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26 September 1987

ENGLISH

TECHNOLOGIES FOR CHEMICAL INDUSTRIES BASED ON BIOMASS

DP/ROM/82/012/11-06/J13424

ROMANIA

Technical Report: Design of Special Enzymatic Reactors*

Prepared for the Government of Romania
by the United Nations Industrial Development Organization, acting as
executing agency for the United Nations Development Programme

BY:
Murray Moo-Young, UNIDO Consultant
in Biotechnology, Design of Special
Enzymatic Reactors

United Nations Industrial Development Organization
Vienna

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Executive Summary

In the first phase of a two-phase proposal to visit the UNIDO-sponsored project in Romania, this fact-finding mission revealed that the project is being carried out essentially in two locations, Bucharest and Timosora. Although most of the funds seem to be allocated to the Bucharest operations, I was not allowed to visit these laboratory facilities and was promised that the next visit would include them. In general, the research team appears to be dedicated and suitably qualified (except for certain areas) to achieve the objectives of the project. Current lack of adequate equipment, especially at the Timosora laboratories, appear to be hampering progress.

Introduction

This report deals with the first phase of a pre-planned program consisting of two phases (of two weeks each) whereby the writer agreed to assist in aspects of biotechnology development in Romania. The official job description is given in Appendix A. This first phase took place during November 2-20, 1986 and the second-phase was scheduled for May 1987. The report is based on a fact-finding mission which involved the following activities.

1. Travel and UNIDO briefing in Vienna (2 days).
2. Fermentation equipment discussions in Zurich (1 day).
3. Seminar and discussions in Bucharest (2 days).
4. Seminars, lab visits and discussions in Timosora (11 days).
5. Travel and report preparation in Waterloo (2 days).

Findings and Recommendations

The identities of the main people contacted are given in Appendix B and the inter-relationships of these within the participating organization, Institute for Energy-Related Chemistry and Biochemistry (IECB), are given in Appendix C. An outline of the UNIDO program, in terms of area responsibilities, as received in Romania is given in Appendix D. In addition

to discussions and laboratory visits (primarily at the Timosora location), I presented several invited lectures and seminars at both locations on designated topics relevant to the project:

1. The multidisciplinary nature of biotechnology (B).
2. Bioreactor design and process scale-up (T).
3. Biotechnology: opportunities and limitations (T)

References were drawn to appropriate literature for further study and reprints of some of my own papers were handed out:

1. Bioreactors: Chapter in Advances in Biochem. Eng., Springer (1981).
2. Process scale-up and techno-economics: Article in "Perspectives in Applied Microbiology and Biotechnology", Elsevier (1986).
3. Ethanol production: Paper from Biotech. Letters (1980).

A complete list of my publications of over 160 papers (for possible reprint requests) was left with the IECB. In addition, pamphlets on typical examples (Sulzer MBR) of commercially-available equipment (fermentor and related bioprocessing ancilliaries) were left with IECB. My reaction to an uncertainty pertaining to a previous Chemap consideration is summarised in a telex I sent to UNIDO at the end of my visit (see Appendix E). Finally, Appendix F is a list of books and journals which is deemed to be desirable for the biotechnology-related sections of the IECB library. This IECB submission, which seems approrpriate, was not discussed in any detail.

In the interest of speed, other observations are enumerated below, not necessarily in any perceived order of importance.

1. I was unable to visit the IECB/Bucharest laboratories, the Polytechnic Biology Institute or a nearby SCP plant, all three having direct relevance to the UNIDO project. Thus, the potential value of the mission is marred by this knowledge gap. Apparently, visits of these kinds must be arranged in advance before arrival of a consultant. From discussions, I am informed that the IECB laboratories are well-equipped with

analytical facilities and fermentation equipment, including a 250-L computer-coupled fermentor, an insinuation which bodes well for the project. I am told that these facilities would definitely be on my agenda in Phase 2 of the mission.

2. By contrast, I was involved with extensive visits and discussions at the laboratories of the Timosora component of the UNIDO project which actually was being conducted in some of the university facilities there. These facilities (small shakers and fermentors) were quite primitive but were clearly being put to good use. Indeed, many innovative home-made equipment were in operation during the visit. The technical calibre of the staff seemed to be good-to-excellent in scientific background knowledge; no engineers are involved. The output of this dedicated and industrious group of researchers is obviously hampered by the lack of suitable equipment and instrumentation. During my visit, the group leader was away. The on-going work is interesting but needs better focussing on the UNIDO project objectives.

3. There appears to be inadequate technical communication and interaction between the Bucharest and Timosora components of the project. Given the geographic separation of the two locations, this may be unavoidable. However, a desirable synergistic effect should be promoted between the two groups based on improved collaborations.

4. A major area of concern expressed (by IECB) was the status over a requisitioned computer-coupled 25-L fermentor of Swiss design. Having not seen the IEC facilities, I failed to understand the immediate need for this facility except possibly, for more ease and reliability of basic data-logging. I met no one who was conversant with aspects of fermentation CAD/CAM (computer aided design/manufacturing), an aspect which the facility would presumably address. The eargerness for equipment acquisition per se probably led to a questionable choice with

regard to budget considerations.

5. If I am to focus on the terms of my consultancy, there is a need to follow up on the ground work laid out in this visit (primarily through seminars and discussions). The specifics include reactor types, bioprocess scale-up criteria, mass and heat transfer correlations and performance expectations as they apply to the enunciated bioprocess development interests in (a) ethanol from lignocellulosics (b) commercial enzyme production (c) SCP production (d) animal feed from biomass.

6. The technical expertise of the team with regards to the biological and biochemical sciences is excellent compared to a rate-limiting component in biochemical engineering. Without this, the exercise is simply one of basic scientific research with little near-term potential of technology transfer. In this context, one of the team members (Emil Geisculsecu) was to come to our university (Waterloo) for training starting May/87: this plan has yet to materialize. We are still prepared to accept E. Geiculescu in a training program in IECB's area(s) of interest: our current activities are outlined in the attached 1986 article I wrote for Chemical Engineering Education.

Concluding Remarks

The role being played by the Timosora group is fairly minor, yet this is the location at which I was primarily stationed. One important aspect of this location is the brain-power and personnel training for possible transfer of human resources into the intended industrial marketplace.

On the non-technical issues, I wish to express my deep gratitude to my Romanian hosts, especially those at Timosora, who demonstrated warmth and friendship beyond all expectations.

Appendix A

H. Haug/ak
27/2/86

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

UNIDO

JOB DESCRIPTION

DP/ROM/82/012/11-06/32.1.1

Post title Expert on design of special enzymatic reactors

Duration 1 month

Date required October 1986 or as soon as possible thereafter

Duty station Bucharest, Romania

Purpose of project To strengthen the research and development activities of the Institute for Energy Related Chemistry and Biochemistry (IECB), Institututul de Energetica Chimica si Biochimica in the field of energy related biochemistry and applied enzymatic technology, particularly in the following areas:

a) Development of biomass processing technologies and new chemical technologies based on enzymatic catalysis for application in the chemical and related industries (i.e. basic technological process design for new industrial biomass based plants and improvement of furfurol, methionine and ethyl alcohol plants);

b) Establishment of a complex experimental multipurpose plant for conversion of biomass into chemical products and useable, non-toxic residues, such as animal fodder or fuel with a view to expanding application of the research to the industrial development.

Duties The expert will be required to review the work at IECB and advise the staff through lectures, seminars, discussions and practical guidance on the following topics:

- The main reactor types for enzymatic catalytic reactions;
- Principles of technological scaling-up of enzymatic catalytic reactors;

..../..

- Kinetic equations of mass and heat transfer for enzymatic catalytic reactors;
- The performance of enzymatic catalytic reactors.

Qualifications Biotechnologist with extensive experience in design and use of enzymatic reactors.

Language English

Background Information

IECB has several objectives in the field of applied biotechnology for the chemical industry:

- To increase and diversify the utilization of non-conventional raw materials for the chemical industry and power/heat generation;
- To develop biomass based biochemical conversion technologies for the production of chemicals and fuels;
- To reduce the energy consumption of chemical processing plants through the application of enzymatic catalysis;
- To develop the industrial production of enzymatic catalysts.

In order to achieve these objectives the research and development capacity of IECB in the field of energy related biochemistry and applied enzymatic technology will be improved using the experience of advanced industrialized countries.

At the present time Romania produces around 8.05 million t/y wheat, 10.83 million t/y corn, 2.89 million t/y potatoes, 9.41 million t/y sugar beet, 0.06 million t/y sorghum, 6.30 million t/y lucerne, 1.30 million t/y rape, 1.15 million t/y sunflower, 2.0 million t/y poplar, and the resulting agricultural residues including 13.5 million t/y stalks, 1.5 million t/y creeping stems, 11 million t/y straw, 0.35 million t/y vine shoots, 2 million t/y corn cobs. In the field of industrial biotechnology Romania produces 100,000 t/y single-cell proteins, 22,000 t/y furfural, 8,000 t/y lysine, etc.. Research activity is directed towards the improvement of ethyl alcohol, fodder yeast and furfural production.

Current research and development work at IECB concerns technologies for enzymatic catalysts and enzymatic catalytic processes. Reactors are the basic equipment for carrying out catalytic processes, and advice and assistance in this area are therefore needed.

Appendix B

Principal People/Organizations Contacted

1. UNIDO/Vienna

   Ms. J. Tobin, Appointment Clerk
   Ms. Winkelmann, Recruitment Officer
   Ms. A.M. Draxler, Area Clerk
   Ms. J. Mazue, Briefing Co-ordinator
   Mr. Robert Williams, Substantive Officer

2. Zurich

   Mr. Canonica, Chemp
   Mr. K. Ruten, Sulzer MBR

3. Romania (Bucharest)/UNDP

   Mr. Noel Eichorn
   Mr. Ionesco

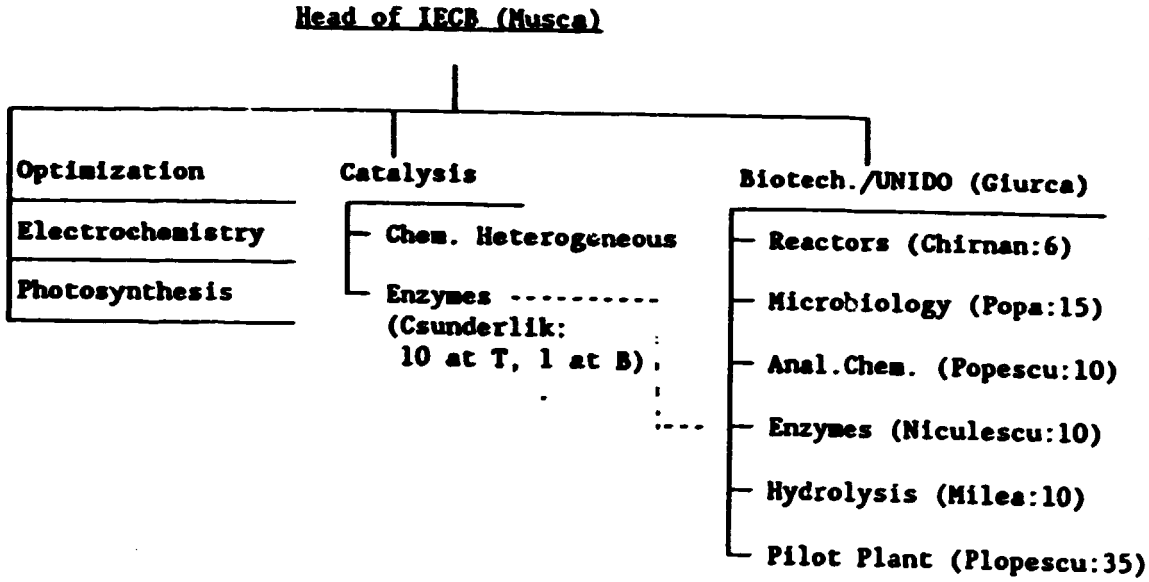
   Romania (Bucharest)/IECB

   Mr. Emil Geisculescu
   Mr. Marius Tudorascu
   Mr. Radu Giurca
   Mr. S. Niculescu
   Mrs. Tania Hogea
   Mr. G. Musca
   Mr. G. Pop
   Mrs. C. Stanan
   Mrs. Carmen Sandulesu
   Mr. S. Straja

   Romania (Timosora)/IECB, etc.

   Mr. Fery Peter
   Ms. Adrianne Stoi
   Mrs. Sigy Eisler
   Mr. P. Romulus
   Mrs. Carmen Boeri
   Mrs. Gaby
   Mr. Radu Bacaloglu

Appendix C



Organization of Divisions and Groups within IECB showing the UNIDO component of the current operations, various adminstrators and approximate numbers of reseachers. T = Timosora, all others located at B = Bucharest. Also, some unspecified connections (not shown) with the Bucharest Institute of Biology.

and Schedules for UNIDO Project
Received during mission visit

RESEARCH ITEMS REGARDING THE
UNIDO PROJECT 84/46o/RCW/o12

I. Obtaining of ethanol from different phytomass categories

1. Ensymatic hydrolysis of lignocellulosic stuffs.

Stages : a) - isolation and selection of microbial strains with high productivity ;
b) - mutagenesis and genetic engeneering techniques ;
c) - tests with microbial hydrolysis in static batches ;
d) - tests with microbial hydrolysis in stirred batches ;
e) - extraction and purification of enzymes ;
f) - the kinetics of enzymatic hydrolysis in bioreactors ;
g) - mathematic modelling

2. With immobilised yeast cells for direct fermentable stuffs

a) - selection of yeast strains tolerating high alcoholic levels ;
b) - standardization of celitative and cantitative analyt methods for sugars, ethanol and by-products determination ;
c) - tests with immobilised cells on standard fermentation substrates (dextrose and sucrose) ;
d) - study of sterilisation and cooling methods of mashes ;
e) - immobilisation of yeast cells on different carriers ;
f) - processing of juices fermentation obtained from Jerusalem artichokes, sweet sorghum, fodder beet in immobilised yeast cells reactor ;
g) - technological tests in pilot-scale plant.

Timing : 1984 - 1985 labor scale
1985 - 1987 labor + pilot scale

Estimated production increase : 15-2o % over the actual technologies through rising up the useful conversion of sugars to alcohol. It is also possible to increase 5-1o fold the fermentation rate.

Work should be done at the Biotechnological department of the Institute of Chemical and Biochemical Energetics.

Team - coordinator : Dr. Radu Ginveă

Team : 3 microbiologists, 4 biochemists, 1 analyst, 1 biophysicist, 3 process engineers and the staff to be hired on the pilot plant.

II. Obtaining of enzimatic preparations

1. Catalase - useful in the diary industry (cold pasteurization of milk).

Stages : a) - obtaining of high productive strains including mutagenesis ;
b) - tests in static batches ;
c) - tests in stirred batches ;
d) - working out of the culture media;
e) - determination of enzyme activities (labor tests) ;
f) - biosynthesis processing on air-lift reactors working out of the optimum process parameters ;
g) - enzyme extraction and purification
h) - enzyme imobilization
i) - pilot-scale technological tests
j) - industrial tests.

Timing : 1984 - 1985 labor scale
1985 - 1987 labor - and pilot scale.

One can appreciate that the milk sterilization through this method could reduce the energy consumption by 3o %.

Team coordinator : Dr. Stelian Nicolescu

Team : 2 microbiologists, 4 biochemists, 1 analyst, 1 biophysicist, 3 engineers and the staff to be hired on the pilot plant.

2. Proteases - for detergents , leather - and textile - industries.

Stages : a) - isolation and selection of microbial strains ;
b) - working out of the culture media ;
c) - tests with static cultures ;
d) - tests with stirred cultures ;
e) - determination of enzyme activities ;
f) - working out of the optimum process parameters on complete stirrer tank reactor ;
g) - processing of biosynthesis media ;
h) - conditioning of enzymatic preparations ;
i) - pilot-scale technological tests.

Timing : 1984 - 1985 laboratory scale
1985 - 1987 laboratory + pilot scale

One can appreciate that detergent efficiency could be rised by 20%.

Team coordinator : biochemist Carmen Săndulescu
Team : 2 microbiologists, 3 biochemists, 1 analyst, 2 process engineers and staff to be hired.

III. Single cell proteins obtained from biomass processing for foddex

Stages : a) isolation and selection of yeast strains having min. 45 % protein contents ;
b) isolation and selection of bacterial strains having min.60% protein contents ;
c) pretreatment and acid hydrolysis of phytomass ;
d) tests in stirred cultures ;
e) tests on air-lift - and complete stirrer tank reactor;
f) working out of the biosynthesis parameters ;
g) processing and conditioning of biosynthesis ;
h) tests on livestock ;
i) pilot-scale technological tests.

Timing : 1984 - 1985 laboratory-scale
1985 - 1987 laboratory-and pilot-scale.

One can appreciate that by such types of biotechnologies one can realise the processing of various types of phytomass wastes into single cell proteins feed.

Team coordinator : eng. Aurelia Chirvase
Team : 3 microbiologists, 3 biochemists, 1 analyst, 3 process engineers, 1 biophysicist and staff to be hired for the pilot instalation.

IV. The pentosanal hydrolysis of the biomass for furfural obtaining and the residues using for animal food

Objectives : production of furfural for chemical industry and animal food which consists in the residual ligno-cellulose.

Stages : a) - substitution of sulfuric acid, as catalyst, with different salts and diluted acetic acid solutions ;

b) - working out the hydrolysis parameters, on laboratory and pilot-scale ;

c) - characterization of the end-products of the hydrolysis process (furfural and ligno-cellulosic residue) ;

d) - analysis of the ligno-cellulose, as fodder, in order to establish its feeding properties ;

e) - testing the obtained fodder as food for animals with short-life cycle ;

f) - technological test on pilot scale.

Timing : 1984 - 1985 laboratory-scale
1985 - 1987 laboratory+pilot plant + farm

We estimate to use the furfural as selective solvent for mineral oils refining, as raw material in organic synthesis, for obtaining fenol-furfuralical resins ; the residual ligno-cellulose will be used as animal food. We estimate 0.700 t oven-dried fodder from 1,000 t oven-dried raw material.

The new technology will avoid the environment pollution produced by the acid lignins.

Team coordinator : Dr. Ioan Milea

Team : 5 engineers, 4 biologists, 2 biochemists, 1 analyst and staff to be hired on the pilot-plant.

Appendix E

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Dr. Robert Williams
UNIDO

Re my telephone conversation Nov. 12, I regret UNIDO feels committed to Chemap. I cannot understand why "Bucharest recommended it" since they will not get two important items requested: fermentor volume flexibility and computer interface capability. Also, the present Chemap quotation is unreasonably high compared to MBR, LH, NBS, Marubushi, etc. Hopefully, it is not too late to rectify a bad situation. I will copy Bucharest this telex. Unfortunately I cannot go on Brazilian mission before January 1987.

Prof. Moo-Young
IBR
Univ Waterloo
CANADA
TLX 06955259

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Appendix F

List of Desirable Biotechnology-Related Books and Journals for the IECB Library

Books

1. Computer Applications in Fermentations, Soc. Chem. Ind., UK (1982).
2. Handbook of Biochemical Engineering and Biotechnology, Nature Press, UK.
3. Advances in Biotechnology, Pergamon Press, UK.
4. Handbook of Heat and Mass Transfer (1985).

Journals

1. Biotech. Letters (>1986).
2. Biotech. Bioeng. (>1988).
3. Process Biochemistry (>1986).
4. J. Fermentation Technol. (>1986).
5. J. of Biotechnology (>1986).
6. J. of Ind. Microbiology (>1986).
7. European J. Appld. Microbiol. Biotechnology (>1986).
8. Biotechnology (>1986).
9. Biotechnology Advances.
10. Advances in Biochem. Eng.

Research in

BIOCHEMICAL ENGINEERING AND INDUSTRIAL BIOTECHNOLOGY

MURRAY MOO-YOUNG
University of Waterloo
Waterloo, Ontario N2L 3G1, Canada

Murray Moo-Young is a professor of chemical engineering and director of the Industrial Biotechnology Centre at Waterloo. He was educated at the universities of London (BSc, PhD), Toronto (MASc) and Edinburgh (postdoctorate). An active consultant worldwide, he is the chief editor of *Comprehensive Biotechnology*, a multi-volume reference treatise, and *Biotechnology Advances*, an international review journal.

BIOCHEMICAL ENGINEERING IS the application of biological and chemical engineering principles in the development and implementation of bio-process systems [1]. As such, it is the handmaiden of industrial biotechnology whereby these systems are put into commercial practice for the production of goods and services [2]. It is predicted that biotechnology will trigger the next industrial revolution [3] and that, within the next decade, more than 25% of new chemical engineering graduates will be involved in biotechnology-related activites [4]. These predictions are based on the current use and future potential of genetic manipulative techniques and biochemical engineering in the development of new and improved processes and products [5].

The following sketch of Waterloo's programs in biochemical engineering and industrial biotechnology highlights its graduate courses, its research activities and its technology transfer mechanism.

WATERLOO CONNECTIONS

For many years the University of Waterloo has been a pioneer in high-tech areas including micro-electronics, computer software, robotics, CAD/CAM and biotechnology. Last year, the Wall Street Journal featured it as the top computer school in North America, ahead of MIT and Stanford. In biotechnology, Waterloo has one of the oldest and largest programs in North America [6,7]. Started in 1966, the graduate program now involves 39 researchers, consisting of 7 of the 31 chemical engineering faculty members (see Table 1), 17 graduate students, 5 technicians, and 10 postdoctoral fellows, visiting scholars and research associates, in addition to collaborating faculty in the biology and chemistry departments. Waterloo is the first North American university to introduce a biotechnology core course in its chemical engineering program, which graduates about 100 students annually.

TABLE 1
ChE Faculty Members Involved in Biotech-Related Research

G. J. Farquhar, PhD (Wisconsin)
R. Y. M. Huang, PhD (Toronto)
R. L. Legge, PhD (Waterloo)
M. Moo-Young, PhD (London)
C. W. Robinson, PhD (UC Berkeley)
J. M. Scharer, PhD (Pennsylvania)
G. R. Sullivan, PhD (London)

In order to encourage the development of appropriate multidisciplinary "critical masses" in our biotech research, the activities have been incorporated into a research consortium, Guelph-Waterloo Biotech (GWB), which combines the resources of Waterloo with those at the neighbouring University of Guelph. At present, the consortium has 103 faculty members who belong to one or more of four constituent units: animal, industrial, microbial and plant biotech centres. Biochemical engineering research is under the general umbrella of the Industrial Biotechnology Centre (IBC), which is administratively located in the Waterloo chemical engineering department. The synergistic co-operation between several departments at the two universities has considerably expanded the versatility and comprehensiveness of our programs.

IBC has about thirty faculty members represent-

. . . to encourage the development of appropriate multidisciplinary "critical masses" in our biotech research, the activities have been incorporated into a research consortium . . . which combines the resources of Waterloo with those at the . . . University of Guelph. At present, the consortium has 103 faculty members.

ing 20% biological, 20% chemical, and 60% engineering-base expertise, and a rough 75/25 split between Waterloo and Guelph. Major aims of IBC include promotion of collaborative research among its faculty members and the provision of "windows" on biotech advances to GWB industrial affiliate members. Within its first year of operation, GWB has already signed up two European and three North American companies: Rhone-Poulenc, Drogocco, Liquid Air, Monsanto, and Allelix.

COURSES

Various courses are offered in biotechnology/ biochemical engineering, and brief descriptions of these courses are given below. Except for the last course listed, all courses are given on a regular basis, annually. Throughout these courses, students are constantly reminded of the necessary multidisciplinary nature of biotechnology. It is noteworthy that graduates of honours non-chemical engineering technical programs are admitted to our programs provided they successfully complete a "qualifying" program of a pre-arranged set of courses usually lasting for one to two years of study.

Introduction to Biotechnology • Biological systems for the production of commercial goods and services. Properties of microbial, plant and animal cells, and of enzymes used in bioprocess applications. Classification and characterization of biological agents and materials. Quantification of metabolism, biokinetics, bioenergetics. Elementary aspects of molecular biology, genetic engineering, biochemistry, microbiology. (The material is based on Reference 8.)

Fermentation Engineering • Application of process engineering principles to the design and operation of fermentation reactors which are widely used in the pharmaceutical, food, brewing and waste treatment industries. Aspects of mass transfer, heat transfer, mixing and rheology with biochemical and biological constraints. (The material is based on References 8,9.)

Food Process Engineering • Applications of unsteady and steady-state heat and/or mass transfer operations to processing natural and texturized foods. Design and analysis of sterilization, low-temperature preservation, concentration, separation and purification processes. Effects of formulation, additives and processing on organoleptic and nutritional quality.

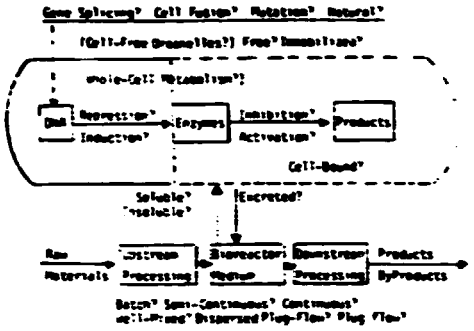

FIGURE 1. Bioreactor heart in industrial biotechnology: Biology selects it, biochemical engineering determines its performance.

(The material is based on Reference 10.)

Principles of Biochemical Engineering • Aspects of mass-transfer, heat-transfer, fluid flow, cell growth and enzyme kinetics related to the design of biological process equipment. Fermentations, sterilization techniques, specialized extraction methods, immobilized-enzyme reactor design. (The material is based on Reference 11.)

Advances in Biochemical Engineering • Design and control of continuous-flow processes for biological systems. Exploration of new methods of producing materials for food and medicinal purposes and of treating effluents. (The material is based on the current literature.)

Selected Topics in Biotechnology • Various courses deemed necessary at intervals. (The material is based on References 12, 13 and the current literature.)

CURRENT RESEARCH ACTIVITIES

A wide range of research projects is conducted in bioprocess and bioproduct developments. As indicated in Table 2 and Figure 1, we address problems involving principles and applications of a theoretical and experimental nature. In addition to the usual research facilities, we are well equipped with computers and a range of pilot-plants including a versatile 1,300-litre fermentation unit (the largest of its kind at a North American university) which is capable of various modes of operation (batch, fed-batch, continuous; stirred tank, air-lift). These facilities are available for graduate studies and contract research. Brief descriptions of a representative sample of our current research projects follow.

Additional benefit in reduced disposal costs and environmental pollution control may be realized.

Desulphurization of Petroleum Crudes

Conventional physiochemical desulphurization methods would add a prohibitive $10+ per barrel to the cost of producing fuel oil from crudes containing 3% or more sulphur. We are evaluating the technoeconomic potential of biotechnology processes for upgrading bitumen and heavy oils in a Canadian environment in terms of microbial desulphurization, demetallization and viscosity reduction.

Delaying Fruit Ripening

This project is focussed on increasing our understanding of the physiological mechanisms underlying fruit ripening as well as chilling injury sustained during low temperature storage. Using this information, we wish to develop suitable treatment and/or containment strategies for extending the storage life of chilling-sensitive fruits such as tomatoes.

Lignocellulosic Materials

Various approaches are being taken to scale up the production of microbial cellulose and to alter its physical characteristics during the process in an attempt to develop unique products. In addition, various white rot fungi, which are capable of lignin degradation, are being studied to produce ligninases. These are earmarked for use in the production of more fermentable feedstocks and for biobleaching.

Disruption of Microbial Cells

Microbial products such as intracellular proteins and hormones require cell wall disruption for recovery. Little or no information is currently available to allow rational design of large-scale cell disruption devices. Cell wall disruption is being studied in a high-pressure capillary-flow device producing stresses of known type and magnitude. Various cell types (bacteria, yeast, algae) are being studied.

rDNA Downstream Processing

Studies are currently in progress to optimize an integrated 8-step process involving fermentation, recovery and purification for the production of protein gene products based on rDNA technology. Investigation of a unique continuous fermentation strategy which, by operating at different temperatures in each stage, will result in maximum expression of the proteins, forms a key part of this study. It is expected that the results will produce an overall optimized process model which has general applicability.

Separation Membranes

In fermentation technology, improved downstream processing techniques are required for the recovery and purification of intracellular bioproducts. We are synthesizing and testing a steam-sterilizable polymeric thin-film composite-membrane micro-filtration system, conceptualized for the separation of whole single cells (bacterial and yeast) and of cell debris (after cell disruption) from fermentation broths without undue damage of protein products left in the liquid fraction required for further processing refinement.

Biological Waste Management

This is a multi-faceted project. One aspect involves examination of some unique microbial systems as potentials for breaking down recalcitrant pollutants such as polychlorinated compounds as found in landfills. Another aspect deals with dynamic modelling of the activated sludge process for handling inlet perturbations of xenobiotics. Finally, a major aspect deals with microbial regeneration of activated carbon often used for the adsorptive removal of water contaminants in industrial effluents, *e.g.* phenols, aromatics.

CONCLUDING REMARKS

The sheer size of the Waterloo programs allows us to cover a full range of graduate interest in biochemical engineering and industrial biotechnology. This comprehensive multidisciplinary mileau is rare in chemical engineering departments. We hold an enviable record of technology transfer via the Waterloo Centre for Process Development (WCPD) (also located in our department) and through Waterloo-trained personnel in virtually every major organization involved in biotechnology in Canada, and in parts of the USA, Europe and Japan.

REFERENCES

1. M. Moo-Young, "Biochemical Engineering" in *Encyclopedia of Science and Technology*, McGraw-Hill (1986)
2. E. L. Gaden, "What is Biochemical Engineering?" in *Advances in Biotechnology*, Moo-Young, *et al* (Eds.), Vol I, Pergamon (1981)
3. J. Naisbitt, *Megatrends*, Warner (1984)
4. A. E. Humphrey, "Biotechnology in the Next Decade," *CEP* (1984)
5. OTA/U.S. Congress, *Commercial Biotechnology*, Pergamon (1984)
6. M. Moo-Young, "Biochemical Engineering Programs," *CEE* (1978)
7. AIChE Faculty Directory (1985)
8. J. E. Bailey and D. F. Ollis, *Biochemical Engineering Fundamentals*, McGraw-Hill (1986)
9. S. Aiba, *et al*, *Biochemical Engineering*, Academic (1979)
10. C. W. Robinson, Personal Notes, Univ. of Waterloo
11. M. Moo-Young, *et al* (Eds.), *Comprehensive Biotechnology*, Pergamon (1985)
12. Moo-Young, *et al* (Eds.), *Advances in Biotechnology*, Pergamon (1981)
13. D. I. C. Wang, *et al*, *Fermentation and Enzyme Technology*, Wiley (1983) □

Transport Processes in Bioreactors

In this ongoing megaproject, multiphase contacting is used to promote transport processes for bioconversion. Novel contacting devices (recirculation loops, scraped tubes, packed beds) are being developed and compared to conventional stirred tanks and bubble columns for Newtonian and non-Newtonian systems. Transport phenomena and process control are the key elements of study.

Codeine Production

Medically important morphine alkaloids such as codeine are normally obtained from opium poppy cultivated in countries with fairly tenuous governments from which Canada (and the USA) import virtually all their supplies. Work is in progress on a bioreactor battery of immobilized enzymes derived from microbial and plant tissue cultures whereby readily available chemical feedstocks are converted into intermediates which are then chemically transformed to codeine.

Production of Monoclonal Antibodies

Animal cells in culture have the potential to be a source of macromolecules for diagnostic, therapeutic and processing applications. To address commercial scale production concerns, we are designing fully instrumented, computer-controlled, robust bioreactors for growing hybridomona cells in the production of monoclonal antibodies. Initially, MAb's with specificity against a cellulase complex enzyme antigen are being used as a model test system.

MBP Production

Agricultural and forestry residues represent potentially valuable renewable resources for fermentation processes which can be used to produce edible protein-rich microbial biomass products (MBP) for animal feed or human food. We are developing novel MBP processes which are based on the aerobic mass cultivation of yeasts and fungi. Computer process simulations, pilot plant evaluations and animal feeding trials are being used to test techno-economic scenarios for both developed and developing countries.

Ethanol Production

A continuous-flow, packed-bed bioreactor based on surface-immobilized yeasts attached to inexpensive wood chips has been developed, modelled and tested for the fermentation of hexose sugars. Stable operation has been achieved at productivities comparable to or greater than any previously reported. A process for fermenting enzymatically-transformed pentose sugars, another component of cellulosics, using the same yeasts is under investigation for possible process integration.

Anaerobic Digestion

The use of organic wastes is being tested for the production of energy (methane) and organic chemicals (fatty acids) under both mesophilic and thermophilic conditions. Bioreactor studies include continuous and intermittently-stirred tanks and fixed-film trickle beds. Performance is evaluated for retention time, loading rate, carbon-to-nitrogen ratio and several physico-chemical parameters.

Biomass Pretreatment

A techno-economic comparison is made of existing and potential chemical and biochemical strategies for cellulosic biomass utilization in the production of fermentation feedstocks suitable for replacing or supplementing traditional substrates, *e.g.*, molasses, starch. In particular, cellulosic materials generated as paper-pulp mill sludge and wood remnants are being studied.

TABLE 2

Current Research Areas in Biotechnology/Biochemical Engineering

BIOREACTOR DESIGN
- mass transfer
- heat transfer
- mixing
- stirred tanks
- air lifts
- packed beds
- biokinetics
- bio-immobilization

BIOCONVERSION AGENT
- microbial cells
- plant cells
- animal cells
- rDNA cells
- hybridoma cells
- psychrophiles
- thermophiles
- enzymes

PRODUCT TYPES
- SCP/MBP
- alcohols
- methane
- organic acids
- enzymes
- biopolymers
- monoclonal antibodies
- morphinans

INSTRUMENTATION
- computer control
- biosensors
- data logging
- modelling
- product assays
- economic analysis
- CAD/CAM

BIOPROCESSING TECHNIQUES
- hydrolysis
- sterilization
- membrane separations
- chromatography
- flotation
- drying
- cell disruption

FEEDSTOCK TYPES
- cellulosics
- starches
- sugars
- oils
- forestry biomass
- agricultural biomass
- biomass pulps
- xenobiotics