The Science and Engineering Research Council (SERC) of the Department of Science and Technology (DST) organized a series of seminars to review and update thrust areas of research in various fields. Seminars were held in: engineering sciences (Jamshedpur, 18–20 November 1988); chemical sciences (Baroda, 24–25 November 1988); life sciences (Lucknow, 6–8 December 1988); physical sciences (Santiniketan, 23–25 February 1989); earth sciences (Dehra Dun, 4–6 August 1989); atmospheric sciences (Pune, 16–18 August 1989).

In the April 20 issue we published the recommendations of the seminar on chemical sciences. In this issue we publish the recommendations of the seminar on life sciences. The introduction to the report gives a background to the approach of SERC, with special reference to life sciences. The report is divided into seven parts representing seven separate reports prepared by the Programme Advisory Committees. This is followed by general recommendations of the seminar. We hope that the issues raised in the report and the recommendations made by the scientific community would open up a national debate on this approach to supporting scientific research in the country. Scientists are welcome to write to Current Science or Adviser (Science and Technology Promotion Division), Department of Science and Technology, New Delhi, regarding suggestions on implementation of the programmes.

—Editor

CHALLENGING AREAS IN LIFE SCIENCES

INTRODUCTION

An important component of the allocation of business of the Department of Science and Technology is 'Promotion of new areas of science and technology'. To fulfil this obligation and to focus national efforts in some specific emerging areas, DST organized a series of national seminars at Baroda during 1980–83. These seminars were in the form of well-prepared debates and provided guidelines for supporting R&D activities. These seminars, now known as the 'Baroda Seminars' identified 'thrust areas' in all branches of science and engineering for support on a preferential basis. The broad guidelines for identification of thrust area programmes were that these should

—lead to growth of indigenous research capabilities
—be challenging to scientists
—be relevant to overall socio-economic development.

To encourage activity in these chosen areas it was planned to

—initiate major coordinated research programmes
—set up core groups/units around scientists
—organize training programmes and summer and winter schools with the help of outstanding scientists
—establish national support facilities in selected areas of high technology.

It may be pointed out that this exercise coincided with unparalleled developments in biological sciences. Molecular biology, genetics, biotechnology and immunology were emerging as new disciplines, with tremendous possibilities of enhancing our knowledge of biological phenomena and immediate application in agriculture, animal and medical sciences.

To initiate, implement and monitor these programmes, DST constituted a Programme Advisory Committee (PAC) in each of the major areas. In the field of life sciences, PACs were constituted in

—molecular biology
—molecular biophysics and biochemistry
—plant sciences
—animal behaviour, ecology and evolution
—medical biology
—immunology
—neurobiology and mechanisms of behaviour.

DST has an apex advisory body, viz. the Science and Engineering Research Council (SERC), consisting of expert scientists and engineers, to evolve policy guidelines, determine priorities and coordinate the activities of all the PACs.

As a result of these efforts initiated in the early eighties, substantial support has been provided to these selected programmes. During the last year or two, through a series of group monitoring workshops, involving PAC members, experts and principal and young investigators of projects, an evaluation of completed and ongoing programmes was carried out.

MOLECULAR BIOLOGY

1. PREAMBLE

BIOCHEMISTRY in the international scene evolved as an interdisciplinary area in the beginning of the 20th century. India started with a strong base in nutrition biochemistry and enzymology. Molecular biology emerged as a branch of biochemistry and soon strongly evolved to have a distinct identity. This happened in the fifties on the international scene and with a gap of a decade in our country. The seventies have seen a strong emergence of genetic engineering in the West. Although, the term signifies a particular technology or methodology, the area has broadened enormously to signify a particular approach to understand the molecular basis of life processes. In other words, molecular biology as such is becoming old-fashioned unless a recombinant DNA approach and the use of the modern nucleic acid methodologies are taken to study the problems. The advent of recombinant DNA research and the associated technologies have revolutionalized the approach used in present day molecular biology and biochemistry. The entire research is an operation in microscales and gadgets have also been developed to handle micro, pico and nano levels of macromolecules. Knowledge about sequence of amino acids in proteins is more easily obtained from the corresponding DNA sequence of appropriate cloned DNA. Active sites of enzymes are more easily and specifically altered by site-specific mutation of the corresponding DNA sequences. Thus, the impact of this technology revolution permeates all disciplines of biology. Thus, our effort at redefining thrust areas has to recognize the revolution that has taken place in terms of a totally new approach to understand and define the molecular basis of life processes.

While, this is the picture that emerges when one is discussing basic biology, an unprecedented situation has also arisen in view of the possible applications, which modern biology holds for the betterment of the quality of life. Thus, new possibilities for treatment and cure of infectious diseases and genetic disorders, control of population explosion, improvement of crop plants and other components of the plant kingdom, a new approach to industry and environment management have arisen. While, the technology content in the new approach cannot be very different between countries, the choice of systems to work with can be totally indigenous, dictated by the needs of our society. Thus, we have an opportunity to combine scientific curiosity and the passion to understand basic biological phenomena with the mundane needs of our society, where a scientist can also legitimately feel proud that he/she has also contributed towards the alleviation of societal suffering.

2. STATE-OF-THE-ART IN NATIONAL CONTEXT

The Baroda seminar resulted in the formation of a Programme Advisory Committee for molecular biology and cellular biology/genetic engineering. At this stage it is rather difficult to sift the projects classified in molecular biology from those belonging to cell biology. Nevertheless, a total of 35 projects were funded during the period and the total amount constituted large per cent of the funds given to life science research.

An indication of the molecular biology carried out in the earlier part of the period can be obtained from an extract of the SERC review containing research highlights for the period 1980–87. It highlights the following aspects:

2.1 Binary complex formation between 16S and 23S RNA as a basis for ribosome assembly
2.2 DNA repair mechanisms in *Vibrio cholerae*
2.3 Methylation/demethylation processes in gene activation in *Drosophila*
2.4 Mitogenic factor in rat testes and its regulation by vitamin A levels.

These are only examples to emphasize the conventional molecular biology that formed the basis of research output in early 1980s, which also resulted in high quality research in a few pockets.

As a follow-up of the Baroda seminar, institutions were invited to submit proposals in the area of recombinant DNA research and ultimately five institutions established Genetic Engineering Units. These were at (i) Bose Institute, Calcutta, (ii) Jawaharlal Nehru University, Delhi, (iii) Indian Institute of Science, Bangalore, (iv) Madurai Kamaraj University, Madurai and (v) Banaras Hindu University, Varanasi. In addition, several specific proposals in molecular biology, where the use of recombinant DNA research has formed the thrust were funded in many institutions. The outcome of this effort is very impressive. From a situation in 1980, where hardly any group could have boasted of a set-up to use recombinant DNA technology, a recent symposium entitled 'Genetic Engineering Research in India' held at Bangalore (July 26–28, 1988) could elicit the participation of about 50 research groups from all over the country. DST funding is largely responsible for this build-up, although recently the Department of Biotechnology has taken over some of the centres and is also funding specific proposals.

The areas, where some competence has been built are:

– molecular biology of disease-producing organisms;
– Basic understanding of eukaryotic gene structure and expression in animal and plant systems;
– molecular biology of organisms of importance in agriculture;
– molecular basis of special phenomena such as DNA repair and recombination, nitrogen fixation, osmoregulation, etc.;
– development of DNA-based probes as diagnostics.

To site specific examples:

A. At the Bose Institute, Calcutta, a strong group has evolved looking at the plant tubulin genes and ribosomal RNA genes in fish and other systems.

B. At the Indian Institute of Chemical Biology, Calcutta, molecular biology of *Leishmania* and *Vibrio cholerae* are being looked at in great detail.

C. At the Indian Institute of Science, Bangalore, structure and expression of genes from liver (genes concerned with biotransformation of chemicals), silk moth and rice have been studied in detail. The complex steps involved in meiotic recombination in eukaryotic systems have been unravelled.

D. At the Jawaharlal Nehru University, Delhi, nitrogen-fixing genes in *Azotobacter* and molecular biology of *Candida* yeast have been investigated.

E. At the Centre for Cellular and Molecular Biology, Hyderabad, significant progress has been made in the understanding of bacterial genes involved in osmoregulation.

F. At the Bhabha Atomic Research Centre, Bombay, the phenomenon of male sterility in plants has been investigated and exploited.

G. The Madurai Kamaraj University, Madurai, and the University of Poona, Pune, have evolved into good centres for teaching M.Sc. programme in molecular biology.

H. At the National Institute of Immunology, Delhi, protein expression systems based on vaccinia virus and baculovirus have been standardized.

In total, there may not be more than a dozen groups in the country, where recombinant DNA and the associated modern technologies can be applied to molecular biology research with confidence.

The development in the country during the last 5–6 years in the area has been phenomenal and very impressive. This competence has also led to larger investments in biotechnology public sectors. These include the establishment of the ASTRA Research Centre at Bangalore and the opening of the new laboratories of the CCMB at Hyderabad. While, this is a heartening progress in itself, an assessment of the international scene would indicate that India is a decade behind the progress achieved in the West.

3. INTERNATIONAL STATUS

Molecular biology research in the West and Japan has seen a phenomenal growth by taking recourse to recombinant DNA approach. Several eukaryotic genes have been cloned and completely sequenced establishing that the eukaryotic gene sequence is a mosaic and is not colinear with the protein sequence. Many proteins have been expressed in suitable expression systems and obtained in gram quantities. Although, commercial exploitation has been possible only in very few cases, large quantities of proteins for purposes of structural studies and X-ray crystallography have been produced. This would indicate that expression systems (*E. coli*, yeast, vaccinia and baculovirus in particular) have been successfully developed and exploited. This has led to an impressive understanding of the structure of receptors and a clue as to the mechanism of transmembrane signalling. Protein domains necessary for translocation across membranes have been identified. A wealth of information on transcription factors, their mode of interaction with promoter sequences and mechanism of transcription activation has been obtained. New concepts based on the commonality of the mechanisms involved in transcription and replication have been proposed. Detailed molecular models are available to explain DNA repair and recombination in prokaryotes. Molecular parasitology has seen the evolution of some exciting concepts. The molecular mechanisms of the strategies employed by the parasite to escape immunosurveillance are beginning to be understood. A new possibility to use cloned proteins as vaccines to protect against infectious diseases has arisen out of an understanding of the functional importance and strategic location of such proteins in the infecting agent

The major systems that have contributed a great deal to understand the structure, organization and expression of eukaryotic genes are the immunoglobulin and oncogene families. A virtual knowledge explosion has taken place in these areas and one is getting to be confident about handling autoimmune diseases and cancer. Although AIDS has created a genuine scare, the amount of knowledge accumulated on the molecular biology of HIV is impressive.

Post-transcriptional mechanisms, which include splicing and RNA processing, RNA editing and transport across nuclear membranes have been understood in great detail. The universality of the genetic code has been questioned. The structure of messenger, ribosomal and transfer RNAs and their participation in protein synthesis have been studied with better tools.

Plant molecular biology lagged behind in the beginning, but is soon catching up. A wealth of information has been obtained on bacterial genes fixing nitrogen and the plant genes involved in a symbiotic relationship. The concept of 'biocides', where the plant makes its own insecticide through a toxin gene cloned into the plant holds tremendous promise in understanding heterologous gene expression in plants besides its economic potential in agriculture. The plant system is still faced with the lack of adequate vectors to incorporate foreign DNA. But, Ti plasmids have worked wonders and newer approaches such as electroporation and DNA-coated tungsten bullets to introduce foreign DNA have been efficiently used.

Considerable information on organelle biogenesis and its implication to cell evolution is now available. These studies have implications for improving plant productivity.

The molecular biology of animal viruses; SV40 and adenovirus, in particular, has been studied in great detail and this has laid the foundation for understanding several aspects of eukaryotic gene structure.

4. GAP AREAS

As already indicated, the progress in molecular biology research in the country during 1980–88 is very impressive. But, virtually a knowledge explosion has taken place elsewhere and therefore Indian scientists are lagging behind by nearly a decade.

The main deficiency in research is not lack of ideas or funds, but a lack of the mastery of modern techniques. For example, DNA sequencing and oligonucleotide synthesis have become commonplace in the West. In India, only very few laboratories have this expertise. Gene cloning and characterization are very widely carried out in the West and not necessarily by molecular biologists only. This tool is used by enzymologists, biophysicists and chemists. In India, gene cloning is still considered a great achievement in itself, although in present day molecular biology it has necessarily become the first step. Similarly, many genes have been successfully expressed in appropriate expression systems and large quantities of many proteins have been prepared for physico-chemical studies. India has a long way to go in this area. Even basic methodologies in nucleic acid and protein analysis such as nicktranslation, end-labelling and blot hybridizations pose major challenges to many in the field in India. Elsewhere, these have become so routine as weighing operations on a balance.

The reasons for this situation are clear. These are:

- poor standards of students at the Master's level in universities.
- poor infrastructure for advanced research in universities. This includes non-availability of continuous power supply and water for research.
- necessity to import all equipment and consumables from abroad and the associated agonies involved in the process.
- poor library facilities in universities.
- unfamiliarity of the senior scientists with the modern techniques.
- lack of a critical mass doing high quality research in any particular aspect of the total field. These groups work in isolation within the country, except for contacts abroad.
- a general lack of self-criticism and pride in one's own work and being Indian.

Thus, these reasons are general and should be applicable to all research areas. Perhaps, the one reason specifically applicable to molecular biology is the requirement of highly perishable imported biochemicals and a variety of plastic and other wares. The research is expensive and strictly time-bound. The other reason could be that the tremendous pace set by the industrial infrastructure created by interested parties in the West can in no way be matched by half-hearted enthusiasms shown by entrepreneurs in the country.

5. NEW THRUST AREAS TO BE PROMOTED

The identification of new thrust areas, as already indicated, has to recognize the following factors:

– Recombinant DNA and the associated technologies have become powerful approaches to study molecular biology.

– While there cannot be much of a compromise in the modern techniques to be used, the systems employed can be totally indigenous and relevant to our societal needs.

– Thrust area is only a listing of areas of relevance and importance but need not be exclusive. Therefore, while a certain percentage of funds (to be decided) may be reserved for thrust areas, perhaps a lesser percentage should also be earmarked for non-thrust areas. It should be made clear that in intellectual pursuit, non-thrust area research is as much valuable as thrust area research, although the latter may attract a greater percentage of total funding.

With this philosophy, the following thrust areas are suggested:

Microbial world

5.1 Molelcular biology of tropical pathogens/parasites
- 5.1.1 Molecular basis of pathogenicity
- 5.1.2 Host-pathogen interaction
- 5.1.3 Genetics of pathogens

5.2 Genetic manipulation of microbes for the production of useful metabolites

5.3 Cell and molecular biology of potentially useful microbes
- 5.3.1 Mycorrhiza/endophytes, cyanobacteria, *Bacillus*, *Streptomyces*
- 5.3.2 Ore leaching bacteria
- 5.3.3 Marine microbes
- 5.3.4 Microbes tolerant of extreme conditions
- 5.3.5 Molecular biology of tropical crop plant viruses
- 5.3.6 Insect viruses
- 5.3.7 Animal viruses causing disease

5.4 DNA transactions.

Plant kingdom

5.5 Cytoplasmic male sterility

5.6 Organelle genetics

5.7 Differentiation in higher plants

5.8 Stress tolerance in plants

5.9 Genetic transformation in plants

5.10 Plant–microbe interaction

5.11 Gene structure and expression

5.12 DNA transactions

Animal kingdom

5.13 Gene structure and expression

5.14 Molecular basis of development and differentiation.
- 5.14.1 Fertility control
- 5.14.2 Fetal development
- 5.14.3 Post-natal development and differentiation
- 5.14.4 Molecular basis of immunity

5.15 Molecular mechanism of transmembrane signalling

5.16 Molecular basis of sex determination

5.17 Gene transformation in animal cells and embryos

5.18 DNA transactions

6. HUMAN RESOURCES DEVELOPMENT

As already indicated, our major concern is the availability of competent manpower. In the light of the largeness of our country and the number and dimensions of problems that can be solved through modern biology and the total amount of scientific manpower available in the country, the lack of a critical mass of competent research groups in the area only reflects a distorted emphasis on manpower development. The often boasted large scientific manpower in the country is actually of inferior quality. The fundamental issue between spread of education among the masses and achieving peaks of excellence has to be solved at the university level. Higher education at the college level has to be exclusively meant for gifted students. While general education should be assured to all segments of society up to say 12th standard, further collegiate education has to be made exclusively on the basis of merit. This is a larger issue and cannot be treated in this document adequately. However, this is a fundamental issue to be kept in mind in terms of approaching the problem of human resource development in any advanced area of science and research.

In the limited context of human resource development in the area of molecular biology the following factors should be recognized:

6.1 Many academic and scientific posts in the area in the country are lying vacant due to the non-availability of suitable candidates.

6.2 The standard of teaching of modern biology in universities is poor, in view of the unfamiliarity of the existing teaching community with current progress in the field.

6.3 Research and laboratory training in the field are of very poor standard, again due to the unfamiliarity of the senior faculty with the present day molecular biology and lack of infrastructure.

6.4 Many state universities have started molecular biology or even biotechnology without adequate preparation in terms of having appropriate faculty and laboratory.

6.5 Bulk of the experimental research done even in National Laboratories and some of the outstanding universities is still only the second best, while the country has always produced at least a few outstanding theoretical groups. This only emphasizes our deficiency in the experimental approach.

Some of the limited and short range solutions to the problem are:

- DST should pool resources with other agencies and start new centres for research in molecular biology in universities in the country. These centres should be built around identified scientists. These centres should be built in not so well known universities, which may still have at least one or two good scientists. An honest search needs be undertaken to identify such individuals and groups, who may not be in the limelight.

- Industries should come forward not only to sponsor research projects in universities, but also fund establishment of new research centres in the university set-up. The universities should receive such proposals with an open mind and facilitate the establishment of such a centre. Competent scientists in industrial set-ups should hold honorary faculty positions in universities.

- Adequate support should be given by the DST to the existing centres/groups that have performed well.

- DST can initiate training associateship programme for scientists in service. There can be two categories one for training within the country and another for training abroad. This scheme appears to be working reasonably well with the Department of Biotechnology.

- Despite the enormous brain drain, still adequate number of well trained Indians have shown interest to return and settle down back home. This group usually consists of young scientists who have spent around 3–5 years abroad. This is also the group most ideal to have back in India. It is necessary for universities to have a mechanism to offer jobs to candidates with good credentials on a priority basis. It should be possible to make a decision within 3 months time. The present procedures adopted in many universities are very slow and good candidates are lost. The second major factor is to create an environment congenial to retain the new comers. This can only be provided with good academic leadership and adequate infrastructure.

- Molecular biology teaching and laboratory at M.Sc. level should be strengthened.

7. NATIONAL FACILITIES REQUIRED

Human resource and infrastructure are essential for progress in research. The subject of human resource development in a limited context has been dealt with earlier. The following suggestions are for infrastructure development:

- The COSIST programme has brought about a qualitative change in research infrastructure in some universities. This programme should be expanded and many more centres and groups should be identified and strengthened.

- Some steps have been taken to liberalize import procedures. It has to be really seen how well the recent liberalizations are implemented. Many times, there is a difference between intention and what is actually implemented in the field.

- Manufacture of biochemicals and research instruments should take place in the country. Best course appears to be to encourage collaborative ventures between Indian and foreign companies, so that the product is manufactured in India.

- The Department of Biotechnology has created several national facilities such as microbial collection centre, centres for animal and plant tissue cultures, bioinformatics and is in the process of creating national facilities for oligonucleotide and peptide synthesis. These facilities will have a direct impact on the quality of molecular biology research in the country. It has to be seen as to how well these national facilities are able to contribute to the growth of molecular biology in the country. Everything should be done to facilitate the optimum performance of these national facilities.

8. OTHER SUGGESTIONS

The following general issues also need to be considered.

8.1 Funding by research agencies in isolation is a serious lacuna. Many agencies are funding similar areas of research. Integration has been talked about, but very little has been done in practise. In the field of molecular biology, a beginning can be made by integrating the efforts of the Department of Biotechnology and DST to start with, perhaps, projects, specialized centres/units, training programmes, Summer/Winter schools, etc. and then a decision made as to which of the two agencies is most appropriate to fund the proposal. In fact, the entire life science programme has to be an integrated effort between DBT and DST, while keeping the overall objectives of the two departments in perspective.

8.2 The PAC mechanism followed at the DST evaluates new proposals and offers mid-course correction to on-going projects. However, no serious analysis and gradation of completed projects take place. This should be made mandatory and the scores obtained in completed projects, should contribute to the decision making process for funding new proposals.

8.3 There is no common evaluation procedure adopted by different PACs. A quantitative scoring procedure should be evolved and decisions made on the basis of the scores obtained by the proposals.

8.4 The large opportunities available at the present time to go abroad for training etc. have led to good and bad results. In many laboratories, even competent scientists tend to carry out the work abroad but do not achieve very much back home and keep waiting for the next trip abroad. While, training in established laboratories in the West is a welcome feature, ultimately Indian science can grow only if things start working in Indian laboratories. Therefore, serious attempts at technology transfer should be made by the individuals who benefit by the exposure. Thus, some kind of monitoring of the laboratories receiving substantial funding from DST is essential. This should include site visits, both for assessing what has been achieved and for sanctioning new major projects, to evaluate the technical competence developed in the laboratories concerned.

MOLECULAR BIOPHYSICS AND BIOCHEMISTRY

1. PREAMBLE

Molecular biophysics and biochemistry forms the foundation for the fundamental and technological advances in the areas of molecular biology, bio-technology and medical physics. Both fields have grown at an extremely fast rate during the past 50 years. The fundamental knowledge about the basis of molecular mechanisms involved in biology started emerging from 1940s and got accelerated with the discovery of molecular structure of proteins and nucleic acids. Our country has picked up these areas at an early stage and the contributions made by Indian scientists in this field are of a very significant nature.

While formulating the thrust area programmes in the two disciplines of biophysics and biochemistry during the Baroda meetings, the activities were divided into various Programme Advisory Committees under the disciplines of physics, chemistry and biology. DST has realized in recent years that the fields of biophysics and biochemistry are intimately connected and such a division of activity may not be advisable in the interest of promoting integrated and interdisciplinary programmes in these overlapping areas. DST therefore took the conscious decision to combine these activities under a common thrust area programme.

2. STATE-OF-THE-ART IN NATIONAL CONTEXT

During the VI and VII Plan Periods, the emphasis of the research programmes had been on enzyme structure and function and conformation of biological molecules. When the VI Plan activities were initiated under the thrust area programme there were very few major facilities to support these activities. Much of the earlier research output was therefore based on good ideas backed by primitive facilities and we were loosing the race with the world. Therefore, the PACs made attempts to create sophisticated facilities and to make Indian scientists aware about the recent trends in these areas through workshops, winter schools, etc. The twin areas received good funding during this period. Money was provided for creating state-of-the-art X-ray facilities at IISc, Bangalore and at the University of Madras, Madras. Another good X-ray diffraction facility for macromolecular study exists at BARC, Bombay which has been built up largely through indigenous efforts. DST also provided funds for creating good NMR facilities at TIFR, Bombay; IISc, Bangalore; CDRI, Lucknow and Bose Institute, Calcutta. For biochemical work, individual researchers were funded so that the basic facilities such as HPLC, centrifuges, etc. are now available in several laboratories. Facilities for tailored DNA and peptide sequences were also made available. In view of the complex nature of these facilities, most of the inputs were made in institutions with good back-up and infrastructural facilities. At the same time, as a result of these investments, we now have expertize and facilities which can be utilized by a more general group of users located in the universities. In particular, it is now possible at least in principal, that small programmes can be funded in the universities without providing major grants for sophisticated instruments and biochemical facilities. As an approach to the VIII Plan, the PAC must encourage such researchers. DST should also ensure that the facilities funded with its money are shared with the users all over the country who have viable research programmes.

3. GAP AREAS

The field of biophysics and biochemistry has blossomed into several new areas which now lie on interface with the emerging trends in biotechnology and bioengineering. Taking this in view, the PAC felt that a major change is required in the structure of programmes which had been identified as thrust areas several years back. PAC also felt that brain storming sessions should be held in the area of protein engineering and protein–DNA interactions. Scientists have been identified to take initiative to organize such sessions. Areas such as biomolecular electronics and protein designing may provide focal themes for future research programmes.

A new interface is developing involving molecular techniques, artificial intelligence and medicine and such areas of medical physics should be encouraged. Examples of the type of problems one is referring to are molecular mechanisms involved in the process of sleep, fatigue, pain, animal behaviour, learning, etc. Such studies have been made possible because of recent developments for monitoring molecular levels through *in vivo* techniques and image reconstruction. Research in these fields requires major investments and bringing together expertize in the fields of molecular, computer and medical sciences working towards a common goal. Since such an area cannot be developed under the present scheme of TAP (funding to individual scientists or a group of collaborators on a fixed time basis), it has been included as a separate item in the list. It is an ideal subject to be looked into by DST and ICMR under the scheme of Intensification of Research in High Priority Areas. The inputs made at this stage can put us in the forefront of this field and can bring a new revolution in health care as well as development in future design of computers based on information gained from nonlinear neural networks.

We can take pride in the fact that in certain areas our research is on the frontline and that we are running the race with the world. However, we should not forget that in most cases we are following the science initiated by scientists in western countries. Even in cases where ideas originate in our own country we soon loose the race because the ideas are picked up by scientists with better resources. One of the things that is lacking in our research is an interdisciplinary approach and sharing of our limited resources and expertize to achieve a concerted and common goal. The areas under discussion require knowledge at the level of physics, chemistry, biology, computer sciences and mathematics. It will be difficult to make a dent unless Indian scientists with various strength can get together and work towards common goals.

4. NEW THRUST AREAS

4.1 Membranes and model systems
4.2 Bioenergetics
4.3 Biochemical evolution
4.4 Molecular structure, interactions and recognition in biological systems
4.5 Protein engineering: (site-direct mutagenesis, cloning and designer proteins)

4.6 Biomolecular electronics
4.7 Catalytic antibodies
4.8 Enzyme structure and function
4.9 Molecular mechanics and dynamics
4.10 Molecular mechanisms of perception and communicaiton (chemoreceptions, cell surface recognition, drug receptor interaction).

5. Important area which may be supported under IRHPA.

Medical physics (details as outlined above).

PLANT SCIENCES

PREAMBLE

As primary producers of renewable resources that provide the basic needs of humans and domestic animals and a variety of raw materials for industry, green plants will continue to be pivotal for our civilization. The full potential of plants and microbes has only been marginally realized. Basic scientific knowledge and its application will have to be pressed into service effectively to mitigate poverty, meet the country's requirements of food, feed, clothing, rural energy and also sustain the rich plant diversity, prevent eco-degradation, recover wastelands and ensure biological conservation. The well-established methods of genetic improvement of plants and microbes need to be speeded by the application of genetic engineering and biotechnology.

A perusal of the Thrust Area Programmes in Life Sciences emanating from the Baroda Seminar shows that it did not identify any aspect of Plant Sciences including microbiology in the area of basic Life Sciences.

However, the following areas were recognized under Applied Biological Sciences.

- Microbial productivity
- Microbial genetics
- Improved strains for fermentation
- Microbial transformation
- Useful biochemicals and micro-organisms
- Biomass as a source of energy
- Fast growing plants
- Biological fuel cells
- Biogas
- Production of alcohol
- Physiology and biochemistry of plants
- Photosynthesis (including photorespiration)
- Nitrogen fixation
- Improved plant proteins
- Protection of endangered species and preservation of genetic diversity of living organisms
- Ecological balance for sustainable utilization of biological resources
- Forests
- Grazing lands
- Cell and tissue culture
- Somatic cell hybridization.

In this list, those areas which pertained to environment were transferred to the newly created Department of Environment.

The programme advisory committee reiterates that excellent and innovative basic research in plant and microbial sciences must be supported by DST in keeping with its past tradition. Nevertheless, certain areas of work which are either relevant to national needs or would fill the present lacunae must be recognized as thrust areas.

In some of the thrust areas multidisciplinary groups should be organized at three or four centres, which should have the potential to become leading research groups in the world. Research in areas such as DNA sequencing in plant mitochondria, chloroplasts and nuclear fragments and study of stress due to water, disease and salt is of such magnitude that a small group working in isolation can make very little progress. It is essential to have collaboration of specialists in biochemistry, membrane biology, plant genetics and rDNA technology. Three or four thrust areas and a few research groups should be identified and a long term (5–10 years) programme initiated. The work of the different centres may be reviewed periodically and the programmes suitably revised in the light of recent developments. Interaction with foreign groups may also be needed in some areas. DST has provision for supporting units and core groups. However, thrust should be given to inter-disciplinary and inter-institutional research on a long term basis. Whereas good work is being done by a few research groups working in isolation, the results have not been commensurate with the talents and facilities available in the country.

It is to be recognized that plant scientists have had a long and rich tradition of research in this country and that they constitute a very large proportion of biologists in India. The list of thrust areas may appear long but it is realistic, considering their basic and applied value in the national context.

2. STATE-OF-THE-ART IN NATIONAL CONTEXT

2.1 Photosynthesis

Extensive work has already been done globally on photosynthesis at the whole plant level. The biochemistry of photosynthesis, environmental effects on photosynthetic carbon dioxide fixation, the relationship between the electron transport capacity and carbon dioxide assimilation rates have been extensively studied. However, it is still obscure how the primary processes in photosynthesis which are ultra fast reactions in the range of femto to pico seconds are controlled. Studies on the genetic regulation of these events by the modification of structure of photosynthetic apparatus is now basically required to be studied.

The conversion of light energy into chemical energy during photosynthesis can be fully understood only when the molecular architecture of the photosynthetic pigment molecules in the membrane is known. The energy absorbed by the pigment proteins is efficiently transferred to the reaction centres of either photosystem I or photosystem II. These multimolecular complexes have been partially characterized by their structural and functional association within a specific photosystem. It is still not clear how the isolated chlorophyll protein complexes are connected with the LHCs *in vivo* to produce photosynthetic units. We do not yet know how many apoprotein molecules are assembled with each other (and with chlorophyll *a* and *b*) to form the LHCs in the thylakoid membranes. Though the structure of pigment complexes in green plants has been moderately established (particularly of LHC II), no crystals suitable for high resolution X-ray analysis have been reported so far for any plant pigment-protein. The oxygen evolving complex has not been totally isolated and its arrangement in the membrane has not yet been delineated.

2.2 Nitrogen fixation

Various aspects of nitrogen fixation have been studied at the Bhabha Atomic Research Centre, Banaras Hindu University and a few other institutes. Work done at BARC has shown that: (i) heterocysts lack phycobiliprotein and PS-II activity; (ii) heterocyst development correlates with nitrogenase activity; (iii) heterocyst is the main site of nitrogen fixation; (iv) sodium is required for nitrogenase activity but not for its synthesis; (v) prolonged incubation of cultures with acetylene brings about conformational changes in the nitrogenase polypeptid; and (vi) glutamine synthetase and glutamate synthetase are the main ammonia assimilating enzymes in cyanobacteria.

Recently, scientists at BARC have successfully cloned *nif* genes both from heterocystous and non-heterocystous cyanobacteria. The major contributions from BHU and Hyderabad have been in understanding the mechanism governing heterocyst differentiation and nitrogenase synthesis. Ammonia *per se* is not the regulator of heterocyst differentiation or nitrogenase activity. Employing amino acid analogues and *nif* mutants it has been shown that glutamine regulates heterocyst differentiation. Glutamine is also involved in maintaining the spacing pattern of heterocysts. Possible linkage between nitrate reductase and nitrogenase has also been suggested. The effects of various physical and chemical factors (e.g. herbicides, nitrogenous fertilizers, growth inhibitors) have been studied on diverse nitrogen fixing cyanobacteria. The symbiotic cyanobacterium *Anabaena azollae* has been isolated and it has been suggested that both morphological and physiological changes occur in the symbiont when it is freed from the host.

Blue-green algae are the only organisms in which the otherwise incompatible processes of nitrogen fixation and photosynthesis occur together in the same filaments.

2.3 Tissue culture

Plant tissue culture research in India was initiated 30 years ago primarily with the objective of using it as a technique for understanding problems related to reproduction in flowering plants. India has carved for itself a place in the international sphere for its basic contributions to *in vitro* pollination and fertilization, production of androgenic haploids and triploid, etc.

Work done in India has stimulated research in several laboratories around the world although in our own country, we have not been able to realize its potential optimally. However, in the past decade there are indications of taking the technique to the level of technology especially in the micropropagation of elite economic plants such as oil-seed crops, legumes, timber and fire wood crops and medicinal and aromatic plants.

One of the main reasons for the slow pace of progress in the full utilization of plant tissue culture is lack of orchestration and interdisciplinary approach to solving specific goal-oriented problems. The seed money grants made to several individuals and groups have resulted in research activities that have given us the confidence to make important dents in agriculture and forestry. The country has produced a critical mass of trained human power to take up the challenges.

2.4 *Microbial productivity*

The country has not made sufficient progress in microbial productivity either in developing efficient microbes or in improving the engineering. Microbial productivity in India is largely centred on production of antibiotics and yeast. Even in these, our yields are below the international standards.

Projects in the thrust area were few and have been unsatisfactory. Thus in this most important area funding has been negligible.

A critical review of the national industries in this area has shown that there is a tendency to maintain *status quo* in terms of production or import of improved strains and adopt them to out dated machinery. This has failed to increase productivity. Bulk production may have gone up, but the unit input cost has not come down.

3. NEW THRUST AREAS

3.1 Reproductive biology
3.2 Differentiation, development and hormones
3.3 Genetics and plant molecular biology
3.4 Biology of stress
3.5 Photosynthesis and photobiology
3.6 Biology of trees
3.7 Plant pathology
3.8 Microbiology.

3.1 *Reproductive biology*

Indian scientists have made significant contributions to descriptive, comparative and phylogenetic aspects of plant embryology. In fact they can be considered as leaders in the world literature in these areas. However, in terms of basic knowledge needed for improvement, utilization and conservation of plants of high economic value, our efforts have been rather minimal. Recognizing the expertize already available within the country, the PAC recommends that the following aspects may be supported:

3.1.1 Pollination biology, especially of forestry species and other economically valuable perennials

3.1.2 Pollen–pistil recognition and interaction

3.1.3 Isolation of male gametes of flowering plants and their use as tools in biotechnology

3.1.4 Regeneration of isolated plant cells and protoplasts following genetic transformation

3.1.5 Molecular and biochemical mechanisms of male sterility, apomixis and somatic embryogenesis

3.1.6 Storage of pollen as gene banks

3.1.7 Biology of seed set, biochemical aspects of seed protein storage, seed viability and germination

3.1.8 Production of artificial seeds (with *Rhizobia* and/or mycorrhizae along with somatic embryos encapsulated with hydrophobic coating)

3.1.9 *In vitro* preservation of germplasm especially of shoot tips or somatic embryos of economic plants with recalcitrant seeds.

3.2 *Differentiation, development and hormones*

The development in multicellular plants involves the formation of several distinct cell types, tissues and organs in a precise time-phased manner at specific locations. The cells of the apical meristems are known to retain the embryonic nature permanently. However, in many plants even the fully differentiated cells upon culture in an artificial medium can be made to divide and develop into whole plants. This reversibility of commitment makes it possible to regenerate and multiply plants through tissue culture and other means. Such systems are also invaluable for understanding the basic features of plant cell differentiation. The overall plant development is regulated by hormones, nutrients, environmental factors such as light and temperature.

The following areas need thrust:

3.2.1 Analysis of cell lineages, developmental commitments and role of genes in development

3.2.2 Hormonal regulation of development and differentiation, temporal and spatial variations in hormones, signal transduction during hormone action, regulation of transcription and translation. Role of calcium.

3.3 *Genetics and plant molecular biology*

Plant genetics and breeding have contributed a great deal towards making the country self-sufficient in food production; increasing export of agricultural produce or products of agro-based industries and contributing to the rural economy.

The overall contribution of genetics to the national economy is far greater than that of any other discipline in plant sciences. Increased investment in research in this discipline can bring even greater returns.

The promise and potential of plant biotechnology is based on the use of cell culture and molecular biology techniques to produce plants that have enhanced consumer (such as improved nutrition) or value added agronomic qualities. These accomplishments have been achieved not in major crop species but in model systems such as *Petunia*, tobacco, tomato, etc. which are easy to manipulate.

The first products of biotechnology concern viruses and bacteria. Unfortunately, no major crop species or plant products improved or produced by biotechnology are yet available.

The following thrust areas are identified:

3.3.1 Genome organization of a few selected cereals, pulses, oil seeds and forest trees

3.3.2 Identification, cloning, horizontal transfer, regulation and expression of useful genes

3.3.3 Genetic and molecular basis of compatible (susceptible) and incompatible (resistant) interactions between plants and pathogens, insects and symbionts

3.3.4 Genetic and molecular basis of resistance to abiotic stresses.

3.4 *Biology of stress*

With increasing human and live stock population, there is an ever increasing demand to produce more on limited cultivable land area as well as to utilize wastelands. In addition to the need to understand how crops adapt themselves to low moisture, flooding, high salinity and other soil stresses, there is an urgent need to probe into the mechanism of tolerance to heat, cold, salinity, alkalinity, etc. Special attention needs to be given to:

3.4.1 Molecular mechanisms that regulate water and salt stress

3.4.2 Adaptation to salinity and alkalinity

3.4.3 Isolation and utilization of *Rhizobia* tolerant to stresses

3.4.4 Genotypic responses and screening for water stress in pulses, oil-seeds and tree species.

3.5 *Photosynthesis and photobiology*

Photobiology is an interdisciplinary science which has undergone remarkable advancement during the past few years. The chemical evolution of the light absorbing pigments such as chlorophylls and carotenoids has led to the harvesting of solar energy and transforming it into chemical energy. Photosynthesis results in the production of high energy organic compounds (biomass) from low energy precursors. The photoautotrophic organisms have an ecological advantage over chemosynthetic organisms since the solar energy is available in a virtually unlimited supply. In addition to energy fixation, plants use light for a wide range of complex sensory processes. The necessity for photo orientation is obvious in photosynthetic organisms which depend on the availability of radiation.

The following areas in photobiology require thrust:

3.5.1 Isolation and sequencing of genes encoding PS subunits

3.5.2 Elucidation of the three-dimensional structure of the functional macromolecular complexes in the thylakoids of the photosynthetic apparatus

3.5.3 Genetic engineering of chloroplasts (chloroplast transformation) for improving yields and conferring herbicide resistance

3.5.4 Study of unclear-coded genes for chloroplast polypeptides

3.5.5 Understanding of the regulation of activity of RUBP carboxylase

3.5.6 Steric configuration of phytochrome

3.5.7 Molecular basis of photomorphogenesis

3.5.8 Photomorphogenesis of mitochondria.

3.6 *Biology of trees*

Tree biology research useful for afforestation is important to meet the needs of national programmes of social forestry, timber production, wasteland afforestation, water-shed afforestation and fuelwood and fodder production. Although India possesses an array of tree species uniquely useful for different purposes, we have very little information on their biology. As in other parts of the world, India can benefit enormously by modern approaches for improving, identifying, modifying and regulating tree species.

The following areas need support:

3.6.1 Forest genetics and tree improvement

a) Screening of genetic variation of wild tree species
b) Identification of chromosome races and multiplication of triploid trees for fast growth and higher productivity
c) Selection of provenances, race and plus trees to be subjected to site-performance evaluation, followed by progeny tests and advanced generation, selective breeding and hybridization
d) Reproductive biology of selected trees
e) Broadening of the genetic base through indigenous and exotic material and evolving procedures for utilization of hybrid vigour.

3.6.2 Tree physiology

a) Physiological aspects of juvenility and maturity
b) Flowering, fruiting and seed development
c) Seed viability, dormancy and germination
d) Storage of recalcitrant seeds
e) Vegetative propagation with special reference to hard-to-root plants
f) Micropropagation of elite trees
g) Photosynthesis and biomass production
h) Growth under stress conditions with special reference to physiology of roots
i) Nitrogen fixation in trees in symbiotic association with rhizobia and actinomycetes
j) Mechanism of mycorrhizal-tree association and its economic utilization
k) Ultra-structural and physiological aspects of cambial activity, wood and bark production
l) Enhancement of secondary metabolite production—especially rubber, gums and resins by growth regulator application.

3.6.3 Tree pathology and protection

3.6.4 Application of biotechnology and tree improvement.

3.7 *Plant pathology*

The basic and applied aspects of plant pathogen interactions have received much attention by scientists the world over. For a predominently agricultural country such as India, plant protection is crucial in crop productivity.

Biological control of plant pathogens is an area in which very little work has been done in the country. The technologies developed in the recent years have demonstrated good potential for the biological control of bacterial and fungal diseases. Programmes on the biological control of important diseases should be strengthened.

In the area of physiological plant pathology, limited information is available on the processes of infection, role of various enzymes and defence mechanisms in plants in relation to plant diseases common in India. These studies require close collaboration among pathologists, physiologists, geneticists and biochemists.

A few aspects which need urgent attention are summarized below:

3.7.1 Plant–microbe–viral interactions

3.7.2 Associative symbiosis for enhanced plant growth (*Frankia*), Pseudomonads, etc.

3.7.3 Biological pest control (excluding work on *Bacillus thuringensis* toxin)—Emphasis on baculoviruses, fungal pathogens of pests, pheromones.

3.7.4 Monoclonal antibodies for detecting, monitoring and effective management of plant diseases.

3.8 *Microbiology*

Realizing that five years from now genetically engineered strains could be used for microbial productivity, it is important to support research in microbial biomass. A complete new strategy has to be worked out. A dialogue with industry will be needed.

The following areas need thrust:

3.8.1 Plant growth regulators of microbial origin

3.8.2 Enzymatic processes for chemical technology reactions and newer process developments (e.g. indigo, arachidonic acid, etc.)

3.8.3 Enzymes for detoxification of major chemical pollutants, pesticides, insecticides, etc.

3.8.4 Enzymes for paper, leather and other commodity industry applications

3.8.5 Enzyme reactions in organic solvents

3.8.6 Synthetic enzymes

3.8.7 Enzymatic, immunological and recombinant DNA methods for disease diagnosis-clinical enzymes and diagnostic kits.

3.8.8 Screening for anti-inflammatory, anti-cholesteremic, anti-parasitic compounds from microbes, new immunosuppressants, etc.

4. HUMAN RESOURCES DEVELOPMENT

4.1 Training and refresher courses in the following areas may be held periodically:

4.1.1 Plant molecular biology and genetic engineering

4.1.2 Plant protoplast isolation, regeneration and transformation

4.1.3 Use of computer software for DNA and protein studies, literature retrieval and statistical analyses

4.1.4 Techniques of plant virology

4.1.5 Environmental toxicology

4.1.6 Environmental impact analyses.

4.2 The syllabi for plant sciences require revision to incorporate recent advances. A committee of experts may be formed in collaboration with UGC to revise the syllabi.

4.3 An integrated B-Tech. programme in microbial engineering (4 years duration after 10+2 years of schooling) must be started.

5. NATIONAL FACILITIES REQUIRED

The following national facilities are needed for rapid progress in several areas of plant sciences:

5.1 Plant hormone assays: A national facility for assay of phytohormones (auxins, cytokinins, gibberellic acid, abscisic acid, ethylene) is required. These hormones play a basic role in cell growth and differentiation and in several cell processes. Sensitive methods based on radio-immunoassay or Elisa, HPLC and gas chromotography are used for their determination which are not available to most research workers. A national facility where the analyses of these hormones can be undertaken will be invaluable.

5.2 Collection and assay of plant viruses: The number of plant viruses of economic importance is very large. A centre for maintaining a collection of viruses and sera banks and monoclonal antibodies for virus assays would greatly extend the scope of research in this important area.

5.3 Controlled environment growth chambers: At many centres of research, work on a particular plant species is seasonal and progress is, therefore, very slow. The availability of controlled environment growth chambers would facilitate the growth of these species throughout the year. The imported growth chambers are very expensive. Research on indigenous production of these chambers should receive high priority. A committee may be formed to make recommendations for planning indigenous production of these chambers.

5.4 Chemicals, enzymes and equipment for research: Several special biochemicals, restriction endonucleases and other enzymes and equipment such as millipore filters, etc. are needed for research. They are presently imported through the CSIR Centre for Biochemicals, but indigenous production and ready availability of these items will be very useful for research.

5.5 Computer software: Research on DNA and protein structure and statistical analyses require software for which DBT is establishing a national network. The provision of computers to different research groups for integration into the network for literature and for use of the software is required.

5.6 Long term ecological studies: At least one site in each biome including agricultural ecosystems, should be made available for long term biological studies. They should be equipped with a field laboratory and skeleton staff.

5.7 Microelement analysis: A national facility equipped with atomic absorption spectrometer/X-ray fluorescence analyser for rapid determination of micronutrients is needed for many projects. Though there are a few centres which carry out these analyses, especially on elements such as iron, molybdenum, manganese and zinc, there are often long delays in carrying out these analyses. Facilities for analysis of other elements such as cobalt, nickel, selenium and fluoride are also needed.

5.8 A national laboratory entrusted with the exclusive study of antibiotic producing strains must be set up. For another 50 years to come microbial antibiotics will be still needed in India inspite of the availability of antibiotics and synthesis.

ANIMAL BEHAVIOUR, ECOLOGY AND EVOLUTION

1. PREAMBLE

ETHOLOGY, the scientific study of animal behaviour, is relatively a recent field of animal sciences integrating animal ecology, neurophysiology endocrinology, sensory physiology and several other fields. Behavioural studies, in the country, have been essentially confined to only a few animal groups in spite of the fact that we in India have the great fortune of having access to a tremendous diversity of plants and animals, notable among which are many groups of insects, birds, primates and human societies which are uniquely suited for modern investigations in ethology and sociobiology. This fact is widely recognized in our country, but this resource is hardly utilized. On the other hand there is a great deal of interest among western scientists to come to India to take advantage of these valuable biological materials. Given a well planned programme, we have an excellent chance of providing international leadership in this area.

2. STATE-OF-THE-ART IN NATIONAL CONTEXT

Behavioural studies in this country have been essentially confined to such principal areas as primatology involving non-human primate behaviour, behavioural dynamics of rodents, migratory behaviour of birds as well as reproductive behaviour of some fishes in relation to endocrine control of reproduction. In addition, in recent years some work has been done on circadian rhythms in bats and to a limited degree on the chelonian and crocodilian behaviour. Compared to information on the behaviour of vertebrates, that on invertebrates is restricted mostly to arthropods. An outline of the current status of research on ecobehaviour and evolution is indicated below.

2.1 Behavioural studies

2.1.1 Vertebrates

– Behavioural ecology of wildlife

Investigations in this particular field have been carried out on such animals as elephant, rhinoceros, lion, tiger, antelopes, etc. with reference to their territorial behaviour, predation, parental care, defensive behaviour, etc. The newly-established Wildlife Institute of India (Dehra Dun), has come up with excellent programmes to study the behaviour and ecology of several species in relation to their habitat.

– Behaviour of non-human primates

Stúdies relating to the behaviour of non-human primates including their sociobiological aspects, territoriality and parental care have been extensively carried out by such centres as the Zoological Survey of India, the University of Jodhpur (Department of Anthropology), Delhi University, Aligarh Muslim University, Meerut University, and at a number of other centres.

– Rodent behaviour

Studies on the socio-ecology of desert rodents are in vogue for the last 30 years at the Central Arid Zone Research Institute (Jodhpur), and on rodents of economic importance to agriculture at 10 centres in India under the ICAR All India Coordinated Project on Rodent Pests. Some work was taken up on the ecology and reproductive behaviour of murids under a DST-funded project at the Garhwal University. Besides considerable work on the ecology of bandicoots and other species has been carried out at the Zoological Survey of India; Haffkine Institute (Bombay), Department of Entomology (Kanpur). Besides, relatively a new field of ethology, the olfactory communication among rodents, is being carried out at BHU (Varanasi), CAZRI (Jodhpur) and at University of Kerala (Trivandrum).

– Circadian rhythm in bats

Much attention has been paid in recent years to the study of the circadian rhythms in bats by the Madurai Kamaraj University (Madurai).

– Behaviour of birds

Extensive investigations have been carried out on the migratory behaviour of birds, their nesting behaviour, parental care, feeding behaviour by the scientists of the Bombay Natural History Society and the Zoological Survey of India, and that of several universities.

– Chelonians and crocodilians

Investigations on the egg laying, feeding, parental care, and captive breeding of chelonians and crocodilians have been made by some of the university centres and Wildlife Institute of India.

– Fishes

The reproductive behaviour of fishes has been investigated in relation to their schooling behaviour, spawning and parental care, by the Inland Fisheries Research Institute, Centre of Advance Studies in Marine Biology (Portonovo), besides other universities.

2.1.2 Invertebrates

The various aspects of invertebrate behaviour investigated in this country are broadly outlined.

– Helminths

– Behavioural ecology of helminths

– Annelids

– Swarming behaviour in polychaetes

– Earthworm behaviour in relation to vermiculture

– Arthropods

– Crustaceans: Crustacean behaviour in relation to their feeding and reproduction, tidal cycles and lunar rhythms of ecology of crustacean parasites.

– Arachids: Behaviour of ticks and mites in relation to their vector potential, web spinning behaviour in spiders

– Molluscs: Oyster, mussel and clam culture and setting behaviour

– Insects.

(i) Feeding behaviour of phytophagous, predatory and parasitic insects

– Host searching and host selection behaviour

– Feeding rhythm of larval and adult insects

– Feeding behaviour of mosquitoes in relation to disease eradication programmes

– Behaviour of parasitoids in relation to host selection

(ii) Distributional pattern

– Vertical horizontal distribution, behavioural ecology of insect communities

– Sociobiological aspects of Hymenoptera

(iii) Courtship behaviour

– Endocrine control of reproductive behaviour.

(iv) Foraging behaviour of pollinators. Energy expenditure in foraging and the role of behavioural studies in pollination.

3. INTERNATIONAL STATUS

4. GAP AREAS

4.1 Biosystematics: Expertize in taxonomy/biosystematics of certain group of taxa is extremely limited within the country specially reckoning the great diversity of fauna and flora occurring in the Indian sub-continent. Researches in biosystematics need to be strengthened, a database should be prepared on the information already available but scattered and therefore, not useful in the decision making process. Attempts should be made to create a National Identification Centre with special reference to insects.

4.2 Behavioural models: Studies on diverse aspects of animal behaviour, ecology and evolutionary aspects have assumed interdisciplinary proportions calling for indepth investigations. From the point of view of animal behaviour, of several emerging areas of considerable relevance some are behavioural rhythms in various animals and plants, the formulation of flow chart or behavioural models of several species of economic importance more particularly among insects, integrated approaches to behaviour through behavioural manipulation as well as through neurophysiological and neurochemical studies. From an ecological angle diverse aspects dealing with mountain ecology, insect–plant interactions in terms of chemical ecology as well as energy flow in ecosystems populations as well as through the individual life cycles, are emerging areas for taking up research. Needless to mention, the reptiles and mammals of north-east India deserve indepth studies from an ecobehavioural viewpoint.

4.3 Evolutionary approach: Evolutionary approaches are interlinked with ecobehavioural studies and an understanding of the various adaptive strategies adopted by diverse groups of organisms in their efforts for survival go a long way in our understanding of this integrated area of research. In this connection, the evolution of reproduction in animals and plants in terms of the photoperiodic and hormonal basis as well as the evolution of feeding behaviour, more particularly in animals with varying habits such as evolution of predation, evolution of parasitism, etc. are areas wherein more information is needed. The interlinking of ecology with physiology (ecophysiology) and ecology with behaviour (ecobehaviour) further highlights the need for investigations on such areas as stress physiology, neurotoxicology and reproductive physiology.

4.4 Marine science: There is a plethora of ecologically interesting, physiologically significant, economically important and potentially useful organisms in the marine environment. Although the detailed study of these several forms will take a very long time, there are some areas in which research can be encouraged right away so that benefits may accrue in another 5–10 years. Among these areas some of the most rewarding are also the most basic. For example, culture of marine forms has never really been developed in this country. Although ecological statements have been made on trophic level interactions, the dietary habits of the several herbivores and carnivores have not been systematically studied. Neither grazing rates nor respiration rates can be measured unless the species is in monospecific culture. Similarly prey recognition, specially for species that are raptorial feeders or avoidance/rejection by filter feeders have not been investigated. Conditions that control spawning have been deduced from environmental studies, they have not been meticulously investigated in controlled conditions. All of these studies require to be done before attempting ecologically valid predictive models.

4.5 Soil biology and fertility: At a general level this project envisages comparative analysis of natural and man-made agroecosystems at a given site with a view to understand: (a) nutrient cycling patterns, (b) nutrient budget in biomass and soils, (c) litter decomposition patterns through soil animals and soil micro-organisms and even (d) soil fertility recovery during succession if habitat types are available. The objective has to incorporate biological processes into soil fertility maintenance in agroecosystems. This may take the form of mixed cropping, agroforestry concepts, earthworm culture being incorporated on the basis of studies on natural systems.

At a specific level the study may involve field studies on biological nitrogen fixation, earthworm biology and nutrient cycling through vermiculture, potassium or phosphorus fertility maintenance, etc.

This is an area relevant to agriculture and yet is not a concern of agricultural scientists. Nutrient release on surface soil layers through no-till agriculture which is being investigated now, for e.g. imitates natural systems in terms of nutrient release on the surface soil through litter fall.

4.6 Ecology of biological invasion: A variety of questions could be asked related to biological invasion by exotics in our terrestrial and freshwater ecosystems.

- What are the factors contributing to invasion?
- Could invasion occur in intact ecosystems or perturbations critical for invasion to occur?
- What are the ecosystem level consequences at the structural and functional levels of the ecosystem?
- What are the social and biological impacts of invasion?
- What are the social and biological consequences of possible control measures?

The answer to these questions and many others is important for managing our natural ecosystems that are being more and more altered by biological invasions altering biological diversity and even affecting productivity of our land and water resources.

4.7 Ecology of succession: Studies on the ecological succession on a variety of habitats like coastal, desert, forest, montane, wetland ecosystems and a host of others appear to be essential not only to understand the resource potential but also for a better idea of the different types of interaction among the biota.

4.8 Behaviour and survival of sympatric species in different ecological conditions: Species complexes are of common occurrence. Within a taxon, sibling species are known to exhibit biological differences with reference to their role in disease transmission, responses to insecticides, preferences to feed on the blood of man and their distribution in space and time.

The sibling species which are morphologically alike have specific ecological preferences thereby resulting in a specific distribution pattern in nature. Further, within a given ecosystem, they may have specific niche preferences with reference to breeding and resting. Knowledge of the environmental conditions which promote the existence and proliferation of such sibling species is essential and is particularly recommended for those taxa which are medically and economically important, in order to plan suitable control strategies.

The sibling species maintain a total reproductive isolation in nature even though they have been found to exist sympatrically. Further, in many extensively studied members of anopheline species, it has been well established that mechanical, seasonal and habitat isolation are not the reasons for their isolation suggesting that ethological barrier may be the major factor operating in mate recognition systems.

However, these mate recognition systems breakdown between some members of the group leading to the production of hybrids between the sibling species. In specific cases, this breakdown could lead to the mixing of genes responsible for disease transmission thereby converting a non vector eventually to a vector. In view of this, it is felt that studies should be undertaken to identify behaviour aspects responsible for their isolation and the environmental factors responsible for their breakdown.

5. NEW THRUST AREAS

Some of the important aspects of animal behaviour and ecology on which immediate research is required are:

5.1 Biological rhythms
5.2 Olfactory behaviour and pheromonal interactions
5.3 Sociobiology
5.4 Behaviour of polymorphic/sibling/sympatric species
5.5 Biological diversity
5.6 Population ecology and genetics
5.7 Succession and community dynamics
5.8 Animal–plant relationship including pollination biology and cecidology
5.9 Ecosystem energetics
5.10 Ecology of biological invasions
5.11 Predation and parasitism
5.12 Pedobiology
5.13 Evolutionary and adaptive strategies

6. HUMAN RESOURCES DEVELOPMENT

6.1 *Summer/winter schools*

To invite attention of senior as well as young scientists in India to take up research on animal behaviour, there is an urgent need of organizing summer/winter schools in specialized areas for a period of 2–3 weeks with a stress on methodologies which should be adopted for taking up research in the area of animal behaviour, ecology and evolution. To start with, experienced scientists may be identified to organize such summer/winter school in the general disciplines of

- Behavioural ecology
- Ethology and sociobiology
- Community ecology
- Vertebrate behaviour.

7. NATIONAL FACILITIES REQUIRED

7.1 *Centres for behavioural Research*

To minimise ad hocism in research, DST can identify 'DST Centres for Behavioural Research' in which ethological research can be supported on a long term or permanent basis with respect to staff and contingent grants.

7.2 *Five-Year Programmes*

To further intensify research within the thrust areas, it is suggested that certain themes should be selected for supporting projects during the next five years. These could be:

(a) Ecosystem/habitat based (ecology and behaviour of fauna of rainforest)

OR

(b) Region-based (ecology and behaviour of vanishing bird species in the Indian desert).

8. OTHER SUGGESTIONS

A fairly large number of projects (all of which do not fall strictly under purview of animal behaviour) have been financially supported by DST. As a consequence, field data and comparative studies have accumulated at an impressive rate. However a number of questions have been raised:

– Have we contributed to some new concepts/theories pertaining to animal behaviour, ecology and evolution?

– Have we developed new techniques?

– Have we created an impact at a national and international level?

– Have we trained enough young research workers to take up work on animal behaviour, ecology and evolution?

In my opinion, a spontaneous reply to all the above questions would be: not much.

Why not, what are the major constraints that these important disciplines of life sciences are not getting attention of the research workers in our country. Why are scientists not interested in carrying out work which can strictly be categorized as that on animal behaviour.

8.1 Project tenure

There are a number of practical difficulties with university/institute scientists to take up actual behavioural work whether it is to be carried out in laboratory, semi natural conditions or in the field. Besides teaching very little time is left with a university teacher to take up extensive field work. There is always a paucity of funds to establish enclosures for ethological work and there is no vehicular facility for undertaking a project the tenure of which is 3–4 years. In fact, it takes 10–15 months to get the staff appointed and for the purchase of equipments. By the time the real work starts, the project tenure comes to an end. Moreover, at present the state of affairs is that when after 3 years, the scientist submits another project on similar lines either to DST or to the Department of Environment or to UGC/ICMR, ICAR so that his work is continued on a permanent basis, more often, this effort does not succeed or there is a gap of one or two years between sanctioning of the two projects from the same source or from different agencies. As such, the research work continues of an adhoc basis or is aimed at getting PhD degrees to students. Consequently, no relevant continuation of the major theme is maintained. With a view to make the DST support to research more purposeful, the projects should be sanctioned for period of 5 years with a provision of extension of 2–3 years.

8.2 Project monitoring

Every project should be strongly monitored/evaluated every year by a senior scientist or an adviser on the report of whom funds for the next year should be released. There should be an in-built system within the project of providing funds for his/her travel etc.

8.3 Data bank

The annual final report of the projects financed by DST are usually lost as cyclostyled/mimeographed matters and the data contained therein are not usually available to other scientists. It is, therefore, suggested that:

(a) A data bank should be established either by DST or with national institute(s) where all the data emanating out of the DST-supported projects should be deposited. It should be a binding on the principal investigator to compile data in a set proforma for depositing it in this bank. A request can be made to a competent (or to a group of) bio-statistician(s) to generate such a proforma which may satiate needs of projects of varied nature.

(b) An executive summary of the final report, preferably incorporating basic data, should be submitted by the PI in a printed form. Funds for printing this abridged final report (about 20 pages) should be provided within the project. Printed copies could be sent to all conventional/agricultural universities/research institutes and to important libraries in the country and abroad.

8.4 Duplication of support

Some mechanism has to be developed so that the overlap/duplication of financial support by different agencies to the same/similar project to the same principal investigator or to his colleague in the same department could be minimized.

IMPORTANT AREAS OF RESEARCH

Vertebrates

1. Pheromonal interaction among fishes, amphibians and reptiles in sex recognition, migration, alarm responses
2. Chemical communication among mammals
3. Influence of habitat type on vertebrate mating systems
4. Behavioural changes in relation to population cycles in rodents
5. Evolutionary strategies in relation to mating in reptiles
6. Sociobiology of smaller carnivores, primates and their translocation.

Invertebrates

A. Behavioural ecology

1. Theoretical and field studies of social insects with a view to understanding the evolution of social behaviour

2. Pollination ecology
3. Use of behavioural data in developing potential biological control agents
   a. Work on predaceous coccinellids
   b. Investigations into behavioural studies on tachinids with a view to improve their effectiveness as biological control agents
   c. Study of biological factors which effect the success/failure of introduced insects as biological control agents
   d. Knowledge about the interaction between ants and parasites used as control agents
   e. Examination into the interactions between arachnids and insects
4. Behaviour of insect populations with special reference to their migration and diapause
5. Biological response of natural insects populations to pheromones with special understanding to the importance of extreme individuals
6. Qualitative and quantitative behavioural studies of symbolic association between insects and micro-organisms
7. Evolution of host selection behaviour during insect pest-host plant coevolution
8. Sensorial ultrastructure and behavioural diversity in insects
9. Behavioural diversity and food web components in aquatic ecosystem and energetics
10. Soil arthropods their behaviour, and their role as potential elements in trophic chains.

B. Behavioural physiology

1. Insects and behaviour-modifying chemicals
2. Feeding and nutrition in insects
3. Environmental and physiological factors regulating reproductive behaviour of insects
4. An examination into the biochemical changes in the internal milieu associated with feeding and mating drives in insects feeding on blood
5. Ovipositional site attractants of blood-feeding insects
6. Electrophysiological studies to identify receptor specificity and host selection behaviour in insects
7. Neuroendocrinological and exocrine studies of insects:
   a. Effect of hormones on pheromone perception and production in insects
   b. Role of hormones in accessory glands functions and their impact on insect reproduction
   c. Role of hormones in neural activities in insect
   d. Effect of insect hormones on biological activities of related animals like spiders, mites, etc.
   e. Effect of vertebrate hormones on insect life activities
   f. Endocrine rhythms in insects
   g. Importance of kairomones in insect behavioural studies, specially those of insect parasites
   h. Bacterial decomposition of organic matter that result in the production of kairomones leading to alterations in the characteristics of ovipositional sites.

Behavioural energetics

1. Estimation of energy budget of economically important insects, specially social and polymorphic forms and to explore the possibility of manipulation the mechanism(s) of energy allocation in these insects.
2. Energetics of vector insects.

Behavioural genetics

1. Genetics of behaviour especially on feeding rhythms of haematophagous insects.

MEDICAL BIOLOGY

1. Fast changing frontiers of bio-medicine have made tremendous impact on medical research. How to integrate these new developments in our research programmes is a major challenge for medical sciences in India, where major emphasis is still on data collection. While it is of utmost importance to generate reliable information on our disease pattern, simultaneously, it is imperative that modern developments in biology must be increasingly applied as investigative tools. Further, if we have to emerge as leaders, it is essential that we not only work in the front-line areas but our scientists must create new frontiers. This could only be achieved by promoting, in a major way, basic research which is the mother of all scientific discoveries.

2. Unfortunately, our medical research organizations lay very little emphasis on basic research. With the result that for generation of new knowledge, we still continue to depend heavily on the developed world. This is justified in certain quarters, on the

grounds that fundamental research is very costly and, therefore, with our limited resources, we cannot compete with the developed world. Often, the slogan 'no need to re-discover the wheel' is used to justify this approach.

3. As a consequence, the medical research has not made significant inroads either into the management of health affairs or in research in the academic sciences in this country.

4. This attitude, which is detrimental to research in medical biology, must change.

5. This can be corrected only by a well planned effort to promote fundamental research in medicine.

6. In a vast country like India, with enormous problems, it would be desirable to focus attention on a few priority areas to maximize utilization of limited resources.

7. The central theme of this approach paper is to identify the thrust areas in health sciences. Obviously, they would be determined by the prevailing disease pattern. Simultaneously, S & T planning should also be futuristic and, therefore, the changing health scene has to be taken into account. Diseases that are knocking at our doors should not be ignored.

8. Communicable diseases, that have vanished from the 'West', continue to be our dominant killers. They are responsible for high infant mortality, paediatric morbidity and economic loss in adults due to loss of wages. Strategies to control these disorders are by and large well known. Improved nutrition and personal and environmental hygiene hold the key to their control, which is now a more or less a managerial problem that needs little research inputs. However, it is recognized that there are lacunae in our knowledge about the host-parasite interaction and the factors that modulate immune response. A better understanding of the host-parasite interaction would provide clues to evolve strategies for immunodiagnosis as well as production of newer vaccines.

9. Despite tremendous progress in all sectors, continued unabated population growth has upset our economic growth. It is, therefore, felt that all novel approaches aimed at generating information on fertility regulation, and development of new contraceptives should be supported on priority basis.

10. Occurrence of cholera, almost in epidemic form in the capital, indicates the fragility of our health services. However, despite the shortcomings, life expectancy is doubled since independence. Therefore, in the next decade, age-related diseases such as cardio- and cerebro-vascular disorders, cancer and degenerative diseases will be of importance to us.

11. Thrust areas should also include technology-oriented topics such as computer modelling, patch clamp technique, etc.

12. Knowledge about the disease process is tremendously improved as soon as a laboratory model is established. All such efforts would be specially encouraged.

13. These have been the major considerations in suggesting the thrust areas (list enclosed). The list is not all inclusive and would be modified keeping in view the trends of discussions on this approach paper.

14. While recognizing the importance of collecting reliable data on disease pattern, this PAC would primarily like to support new, innovative idea-oriented interdisciplinary investigative projects aimed at understanding disease mechanisms.

15. Projects aimed at merely data collection, case reporting, drug testing, routine clinical and community field research would receive low priority.

16. One of the major challenges in medical biology is the *man-power development*. There are hardly any medical scientists involved in basic research. The main factors are the lack of motivation in most of the physicians, who prefer service and practice-oriented lucrative clinical work and have little aptitude for research. The medical curricula are somewhat outdated and hardly prepare students for a research career. The number of medical colleges have increased by 8 to 10-fold since independence. But in this process the quality has suffered. Majority of our medical colleges lack infrastructure required for basic research. Research is usually done through MD theses and lack depth and long-term perspective. Because of these factors the research culture is often lacking. As a consequence, much of our medical research still centres around mere data collection. Even in this area, unfortunately, little emphasis is paid to proper documentation, biostatistics and epidemiology. The results are not able to often stand the scientific scrutiny. The man-power developments in medical biology would need a change in the attitude and aptitude of our physicians. Teaching curricula, even at the high-school and pre-university levels, will have to be up-dated to include developments in contemporary sciences. Simultaneously, the medical curricula need drastic alterations to train our physicians more as scientists and not only as 'healers'. This is obviously a long-term complex issue.

17. Much could be achieved, even in the prevailing conditions, by promoting collaborative research between medical scientists and basic biologists. Physicians often find themselves somewhat deficient in knowledge about modern biology and, therefore, feel shy of undertaking investigations using newer emerging technologies. On the other hand, the basic scientists, who are equipped with such knowledge, have little appreciation of disease process. As a short-term measure, this imbalance could be removed, to some extent, by supporting workshops, seminars, training programmes, etc. of interdisciplinary nature on disease-oriented modern biology. Topics for such activities would be identified through broad-based consultation with members of different disciplines.

18. Infrastructural facilities: Majority of our medical colleges, and even the universities, are poorly equipped to conduct front-line bio-medical research. To support investigative laboratory-based research, it would be essential to strengthen infrastructural facilities, specially in newly emerging areas, so that the investigators are equipped to use modern technology. As the first step, this PAC recommends that modest infrastructural facilities could be developed in a few medical colleges in different parts of India, specially in the university towns, so that common forum is provided for physicians and biologists to work together.

19. International interaction specially with neighbouring nations: This PAC would like to enlarge the scope of its activities and promote collaborative research, specially with the neighbouring SAARC countries. As the first step, the PAC would like to organize small interdisciplinary group meetings, seminars and training programmes on common bio-medical problems. It is hoped that such activities would provide meeting ground for bio-medical scientists of the neighbouring countries and enable them to identify and organize collaborative research projects. Such workshops could be held under bilateral agreement involving, if necessary, international agencies. For this purpose, the PAC would like to identify a few leading bio-medical institutes which could provide opportunities and facilities for guest scientists from the neighbouring countries.

LIST OF THE SUGGESTED THRUST AREAS

1. Cellular and molecular aspects of host-parasite interaction including the study of factors modulating immune response in relation to our dominant communicable disorders
2. Novel approaches to the development of vaccines specially polyvalent vaccines relevant to India
3. Fertility regulation
4. Infant and childhood diarrhoeas, their etiology and mechanisms, specially the aspects of gut immunity
5. Molecular biology of genetic disorders
6. Thrombosis and platelet biology, specially in relation to cardio- and cerebro-vascular accidents
7. Cellular and molecular aspects of cell transformation, growth signalling, metastasis and cancer chemotherapy
8. Epidemiological modelling
9. Computer modelling
10. Whole body energetics
11. Patch-clamp techniques
12. Material science, specially the study of novel biopolymers/bioimplants
13. Animal models in human diseases.

IMMUNOLOGY

1. PREAMBLE

The Science and Engineering Research Council of the Department of Science and Technology, Govt. of India has adopted an approach of supporting creative research in a major way in a few selected areas of research identified as Thrust Areas for the period 1980–1990. The objective was to concentrate effort in newly emerging and frontier areas of interdisciplinary fields to make significant impact on the scientific scene. The time has come to review the progress made and have a look for future directions.

In the field of medical sciences (which was one of the four areas under life sciences) immunology was given the pride of place. Immunological control of tropical diseases (in early part human reproduction was also included) was identified as one of the two thrust areas under medical sciences. However, there have been few takers of this opportunity. Whatever proposals came were predominantly in the area of immunodiagnostics and monoclonals. Some other proposals focused on the evaluation of immune response and understanding of pathogenesis. It is only in recent years that some basic and frontline proposals have started coming.

Immunology continues to play a dominant role in modern medical research. Understanding the pathogenetic process of immune-mediated disorders on one hand and tailoring of vaccines as well as successful modulation of immune response on the other hold promise of providing solutions to control of more difficult to manage infectious diseases as well as malignancies. Monoclonals, lymphokines, interferons and other molecules which can act as biological response modifiers are on centre stage. Equally importantly the discipline of clinical immunology dealing with diseases of immune organ is gaining ground. Emergence of AIDS has not only forced to take immune deficiency seriously, but has also given a major boost to study the immune system especially in the western world. The progress in the field of immunoinflammatory diseases is also spectacular. Emphasis has shifted from symptomatic anti-inflammatory agents to disease-modifying drugs/immunomodulating agents. However, inspite of some success the very basis of autoimmune diseases continues to remain an enigma. Considerable advances have been made in understanding the structure and function of HLA molecules and their disease association but the role of genetic regulation of immune response in humans still remains hypothetical. Cell sorting and cell cloning could provide better understanding of specific subsets of cells but without understanding of idiotype, clonotype and cellular networking in the immune system, our understanding of aberrations of immune response and their control will remain a challenge. This is also applicable to genetic engineering of vaccines and molecules of biological response modifiers which have far reaching potentials.

In the above context there could be little doubt that research in the field of immunology continues to remain a thrust area. However, there is great need to precisely delineate specific areas in this field where Indian scientists could make meaningful contribution and international impact. Equally important are the aspects of research and development in the field of immunology which will help us deliver better health care to the population of India. There is also a need to strengthen manpower base and develop adequate infrastructure facilities which can support research in frontline areas.

2. STATE-OF-THE-ART IN NATIONAL CONTEXT

Infectious diseases continue to remain the major cause of morbidity and mortality in India. Besides, other diseases or situations where knowledge of immunology could be applied (except for AIDS) appear to be no different in our country from those in the West. With the population base of our country, the absolute dimensions of these problems could be huge in India. In a recent population survey it was found that only one of the immunoinflammatory diseases, viz. rheumatoid arthritis had a point prevalence of 1.18%, giving a projected prevalence of over 7 million patients in India.

In India, there are about 40 centres and over 400 immunologists who are engaged in research in immunology (Appendix 1). If the number of papers presented at the annual meeting of the Indian Immunology Society is taken as an indicator there has been modest but continuous increase in research activity in this field (125, 152 and 206 abstracts were submitted in 1985, 1986 and 1987, respectively). A full fledged National Institute of Immunology has been established at New Delhi. In addition the facilities for immunological research have been either created or strengthened in many universities, national institutes and medical institutions. More than a dozen laboratories have been reported to be engaged in raising monoclonals in various parts of the country (Appendix 2). Research in this field has been actively supported by DST, ICMR and CSIR. To monitor the menace of AIDS, ICMR has established a network of screening centres. Lately research and developmental effort in the field of immunology has also been picked up by the industry. One of the most spectacular of these is the high technology laboratories of ASTRA at Bangalore. Immunodiagnostics and Hoechst (Boehringer) have marketed several immunological reagents and test kits in India. In particular, the immunological tests for pregnancy are now marketed by several firms. Ranbaxy has also entered in the field of immunologicals. Several others are promoting the reagents of the foreign principals. However, the supply of these reagents is still not satisfactory. One of the major limiting factors for the progress of laboratory investigations in this field has been lack of availability of tissue culture grade plasticware in India.

During the period from 1979 to 1986 DST has funded 19 research projects in the field of immunology for a total cost of 161.95 lakhs (Appendix 3). This accounted for 22% of the projects (as well as funds) sanctioned in the field of medical biology as a whole. More than 100 publications have emerged from these studies and 26 persons have qualified for PhD. Besides, at least 100 technical persons have been engaged in these research projects. Out of 19 projects 11 were in the field of infectious diseases and 5 on cancer.

ICMR has supported a large multicentric study on seroepidemiology of malaria and another one on HLA typing. Besides, its own institutes have also been conducting research on various aspects of immunology. The same has been true of CSIR laboratories as well.

An analysis of abstracts presented at the Indian Immunology Society indicates that the largest number (172) of papers dealt with infectious diseases. It was followed by studies on malignancies (73), clinical aspects (57), basic aspects (53), reproductive immunology (28), immunogenetics (20), immunopharmacology (19), veterinary immunology (6) and allergy (5). It should only be taken as representative of trend only because papers dealing with immunological aspects are presented at several other forums as well (Indian Association of Medical Microbiology, Indian Rheumatism Association, etc.).

On overall analysis, Indian immunologists have not yet graduated into modern immunology. Barring aside few laboratories the activity has mainly revolved around development of immunoassays and evaluation of immune competence (quantitation of immunoglobulins, subsets of lymphocytes, etc.). Hybridoma technology and genetic engineering for vaccine development are still in infancy. Of late there are some signs of recovery but a very intensive effort is required to join the mainstream. A few high level workshops have been held in recent years to develop the manpower but there is no follow-up information on the outcome of these exercises.

3. INTERNATIONAL STATUS

The field of immunology is one of the most active fields of research internationally. The number of Nobel awards, books and journals, national and international conferences in the discipline and the volume of marketed immunologicals and immunochemicals is a good testimony to it. The great advances in immunology in recent years have mainly resulted from influx of investigators from multiple disciplines ranging from highly molecular to highly clinical areas. There is no area in biology that has remained untouched by immunology and there is no methodology that has either not given or accepted something from it. In recent years, more and more emphasis is being given to understand the structure and function at molecular level. Some of the areas that are being hotly pursued include T- and B-cell biology, T-cell receptors, anti-idiotypes, lymphokines, monokines and their receptors, antigen recognition and processing at molecular level, antibody combining site, regulation of antibody class expression, molecular mechanisms of signal transduction in immunocytes, non specific MHC-unrestricted killer cells and their receptors, regulatory structures on the V and C regions of immunoglobulin molecules, immune-response gene function, genetic aspects of antibody V regions, genetic origin of auto-antibodies and origin and significance of anti-DNA antibodies, etc. In the area of immune intervention in disease states significant progress has been made in the form of development of new generation vaccines, monoclonal antibodies as therapeutic measures, anti-idiotypic antibodies as vaccines, interleukins, interferons, certain compounds identified as immunomodulators and total lymphoid irradiation. Significant strides have also been made in the field of transplantation immunity including cardiac, bone marrow, renal and other organs transplantation. The modern pandemic of AIDS is also being chased from various angles including the prospects of development of potent antiviral drugs, immune response modifiers and vaccine. It is humanly impossible to review the entire field in this space.

4. GAP AREAS

5. NEW THRUST AREAS

There is so much going on and at such high level in the field of immunology in the rest of the world that it would be impossible for us to match unless efforts are intensified and concentrated towards areas of national relevance. This requires taking concious decisions in identification of areas for vigorous pursuit. This approach does not preclude independent research.

In identifying thrust areas the debate about basic and applied is futile. The choice has to depend on available resources, both in manpower and material. The ideal would be that all the active labs are visited and discussions are held with the scientists in these labs about their interests and future plans. The identified thrust areas should match our capabilities. However, since the available base is limited we will also have to identify areas which are contemporary and befitting with national needs to which scientists can be attracted. In the latter category the following areas deserve consideration:

5.1 Immunochemical characterization of Indian strains of parasites and other infectious agents; identification of their protective antigens and functional epitopes and understanding of factors determining immune response (antigen recognition, presentation, processing, cell interactions, effect molecules and cells, etc.) to these epitopes, including genetic factors (HLA, IR genes and T-cell receptors) and idiotypic net working mechanisms.
5.2 Development of monoclonals and immunodiagnostics.
5.3 Identification of genetically determined variations in immune response including genetic immune-deficiency diseases and aberrant immune responses including cancer immunology and that of immuno-inflammatory auto-immune diseases for understanding the development and functioning of immune apparatus by dissecting the underlying mechanisms of variation.
5.4 Search for the immune modulators and other biological response modifiers among indigenous systems of medicine including clinical evaluation of emerging agents.
5.5 Development of genetically engineered vaccines of national interest.

6. HUMAN RESOURCES DEVELOPMENT

More important than financial constraint is the constraint of available trained manpower in the field. Immunology is not yet commonly adopted as a standard undergraduate or postgraduate subject. It is mostly taught as a part of zoology, biology, or life-sciences and that too only at few places. Its content in medical school curriculum is negligible. The only source of manpower in the field of immunology is PhD programmes. The latter are essentially project-based and do not include broad-based formal training. There is an urgent need to generate human resource in immunology if we wish to make meaningful contributions in this field. The following is suggested:

6.1 Courses in immunology with laboratory facilities should be included in graduate, postgraduate and medical curricula all over the country. Optional specialization in immunology can be offered at postgraduate level.
6.2 A regular summer/winter school in immunology be held at an identified place every year on a long term basis.
6.3 More frequent intensive workshops to be held in different parts of the country according to expertize of individual laboratories which should include a follow-up programme as well.

7. NATIONAL FACILITIES REQUIRED

Research has become highly technical these days. Some of the requirements are quite fastidious and often have to be imported. High-tech research is infeasible without such facilities. Unfortunately, the industry does not seem to be ready to accept this challenge. The only recourse is to establish national facilities. Some of the requirements for research in immunology are identified as follows:

7.1 SPF defined strains of inbred mice
7.2 Bank of Indian strains of parasites and other infectious agents
7.3 Cell banks of immunological clones including target cells, lymphokine-producing cells and hybridoma clones secreting commonly used phenotype and marker-specific monoclonals
7.4 Reference antigen and sera banks providing international and national standard of antigens, and positive and negative antisera, conjugated second antibodies, etc.
7.5 Facilities for setting up hybridomas.

Simultaneously, it is also important to take steps for
— developing our own clones producing specific reagents and,
— improving the supplies of immunological reagents and tissue culture grade plasticware. Although it is not in the realm of research but it calls for strong administrative action.

APPENDIX 1

Centres engaged in research in immunology

1. All India Institute of Medical Sciences, New Delhi
2. Aligarh Muslim University, Aligarh
3. Amla Cancer Research Centre, Trichur
4. Banaras Hindu University, Varanasi
5. Biology Group and Radiation Medicine Centre, Bhabha Atomic Research Centre, Bombay
6. Cancer Research Institute, Bombay

7. Cancer Research Institute, Madras
8. Central Drug Research Institute, Lucknow
9. Central Jalma Institute of Leprosy, Agra
10. Centre for Biochemicals, Delhi
11. Centre for Cellular and Molecular Biology, Hyderabad
12. Chittaranjan National Cancer Research Centre, Calcutta
13. Christian Medical College, Vellore
14. Hindustan Ciba-Geigy Research Institute, Bombay
15. Cytology Research Centre, New Delhi
16. Foundation for Medical Research, Bombay
17. Haffkine Institute, Bombay
18. Haryana Agricultural University, Hisar
19. Institute for Research in Reproduction, Bombay
20. Indian Institute of Science, Bangalore
21. Institute of Immunohaematology, Bombay
22. Institute of Pathology, New Delhi
23. Industrial Toxicology Research Centre, Lucknow
24. Indian Veterinary Research Institute, Izatnagar
25. Jawaharlal Nehru University, Delhi
26. K.E.M. Hospital, Bombay
27. K.G. Medical College, Lucknow
28. Madurai Kamaraj University, Madurai
29. Malaria Research Centre, New Delhi
30. National Institute of Communicable Diseases, Delhi
31. North Bengal University, Siliguri
32. National Institute of Immunology, New Delhi
33. National Institute of Virology, Pune
34. National Institute of Nutrition, Hyderabad
35. Post-Graduate Institute of Medical Education and Research, Chandigarh
36. Regional Cancer Research Centre, Trivandrum
37. Regional Medical Research Centre, Bhubaneswar
38. Sanjay Gandhi Post-Graduate Institute of Medical Sciences, Lucknow
39. Sher-i-Kashmir Institute of Medical Sciences, Srinagar
40. Tuberculosis Research Centre, Madras.

APPENDIX 2

Laboratories involved in raising monoclonal antibodies in India

S. No.	Institution	Monoclonal antibodies against
1.	National Institute of Immunology, New Delhi	(i) *E. histolytica* (ii) HBsAG (iii) *S. typhi* (iv) *M. tuberculosis*
2.	All India Institute of Medical Sciences, New Delhi	(i) Herpes simplex virus types 1 and 2 (ii) *S. typhi*
3.	Cancer Research Institute, Bombay	(i) Myeloid leukemic cells (ii) Alphafetoprotein (iii) Squamous cell carcinoma, oral cavity
4.	Tata Memorial Hospital, Bombay	Myeloid leukemic cells
5.	Foundation for Medical Research, Bombay	*M. leprae*
6.	Institute for Research in Reproduction, Bombay	Thyroglobulin
7.	Hindustan Ciba-Geigy Research Institute, Bombay	Filaria
8.	Cancer Research Institute, Madras	Lymphoma-specific antigen
9.	National Institute of Virology, Pune	*Japanese encephalitis* virus
10.	School of Biological Sciences, Madurai Kamaraj University, Madurai	Porin (*S. typhi*)

APPENDIX 3

DST-funded research projects in the field of immunology

S. No.	Title	Principal investigator	Institution	Period	Grant (Rs. in lakhs)
1.	Etiological factors, pathogenic mechanism, immunological status and appropriate dietary schedule in intractable diarrhoea patients	O. P. Ghai	AIIMS, New Delhi	84–87	9.14
2.	Immunodiagnostic and other studies in Bancroftian filariasis	B. C. Harinath	Wardha	79–82	9.47
3.	Immunity in amoebiasis: study of the host–parasite interaction at the macromolecular level	Sohail Ahmed	AMU, Aligarh	80–83	4.01
4.	Evaluation of endogenous interferon inducers and antiviral drugs for the prophylactic and therapeutic use in man	S. N. Ghosh	NIV, Pune	80–84	4.43
5.	Immunological studies in typhoid fever	Ramesh Kumar AN Malviya	AIIMS, New Delhi	81–83	—
6.	Cell-mediated immune responses in childhood tuberculosis	V. Seth	AIIMS, New Delhi	81–85	—
7.	Hybridoma produced monoclonal radiolabelled antibody in specific targetting both in neoplastic and infective lesions	D. K. Hazra	S. N. Med. College, Agra	84–88	—
8.	Detection of antigens for a rapid and improved laboratory diagnosis of typhoid fever	Ramesh Kumar	AIIMS, New Delhi	84	6.71
9.	Interaction between nutrition, immunology and drug response in man	N. A. Kshirsagar	GSMC, Bombay	82–86	4.0
10.	Use of monoclonal antibodies in the studies of development and differentiation of nervous system TSA	Shail Sharma	AIIMS, New Delhi	82–86	4.0
11.	Epidemiological study of viral hepatitis and immunological aspects in pregnancy	R. S. Karrat	Haffkine Inst., Bombay	83–87	1.0
12.	Studies on the characterization and protective roles of defined antigen of axenic *E. histolytica* by use of monoclonal antibody	V. K. Vinayak	PGIMER, Chandigarh	86–89	
13.	Lepromin conversion, natural or induced by agents, and its competency in clearing *M. leprae*	S. Chaudhary	School of Trop. Med., Calcutta	85–86	5.0
14.	Role of IL-1 in microbicidal killing in pulmonary TB	R. S. Padma	AIIMS, New Delhi	86–88	1.0
15.	Assessment of immunological alterations caused by some common pesticides in experimental animals	B. D. Banerjee	NICD, Delhi	85–87	0.9

16.	Studies on the HLA system with special reference to distribution, genetics and disease association	R. M. Pitchappan	MKU, Madurai	84–88	10.6
17.	Immunodiagnostic tests for detection of asymptomatic malignant neoplasms	Uday Chander	CRI, Madras	81–85	29.45
18.	Development of monoclonal antibodies reactive against tumour or associated antigens of human leukemias and murine mammary tumour virus	Sudha Gangal	CRI, Bombay	84–87	7.62
19.	Monoclonal antibodies to lymphoma associated antigen (LAA) and their application in early diagnosis and therapy	Uday Chander	CRI, Madras	85–88	13.43

NEUROBIOLOGY AND MECHANISMS OF BEHAVIOUR

1. PREAMBLE

FOLLOWING the 'Baroda Seminar', SERC identified thrust areas for major research programmes for 1980–90 period. Among the areas identified in the life sciences there were two primarily concerned with the broad field of neuroscience—Neurobiology and mechanism of behaviour, and Human neurobiology in relation to mental health.

Realising the overlap between these two fields a single PAC was constituted to encourage work in these areas. The paucity of ongoing research in these areas became very apparent during the initial meetings of the first PAC on neurobiology. It was, therefore, decided to organise a 'Brain Storming Session', to take stock of the existing situation and stimulate future activity. This session was held at Bangalore in November 1984. The proceedings and recommendations of this session were widely circulated. This resulted in a distinct increase in interest in the field, though much more needs to be done. The present report provides a review of the current status and suggestions for future directions. This is based on discussions in the PAC on neurobiology on several occasions, as well as comments received from some other colleagues working in this area who gave their suggestions on the basis of a preliminary paper circulated to them.

2. STATE-OF-THE-ART IN NATIONAL CONTEXT

A survey of neurosciences activity in the country reveals that in various fields of neurosciences, neuroanatomy, neurophysiology, neuropharmacology and toxicology, neurogenetics, neuropathology, clinical neurological and behavioural sciences, nuclei and groups exist scattered all over the country. There was unmistakable evidence of some very good and a few outstanding units in each field, but in general the overall activity in this very important field is still limited. There is a real dirth of interdisciplinary, comprehensive and coordinated activity cutting across the artificial barriers. As a matter of fact most workers belonging to any of the disciplines mentioned above, not only seldom interact with each other, but are not even fully aware of the existing expertize available. Neuroscience research is a continuum of study from the molecular to the behavioural level. To quote the office of Science and Technology Policy, USA (1985): Neuroscience was defined as 'that body of research directed towards understanding the molecular, cellular, intercellular, processes in the central nervous system and the ways in which those processes are integrated in CNS functional control system, with emphasis on research relating CNS functions with behaviour.

The Thrust Area Programmes (1980–90) identified the following subjects in the field of neurobiology.

Neurobiology and mechanisms of behaviour.
Biophysics of the nervous system
Sensory and motor mechanisms
Brain structure and development
Higher functions of central nervous system (learning memory)

Chemical modulation of CNS functions
Neurogenetics
Human neurobiology in relation to mental health.
Neurobiological investigations with emphasis on neuronal transmission mechanisms, psychopharmacology developmental neurobiology of human foetus.

As a result of the efforts of the PAC during the last 5 years SERC supported the following programmes:

2.1 Units supported under the IRHPA programme

Unit of Neurobiology and Mechanism of Behaviour at the School of Biological Sciences, MKU, Madurai. (Programme Director, Prof. M. K. Chandrashekaran 1983–88): This unit has done creditable work on the nature of entrainment of circadian rhythms, social synchronization of these rhythms, electrophysiology of ecolocation in bats. Besides, a chronocubicle complex with isolation facility for experiments with human subjects, the only of its kind in the country and one of the few in the world, has been established and is currently being regularly utilized.

Unit on Neural Transplantation in Mammals at AIIMS, New Delhi (Programme Director, Prof. P. N. Tandon): A centralized facility to initiate research and training in this frontier area was established in March 1986. This unit has already carried out a variety of embryonic neural transplants in adult rodents and monkeys. It has organized two National Training Programmes.

2.2 Individual projects

During the last five years the following individual projects were supported and a few others are now being evaluated.
– Studies on myelin synthesis in developing brain—Prof. P. S. Sastry, IISc., Bangalore.
– A comparative study of nervous system and platelets with particular reference to the amine-sensitive arylacylamidases and acetylation-deacetyltion processes - Prof. A. S. Balasubramanian, CMC, Vellore.
– Functional organization of the skeleto-motor correlates of the hand with respect to skilled movements—Prof. M. S. Devanandan, CMC, Vellore.
– Identification of domains responsible for arylacylamidase and peptidase activities in acetylcholinesterase and pseudocholinesterase—Prof. A. S. Balasubramanian, CMC, Vellore.
– Mechanisms of peripheral nerve damage in leprosy and approaches for its prevention and treatment—Dr. N. H. Antia, The Foundation for Medical Research, Bombay.
– Studies on neurotransmitter receptors in platelets of Parkinsonian patients—Prof. Devika Nag, KG Medical College, Lucknow.

2.3 Training programmes

– National workshop on reconstruction of the central nervous system: Organised by Prof. P. N. Tandon, AIIMS, New Delhi, 1986.
– National course in basic neurosciences for postgraduates in clinical neurosciences: Organized by Prof. P. N. Tandon, AIIMS, New Delhi, October 1987. Second course planned from November 14 to 25, 1988.

Obviously this is not the only activity going on in the field of neuroscience in the country. Unfortunately there is no single source from where one could gather a comprehensive information on the subject. The need for creating a 'National Neuroscience Information Unit' has already been approved in principle by SERC.

2.4 Work going on in the country in the areas identified by SERC though not necessarily supported by DST is given below. This information is based on the personal knowledge of the members of PAC and hence is most likely incomplete.

Neurobiology and mechanism of behaviour

Besides the work at the Madurai Unit mentioned above the Department of Physiology of the AIIMS has a continuing interest in this field over the last two decades. The role of limbic system, hypothalamus and other regions of the brain in a variety of behaviours, e.g. feeding, sex, reproduction, sleep and response to pain have been the subject of a large number of studies.

– *Biophysics of the nervous system*

We are not aware of any significant contributions in this field from any individual or group in the country.

– *Sensory and motor mechanisms*

Some work is going on in this area at CMC, Vellore; AIIMS, New Delhi, and NIMHANS, Bangalore.

– *Brain structure and development*

The group at AIIMS is undoubtedly the most active group in this field. Their work in the field of development of the visual and pain pathways in human embryos is certainly of international standard. Important contributions have also been made by this group on the effect of malnutrition, radiation and thyroid hormone on developing brain.

Three or four groups, i.e. at AIIMS, PGI, NIMHANS, Institute of Neurology, Madras and Bombay are actively involved in the field of neurooncology. More basic investigations are, however, necessary to improve our understanding of the brain tumours, a majority of them still not being curable.

– *Higher functions of central nervous system (learning, memory)*

To the best of our knowledge hardly any activity is going on in the country in this vital area. The studies on neurophysiology of Yoga carried out initially at AIIMS, New Delhi and currently at NIMHANS, Bangalore, are the only important contributions worth mentioning.

– *Chemical modulation of CNS function*

A few groups at Vellore, Bangalore, New Delhi, Lucknow, Hyderabad and Calcutta are working in the field of neurochemistry and chemical modulation of the central nervous activity.

– *Neurogenetics*

The group at TIFR Bombay, has made outstanding contributions in this field. Some work has also started in CCMB, Hyderabad, on molecular genetics, which has bearing on neurogenetics. Department of Zoology, BHU, Varanasi has been working on genetics of aging which has some relevance for CNS.

It would, thus be seen from the above account that the overall activity in the field of basic neuroscience in India is grossly inadequate. There are very few individuals/groups/institutions currently engaged in this field. The importance of this field can hardly be overstated. Better understanding of the human brain and behaviour may be the key to survival of the human race itself. Even in the short term, a large number of neurological and psychiatric disorders, till now ill understood and thus untreatable, demand urgent attention for better understanding and relief.

3. INTERNATIONAL STATUS

The extensive excitement witnessed globally in the field of neuroscience is reflected in the increasing number of scientists engaged in research in this area all over the world. In USA in 1971, the Neuroscience Society had 250 members, which in 1985 had increased to over 8,000. In China in a single institute in Beijing or Shanghai there were more scientists working in narrow areas like visual or auditory system than the total number of neuroscientists in India. This spurt of interest in the field is because of the recent developments in diverse fields like molecular biology, biotechnology, imaging and biochemical techniques, advances in solid state electronics and computers. Thus, new analytical techniques like mass spectroscopy, nuclear magnetic resonance spectroscopy, high pressure liquid chromatography, radioimmunoassay, etc. now permit isolation and identification of specific molecules used by nerve cells for intercellular communication. It is now possible to identify and characterize the gene sequences responsible for the various neuropeptides, neuromodulators and neurohormones and thus modify any defects. The technique of 'patch clamping' enables an investigator to record from the tiniest of neurons and detect the opening and closing of a single ion channel as a small patch of membrane responds to neurotransmitters. Much useful information on the cellular properties of the nervous system is being gained through the use of cell-culture, *in vitro* study of brain slices and more recently using neural transplantation. The technique of genetic hybridization today permits development of animal strains with specific neurological or behavioural properties, ranging from resistance to alcohol intoxication to the ability to acquire new reflex skills. These strains then permit studies for their underlying structural or biochemical defects.

The techniques for recording the activity of the brain during behaviour have expanded greatly. Methods now range from study of the activity of single neuron in animals to the ability to visualize regional cerebral blood flow or metabolism in intact human brain. Thus nuclear magnetic resonance, imaging and spectroscopy, positron emission tomography, single photon emission computerized tomography, telemetry, electromagnetic field registration, etc. have lead to sophisticated analysis of behaviour hitherto impossible to imagine.

Intense activity is going on in the field of artificial intelligence, computer modelling and simulations, to provide better understanding of neural activity on the one hand and simulate it for development of more sophisticated and powerful computers on the other.

These techniques have thus made it possible to explore certain basic questions about the brain, its growth, connectivity, organization, means of intercellular communication, anatomical and biochemical circuitory which have direct relevance to the understanding of its functions in health and disease. Neural transplantation, with its vast potentialities for relief of neurological disorders, like Parkinsonism, dementia, etc. has already attracted thousands of neuroscientists around the world. It is already a reality, its wider application depends upon a better understanding of the underlying biology.

Global reviews further highlighted that today for any worthwhile neuroscience research the traditional compartmentalized efforts are not likely to succeed. Modern techniques of molecular biology, cell culture hybridoma technology and immunology are equally important for workers in most areas of neuroscience referred to above. Furthermore it is obvious that to break new grounds inter-disciplinary interaction is necessary not only among the scientists in various neuroscience disciplines but also with mathematicians, physicists, chemists and computer scientists. It is neither necessary nor desirable to catalogue all possible areas of research in neuroscience. However, on the basis of the discussion some general guidelines emerged on identification of new thrust area, which are listed here not necessarily in their order of priority or importance. Nevertheless this list is drawn taking into consideration the existing talent, potentials and the national needs.

4. GAP AREAS

From the above description it will be seen that there are major areas of research in neuroscience which are either being pursued at subcritical level or not at all, cataloguing these would serve no useful purpose. However, the areas identified for preferential support are given under the next section.

5. NEW THRUST AREAS

5.1 *Developmental neurobiology*

The large resource of human foetuses and adult brains from autopsies available in the country could be exploited to study developmental neurobiology utilizing modern neuroanatomical, and neurochemical techniques combining various newer labelling methods (antegrade and retrograde Golgi, double labelling, immunoflourescent and immunocytological investigations) along with quantitative morphometery routine, flourescent and electron-microscopy, on the one hand and evaluation of regional distribution of various neurotransmitters and neuropeptides on the other.

This would provide valuable information on (a) the development of normal human brain, its organization, biochemical correlates and connectivity, since large areas of human brain even today remain uncharted, and modern techniques can provide quick and reliable information which was not possible till recently, (b) this basic information about the normal state is important to answer a large number of questions regarding pathological states.

– *The effects of malnutrition*

A large amount of controversial data exist on this subject, however, specific answers are not yet available for many vital questions of great practical importance. Thus so far quantification of the damage, its precise extent, pathogenetic mechanism, and reversibility, etc. have not been possible because the available techniques till recently were inadequate or too slow or too complicated to answer these questions.

– This knowledge could be utilized to understand the basis of a number of ill-understood developmental defects, and permit quantitative study of changes associated with ageing.

– It is likely to throw new light on plasticity and regeneration of the nervous tissue both at the central and peripheral levels. This information is of great practical value in managing patients with neurological damage. To enable such studies to be carried out it will be necessary to develop facilities for:

– Foetal and adult brain banks

– Quantitative morphometry

– Modern labelling techniques, specially possibilities to raise monoclonal antibodies and various marker isotopes

– Microanalytic methods to measure minute levels of neurotransmitters/hormones/modulators, etc.

– Tissue culture, and explant and organ culture, which can help provide several answers in neurobiology

- High-voltage electron microscope facilites.

Besides enhancing our knowledge of basic neurobiology such studies are directly relevant for the newly emerging area of neural transplant for treatment of human diseases.

5.2 *Neurophysiology*

A number of new techniques for neurophysiological studies have developed in recent years. Thus, in addition to the classical macro- and micro-electrode studies, patch-clamp technique, studies of brain slices *in vitro*, quantitation of behavioural parameters using computerized facilities and telemetry are some of the examples, which need to be developed.

5.3 *Neurochemistry*

Recent developments in neurochemistry have opened up completely new vistas to study normal and abnormal nervous system from the molecular to behavioural level. The existing expertize in this field could be utilized and strengthened to permit research to the frontier areas, static and dynamic studies of conformation of the transmitters and receptors and their modification by drugs and pathological states.

5.4 *Neuropharmacology*

Pharmacodynamic and pharmacokinetic action of known drugs, development of newer drugs utilizing computer modelling techniques are two emerging areas. Investigations for developing reliable and cheaper monitoring kits for drug levels, for clinical use need to be encouraged, studies on selected drugs used in traditional systems of medicine for modifying CNS function, need to be explored.

5.5 *Neuroimmunology*

A number of neurological disorders are now being recognized to have an immunological basis. On the other hand involvement of nervous system in regulation of immune system is no more a matter of speculation. In view of the available evidence of the role of CNS in modulating the immune system, studies are needed both to delineate the role of central mechanisms in immune diseases and to evaluate the usefulness of centrally acting drugs to modify the same.

5.6 *Neurogenetics*

It is obvious that the techniques of modern genetics could be used not only to study the manifestations of various genetic traits for normal and abnormal structure and function of animals (and human), but these new techniques could be utilized to understand some of the basic neurobiological mechanisms/phenomenon, e.g. neuronal organization, connectivity and even, behaviour.

5.7 *Neuroendocrinology*

This is a fast developing field still in its infancy in India. Facilities for modern neuroendocrinological investigations are available in only few centres. These studies are of great importance to understand normal growth and development, effect of undernutrition and malnutrition on mental development (classical example iodine deficiency and mental retardation).

5.8 *Study of pathological states*

Whole range of pathological states affecting the nervous system, central and peripheral, remain ill understood or un-understood. Some of these disorders specific to India are of greater interest to us. These are malnutrition, infective disorders (tuberculosis, leprosy, viral and parasitic), degenerative disorders (motor neuron disease, ataxias), and certain toxic substances of national relevance (lathyrism, connibas, country liquor).

Another important area is that of neurooncology, with the availability of newer techniques like *in vitro* and *in vivo* cell kinetics tissue culture, use of tumour markers, etc. It has now become possible to investigate brain tumour to get a better insight in their histogenesis, biological behaviour and response to chemotherapy, etc.

5.9 *Neurotoxicology*

Neurotoxicology is of great concern in view of the increasing exposure of man to a variety of neurotoxins of pharmacological, environmental and industrial origin. Furthermore, recent studies have provided a clue to the role of neurotoxins in the aetiopathogenesis of several neurodegenerative disorders such as Parkinsonism, motor neuron disease, dementia, etc. The following areas of research are, therefore, identified.

5.9.1 *Development of animal models*

Animal model need to be developed for testing of environmental toxins and industrial pollutants; priority should be given to solvents (particularly hydrocarbons and halogenated hydrocarbons), heavy metals (lead and manganese), pesticides and polymers.

An integrated approach using biochemical, electrophysiological, behavioural and morphological methods has to be used for the development of animal models. Biochemical evaluation would essentially involve the study of receptor changes, glycolytic enzymes and marker enzymes for subcellular components. Electrophysiological studies of peripheral and central nervous system including electromyography, neuro-muscular transmission, nerve conduction and evoked potentials are necessary to provide essential information of the functional status. Behavioural studies would involve motility monitoring, maze test for memory and tailflick test for pain sensation. Morphological studies of peripheral and central nervous system using histological, histochemical and ultrastructural methods, need to be carried out.

5.9.2 Study of mechanism of action of neurotoxins

It is important to delineate the precise site of action of neurotoxins. To achieve this objective, *in vitro* methods using brain slices, tissues cultured cells and subcellular fractions have to be developed. These studies would be critical in devising, *in vitro* assays for rapid screening of potential neurotoxins, while *in vitro* testing cannot completely replace *in vivo* studies, such methods would obviously reduce the number of compounds that need to be tested *in vivo*, saving valuable animals, time and expense.

5.9.3 Application to human studies

The information obtained from basic work has to be applied to the actual human situation. Well designed neuroepidemiological studies will provide the framework for obtaining prevalence data and allow intervention methods. Such studies will have to be conducted in selected population at high risk of exposure.

- The neurotoxicological data obtained from animal studies will be valuable in determining the maximum permissible levels of exposure. In the Indian context, the influence of nutritional status has to be given due consideration while formulating the guidelines. Therefore, studies have to be designed to assess the inter-relationship between the effect of toxin and nutritional factors.

5.10 Biological psychiatry

Another area of behavioural science research which has become possible today is the field of structural, biochemical, functional and behavioural correlates of a variety of psychological or psychiatric disorders. With the availability of techniques for precisely delineating structural, biochemical and metabolic abnormalities in intact animals (including human), it is now possible to explore various higher mental fuctions and their disorders from a biological stand point.

The study of memory mechanism, its neuroanatomical biochemical, physiological and behavioural basis constitutes a vital area of neurological research.

5.10.1 Drug/substance abuse

In view of the current global concern in this subject and the specific problems peculiar to India, urgent attention is needed in this field.

5.10.2 Drug abuse

Basic studies on drug abuse are needed in certain areas of special relevance to India. Important problems should include:

- Development of animal models to study substances abuse, for example opium, Indian alcoholic liquors, cannabis, etc. need detailed studies as their response may differ from the more thoroughly studied pure compounds like morphine, heroin, cocaine, etc.
- The abuse potential of some new psychotropic drugs developed and introduced in India needs to be studied.
- Morphine and opioid peptides have now been shown to have marked effect on immune system. Their effect on time course of tropical infections has not been investigated so far.
- With drug rules and surveillance becoming more strict in Western countries a new class of drugs of abuse has developed called the Designer's drugs. These are derivatives of drugs of abuse which are not legally banned and can thus escape the enforcement network. It is necessary to have assay procedures for such compounds at least at some centres in the country so that their abuse can be detected before it becomes uncontrollable.

A major problem faced by research workers is the high cost and difficulty in procurement of necessary ligands, narcotic substances, biochemicals, etc. The

National Institute on Drug Abuse, USA supplies these agents free to bonafide investigators through an approved national agency. Immediate steps need be taken to make this facility available to Indian investigators.

5.11 Neuromodelling: Neural implants and neural prosthesis

Active interaction is required between neuroscientists, mathematicians, electronics and computer specialists and experts in biomaterials to develop these exciting areas which promise to provide better understanding of the functioning of the nervous system and help developing implantable devices to replace lost function.

6. HUMAN RESOURCES DEVELOPMENT

It is obvious that there is a paucity of scientists working in the various fields of neuroscience. Those engaged in this activity usually work in isolated disciplinary boundaries, e.g. as neuroanatomists, neurophysiologists, neurochemists, etc. There are very few institutions where groups in all neuroscience disciplines exist. Even these groups are not adequately exposed to modern developments in molecular biology, biotechnology, computer modelling, etc. which are now integral part of frontline research in neuroscience. Hence it is important to create an awareness of these developments, attract younger scientists to neuroscience, provide for multidisciplinary interaction and bring together various groups to learn from each other and develop collaborative research programmes. For this purpose the following activities are recommended:

a) Summer–winter schools conducted by established high quality scientists/groups: Some of the identified individuals and institutions are given below: (This is not an exclusive list but an indicative one.)

i) Neuromorphology: AIIMS, New Delhi
ii) Neuronal membranes: CDRI, Lucknow
iii) Neurotoxicology: ITRC, Lucknow
iv) Neurogenetics: TIFR, Bombay
v) Biology of brain tumours: AIIMS, New Delhi
vi) Animal behaviour: Madurai Kamaraj University, Madurai
vii) Higher nervous activity including Yoga etc: NIMHANS, Bangalore.

b) Seminars and symposia on emerging areas if necessary, supported by international experts

c) Brain storming session: specially in multidisciplinary areas

d) Travelling symposia

e) Training abroad: Young scientists should be selected for training abroad in newly emerging areas not yet developed in India. Some examples are neuroimmunology, neurogenetics and computer modelling of CNS activity. These selected persons could then nucleate this activity in the country.

7. NATIONAL FACILITIES REQUIRED

7.1 There is an urgent need for creating centralized or regional facilities, fully equipped with latest technological advances like nuclear magnetic resonance both imaging and spectroscopy, total body scanner, positron emitting tomography, SPECT, etc. These facilities, no doubt very costly, have opened up completely new vistas to study the morphology, biochemistry, metabolism, circulation and even pharmacokinetics in intact human brain. This would be unimaginable only a few years ago. The investment will pay rich dividends not only for exploring the functions of the normal human brain, but also for the study of a large number of ill-understood diseases of the nervous system.

7.2 Another centralized facility identified was a 'Brain Bank' which could act as a respository of specimens of brains, at all stages of development, at various ages and those afflicted with diseases. These can then be made available to interested researchers. Since the legalization of medical termination of pregnancy the country has a valuable resource of human foetuses, which could be used for studying all aspects of developmental neurobiology. Possibilities of utilizing this for neural transplant work opens up a challenging area of frontline research. Centralized facilities are also necessary for quantitative morphometric studies which would be required for a large number of morphological investigations of the normal and pathological brains.

7.3 Centralized facilities need to be created for procuring and raising special strains/species of genetic mutants required for basic neurobiology research.

7.4 National Information Centre for Neurosciences: There is a need to collect, collate and computerize information regarding current neuroscience activities in the country, procure literature and information at the international level, critically evaluate this data and make it available to neuroscientists in the country.

7.5 Strengthen and support unit of neuroscience in institutions where nuclei of activity of high quality already exists on the lines of advanced centres of COSIST programmes.

ANNEXURES

Annexure 1

RECOMMENDATIONS REGARDING IMPROVEMENT IN EXISTING STATUS OF MEDICAL RESEARCH

1. The condition of investigative medicine is precarious in India. This is no new development. The lack of creativity dates back to hundreds of years. The adventure of Western medicine and political independence produced medical colleges and doctors but their collective contribution to medical knowledge has had little impact on the course of global medicine. Any measures to revive investigative medicine cannot ignore the deep seated nature of the present malady.

2. The reasons for the weakness of investigative medicine are many. A list would include a total alienation from our medical past; poor preparedness in basic sciences such as mathematics, physics, chemistry, etc. when a student enters the medical college; orientation of curricula at undergraduate and postgraduate levels towards passing examinations rather than developing investigative attitudes; selection and promotion of medical teachers on considerations other than competence in research and professional work; frequent transfer of faculty, etc.

3. The Indian Council of Medical Research primarily serves its own institutions and has played a limited role in funding, and working for remedies for the present situation.

4. The remedies must be found at short and long term levels. Both are equally important as one without the other would be less than productive.

4.1 Short-term steps

4.1.1 Seminars on three themes should be organized regionally with investigators of proven ability in medicine and related areas as faculty. The themes suggested are: (a) introduction to medical research (historical, epidemiology, biostatistics, experimental design, medical writing, how to get research funds etc.); (b) common frontiers of medicine and biology; and (c) common frontiers of medicine and engineering. The selection of faculty as well as participants should be done with great care so that the exercise will result in discovery of at least a small number of competent young people who wish to take up medical research seriously. Persons so identified should not only be helped and encouraged to prepare research proposal but also given some incentives to attract them to research.

4.1.2 The participants of the seminars should be assisted by senior investigators constituting the faculty of the seminars in giving formal shape to their proposals which should receive expeditious consideration. The stress should be on young investigations under 40 years and the search should be for a 'spark' in their projects.

4.1.3 Resources should be allocated to arrange for the visits by selected young investigators to spend sometime with institutions. Individuals actively engaged in research, specially to learn newer techniques and technologies.

4.1.4 It is worth considering if some of the selected persons from peripheral institutions may be encouraged to have a 'perceptor/guide' from better endowed institutions.

4.2 Long-term steps

4.2.1 Students must have a much stronger base in mathematics, physics, chemistry and language skills than at present, before they enter the MBBS course.

4.2.2 Undergraduate and postgraduate courses should have less stress of examinations and more emphasis on investigating things for themselves. This may involve literature search, clinical search, experimental electives and so on. Achievements in these should be given as much credit as for grades in examinations.

4.2.3 The selection and promotion of teachers should give as much importance to research capability and achievements as teaching experience, seniority, etc. Prior to recruiting a lecturer, it should be mandatory that he has spent at least two years in a research laboratory, as is done in all advanced countries.

4.2.4 All medical colleges should have adequately equipped research laboratories as also research positions to enable those aspiring to academic careers to work in these laboratories.

4.2.5 Medical colleges should be delinked from government service and be an integral part of a university.

4.2.6 Till a culture for investigative work is created, some seed money and opportunity for members of the medical college faculty be provided to enable them to undergo 'short term' courses in medical research in established research institutes in India or abroad.

4.2.7 Role of various grant giving agencies for promoting medical research be critically evaluated and ways and means found to strengthen these and provide for greater co-ordination amongst them. The question of having one single agency, which is not only for giving grant, but also promote research needs to be debated.

4.2.8 The new agency should encourage medical research in the medical colleges as a matter of policy.

Annexure 2

COMPOSITION OF SCIENCE AND ENGINEERING RESEARCH COUNCIL

Dr Vasant Gowariker
Secretary
Department of Science and Technology
Technology Bhavan
New Mehrauli Road
New Delhi 110 016
—Chairman

Dr M. S. Valiathan
Director
Sree Chitra Tirunal Institute
of Medical Sciences and Technology
Trivandrum 695 001
—Member

Prof. G. Mehta
School of Chemistry
University of Hyderabad
Hyderabad 500 134
—Member

Dr P. Rama Rao
Director
Defence Metallurgical Research
Laboratory
Kanchan Bagh
Hyderabad 500 258
—Member

Dr D. V. Singh
Head
Department of Mechanical and
Industrial Engineering
University of Roorkee
Roorkee 247 667
—Member

Prof. P. N. Tandon
Head
Department of Neurosurgery
All India Institute of Medical Sciences
New Delhi 110 029
—Member

Dr S. Ganguly
Executive Vice Chairman &
Managing Director
Associated Cement Companies Ltd.
Cement House
121, Maharishi Karve Road
Bombay 400 020
—Member

Prof. H. Y. Mohan Ram
Department of Botany
University of Delhi
Delhi 110 007
—Member

Prof. G. Padmanaban
Department of Biochemistry
Indian Institute of Science
Bangalore 560 012
—Member

Dr R. A. Mashelkar
Head
Chemical Engineering Division
National Chemical Laboratory
Pune 411 008
—Member

Dr G. Venkataraman
Director
STAR Group ANURAG
Kanchan Bagh P.O.
Hyderabad 500 258
—Member

Dr D. P. Dhoundliyal
Director-General
Geological Survey of India
27 Jawaharlal Nehru Road
Calcutta 700 016
—*Member*

Dr J. J. Irani
President
Tata Iron and Steel Company Ltd.
Jamshedpur 831 001
—*Member*

Dr P. R. Pisharoty
Physical Research Laboratory
Navarangpura
Ahmedabad 380 009
—*Member*

Dr I. P. Abrol
Deputy Director-General
Indian Council of Agricultural Research
Krishi Bhavan
New Delhi 110 001
—*Member*

PROGRAMME ADVISORY COMMITTEES

MOLECULAR BIOLOGY

Dr G. Padmanaban
Department of Biochemistry
Indian Institute of Science
Bangalore 560 012
—*Chairman*

Dr K. Dharmalingam
School of Biological Sciences
Madurai Kamaraj University
Madurai 625 021
—*Member*

Dr J. Das
Biophysics Division
Indian Institute of Chemical Biology
4, Raja SC Mullick Road
Jadavpur
Calcutta 700 032
—*Member*

Prof. R. K. Mandal
Bose Institute
93/1 Acharya Prafulla Chandra Road
Calcutta 700 009
—*Member*

Prof. D. Deobagkar
Department of Zoology
University of Poona
Pune 411 007
—*Member*

Dr M. R. Das
Centre for Cellular and Molecular Biology
Hyderabad 500 007
—*Member*

Dr P. K. Khandekar
National Institute of Immunology
Shahid Jeet Singh Marg
JNU Complex
New Delhi 110 067
—*Member*

Dr (Ms) Kunthala Jayaraman
Department of Biochemistry
Anna University
AC College of Technology
Madras 600 025
—*Member*

Dr Deepak Pental
Tata Energy Research Institute
90, Jor Bagh
New Delhi 110 003
—*Member*

Dr Joseph Thomas
Biotechnology Division
SPIC Research Foundation
Mount View, 110 Mount Road
Madras 600 032
—*Member*

MOLECULAR BIOPHYSICS AND BIOCHEMISTRY

Prof. G. Govil
Tata Institute of Fundamental Research
Homi Bhabha Road
Bombay 400 005
—*Chairman*

Prof. U. N. Singh
Department of Biophysics
Delhi University
South Campus
Benito Juarez Road
New Delhi 110 021
—Member

Dr C. M. Gupta
Central Drug Research Institute
Chattar Manzil
Lucknow 226 001
—Member

Prof. N. Appaji Rao
Department of Biochemistry
Indian Institute of Science
Bangalore 560 012
—Member

Dr K. K. Kannan
Neutron Physics Division
Purnima Laboratory
Bhabha Atomic Research Centre
Bombay 400 085
—Member

Prof. N. Yathindra
Department of Biophysics and Crystallography
University of Madras
Madras 600 025
—Member

Prof. V. S. Chauhan
Department of Chemistry
Delhi University
Delhi 110 007
—Member

Prof. D. Balasubramanian
Centre for Cellular and Molecular Biology
Hyderabad 500 007
—Member

PLANT SCIENCES

Prof. H. Y. Mohan Ram
Department of Botany
Delhi University
Delhi 110 007
—Chairman

Dr P. V. Sane
National Botanical Research Institute
Rana Pratap Marg
Lucknow 226 001
—Member

Prof. V. S. Rama Das
Department of Botany
University of Hyderabad
Hyderabad 500 007
—Member

Dr C. R. Bhatia
Nuclear Agriculture Division
Bhabha Atomic Research Centre
Bombay 400 085
—Member

Prof. V. Jagannathan
Tata Energy Research Institute
Jor Bagh
New Delhi 110 003
—Member

Dr S. Mahadevan
Department of Biochemistry
Indian Institute of Science
Bangalore 560 012
—Member

Prof. M. M. Johri
Molecular Biology Unit
Tata Institute of Fundamental Research
Homi Bhabha Road
Bombay 400 005
—Member

Prof. H. D. Kumar
Department of Botany
Banaras Hindu University
Varanasi 221 005
—Member

Dr Hari Om Agarwal
Department of Biosciences
HP University, Summer Hill
Shimla 171 005
—Member

Dr H. K. Srivastava
Project Coordinator
Department of Biotechnology
Block II/8th floor
CGO Complex, Lodhi Road
New Delhi 110 003
—Member

Others consulted:

Dr S. K. Sinha
Water Technology Centre
Indian Agricultural Research Institute
New Delhi 110 012

Dr M. C. Srinivasan
Division of Biochemical Sciences
National Chemical Laboratory
Pune 411 008

Prof. Anupam Verma
Department of Microbiology
Indian Agricultural Research Institute
New Delhi 110 012

Dr B. B. Chatto
Department of Microbiology
M. S. University of Baroda
Baroda 390 002

ANIMAL BEHAVIOUR ECOLOGY AND EVOLUTION

Dr Ishwar Prakash
Central Arid Zone Research Institute
Jodhpur 342 003
—*Chairman*

Prof. T. N. Ananthakrishnan
Entomology Research Institute
Loyola College
Madras 600 034
—*Member*

Prof. M. K. K. Pillai
Department of Zoology
Delhi University
Delhi 110 007
—*Member*

Prof. R. Ramamurthi
Department of Zoology
S. V. University
Tirupati 517 502
—*Member*

Prof. K. Krishnamurthi
Centre for Advanced Studies in Marine Biology
Annamalai University
Parangipettai
Tamil Nadu 608 502
—*Member*

Shri H. S. Panwar
Director
Wild Life Institute of India
New Forest
Dehra Dun 248 006
—*Member*

Shri J. C. Daniel
Bombay Natural History Society
Hornbill House (Museum Compound)
Shaheed Bhagat Singh Road
Bombay 400 023
—*Member*

Dr P. S. Ramakrishnan
School of Environmental Sciences
Jawaharlal Nehru University
New Delhi 110 067
—*Member*

Prof. Uma Kant
Department of Botany
Rajasthan University
Jaipur 302 002
—*Member*

Dr Sarla K. Subba Rao
Malaria Research Centre
22 Sham Nath Marg
Delhi 110 054
—*Member*

Dr Ipe M. Ipe
School of Entomology
St. John's College
Agra 282 002
—*Member*

Dr Aditi Pant
National Institute of Oceanography
Dona Paula
Goa 403 004
—*Member*

Dr Raghavendra Gadagkar
School for Ecological Sciences
Indian Institute of Science
Bangalore 560 012
—*Member*

Dr K. M. Alexander
Department of Zoology
Kerala University
Trivandrum 695 007
—*Member*

MEDICAL BIOLOGY

Dr M. G. Deo
Research Director
Cancer Research Institute
Parel
Bombay 400 012
—*Chairman*

Dr N. C. Nayak
Department of Pathology
All India Institute of Medical Sciences
Ansari Nagar
New Delhi 110 029
—*Member*

Dr Victor Solomon
Department of Thoracic Surgery
Madras Medical College
Government General Hospital
Madras 600 003
—*Member*

Dr Umesh Chaturvedi
PG Department of Microbiology
K. G. Medical College
Lucknow 226 001
—*Member*

Dr G. V. Satyavati
Senior Deputy Director-General
Indian Council of Medical Research
Ansari Nagar
New Delhi 110 029
—*Member*

Dr V. P. Kamboj
Central Drug Research Institute
Chattar Manzil Place
Lucknow 226 001
—*Member*

Dr B. N. Walia
Post-Graduate Institute of Medical Education and Research
Chandigarh 160 012
—*Member*

Dr D. K. Hazra
Nuclear Medicine Unit
PG Department of Medicine
S. N. Medical College
Agra 282 003
—*Member*

Dr V. Sitaramam
Department of Zoology
University of Poona
Ganeshkhind
Pune 411 007
—*Member*

Dr Indira Chakravarty
Department of Biochemistry
Indian Institute of Hygiene and Public Health
Chitaranjan Avenue
Calcutta 700 073
—*Member*

Dr P. S. Shetty
Nutrition Research Centre
St John's Medical College
Bangalore 560 034
—*Member*

IMMUNOLOGY

Dr S. S. Agarwal
Genetics and Immunology
Sanjay Gandhi P. G. Institute of Medical Sciences
Lucknow–Raebareli Road
Lucknow 226 001
—*Chairman*

Dr Indra Nath
Department of Biotechnology
All India Institute of Medical Sciences, Ansari Nagar
New Delhi 110 029
—*Member*

Dr Pradeep Seth
Department of Microbiology
All India Institute of Medical Sciences, Ansari Nagar
New Delhi 110 029
—*Member*

Dr V. R. Muthukkaruppan
Department of Immunology
School of Biological Sciences
Madurai Kamaraj University
Madurai 625 021
—*Member*

Dr U. C. Chaturvedi
Department of Microbiology
K. G. Medical College
Lucknow 226 003
—*Member*

Dr Shobha Sehgal
Department of Immunology
Post Graduate Institute of Medical Education and Research
Chandigarh 160 012
—*Member*

Dr Rama Mukerji
National Institute of Immunology
JNU Campus, Shahid Jeet Singh Marg
New Delhi 110 067
—*Member*

Dr Sudha Gangal
Cancer Research Institute
Tata Memorial Centre
Dr E. Borge's Marg
Bombay 400 012
—*Member*

Dr Kunthala Jayaraman
Department of Biotechnology
Anna University
AC College of Technology
Madras 600 025
—*Member*

NEUROBIOLOGY

Dr P. N. Tandon
Department of Neurosurgery
All India Institute of Medical Sciences
Ansari Nagar
New Delhi 110 016
—*Chairman*

Dr B. N. Dhawan
Director
Central Drug Research Institute
P. B. No. 173
Lucknow 226 001
—*Member*

Prof. M. Gaurie H. Devi
Department of Neurobiology
National Institute of Mental Health and Neuro Sciences
Bangalore 560 029
—*Member*

Dr Veena Bijlani
Department of Anatomy
All India Institute of Medical Sciences
Ansari Nagar
New Delhi 110 029
—*Member*

Dr B. Ramamurthi
Department of Neurosurgery
V. H. S. Medical Centre
Madras 600 113
—*Member*

Prof. Venkoba Rao
Institute of Physiology and Psychiatry
Madurai Medical College and Government Rajaji Hospital
Madurai 625 020
—*Member*

Prof. P. S. Sastry
Department of Biochemistry
Indian Institute of Science
Bangalore 560 012
—*Member*

Dr N. H. Wadia
Department of Neurology
The Jaslok Hospital and Research Centre
Dr G Deshmukh Marg
Bombay 400 026
—*Member*