shortfall, but also act as focal points for the modernization of indigenous vaccine units in particular. I do hope that the R&D components of these deals are flexible enough to be exploited elsewhere in the country. There is also the unresolved controversy of the potency of the oral polio vaccine versus killed polio vaccine. Flexibility should be provided to convert the OPV unit into a KPV unit if the situation so demands.

## Do national infrastructural facilities function optimally?

Many of the national facilities funded by DBT are almost fully established and their performance will come in for a critical examination soon. However, traditionally, scientists in this country do not have much faith in the performance of national infrastructural facilities supporting research. They are usually considered to be small empires built for individual scientists. Some of the national facilities established earlier have not exactly covered themselves with glory. The users should make a demand on these facilities, which in turn should respond readily. However, if the performance of bioinformatics centres (DBT) and central NMR facilities (DST) is any indication, there is hope that basic research in the country will be largely benefitted by these national facilities. We have, however, miserably failed in one vital area of infrastructure for research.

That is in the area of the manufacture of fine biochemicals and enzymes needed for modern biotech research. Almost the entire requirement is imported, which arrangement is also far from satisfactory.

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I do not believe that we can compete in international research with imported materials, whose quality is not assured after their sojourn in Indian airports and customs! Our manufacture and supply of radiolabelled biomolecules for purposes of research falls very much short of requirements in terms of schedule, frequency and uniform maintenance of quality. Of late, there has been a perceptible improvement in the quality and maintenance of schedule by the Board of Radiation and Isotope Technology (BRIT) of the Bhabha Atomic Research Centre (BARC). I hope this will continue. Nearly 150 universities and even national laboratories suffer owing to the inadequate availability and supply of raw materials for basic research in life sciences. Manufacture of sophisticated research equipment has never been considered seriously in this country. We are trying to build castles, but where are the bricks? It is not a consolation that the entire Third World or even the eastern part of the West is in a similar situation.

## Are we spreading thin?

I do not think so. There are some who believe that we should concentrate on one or two items and come up with spectacular success. Whom are we trying to impress? If our real concern are the common man, the poor and the downtrodden, our priorities cannot be one or two spectacular successes, but a silent revolution in many areas. As already indicated, biotechnology lends itself to exploitation in a wide variety of areas of priority to this country. What we need is an integrated approach; we have the capabilities. We have to work on several fronts. But DBT should be able to jettison projects, beyond feasibility stage, so that the appropriate user sector, private or government, will take over. This will also help them to keep moving and looking for newer pastures. In particular, I do not favour the DBT starting its own biotech corporations. That will tie its hands for ever.

## Can territorial integrities be broken?

I believe India has a very good organizational set-up in general. After all, we were able to take smallpox vaccine to the doorstep of almost every family in the country and abolish the disease. Looking at it another way, you name the disease, we have an institute to deal with it! You name the crop, we have an institute to deal with it! But territorial integrities are zealously guarded at the level of each research institute, the agency covering these institutes, and the ministry under which the agency functions. DBT assures us that every one of its programmes is implemented in collaboration through the agricultural, medical or other networks operating under appropriate ministries. But still, the other agencies have their own overlapping programmes and their own biotech experts as well. These do work at cross purposes. The worst scenario is partitioning of new and old biotechnology along the new and old government departments dealing with the sciences relating to agriculture, medicine and environment. Biotech is only a component in our overall strategy to banish infectious diseases or grow more food or regreen the denuded forests. For example, vaccines are only a second-line defence against infectious diseases. The primary concern is sanitation. But the two are not mutually exclusive. There is not much communication between

scientists who man the top positions of science departments in the government. Communication is often by proxy, through 'experts' who try to please all the agencies and keep their own positions intact!

## Biotech research in industry

The response of private industry to biotechnology had been lukewarm despite the curiosity. India has more traders than industrialists in the sense that one feels content with acting as agent for foreign companies. Industry is also more keen on foreign tie-ups than on relying on indigenous expertise. It should also be stated that the credibility of locally generated expertise is also not very high for a variety of reasons. There is every reason to believe that all these attitudes are changing, at least in the area of biotechnology. At the moment there are about a dozen private establishments that are interested in exploiting the indigenous expertise and are also carrying out in-house research.

## Need for a positive approach

Despite all the problems, there is a feeling of great expectation. One feels like a pre-university student who has done exceedingly well so far and is looking at the future with starry-eyed wonder and ambition. It would be cruel to dampen this enthusiasm with cynicism and bad forebodings. The best thing that DBT has been able to achieve is generating enthusiasm for a science–industry consortium. I am told that 60–70 industrialists have shown tremendous enthusiasm for biotechnology and financial institutions are itching to step in. If this really happens the girl (or boy!) is quite mature for her age. She holds great promise for the welfare of the country and a challenge to the scientists, and she needs all the help and care we can give.

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# The role and present status of biotechnology in India

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*India has several advantages that augur well for development of biotechnology. But a central agency like the Department of Biotechnology should break new ground.*

The revolution in biotechnology has come about as a consequence of the development of a number of techniques, prominent among which are recombinant-DNA technology, hybridoma technology, tissue culture, chemical synthesis of proteins and DNA, techniques of sequencing of protein and DNA, and *in vitro* fertilization. The use of these techniques against the background of knowledge acquired in the last four decades in regard to the structure and function of living systems has opened up new vistas of application.

## The developed countries

The use of recombinant-DNA and hybridoma technologies, plant and animal tissue culture, the metabolic abilities of microorganisms, and the new enzyme and synthetic technologies is already revolutionizing chemical industry in the developed countries by providing cheaper, better and less pollutive ways of producing both known and new, simple and complex, useful chemical substances. There are today over 170 firms in 18 countries (but none in India) engaged in the development of the technologies for and/or production of nearly a hundred pharmaceutical and industrially important proteins through genetic engineering. The monoclonal-antibody business is expected to touch two billion dollars per year by the end of 1990. And several countries are investing heavily, in terms of both manpower and financial resources, in the development of vaccines based on antigens produced through recombinant-DNA techniques for virtually all the major infectious diseases. India's contribution towards this global effort is, as of today, virtually nil--in spite of the fact that we are the second most populous country in the world, that we have a very large scientific and technological manpower, that we are among the world's ten most industrialized countries, and that we have the need for doing what have been mentioned above on a large scale.

Then there is *in vitro* fertilization, which has successfully led to the establishment of pregnancies in thousands of women, who were otherwise considered infertile, since the pioneering work of R. G. Edwards and the late Patrick Steptoe some ten years ago. Embryo-transfer technology is also bound to revolutionize the practice of animal husbandry. The application of modern biotechnology to medicine is diverse—be it the enhanced ability to accept organ transplants and the development of artificial organs as a consequence of the understanding of immune response and of organ function at the molecular level, or the development of new techniques of diagnosis.

In summary, in the more advanced countries of the world, the advances in modern biology, especially in molecular