OBAFEMI AWOLOWO UNIVERSITY, ILE-IFE, NIGERIA

Inaugural Lecture Series 127

THE POTENTIALS OF BIOCHEMICAL ENGINEERING IN INDUSTRIAL DEVELOPMENT

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An Inaugural Lecture Delivered at Oduduwa Hall,
Obafemi Awolowo University, Ile-Ife,
on Tuesday, August 11, 1998

Inaugural Lecture Series 127

Obafemi Awolowo University Press Limited,
Ile-Ife, Nigeria.

ISSN 0189-7845

Printed by
Obafemi Awolowo University Press Limited,
Ile-Ife, Nigeria.

POTENTIAL APPLICATIONS OF BIOCHEMICAL ENGINEERING IN INDUSTRIAL DEVELOPMENT

I was at the University of Ibadan in October 1964 using a West Regional Scholarship but the Federal Scholarship was richer hence I applied for it. My application succeeded but simultaneously the Bureau for External Aid for Education offered me a foreign scholarship to study chemical engineering in Romania- a Latin speaking country. I accepted (I studied Latin at Christ School Ado-Ekiti) and left Nigeria early in December 1964 and joined the on going lectures at the Polytechnic Institute of Bucharest, an engineering institution with a student enrollment then of about 40,000. Chemical Engineering was a Faculty in the Institute and there were only two of its kind in that country. There was discipline, there were facilities and welfare was good. I completed the Dipl-Ing (M.Sc.) degree programme in June 1970 in the distinction bracket and was invited to continue for the doctoral study at the Chemical Research Institute of Bucharest (an arm of the academy). My Dipl-Ing thesis project was on the Synthesis and Plant Design for the Production of Tetra-alkyl (-aryl) Thiuram disulfides (a class of chemicals with anti-addiction properties). But, for a change, I intended going to the University of California, Los Angeles where I had also been offered admission. However, a visit to Nigeria in July 1970 changed all that for I was posted to the Federal Ministry of Industries from where I joined the University of Ife (now OAU) in December 1970 as the first Graduate Assistant on an enhanced scale in the Department of Chemical Engineering. In September 1971, I left for the University College, London as a Commonwealth Academic Staff Scholar for the M.Sc. degree course in Biochemical Engineering.

This discipline Biochemical Engineering-acquired its standing by backward integration. While it has enjoyed tremendous development and application in the developed countries, it is still in its infancy in the developing countries. As such this lecture has to be presented in its global perspective rather than focus on a narrow research area.

Harnessing the forces of nature for the service and convenience of man is the main object of the Charters of the Institutions of Professional Engineers worldwide. George E. Davis gave the first course of lectures in Chemical Engineering in 1887 while Sir Harold Hartley gave the first course of lectures in Biochemical Engineering in 1957 both at Manchester in England (R. Steel, 1958). At this time, chemical engineering, activated by chemical warfare activities in the 1930s to 1940s had become established in Europe, America, Japan and USSR (Layokun, 1975) but the discovery of the potentials in

harnessing of the ability of micro-organism to synthesize highly useful and complex molecules under relatively mild conditions was an incentive for Harold Hartley to propose biochemical engineering as a viable extension to chemical engineering practice. This proposal has met with universal approval and is enjoying wide applications.

Definition of Biochemical Engineering

The current definition of Biochemical Engineering is the application of engineering principles to industrial biological processes such as fermentation, enzymes extraction and use, food preservation and waste treatment. Hence the industrial application of a biochemical process is a combined operation in which the biochemist, the microbiologist, the geneticist and the chemical engineer are all intimately concerned. The special role of biochemical engineers is to translate the understanding of the biological scientists, by empirical means in many cases into increased productivity. While many problems in biochemical engineering are analogous to those encountered elsewhere in the chemical process industries, others require a more specialized knowledge dictated by the complex limitations imposed on design by the biological nature of the materials and processes. Additional unit operations over purely chemical processes include sterilization, aeration, freezing/de-freezing and pasteurization as well as those procedures encountered in product recovery from fermentation broth.

The Scope of Biochemical Engineering

The exploitation of micro-organisms is at the heart of biochemical engineering practice. The new science of molecular biology has produced a remarkable outpouring of new ideas and powerful techniques. From this revolution has sprung, in particular, a new discipline called genetic engineering which give us the power to alter living organisms for important purposes in medicine, agriculture and industry. The resulting biotechniques span the range from the ancient art of fermentation principles (about 7,000 BC) to the new esoteric use of gene splicing and monoclonal antibodies. Of special importance is fermentation among other bioprocesses briefly described as follows:

1. Fermentation - aerobic and anaerobic: These include the production of primary products such as alcohol, butanol, acetone, citric acid and secondary products such as vinegar and antibiotics as well as activities in sewage disposal, curing of

hides, retting of flax, silage making and all the food products which depend on microorganisms and enzyme systems for their character and flavour e.g. beer, cheese, wine and cocoa. It is important to know that fermentation itself can be divided into four commercially viable groups namely:

(a) those that deal with cell mass production i.e. production of single cell protein as well as cultivation of plant and animal cells. The Imperial Chemical Industries in the U.K and some ventures in the old Soviet Union were producing single cell protein (SCP) from methane while the Germans were producing *Candida* spp. as a source of food for soldiers during the world wars. Currently there is high turnage turnout in the developed countries. In Nigeria, the Nigerian Yeast and Alcohol Manufacturing Company (NIYAMCO) located at Bacita is struggling to produce ethanol from molasses with little to show on yeast production. Attempts to produce yeast on a pilot scale is however going on at Federal Institute for Industrial Research, Oshodi (Odunfa, 1996).

(b) those that produce microbial enzymes: Nigeria imports all grades of enzymes from Europe and America. The amylases and glucosidase used in the industries are all imported from Denmark. Apart from enzymes generated *in situ* in various university laboratories for research purposes, there is no known industrial enterprise engaged in large scale production.

(c) those that produce microbial metabolites. Products are elaborated either as growth associated or non growth associated depending upon the microbial growth phase in which the product is produced. Generally, the initial products such as ethanol and butanol are subject to bioconversion to secondary metabolites. Biochemicals and solvents as well as antibiotics are produced. The locally distilled gin (ogogoro) is inefficiently manufactured or distilled as it sometimes contains traces of methanol acetaldehyde and esters. There is need for improvement.

(d) transformation processes: in this process a compound is transformed into a structurally related but potentially more valuable product by the action of microorganism whether as wild type or genetically engineered. The unit operational procedures are quantitatively accomplished offering at the same time the advantages of low temperature requirement and non-usage of potentially polluting heavy metal catalyst. Some of the operations include: amination, deamination, dehydrogenation, hydroxylation, oxidation, alkylation, decarboxylation, isomerization etc. Active steroids, semi-synthetic, antibiotics and prostaglandin are notable examples of biotransformed chemicals (Kieslich, 1982). A look at the catalogues of Aldrich chemicals and Sigma chemicals gives an insight into the versatility of this fermentation scope.

2. The manufacturing of sera and vaccines.

3. Extraction processes for insulin and other hormones, fat from oil seeds, essential oils and perfumes, infusion such as tea and coffee and bone products such as glue and gelatin.

4. Processing of forest and crop products including agricultural wastes such as cereal straws, leaves, grass, algae and seaweed. The prospect for the harnessing of photosynthesis are very high. Of the polysaccharides present in agricultural wastes cellulose has proved to be the most valuable. And it is renewable. Approximately, 0.1% of the solar energy incident on earth is fixed by green plants through photosynthesis. The annual net yield of the process amounts to about 20×10^{10} tons of organic plant substance. Half of this is cellulose (Tracey, 1964; Bellamy, 1969). Since one man requires 500g of food (70g protein, 80g fat, 350g carbohydrates) per day to maintain himself (Klicks, 1970), the present world population of around 6 billion (6×10^9) requires more than 8×10^8 tons of food per year and this demand is steadily increasing. Cellulose is also a substance for single cell protein (SCP) and as a material for fermentation. The wastes from the processing of cellulose materials offer the most immediate promise for

economic utilization even though composting, use as manure, landfill and even burning without undue pollution can be expensive. The use of cellulose as an energy source appears to offer the greatest incentive.

5. Downstream processing in the chemical; petroleum-petrochemical industries. The obvious need for a clean environment has generated so much effort in effluent treatment and the design of solid, liquid and gaseous effluent treatment plants. Of particular interest are the petroleum/petrochemical industries where hydrocarbon-degrading organisms are required. These organisms are preferably isolated from hydrocarbon-polluted environment such as soil or sewage or activated sludge system. This is a strictly biochemical events in which the growth characteristics and bioenergetic regularities of an organism dictates its preference to others capable of performing the same duty. Dispersants are prepared to be used in the cleansing of terrestrial oil spills. *Pseudomonas aeruginosa, P. fluorescens, P. putida* have been found useful.

6. Industrial 'typing' of microorganisms: this involve the selection, isolation and screening of microorganisms and identifying the functions they can perform at the industrial level. It may have to go beyond the wild type strain in which case genetic engineering principles are invoked. Genetic engineering is a loose term used to describe any gene manipulation technique especially recombinant DNA techniques. Recombinant DNA (r-DNA) is the hybrid DNA produced by joining pieces of DNA from different organisms together in vitro while recombinant DNA technique is the use of r-DNA for a specific purpose such as the formation of a product or the study of a gene. This is desirable for selectivity and increased productivity. This procedure would be useful as a bases for classifying various organisms in a culture collection center. The idea of gene cloning in humans is another venture altogether.

7. Teaching and research in biochemical engineering - "I am very glad that the first course of lectures in Britain on biochemical engineering should be given in the Manchester College of Science of Technology since it was in its forerunner-the Manchester Technical School that George Davis gave the first

course of lectures on chemical engineering 70 years ago. It is a good omen for a subject that has a great future". This was the opening paragraph of the first lecture ever on biochemical engineering given by Sir Harold Hartley in the spring of 1957 in Manchester, England (R. steel, 1958). The component disciplines of biochemical engineering - biochemistry, microbiology, elements of genetics and chemical engineering - were already being well articulated and taught in various departments in Europe, America and Japan but the introduction of the teaching of biochemical engineering was a later event. The Handbook of Chemical Engineering by G.E. Davis published in 1901 is said to have been the first textbook of Chemical Engineering. The next set of books which appeared in the mid 60s were "Biochemical Engineering" by Aiba, Humphrey and Millis; "Biochemical Engineering" by F.C.Webb and "Biochemical and Biological Engineering Science". Volumes 1-3, edited by Blakebrough. Aiba was at Kyoto University in Japan, Humphrey and Millis at Pennsylvania State University, USA, F.C. Webb at University College, London and N. Blakebrough at the University of Birmingham, England. These chemical engineering departments started the teaching and research in biochemical engineering at the postgraduate level offering both M.Sc. and Ph.D. degree programmemes. To my knowledge, only the University College, London has scaled it down to offering the B.Sc. and B.Eng. degree programmemes. There are of course several research institutes in Canada, America, Germany, Holland, Japan and USSR. Some institutes and University departments name them as biotechnology departments or institutes or units. In a typical biotechnology research institute, the scope is about 75% biochemical engineering, the rest being on related biological and biomedical engineering. Only recently the Department of Chemical Engineering and Biochemical Engineering at the University College, London where I trained for the M.Sc., DUC, completed a £12.5 million interdisciplinary Biochemical Engineering Research Center in conjunction with the ministry of the environment and funded by the British Government. A department of chemical engineering with a strong biochemical engineering division was set up by N. Blakebrough at the Indian Institute of Technology, New Delhi in 1973. Recognizing the importance of biochemical engineering in the industrial

development of a nation, the new NUC programmemes includes biochemical engineering as a compulsory 3 unit course in Part III and an elective of 3 unit course in Part V of the Chemical Engineering degree programmeme.

Some Organizations Engaged in Biochemical Engineering Practice

One of the gains of conference attending is interaction with both researchers and those working in industries. During these interactions, the problems associated with products development from research findings are freely discussed. It also offers the opportunity to fashion some form of collaboration with the industry. In fact most industrial organizations sponsor conferences and the workshops to achieve these interactions. Over the years I have come to know the thrust of several companies and the multinationals who unfortunately have hitherto found our industrial climate and altitude in Nigeria uncomfortable. However, I am giving a few examples to illustrate how well biochemical engineering has gained ground in Europe and America.

Glaxo, UK.

The company is engaged in genetic research among others. BIOGEN, based in Geneva is its subsidiary and is now called Glaxo Institute for Molecular Biology. It has some marketing right for cancer and AIDS drugs. Its Montrose (in Scotland)- based Glaxochem is now actively engaged in the increased production of Canitidine- the active ingredient of Zantac (an antiulcer agent).

Porton International, UK.

The number of companies under this organization reaches double figures. Porton Instruments produces progenitor- a protein sequencer. Its biotechnology computer systems company has produced two control programmes in collaboration with University College, London. BIO1 is a package design for DEC computers providing process management for large fermentation plants. BIOPC which runs on the IBM AT or similar systems is described as a versatile small scale control programmes for up to four bioreactors.

Beecham, UK.

Has streamlined its organization and concentrated on health and personal care interest. The combination antibiotic- Augmentia consisting of Penicillin, Amoxycillin plus the beta-lactamase inhibitor Clavulanic acid are currently on high production.

ICI, UK.

The organization has operational sections all over the world specializes in the production of wide range of chemicals used to control the production of hybrid wheat and barley seeds. Many inventions are under patents

Dupont, USA.

Newly introduced DNA sequencer which allows a laboratory technician to sequence the AIDS virus genome in one day something which originally took six Dupont Ph.D. scientists six months. Also under investigation is a range of biomaterials for implant and prosthetic devices for surgical instruments and arterial handling. There is a lot of interest in the production of antiviral, antifungal and antibacterial agents as well as in drugs to treat AIDS and cardiovascular problems.

Novo, Denmark.

The company engages in the manufacture of pharmaceuticals and enzymes. Its company (Bio) handles diagnostic problems. It develops kits for the detection of hormones and infectious diseases mostly based on antibodies but they rely on enzymes for amplification purposes. It is a major supplier of saccharifying enzymes to the breweries and allied companies in Nigeria.

Inotec, UK.

Produces soil inocula for assisting the germination and growth of leguminous food crops especially soy beans. Supplies its products to USA, Canada, Africa, Middle East, Europe and South America.

Monsanto, USA.

It is currently developing a major biotechnology programmes to insert genes into crop plants and to create drugs resistant to herbicides.

Ciba Geigy, Switzerland.

Engages in pharmaceutical research and is prosecuting about twelve projects in new drugs-interferon, microphage inhibition factor and muramyl tripeptide as possible cancer therapist. They also engaged in the manufacture of drugs for the treatment of thrombosis and shock. For instance hirudin, originally obtained from leaches are now being made by fermentation in baker's yeast.

Brewing Foundation,UK.

The Brewing Foundation started in the 70s is headed by Professor B. Atkinson, a biochemical engineer. One fundamental feature of this foundation is its Research and Development Programmes which involve among other thrust the principles of scale up from laboratory scale to pilot scale and then to commercial scale. Process optimization and control as well as the integration of cleaner technology concept are essential part of their R & D. Naturally not all items of information on brewing strategies are accessible.

MY CONTRIBUTIONS

On my return to the department after the Ph.D. degree study at the Imperial College, London, I-realizing the conscious efforts of the developed countries to prosecute and fund research in biochemical engineering/biotechnology in their respective domains, opted to start biochemical engineering inspite of the lack of equipment and specific infrastructure.

Essentially, my contribution have been in the areas of teaching, research and contact with industry. My first real encounter was in 1971/72 academic session at the University College, London as an M.Sc. student of biochemical engineering. It was exciting going through the new rigours of microbiology and genetic engineering, biochemistry and the design procedures marrying the characteristics of microorganisms as catalysts and reactants with the existing chemical engineering operations. My thesis project was on "n-Hexadecane Utilization by *Pseudomonas aeruginosa*" (Layokun S.K., 1972, 1982). The system was designed and executed on both batch and continuous modes (Layokun, 1982). Of immense pleasure is the fact that the system worked perfectly. Important findings which have found industrial applications are:

(i) *P. aeruginosa* is a good fermenter of hydrocarbons and therefore widely used in bioremediation of oil spills.

(ii) *P. aeruginosa* accumulates internal reserves such as poly *β*-hydroxybutyrate under nutrient sufficiency. This was a clue to the formation of microbial polymers.

(iii) Metabolic reactions of this nature do not fit into simple kinetic models. It was not until 1985 that Layokun *et al.* developed the appropriate model.

The question of "how one molecule begets another" could be answered chemically or biochemically. I became part of the answer package

chemically at the Imperial College, London from October, 1972 to January, 1975 this time developing high temperature reactors analytical systems with the corresponding computer programmes (Layokun S.K., 1975). Highlight of experience on this Ph.D. study are:

(i) Design of a reentrant reactor attaining 1200°C internally but only 22°C on the outside.

(ii) Coupling of the reactor system to the GC-MS

(iii) Deconvolution or resolution of the superimposed mass spectra by self-developed computer programme

(iv) Development of an integration programme devoid of steady state assumptions to resolve the chain reaction schemes (Layokun *et al.*, 1979). The project was funded by ICI, UK.

The aspects of my research works at OAU relevant to this lecture are on biochemical reaction engineering. Reactants of interest have been hydrocarbons, simple and mixed sugars, lignocellulosics (cellulosic wastes, cereal straws, agricultural wastes), molasses and microorganisms of industrial importance with conversions effected in batch, fed-batch or continuous flow fermentors designed or acquired. Efforts were geared towards evolving the kinetics and the development of processes for the production of chemicals, single cell protein (SCP) and other growth associated products. In investigations involving microbial propagation with or without product formation, consistency test based on available electrons, energy and material balances were invoked. This also allowed the partition of substrate energy into maintenance, growth and products formation. Some models have been either newly evolved or by reparameterization of existing but inadequate models. Thus the overall kinetic parameters could be properly and adequately evaluated for the purposes of design and scale up. Some of these research outputs are briefly discussed below:

(1) Use of Palmwine Cultures for Ethanol Production (Layokun, 1984)

Palmwine culture is native to the tropics. It coontains seventeen strains of yeast and seven bacteria. It is a source from which single organism can be isolated. The dominant yeast is *Saccharomyces cerevisiae*. The Nigeria Yeast and Alcohol Manufacturing Company (NIYAMCO) at Bacita uses imported engedura yeast to produce alcohol from molasses. Their yield is only 7%w/v. My work with palmwine culture yields 14.7%w/v. This palmwine culture should therefore be a

substitute for engedura yeast. This was communicated to NIYAMCO, Bacita.

(2) Ethanol Production from

(a) Cellulose and holocellulose by *Pachysolen tannophylus* (Layokun, 1985). This involved delignification of wood waste (sawdust) followed by acid hydrolysis. The hydrolysates contains both hexose and pentose sugars. The organism fermented these substrates simultaneously to ethanol. No diauxic is observed. This organism should be a good replacement for *S. cerevisiae*.

(b) Cashew Apple Juice by *S. cerevisiae* (Layokun *et al.*, 1986). The juice contained about 15%w/v reducing sugars made up of glucose, sucrose and fructose. The sugars were all converted in a diauxic fashion with secreted invertase by the organism to hydrolyze sucrose into glucose and fructose fermented sequentially. This is extrapolatable to other fruit juices.

(3) Single Cell Protein Production- The cell mass of eaible organism is referred to as single cell protein (SCP). SCP contains approximately 50% protein and can be obtained by cultivating the organism on balanced substrate medium or by enrichment procedures such as fermenting the pomace of the fruit with or without nutrient supplementation.

(a) Both cashew apple juice (Layokun *et al.*, 1986) and the pomace (Solomon *et al.*,1988) were fermented using *Saccharomyces cerevisiae*. An important observation was how the capacity of a fermentor can be exhausted. The initial culture with sufficient substrate and nutrients under agitation was growing very well, then suddenly it stopped. On examination, more nutrients were added, the growth picked up. After some time, the growth ceased again only to pick when agitation was increased. When finally it stopped there was sufficient substrate and nutrients and no amount of agitation improved the yield. This indicated the limit or the capacity of the fermentor and any improvement would only occur in a bigger fermentor or one of a different configuration.

the capacity of the fermentor and any improvement would only occur in a bigger fermentor or one of a different configuration.

(b) Cellulosic wastes are promising sources of single cell protein. Collection, drying, cominution and hydrolysis with dilute sulphuric acid followed by fermentation produces SCP. In the case of corn straw (Omobuwajo *et al.*,1987), glucose, fructose and xylose were the reducing sugars. The supplemented hydrolysate was fermented with *Candida intermedia* which gave high yield of SCP as it is also a fermenter of D-xylose. Other cereal straws can be treated similarly.

4. Growth Characteristics of Ife Cowpea *Rhizobium 9*- IFE CR9 (Layokun *et al.*, 1988). The *Rhizobium* species are the major nitrogen fixing bacteria which have great applications in agriculture. They are non spore-forming obligate aerobes and numerically non abundant in the soil but form nodules on legumes. To ensure their presence in adequate quantity in the soil *Rhizobium* inoculants are either added to the soil, impregnated into legume seeds or coated on them at the growing time (Kumar-Rao *et al.*, 1973; Sekhon *et al.*,1978). We propagated the IFE CR9 on glucose and sucrose instead of the usual expensive manitol. Appropriate medium was formulated using different nitrogen sources. The best growth (high yield and low maintenance) was obtained with potassium nitrate as the nitrogen source.

5. Selection of Microorganisms for Treatment of Oil Spills and Hydrocarbon Effluents- A general balanced equation for the growth of microorganisms on organic substrates is given by Ferrer and Erickson (1980) as:

$$CH_aO_b + aNH_3 + bO_2 \rightarrow y_cCH_pO_qN_r + zCH_iO_jN_k + CH_2O + dCO_2$$

where CH_aO_b, $CH_pO_qN_r$ and $CH_iO_jN_k$ represent the elemental compositions of the substrate, biomass and extracellular products respectively and a, b, y_c, z, c and d are constants. From this, models for maintenance, biomass energetic yield and specific growth rates are developed (Solomon *et al.*, 1986). The results indicate that while bacteria treatment may be

preferred for oil spills, yeast are mostly favoured for treatment of hydrocarbon effluents because of the accompanying by products which can be used for protein supplementation in human and animal diets.

6. Data Consistency and Analysis of Data- Accurate design can only emanate from accurate data. An erroneous parameter as a component of a mathematical model throws the model into jeopardy. Reproducible but inconsistent data are very common in biological reactions and these can only be detected through application of consistency tests which are carried out by invoking the concept of carbon and available electron balances (capable of detecting out liers) (Erickson, 1979; Solomon *et al.*, 1984). Also the role of statistical techniques in data analysis and parameter estimation has gained prominence (Yang *et al.*, 1984). We (Layokun *et al.*, 1985) deliberately worked with organisms of proven industrial applicability. For instance the analysis of data on the growth of *Candida lypolytica* and *Pseudomonas aeruginosa* on *n*-hexadecane was motivated by the fact that *C. lypolytica* was a potential source of single cell protein while *P. aeruginosa* has been known to produce secondary metabolites and it is one of the few Gram negative organisms which can be genetically transformed to secrete and correctly process human growth hormones. Besides both organisms are fermenters of hydrocarbons.

This concept of material and energy balances was used to interpret the intermediate products build-up during the growth of *P. aeruginosa* on n-hexadecane. The inconsistency in the data had earlier been observed by Layokun in 1972. Now in this work, sets of data of each specific growth rate were checked for consistency. The explanation lies in the fact that the PHB which accumulated during the early stages of growth was metabolized at layer stages during nutrient insufficiency. This role of PHB which was elusive in 1972 became exposed in 1985 and so the finer features of the mechanism of reaction is now clear. The appropriate reparameterized Pirt's model now fits the entire data. The integrity of data must be preserved.

The publication on "Efficiency of Product Formation in Fermentation Processes" (Layokun *et al.*, 1985) revealed the behaviour of nine different organisms of industrial importance

in so far as they converted Jerusalem artichokes anaerobically. Large values of the maintenance coefficients and small values of the true biomass energetic yield are desirable for maximizing the efficiency of product formation.

Applying the same statistical procedure on the data acquired during the growth of *Trichosporon cutaneum* on glucose (Solomon *et al.*, 1985)it was revealed that *T. cutaneum* has a higher true biomass energetic yield and lower maintenance requirement than *Candida utilis*, is major competitor in SCP production. In addition to giving good yield and no foam formation when grown on molasses, *T. cutaneum*, unlike *S. cerevisiae*, *C. tropicalis*, and *C. utilis* is insensitive to both glucose repression and oxygen limitation.

7. Waste Management (conversion and control)- Major wastes apart from hydrocarbon based ones are cellulosic in character. Wood wastes are in the main lignocelluosic. Many pretreatment methods have been applied but caustic swelling under autoclave conditions has proved most effective (Mwesigye, 1988). Cellulase enzyme from *Trichoderma viride* and its mutants have proved very effective in degrading soluble cellulose. However, we have found that the cellulase from *Aspergillus flavus*- a phytopathogenic fungus responsible for the internal mouldness of cocoa beans and other tropical cash crops has all the essential components to synergistically degrade cellulose to D-glucose. Its optimum activity is at 45°C and pH 5.0. The kinetic behaviour is modeled by a simple expression:

$X = kt^n$.

Where X is the extent of hydrolysis, t is time and n is a constant.

Both the initial fast rate period (Layokun *et al.*, 1990) and period beyond this (Solomon *et al.*, 1990) have been reported. It is worthy of note here that results on further works and detailed explanation of procedural steps leading into eventual mathematical model was accepted and presented at the 1993 Annual Research Event of the Institution of Chemical Engineers. Also the paper presented by Layokun at the BESG-IChemE Annual Research Event in 1994 was awarded a grant for its depth and exposé (Layokun S.K., 1994). Further work is going on to improve the quality and efficiency of the cellulase

enzyme from *A. flavus* because it is indigenous.

8. Teaching of Biochemical Engineering- I started the teaching of biochemical engineering in the Department of Chemical Engineering, University of Ife (now OAU) in 1976 and with thesis projects made available to final year students. About fifteen students now take B.Sc. projects in this division every year and several M.Sc. students have been graduated. I introduced biochemical engineering to the University of Lagos, Chemical Engineering Department in 1978. I was a member of the team that drew up the B.Eng. programme in biotechnology for the Federal University of Technology, Minna in 1986 and have being involved in biotechnology teaching also at the Federal University of Technology, Akure since 1988. Mindful of the deep relationship between chemical engineering and biochemical engineering in both theory and applications, it seems to me appropriate for the current Department of Chemical Engineering, OAU to metamorphose to a Department of Chemical Engineering and Biochemical Engineering similar to what operates at the University College, London.

The development of this discipline at OAU, Chemical Engineering Department started through improvisation of some laboratory equipment. In 1979 the modular 19 batch fermentor and a chemostat were acquired from New Brunswick Scientific Instruments, N.J., USA and in 1983 the Microferm Twin Fermentor also from New Brunswick was purchased with a faculty grant. Dr. Fatile (RIP) a biochemical engineer joined the department in 1979 while Dr. Solomon also a biochemical engineer joined in 1983. It was a pleasure to have other ideas and problems to resolve or investigate in the biochemical engineering division. We started to design and fabricate fermentor jars and thermostated water baths to augment the purchased ones. Mutual interactions with Microbiology and Biochemistry Departments intensified. Right now this division is the most viable in the department and deserves encouragement.

PROSPECTS/CHALLENGES IN NIGERIA.

A cursory look at the scope of biochemical engineering as listed above would indicate the potential benefits derivable from its various applications in industry, medicine and agriculture. The raw materials are present in abundant while available technology can be adapted to

suit our local needs. Properly planned and executed, the production processes can be elevated to the extent that importation would be drastically reduced. Challenges abound in the following areas:

(1) Agriculture:

(a) Production of fertilizers and soil conditions from agricultural wastes i.e. an intensification of the National Agricultural Research Programme (N.A.R.P) on the use of organic wastes along the lines being prosecuted by Adepetu *et al.* in the Department of Soil Science of this University.

(b) Production of microbial inoculants for various crops, in particular rhizobium inoculants for legumes. Crops improvement programmes leading to high yield rice varieties, bigger potatoes that are rich in protein, tomatoes that will not go soft when ripe, yam that is as sweet as potato and plants that are resistant to insect attack. r-DNA techniques are highly feasible along the focus of IITA in Ibadan on cowpea, maize, plantain/banana, soybean, yam and cassava.

Large scale anaerobic digestion of cellulosic, poultry and animal wastes for the production of biogas and the sludge for manure. Natural gas is plentiful though and may stifle biogas project for now but it an option where these wastes are plentiful.

(2) Industry:

(a) Design of bioreactors and ancillaries as well as other unit operational equipment i... fermentation and products formation/recovery systems.

(b) development of raw materials from plant, animal and microbial sources for the production of chemicals, biochemical, fuels, solvents etc.

(c) Production of industrial enzymes and development of the brewing industries. The food processing industries also offers exciting possibilities for the application of biological processing technologies. Amino acids can be produced via fermentation (Reed, 1982), particularly glutamate, lysine and methionine. Similarly sweeteners and vitamins can be economically produced (Daily *et al.*, 1981).

(3) Medicines and Pharmaceuticals:

The application of biotechnological processes in this field is

very attractive. The use of engineered organisms increases selectivity and productivity. Capital layout can be inexpensive. Products such as insulin, pancreatic enzymes, pituitary hormones and heparin are good examples. The genes for most of these products have been cloned and expressed in certain bacteria. Genetic engineering practice has led to the production of vaccines against smallpox, diphtheria, mumps, polio and whooping cough (*The Economist*, June 1996). Other prospects include:

Production of Antibodies.

(i) Bacterial Production of interferon.

(ii) Production of Human Hormones, and

(iii) Gene Therapy.

The above are necessary and achievable but there must be funds, discipline and commitment by the regulatory bodies as well as the producers.

(4) Warfare and Biological Weapons:

Biological or microbial warfare is the deliberate cultivation, propagation and dissemination of bacteria and their poisonous products which naturally cause epidemic diseases in human beings for warfare purposes. Despite the vehement denials that always greet the accusation that the advanced countries are actively engaged in developing warfare potentials, sizable part of their defense spendings go into the development of biological weapons. During the Gulf war in 1991, the possibility of Iraq unleashing its biological arsenal on the allied forces appeared real. Israel threatened revenge should this happen. Most of the US Department of Defense funded biological research are focused on the development of vaccines against deadly and exotic diseases which can conceivably be unleashed as part of biological warfare campaign. Other known areas of interest are genes of dangerous viruses, bacteria and parasites that cause leishmaniasis, shigellasis and Rocky Mountain spotted fever. Recent converts into the nuclear arms terror are India and Pakistan. That the technology can be developed here is a high probability but that it is desirable becomes questionable in the face of possible misapplication. Such arsenal needs expert handling. I believe the UN treaty of non proliferation is inadequate. Existing weaponry of such destructive capability should be destroyed and energy channeled into agriculture and health care.

Caution on Gene Cloning

The British Scientists achievements ranks as a major first. They showed that DNA from an adult mammal can revert to an embryonic state and then duplicate the animal from which it came. A female biologist enthused "there will be no more need for men". She forgot that sex goes beyond fun and that cloning can make for bad breeding. Uncontrolled use of this technology may lead to the production of bacteria or viral strains that may accidentally acquire novel pathogenic characteristic never known to mankind. Our microbial enemies constantly evolve ways to defeat our defenses and invades our cells. Sex is the brilliant counter measure originated in evolution ages ago. By mingling genes, male and female creatures arm their offspring's with novel DNA combinations. Microbes equipped to burglarize one generation's cells find the cellular locks changed in the next. In short without sex, we'd soon be toast for germs. And cloned, genetically identical cows would be sitting ducks for epidemics. Cloning gene-tweaked animals that make human medicines in their milk has merit. It would keep the beasts' precious genome from being sullied overtime by sexual gene-mixing. But there seems to be better ways already to generate living drug factories. Remember there was only one success in 277 cloning tries of Ian Wilmot. In March 1997 for example, researchers reported making human hemoglobin needed for blood substitute in bioengineered tobacco plant of all things. It seems therefore that the benefit of gene cloning won't be compelling enough to induce scientists to risk their careers and possibly their necks trying to realize them. But they will risk much to understand how genes work. That knowledge will pay in ways cloning never can. Humanity may ultimately be served better by restricting DNA manipulations to enhancing the capacity of microorganisms to produce higher yields of existing and novel products.

RECOMMENDATIONS

(1) Teaching, Training and Research Facilities

The educational background of a potential engineering practitioner must be thoroughly adequate. He must have been well taught (good theoretical background), laboratory-trained and be able to handle machinery and equipment before graduation. To this end, up to date textbooks and journals must be made available to students both undergraduates and postgraduates. In particular the unit operations laboratory

should be well equipped. So also is the technological workshop where components can be fabricated. Facilities for metal, metal-glass and all glass welding should be provided. Quality analytical instruments should be provided. It is vital that students should be computer literate. Adequate research funds should be made available to researchers under nationally focused directive. It is also important that productive mutual interaction with the industrial sector and research institutes should be made obligatory. Expansion of engineering departments and their infrastructures is what is desirable not their proliferation.

(2) Bioengineering/Biotechnology Research Institute

I propose that a National Bioengineering-Biotechnology Research Institute should be set up with the following terms of reference

(i) to monitor developments in the field and direct the research thrust in this area in the various universities and other institutions.

(ii) to engage in the Industrial Typing of microorganisms indicating their sources and capabilities and hence to develop and maintain a culture collection center.

(iii) to engage in genetic engineering studies particularly on microorganisms in aid of (ii) above and also in the production of industrial enzymes and specialized biochemicals.

(iv) to engage in the design and fabrication of bioreactors and ancillaries, biochemical measurement equipment such as pH probes, oxygen probes etc. in its own workshop.

(v) to offer extension services to biotechnology related industries in the country and oversee the adaptation and scale-up of local technologies.

(vi) to ascertain the quality of the bioproducts before marketing approval within and outside of the country.

(3) Activation and Sustenance of Engineering Materials Industries.

Empirical technology is always well in advance of theoretical understanding. The bulk of small scale productions in the rural area are based on trials. To scale them up by applying theoretical concept will require the right material of construction. Over reliance on importation is the cause of our erratic and low output. For example, the petroleum refineries will not be in the poor state they are if materials were

available within the country to resuscitate them. No developed nation will assist us to become industrial competitors with them. It would be economically wise to activate the existing iron and steel industries and other materials industries and even create new ones. It is in large scale manufacturing for both domestic and external supply that the nation's well being can be guaranteed.

ACKNOWLEDGEMENT

I thank God Almighty for His infinite mercies at all times. He is at hand to uplift at worrying times and at hand to moderate at moments of supreme joy. My deep appreciation goes to my wife Mrs. OLUKEMI LAYOKUN for her unflinching support and love. I thank my children Kolawole, Ayodele, Bankole and Oluyomi for their respect, love and understanding. Special gratitude goes to my parents- effusive, disciplined and honest Chief Bisi Adeola Layokun and Mrs. (Princess) Julianah Oja Layokun for their natural care and love at all times. To my eldest brother Mr. Michael Layokun and his family, I express sincere appreciation, and to my other brothers and sisters, cousins and relations I also extend my unreserved gratitude.

I sincerely appreciate the encouragement and collaboration of colleagues and students in Chemical Engineering Department and other Departments in this University and elsewhere. Many thanks to the technical and administrative staff of Chemical Engineering Department.

I very much appreciate the research grant provided by the University through the URC, the professional cooperation by the Nigerian Society of Chemical Engineers (NSChE), Mobil Producing Nigeria Unlimited, NNPC, Elf Petroleum and Imperial Chemical Industries (ICI), UK.

Finally to all of you present here today accept my sincere thanks. May God bless you all.

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