The role and present status of biotechnology in India: A commentary

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The revolution in biotechnology has been brought about as a consequence of the development of a number of techniques, prominent among which are recombinant DNA technology, hybridoma technology, tissue culture (both plant and animal), 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 that we have acquired in the last four decades in regard to the chemistry, the biochemistry, structure and the function of living systems, and our ability to explain function in terms of chemistry, biochemistry and structure, has opened up unimagined new vistas of application.

The developed countries

We have recently reviewed the application of biotechnology, including in the area of production of chemicals[1,2]. The use of recombinant DNA and hybridoma technologies, plant and animal tissue culture, the metabolic abilities of microorganisms, the new enzyme technologies, and the 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 was expected to touch two billion dollars per year by the end of 1990. And several countries of the world are investing heavily, both in terms of 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 the third largest scientific and technological manpower in the world, that we are among the world's ten most industrialized countries, and that we have the need for doing what we have mentioned above on a large scale.

Then, we have *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 bound to revolutionize the practice of animal husbandry. The application of modern biotechnology to medicine is not only highly sophisticated but also so diverse that it would be impossible even to list the areas of application — 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 (such as computer-aided tomography, positron emission tomography and nuclear magnetic resonance scanning), or laser surgery.

In summary, in the more advanced countries of the world, the advances in modern biology, especially in molecular and cellular biology and related areas such as immunology, have become so deeply and intricately intermeshed with the fabric of our daily existence, that the structure of biotechnology is being built there rapidly, over a solid foundation.

Why has it been possible in developed countries such as the USA, the UK, France, the Netherlands, Sweden, Italy and Japan to sow the seeds of the development of biotechnology so far and wide, and then to be able to nurture the infant industry appropriately? Three reasons stand out. The first is the recognition of the importance of investment in basic biological research, the second is the ability to peep into the future of both biology and biotechnology, and the third is an understanding of the specific requirements of biotechnology, for example the close relationship between basic research and its application in the area of modern biology.

The future

Looking at the prospects for the future, which the developed countries mentioned above have perceived so much better than us, in a likely scenario 20 years from now, biotechnology would have overtaken chemical technology, and a large proportion of those chemicals that are today made through chemical technology would be made through biotechnology. Many products of everyday use would be cheaper and better — to the extent that it all might even change our lifestyles. For example, if amino acids; vitamins and the few other nutrients that are essential for man become as cheap as is theoretically possible, the cheapest diet that would take care of one's everyday's nutritional requirements would be a synthetic diet. One can then conceive of a situation where satisfaction of hunger and the need of adequate nutrition would be dissociated from the satisfaction of the desire to eat food that one finds delicious and is fond of. Production of alcohol from cellulose through its enzymatic hydrolysis could make alcohol so cheap that alcohol-based industry would be revolutionized. Availability of biodegradable plastics and home diagnostic kits would make life different from what it is today, as would the ability to determine the sex of early embryos, including human embryos, development of new species (especially plant species), and availability of techniques that would allow preservation of food for long periods without refrigeration. The control of those few diseases which cannot be fully cured today — such as cancer, leprosy, heart diseases, brain disorders, and viral diseases like AIDS — coupled with improved environment and an increased understanding of the requirements for maximal longevity, would increase our life span to an extent that the entire social security system would need to be revised.

What biotechnology can do for India

It would be obvious that biotechnology can do a lot for India — everything that it is doing or is poised to do for the more developed countries where it has come of age. But, that, in our perception, would not be the primary reason for investing adequately in the development of biotechnology in our country. The main reason would be that, if we do nothing in the area of modern biology and biotechnology, we will be exploited by others, and in a manner and through means that history has not known before. Neocolonialism, and domination of one nation by another tomorrow, will operate through superiority in regard to biological knowledge and practice. We already have experience of recent dramatic reduction of coffee production in Africa through deliberate marketing of a harmful agrochemical by interested nations. In our own country, there have been at least two cases of possible infiltration of our agriculture in a similar way; we were able to overcome them as we had expertise in the area. Indeed, if we wish to have a place of

our own in the community of nations, we must not only have this expertise but we must also be leaders at least in some areas of basic biology and biotechnology.

Being a large and the second most populous country of the world, it would not be enough for us to be doing just *some* biotechnology. It would be important that we do enough to make our chances of being a leader in some areas of biotechnology bright, so that we may be able to find for ourselves a place of honour in the community of nations in the 21st century. Specifically, we ought to invest in biotechnology that will lead to the production of chemicals through non-pollutive processes, of drugs, of diagnostic kits, of vaccines, and of agricultural chemicals. We ought to use it for improving our cattle—for example, through embryo transfer technology—and our environment. Biotechnology can, through development of appropriate energy plantations, take care of part of our energy requirements in the immediate or near future. It can be used to boost our exports by allowing rapid production of quality plants, including normal plants, which can probably be produced cheaper here than anywhere else in the world. Countries like Thailand already have orchids grown through tissue culture as one of their main exports. We can be a pioneer in the use of DNA fingerprinting for identification of plants and germ-plasm. And these are but a few examples.

We should also remember that India is today uniquely placed for the development of biotechnology, among others for the following reasons.

(i) Its stage of scientific development today is the highest among all the developing countries of the world. Every item of consumer goods that one buys in India is today made in India, and the range and variety is large, and the quality often good. It exports more than 150 categories of goods, including sophisticated finished products made entirely in India. Its systems capabilities today are next to none. Its engineering and construction firms have won a large number of major contracts abroad in competition with unscrupulous multinationals. It has an elaborate infrastructure for science and an expertise of a very high order in a whole range of areas in science and technology. It is the only developing country which publishes more than 10,000 scientific papers in a year in journals indexed in *Current Contents*. Out of about 20 countries producing more than 1000 such papers, it ranks amongst the top 10.

(ii) Although the quality is not always high, it has a large number of persons trained as biologists in a number of disciplines, in institutions spread over the length and breadth of the country.

(iii) In the past five years or so, the Government of India, the various scientific agencies in the country, and the succesive Prime Ministers, have recognized the importance of investment in biology and have given basic research in biology and development of biotechnology high priority.

(iv) India has a strong, organized 'public sector as well as a large private sector, both with a tradition of entrepreneurship.

(v) It has strong professional societies in the area of biology.

(vi) It is rich in biological natural resources.

(vii) It has sunshine almost throughout the year in most places.

(viii) Its biologists are aware of what is happening elsewhere, so that the country is in a position to learn lessons from other's successes and failures.

(ix) Biotechnology is labour-intensive and labour is cheap in India.

It is, therefore, not only India's prerogative but also its obligation to show the way to other developing nations in regard to large-scale development of modern biology and biotechnology.

If we, as a country, do not keep pace, we will open the doors for a new kind of neocolonialism of which we will be the victims as we enter the twentyfirst century, for our lack of progress in the areas of modern biology and biotechnology, which are bound to act as major determinants of life-styles and of 'Power and influence' by the turn of this century, is bound to make us dependent on other countries for ideas, for know-how, and for biotechnology-based products. In fact, any talk of our entry into the twentyfirst century with our heads high in the community of nations—no matter what we may have done in other areas—would make little practical sense if we are not at part with the rest of the world in regard to modern biology and biotechnology, and if our government, our scientists, and our countrymen at large do not understand that the social, political, economic, legal, moral, ethical and philosophical implications of the likely advances in biology and biotechnology are going to be far greater than those of any other scientific advance made so far or likely to be made in the next two decades, including any in the areas of microelectronics and space, important no doubt as they are.

Development of biotechnology in India

As we have already mentioned, the development of biotechnology has been closely related to that of basic modern biology, which would include sub-disciplines such as biochemistry, molecular biology, cellular biology, immunology, genetics and virology, many of which overlap substantially with the others. One should, therefore, first look at the development of modern biology in India—which was, in two words, extremely slow. For a long time, the first and the only groups doing any serious biochemistry—which was the first of the modern experimental biological sciences to develop in the country—were at the Indian Institute of Science in Bangalore, the National Chemical Laboratory in Pune, and the Department of Applied Chemistry at the University of Calcutta, the persons responsible for them being P. S. Sarma, M. Damodaran and V. Jagannathan, and B. C. Guha respectively. Subsequently, groups developed at the Regional Research Laboratory in Hyderabad [which later became the nucleus for the development of the Centre for Cellular and Molecular Biology (CCMB) at Hyderabad], the Tata Institute of Fundamental Research in Bombay (led by Obaid Siddiqi), the All-India Institute of Medical Sciences in Delhi (led by Pran Talwar), the Bose Institute in Calcutta which group shifted later to Banaras Hindu University (led by Debi Burma), and the Christian Medical College in Vellore (led by Bimal Bachchawat and the late A. N. Radhakrishnan). These groups can be truly considered as the nuclei of the development of modern biology in India; they all started their activity in the late fifties or early sixties. Two organizations that helped to bring these and other small groups that subsequently came up all over the country with the opening of departments of biochemistry both in the universities and in the medical colleges, and also helped modernize the departments that related to biological sciences of various kinds, were the Society of Biological Chemists of India, which should be soon celebrating its 60th anniversary, and the Guha Research Conferences, which just celebrated their 30th anniversary. Till 1977, however, there was no institution devoted totally to research in modern biology. In 1977, CCMB was set up in Hyderabad by the CSIR, and a few years later the National Institute of Immunology in New Delhi by the DST. The support to biological research outside of the institutional grants given by agencies such as CSIR, ICMR, ICAR, DAE and DST to own institutions, came largely through SERC (Science and Engineering Research Council) administered by DST. Today, the facilities that exist for biological research in the country are comparable with the best anywhere in the world. Expertise exists somewhere or the other in the country for most of the sophisticated techniques on which modern biology is so dependent today. In regard to at least one technique, that of DNA fingerprinting, India is now regarded as a pioneer—being the second country in the world to develop its own technique in this area and use it.

What about biotechnology? Some of us did recognize that we were going soon to start living in the age of biotechnology as far back as the early seventies by which time the technique of tissue culture was well established and it was possible to transfer new (but only homologous) genetic information into microorganisms through conjugation, transduction, transformation and, later, transfection. Those who were guiding the destiny of science in the country around that time were fortunately receptive to these ideas, and there were several meetings held in Hyderabad, one of them called on 29th July 1980 by the then President of INSA, Dr V. Ramalingaswami, and another one on 5th April 1981 by the then Director-General of CSIR and Secretary, DST, Prof M. G. K. Menon, to discuss the strategy for the development of biotechnology in India. As a sequel to the last-mentioned meeting, a high-power meeting was held on 28th July 1981 in the DST, New Delhi, presided over by Prof. Menon which, following a decision at a meeting of

the Scientific Advisory Committee to the Cabinet (SACC) held on the next two days (29th and 30th July 1981), led to the establishment of the National Biotechnology Board (NBTB). Unfortunately for those of us who had been advocating a major, planned investment in biotechnology, the establishment of the NBTB, although a welcome first step, did not seem entirely satisfactory. One of us, following letters to two successive Prime Ministers, Mrs Indira Gandhi and Mr Rajiv Gandhi, requesting them to establish a separate department of biotechnology, and a personal meeting with the former in this connection, said the following in an article[3] published in 1985.

'We did recognize the need of investment in biotechnology in time—that is, in the late seventies. But, as happens in our country often, a lack of the ability to identify our requirements for a programme *expeditiously*, and of the determination to convert a laudable idea into action *in time*, has prevented the biotechnology programme in the country from developing as rapidly as it should and could have. Although a detailed plan of development of biotechnology in the country was available at the beginning of this decade, there is no new fully indigenous biotechnology-based research-cum-development-cum-production unit that has been set up in the country yet; there are not even plans ready for setting up of such an indigenous unit in the immediate future. We have a separate Department of Electronics, of Ocean Development, of Environment, of New Energy Sources, but we do not have a separate department of biotechnology at the level of the Government of India. The executing agency for biotechnology programmes in the country, as of today, is the National Biotechnology Board (NBTB). But, with the best of intentions and the best of people that it has to run its affairs and with all the goodwill, it is unlikely to deliver the goods as it is structured.

'Given the realities of bureaucratic functioning, I doubt very much if the biotechnology programme in the country would make much headway unless a separate department of biotechnology is created, manned by competent people and supported adequately. Would, for example, our atomic energy or space programmes, or, for that matter, even coal and steel industry, have progressed as much as they have, had these activities been a part of another department of the government, instead of being independently structured as they are now?

'We have, therefore, lost some five to six valuable years on account of inadequate action at the governmental level in the area of biotechnology. One can only hope that the new government will set up a new department of biotechnology directly under the prime minister, expeditiously, and staff and fund it *adequately* (not subcritically as often happens in the country).'

The Department of Biotechnology

It was, therefore, a step forward when, in early 1986, the government of the then prime minister, Mr Rajiv Gandhi, decided to set up a full-fledged Department of Biotechnology under the auspices of the Government of India. The expectations of the authors at the time were that the department's primary objective would be to set up *research-cum-development organizations*—somewhat on the lines of corporations—*in the following* areas.

(i) Genetic engineering of all types, including recombinant-DNA technology and somatic-cell hybridization. This would allow one to produce substances otherwise unavailable or extremely expensive that would be useful in medicine, agriculture and industry.
(ii) Tissue culture, both of plant and animal cells. This would allow one to clonally propagate useful or elite plants which cannot be grown vegetatively, e.g. eucalyptus, tamarind, coconut, turmeric and cashew. One could also use these techniques for development of new plant species, of disease-resistant plants, and of haploid or diploid embryos that would give primarily flowers or fruits, or even fruits with no seeds.
(iii) Enzyme engineering and technology involving stabilization and reuse of enzymes. It is this technology that would be largely responsible for replacing chemical industry with biological industry in the future.
(iv) Immunotechnology, including hybridoma technology. This area has the potential of allowing one to localize and recognize a disease easily, to control events like fertility, to allow organ transplantation, and to provide new techniques for prophylaxis and therapy for diseases such as malaria, filaria and leprosy.
(v) Production of alcohol from non-conventional sources such as grass.
(vi) Energy plantations, i.e. development of trees that grow faster and give better and more wood, and can be grown in arid and semi-arid areas in a range of climatic conditions.
(vii) Indigenous drugs. The first effort here should be to find out which are effective and which are not, and develop standards for the effective ones.

The idea was that India would do it largely on its own, using its own capital and expertise, and obtaining help, where needed, for specific purposes. Unfortunately, it is now more than four years since the Department of Biotechnology (DBT) was set up, and it has no doubt done several worthwhile things, but it has not spawned any *indigenous*, commercially oriented research-cum-development-cum-production unit in any area of biotechnology. The department has augmented the educational facilities for modern biology in the country, and sent people abroad for training (even though those going abroad under the auspices of DBT have represented a small proportion of those who go abroad through other sources); it has also funded research in a variety of areas like any other funding agency. Whatever has been done in establishing industries in the country has been done with foreign collaboration—with their capital and technology. And like any other scientific department, the Depar*tment of Biotechnology*, set up exclusively t develop biotechnology in the country, running an institution, the National Institute of Immunology, which was started unde the auspices of DST. If one were to ask th question, 'what would have been the scenari if the DBT were not there?' the answer woul be: not *very* different from what it is today, a DBT has been performing largely activitie that were being (or could be) carried ou under the auspices of other departments lik DST, ICAR or ICMR. The department ha yet to acquire a personality of its own b engaging primarily, if not exclusively, i activities that would not have been possibl had the department not existed. This is in n way to underrate the activities of the department or their importance; it is merely to say that what has been done is far from enough and there is need for the department to break new ground.

In terms of commercialization of materials developed in the country, the success has been extremely limited, though it is to the country's credit that several hybridomas developed in the country, for example, at the National Institute of Immunology and its predecessor, the All India Institute of Medical Sciences, have found a market in the country and abroad. What is perhaps of even greater concern is that neither the private nor the public sector in the country is geared today to exploit something that might be developed within the country within a reasonable time beyond which the country would lose the lead. There are several examples available today of materials developed in the country that could have been produced commercially and for which an international market exists; India *could* have acquired leadership in these areas but it did not.

Why this unsatisfactory scenario?

The reasons are as much sociological as scientific. We are obsessed with foreign technology and foreign training. The high ratio of mediocrity to excellence in the area of scientific research—as much in biology as in any other field—shows itself in our lack of will and confidence, which, in turn, prevents any risks whatever from being taken. In a society like ours, only the government can take risks, the private sector will not—a situation just the reverse of countries such as the United States. Not that there are no ideas and no people, but mediocrity dilutes and invalidates excellence in a most insiduous way.

What must we do now?

We should, first of all, comprehend the significance of the fact that we have a department of biotechnology (DBT) today but *not* a department of, say, chemical technology, at the level of the Government of India. One could argue that this is so because chemical technology is all-pervading, but so is biotechnology, and the fact is that none of the developed countries has a department of biotechnology.

There are three important reasons on account of which the existence of a department of biotechnology at the level of the Government of India is fully justified.

(i) Biotechnology is high technology in which, unlike in other technologies, research, development and production are intimately linked.
(ii) Whereas other technologies such as chemical technology or physics-based technology grew slowly, biotechnology developed very fast. What has happened in other areas in a matter of centuries has been compressed in just two to three decades in the area of biotechnology, making an apex body at the governmental level essential to give the activities in the area adequate support and direction to ensure maximal benefit at the national level.
(iii) Biotechnology, for reasons already stated, has special relevance to India today.

In fact, the above reasons are very similar to those that were applicable to electronics when we very rightly set up a separate Department of Electronics.

In view of the above, the nation would be justified in having the following expectations of DBT.

(i) The department would identify and develop areas of a high-tech nature in the area of modern biology that are most relevant to us and/or in which we would have the potential of emerging as one of the world's leaders, and then set up R&D-cum-production units in these areas. Examples of areas in which the department should invest on its own would be genetic engineering, enzyme technology and engineering, immunotechnology (including vaccines and immunodiagnostics), production of alcohol through non-conventional sources, and tissue culture (both plant and animal). It is only when the department sets up its own R&D-cum-production units that activity in these areas carried out elsewhere in the country, with or without the support from DBT, would be appropriately focused and yield optimal returns. These units do not necessarily have to be in the public sector; they could very well be in the joint sector.
(ii) The department would also set up suitable R&D-cum-production units in selected conventional areas in which the effort has so far been suboptimal, scattered or unfocused. The rationale for DBT's involvement in such areas would be that it can bring to bear on these areas the techniques of modern biology. One such area is indigenous drugs.
(iii) The department would provide only the critical inputs in regard to those commercial activities that are 'repetitive' in nature (that is, that would not require any new research or development) and can and should be pursued, with the sole objective of wide-scale application in the country under the auspices of other departments. As of now such activities have been the *primary* focus of DBT's attention.
(iv) The department would serve as the eyes and ears of the modern-biology community in the country, and help them identify processes and products emerging out of their research that could be commercially exploited; DBT should then take steps to ensure such exploitation speedily and efficiently. There are already several cases where this could have been done but has not been done. One of them is the DNA fingerprinting technology developed in our laboratory at Hyderabad by Dr Lalji Singh and Dr Sridevi. In any other country, by now, steps would have been taken to make this technique available widely. The CCMB cannot be expected to perform the function of a commercial organization, and the related functions of publicity and ensuring appropriate legislation. The point we wish to emphasize here is that it should be the responsibility of DBT to keep a tab on such activities and to take the initiative for doing whatever is required for commercial exploitation of work done in research laboratories.

If these are done diligently, intelligently and expeditiously, at the end of the Eighth Plan we may be poised to provide leadership in some areas of biotechnology in the following years, with a promise of commercialization and application on a substantial scale and on a solid foundation.

The optimism is not unfounded

We must add that, if we take into account the realities of the situation, it would be unfair to expect biotechnology to perform any better than other sciences or technologies in the country. The chance that we had of doing so when it all started has been lost. If we had exhibited confidence, courage and imagination at *that* time, biotechnology would have, by now been poised not only to bring substantial material benefit to the nation in the coming decade, but also to provide world leadership in a few areas. Today the outlook cannot be any better than for any other area of endeavour in our country: be it water, power, education or microelectronics. Only those areas where a good and solid beginning was made, such as space, are an exception today. We therefore have no recipe for putting the biotechnology programme in the country on the fast track, so that it may meet the expectations we have stated above. Nevertheless, we are optimistic and have no doubt that when our country decides to set up research-cum-development-cum-production units on its own in the desired areas of biotechnology, it will find that it has enough talent, ability and expertise, and enough ideas, to support a viable biotechnology programme based on self-reliance. We would have then reached the take-off point. Let us hope that this day will come sooner than later, or else we may have to pay a penalty higher than we did during colonial rule.

1. Chakrabarti, C., *J. Sci. Ind. Res.*, 1989, 48, 211.
2. Chakrabarti, C. and Bhargava, P. M., *Impact*, 1990, no. 157, 81.
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