A Course in

BIOCHEMICAL ENGINEERING

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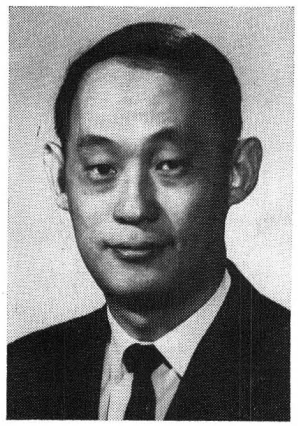

George T. Tsao received a B.S. degree from National Taiwan University in 1953, a M.S. degree from University of Florida in 1956 and a Ph.D. degree from University of Michigan in 1960, all in Chemical Engineering. He joined Iowa State University in November, 1966 as an associate professor and was promoted to the rank of full professor in July, 1970. Dr. Taso's teaching and research interests are in the areas of biochemical engineering, enzyme technology and biological waste treatment. Before joining Iowa State, he was an assistant director of research of Union Starch & Refiing Co., a Division of Miles Laboratories, Inc.

I. The Need

BIOCHEMICAL INDUSTRIES are those involving biochemical and microbiological processes. The oldest example is fermentation by which a large number of chemicals and pharmaceuticals can be produced. Industrial food processing is another area in which a chemical engineer is often required to consider biochemical and microbiological problems such as preservation of taste, flavor and nutritional value and prevention of spoilage.

Besides the normal growth in fermentation and certain sections of food processing and pharmaceutical industries, there are three areas which are currently stimulating additional interest in learning biochemical engineering. They are briefly described below.

Enzyme Engineering: Enzymes are proteins which catalyze biochemical reactions. Enzymes are, in fact, excellent catalysts judging from their high specificity and rapid reaction rates. Recently, enzymes are becoming more important not only in biochemical laboratories and in medical applications but as industrial catalysts in chemical processing. The major factors currently restraining the broad application of enzymes in industry are the high cost and the relative unstable nature of enzymes. More efficient methods of enzyme production and purification, better methods in enzyme recycling and better engineering in kinetics and reactor design will require the talents of chemical engineers who have had training in biochemical engineering.

Single Cell Protein: The cells of microorganisms contain high levels of protein which are commonly known as the single cell protein (SCP). Production of SCP from carbohydrates and more recently from hydrocarbons has been considered most promising in solving the problem of immediate and long range world food supply. Microorganisms not only can convert non-food materials such as hydrocarbons, ammonia, and potassium phosphates into edible proteins but also can make the conversion in extremely high rates and with good efficiency. Dynamics of cell growth processes and oxygen absorption in multiple-phase hydrocarbon fermentations are all challenging problems of biochemical engineering.

Biological Waste Treatment: In water pollution, the problem of oxygen supply is of great importance. The oxygen solubility in water is about 10 milligrams per liter. When water is polluted with, say, one gram of glucose, the microbiological activity stimulated by the presence of this gram of food is sufficient to exhaust dissolved oxygen in more than 100 liters of water. Unless re-absorption of oxygen from the atmosphere is fast enough, fish and other marine organisms will receive irreversible damage. In (micro-) biological waste treatment, the contaminated water is processed through highly efficient gas-liquid contactors to absorb oxygen to biologically convert all the biodegradable pollutants into either escapable gases or filterable solid cell mass. Thus, a good portion of the water pollution control technology centers around microbiological activities and particularly biological oxidation. This is true in pollution damage to water resources and also true in waste treatment. With additional training in biochemical engineering, a chemical engineer is probably the best qualified engineer in pollution abatement.

A course in biochemical engineering covers the engineering aspects of biochemical and microbiological processes . . . It provides supplementary training to ChE students . . .

II. The General Philosophy

IN ADDITION TO ALL regular chemical engineering subjects including stoichiometry, unit operations, transport phenomena, thermodynamics, kinetics and process control, chemical engineers serving biochemical industries can work more effectively if they also have training in the fundamentals of biochemical engineering. Most chemical engineering students have taken non-major courses in mathematics, physics, and chemistry. For those whose work will involve biochemical and microbiological processes, certain additional exposure to elementary biochemistry and microbiology will be helpful.

Biochemical engineering is not a separate discipline from chemical engineering. It is neither "condensed biochemistry and microbiology'" made easy for chemical engineers. A course in biochemical engineering covers rather the engineering aspects of biochemical and microbiological processes that are not normally covered in regular chemical engineering courses. It is to provide supplementary training to chemical engineering students so that they are better prepared as chemical engineers for work that involves biological and microbiological processes. A biochemical engineering course covers either (1) topics unique to biochemical and microbiological processes such as microbial cell growth or (2) those chemical engineering topics that are of particular importance to biochemical industries such as gas-liquid interfacial mass transfer of oxygen.

A course entitled Biochemical Engineering has been offered to graduate students and qualified seniors at Iowa State University to provide the supplementary training as described above. For those graduate students who intend to become specialized in biochemical engineering, additional training is of course needed.

An additional objective of this course is to arouse awareness and stimulate interest in biochemical engineering research among chemical engineering students. There have been very few universities offering such training for chemical engineers, although there is a trend toward greater interest in this area. This is quite in step with the current trend towards interdisciplinary studies.

III. Outline of the Course

Course title: Biochemical Engineering
Textbook: none (There is a lack of a suitable textbook.)
Prerequisites:

(1) No previous training in biochemistry or microbiology is assumed. A sufficient coverage of the basics of biochemistry and microbiology is included in this course so as to allow intelligent discussion of the related biochemical engineering problems.
(2) Graduate students and qualified seniors (have had courses dealing with chemical kinetics and mass transfer) of chemical engineering.
(3) Non-chemical engineering majors by permission. (note: Qualified students from Departments of Sanitary Engineering, Biochemistry, Bacteriology and Food Technology can often follow this course with some extra help from the instructor on basic chemical engineering principles.

Chapter 1: **Basic Biology**

1. major microbial cell structures
2. cells and populations
3. DNA and double helix
4. RNA
5. enzymes
6. protein synthesis
7. genetic information

reference: Part 1 "Biochemistry of Bacterial Growes" by J. Mandelstam and K. McQuillen (Wiley, 1968).

Chapter 2: **Microbial Cell Growth**

1. Quantitation of growth
2. batch growth curve
3. lag phase and its shortening
4. exponential phase
5. mathematical description of growth curve
6. Monod equation and its extensions
7. Perret's growth model
8. Hinshelwood's balanced cell expansion model
9. production of single cell production

reference: Chapters 2, 3 and 5 in "Growth, Function and Regulation in Bacterial Cells" by A. C. R. Dean and Sir Cyril Hinshelwood (Oxford Press, 1966).

Chapter 3: **Applied Microbiology and Industrial Fermentation**

1. yeast, mold and bacteria
2. basic nutrients
3. pH effect
4. temperature effect
5. classifications: aerobic vs. anaerobic, etc.
6. concept of pure culture and controlled mixed culture
7. design of typical industrial fermentors and accessories

8. identification of areas for engineering investigation (as an introduction to the later chapters)
9. examples of typical industrial fermentation processes

references: Chapters 1 and 2 in "Biochemical and Biological Engineering Science" vol. 1, by N. Blakebrough (Academic press, 1967).
Chapters 1 and 2 "Biochemical Engineering" by S. Aiba, A. E. Humphrey and N. F. Millis (Academic Press, 1965).

Chapter 4: **Continuous Process of Cell Growth, Substrate Utilization (Waste Disposal) and Product Formation**

1. single stage, perfect mixed cell propagator (chemostat)
2. mathematical equations for cell growth, nutrient depletion and product accumulation
3. concept of wash-out
4. cell recycle and effect on cell yield
5. multiple stage cell propagator
6. design of continuous process—method by leudeking
7. plug flow and non-ideal reactor in cell growth
8. new techniques—concentrated cell population, dialysis cell propagator

references: Chapter 5 in "Biochemical Engineering" by S. Aiba, A. E. Humphrey and N. F. Millis (Academic Press, 1965)
Supplementary handout.

Chapter 5: **Enzyme Kinetics**

1. enzymes
2. Michaelis-Menten equation
3. equilibrium approach and steady state approach
4. Lineweaver-Burk and other plots
5. Monod equation and Langmuir equation
6. enzyme inhibitions
7. reversible competitive inhibition and Lineweaver-Burk plot
8. multiple and simultaneous enzymatic reactions
9. temperature effect

references: Chapter 6 in "Biochemical and Biological Engineering Science" vol. 1 by N. Blakebrough Academic Press, 1967).
Chapter 4 in "Enzymes" 2nd ed. by M. Dixon and E. C. Webb (Academic Press, 1964).

Chapter 6: **Industrial Enzymology**

1. types of enzymes: intracellular vs. extracellular, etc.
2. methods of isolation and purification (grinding, ultrasoundics, alcohol precipitation, salting out, etc.)
3. new techniques in enzyme applications (ultrafiltration, enzyme analogs, enzyme insolubilization)
4. available commercial enzymes and applications
5. important industrial enzymatically catalyzed reactions
6. enzymatic starch hydrolysis and glucose isomerase application

references: Chapters 2 and 3 in "Enzymes" 2nd ed. by M. Dixon and E. C. Webb (Academic Press, 1964).
Supplementary handout.

Dynamics of cell growth processes and oxygen absorption . . . are challenging problems of biochemical engineering.

Chapter 7: **Energetics and Metabolic Pathways**

1. high energy bonds (ATP, etc.)
2. coenzymes
3. concept of pathways
4. outlines of EMP, TCA, pentose pathways
5. amino acid synthesis and protein synthesis
6. beta-oxidation
7. biological oxidation
8. energy from glycolysis
9. anaerobic formation of methane, ethanol, lactic acid and glycerol
10. biological oxidation of Fe, S, and N compounds

references: Part 1 in "Biochemistry of Bacterial Growth" by J. Mendelstam and K. McQuillen (Wiley, 1968).
Supplementary handout.

Chapter 8: **Interfacial Mass Transfer**

1. oxygen solubility in water
2. BOD
3. methods for measuring dissolved oxygen
4. methods for measuring rate of oxygen absorption
5. empirical correlations for interfacial mass transfer coefficient
6. application of theory of turbulence
7. interfacial mass transfer theories of Whitman, Higbie and Danckwerts
8. effect of absorbing small particles
9. hydrocarbon-aqueous-gaseous multiple phase mass transfer

references: Chapter 5 in "Biochemical and Biological Engineering Science" by N. Blakebrough (Academic Press, 1967).
Book "Gas-Liquid Reactions" by P. V. Danckwerts, (McGraw Hill, 1970).

Chapter 9: **Gas-Liquid and Liquid-Liquid Dispersions**

1. interfacial area measured by optical methods
2. measured by chemical method of Danckwerts and Sharma
3. Sauter's mean bubble dismeter
4. surface area correlations—Weber number
5. gas-liquid contactors and liquid-dispersion equipment
6. power input
7. foam and emulsion

references: Chapter 5 in "Biochemical and Biological Engineering Science" vol. 1 by N. Blakebrough (Academic Press, 1967).
Chapter on "Dispersion" by Resnick and Gal-Or in Advances in Chemical Engineering (Academic Press, 1969).

Chapter 10: **Sterilization of Air**

1. sterilization by heat due to adiabatic compression
2. use of packed bed
3. theory of Gaden and Humphrey
4. Friedlander's analysis
5. mechanisms of particles removal from air
6. Pelect number
7. correlation of experimental data

references: Chapter 3 in "Biochemical and Biological Engineering Science" vol. 1 by N. Blakebrough

Chapter 11: **Sterilization of Liquid**

1. chemical methods
2. cationic detergent, ethylene and propylene oxide
3. chlorination in water treatment
4. phenol number
5. sterilization and pasteurization by heat
6. logrithmic death equation
7. Q-10 theory
8. temperature profile and its integration
9. Z-value and F-value
10. continuous sterilization process and equipment
11. inactivation by heat.

reference: Chapter 13 in "Biochemical Engineering" by F. C. Webb (Van Nostrand 1964)
Chapter 8 in "Biochemical Engineering" by S. Aiba, A. E. Humphrey, and N. F. Millis

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HEAT & MASS TRANSFER: Toor & Condiff

Toor & Condiff (Continued from page 191)

This form is specialized to obtain the general mass, momentum, and energy balances wherein conservation of mass, Newton's law of mechanics, and the first law of thermodynamics are each identified as a condition on the respective source terms. The assumption of local equilibrium is then introduced and employed to obtain the entropy balance, with identification of the positive definiteness of the source term as the second law of thermodynamics. Then follows a short survey of the highlights of irreversible thermodynamics using polyadics as a means of providing (i) a compact description of the linear laws of transport for an anisotropic medium, and (ii) a demonstration of Curie's theorem as a mathematical consequence of the assumption of isotropic transport coefficient tensors. It is hopefully made "crystal clear" that a violation of Onsager reciprocal relations is not excluded by any of the macroscopic principles.

With the closed and simplified versions of transport equations derived, methods of getting approximate and exact solutions for special heat transfer and analogous mass transfer problems are examined, though somewhat briefly. The sequence of study starts with the solution of problems categorized as (i) constant wall temperature penetration (BSL 10.R. 9.P, ex. 11.1-1, plug flow past a flat plate, etc.) all treated together by a similarity argument, (ii) constant wall heat flux penetration (BSL ex. 11.2-2, 9.R, etc.) also solved simultaneously by a similarity argument, and (iii) penetration in combination with external wall resistance. For case (iii) the similarity arguments are shown to break down and so the Laplace transform method is introduced, applied here, and pursued a bit further. Next the separation solutions are developed generally in conjunction with a concise survey of the Sturm-Liouville eigenvalue problem. This permits in particular a look at the general solution forms for forced convection heat transfer to fluid flowing in a conduit with boundary conditions of *constant wall temperature* or of transfer in series with an *external resistance* (e.g., the insulated pipe). The relationship of the lead eigenvalue to the asymptotic internal transfer coefficient is established at this point.

The separations solutions, and their special suitability for long time results provides a natural lead into the concept of relaxation time, which in turn is expanded into the ideas of multiple time scale analysis and their use in the justification of quasi steady state (qss) approximations. An example is the estimate of the time required to freeze a can of beer (for simplicity the beer is taken to be water) which is made using a one dimensional qss approximation. This approximation is then shown by a simple comparison of time scales to be necessarily invalid at the initial and final stages of the freezing process. Another example is the qss estimate of the time and distance of fall of an evaporating spherical raindrop with Stokes law drag, heat transfer correlations, and an analogy assumption for heat and mass transfer.

Problems emphasize the use of qss approximations with intuitive understanding of when they would not be accurate. Additional attention is given to problems with transfer across moving boundaries, especially boundaries where phase changes or fast reactions occur. There is a lecture devoted to the convective diffusion towards a rotating disc, and in this discussion the essential boundary-layer like character of the exact solution is brought out. This points the way to a development of boundary layer equations by simplified asymptotic arguments, with the Von