

How ABPDU is Training the Next Generation of Bioprocess Engineers

Overview Presentation and Panel Discussion

September 16, 2021



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About the Bioenergy Communicators (BioComms) Working Group

Sponsor:

- U.S. Department of Energy (DOE)
Bioenergy Technologies Office (BETO)



BETO & DOE National Laboratory Members:

- Bioenergy communicators, laboratory relationship managers, BETO tech team, and education and workforce development professionals



Purpose:

- Communications strategy for BETO-funded bioenergy research and development

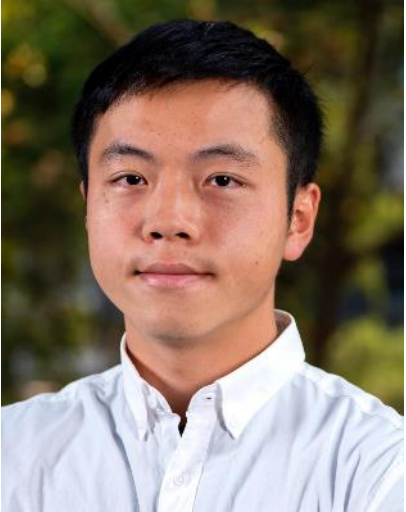


Today's Agenda

- I. **Presentation: How UC Berkeley and the Advanced Biofuels and Bioproducts Process Development Unit (ABPDU) Are Training the Next Generation of Bioprocess Engineers**
- II. **Panel Discussion with Key Stakeholders**

Photo courtesy of iStock

Today's Presenters and Panelists



Jason Ryder
Adjunct Professor &
Executive Director
Master of
Bioprocess
Engineering
Program, UC
Berkeley

James Gardner
Program Manager
for the ABPDU and
the Agile BioFoundry

**Jan-Philip (JP)
Prah**
Senior Process
Engineer in
Fermentation and
Recovery at LBNL's
ABPDU

Monica Bhatia
Former VP of
Process
Development, Geltor

David Chang
Senior Research
Associate at LBNL's
ABPDU



I. Presentation: How UC Berkeley and ABPDU Are Training the Next Generation of Bioprocess Engineers

Photo courtesy of iStock

How UC Berkeley and ABPDU Are Training the Next Generation of Bioprocess Engineers

2021 September 16

Jason Ryder, Ph.D.
Adjunct Professor
Department of Chemical & Biomolecular Engineering
Executive Director
Master of Bioprocess Engineering (MBPE) Program
University of California, Berkeley
306 Lewis Hall
ryder@berkeley.edu

1. Introductions

- Jason Ryder Bio
- Industrial Advisory Board

2. Master of Bioprocess Engineering (MBPE) Program

- Program scope
- Curriculum & required course content
- **CHMENG 275 Advanced Bioprocess Engineering Laboratory at ABPDU**
- Admissions requirements

UC Berkeley's Master of Bioprocess Engineering Program

Executive Director: Jason Ryder

Education



B.S. Chemical Engineering, University of Alabama (1997)



Ph.D. Chemical Engineering, UC Berkeley (2003) Bell & Chakraborty

Professional



(2003 – 2006) Semiconductor tool product development



(2006 – 2013) Farnesene process development, scale up, commercialization



(2013 – 2016) Recombinant spider silk proteins and premium clothing



(2016 – 2018) Plant-based proteins, “egg-free” Just Egg, clean meat



(2018 – present) Plant- and fermentation-based sweet fruit proteins and foods



(2018 – present) Growing and developing the next generation of bioprocess scientists and engineers

Passions



Bioprocessing in all forms (they are all my favorites)



Sustainable chemical engineering in all forms, mass and energy balances hugging the world



Growing and developing microbes, plants, people, scientists, engineers, companies



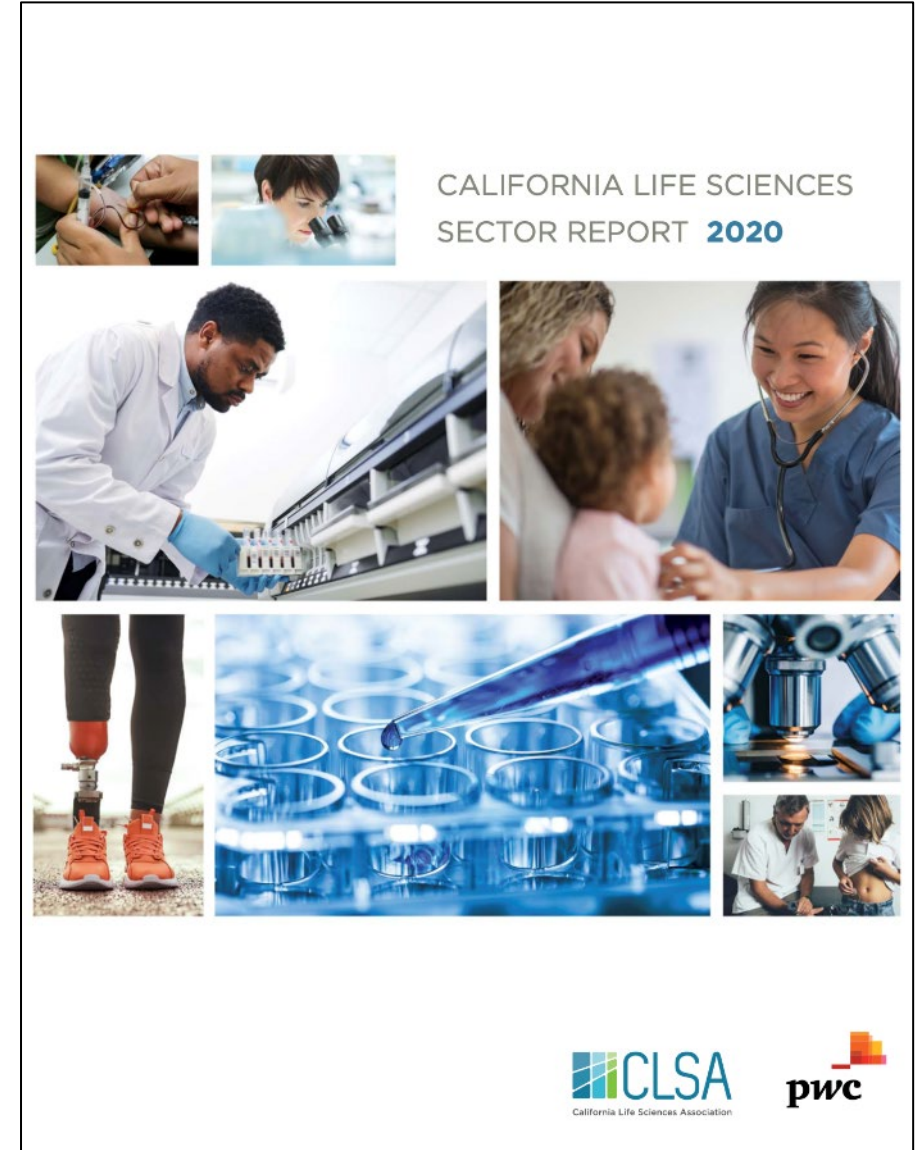
UC Berkeley's Master of Bioprocess Engineering Program

California's Life Sciences Industry

Life Sciences Sector Report 2020

biopharma, industrial biotech, food tech, advanced biologics, and more

- **3,700+** companies
- **\$191.6B** revenue
- **323,723** directly employed Californians
- **\$123,000** average salary
- **1,300** new medicines in clinical trials
- **\$6.5B** in venture capital



Problem: How To Prepare Bioprocess Engineers for Industry?

- Bioprocess industry has benchmarks on training to perform role as **Associate Scientist** or **Process Engineer**
- Many graduating students do not know or meet benchmark, are hired into operations roles with no growth and development path
- Industry is increasingly relying on temp agencies & contract positions, not investing in scientists and engineers they will need in 10 years
- Biotechnology field is growing faster than supply of trained bioprocess scientists and engineers required to develop, scale, commercialize
- This is a recipe for failure for students, industry, and field

Ask the Bioprocess Industry Experts: Industrial Advisory Board



Paul Hill
(Amyris)



Ashley Hesslein
(Bayer)



Paul Wu
(Bayer)



Marcella Yu
(Boehringer Ingelheim)



Brian Kelley
(VIR)



Jay Keasling



Brian Maiorella



Jason Ryder



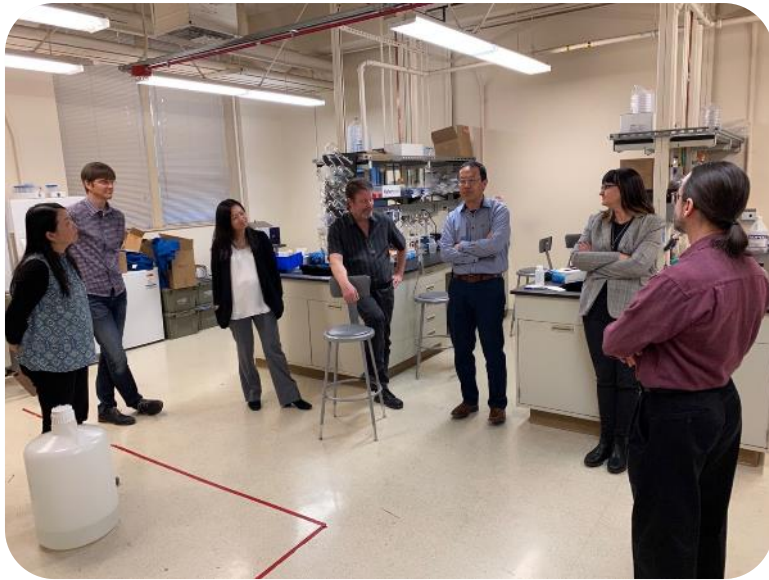
Wenjun Zhang

UC Berkeley's Master of Bioprocess Engineering Program

What the Bioprocess Industry Experts Said

First MBPE Industrial Advisory Board Meeting, 25 February 2020

- Goal: review of current program scope, facilities, curriculum, financing, keys to MBPE success
- Discussion on industry needs, key recommendations for program



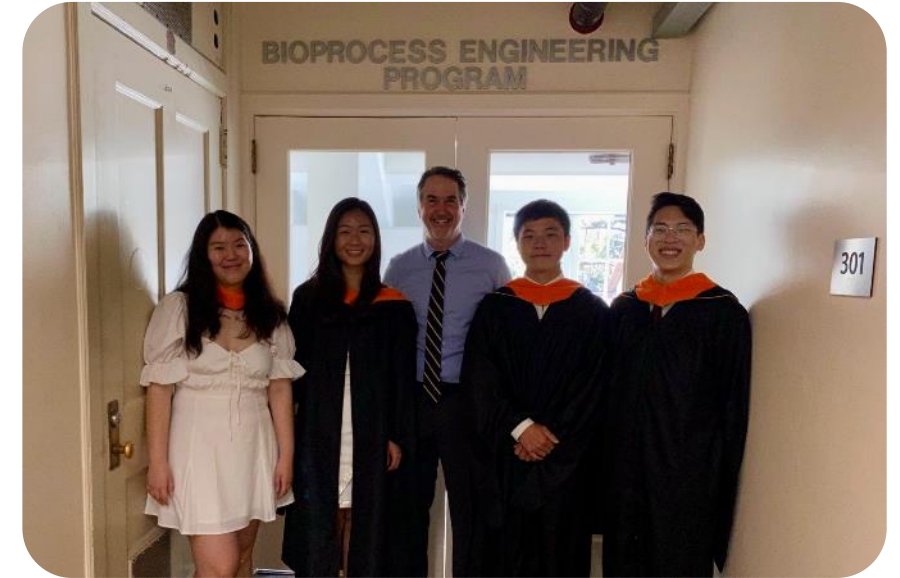
Key recommendation for hands-on training with common bioprocess equipment

- Upstream: shake flask, stainless steel fermentor, steam sterilization, filter sterilization, Ambr250
- Downstream: centrifugation, depth and crossflow filtration, chromatography (ÄKTA)

Solution: How to Train Bioprocess Engineers for Industry!

- **9-month Master of Bioprocess Engineering (MBPE)** curriculum
- **Benchmarks** agreed to by bioprocess industry, supported by **Industrial Advisory Board**
- Curriculum of bioprocess fundamentals and hands-on applications spanning laboratory- and pilot-scale bioprocessing equipment
- Graduating students qualify for and are hired for **Associate Scientist** or **Process Engineer** roles
- Industry gets well-prepared students who can be hired afterward with minimal to no search effort

UC Berkeley's Master of Bioprocess Engineering Program Inaugural MBPE Class of 2020-21



UC Berkeley's Master of Bioprocess Engineering Program MBPE Class of 2021-22



UC Berkeley's Master of Bioprocess Engineering Program Curriculum for 2021-22

Fall Semester	Spring Semester
CHMENG 170A Biochemical Engineering (4 units)	CHMENG 170B Biochemical Engineering (4 units)
Elective (3 units)	CHMENG 275 Advanced Bioprocess Engineering (3 units)
CHMENG 170L Biochemical Engineering Laboratory (3 units)	CHMENG 275L Advanced Bioprocess Engineering Lab (4 units)
CHMENG 298B Seminar in Bioprocess Engineering (1 unit)	CHMENG 298B Seminar in Bioprocess Engineering (1 unit)
Elective (3 units)	Elective (3 units)
TOTAL (14 units)	TOTAL (15 units)

UC Berkeley's Master of Bioprocess Engineering Program

CHMENG 170 A, B, L Biochemical Engineering Series

- The CBE 170 series is designed to introduce the essential concepts of bioprocessing to chemical engineers for applications in the biopharmaceutical, industrial biotech, and food tech industries



- The combined curriculum provides a comprehensive biochemical engineering training and toolkit in the analysis, design, development, scale-up, and commercialization of bio-based processes and products

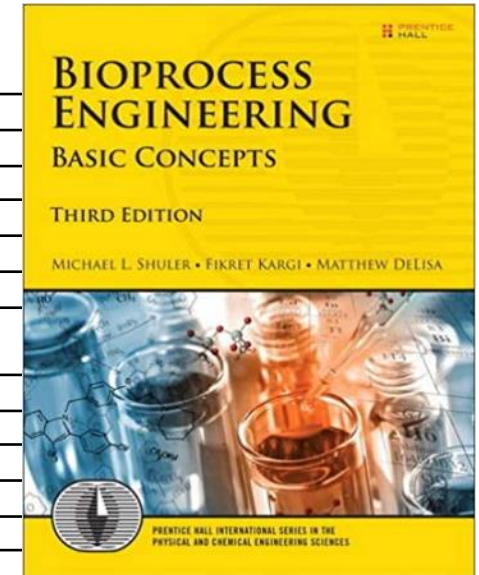
CHMENG 170A Biochemical Engineering (Fall Semester)

The emphasis of the 170A lecture course is on cells and how to make products by designing unit operations and processes around living systems.



Example of Topics (Fall 2020)

Biotechnology and biochemical engineering
Overview of biological basics
Enzymes: mechanisms, kinetics, and inhibition
Enzymatic reactions and immobilized enzymes
How cells work, major metabolic pathways
Recombinant microbes for bioprocesses
How cellular information is altered
Stoichiometry of growth and product formation
How cells grow, cell growth in continuous culture
Mass balances for two-phase bioreactors
Oxygen limitation in pellet culture
Gas-liquid mass transfer and k_La
Genetic instability
Microbial fermentation and host selection: Yeast, <i>E. coli</i> , and filamentous fungi
Bioreactor design for microbial fermentation
Scale-up of microbial fermentation
Scale-down of microbial fermentation
Bioprocess monitoring and controls, sensors, control strategy for ideal systems
Media preparation and continuous sterilization, sterilize-in-place (SIP)
Dead-end sterilization, clean-in-place (CIP), aseptic design and operations
Bioreactor design for animal cell culture
Mammalian cell culture medium development and fed-batch process optimization
Mammalian cell perfusion culture
Genetic engineering for mammalian cell expression
Biopharmaceutical process economics
Advanced biologics: nucleic acid, gene, cell therapies
Industrial biotech / food tech process economics
Illustrative examples (throughout)



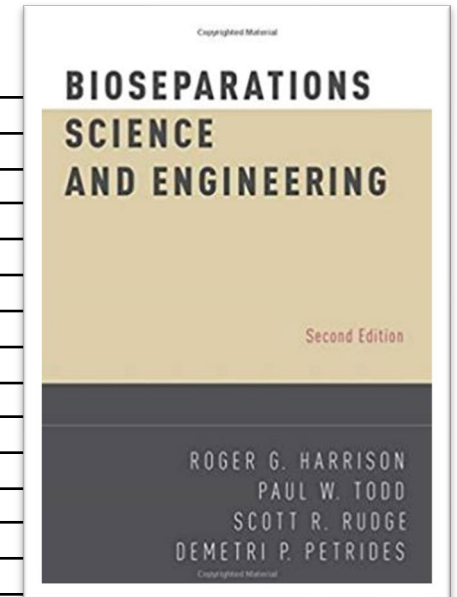
CHMENG 170B Biochemical Engineering (Spring Semester)

The focus of the 170B lecture course is primarily on the recovery, separations, and purification of bio-based products.



Example of Topics (Spring 2021)

- Introduction to bioproducts and bioseparations
- Bioprocess design and quality frameworks
- Analytical methods
- Homogenization and cell lysis
- Flocculation and sedimentation
- Bioprocess design and economics
- Centrifugation
- Centrifugation equipment, scale-up
- Filtration and membrane separations
- Harvest clarification: centrifugation vs. crossflow filtration
- Extraction
- Adsorption and liquid chromatography
- Chromatography and column dynamics
- Chromatography equipment and scale-up
- Precipitation fundamentals
- Precipitation equipment and scale-up
- Crystallization
- Bioprocess design and economics
- Integrated purification process design for macromolecules
- Protein products from *E. coli*
- Protein analytical characterization
- Evaporation and drying fundamentals
- Evaporation and drying equipment, scale-up
- Plant-based protein processing
- Illustrative examples (throughout)



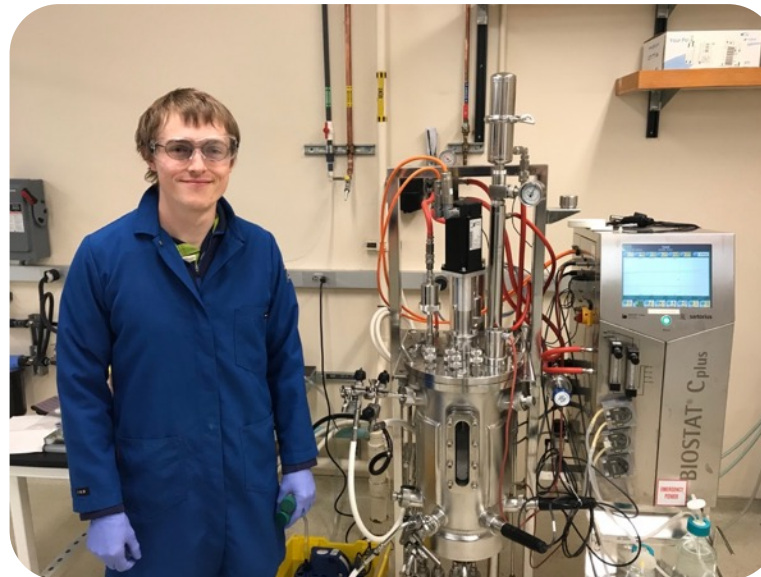
UC Berkeley's Master of Bioprocess Engineering Program

CHMENG 170L Biochemical Engineering Laboratory

The 170L laboratory provides hands-on opportunities to translate fundamentals learned in the 170A and 170B lecture courses into meaningful bench-scale applications.

Example of Topics and Experiments (170L)

- Employ basic molecular cloning and cellular biology techniques at lab scale
- Practice basic techniques for cell growth and harvesting
- Apply theory related to protein expression and purification to lab experiments
- Differentiate and apply common methods for protein and small molecule recovery and purification
- Use empirical and theoretical models to appraise enzyme kinetics
- Perform activity assays to assess protein quality
- Perform analytical assays to assess small molecule purity
- Sartorius BIOSTAT B
- Sartorius BIOSTAT C Plus
- Prepare and operate a bioreactor for batch fermentation
- Manage a laboratory notebook for reproducibility of experimental set-ups
- Prepare formal written and oral reports on experimental results and observations



UC Berkeley's Master of Bioprocess Engineering Program

CHMENG 275 Advanced Bioprocess Engineering

The 275 capstone course is designed to provide a thorough training in the integrated application of quality by design (QbD), statistical experimental design, and other concepts co-taught by industry experts from Amyris, Bayer, Boehringer Ingelheim, Genentech, Lilly, Vir Biotechnology, and more.

Example of Topics (Spring 2021)

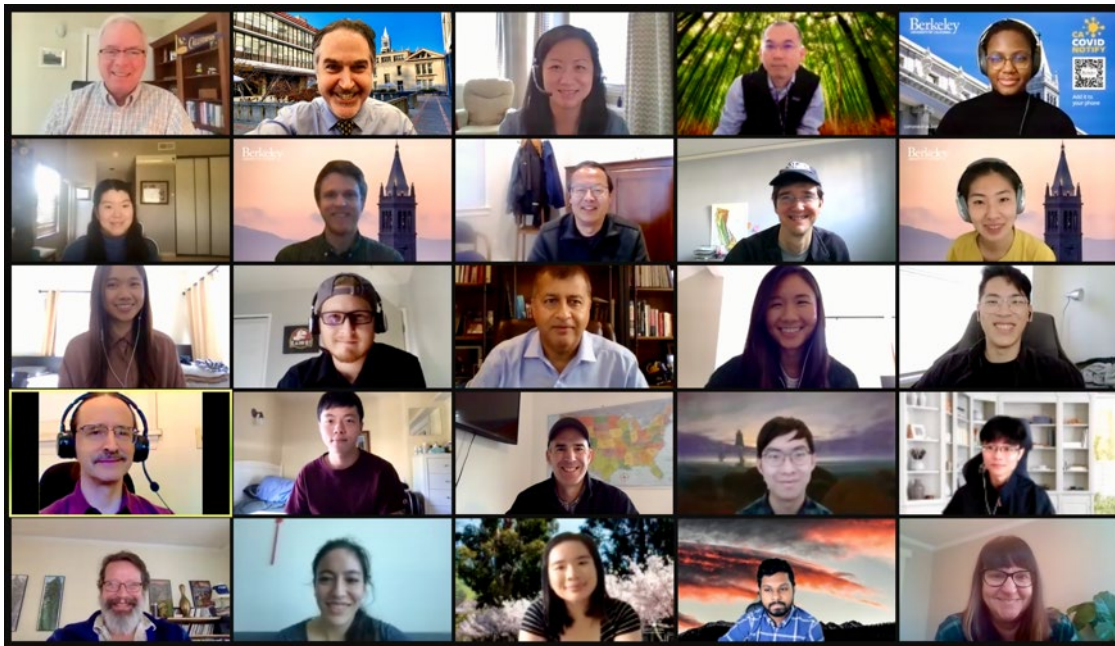
Introduction to Quality by Design (QbD)
Target product profile, molecule design
Identification, risk assessment of quality attributes
Examples of quality attribute risk assessment
Testing plan as a part of control strategy
Principles of noise
Effective data management
Fundamentals of applied statistics
Measurement system analysis
Optimization using design of experiments (DOE)
An R&D quality management system
Real-world examples of experimental design
Upstream manufacturing process development
Upstream process characterization
Defining design space for production bioreactor
Control strategy for upstream process
Case studies on practical implementation of QbD
Applications to non-therapeutic products
Downstream process description, prior knowledge
Downstream process characterization
Control strategy for downstream process
Understanding product quality
SARS-CoV-2 neutralizing antibodies for treatment and prevention of COVID-19
Mechanistic modeling of chromatography
Quality target product profile
Control strategy
Design space and lifecycle management

A-Mab: a Case Study in Bioprocess Development

CMC Biotech Working Group

Version 2.1
30th October 2009

The CMC Biotech Working Group has requested that this document be placed in the public domain by CAES and EDC



UC Berkeley's Master of Bioprocess Engineering Program

CHMENG 275L Advanced Bioprocess Engineering Laboratory

The 275L capstone laboratory course is designed to provide hands-on training and experience through pilot-scale bioprocess experiments at the **Advanced Biofuels and Bioproducts Process Development Unit (ABPDU)**.



JP Prahl, Senior Fermentation/Recovery Process Engineer (ABPDU)

CBE 275L – Advanced Bioprocess Engineering Laboratory – Spring 2021

Department of Chemical and Biomolecular Engineering
University of California, Berkeley
Advanced Biofuels and Bioproducts Process Development Unit (ABPDU)
5885 Hollis Street 3rd Floor, Emeryville
Tue/Thu 2:00 pm – 6:00 pm PT

Instructors

Jay Keasling, Professor
5885 Hollis Street 4th Floor, Emeryville
keasling@berkeley.edu
Office hours: TBD

Jan-Philip (JP) Prahl
Senior Fermentation/Recovery Process Engineer
5885 Hollis Street 3rd Floor, Emeryville
jprahl@lbl.gov
Office hours: TBD

Required Textbook

- Woodard B., Knapstein, K., Barrett J., *Fermentation Science & Biopharmaceutical Production*. 2nd ed. Maryland: Mandalay Publishing, 2020.

Recommended References

- Shuler L.S., Kargi F., DeLisa, M. *Bioprocess Engineering*. 3rd ed. New Jersey: Prentice-Hall, 2017.
- Harrison R.G., Todd P.W., Rudge S.R., Petrides, D.P., *Bioseparations Science and Engineering*. 2nd ed. New York: Oxford University Press, 2015.

Course Description

The CBE 275 series of courses is designed to introduce advanced concepts of bioprocessing to chemical engineers for applications in the biopharmaceutical, industrial biotech, and food tech industries. The emphasis of the 275 lecture course will be on integrated application of quality by design (QbD) framework, good manufacturing practice (GMP), statistical experimental design, and other advanced concepts addressing current industry needs. The 275L laboratory will provide hands-on opportunities to translate fundamentals learned in 170A, 170B, and 275 to meaningful pilot-scale unit operations and bioprocess applications. The combined curriculum provides an advanced bioprocess engineering training and toolkit in the analysis, design, development, scale-up, and commercialization of biochemical processes and products.

Prerequisites

- CBE 170A and CBE 170L
- CBE 170B concurrent (or consent of instructor)

UC Berkeley's Master of Bioprocess Engineering Program

CHMENG 275L Advanced Bioprocess Engineering Laboratory: Overview



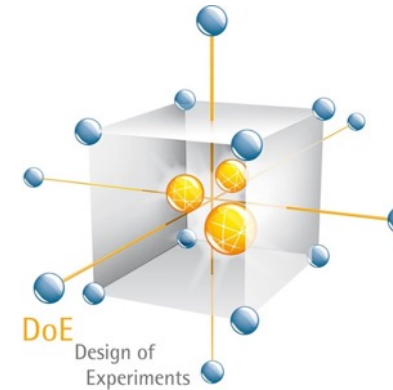
1. **Sartorius ambr®250** – design of experiment & multi parallel bioreactors – yeast

2. **ABEC 300L** – reactor setup & operations – yeast

3. **Alfa Laval Disc Stack Centrifuge** – cell separations – yeast

4. **Alfa Laval M20** – spiral membrane filtration – milk protein (LGB)

5. **GE ÄKTA Avant** – chromatography (protease)



CHMENG 275L: High Throughput Bioreactor Platform

Sartorius Ambr250 High Throughput Bioreactor Platform

S. cerevisiae – indigoidine

Design of Experiments (DOE)

Four factors, two levels (12 tanks)

→ carbon source, temp, pH, feed rate

Learnings:

Custom design (DOE) w/blocking

Software writing (basic/advanced)

Hardware setup & sampling



Sartorius Ambr250 High Throughput Bioreactor Platform

CHMENG 275L: Stainless Steel Bioreactor Setup & Operation

ABEC 300 L Stainless Steel Bioreactor

300L vessel prep + media batching

Scale-up (Ambr250 → 300 L)

Yeast fermentation

Learnings:

Steam sterilization of batch nutrients

Post sterile additions through cartridge filter

Probe calibration

Inoculation (generation of cell material*)



ABEC 300 L Stainless Steel Bioreactor and Supporting Equipment

CHMENG 275L: Cell Separations via Centrifugation

Alfa Laval MBPX 404S

Continuous disc stack centrifuge setup

Processing of whole cell broth

Learnings:

Solid liquid separation

Process optimization (time, flow rate)

Sample processing (spin tests)

Material handling (holding tanks, pumps, etc.)

Mass balance



Alfa Laval MBPX 404S and ABEC 300 L Stainless Steel Bioreactor

CHMNEG 275L: Protein Purification via Spiral Wound Membrane Filtration

Alfa Laval M20 Test Unit

Cross-flow filtration (TFF)

Ultrafiltration (5 kDa membrane)

Milk protein (19.8 kDa LGB)

Learnings:

Protein concentration

Diafiltration (desalination)

Analytics (ex. SDS page, conductivity)



Alfa Laval M20 Filtration Test Unit

CHMENG 275L: Protein Purification Via Chromatography

Cytiva ÄKTA Avant Chromatography

Protease purification

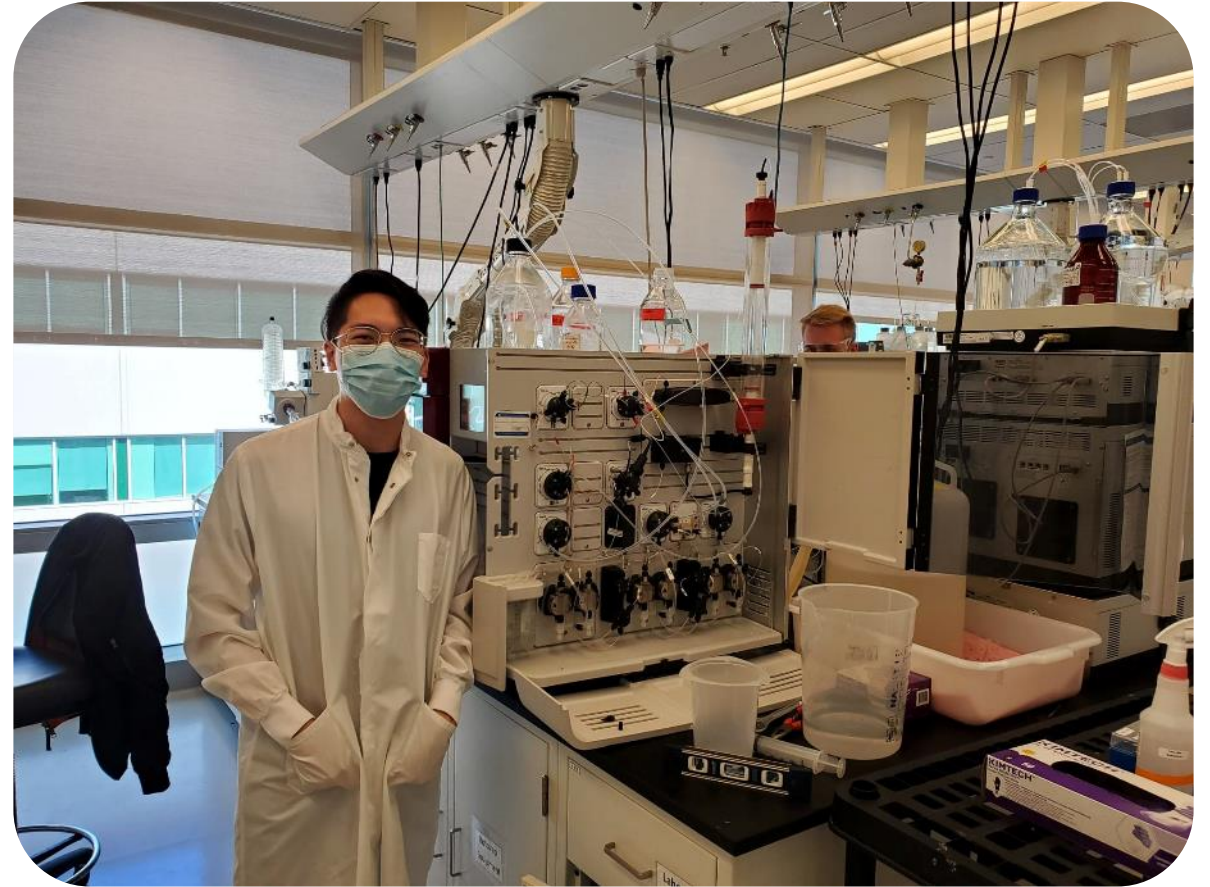
Column chromatography

Learnings:

Column packing

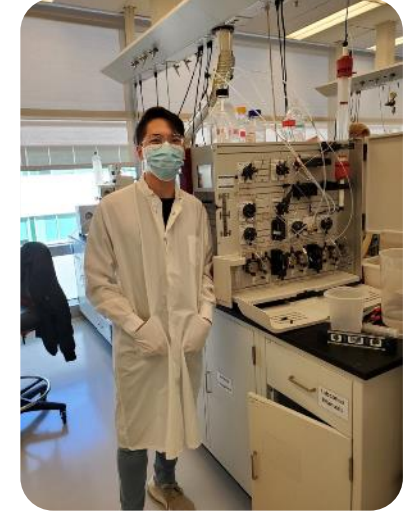
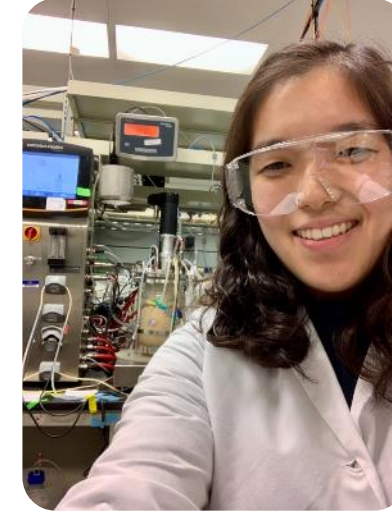
Recovery of protease from broth

Protein analytics (ex. SDS page)



Cytiva ÄKTA Avant Chromatography System

UC Berkeley's Master of Bioprocess Engineering Program What Success Looks Like for Both Industry and Students!



UC Berkeley's Master of Bioprocess Engineering Program

Admissions for MBPE 2022-23

Requirements

- Chemical Engineering background (B.S.)
- Undergraduate biochemistry/molecular biology course equivalent to BIOENG 11 or MCELLBI 102
- Minimum GPA of 3.0 on a 4.0 scale
- Minimum TOEFL score of at least 90 for the internet-based test (IBT) or 570 for the paper-based test (PBT)

UC Berkeley's Master of Bioprocess Engineering Program

Admissions for MBPE 2022-23

Program information and application

- <https://chemistry.berkeley.edu/grad/cbe/bioprocess-engineering>

Send an email


- mbpe@berkeley.edu

Deadline for applications

- **Friday 14 January 2022**

Admissions decisions

- **Monday 14 February 2022**



II. Panel Discussion with
Key Stakeholders

Photo courtesy of iStock

Today's Presenters and Panelists



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Monica Bhatia
Former VP of
Process
Development, Geltor

David Chang
Senior Research
Associate at LBNL's
ABPDU

Thank you!

Key Dates for MBPE 2022-23 Admissions

Program information and application: chemistry.berkeley.edu/grad/cbe/bioprocess-engineering

Send an email: mbpe@berkeley.edu

Deadline for applications: Friday, 14 January 2022

Admissions decisions: Monday, 14 February 2022

Questions for the ABPDU team?

General email: abpdu@lbl.gov

Website: abpdu.lbl.gov

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