Unit Operations for Bioprocess Engineers

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Abstract

Unit Operations in Biological Systems Engineering was introduced into the curriculum at Virginia Tech in 2000. It is a lecture and laboratory combined course. The lectures and experiments covered in the course had a narrow focus before the author took over in 2002. To broaden the education for students selecting the Bioprocess Engineering option within the curriculum, the author has revised the content of the course to give the students an opportunity to understand that different unit operations can be applied in various industries, namely food, biochemical, and biotechnology. The experiments have been decreased from 14 to 8 so the students could have a better grasp of the theories and applications. Students' responses showed that it is important to design the experiments in a way to stimulate their desire to learn and perform. The author found that it is possible to give the students a better view of the various unit operations in bioprocess engineering.

Introduction

As defined by Shuler and Kargi (2002), "Bioprocess engineers are engineers working to apply the principles of various disciplines, such as chemical, mechanical, electrical, and industrial, to processes based on using living cells or subcomponents of such cells." In other words, bioprocess engineers are engineers who process biological materials to produce useful goods for society. Without question, bioprocess engineering is a broad-based engineering discipline. As educators, it is our job to broaden the view of the students, so they can take advantage of numerous, diverse job opportunities presented to them when they finish their BS degree.

In the Department of Biological Systems Engineering (BSE) at Virginia Tech, we offer an option in Bioprocess Engineering. Our main goal is to train students so they can have successful careers in bioprocess related industries, such as food, biochemical, and biopharmaceutical. Unit Operations in Biological Systems Engineering (BSE 3524), hereafter referred to as "Unit Ops", is offered to the students in the second semester of their junior year, and it consists of two 50-minute lectures and one 165-minute laboratory session per week. This course is the first technical elective course for students electing the Bioprocess Engineering option. Before taking this course, the students will have taken the following courses: calculus, physics, freshman chemistry, mathematics, Biological Systems Engineering Laboratories (sophomore); Thermodynamics of Biological Systems (first semester in junior year); and Transport Processes in Biological Systems Engineering (BSE 3504), which is taken in the same semester as Unit Ops. After taking Unit Ops, the students will take the following courses: Food Engineering, Protein Separation Engineering, Bioprocess Engineering, Industrial Bioprocessing,

Bioprocessing Plant Design, and Senior Design Project and Report. Fundamentals the students learn in Unit Ops will be applied to all these courses. Therefore, it is not exaggerating to say that Unit Ops is the cornerstone course for students pursuing the Bioprocess Engineering option in BSE. Given the importance of Unit Ops, it is imperative that the course be designed to give the students a very complete overview of bioprocess engineering.

Comparison of lecture content

1. Course content before modification (schedule by week):

- Introduction to unit operations, review of heat and mass transfer;
- Heat exchangers (plate, tubular, and shell-in-tube);
- Solid-liquid separation – filtration;
- Solid-solid separation and size reduction – sorting, sieving, milling, grinding;
- Membrane separation – liquid-gas permeation membranes, reverse-osmosis, ultrafiltration;
- Mixing and homogenization;
- Drying – dryer design and calculations for constant and falling rate drying;
- Freeze drying, spray drying, and design calculations;
- Evaporation;
- Liquid-gas separation – absorption in plate and packed towers;
- Liquid-vapor separation – phase rule, boiling point, and McCabe-Theile design calculations;
- Transportation – conveyors;

- General principles in process control.

2. Course content after modification:

- Introduction to unit operations, evaporation;
- Evaporation, drying;
- Drying – equipment, principles, and design;
- Gas-liquid separations;
- Gas-liquid separations;
- Vapor-liquid separations;
- Vapor-liquid separations;
- Adsorption – solid-liquid separation;
- Crystallization – introduction and theory;
- Crystallization – case study;
- Membrane separations;
- Membrane separations;
- Membrane separations – gas permeation, reverse osmosis, ultrafiltration, and microfiltration.

The comparison of the course content before and after modification is illustrated in Figure 1. The topics with the most significant increase in coverage are Crystallization and Membrane Separations. Crystallization was not included before modification, and the coverage for Membrane Separation is increased from two to six class periods. On the other hand, Mechanical Separation and Transportation were eliminated. The reasons for the changes are explained below.

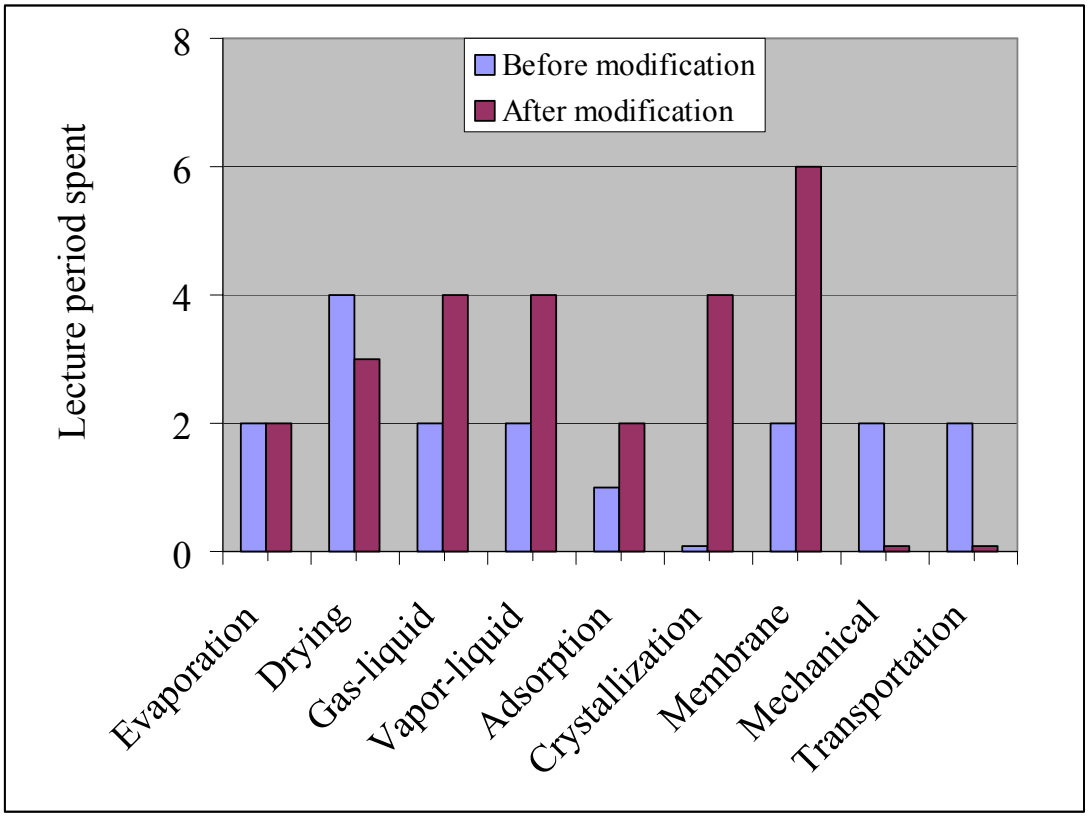

Figure 1. Comparison of the course content before and after modification.

Crystallization is a solid-liquid separation process in which mass transfer of a solute occurs from the liquid solution to a pure solid crystalline phase. Most bulk pharmaceutical and organic fine chemicals are marketed as crystalline products. It is a very important unit operation because 1) crystals are usually of exceptional purity; 2) the production of uniform crystals facilitates subsequent finishing steps, like filtration or drying; and 3) crystallization improves the product's appearance (Geankoplis, 2003). Crystallization is used in the food industry for production of sucrose from sugar beet, where sucrose is crystallized out from an aqueous solution. It is used in the biochemical and biotechnology industries, where the technique is often applied to produce highly purified products such as antibiotics and proteins. The content covered in the class includes an introduction and definition of the types of crystals; equilibrium solubility;

heat effect on crystallization; equipment and basic operation principles; crystallization theory including supersaturation, nucleation, and crystal growth; and the Δl law of crystal growth. Crystal growth is measured as the increase in length, Δl, in linear dimension of one crystal. This increase is independent of the initial size of the crystal, provided that all the crystals are subjected to the same environmental conditions. In addition, a method to determine the crystallization kinetics is introduced, and finally, a case study, sucrose crystallization, is studied to connect theory and practice. In the data analysis of the case study, the following concepts are also introduced: weight distribution as a function of the crystal sizes (sieving), number density, growth rate, nucleation rate, and dominant crystal size.

A membrane is a sheet of solid medium containing pores with well-defined size. It acts as a semipermeable barrier, which controls the rate of movement of various molecules between two fluid phases, liquid-liquid, liquid-gas, and gas-gas. Membrane separation is becoming increasingly important in almost all the process industries. Its applications include separation of gas mixture, such as separating helium from natural gas (gas permeation); chemical separation, such as H_2SO_4 from nickel and copper sulfate in aqueous solutions (liquid permeation); food processing, such as reduction of alcohol in beer (liquid permeation); artificial kidney – removal of urea from blood (dialysis); water treatment, such as the desalination of seawater (reverse osmosis); concentration of enzymes (reverse osmosis); and separation of macromolecules, such as proteins, separation of polymers from components with smaller molecular weight, recovery of whey proteins, and removal of bacteria to sterilize wine (ultrafiltration). To give students a broad view about membrane separation, the classification of various membrane

processes is first introduced, followed by the principles of the liquid permeation membrane process and dialysis, the principles of gas permeation membrane process, equipment and design, the principles of reverse osmosis, operation, and design, and the principles of ultrafiltration and operations. Each part was accompanied by examples to illustrate the principles.

Comparison of the laboratory content

Typically, there are 15 laboratory sessions each semester. Before modifications, one experiment was covered in each session. In addition to a field trip and a lab safety session, the following experiments were covered:

- Heat exchangers
- Filtration
- Size reduction and sieve separation
- Membrane separation
- Supercritical fluid extraction
- Thermal processing – canning
- Drum drying
- Spray drying/freeze drying/conventional drying
- Beef jerky
- Microwave and conventional oven
- Chromatography
- Fermentation
- Extrusion

After modification, the experiments were reduced to eight plus a lab safety session. The number of sessions for each experiment is included in parentheses.

- Freeze drying (1)
- Heat exchange (2)
- Fermentation (2)
- Liquid chromatography (2)
- Filtration (plate and frame) (2)
- Crystallization (2)
- Ultrafiltration (2)
- Continuous centrifugation (1)

Six of the eight experiments are covered in two sessions. Table 1 shows the modification of lab content. Out of the thirteen experiments previously taught, seven are eliminated.

Table 1. Modification of the experiments covered in the laboratory sessions.

Experiments eliminated	**Experiments added**	**Experiments changed**
1. Size reduction and sieve separation 2. Supercritical fluid extraction 3. Thermal processing – canning 4. Drum drying 5. Beef jerky 6. Microwave and conventional oven 7. Extrusion	1. Crystallization 2. Continuous centrifugation	1. Filtration 2. Heat Exchange 3. Fermentation 4. Liquid chromatography 5. Ultrafiltration

All seven of the eliminated experiments were narrowly focused and had limited application in the biochemical and biotechnology industries. Two new experiments, crystallization and continuous centrifugation, were added, and the other five experiments were all increased from one session to two sessions. With two-session coverage, the students have opportunities to not only gain valuable hands-on experience, but they also gain a deeper understanding of the principles of the unit operation involved. Using crystallization as an example, the following discussion demonstrates how the experiment is covered in a two-session period.

The crystallization experiment uses the operation of a batch crystallizer to understand the kinetics of crystal growth, and the influence of agitation rate on kinetics. Ideally, the experiment should be carried out in a continuously stirred tank reactor; however, a batch reactor is adequate to demonstrate the principles. The following information is given to the students before the experiment:

- Salt: potassium aluminum sulfate [$AlK(SO_4)_2 \cdot 12H_2O$], density and crystal shape factor.
- The solubility of potassium aluminum sulfate in water as a function of temperature.
- Theories covered in the class.

In the first session, the students need to complete the following tasks:

- Heat water to certain temperature;
- Calculate the amount of salt needed for a saturated solution at elevated temperature and make the saturated solution;
- Cool the salt solution while maintaining a certain agitation rate;

- Collect the crystals after certain time period;
- Allow crystals to dry;
- Repeat the above steps for a different agitation rate.

In session two, the following tasks are completed:

- Weigh total crystal weight (thoroughly dried);
- Fractionate the crystals using sieve (sieving is covered here);
- Weigh the crystals in every size fraction;
- Repeat for the second batch of crystals.

For the experiment report, the following components are required to be included for data analysis,

- Calculate overall yields;
- Calculate number density and determine the size distributions on mass and number basis;
- Assuming a continuous operation, determine the crystal growth kinetics, nucleation, and growth rate;
- Determine the dominant crystal sizes;
- Determine the effect of the agitation rate on crystallization.

Figure 2 shows the expected result for determination of the kinetics of the crystallization. The linear relationship between the crystal number density and the average crystal size is a characteristic of a continuous crystallizer. This also shows that with proper design of experiments, the kinetics of crystallization can be demonstrated with a batch type reactor. Eq. (1) gives the crystal growth rate (Belter, et al. 1988),

$$\ln(n) = \ln(n_0) - \left(\frac{1}{G \cdot \tau}\right) l \qquad (1)$$

where n is the number density of crystals with average size of l, G is the growth rate, τ is the residence time, and n_0 is the number density of the crystals with critical size. Then the nucleation rate, B, can be determined using Eq. (2),

$$B = n_0 \cdot G \qquad (2)$$

The effect of the agitation rate on crystallization kinetics is shown in Table 2.

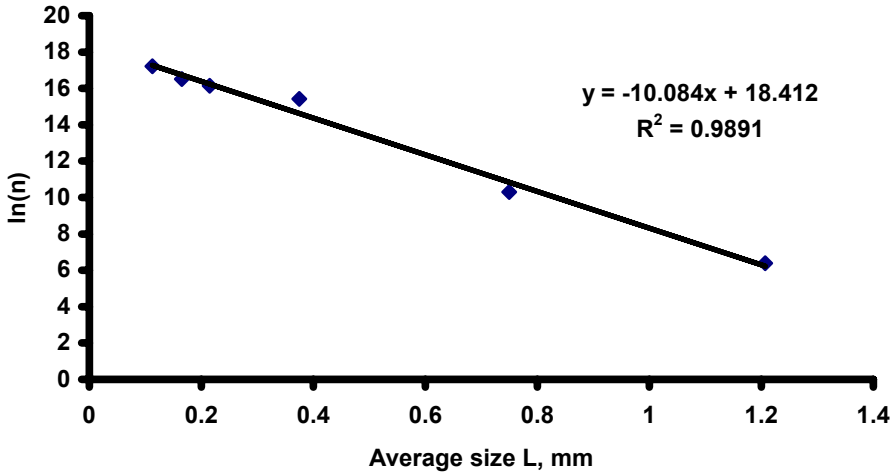

Figure 2. Number density of crystals as a function of the average crystal size.

Table 2. The effect of agitation rate on crystal growth.

Agitation Rate	Mass Average Size	Number Average Size	Dominant Size	Growth Rate	Nucleation Rate
(rpm)	(mm)	(mm)	(mm)	(mm/hr)	(10^7/L hr)
1678	0.371	0.025	0.298	0.331	3.28
7018	0.371	0.024	0.275	0.305	5.34

This experiment illustrates various unit operations such as filtration, sieving, mixing, and crystallization. The application of this technique can be easily generalized to

the crystallization of other components, such as proteins and sugars. More importantly, the students enjoy the experiment, thus their learning is enhanced.

Summary

Unit Operations in Biological Systems Engineering is a cornerstone course for students electing the Bioprocess Engineering option. Significant changes were made to increase emphasis on two operations, crystallization and membrane separation. The laboratory experiments were greatly modified, and most experiments were extended into two sessions for better understanding of the operation and associated principles. The Unit Ops course is now more appropriate for students with a broad interest in bioprocess engineering.

Acknowledgement

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