DEVELOPMENT IN BIOTECHNOLOGY-WITH REFERENCE TO MALAYSIA

ABU BAKAR SALLEH^a AND JOHN E. SMITH^b

^aJabatan Biokimia & Mikrobiologi,
Universiti Pertanian Malaysia,
Serdang, Malaysia

^bDept. Bioscience and Biotechnology,
University of Strathclyde,
Glasgow, Scotland.

ABSTRACT

Biotechnology is an interdisciplinary subject evolving from four developmental stages namely microbiological production of food and beverages, microbiological processes initially developed under non-sterile conditions, use of sterile containment and exclusion processes, and the 'new' biotechnology comprising genetic engineering, enzyme technology and process engineering. Biotechnology is highly developed in the European countries, USA and Japan where there is close cooperation between governments and private sectors.

Biotechnology is being developed in Malaysia and urgent consideration must be given to identifying the specific needs here and how best it can be achieved in the near future. Appropriate training programme has to be set up with the correct organisational structure and framework established. Health care has been identified as a priority area where biotechnology can offer major contributions, but agriculture seems to be a prime area for biotechnological innovation. Agriculture based biotechnological research towards enhancement of crop yield, production of 'new' food, finding new sources of energy and control of environment should be propagated.

BIOTECHNOLOGY

Biotechnology involves the practical application of biological organisms, systems or processes to manufacturing and service industries as well as to environmental management. Biotechnology will utilize bacteria, fungi yeasts, algae, plant cells and cultured mammalian cells and constituents of industrial processes. Biotechnological processes will mainly function at near ambient temperature, will consume little energy and mainly use inexpensive substrates for biosynthesis.

The main industrial impact of biotechnology will be in human and animal food production, provision of chemical services, waste recycling, pollution control, agriculture and new products to aid and revolutionise many aspects of medicine, the veterinary sciences and the production of pharmaceuticals. Many biotechnological industries will be based mainly on renewable and recyclable materials and countries with easy access to organic material such as wood, agricultural crops or organic wastes are well situated to enter this new area of activity. In particular, tropical countries with abundance of rainfall must be major candidates for certain areas of biotechnological innovation.

Although many aspects of biotechnology are of ancient origin much of 'new' biotechnology is embryonic and will require much skilful control of its development but the potential is vast and diverse and will play a major role in many future industrial processes as well as to the economics of nations.

The interdisciplinary nature of biotechnology cannot be over emphasised. Microbiology, initially the primary discipline, requires the support of biochemistry, molecular and cell biology, engineering and computer technology and these disciplines in addition to other minor ones need to be integrated for successful application of biotechnology. To achieve maximum impact these scientists and technologists must have close working relationship with specialists in other related fields such as agriculture (and veterinary), nutrition, medicine, pharmaceutical and chemical industries and economy.

Bioscientists and engineers of various specialisations will make their individual contributions to biotechnology. However, the term **Biotechnologist** should be considered as an all-embracing description of scientists or engineers engaged in applying their skills and knowledge to the **processing** of biological materials. In contrast a **Biochemical Engineer** is a process engineer whose role is to **transfer** the knowledge of the biological scientist into practical operation. A biochemical engineer will have been trained in the scientific and engineering principles underlying the design and operation of biological operations.

A "complete biotechnologist" will never exist, since no one person can be expert in the skills of microbiology, molecular biology, chemical and process engineering, etc. However, for those who practice in this subject every effort must be made to understand the language of the other component subjects.

A high proportion of the processes practiced in biotechnology are more economic, safer than current traditional industrial processes, less energy demanding and with most processes the residues are biodegradable and non-toxic. It is now abundantly clear that biotechnology offers a means of solving some of the world's major problems in particular those related to medicine, agriculture, pollution control and the development of new energy sources.

In commercial practice the continued successful growth of biotechnology will be dependent to a large extent on three premises.

- (a) An expanding range of valuable products from both traditional and genetically engineered systems.
- (b) The ability to obtain the raw materials from renewable resources.
- (c) The growing awareness that biotechnological processes will in many cases become economical against the present chemical processing of vegetable materials.

Biotechnology, in particular, offers major advantages for the conversion of agricultural by-products and other organic wastes to more valuable products. Thus renewable resources from agriculture, forestry and industrial organic wastes are gaining increasing importance since they offer, by biotechnological processing, a politically and strategically important base for food, feed, basic chemicals and energy production. However, to achieve this will require wide ranging programmes not only in the component aspects of biotechnology but also in land management.

DEVELOPMENT OF BIOTECHNOLOGY

How has biotechnology evolved? Contrary to popular belief biotechnology is not a new pursuit but in reality dates far back into history. The present position of biotechnology in world economics has arisen by way of four major developmental stages.

1. Microbiological production of foods and beverages

The important processes of baking, brewing and wine making have been practiced in most parts of the world for thousands of years yet the recognition of the central role of the yeast microorganism was only first observed in the 17th century by the microscopist Anton van Leeuwenhoeck and then proved experimentally by Louis Pasteur between 1857-1876. Other microbiologically based processes of ancient origin are cheese and yoghurt production, oriental foods and wines, and the many forms of mushroom products. Most of these processes are practiced at large industrial levels and are constantly being improved upon and expanded. Through biotechnological approach these industries have further developed (Kirsop, 1981; Jarvis & Holmes, 1982).

2. Microbiological processes initially developed under non-sterile conditions

Using open systems free of complicated engineering practice by the end of the 19th century where were many processes producing at an industrial level important compounds such as ethanol, acetic acid, organic acids, butanol, acetone etc. Later it was shown that these compounds could be more cheaply produced from the by-products of petroleum production (Gibbs, 1983). However, in present times there has been a major reappraisal of these processes and the economics have begun to change and an increasing volume of these products are now being produced throughout the world by microbiological means. For tropical countries the choice is even more obvious.

Yet other examples include waste-water treatment and composting of solid waste, which are essential requirement in affluent societies. Quite a number of treatment processes are linked to production of food or energy (Coombs, 1981; Boyles, 1982; Howells, 1982; Litchfield, 1983).

3. The use of sterile containment and exclusion processes

In the 1940's new directions in the industrial use of microorganisms came with the introduction of complicated engineering techniques to the mass cultivation of microorganisms which allowed the exclusion of other contaminant microorganisms to the process. Prior sterilisation of the medium, bioreactor and all other systems allowed pure culture technology to develop and contribute to industrial processes. By the nature of the system these processes are costly and suitable only for high value products. Current examples include antibiotics and fine chemicals (Dunhill, 1981), plant cell culture (Kurz & Constable, 1979; Fowler, 1981) and animal cell processors (Spier, 1982).

4. The 'new' biotechnology

In more recent times there have been major developments in molecular biology and in fermentation technology which are creating new and exciting opportunities to lead biotechnology into even greater areas of economic value.

In particular these new innovations have centred around genetic engineering, enzyme technology and process engineering.

a. Genetic Engineering

Manipulation of the genome of industrially important organisms by sexual recombination and/or by mutation has long been part of the innovative repertoire of the

industrial bioscientist. New recombinant techniques involve the systematic manipulation of DNA by involving a mild breakage of living cells, the extraction of DNA, its purification and subsequent selective fragmentation by highly specific enzymes; the sorting, analysis, selection and purification of the fragment containing the required gene, its chemical bonding to the DNA of a carrier molecule and the introduction of the hybrid DNA into a selected cell for reproduction and cellular synthesis (Pittard, 1982). Recombinant DNA technologies permit easier manipulation of organism DNA and can readily by-pass interspecies and intergeneric incompatibility (Schaffner, 1980). Unlimited possibilities exist and already human insulin and interferon genes can be transferred into and expressed by microbial cells (Malik, 1982).

b. Enzyme technology

Isolated enzymes have long being a part of many biotechnological processes and their catalytic properties are being further utilised with the development of immobilisation techniques. Enzymes can be entrapped, adsorped or covalently linked to insoluable matrices immobilised by various methods (Fig. 1). Immobilised enzymes are apparently more stable, can be reused or used in continuous mode and are more convenient to handle (Chibata, 1978). A further development is the immobilisation of whole cells allowing for multi-step biocatalytic processes (Fukui & Tanaka, 1982).

Fig. 1 Methods for Immobilisation of Enzymes and Cells.

c. Process Engineering

Bioreactors play a central role in biotechnological processes by providing a link between the starting materials or substrates and final products (Fig. 2). Major advances have been made in bioreactor designs, though the batch reactors still dominate in industrial use (Sittig, 1982; Cooney, 1983). With improvement in process monitoring techniques where computers are becoming an essential component of a biotechnological process, high yield and quality products can be expected. However, the application of process control in biotechnological industries are many years behind that already in operation in the chemical process industry. New approaches to the processing of the products of biotechnology (Downstream processing) will improve the economics of all processes (Atkinson & Sainter, 1982). However, downstream processing is still the Cinderella subject of biotechnology, particularly at University research level.

Fig. 2 Schematic view of a Biotechnological Process. A typical aerobic system. Air and sterilisation may not be essential in all processes.

THE ATTAINMENT OF BIOTECHNOLOGY AT NATIONAL LEVEL

A full and meaningful development of biotechnology will reflect national levels of training both at technical and managerial level (Anon, 1981). Without suitable and sufficient personnel, biotechnology will not achieve its full potential.

Each biotechnological scenario will require continuous assessment of the resources available, the economics and the impact on the environment, together with the health and safety of operators and users. Biotechnology if correctly planned should help to achieve a proper balance between natural resources, human needs and the environment.

Furthermore, when considering the applications of biological discoveries to future industrial applications the importance of time should not be underestimated. Between the amount when a new discovery has been made the successful commercial production achieved 5-20 years could have passed. Thus significant developments involving 'new' biotechnology must not be expected until the 1990s.

There can be little doubt now that the techniques of biotechnology will offer commercial advancement to industries and nations who realistically apply them. The rapid advances in new areas of biotechnology have prompted many nations to examine the possibility for internal development and to assess their own ability of supplying the necessary trained personnel to put new biotechnology into application.

Much emphasis is being put into biotechnological research in Europe (Rehm, 1982). In France a commission of experts has been set up by the French Government to guide companies in a three year 1 billion French franc investment programme. In Canada a 'Task Force on Biotechnology' was established by the government in 1980 and in its recommendations charge the government with the responsibility of setting up a ten-year national development plan with massive financial input to strengthen the research basis

particularly at an interdisciplinary level. In particular, additional funding was given to the National Science Council. Particular attention was to be given to graduate training and post-doctoral activity. In line with most other countries Canada has recognised that the major foreseeable stumbling block to successful biotechnology development is not funding or ideas but rather the worldwide shortage of suitably trained and experienced practitioners.

Germany has been particularly active in biotechnology and in 1972 an investigation by the German Chemical Apparatus Association (DECHEMA) promoted the government of the Federal Republic of Germany to set out a major national programme on biotechnology. Major funding is given to the Federal Ministry of Research and Technology for industrial studies which the *Deutsche Forschungsgemeinschaft* extensively supports to academic and institute development of the core subjects of biotechnology. There are now many active centres of biotechnological development in Germany.

In the United Kingdom the Spinks Report strongly advised the government to increase the level of funding for the research base of biotechnology. This has been accepted by the government and considerable increase in funding has been given to the various research councils. In particular academic centres with established expertise in the core aspects of biotechnology have been awarded additional funding. Also within the U.K. the British Co-ordinating Committee on Biotechnology has been established. This is in fact an association of learned societies with interests in biotechnology that attempts to co-ordinate the many activities of biotechnology viz academic and applied for the benefit of the nation and the subject. The committee also relates with European Biotechnology Societies and functions actively on the many working groups on specific areas of interest e.g. Downstream Processing, Enzyme Technology, Education, Environmental Pollution, etc. As an example of how biotechnology should be co-ordinated nationally the BCCB sets a useful example. Within the U.K. there are a large number of outstanding industrial bases of biotechnology, involving national and multinational companies.

Biotechnology is being developed actively in Russia, Czechoslovakia, Hungary and the German Democratic Republic with particular emphasis on the utilization of microorganism for biotechnological application.

In the U.S.A. there have been strong attempts to improve communications between research institutes and industry, but in general the level of government funding for biotechnology is less than would be expected. The U.S.A. has been one of the leading research bases for recombinant DNA studies and much of the exciting new developments in this area have been supported by venture capital with the establishment of numerous small but highly specialised genetic engineering companies. Most major pharmaceutical and fermentation companies have now vigorously entered the new area of biotechnology (Anon, 1984a). The Office of Technology Assessment has recently produced a most worthwhile document on the impacts of applied genetics to biotechnology.

In the Far East, Japan has always been a world leader in many aspects of biotechnology, in particular, in the use of microorganism for product formation. Japan was slow to enter the area of recombinant DNA technology but more recently has devoted major concentration of funding to this end. Fermentation technology and related areas of downstream processing are well developed in the Japanese industrial programme. The level of activity can be assessed by the scale of the Japanese government's support which has been increasing since 1973 for research and development in biotechnology (Rogers, 1982). Table 1 gives key reports on biotechnology.

TABLE 1
KEY REPORTS IN BIOTECHNOLOGY

Date	Country	Report
1974	W. Germany	DECHEMA, for BMFT : Biotechnologie
1976	Japan	MITSUI : Present and Future of Enzyme Technology.
1976	U.K.	A.N. EMERY, for Science Research Council : Biochemical Engineering.
1977	Commission of the E.C.	D.G. XII : Possible Action of the European Communities for the optimal exploitation of the fundamentals of the new biology in applied research.
1978	Europe	DECHEMA organise first European Congress of Biotechnology, Interlaken, Switzerland; European Federation of Biotechnology founded.
1979	France	F. GROS, F. JACOB, P. ROYER : Sciences de la vie et societe, pour le President de la Republique.
1979	France	J. de ROSNAY : Biotechnologies et Bio-Industrie
Jan 1980	W. Germany	BMFT Leistungsplan 04 : Biotechnologie
Mar 1980	U.K.	"SPINKS REPORT" Biotechnology : report of a joint Working Party (ACARD, ABRC, Royal Society).
May 1980	Belgium	SPPS: Developments en matiere de biotechnologies.
Sep 1980	Canada	MILLER et al : Biotechnology in Canada.
Feb 1981	Canada	Report to Minister for Science and Technology : Biotechnology : a development plan for Canada.
Feb 1981	France	J.C. PELISSOLO : La biotechnologie, demain?
Mar 1981	U.K.	Govt. White Paper : Biotechnology (response to SPINKS).
Apr 1981	U.S.A.	O ZABORSKY : Biotechnology at the National Science Foundation.
Apr 1981	U.S.A.	Office of Technology Assessment : Impacts of Applied Genetics : Micro-Organisms, Plants and Animals.
May 1981	Netherlands	STT : Biotechnology : a Dutch perspective.
May 1981	Ireland	NBST : Biotechnology Trends.
Sep 1981	U.S.A.	Office to Technology Assessment : Project Proposal for a Comparative Assessment of Biotechnology.
Sep 1981	Spain	La ingenieria genetica en la biotecnologia (Centro para el Desarrollo Tecnologico Industrial, Ministerio de y Energia)
Oct 1981	Japan	Report : Heading toward new Research and Development, by the Study Association for the Foundation of a Long-Term Plan for the Development of Industrial Technology.
Nov. 1981	UNIDO	The Establishment of an international Centre for Genetic Engineering and Biotechnology (ICGEB) report of a group of experts.
Dec 1981	U.S.S.R.	Speech by Academician OVCHINNIKOV at the Annual General Meeting of the Soviet Academy of Sciences.
Apr 1982	Netherlands	Programmacommissie Biotechnologie : Innovatieprogramma Biotechnologie (Chairman : Prof. R.A. SCHILP EROORT).
Sep 1982	OECD	International Trends & Perspectives in Biotechnology : A State of the Art Report by A.T. BULL, G. HOLT and M.D. LILLY.

BIOTECHNOLOGY IN MALAYSIA

The interest in biotechnology can be assessed by a series biotechnologically-oriented meetings organised in Malaysia in recent years as well as reports on biotechnology (Ahmad Zaharuddin, 1983; Mohd. Salleh Ismail, 1983; Cheah, 1983; Salleh & Smith, 1983).

Training

The importance of biotechnology to the Malaysian economy is obvious. How it will be realised is less clear. Underpinning strong industrial biotechnology is the availability of well trained scientists and engineerings.

Urgent consideration must be given to identifying the specific needs of Malaysia and how best they can be achieved in the near future. There is an obvious vacuum at the organisational level and rapid co-ordination should be carried out to established a graduate training and research programme interwoven with industrial application. Though a few Universities have developed undergraduate programmes, most Universities throughout the world have recognised that biotechnology is best taught not at an undergraduate level but rather at postgraduate. Here those graduates in Bioscience (i.e. Microbiology, Biochemistry, Genetics) or in Chemical Engineering will be taught the rudiments and language of the other discipline. The full application of biotechnology will require an interdisciplinary approach and a core of highly qualified scientist/engineerings will be required to achieve maximum return.

It must further be realised that the dominant forces in biotechnology will be the specialist microbiologists, biochemists, genetists and chemical and biochemical engineers. Such people do already exist in considerable numbers in Malaysia and the first priority must be to establish the correct organisational structure and framework within the country's centres of higher education. No one group should seek to control all the activities of biotechnology. Collaboration and a willingness to establish the correct environment for creative activity must be the rule of the day.

Research

At the research level even more selectivity must be exercised. Biotechnology is a vast field of activity and in forward planning much care must be taken to identify the areas that would best suit the needs of Malaysia. Malaysia must decide whether they seek to establish an involvement with the highly expensive areas of biomolecular engineering and process technology or whether to leave these areas to the more technological advanced nations and to concentrate on a lower level of technology more appropriate to their ability to support both educationally and financially.

It is perhaps in the general area of agriculture that Malaysia may seek to enter actively into the field of biotechnology. The ability to produce an abundance of biomass can be a significant factor to many aspects of biotechnology.

Most biotechnological processes depend at some stage, upon the availability of carbohydrates. Carbohydrate and polysaccharides in their many forms, are derived from biomass and countries with high agricultural and forestry productivity are richly endowed with the basic feedstock for practically every conceivable biotechnological process. Many agricultural crops are already being used for conversion into other products by fermentation processes. Notable at Malayan Agricultural Research & Development Institute (MARDI) research to produce hygienic and high quality products on many traditional fermented food are being pursued. Advances have been made in the production of tapai

(fermented cassava or glutinous rice) and tempeh (fermented soya bean cake) Leow, 1983). Though there is no indication yet that this aspect of research is to turn into large scale biotechnology processes, new technologies are being passed on to small entrepreneurs, and will go a long way towards improving the economic status of the population. Another aspect of food production is cocoa fermentation research. Various parameters for fermentation of cocoa such as microbiological populations, design of fermentation vessels as well as control of process are being investigated to produce high quality cocoa products (Anon, 1982a). Single cell protein as a source of food is another area of interest. Much work is focussed on the use of agrowaste such as palm oil mill waste for the growth of cells (Anon, 1982b). Other substrates such as rubber mill effluent, starch mill effluent and animal waste are being studied at many Universities, Standard Institution & Industrial Research of Malaysia (SIRIM), Rubber Research Institute of Malaysia (RRIM), & MARDI.

Malaysia is still dependent on oil for its energy requirement, but there is still the gas and hydro options to be taken up. There is abundant supply of biomass either for direct burning or for conversion to alcohol or biogas and research in this area should be considered a major area of biotechnology study in Malaysia (Zohadie Bardaie, 1981). Most research projects on energy production in Universities and Research Institutions are directed towards the utilisation of wastes, thus, achieving a parallel objective of waste management (Rahim Bidin et. al, 1981; Mohd. Salleh, 1981).

Alcoholic fermentation to ethanol is an ancient art and in most part of the world has been practiced for the production of potable drinks. The production of alcohol for energy purposes has also been carried out but with less vigour, particularly since it compared badly with the more economic production from petroleum. However there has been a dramatic change in this view since the major change in oil prices and more so by the realisation that fossil fuels are limited items. Much basic research continues and it is anticipated that the use of new areas of biotechnology such as the improvement of yeast efficiency by genetic engineering will improve the economic viability of ethanol from biomass for fuel use. Local biogas can replace fuels such as kerosene and is widely practiced in many countries. Biotechnology is improving the anaerobic for digesters that produce this and the resultant residues may be used to enhance soil fertility.

There is a pilot plant for biogas production from palm oil mill effluent, built under Japanese aid at SIRIM. However most work is still very much at the preliminary stages. The use of alcohol as fuel may be of no immediate need but there is every possibility of using small bioreactors for biogas in the rural communities where there is abundant biomass (agrowastes). Of interest in the energy front is the announcement of Palm Oil Research Institute of Malaysia (PORIM) recently that there is the possibility of converting palm oil to diesel (Anon, 1983a, 1984b).

Genetic Engineering and Agriculture

The technique of gene splicing has become a common laboratory tool. But by most account genetic engineering research is an expensive and long term investment. No doubt there has been tremendous development in the health care side such as microbial production of human interferons, insulin and monoclonal antibodies, mainly largely through venture capitals funding research in many biotechnology companies such as Genentech, Biogen and Cetus. In Malaysia such funding is remote. This is much discussion on genetic manipulation of crop plants. Vegetative propagation for selection of high quality clones for oil palms (Corley, et al. 1982) and cocoa (Anon, 1983b) have been achieved with

some measure of success. Primary studies on the genetic make up of perennial plants such as rubber, oil palm and cocoa are required and the relevant research institutions and the Universities are pursuing this line of research. Much more money, time and, particularly, expertise are needed if genetic manipulation is to be incorporated into plant research to acquire high yielding and hardy crop plants.

Health care

Health care aspects of biotechnology have gained world acclaim and to become involved in such studies would be natural for such a nation with a high population. More so little attention is given to tropical diseases by the advanced nations. However even in those nations many aspects of biotechnologically directed health care studies are becoming less attractive to industrial concerns because of prolonged and expensive testing systems required by law and finally the length of time that will be required before financial returns are made. At the moment this aspect of biotechnology does not appear to progress in Malaysia.

However, there is some indication that biotechnological approach may be made in veterinary medical research such as for the production of vaccines and monoclonal antibodies to combat animal diseases.

CONCLUSION

The rapid technological advance in biotechnology, threatens to increase rather than to decrease the scientific and technical gap between the Third World and the industrialised nations and to severely influence the traditional exporters of primary raw materials.

But there can be no doubt that biotechnology can reduce the poverty, vulnerability and dependence of developing countries. However, very special care must be given to the manner in which the various biotechnological programmes are transferred, used and put into practice in the social and economic contexts of the developing nations. Specific attention must be given to local conditions and needs.

To achieve a realistic interaction between the Third World and biotechnologically advanced nations the initial steps must be to develop traditional and small-scale biotechnology by adopting the following policy:

1. Improve the basic and applied knowledge of the various applicable techniques, e.g. comparative waste treatment, traditional fermentations, mushroom production.
2. Greatly increase the training of specialists able to understand and practice biotechnology, in particular, applied microbiologists, biochemists, food technologists and chemical engineers.
3. Advance the cause of appropriate, locally relevant solutions and uses.

REFERENCES

- Ahmad Zaharuddin Idrus (1983) *New Frontiers of Science in Agriculture*, Paper presented at the 9th Annual Conference Malaysian Biochemical Society, 13-14 Sept. 1983, Serdang, Malaysia.
- Anon (1981) *Biotechnology and Education*, The Report of a Working Group, The Royal Society, London.

- Anon (1982a) Annual Report 1982, Food Technology Division, MARDI, Malaysia.
- Anon (1982b) PORIM Annual Research Report 1982, PORIM, Malaysia.
- Anon (1983a) Enter the Palm Diesel, *New Sunday Times*, 1 May 1983.
- Anon (1983b) Mardi's Big Success in Cocoa Cloning, *New Straits Times*, 24 May 1983.
- Anon (1984a) Biotech Comes of Age, *Businessweek*, January 23, 1984, 48-54.
- Anon (1984b) Palm diesel on the way. *New Straits Times*, 25 February, 1984.
- Atkinson, R. & Sainter, P. (1982) Development of Downstream Processing. *J. Chem. Tech. Biotech.* 32(1), 100-108.
- Boyles, D.T. (1982) Fuels from Renewables, *Chem. Ind.*, 15, 522-527.
- Cheah, S.C. (1983) Biotechnology – An overview. *PORIUM Bull.*, 6, 16-28.
- Chibata, I. (1978) *Immobilised Enzymes – Research and Development*, Tokyo, Kondansha Ltd.
- Coombs, J. (1981) Biogas and Power Alcohol, *Chem. Ind.* 7, 223-229.
- Cooney, C.L. (1983) Bioreactors : Design and Operation. *Science*, 219, 728-733.
- Mohd Salleh Ismail (1983) Biotechnology in Developing Countries. Paper presented at the Regional Conference on Impact of Microbiology in Tropical Agriculture, 24-26 October, 1983, Serdang, Malaysia.
- Pittard, A.J. (1982) A Perspective on Recombinant DNA and Genetic Engineering. In *"Microbial Physiology and Genetics of Industrial Processes"*, eds. Millis, N.F. and Pittard, A.J., p. 227-237. University of Melbourne, Melbourne.
- Rahim Bidin, Chong, C.N., Badaruddin Baharum (1982) Biogas Technology in Malaysia. Paper presented at The Regional Workshop/Symposium 4-11 May 1981, Serdang.
- Rebm, H.J. (1982) Biotechnological Research in Europe, *J. Chem. Tech. Biotechnol.* 32(2), 9-13.
- Rogers, M.D. (1982) The Japanese Government Role in Biotechnology Research and Development. *Chem. Ind.* 15. 533-537.
- Salleh, A.B. & Smith, J.E. (1983) Biotechnology: A Field of Research in Focus. *Pertanika*, (Review Supplement) 6, 19-36.
- Schaffner, W. (1980) Direct Transfer of Cloned Genes from bacteria to Mammalian Cells. *Proc. Natl. Acad. Sci. U.S.* 77, 2163-2167.
- Sittig, W. (1982) The Present State of Fermentation Reactors. *J. Chem. Tech, Biotech.*, 32(1), 47-58.
- Spier, R.E. (1982) Animal Cell Technology: an overview. *J. Chem. Tech. Biotechnol.* 32(1), 304-312.
- Zohadie Bardaie (1981) *Energy and Agriculture*, UPM, Serdang.

- Corley, R.V.V., Wong, C.Y, Wooi, K.C. Jones, L.H. (1982) Early Results from the First Oil Palm Clone Trials. In *"The Oil Palm in Agriculture in the Eighties,"* Incorporated Society of Planters, p. 173-196.
- Dunhill, p. (1981) Biotechnology and Industry. *Chem. Ind.*, 7, 204-217.
- Fowler, M.W. (1981) Plant Cell Biotechnology to Produce Desirable Products., *Chem. Ind.* 7, 229-233.
- Fukui, S & Tanaka, A. (1982) Immobilised Microbial Cells. *Ann. Rev. Microbiol.* 36, 145-172.
- Gibbs, D.F. (1983) The Rise and Fall (..... and Rise?) of Acetone/Butanol Fermentations. *Trends Biotech.*, 1(1), 12-15.
- Howells, E.R. (1982): Single Cell Proteins and Related Technology *Chem. Ind.* 15, 508-511
- Jarvis, B., & Holmes, A.W. (1982) Biotechnology in relation to the Food Industry, *J. Chem. Tech. Biotech.*, 32(1), 224-232.
- Kirsop, B.H. (1981) Biotechnology in the Food Processing Industry, *Chem. Ind.* 7, 218-222.
- Kurz, W.G.W., & Constable, F. (1979) Plant Cell Culture. A Potential Source of Pharmaceuticals. *Adv. Appl. Microbiol.*, 25, 209-240.
- Leow, P.T. (1983) Times Focus : Mardi's Many First. *New Straits Times*, 18 July 1983.
- Litchfield, J.H. (1983) Single Cell Protein, *Science*, 219 740.
- Malik, V.S. (1982) o Biotechnology and Where it is Going. *Proc. Biochem.*, 17(2), 38-41.
- Mohd Salleh Ismail (1981) Biofuel Production in Malaysia – Research and Development. Paper presented at the Regional Workshop on Biofuel Conversion for Fuel Production, 20-23 October, 1981, Serdang.