BIOCHEMICAL ENGINEERING

With Extensive Use of Personal Computers

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A COURSE IN biochemical engineering fundamentals was recently described by the authors of one of the best textbooks on the subject [1]. At RPI we take a much different approach to biochemical engineering and make very heavy use of personal computers (PC's) for homework assignments. In addition to games and exercises that have been published [2], we have developed computerized interactive tutorials and numerous problems that require computer simulation of differential equations.

Despite the practices at most institutions, we think it is inappropriate to have biochemistry, microbiology, and genetics taught by engineers. Of course, such training is absolutely essential, but we feel that the beauty of a topic is best conveyed by those scientists who are devoted to it. We require formal training in sciences for our graduate students. By teaching only the bare minimum of sciences, we have time to develop more topics in biotechnology and biochemical engineering. Remedial material is supplied as supplemental readings and commercial packages of audio cassettes with slides to help students in our first biochemical engineering course. Sufficient biochemistry for comprehending the engineering problems is taught outside of the regular class periods by interactive tutorials that do not slow down the student who has already had exposure to this material.

Our course starts with the substrates (raw materials) that may be chosen for a bioprocess. The future impact of inexpensive sugars from lignocellulosic biomass is stressed, and it is logical to digress to discussion of nutrition, alternate processes for biomass refining, carbohydrate structures, cellulases, feedback inhibition, byproducts from lignin, and economics. The next section of the course addresses microbial growth, aseptic techniques, culture preservation and handling, and commercial practices and problems. By this time, the students are comfortable with personal computers because of the tutorials and are ready for simulation problems. We use a barebones BASIC program that can be learned in about fifteen minutes. Adding special features to this program is illustrated by many different homework problems. The success of this program comes from providing a working example. Students have little difficulty in taking a program that executes nicely and modifying it for new problems.

Henry Bungay has been a professor at three universities, has spent ten years in industry, and has had appointments with NSF, USERDA, and New York State ERDA. His research in biochemical engineering addresses biomass refining, microscale effects of oxygen transfer, and high-rate continuous culture. He has owned a personal computer for ten years.

Production fermenters are studied in considerable detail, and novel designs are introduced. The reasons that biological reactors are different from chemical reactors are covered, but there is no time devoted to classical approaches to reactor design. Pilot plant fermentation equipment is studied with emphasis on automation, control, foam problems, assays, and costs. Lectures on fermentation rheology and mixing follow the usual textbooks quite closely, but aeration advances beyond standard practice because of the professor's interest in oxygen microelectrodes and oxygen transfer at the microscopic scale.

A very intensive coverage of continuous culture makes particularly good use of computer simulation. The systems of differential equations are modeled, and basic concepts of effects on yield coefficient, maintenance, and the like take on real meaning for the students. Mixed culture processes are also covered in detail, with simulation homework. This leads into lectures on dynamics of microbial processes.

On alternate years, the entire class (and the students that missed out the previous year) visit Bristol Laboratories in Syracuse, courtesy of Dr. Richard Elander, Vice-President for Fermentation Research and Development. He also lectures in our summer short course on advanced topics in biochemical engineering. Because of the coverage of practical fermentation processes and equipment, the students remark on how interesting it was to see real examples of topics they had studied.

We are blessed at RPI with several excellent courses on purification [3], so the biochemical engineering course does not go into detail on the newer, more advanced technology. Nevertheless, three or four lectures are needed for conventional practices for isolation of products.

TABLE 1
PC Assignments for Biochemical Engineering

ASSIGNMENT	PURPOSE
FERMT game from book	Develop intuition for process development
SUGAR tutorial	Refresher for carbohydrate structures
AMINO tutorial	Amino acid and protein structures
SIMBAS program from book	Simulation of differential equations
Kinetics problems	SIMBAS practice
Exercise using log graphs	Improve graphics skills
Oxygen transfer problem	SIMBAS practice and reinforce lectures
Partial harvest/refill	Reinforce lectures
Growth problems	In depth study; improved input/output
Air filtration	Practice in scaling computer graphs
Oxygen dynamics	Reinforce lectures
Normal distribution curve	Handling statistical distributions
Continuous fermentation	Practice with steady-state mass balances
MONOD game	Analysis of chemostat relation ships (best assignment of all)
LOTKA-VOLTERRA, TWOCUL, and improved predation model	Study of microbial interactions
BODE tutorial	Refresher on process dynamics
CHROMO game	Insight into protein precipitation and column chromatography
LEACH program	Tool for countercurrent extraction
MEMBRANE tutorial	Supplement lectures
ADSORB program	Langmuir and Freundlich isotherms and breakthrough calculations
STERIL game	Introduce continuous sterilization
Sterilization problems	Reinforce lectures
ENZYME tutorial	Teach enzyme kinetics

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TABLE 2
Student Term Projects

TOPIC	STUDENT ACCOMPLISHMENT
Rheology	Interactive tutorial with graphs and quizes.
Multistage Culture	Cascade of chemostats for exploration of feeding and recycle. PC version of game from book.
Enzyme kinetics	Interactive tutorial: theory, Michaelis-Menten kinetics, and types of inhibition.
Fermentation	Translation of Jermferm game (4) to IBM PC.
Genetics	Interactive tutorial on nucleic acid structure and gene splicing.

The remainder of the course is on processes using immobilized enzymes or immobilized cells. There is brief mention of tissue culture. The final lectures cover economics, process development strategy, and the future of biotechnology.

The course has had some computer teaching games and simulation exercises since the early 1970's [2], but many more computer assignments were recently added. Among the options for a term project are creating or improving the computer assignments. About half of the students choose a computer assignment, and the others cast a term paper in the form of a research proposal to the National Science Foundation. Students do quite well in devising interactive tutorials but only a very few have created a good computer game for teaching. The regular computer assignments are shown in Table 1. SIMBAS is the program for handling simultaneous, ordinary differential equations. All the programs are in the public domain and are written in BASIC to encourage others to tailor them to their own needs.

The table does not show the progression in computer skills. The students learn how to make the graphics more elegant, to add delays, logic, and other features, and to improve interaction with the computer. Interspersed with problems are games and exercises from the book [2]. Although this course has been taught many times, it continues to evolve. A deep investment of time for computer programming

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2. Define $k = \min \rho(z_i) - 1$, where $\rho(z_i)$ is the number of equations in which the variable z_i appears.
3. Identify sets of k equations which have the property that when the set is deleted there remains an array containing at least one variable which appears in only one equation.
4. Delete one such equation set.
5. Apply the design variable selection algorithm to the array which remains.
6. If no precedence order is obtained in Step 5, try another set of k equations.
7. If the deletion of no set of k equations results in an array that can be precedence-ordered, increase k by one and return to Step 3.

Returning to the situation of Figure 6 and applying Step 2 above, we determine that $\rho(z_i) = 4$ for the variables x_2 and t, and that is equal to two for each of the remaining six variables. Thus, $k = \min \rho(z_i) - 1 = 1$, which means that one of the remaining eight equations is to be *temporarily* deleted. Specifically, following Step 3 above, equations which qualify are Eqs. (18) through (24). Proceeding to Step 4, let us choose Eq. (18) to be temporarily deleted or relaxed. This temporary deletion has the effect of temporarily providing one more degree of freedom. This, in turn, allows the temporary election of one more problem variable as a design variable. The proper variable to so elect is determined in Step 5; the algorithm is successful in this case and results in the selection of the temperature (t) as the temporary design variable. Thus, these calculations are to be performed with initially assigned values for the two design variables x_1 and Π, and some initial estimate for the temporary design variable t. The calculations are then to be repeated with successively refined values of t until the relaxed Eq. (18) is satisfied. This calculation precedence order, with the recycle calculation loop, is illustrated in Figure 7. Chemical engineers will again readily recognize this sequence as the customary one in which they perform bubble-point calculations.

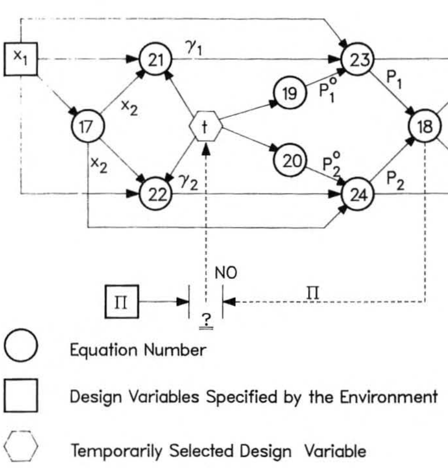

FIGURE 7. Calculation precedence order for isobaric VLE problem

SUMMARY

Methods have been presented for 1) determining the number of degrees of freedom in engineering calculations, 2) identifying information recycle loops in such calculations, and 3) developing calculation precedence orders to minimize or eliminate such loops. These methods have been illustrated manually with several simple examples. For more complex, realistic systems of engineering calculations, these methods are easily programmed on a digital computer, particularly in view of the Boolean logic nature of these methods.

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is essentially over because changes in the course are now coming from the students themselves as they develop new computer packages. Recent contributions by students are listed in Table 2. There have been no controlled experiments on the effectiveness of the course, but with very few exceptions students have rated the course highly and praise the computer assignments.

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