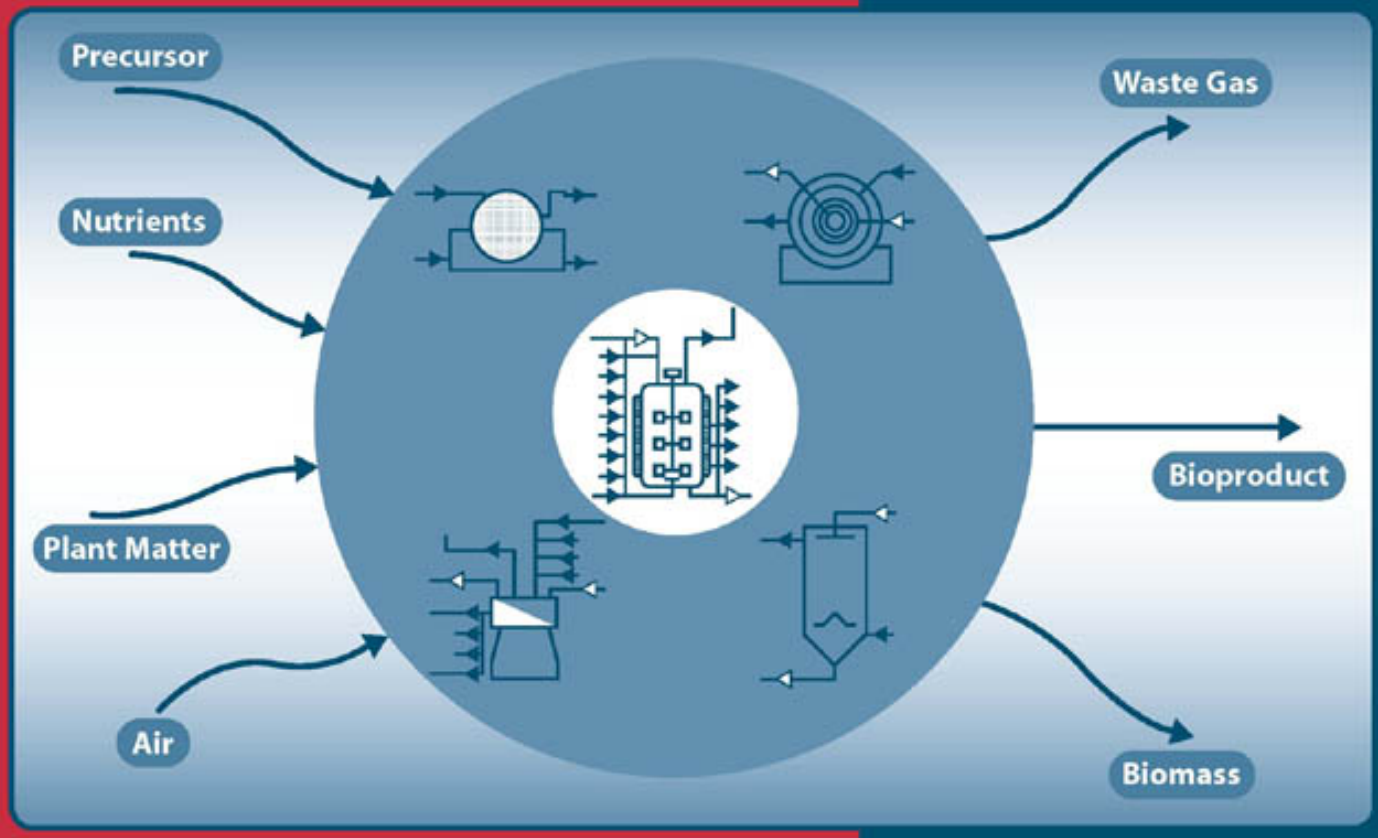
Separation Process Principles

Chemical and Biochemical Operations



Seader | Henley | Roper

3rd Edition

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SEPARATION PROCESS PRINCIPLES

Chemical and Biochemical Operations

THIRD EDITION

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About the Authors

J. D. Seader is Professor Emeritus of Chemical Engineering at the University of Utah. He received B.S. and M.S. degrees from the University of California at Berkeley and a Ph.D. from the University of Wisconsin-Madison. From 1952 to 1959, he worked for Chevron Research, where he designed petroleum and petrochemical processes, and supervised engineering research, including the development of one of the first process simulation programs and the first widely used vapor-liquid equilibrium correlation. From 1959 to 1965, he supervised rocket engine research for the Rocketdyne Division of North American Aviation on all of the engines that took man to the moon. He served as a Professor of Chemical Engineering at the University of Utah for 37 years. He has authored or coauthored 112 technical articles, 9 books, and 4 patents, and also coauthored the section on distillation in the 6th and 7th editions of *Perry's Chemical Engineers' Handbook*. He was a founding member and trustee of CACHE for 33 years, serving as Executive Officer from 1980 to 1984. From 1975 to 1978, he served as Chairman of the Chemical Engineering Department at the University of Utah. For 12 years he served as an Associate Editor of the journal, *Industrial and Engineering Chemistry Research*. He served as a Director of AIChE from 1983 to 1985. In 1983, he presented the 35th Annual Institute Lecture of AIChE; in 1988 he received the Computing in Chemical Engineering Award of the CAST Division of AIChE; in 2004 he received the CACHE Award for Excellence in Chemical Engineering Education from the ASEE; and in 2004 he was a co-recipient, with Professor Warren D. Seider, of the Warren K. Lewis Award for Chemical Engineering Education of the AIChE. In 2008, as part of the AIChE Centennial Celebration, he was named one of 30 authors of groundbreaking chemical engineering books.

Ernest J. Henley is Professor of Chemical Engineering at the University of Houston. He received his B.S. degree from the University of Delaware and his Dr. Eng. Sci. from Columbia University, where he served as a professor from 1953 to 1959. He also has held professorships at the Stevens Institute of Technology, the University of Brazil, Stanford University, Cambridge University, and the City University of New York. He has authored or coauthored 72 technical articles and 12 books, the most recent one being *Probabilistic Risk Management for Scientists and Engineers*. For 17 years, he was a trustee of CACHE, serving as President from 1975 to 1976 and directing the efforts that produced the seven-volume *Computer Programs for Chemical Engineering Education* and the five-volume *AIChE Modular Instruction*. An active consultant, he holds nine patents, and served on the Board of Directors of Maxxim Medical, Inc., Procedyne, Inc., Lasermedics, Inc., and Nanodyne, Inc. In 1998 he received the McGraw-Hill Company Award for ''Outstanding Personal Achievement in Chemical Engineering,'' and in 2002, he received the CACHE Award of the ASEE for ''recognition of his contribution to the use of computers in chemical engineering education.'' He is President of the Henley Foundation.

D. Keith Roper is the Charles W. Oxford Professor of Emerging Technologies in the Ralph E. Martin Department of Chemical Engineering and the Assistant Director of the Microelectronics-Photonics Graduate Program at the University of Arkansas. He received a B.S. degree (magna cum laude) from Brigham Young University in 1989 and a Ph.D. from the University of Wisconsin-Madison in 1994. From 1994 to 2001, he conducted research and development on recombinant proteins, microbial and viral vaccines, and DNA plasmid and viral gene vectors at Merck & Co. He developed processes for cell culture, fermentation, biorecovery, and analysis of polysaccharide, protein, DNA, and adenoviral-vectored antigens at Merck & Co. (West Point, PA); extraction of photodynamic cancer therapeutics at Frontier Scientific, Inc. (Logan, UT); and virus-binding methods for Millipore Corp (Billerica, MA). He holds adjunct appointments in Chemical Engineering and Materials Science and Engineering at the University of Utah. He has authored or coauthored more than 30 technical articles, one U.S. patent, and six U.S. patent applications. He was instrumental in developing one viral and three bacterial vaccine products, six process documents, and multiple bioprocess equipment designs. He holds memberships in Tau Beta Pi, ACS, ASEE, AIChE, and AVS. His current area of interest is interactions between electromagnetism and matter that produce surface waves for sensing, spectroscopy, microscopy, and imaging of chemical, biological, and physical systems at nano scales. These surface waves generate important resonant phenomena in biosensing, diagnostics and therapeutics, as well as in designs for alternative energy, optoelectronics, and micro-electromechanical systems.

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Preface to the Third Edition

Separation Process Principles was first published in 1998 to provide a comprehensive treatment of the major separation operations in the chemical industry. Both equilibrium-stage and mass-transfer models were covered. Included also were chapters on thermodynamic and mass-transfer theory for separation operations. In the second edition, published in 2006, the separation operations of ultrafiltration, microfiltration, leaching, crystallization, desublimation, evaporation, drying of solids, and simulated moving beds for adsorption were added. This third edition recognizes the growing interest of chemical engineers in the biochemical industry, and is renamed *Separation Process Principles—Chemical and Biochemical Operations*.

In 2009, the National Research Council (NRC), at the request of the National Institutes of Health (NIH), National Science Foundation (NSF), and the Department of Energy (DOE), released a report calling on the United States to launch a new multiagency, multiyear, multidisciplinary initiative to capitalize on the extraordinary advances being made in the biological fields that could significantly help solve world problems in the energy, environmental, and health areas. To help provide instruction in the important bioseparations area, we have added a third author, D. Keith Roper, who has extensive industrial and academic experience in this area.

NEW TO THIS EDITION

Bioseparations are corollaries to many chemical engineering separations. Accordingly, the material on bioseparations has been added as new sections or chapters as follows:

- Chapter 1: An introduction to bioseparations, including a description of a typical bioseparation process to illustrate its unique features.
- Chapter 2: Thermodynamic activity of biological species in aqueous solutions, including discussions of pH, ionization, ionic strength, buffers, biocolloids, hydrophobic interactions, and biomolecular reactions.
- Chapter 3: Molecular mass transfer in terms of driving forces in addition to concentration that are important in bioseparations, particularly for charged biological components. These driving forces are based on the Maxwell-Stefan equations.
- Chapter 8: Extraction of bioproducts, including solvent selection for organic-aqueous extraction, aqueous two-phase extraction, and bioextractions, particularly in Karr columns and Podbielniak centrifuges.
- Chapter 14: Microfiltration is now included in Section 3 on transport, while ultrafiltration is covered in a new section on membranes in bioprocessing.
- Chapter 15: A revision of previous Sections 15.3 and 15.4 into three sections, with emphasis in new Sections 15.3 and 15.6 on bioseparations involving adsorption and chromatography. A new section on electrophoresis for separating charged particles such as nucleic acids and proteins is added.
- Chapter 17: Bioproduct crystallization.
- Chapter 18: Drying of bioproducts.
- Chapter 19: Mechanical Phase Separations. Because of the importance of phase separations in chemical and biochemical processes, we have also added this new chapter on mechanical phase separations covering settling, filtration, and centrifugation, including mechanical separations in biotechnology and cell lysis.

Other features new to this edition are:

- Study questions at the end of each chapter to help the reader determine if important points of the chapter are understood.
- Boxes around important fundamental equations.
- Shading of examples so they can be easily found.
- Answers to selected exercises at the back of the book.
- Increased clarity of exposition: This third edition has been completely rewritten to enhance clarity. Sixty pages were eliminated from the second edition to make room for biomaterial and updates.
- More examples, exercises, and references: The second edition contained 214 examples, 649 homework exercises, and 839 references. This third edition contains 272 examples, 719 homework exercises, and more than 1,100 references.

SOFTWARE

Throughout the book, reference is made to a number of software products. The solution to many of the examples is facilitated by the use of spreadsheets with a Solver tool, Mathematica, MathCad, or Polymath. It is particularly important that students be able to use such programs for solving nonlinear equations. They are all described at websites on the Internet. Frequent reference is also made to the use of process simulators, such as

ASPEN PLUS, ASPEN HYSYS.Plant, BATCHPLUS, CHEMCAD, PRO/II, SUPERPRO DESIGNER, and UNISIM. Not only are these simulators useful for designing separation equipment, but they also provide extensive physical property databases, with methods for computing thermodynamic properties of mixtures. Hopefully, those studying separations have access to such programs. Tutorials on the use of ASPEN PLUS and ASPEN HYSYS. Plant for making separation and thermodynamic-property calculations are provided in the Wiley multimedia guide, ''Using Process Simulators in Chemical Engineering, 3rd Edition'' by D. R. Lewin (see www.wiley.com/college/lewin).

TOPICAL ORGANIZATION

This edition is divided into five parts. Part 1 consists of five chapters that present fundamental concepts applicable to all subsequent chapters. Chapter 1 introduces operations used to separate chemical and biochemical mixtures in industrial applications. Chapter 2 reviews organic and aqueous solution thermodynamics as applied to separation problems. Chapter 3 covers basic principles of diffusion and mass transfer for rate-based models. Use of phase equilibrium and mass-balance equations for single equilibrium-stage models is presented in Chapter 4, while Chapter 5 treats cascades of equilibrium stages and hybrid separation systems.

The next three parts of the book are organized according to separation method. Part 2, consisting of Chapters 6 to 13, describes separations achieved by phase addition or creation. Chapters 6 through 8 cover absorption and stripping of dilute solutions, binary distillation, and ternary liquid–liquid extraction, with emphasis on graphical methods. Chapters 9 to 11 present computer-based methods widely used in process simulation programs for multicomponent, equilibrium-based models of vapor–liquid and liquid–liquid separations. Chapter 12 treats multicomponent, rate-based models, while Chapter 13 focuses on binary and multicomponent batch distillation.

Part 3, consisting of Chapters 14 and 15, treats separations using barriers and solid agents. These have found increasing applications in industrial and laboratory operations, and are particularly important in bioseparations. Chapter 14 covers rate-based models for membrane separations, while Chapter 15 describes equilibrium-based and rate-based models of adsorption, ion exchange, and chromatography, which use solid or solid-like sorbents, and electrophoresis.

Separations involving a solid phase that undergoes a change in chemical composition are covered in Part 4, which consists of Chapters 16 to 18. Chapter 16 treats selective leaching of material from a solid into a liquid solvent. Crystallization from a liquid and desublimation from a vapor are discussed in Chapter 17, which also includes evaporation. Chapter 18 is concerned with the drying of solids and includes a section on psychrometry.

Part 5 consists of Chapter 19, which covers the mechanical separation of phases for chemical and biochemical processes by settling, filtration, centrifugation, and cell lysis.

Chapters 6, 7, 8, 14, 15, 16, 17, 18, and 19 begin with a detailed description of an industrial application to familiarize the student with industrial equipment and practices. Where appropriate, theory is accompanied by appropriate historical content. These descriptions need not be presented in class, but may be read by students for orientation. In some cases, they are best understood after the chapter is completed.

HELPFUL WEBSITES

Throughout the book, websites that present useful, supplemental material are cited. Students and instructors are encouraged to use search engines, such as Google or Bing, to locate additional information on old or new developments. Consider two examples: (1) McCabe–Thiele diagrams, which were presented 80 years ago and are covered in Chapter 7; (2) bioseparations. A Bing search on the former lists more than 1,000 websites, and a Bing search on the latter lists 40,000 English websites.

Some of the terms used in the bioseparation sections of the book may not be familiar. When this is the case, a Google search may find a definition of the term. Alternatively, the ''Glossary of Science Terms'' on this book's website or the ''Glossary of Biological Terms'' at the website: www.phschool.com/science/biology_place/glossary/a.html may be consulted.

Other websites that have proven useful to our students include:

(1) www.chemspy.com—Finds terms, definitions, synonyms, acronyms, and abbreviations; and provides links to tutorials and the latest news in biotechnology, the chemical industry, chemistry, and the oil and gas industry. It also assists in finding safety information, scientific publications, and worldwide patents.

(2) webbook.nist.gov/chemistry—Contains thermochemical data for more than 7,000 compounds and thermophysical data for 75 fluids.

(3) www. ddbst.com—Provides information on the comprehensive Dortmund Data Bank (DDB) of thermodynamic properties.

(4) www.chemistry.about.com/od/chemicalengineerin1/index.htm—Includes articles and links to many websites concerning topics in chemical engineering.

(5) www.matche.com—Provides capital cost data for many types of chemical processing

(6) www.howstuffworks.com—Provides sources of easy-to-understand explanations of how thousands of things work.

RESOURCES FOR INSTRUCTORS

Resources for instructors may be found at the website: *www.wiley.com/college/seader.* Included are:

(1) Solutions Manual, prepared by the authors, giving detailed solutions to all homework exercises in a tutorial format.

(2) Errata to all printings of the book

(3) A copy of a Preliminary Examination used by one of the authors to test the preparedness of students for a course in separations, equilibrium-stage operations, and mass transfer. This closed-book, 50-minute examination, which has been given on the second day of the course, consists of 10 problems on topics studied by students in prerequisite courses on fundamental principles of chemical engineering. Students must retake the examination until all 10 problems are solved correctly.

(4) Image gallery of figures and tables in jpeg format, appropriate for inclusion in lecture slides.

These resources are password-protected, and are available only to instructors who adopt the text. Visit the instructor section of the book website at www.wiley.com/college/seader to register for a password.

RESOURCES FOR STUDENTS

Resources for students are also available at the website: *www.wiley.com/college/seader.* Included are:

(1) A discussion of problem-solving techniques

(2) Suggestions for completing homework exercises

(3) Glossary of Science Terms

(4) Errata to various printings of the book

SUGGESTED COURSE OUTLINES

We feel that our depth of coverage is one of the most important assets of this book. It permits instructors to design a course that matches their interests and convictions as to what is timely and important. At the same time, the student is provided with a resource on separation operations not covered in the course, but which may be of value to the student later. Undergraduate instruction on separation processes is generally incorporated in the chemical engineering curriculum following courses on fundamental principles of thermodynamics, fluid mechanics, and heat transfer. These courses are prerequisites for this book. Courses that cover separation processes may be titled: Separations or Unit Operations, Equilibrium-Stage Operations, Mass Transfer and Rate-Based Operations, or Bioseparations.

This book contains sufficient material to be used in courses described by any of the above four titles. The Chapters to be covered depend on the number of semester credit hours. It should be noted that Chapters 1, 2, 3, 8, 14, 15, 17, 18, and 19 contain substantial material relevant to bioseparations, mainly in later sections of each chapter. Instructors who choose not to cover bioseparations may omit those sections. However, they are encouraged to at least assign their students Section 1.9, which provides a basic awareness of biochemical separation processes and how they differ from chemical separation processes. Suggested chapters for several treatments of separation processes at the undergraduate level are:

SEPARATIONS OR UNIT OPERATIONS:

3 Credit Hours: Chapters 1, 3, 4, 5, 6, 7, 8, (14, 15, or 17)

4 Credit Hours: Chapters 1, 3, 4, 5, 6, 7, 8, 9, 14, 15, 17

5 Credit Hours: Chapters 1, 3, 4, 5, 6, 7, 8, 9, 10, 13, 14, 15, 16, 17, 18, 19

EQUILIBRIUM-STAGE OPERATIONS:

3 Credit Hours: Chapters 1, 4, 5, 6, 7, 8, 9, 10

4 Credit Hours: Chapters 1, 4, 5, 6, 7, 8, 9, 10, 11, 13

MASS TRANSFER AND RATE-BASED OPERATIONS:

3 Credit Hours: Chapters 1, 3, 6, 7, 8, 12, 14, 15

4 Credit Hours: Chapters 1, 3, 6, 7, 8, 12, 14, 15, 16, 17, 18

BIOSEPARATIONS:

3 Credit Hours: Chapter 1, Sections 1.9, 2.9, Chapters 3, 4, Chapter 8 including Section 8.6, Chapters 14, 15, 17, 18, 19

Note that Chapter 2 is not included in any of the above course outlines because solution thermodynamics is a prerequisite for all separation courses. In particular, students who have studied thermodynamics from ''Chemical, Biochemical, and Engineering Thermodynamics'' by S.I. Sandler, ''Physical and Chemical Equilibrium for Chemical Engineers'' by N. de Nevers, or ''Engineering and Chemical Thermodynamics'' by M.D. Koretsky will be well prepared for a course in separations. An exception is Section 2.9 for a course in Bioseparations. Chapter 2 does serve as a review of the important aspects of solution thermodynamics and has proved to be a valuable and popular reference in previous editions of this book.

Students who have completed a course of study in mass transfer using ''Transport Phenomena'' by R.B. Bird, W.E. Stewart, and E.N. Lightfoot will not need Chapter 3. Students who have studied from ''Fundamentals of Momentum, Heat, and Mass Transfer'' by J.R. Welty, C.E. Wicks, R.E. Wilson, and G.L. Rorrer will not need Chapter 3, except for Section 3.8 if driving forces for mass transfer other than concentration need to be studied. Like Chapter 2, Chapter 3 can serve as a valuable reference.

Although Chapter 4 is included in some of the outlines, much of the material may be omitted if single equilibrium-stage calculations are adequately covered in sophomore courses on mass and energy balances, using books like "Elementary Principles of Chemical Processes" by R.M. Felder and R.W. Rousseau or "Basic Principles and Calculations in Chemical Engineering" by D.M. Himmelblau and J.B. Riggs.

Considerable material is presented in Chapters 6, 7, and 8 on well-established graphical methods for equilibrium-stage calculations. Instructors who are well familiar with process simulators may wish to pass quickly through these chapters and emphasize the algorithmic methods used in process simulators, as discussed in Chapters 9 to 13. However, as reported by P.M. Mathias in the December 2009 issue of *Chemical Engineering Progress*, the visual approach of graphical methods continues to provide the best teaching tool for developing insight and understanding of equilibrium-stage operations.

As a further guide, particularly for those instructors teaching an undergraduate course on separations for the first time or using this book for the first time, we have designated in the Table of Contents, with the following symbols, whether a section (§) in a chapter is:

* Important for a basic understanding of separations and therefore recommended for presentation in class, unless already covered in a previous course.

O Optional because the material is descriptive, is covered in a previous course, or can be read outside of class with little or no discussion in class.

• Advanced material, which may not be suitable for an undergraduate course unless students are familiar with a process simulator and have access to it.

B A topic in bioseparations.

A number of chapters in this book are also suitable for a graduate course in separations. The following is a suggested course outline for a graduate course:

GRADUATE COURSE ON SEPARATIONS

2–3 Credit Hours: Chapters 10, 11, 12, 13, 14, 15, 17

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J. D. Seader
Ernest J. Henley
D. Keith Roper

Brief Contents

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Contents

* Suitable for an UG course
o Optional
• Advanced
B Bioseparations

Nomenclature

All symbols are defined in the text when they are first used. Symbols that appear infrequently are not listed here.

Latin Capital and Lowercase Letters

A	area; absorption factor = L/KV; Hamaker constant
A_M	membrane surface area
a	activity; interfacial area per unit volume; molecular radius
a_v	surface area per unit volume
B	bottoms flow rate
B^0	rate of nucleation per unit volume of solution
b	molar availability function = $h - T_0 s$; component flow rate in bottoms
C	general composition variable such as concentration, mass fraction, mole fraction, or volume fraction; number of components; rate of production of crystals
C_D	drag coefficient
C_F	entrainment flooding factor
C_P	specific heat at constant pressure
$C^o_{P_V}$	ideal-gas heat capacity at constant pressure
c	molar concentration; speed of light
$c*$	liquid concentration in equilibrium with gas at its bulk partial pressure
c'	concentration in liquid adjacent to a membrane surface
$\bar{c}_b$	volume averaged stationary phase solute concentration in (15-149)
c_d	diluent volume per solvent volume in (17-89)
c_f	bulk fluid phase solute concentration in (15-48)
c_m	metastable limiting solubility of crystals
c_o	speed of light in a vacuum
c_p	solute concentration on solid pore surfaces of stationary phase in (15-48)
c_s	humid heat; normal solubility of crystals; solute concentration on solid pore surfaces of stationary phase in (15-48); solute saturation concentration on the solubility curve in (17-82)
c^s	concentration of crystallization-promoting additive in (17-101)
c_t	total molar concentration
Δc_{limit}	limiting supersaturation
D, $\mathcal{D}$	diffusivity; distillate flow rate; diameter
D'_{ij}	multicomponent mass diffusivity
D_B	bubble diameter
D_E	eddy-diffusion coefficient
D_{eff}	effective diffusivity
D_i	impeller diameter
D_{ij}	mutual diffusion coefficient of i in j
D_K	Knudsen diffusivity
D_L	longitudinal eddy diffusivity
$\bar{D}_N$	arithmetic-mean diameter
D_P	particle diameter
$\bar{D}_p$	average of apertures of two successive screen sizes
D_S	surface diffusivity
D_s	shear-induced hydrodynamic diffusivity in (14-124)
$\bar{D}_S$	surface (Sauter) mean diameter
D_T	tower or vessel diameter
$\bar{D}_V$	volume-mean diameter
$\bar{D}_W$	mass-mean diameter
d	component flow rate in distillate
d_e	equivalent drop diameter; pore diameter
d_H	hydraulic diameter = $4r_H$
d_i	driving force for molecular mass transfer
d_m	molecule diameter
d_p	droplet or particle diameter; pore diameter
d_{vs}	Sauter mean diameter
E	activation energy; extraction factor; amount or flow rate of extract; turbulent-diffusion coefficient; voltage; evaporation rate; convective axial-dispersion coefficient
E^0	standard electrical potential
E_b	radiant energy emitted by a blackbody
E_{MD}	fractional Murphree dispersed-phase efficiency
E_{MV}	fractional Murphree vapor efficiency
E_{OV}	fractional Murphree vapor-point efficiency
E_o	fractional overall stage (tray) efficiency
ΔE^{vap}	molar internal energy of vaporization
e	entrainment rate; charge on an electron
F, $\mathfrak{F}$	Faraday's contant = 96,490 coulomb/g-equivalent; feed flow rate; force
F_d	drag force
f	pure-component fugacity; Fanning friction factor; function; component flow rate in feed

G	Gibbs free energy; mass velocity; rate of growth of crystal size
g	molar Gibbs free energy; acceleration due to gravity
g_c	universal constant $= 32.174\ \text{lb}_\text{m} \cdot \text{ft}/\text{lb}_\text{f} \cdot \text{s}^2$
H	Henry's law constant; height or length; enthalpy; height of theoretical chromatographic plate
ΔH_{ads}	heat of adsorption
ΔH_{cond}	heat of condensation
ΔH_{crys}	heat of crystallization
ΔH_{dil}	heat of dilution
$\Delta H_{\text{sol}}^{\text{sat}}$	integral heat of solution at saturation
$\Delta H_{\text{sol}}^{\infty}$	heat of solution at infinite dilution
ΔH^{vap}	molar enthalpy of vaporization
H_G	height of a transfer unit for the gas phase $= l_T/N_G$
H_L	height of a transfer unit for the liquid phase $= l_T/N_L$
H_{OG}	height of an overall transfer unit based on the gas phase $= l_T/N_{OG}$
H_{OL}	height of an overall transfer unit based on the liquid phase $= l_T/N_{OL}$
$\mathcal{H}$	humidity
$\mathcal{H}'_m$	molal humidity
$\mathcal{H}_P$	percentage humidity
$\mathcal{H}_R$	relative humidity
$\mathcal{H}_S$	saturation humidity
$\mathcal{H}_W$	saturation humidity at temperature T_w
HETP	height equivalent to a theoretical plate
HETS	height equivalent to a theoretical stage (same as HETP)
HTU	height of a transfer unit
h	plate height/particle diameter in Figure 15.20
I	electrical current; ionic strength
i	current density
J_i	molar flux of i by ordinary molecular diffusion relative to the molar-average velocity of the mixture
j_D	Chilton–Colburn j-factor for mass transfer $\equiv N_{\text{St}_\text{M}}(N_{\text{Sc}})^{2/3}$
j_H	Chilton–Colburn j-factor for heat transfer $\equiv N_{\text{St}}(N_{\text{Pr}})^{2/3}$
j_M	Chilton–Colburn j-factor for momentum transfer $\equiv f/2$
j_i	mass flux of i by ordinary molecular diffusion relative to the mass-average velocity of the mixture
K	equilibrium ratio for vapor–liquid equilibria; overall mass-transfer coefficient
K_a	acid ionization constant
K_D	equilibrium ratio for liquid–liquid equilibria; distribution or partition ratio; equilibrium dissociation constant for biochemical receptor-ligand binding
K'_D	equilibrium ratio in mole- or mass-ratio compositions for liquid–liquid equilibria; equilibrium dissociation constant
K_e	equilibrium constant
K_G	overall mass-transfer coefficient based on the gas phase with a partial-pressure driving force
K_L	overall mass-transfer coefficient based on the liquid phase with a concentration-driving force
K_w	water dissociation constant
K_X	overall mass-transfer coefficient based on the liquid phase with a mole ratio driving force
K_x	overall mass-transfer coefficient based on the liquid phase with a mole fraction driving force
K_Y	overall mass-transfer coefficient based on the gas phase with a mole ratio driving force
K_y	overall mass-transfer coefficient based on the gas phase with a mole-fraction driving force
K_r	restrictive factor for diffusion in a pore
k	thermal conductivity; mass-transfer coefficient in the absence of the bulk-flow effect
k'	mass-transfer coefficient that takes into account the bulk-flow effect
k_A	forward (association) rate coefficient
k_B	Boltzmann constant
k_c	mass-transfer coefficient based on a concentration, c, driving force
$k_{c,tot}$	overall mass-transfer coefficient in linear driving approximation in (15-58)
k_D	reverse (dissociation) rate coefficient
k_i	mass-transfer coefficient for integration into crystal lattice
$k_{i,j}$	mass transport coefficient between species i and j
k_p	mass-transfer coefficient for the gas phase based on a partial pressure, p, driving force
k_T	thermal diffusion factor
k_x	mass-transfer coefficient for the liquid phase based on a mole-fraction driving force
k_y	mass-transfer coefficient for the gas phase based on a mole-fraction driving force
$\bar{L}$	liquid molar flow rate in stripping section
L	liquid; length; height; liquid flow rate; crystal size; biochemical ligand
L'	solute-free liquid molar flow rate; liquid molar flow rate in an intermediate section of a column
L_B	length of adsorption bed
L_e	entry length
L_p	hydraulic membrane permeability
L_{pd}	predominant crystal size
L_S	liquid molar flow rate of sidestream

LES	length of equilibrium (spent) section of adsorption bed
LUB	length of unused bed in adsorption
l_M	membrane thickness
l_T	packed height
M	molecular weight
M_i	moles of i in batch still
M_T	mass of crystals per unit volume of magma
M_t	total mass
m	slope of equilibrium curve; mass flow rate; mass; molality
m_c	mass of crystals per unit volume of mother liquor; mass in filter cake
$\bar{m}_i$	molality of i in solution
m_s	mass of solid on a dry basis; solids flow rate
m_v	mass evaporated; rate of evaporation
MTZ	length of mass-transfer zone in adsorption bed
N	number of phases; number of moles; molar flux $= n/A$; number of equilibrium (theoretical, perfect) stages; rate of rotation; number of transfer units; number of crystals/unit volume in (17-82)
N_A	Avogadro's number $= 6.022 \times 10^{23}$ molecules/mol
N_a	number of actual trays
N_{Bi}	Biot number for heat transfer
$N_{\mathrm{Bi_M}}$	Biot number for mass transfer
N_D	number of degrees of freedom
N_{Eo}	Eotvos number
N_{Fo}	Fourier number for heat transfer $= \alpha t/a^2 =$ dimensionless time
$N_{\mathrm{Fo_M}}$	Fourier number for mass transfer $= Dt/a^2 =$ dimensionless time
N_{Fr}	Froude number = inertial force/gravitational force
N_G	number of gas-phase transfer units
N_L	number of liquid-phase transfer units
N_{Le}	Lewis number $= N_{\mathrm{Sc}}/N_{\mathrm{Pr}}$
N_{Lu}	Luikov number $= 1/N_{\mathrm{Le}}$
N_{min}	mininum number of stages for specified split
N_{Nu}	Nusselt number $= dh/k =$ temperature gradient at wall or interface/temperature gradient across fluid (d = characteristic length)
N_{OG}	number of overall gas-phase transfer units
N_{OL}	number of overall liquid-phase transfer units
N_{Pe}	Peclet number for heat transfer $= N_{\mathrm{Re}}N_{\mathrm{Pr}} =$ convective transport to molecular transfer
$N_{\mathrm{Pe_M}}$	Peclet number for mass transfer $= N_{Re}N_{Sc} =$ convective transport to molecular transfer
N_{Po}	Power number
N_{Pr}	Prandtl number $= C_P\mu/k =$ momentum diffusivity/thermal diffusivity
N_{Re}	Reynolds number $= du\rho/\mu =$ inertial force/viscous force (d = characteristic length)
N_{Sc}	Schmidt number $= \mu/\rho\, D =$ momentum diffusivity/mass diffusivity
N_{Sh}	Sherwood number $= dk_c/D =$ concentration gradient at wall or interface/concentration gradient across fluid (d = characteristic length)
N_{St}	Stanton number for heat transfer $= h/GC_P$
$N_{\mathrm{St_M}}$	Stanton number for mass transfer $= k_c\rho/G$
NTU	number of transfer units
N_t	number of equilibrium (theoretical) stages
N_{We}	Weber number = inertial force/surface force
$\mathcal{N}$	number of moles
n	molar flow rate; moles; crystal population density distribution function in (17-90)
P	pressure; power; electrical power
P_c	critical pressure
P_i	molecular volume of component i/molecular volume of solvent
P_M	permeability
$\bar{P}_M$	permeance
P_r	reduced pressure, P/P_c
P^s	vapor pressure
p	partial pressure
$p*$	partial pressure in equilibrium with liquid at its bulk concentration
pH	$= -\log(a_{\mathrm{H+}})$
pI	isoelectric point (pH at which net charge is zero)
$\mathrm{p}K_a$	$= -\log(K_a)$
Q	rate of heat transfer; volume of liquid; volumetric flow rate
Q_C	rate of heat transfer from condenser
Q_L	volumetric liquid flow rate
Q_{ML}	volumetric flow rate of mother liquor
Q_R	rate of heat transfer to reboiler
q	heat flux; loading or concentration of adsorbate on adsorbent; feed condition in distillation defined as the ratio of increase in liquid molar flow rate across feed stage to molar feed rate; charge
R	universal gas constant; raffinate flow rate; resolution; characteristic membrane resistance; membrane rejection coefficient, retention coefficient, or solute reflection coefficient; chromatographic resolution
R_i	membrane rejection factor for solute i
R_{min}	minimum reflux ratio for specified split
R_p	particle radius
r	radius; ratio of permeate to feed pressure for a membrane; distance in direction of diffusion; reaction rate; molar rate of mass transfer per

	unit volume of packed bed; separation distance between atoms, colloids, etc.
r_c	radius at reaction interface
r_H	hydraulic radius = flow cross section/wetted perimeter
S	entropy; solubility; cross-sectional area for flow; solvent flow rate; mass of adsorbent; stripping factor = KV/L; surface area; Svedberg unit, a unit of centrifugation; solute sieving coefficient in (14-109); Siemen (a unit of measured conductivity equal to a reciprocal ohm)
S_o	partial solubility
S_T	total solubility
s	molar entropy; relative supersaturation; sedimentation coefficient; square root of chromatographic variance in (15-56)
s_p	particle external surface area
T	temperature
T_c	critical temperature
T_0	datum temperature for enthalpy; reference temperature; infinite source or sink temperature
T_r	reduced temperature = T/T_c
T_s	source or sink temperature
T_υ	moisture-evaporation temperature
t	time; residence time
$\bar{t}$	average residence time
t_{res}	residence time
U	overall heat-transfer coefficient; liquid sidestream molar flow rate; internal energy; fluid mass flowrate in steady counterflow in (15-71)
u	velocity; interstitial velocity
$\bar{u}$	bulk-average velocity; flow-average velocity
u_L	superficial liquid velocity
u_{mf}	minimum fluidization velocity
u_s	superficial velocity after (15-149)
u_t	average axial feed velocity in (14-122)
V	vapor; volume; vapor flow rate
V'	vapor molar flow rate in an intermediate section of a column; solute-free molar vapor rate
V_B	boilup ratio
V_V	volume of a vessel
$\bar{V}$	vapor molar flow rate in stripping section
$\bar{V}_i$	partial molar volume of species i
$\hat{V}_i$	partial specific volume of species i
V_{max}	maximum cumulative volumetric capacity of a dead-end filter
υ	molar volume; velocity; component flow rate in vapor
$\bar{\upsilon}$	average molecule velocity
υ_i	species velocity relative to stationary coordinates
υ_{i_D}	species diffusion velocity relative to the molar-average velocity of the mixture
υ_c	critical molar volume
υ_H	humid volume
υ_M	molar-average velocity of a mixture
υ_r	reduced molar volume, v/v_c
υ_0	superficial velocity
W	rate of work; moles of liquid in a batch still; moisture content on a wet basis; vapor sidestream molar flow rate; mass of dry filter cake/filter area
W_D	potential energy of interaction due to London dispersion forces
$W_{\min}$	minimum work of separation
WES	weight of equilibrium (spent) section of adsorption bed
WUB	weight of unused adsorption bed
W_s	rate of shaft work
w	mass fraction
X	mole or mass ratio; mass ratio of soluble material to solvent in underflow; moisture content on a dry basis
X^*	equilibrium-moisture content on a dry basis
X_B	bound-moisture content on a dry basis
X_c	critical free-moisture content on a dry basis
X_T	total-moisture content on a dry basis
X_i	mass of solute per volume of solid
x	mole fraction in liquid phase; mass fraction in raffinate; mass fraction in underflow; mass fraction of particles; ion concentration
x'	normalized mole fraction = $x_i / \sum_{j=1}^{N} x_j$
Y	mole or mass ratio; mass ratio of soluble material to solvent in overflow
y	mole fraction in vapor phase; mass fraction in extract; mass fraction in overflow
Z	compressibility factor = $P\upsilon/RT$; height
z	mole fraction in any phase; overall mole fraction in combined phases; distance; overall mole fraction in feed; charge; ionic charge

Greek Letters

α	thermal diffusivity, $k/\rho C_P$; relative volatility; average specific filter cake resistance; solute partition factor between bulk fluid and stationary phases in (15-51)
α^*	ideal separation factor for a membrane
α_{ij}	relative volatility of component i with respect to component j for vapor–liquid equilibria; parameter in NRTL equation
α_T	thermal diffusion factor
β_{ij}	relative selectivity of component i with respect to component j for liquid–liquid

	equilibria; phenomenological coefficients in the Maxwell–Stefan equations
Γ	concentration-polarization factor; counterflow solute extraction ratio between solid and fluid phases in (15-70)
γ	specific heat ratio; activity coefficient; shear rate
γ_w	fluid shear at membrane surface in (14-123)
Δ	change (final – initial)
δ	solubility parameter
δ_{ij}	Kronecker delta
$\delta_{i,j}$	fractional difference in migration velocities between species *i* and *j* in (15-60)
$\delta_{i,m}$	friction between species *i* and its surroundings (matrix)
ϵ	dielectric constant; permittivity
ϵ_b	bed porosity (external void fraction)
ϵ_D	eddy diffusivity for diffusion (mass transfer)
ϵ_H	eddy diffusivity for heat transfer
ϵ_M	eddy diffusivity for momentum transfer
ϵ_p	particle porosity (internal void fraction)
$\epsilon_p{}^*$	inclusion porosity for a particular solute
ζ	zeta potential
ζ_{ij}	frictional coefficient between species *i* and *j*
η	fractional efficiency in (14-130)
κ	Debye–Hückel constant; $1/\kappa$ = Debye length
λ	mV/L; radiation wavelength
λ_+, λ_-	limiting ionic conductances of cation and anion, respectively
λ_{ij}	energy of interaction in Wilson equation
μ	chemical potential or partial molar Gibbs free energy; viscosity
μ_o	magnetic constant
ν	momentum diffusivity (kinematic viscosity), μ/ρ; wave frequency; stoichiometric coefficient; electromagnetic frequency
π	osmotic pressure
ρ	mass density
ρ_b	bulk density
ρ_p	particle density
σ	surface tension; interfacial tension; Stefan–Boltzmann constant = 5.671×10^{-8} W/m$^2 \cdot$ K^4
σ_T	Soret coefficient
σ_I	interfacial tension
τ	tortuosity; shear stress
τ_w	shear stress at wall
Φ	volume fraction; statistical cumulative distribution function in (15-73)
φ	electrostatic potential
ϕ	pure-species fugacity coefficient; volume fraction
ϕ_s	particle sphericity
Ψ	electrostatic potential
Ψ_E	interaction energy
ψ	sphericity
ω	acentric factor; mass fraction; angular velocity; fraction of solute in moving fluid phase in adsorptive beds

Subscripts

A	solute
a, ads	adsorption
avg	average
B	bottoms
b	bulk conditions; buoyancy
bubble	bubble-point condition
C	condenser; carrier; continuous phase
c	critical; convection; constant-rate period; cake
cum	cumulative
D	distillate, dispersed phase; displacement
d, *db*	dry bulb
des	desorption
dew	dew-point condition
ds	dry solid
E	enriching (absorption) section
e	effective; element
eff	effective
F	feed
f	flooding; feed; falling-rate period
G	gas phase
GM	geometric mean of two values, A and B = square root of A times B
g	gravity; gel
gi	gas in
go	gas out
H, *h*	heat transfer
I, I	interface condition
i	particular species or component
in	entering
irr	irreversible
j	stage number; particular species or component
k	particular separator; key component
L	liquid phase; leaching stage
LM	log mean of two values, A and B = (A – B)/ln (A/B)
LP	low pressure
M	mass transfer; mixing-point condition; mixture
m	mixture; maximum; membrane; filter medium
max	maximum
min	minimum
N	stage
n	stage

O	overall
o, 0	reference condition; initial condition
out	leaving
OV	overhead vapor
P	permeate
R	reboiler; rectification section; retentate
r	reduced; reference component; radiation
res	residence time
S	solid; stripping section; sidestream; solvent; stage; salt
SC	steady counterflow
s	source or sink; surface condition; solute; saturation
T	total
t	turbulent contribution
V	vapor
w	wet solid–gas interface
w, *wb*	wet bulb
ws	wet solid
X	exhausting (stripping) section
x, *y*, *z*	directions
0	surroundings; initial
∞	infinite dilution; pinch-point zone

Superscripts

a	α-amino base
c	α-carboxylic acid
E	excess; extract phase
F	feed
floc	flocculation
ID	ideal mixture
(*k*)	iteration index
LF	liquid feed
o	pure species; standard state; reference condition
p	particular phase
R	raffinate phase
s	saturation condition
VF	vapor feed
¯	partial quantity; average value
∞	infinite dilution
(1), (2)	denotes which liquid phase
I, II	denotes which liquid phase
$*$	at equilibrium

Abbreviations and Acronyms

AFM	atomic force microscopy
Angstrom	1×10^{-10} m
ARD	asymmetric rotating-disk contactor
ATPE	aqueous two-phase extraction
atm	atmosphere
avg	average
B	bioproduct
BET	Brunauer–Emmett–Teller
BOH	undissociated weak base
BP	bubble-point method
BSA	bovine serum albumin
B–W–R	Benedict–Webb–Rubin equation of state
bar	0.9869 atmosphere or 100 kPa
barrer	membrane permeability unit, 1 barrer = 10^{-10} cm^3 (STP)-cm/(cm^2-s cm Hg)
bbl	barrel
Btu	British thermal unit
C	coulomb
C_i	paraffin with i carbon atoms
$C_i^=$	olefin with i carbon atoms
CBER	Center for Biologics Evaluation and Research
CF	concentration factor
CFR	Code of Federal Regulations
cGMP	current good manufacturing practices
CHO	Chinese hamster ovary (cells)
CMC	critical micelle concentration
CP	concentration polarization
CPF	constant-pattern front
C–S	Chao–Seader equation
CSD	crystal-size distribution
°C	degrees Celsius, K-273.2
cal	calorie
cfh	cubic feet per hour
cfm	cubic feet per minute
cfs	cubic feet per second
cm	centimeter
cmHg	pressure in centimeters head of mercury
cP	centipoise
cw	cooling water
Da	daltons (unit of molecular weight)
DCE	dichloroethylene
DEAE	diethylaminoethyl
DEF	dead-end filtration
DLVO	theory of Derajaguin, Landau, Vervey, and Overbeek
DNA	deoxyribonucleic acid
dsDNA	double-stranded DNA
rDNA	recombinant DNA
DOP	diisoctyl phthalate
ED	electrodialysis
EMD	equimolar counter-diffusion
EOS	equation of state
EPA	Environmental Protection Agency
ESA	energy-separating agent

ESS	error sum of squares
EDTA	ethylenediaminetetraacetic acid
eq	equivalents
°F	degrees Fahrenheit, °R- 459.7
FDA	Food and Drug Administration
FUG	Fenske–Underwood–Gilliland
ft	feet
GLC-EOS	group-contribution equation of state
GLP	good laboratory practices
GP	gas permeation
g	gram
gmol	gram-mole
gpd	gallons per day
gph	gallons per hour
gpm	gallons per minute
gps	gallons per second
H	high boiler
HA	undissociated (neutral) species of a weak acid
HCP	host-cell proteins
HEPA	high-efficiency particulate air
HHK	heavier than heavy key component
HIV	Human Immunodeficiency Virus
HK	heavy-key component
HPTFF	high-performance TFF
hp	horsepower
h	hour
I	intermediate boiler
IMAC	immobilized metal affinity chromatography
IND	investigational new drug
in	inches
J	Joule
K	degrees Kelvin
kg	kilogram
kmol	kilogram-mole
L	liter; low boiler
LES	length of an ideal equilibrium adsorption section
LHS	left-hand side of an equation
LK	light-key component
LLE	liquid–liquid equilibrium
LLK	lighter than light key component
L–K–P	Lee–Kessler–Plöcker equation of state
LM	log mean
LMH	liters per square meter per hour
LRV	log reduction value (in microbial concentration)
LUB	length of unused sorptive bed
LW	lost work
lb	pound
lb_f	pound-force
lb_m	pound-mass
lbmol	pound-mole
ln	logarithm to the base e
log	logarithm to the base 10
M	molar
MF	microfiltration
MIBK	methyl isobutyl ketone
MSMPR	mixed-suspension, mixed-product-removal
MSC	molecular-sieve carbon
MSA	mass-separating agent
MTZ	mass-transfer zone
MW	molecular weight; megawatts
MWCO	molecular-weight cut-off
m	meter
meq	milliequivalents
mg	milligram
min	minute
mm	millimeter
mmHg	pressure in mm head of mercury
mmol	millimole (0.001 mole)
mol	gram-mole
mole	gram-mole
N	newton; normal
NADH	reduced form of nicotinamide adenine dinucleotide
NF	nanofiltration
NLE	nonlinear equation
NMR	nuclear magnetic resonance
NRTL	nonrandom, two-liquid theory
nbp	normal boiling point
ODE	ordinary differential equation
PBS	phosphate-buffered saline
PCR	polymerase chain reaction
PEG	polyethylene glycol
PEO	polyethylene oxide
PES	polyethersulfones
PDE	partial differential equation
POD	Podbielniak extractor
P–R	Peng–Robinson equation of state
PSA	pressure-swing adsorption
PTFE	poly(tetrafluoroethylene)
PVDF	poly(vinylidene difluoride)
ppm	parts per million (usually by weight for liquids and by volume or moles for gases)
psi	pounds force per square inch
psia	pounds force per square inch absolute
PV	pervaporation
PVA	polyvinylalcohol
QCMD	quartz crystal microbalance/dissipation
R	amino acid side chain; biochemical receptor

RDC	rotating-disk contactor
RHS	right-hand side of an equation
R–K	Redlich–Kwong equation of state
R–K–S	Redlich–Kwong–Soave equation of state (same as S–R–K)
RNA	ribonucleic acid
RO	reverse osmosis
RTL	raining-bucket contactor
°R	degrees Rankine
rph	revolutions per hour
rpm	revolutions per minute
rps	revolutions per second
SC	simultaneous-correction method
SDS	sodium docecylsulfate
SEC	size exclusion chromatography
SF	supercritical fluid
SFE	supercritical-fluid extraction
SG	silica gel
S.G.	specific gravity
SOP	standard operating procedure
SPM	stroke speed per minute; scanning probe microscopy
SPR	surface plasmon resonance
SR	stiffness ratio; sum-rates method
S–R–K	Soave–Redlich–Kwong equation of state
STP	standard conditions of temperature and pressure (usually 1 atm and either 0°C or 60°F)
s	second
scf	standard cubic feet
scfd	standard cubic feet per day
scfh	standard cubic feet per hour
scfm	standard cubic feet per minute
stm	steam
TBP	tributyl phosphate
TFF	tangential-flow filtration
TIRF	total internal reflectance fluorescence
TLL	tie-line length
TMP	transmembrane pressure drop
TOMAC	trioctylmethylammonium chloride
TOPO	trioctylphosphine oxide
Tris	tris(hydroxymethyl) amino-methane
TSA	temperature-swing adsorption
UF	ultrafiltration
UMD	unimolecular diffusion
UNIFAC	Functional Group Activity Coefficients
UNIQUAC	universal quasichemical theory
USP	United States Pharmacopeia
UV	ultraviolet
vdW	van der Waals
VF	virus filtration
VOC	volatile organic compound
VPE	vibrating-plate extractor
vs	versus
VSA	vacuum-swing adsorption
WFI	water for injection
WHO	World Health Organization
wt	weight
X	organic solvent extractant
y	year
yr	year
μm	micron = micrometer

Mathematical Symbols

d	differential
∇	del operator
e, exp	exponential function
erf$\{x\}$	error function of $x = \frac{1}{\sqrt{\pi}} \int_0^x \exp(-\eta^2) d\eta$
erfc$\{x\}$	complementary error function of $x =$ 1 – erf(x)
f	function
i	imaginary part of a complex value
ln	natural logarithm
log	logarithm to the base 10
∂	partial differential
{ }	delimiters for a function
||	delimiters for absolute value
Σ	sum
π	product; pi ≅ 3.1416

Dimensions and Units

Chemical engineers must be proficient in the use of three systems of units: (1) the International System of Units, SI System (Systeme Internationale d'Unites), which was established in 1960 by the 11th General Conference on Weights and Measures and has been widely adopted; (2) the AE (American Engineering) System, which is based largely upon an English system of units adopted when the Magna Carta was signed in 1215 and is a preferred system in the United States; and (3) the CGS (centimeter-gram-second) System, which was devised in 1790 by the National Assembly of France, and served as the basis for the development of the SI System. A useful index to units and systems of units is given on the website: http://www.sizes.com/units/index.htm

Engineers must deal with dimensions and units to express the dimensions in terms of numerical values. Thus, for 10 gallons of gasoline, the dimension is volume, the unit is gallons, and the value is 10. As detailed in NIST (National Institute of Standards and Technology) Special Publication 811 (2009 edition), which is available at the website: http://www.nist.gov/physlab/pubs/sp811/index.cfm, units are *base* or *derived.*

BASE UNITS

The base units are those that are independent, cannot be subdivided, and are accurately defined. The base units are for dimensions of length, mass, time, temperature, molar amount, electrical current, and luminous intensity, all of which can be measured independently. Derived units are expressed in terms of base units or other derived units and include dimensions of volume, velocity, density, force, and energy. In this book we deal with the first five of the base dimensions. For these, the base units are:

Base	SI Unit	AE Unit	CGS Unit
Length	meter, m	foot, ft	centimeter, cm
Mass	kilogram, kg	pound, lb_m	gram, g
Time	second, s	hour, h	second, s
Temperature	kelvin, K	Fahrenheit, °F	Celsius, °C
Molar amount	gram-mole, mol	pound-mole, lbmol	gram-mole, mol

ATOM AND MOLECULE UNITS

atomic weight = atomic mass unit = the mass of one atom

molecular weight (MW) = molecular mass (M) = formula weight* = formula mass* = the sum of the atomic weights of all atoms in a molecule (*also applies to ions)

1 atomic mass unit (amu or u) = 1 universal mass unit = 1 dalton (Da) = 1/12 of the mass of one atom of carbon-12 = the mass of one proton or one neutron

The units of MW are amu, u, Da, g/mol, kg/kmol, or lb/lbmol (the last three are most convenient when MW appears in a formula).

The number of molecules or ions in one mole = Avogadro's number = 6.022×10^{23}.

DERIVED UNITS

Many derived dimensions and units are used in chemical engineering. Several are listed in the following table:

Derived Dimension	SI Unit	AE Unit	CGS Unit
Area = Length^2	m^2	ft^2	cm^2
Volume = Length^3	m^3	ft^3	cm^3
Mass flow rate = Mass/Time	kg/s	lb_m/h	g/s
Molar flow rate = Molar amount/Time	mol/s	lbmol/h	mol/s
Velocity = Length/Time	m/s	ft/h	cm/s
Acceleration = Velocity/Time	m/s^2	ft/h^2	cm/s^2
Force = Mass · Acceleration	newton, N = $1 kg \cdot m/s^2$	lb_f	dyne = $1 g \cdot cm/s^2$
Pressure = Force/Area	pascal, Pa = $1 N/m^2$ = $1 kg/m \cdot s^2$	$lb_f/in.^2$	atm
Energy = Force · Length	joule, J = $1 N \cdot m$ = $1 kg \cdot m^2/s^2$	$ft \cdot lb_f$, Btu	erg = $1 dyne \cdot cm$ = $1 g \cdot cm^2/s^2$, cal
Power = Energy/Time = Work/Time	watt, W = $1 J/s$ = $1 N \cdot m/s$ $1 kg \cdot m^2/s^3$	hp	erg/s
Density = Mass/Volume	kg/m^3	lb_m/ft^3	g/cm^3

OTHER UNITS ACCEPTABLE FOR USE WITH THE SI SYSTEM

A major advantage of the SI System is the consistency of the derived units with the base units. However, some acceptable deviations from this consistency and some other acceptable base units are given in the following table:

Dimension	Base or Derived	Acceptable SI Unit
Time	s	minute (min), hour (h), day (d), year (y)
Volume	m^3	liter (L) = 10^{-3} m^3
Mass	kg	metric ton or tonne (t) = 10^3 kg
Pressure	Pa	bar = 10^5 Pa

PREFIXES

Also acceptable for use with the SI System are decimal multiples and submultiples of SI units formed by prefixes. The following table lists the more commonly used prefixes:

Prefix	Factor	Symbol
tera	10^{12}	T
giga	10^9	G
mega	10^6	M
kilo	10^3	k

deci	10^{-1}	d
centi	10^{-2}	c
milli	10^{-3}	m
micro	10^{-6}	μ
nano	10^{-9}	n
pico	10^{-12}	p

USING THE AE SYSTEM OF UNITS

The AE System is more difficult to use than the SI System because of the units for force, energy, and power. In the AE System, the force unit is the pound-force, lb_f, which is defined to be numerically equal to the pound-mass, lb_m, at sea-level of the earth. Accordingly, Newton's second law of motion is written,

$$F = m\frac{g}{g_c}$$

where F = force in lb_f, m = mass in lb_m, g = acceleration due to gravity in ft/s^2, and, to complete the definition, the constant $g_c = 32.174\ \text{lb}_\text{m} \cdot \text{ft/lb}_\text{f} \cdot \text{s}^2$, where 32.174 ft/s^2 is the acceleration due to gravity at sea-level of the earth. The constant g_c is not used with the SI System or the CGS System because the former does not define a kg_f and the CGS System does not use a g_f.

Thus, when using AE units in an equation that includes force and mass, incorporate g_c to adjust the units.

EXAMPLE

A 5.000-pound-mass weight, m, is held at a height, h, of 4.000 feet above sea-level. Calculate its potential energy above sea-level, P.E. = mgh, using each of the three systems of units. Factors for converting units are given on the inside front cover of this book.

SI System:

$$\begin{aligned} m &= 5.000\ \text{lb}_\text{m} = 5.000(0.4536) = 2.268\ \text{kg} \\ g &= 9.807\ \text{m/s}^2 \\ h &= 4.000\ \text{ft} = 4.000(0.3048) = 1.219\ \text{m} \\ \text{P.E.} &= 2.268(9.807)(1.219) = 27.11\ \text{kg} \cdot \text{m}^2/\text{s}^2 = 27.11\ \text{J} \end{aligned}$$

CGS System:

$$\begin{aligned} m &= 5.000\ \text{lb}_\text{m} = 5.000(453.6) = 2268\ \text{g} \\ g &= 980.7\ \text{cm/s}^2 \\ h &= 4.000\ \text{ft} = 4.000(30.48) = 121.9\ \text{cm} \\ \text{P.E.} &= 2268(980.7)(121.9) = 2.711 \times 10^8\ \text{g} \cdot \text{cm}^2/\text{s}^2 \\ &= 2.711 \times 10^8\ \text{erg} \end{aligned}$$

AE System:

$$\begin{aligned} m &= 5.000\ \text{lb}_\text{m} \\ g &= 32.174\ \text{ft/s}^2 \\ h &= 4.000\ \text{ft} \\ \text{P.E.} &= 5.000(32.174)(4.000) = 643.5\ \text{lb}_\text{m} \cdot \text{ft}^2/\text{s}^2 \end{aligned}$$

However, the accepted unit of energy for the AE System is $\text{ft} \cdot \text{lb}_\text{f}$, which is obtained by dividing by g_c. Therefore, P.E. = 643.5/32.174 = 20.00 ft lb_f.

Another difficulty with the AE System is the differentiation between energy as work and energy as heat. As seen in the above table of derived units, the work unit is $\text{ft} \cdot \text{lb}_\text{f}$, while the heat unit is Btu. A similar situation exists in the CGS System with corresponding units of erg and calorie (cal). In older textbooks, the conversion factor between work and heat is often incorporated into an equation with the symbol J, called Joule's constant or the mechanical equivalent of heat, where

$$J = 778.2\ \text{ft lb}_\text{f}/\text{Btu} = 4.184 \times 10^7 \text{erg/cal}$$

Thus, in the previous example, the heat equivalents are

AE System:

$$20.00/778.2 = 0.02570\ \text{Btu}$$

CGS System:

$$2.711 \times 10^8 / 4.184 \times 10^7 = 6.479 \text{ cal}$$

In the SI System, the prefix M, mega, stands for million. However, in the natural gas and petroleum industries of the United States, when using the AE System, M stands for thousand and MM stands for million. Thus, MBtu stands for thousands of Btu, while MM Btu stands for millions of Btu.

It should be noted that the common pressure and power units in use for the AE System are not consistent with the base units. Thus, for pressure, pounds per square inch, psi or $lb_f/in.^2$, is used rather than lb_f/ft^2. For power, hp is used instead of $ft \cdot lb_f/h$, where the conversion factor is

$$1 \text{ hp} = 1.980 \times 10^6 \text{ft} \cdot \text{lb}_\text{f}/\text{h}$$

CONVERSION FACTORS

Physical constants may be found on the inside back cover of this book. Conversion factors are given on the inside front cover. These factors permit direct conversion of AE and CGS values to SI values. The following is an example of such a conversion, together with the reverse conversion.

EXAMPLE

1. Convert 50 psia ($lb_f/in.^2$ absolute) to kPa:
   The conversion factor for $lb_f/in.^2$ to Pa is 6,895, which results in

$$50(6{,}895) = 345{,}000 \text{ Pa or } 345 \text{ kPa}$$

2. Convert 250 kPa to atm:
   250 kPa = 250,000 Pa. The conversion factor for atm to Pa is 1.013×10^5. Therefore, dividing by the conversion factor,

$$250{,}000/1.013 \times 10^5 = 2.47 \text{ atm}$$

Three of the units [gallons (gal), calories (cal), and British thermal unit (Btu)] in the list of conversion factors have two or more definitions. The gallons unit cited here is the U.S. gallon, which is 83.3% of the Imperial gallon. The cal and Btu units used here are international (IT). Also in common use are the thermochemical cal and Btu, which are 99.964% of the international cal and Btu.

FORMAT FOR EXERCISES IN THIS BOOK

In numerical exercises throughout this book, the system of units to be used to solve the problem is stated. Then when given values are substituted into equations, units are not appended to the values. Instead, the conversion of a given value to units in the above tables of base and derived units is done prior to substitution into the equation or carried out directly in the equation, as in the following example.

EXAMPLE

Using conversion factors on the inside front cover of this book, calculate a Reynolds number, $N_{Re} = D\upsilon\rho/\mu$, given $D = 4.0$ ft, $\upsilon = 4.5$ ft/s, $\rho = 60$ lb_m/ft^3, and $\mu = 2.0$ cP (i.e., centipoise).

Using the SI System (kg-m-s),

$$N_{Re} = \frac{D\upsilon\rho}{\mu} = \frac{[(4.00)(0.3048)][(4.5)(0.3048)][(60)(16.02)]}{[(2.0)(0.0001)]} = 804{,}000$$

Using the CGS System (g-cm-s),

$$N_{Re} = \frac{D\upsilon\rho}{\mu} = \frac{[(4.00)(30.48)][(4.5)(30.48)][(60)(0.01602)]}{[(0.02)]} = 804{,}000$$

Using the AE System (lb_m-ft-h) and converting the viscosity 0.02 cP to lb_m/ft-h,

$$N_{Re} = \frac{D\upsilon\rho}{\mu} = \frac{(4.00)[(4.5)(3600)](60)}{[(0.02)(241.9)]} = 804{,}000$$

Part One

Fundamental Concepts

Chapters 1–5 present concepts that describe methods for the separation of chemical mixtures by industrial processes, including bioprocesses. Five basic separation techniques are enumerated. The equipment used and the ways of making mass balances and specifying component recovery and product purity are also illustrated.

Separations are limited by thermodynamic equilibrium, while equipment design depends on the rate of mass transfer. Chapter 2 reviews thermodynamic principles and Chapter 3 discusses component mass transfer under stagnant, laminar-flow, and turbulent-flow conditions. Analogies to conductive and convective heat transfer are presented.

Single-stage contacts for equilibrium-limited multiphase separations are treated in Chapters 4 and 5, as are the enhancements afforded by cascades and multistage arrangements. Chapter 5 also shows how degrees-of-freedom analysis is used to set design parameters for equipment. This type of analysis is used in process simulators such as ASPEN PLUS, CHEMCAD, HYSYS, and SuperPro Designer.

Chapter 1

Separation Processes

§1.0 INSTRUCTIONAL OBJECTIVES

After completing this chapter, you should be able to:

- Explain the role of separation operations in the chemical and biochemical industries.
- Explain what constitutes the separation of a mixture and how each of the five basic separation techniques works.
- Calculate component material balances around a separation operation based on specifications of component recovery (split ratios or split fractions) and/or product purity.
- Use the concept of key components and separation factor to measure separation between two key components.
- Understand the concept of sequencing of separation operations, particularly distillation.
- Explain the major differences between chemical and biochemical separation processes.
- Make a selection of separation operations based on factors involving feed and product property differences and characteristics of separation operations.

Separation processes developed by early civilizations include (1) extraction of metals from ores, perfumes from flowers, dyes from plants, and potash from the ashes of burnt plants; (2) evaporation of sea water to obtain salt; (3) refining of rock asphalt; and (4) distilling of liquors. In addition, the human body could not function if it had no kidney—an organ containing membranes that separates water and waste products of metabolism from blood.

Chemists use chromatography, an *analytical separation method*, to determine compositions of complex mixtures, and *preparative separation techniques* to recover chemicals. Chemical engineers design industrial facilities that employ separation methods that may differ considerably from those of laboratory techniques. In the laboratory, chemists separate light-hydrocarbon mixtures by chromatography, while a manufacturing plant will use distillation to separate the same mixture.

This book develops methods for the design of large-scale separation operations, which chemical engineers apply to produce chemical and biochemical products economically. Included are distillation, absorption, liquid–liquid extraction, leaching, drying, and crystallization, as well as newer methods such as adsorption, chromatography, and membrane separation.

Engineers also design small-scale industrial separation systems for manufacture of specialty chemicals by batch processing, recovery of biological solutes, crystal growth of semiconductors, recovery of chemicals from wastes, and development of products such as lung oxygenators and the artificial kidney. The design principles for these smaller-scale operations are also covered in this book. Both large- and small-scale industrial operations are illustrated in examples and homework exercises.

§1.1 INDUSTRIAL CHEMICAL PROCESSES

The chemical and biochemical industries manufacture products that differ in composition from feeds, which are (1) naturally occurring living or nonliving materials, (2) chemical intermediates, (3) chemicals of commerce, or (4) waste products. Especially common are oil refineries (Figure 1.1), which produce a variety of products [1]. The products from, say, 150,000 bbl/day of crude oil depend on the source of the crude and the refinery processes, which include distillation to separate crude into boiling-point fractions or cuts, alkylation to combine small molecules into larger molecules, catalytic reforming to change the structure of hydrocarbon molecules, catalytic cracking to break apart large molecules, hydrocracking to break apart even larger molecules, and processes to convert crude-oil residue to coke and lighter fractions.

A chemical or biochemical plant is operated in a *batchwise*, *continuous*, or *semicontinuous* manner. The operations may be *key operations* unique to chemical engineering because they involve changes in chemical composition, or *auxiliary operations*, which are necessary to the success of the key operations but may be designed by mechanical engineers because the operations do not involve changes in chemical composition. The key operations are (1) chemical reactions and (2) separation of chemical mixtures. The auxiliary operations include phase separation, heat addition or removal (heat exchangers), shaft work (pumps or compressors), mixing or dividing of streams, solids agglomeration, size reduction of

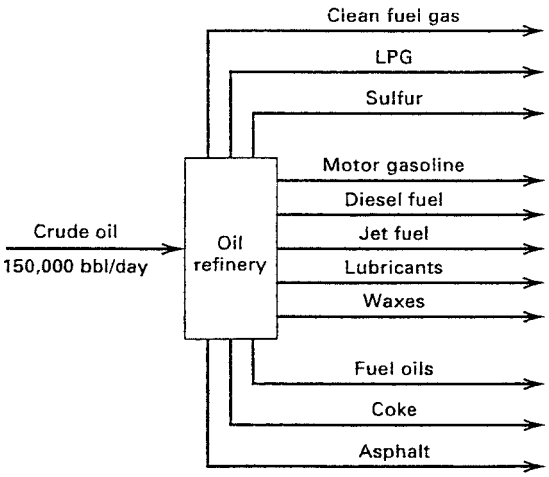


Figure 1.1 Refinery for converting crude oil into a variety of marketable products.

solids, and separation of solids by size. Most of the equipment in biochemical or chemical plants is there to purify raw material, intermediates, and products by the separation techniques discussed in this book.

Block-flow diagrams are used to represent processes. They indicate, by square or rectangular blocks, chemical reaction and separation steps and, by connecting lines, the process streams. More detail is shown in *process-flow diagrams*, which also include auxiliary operations and utilize symbols that depict the type of equipment employed. A block-flow diagram for manufacturing hydrogen chloride gas from chlorine and hydrogen [2] is shown in Figure 1.2. Central to the process is a reactor, where the gas-phase combustion reaction, $H_2 + Cl_2 \rightarrow 2HCl$, occurs. The auxiliary equipment required consists of pumps, compressors, and a heat exchanger to cool the product. No separation operations are necessary because of the complete conversion of chlorine. A slight excess of hydrogen is used, and the product, 99% HCl and small amounts of H_2, N_2, H_2O, CO, and CO_2, requires no purification. Such simple processes that do not require separation operations are very rare, and most chemical and biochemical processes are dominated by separations equipment.

Many industrial chemical processes involve at least one chemical reactor, accompanied by one or more separation trains [3]. An example is the continuous hydration of

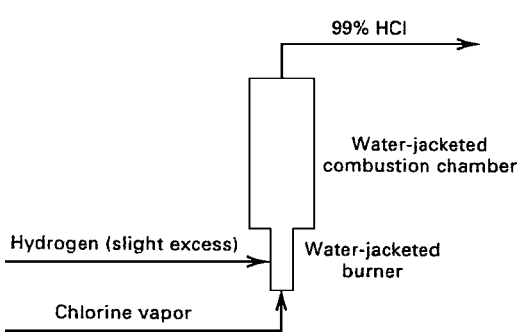


Figure 1.2 Process for anhydrous HCl production.

ethylene to ethyl alcohol [4]. Central to the process is a reactor packed with catalyst particles, operating at 572 K and 6.72 MPa, in which the reaction, $C_2H_4 + H_2O \rightarrow C_2H_5OH$, occurs. Due to equilibrium limitations, conversion of ethylene is only 5% per pass through the reactor. However, by recovering unreacted ethylene and recycling it to the reactor, near-complete conversion of ethylene feed is achieved.

Recycling is a common element of chemical and biochemical processes. If pure ethylene were available as a feedstock and no side reactions occurred, the simple process in Figure 1.3 could be realized. This process uses a reactor, a partial condenser for ethylene recovery, and distillation to produce aqueous ethyl alcohol of near-azeotropic composition (93 wt%). Unfortunately, impurities in the ethylene feed—and side reactions involving ethylene and feed impurities such as propylene to produce diethyl ether, isopropyl alcohol, acetaldehyde, and other chemicals—combine to increase the complexity of the process, as shown in Figure 1.4. After the hydration reaction, a partial condenser and high-pressure water absorber recover ethylene for recycling. The pressure of the liquid from the bottom of the absorber is reduced, causing partial vaporization. Vapor is then separated from the remaining liquid in the low-pressure flash drum, whose vapor is scrubbed with water to remove alcohol from the vent gas. Crude ethanol containing diethyl ether and acetaldehyde is distilled in the crude-distillation column and catalytically hydrogenated to convert the acetaldehyde to ethanol. Diethyl ether is removed in the light-ends tower and scrubbed with water. The final product is prepared by distillation in the final purification tower, where 93 wt% aqueous ethanol product is withdrawn several trays below the top tray, light ends are concentrated in the so-called pasteurization-tray section above the product-withdrawal tray and recycled to the catalytic-hydrogenation reactor, and wastewater is removed with the bottoms. Besides the equipment shown, additional equipment may be necessary to concentrate the ethylene feed and remove impurities that poison the catalyst. In the development of a new process, experience shows that more separation steps than originally anticipated are usually needed. Ethanol is also produced in biochemical fermentation processes that start with plant matter such as barley, corn, sugar cane, wheat, and wood.

Sometimes a separation operation, such as absorption of SO_2 by limestone slurry, is accompanied by a chemical reaction that facilitates the separation. Reactive distillation is discussed in Chapter 11.

More than 95% of industrial chemical separation operations involve feed mixtures of organic chemicals from coal, natural gas, and petroleum, or effluents from chemical reactors processing these raw materials. However, concern has been expressed in recent years because these fossil feedstocks are not renewable, do not allow sustainable development, and result in emission of atmospheric pollutants such as particulate matter and volatile organic compounds (VOCs). Many of the same organic chemicals can be extracted from renewable biomass, which is synthesized biochemically by cells in agricultural or fermentation reactions and recovered by bioseparations. Biomass components include carbohydrates, oils,

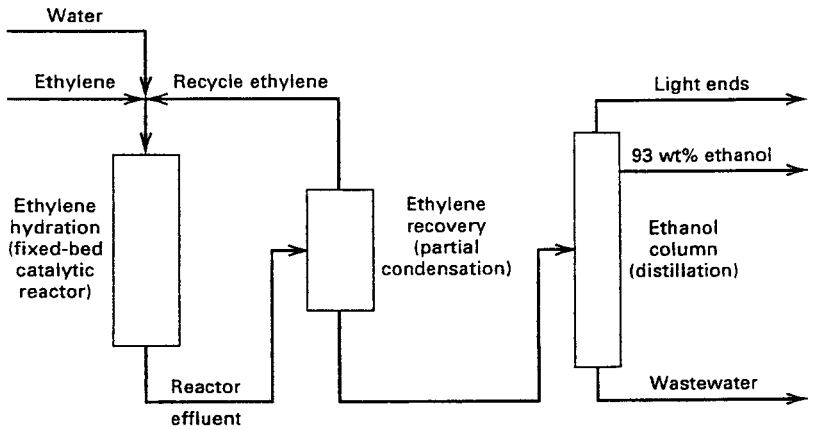


Figure 1.3 Hypothetical process for hydration of ethylene to ethanol.

and proteins, with carbohydrates considered to be the predominant raw materials for future biorefineries, which may replace coal and petroleum refineries if economics prove favorable [18, 19, 20].

Biochemical processes differ significantly from chemical processes. Reactors for the latter normally operate at elevated temperatures and pressures using metallic or chemical catalysts, while reactors for the former typically operate in aqueous solutions at or near the normal, healthy, nonpathologic (i.e., physiologic) state of an organism or bioproduct. Typical physiologic values for the human organism are 37°C, 1 atm, pH of 7.4 (that of arterial blood plasma), general salt content of 137 mM/L of NaCl, 10 mM/L of phosphate, and 2.7 mM/L of KCl. Physiologic conditions vary with the organism, biological component, and/or environment of interest. Bioreactors make use of catalytic enzymes (products of *in vivo* polypeptide synthesis), and require residence times of hours and days to produce particle-laden aqueous broths that are dilute in bioproducts that usually require an average of six separation steps, using less-mature technology, to produce the final products.

Bioproducts from fermentation reactors may be inside the microorganism (*intracellular*), or in the fermentation broth (*extracellular*). Of major importance is the extracellular case, which can be used to illustrate the difference between chemical separation processes of the type shown in Figures 1.3 and 1.4, which use the more-mature technology of earlier chapters in Part 2 of this book, and bioseparations, which often use the less-mature technology presented in Parts 3, 4, and 5.

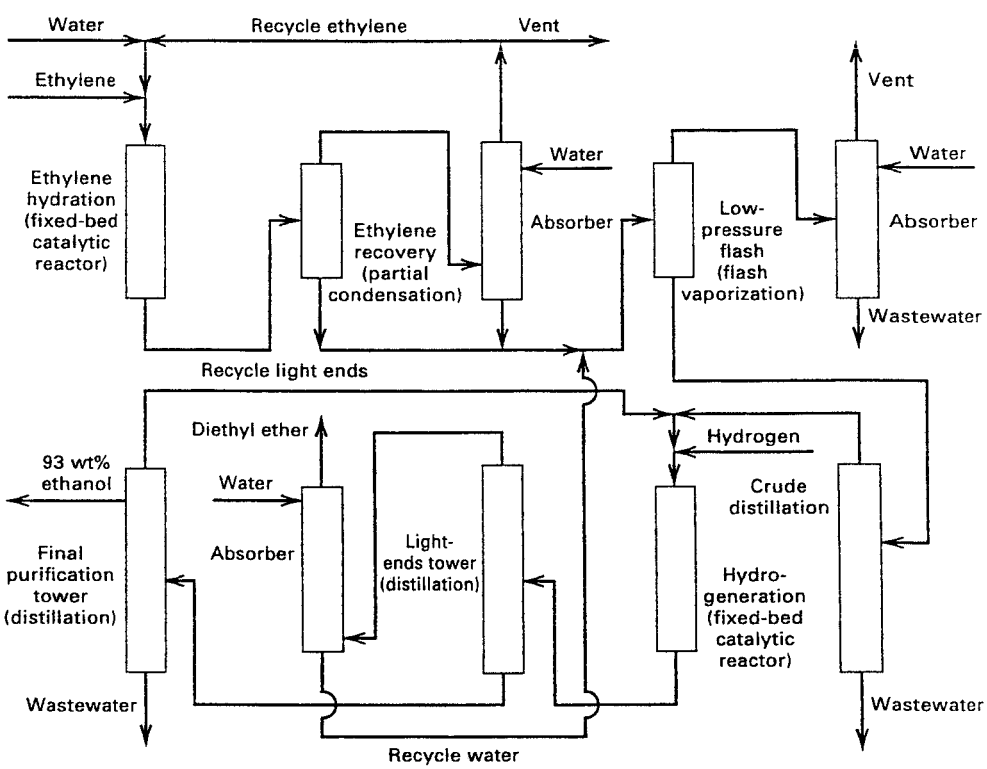


Figure 1.4 Industrial processes for hydration of ethylene to ethanol.

Consider the manufacture of citric acid. Although it can be extracted from lemons and limes, it can also be produced in much larger quantities by submerged, batch *aerobic fermentation* of starch. As in most bioprocesses, a sequence of reactions is required to go from raw material to bioproduct, each reaction catalyzed by an *enzyme* produced in a living cell from its DNA and RNA. In the case of citric acid, the cell is a strain of *Aspergillus niger*, a *eukaryotic fungus*. The first step in the reaction is the hydrolysis of starch at 28°C and 1 atm in an aqueous media to a *substrate* of dextrin using the enzyme α-amylase, in the absence of the fungus. A small quantity of viable fungus cells, called an *inoculum*, is then added to the reactor. As the cells grow and divide, dextrin diffuses from the aqueous media surrounding the cells and crosses the fungus cell wall into the cell cytoplasm. Here a series of interrelated biochemical reactions that comprise a *metabolic pathway* transforms the dextrin into citric acid. Each reaction is catalyzed by a particular enzyme produced within the cell. The first step converts dextrin to glucose using the enzyme, glucoamylase. A series of other enzyme-catalyzed reactions follow, with the final product being citric acid, which, in a process called secretion, moves from the cytoplasm, across the cell wall, and into the aqueous broth media to become an extracellular bioproduct. The total residence time in the fermentation reactor is 6–7 days. The reactor effluent is processed in a series of continuous steps that include vacuum filtration, ultrafiltration, ion exchange, adsorption, crystallization, and drying.

Chemical engineers also design products. One product that involves the separation of chemicals is the espresso coffee machine, which leaches oil from the coffee bean, leaving behind the ingredients responsible for acidity and bitterness. The machine accomplishes this by conducting the leaching operation rapidly in 20–30 seconds with water at high temperature and pressure. The resulting cup of espresso has (1) a topping of creamy foam that traps the extracted chemicals, (2) a fullness of body due to emulsification, and (3) a richness of aroma. Typically, 25% of the coffee bean is extracted, and the espresso contains less caffeine than filtered coffee. Cussler and Moggridge [17] and Seider, Seader, Lewin, and Widagdo [7] discuss other examples of products designed by chemical engineers.

§1.2 BASIC SEPARATION TECHNIQUES

The creation of a mixture of chemical species from the separate species is a spontaneous process that requires no energy input. The inverse process, separation of a chemical mixture into pure components, is not a spontaneous process and thus requires energy. A mixture to be separated may be single or multiphase. If it is multiphase, it is usually advantageous to first separate the phases.

A general separation schematic is shown in Figure 1.5 as a box wherein species and phase separation occur, with arrows to designate feed and product movement. The feed and products may be vapor, liquid, or solid; one or more separation operations may be taking place; and the products differ in composition and may differ in phase. In each separation

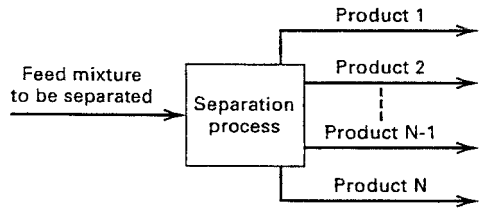


Figure 1.5 General separation process.

operation, the mixture components are induced to move into different, separable spatial locations or phases by any one or more of the five basic separation methods shown in Figure 1.6. However, in most instances, the separation is not perfect, and if the feed contains more than two species, two or more separation operations may be required.

The most common separation technique, shown in Figure 1.6a, *creates* a second phase, immiscible with the feed phase, by energy (heat and/or shaft-work) transfer or by pressure reduction. Common operations of this type are distillation, which involves the transfer of species between vapor and liquid phases, exploiting differences in volatility (e.g., vapor pressure or boiling point) among the species; and crystallization, which exploits differences in melting point. A second technique, shown in Figure 1.6b, *adds* another fluid phase, which selectively absorbs, extracts, or strips certain species from the feed. The most common operations of this type are liquid–liquid extraction, where the feed is liquid and a second, immiscible liquid phase is added; and absorption, where the feed is vapor, and a liquid of low volatility is added. In both cases, species solubilities are significantly different in the added phase. Less common, but of growing importance, is the use of a barrier (shown in Figure 1.6c), usually a polymer membrane, which involves a gas or liquid feed and exploits differences in species permeabilities through the barrier. Also of growing importance are techniques that involve contacting a vapor or liquid feed with a solid agent, as shown in Figure 1.6d. Most commonly, the agent consists of particles that are porous to achieve a high surface area, and differences in species adsorbability are exploited. Finally, external fields (centrifugal, thermal, electrical, flow, etc.), shown in Figure 1.6e, are applied in specialized cases to liquid or gas feeds, with electrophoresis being especially useful for separating proteins by exploiting differences in electric charge and diffusivity.

For the techniques of Figure 1.6, the size of the equipment is determined by rates of mass transfer of each species from one phase or location to another, relative to mass transfer of all species. The driving force and direction of mass transfer is governed by the departure from thermodynamic equilibrium, which involves volatilities, solubilities, etc. Applications of thermodynamics and mass-transfer theory to industrial separations are treated in Chapters 2 and 3. Fluid mechanics and heat transfer play important roles in separation operations, and applicable principles are included in appropriate chapters of this book.

The extent of separation possible depends on the exploitation of differences in molecular, thermodynamic, and transport properties of the species. Properties of importance are:

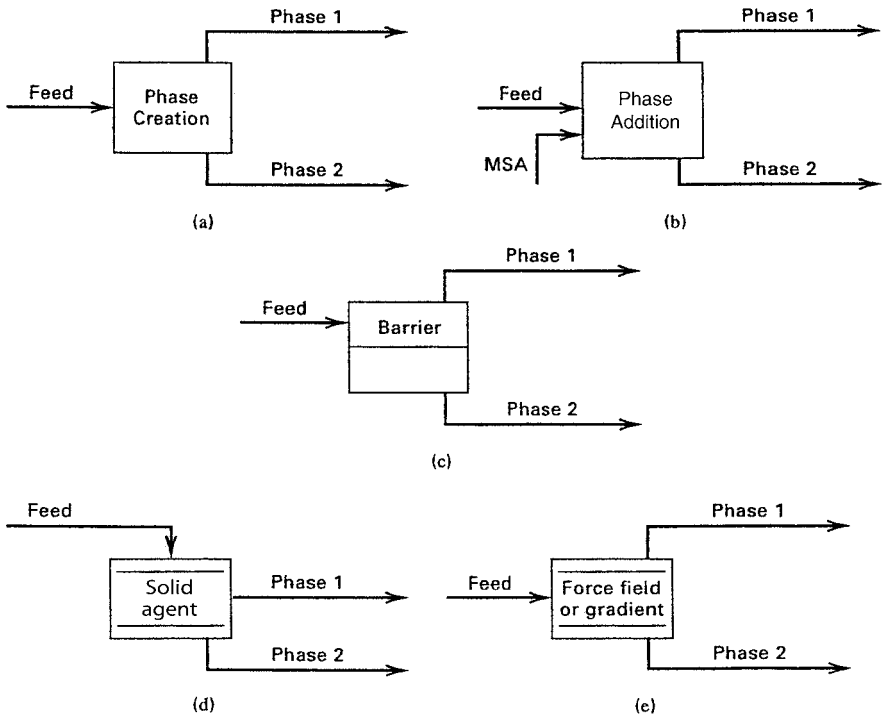


Figure 1.6 Basic separation techniques: (a) separation by phase creation; (b) separation by phase addition; (c) separation by barrier; (d) separation by solid agent; (e) separation by force field or gradient.

1. Molecular properties

Molecular weight	Polarizability
van der Waals volume	Dielectric constant
van der Waals area	Electric charge
Molecular shape (acentric factor)	Radius of gyration
Dipole moment	

2. Thermodynamic and transport properties

Vapor pressure	Adsorptivity
Solubility	Diffusivity

Values of these properties appear in handbooks, reference books, and journals. Many can be estimated using process simulation programs. When property values are not available, they must be estimated or determined experimentally if a successful application of the separation operation is to be achieved.

EXAMPLE 1.1 Feasibility of a separation method.

For each of the following binary mixtures, a separation operation is suggested. Explain why the operation will or will not be successful.

(a) Separation of air into oxygen-rich and nitrogen-rich products by distillation.

(b) Separation of *m*-xylene from *p*-xylene by distillation.

(c) Separation of benzene and cyclohexane by distillation.

(d) Separation of isopropyl alcohol and water by distillation.

(e) Separation of penicillin from water in a fermentation broth by evaporation of the water.

Solution

(a) The normal boiling points of O_2 (−183°C) and N_2 (−195.8°C) are sufficiently different that they can be separated by distillation, but elevated pressure and cryogenic temperatures are required. At moderate to low production rates, they are usually separated at lower cost by either adsorption or gas permeation through a membrane.

(b) The close normal boiling points of *m*-xylene (139.3°C) and *p*-xylene (138.5°C) make separation by distillation impractical. However, their widely different melting points of −47.4°C for *m*-xylene and 13.2°C for *p*-xylene make crystallization the separation method of choice.

(c) The normal boiling points of benzene (80.1°C) and cyclohexane (80.7°C) preclude a practical separation by distillation. Their melting points are also close, at 5.5°C for benzene and 6.5°C for cyclohexane, making crystallization also impractical. The method of choice is to use distillation in the presence of phenol (normal boiling point of 181.4°C), which reduces the volatility of benzene, allowing nearly pure cyclohexane to be obtained. The other product, a mixture of benzene and phenol, is readily separated in a subsequent distillation operation.

(d) The normal boiling points of isopropyl alcohol (82.3°C) and water (100.0°C) seem to indicate that they could be separated by distillation. However, they cannot be separated in this manner because they form a minimum-boiling azeotrope at 80.4°C and 1 atm of 31.7 mol% water and 68.3 mol% isopropanol. A feasible separation method is to distill the mixture in the presence of benzene, using a two-operation process. The first step produces almost pure isopropyl alcohol and a heterogeneous azeotrope of the three components. The azeotrope is separated into two phases, with the benzene-rich phase recycled to the first step and the water-rich phase sent to a second step, where

almost pure water is produced by distillation, with the other product recycled to the first step.

(e) Penicillin has a melting point of 97°C, but decomposes before reaching the normal boiling point. Thus, it would seem that it could be isolated from water by evaporation of the water. However, penicillin and most other antibiotics are heat-sensitive, so a near-ambient temperature must be maintained. Thus, water evaporation would have to take place at impractical, high-vacuum conditions. A practical separation method is liquid–liquid extraction of the penicillin with *n*-butyl acetate or *n*-amyl acetate.

§1.3 SEPARATIONS BY PHASE ADDITION OR CREATION

If the feed is a single-phase solution, a second separable phase must be developed before separation of the species can be achieved. The second phase is created by an *energy-separating agent* (ESA) and/or added as a *mass-separating agent* (MSA). An ESA involves heat transfer or transfer of shaft work to or from the mixture. An example of shaft work is the creation of vapor from a liquid phase by reducing the pressure. An MSA may be partially immiscible with one or more mixture components and frequently is the constituent of highest concentration in the added phase. Alternatively, the MSA may be miscible with a liquid feed mixture, but may selectively alter partitioning of species between liquid and vapor phases. This facilitates a separation when used in conjunction with an ESA, as in extractive distillation.

Disadvantages of using an MSA are (1) need for an additional separator to recover the MSA for recycle, (2) need for MSA makeup, (3) possible MSA product contamination, and (4) more difficult design procedures.

When immiscible fluid phases are contacted, intimate mixing is used to enhance mass-transfer rates so that the maximum degree-of-partitioning of species can be approached rapidly. After phase contact, the phases are separated by employing gravity and/or an enhanced technique such as centrifugal force. Table 1.1 includes the more common separation operations based on interphase mass transfer between two phases, one of which is created by an ESA or added as an MSA. Design procedures have become routine for the operations prefixed by an asterisk (∗) in the first column. Such procedures are incorporated as mathematical models into process simulators.

When the feed mixture includes species that differ widely in volatility, expressed as vapor–liquid equilibrium ratios (*K*-values)—*partial condensation* or *partial vaporization*—Operation (1) in Table 1.1 may be adequate to achieve the desired separation. Two phases are created when a vapor feed is partially condensed by removing heat, and a liquid feed is partially vaporized by adding heat. Alternatively, partial vaporization can be initiated by *flash vaporization*, Operation (2), by reducing the feed pressure with a valve or turbine. In both operations, after partitioning of species has occurred by interphase mass transfer, the resulting vapor phase is enriched with respect to the species that are more easily vaporized, while the liquid phase is enriched with respect to the less-volatile species. The two phases are then separated by gravity.

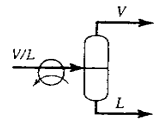
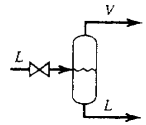
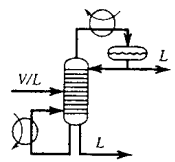
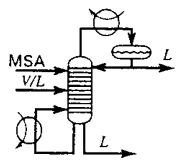
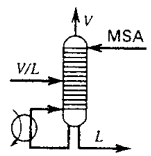
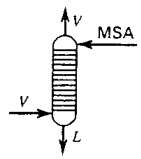
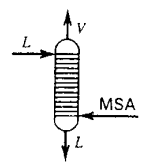
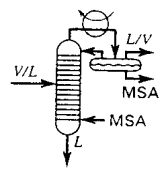
Often, the degree of separation achieved by a single contact of two phases is inadequate because the volatility differences among species are not sufficiently large. In that case, distillation, Operation (3) in Table 1.1 and the most widely utilized industrial separation method, should be considered. Distillation involves multiple contacts between countercurrently flowing liquid and vapor phases. Each contact, called a *stage*, consists of mixing the phases to promote rapid partitioning of species by mass transfer, followed by phase separation. The contacts are often made on horizontal trays arranged in a column, as shown in the symbol for distillation in Table 1.1. Vapor, flowing up the column, is increasingly enriched with respect to the more-volatile species, and liquid flowing down the column is increasingly enriched with respect to the less-volatile species. Feed to the column enters on a tray somewhere between the top and bottom trays. The portion of the column above the feed entry is the *enriching* or *rectification section*, and that portion below is the *stripping section.* Vapor feed starts up the column; feed liquid starts down. Liquid is required for making contacts with vapor above the feed tray, and vapor is required for making contacts with liquid below the feed tray. Commonly, at the top of the column, vapor is condensed to provide down-flowing liquid called *reflux*. Similarly, liquid at the bottom of the column passes through a reboiler, where it is heated to provide up-flowing vapor called *boilup*.

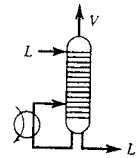
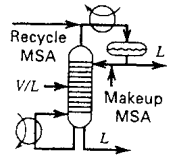
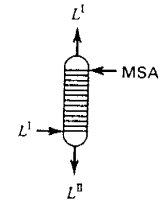
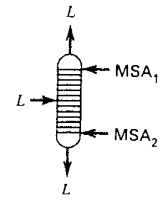
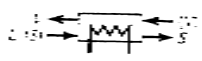
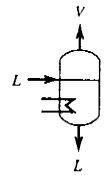
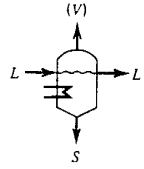
When the volatility difference between two species to be separated is so small as to necessitate more than about 100 trays, *extractive distillation*, Operation (4), is considered. Here, a miscible MSA, acting as a solvent, increases the volatility difference among species in the feed, thereby reducing the number of trays. Generally, the MSA is the least volatile species and is introduced near the top of the column. Reflux to the top tray minimizes MSA content in the top product. A subsequent operation, usually distillation, is used to recover the MSA for recycling.

If it is difficult to condense the vapor leaving the top of a distillation column, a liquid MSA called an *absorbent* may be fed to the top tray in place of reflux. The resulting operation is called *reboiled absorption*, (5). If the feed is vapor and the stripping section of the column is not needed, the operation is referred to as *absorption*, (6). Absorbers generally do not require an ESA and are frequently conducted at ambient temperature and elevated pressure. Species in the feed vapor dissolve in the absorbent to extents depending on their solubilities.

The inverse of absorption is *stripping*, Operation (7) in Table 1.1, where liquid mixtures are separated, at elevated temperature and ambient pressure, by contacting the feed with a vapor stripping agent. This MSA eliminates the need to reboil the liquid at the bottom of the column, which may be important if the liquid is not thermally stable. If trays are needed above the feed tray to achieve the separation, a *refluxed stripper*, (8), may be employed. If the bottoms

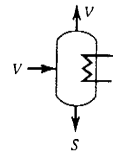
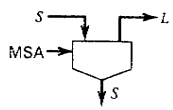
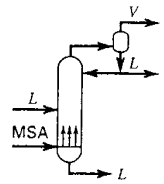
Table 1.1 Separation Operations Based on Phase Creation or Addition

Separation Operation	Symbol[a]	Initial or Feed Phase	Created or Added Phase	Separating Agent(s)	Industrial Example[b]
Partial condensation or vaporization* (1)		Vapor and/or liquid	Liquid or vapor	Heat transfer (ESA)	Recovery of H_2 and N_2 from ammonia by partial condensation and high-pressure phase separation
Flash vaporization* (2)		Liquid	Vapor	Pressure reduction	Recovery of water from sea water
Distillation* (3)		Vapor and/or liquid	Vapor and liquid	Heat transfer (ESA) and sometimes work transfer	Purification of styrene
Extractive distillation* (4)		Vapor and/or liquid	Vapor and liquid	Liquid solvent (MSA) and heat transfer (ESA)	Separation of acetone and methanol
Reboiled absorption* (5)		Vapor and/or liquid	Vapor and liquid	Liquid absorbent (MSA) and heat transfer (ESA)	Removal of ethane and lower molecular weight hydrocarbons for LPG production
Absorption* (6)		Vapor	Liquid	Liquid absorbent (MSA)	Separation of carbon dioxide from combustion products by absorption with aqueous solutions of an ethanolamine
Stripping* (7)		Liquid	Vapor	Stripping vapor (MSA)	Stream stripping of naphtha, kerosene, and gas oil side cuts from crude distillation unit to remove light ends
Refluxed stripping (steam distillation)* (8)		Vapor and/or liquid	Vapor and liquid	Stripping vapor (MSA) and heat transfer (ESA)	Separation of products from delayed coking

Reboiled stripping* (9)		Liquid	Vapor	Heat transfer (ESA)	Recovery of amine absorbent
Azeotropic distillation* (10)		Vapor and/or liquid	Vapor and liquid	Liquid entrainer (MSA) and heat transfer (ESA)	Separation of acetic acid from water using *n*-butyl acetate as an entrainer to form an azeotrope with water
Liquid–liquid extraction* (11)		Liquid	Liquid	Liquid solvent (MSA)	Recovery of penicillin from aqueous fermentation medium by methyl isobutyl ketone. Recovery of aromatics
Liquid–liquid extraction (two-solvent)* (12)		Liquid	Liquid	Two liquid solvents (MSA_1 and MSA_2)	Use of propane and cresylic acid as solvents to separate paraffins from aromatics and naphthenes
Drying (13)		Liquid and often solid	Vapor	Gas (MSA) and/or heat transfer (ESA)	Removal of water from polyvinylchloride with hot air in a fluid-bed dryer
Evaporation (14)		Liquid	Vapor	Heat transfer (ESA)	Evaporation of water from a solution of urea and water
Crystallization (15)		Liquid	Solid (and vapor)	Heat transfer (ESA)	Recovery of a protease inhibitor from an organic solvent. Crystallization of *p*-xylene from a mixture with *m*-xylene

(*Continued*)

Table 1.1 (*Continued*)

Separation Operation	Symbol[a]	Initial or Feed Phase	Created or Added Phase	Separating Agent(s)	Industrial Example[b]
Desublimation (16)		Vapor	Solid	Heat transfer (ESA)	Recovery of phthalic anhydride from non-condensible gas
Leaching (liquid–solid extraction) (17)		Solid	Liquid	Liquid solvent	Extraction of sucrose from sugar beets with hot water
Foam fractionation (18)		Liquid	Gas	Gas bubbles (MSA)	Recovery of detergents from waste solutions

*Design procedures are fairly well accepted.

[a]Trays are shown for columns, but alternatively packing can be used. Multiple feeds and side streams are often used and may be added to the symbol.

[b]Details of examples may be found in *Kirk-Othmer Encyclopedia of Chemical Technology*, 5th ed., John Wiley & Sons, New York (2004–2007).

product from a stripper is thermally stable, it may be reboiled without using an MSA. In that case, the column is a *reboiled stripper*, (9). Additional separation operations may be required to recover MSAs for recycling.

Formation of minimum-boiling azeotropes makes *azeotropic distillation* (10) possible. In the example cited in Table 1.1, the MSA, *n*-butyl acetate, which forms a two-liquid (heterogeneous), minimum-boiling azeotrope with water, is used as an *entrainer* in the separation of acetic acid from water. The azeotrope is taken overhead, condensed, and separated into acetate and water layers. The MSA is recirculated, and the distillate water layer and bottoms acetic acid are the products.

Liquid–liquid extraction, (11) and (12), with one or two solvents, can be used when distillation is impractical, especially when the mixture to be separated is temperature-sensitive. A solvent selectively dissolves only one or a fraction of the components in the feed. In a two-solvent extraction, each has its specific selectivity for the feed components. Several countercurrently arranged stages may be necessary. As with extractive distillation, additional operations are required to recover solvent from the streams leaving the extraction operation. Extraction is widely used for recovery of bioproducts from fermentation broths. If the extraction temperature and pressure are only slightly above the critical point of the solvent, the operation is termed *supercritical-fluid extraction.* In this region, solute solubility in the supercritical fluid can change drastically with small changes in temperature and pressure. Following extraction, the pressure of the solvent-rich product is reduced to release the solvent, which is recycled. For the processing of foodstuffs, the supercritical fluid is an inert substance, with CO_2 preferred because it does not contaminate the product.

Since many chemicals are processed wet but sold as dry solids, a common manufacturing step is *drying*, Operation (13). Although the only requirement is that the vapor pressure of the liquid to be evaporated from the solid be higher than its partial pressure in the gas stream, dryer design and operation represents a complex problem. In addition to the effects of such external conditions as temperature, humidity, air flow, and degree of solid subdivision on drying rate, the effects of internal diffusion conditions, capillary flow, equilibrium moisture content, and heat sensitivity must be considered. Because solid, liquid, and vapor phases coexist in drying, equipment-design procedures are difficult to devise and equipment size may be controlled by heat transfer. A typical dryer design procedure is for the process engineer to send a representative feed sample to one or two reliable dryer manufacturers for pilot-plant tests and to purchase equipment that produces a dried product at the lowest cost. Commercial dryers are discussed in [5] and Chapter 18.

Evaporation, Operation (14), is defined as the transfer of volatile components of a liquid into a gas by heat transfer. Applications include humidification, air conditioning, and concentration of aqueous solutions.

Crystallization, (15), is carried out in some organic, and in almost all inorganic, chemical plants where the desired product is a finely divided solid. Crystallization is a purification step, so the conditions must be such that impurities do not precipitate with the product. In *solution crystallization*, the mixture, which includes a solvent, is cooled and/or the solvent is evaporated. In *melt crystallization*, two or more soluble species are separated by partial freezing. A versatile melt-crystallization technique is *zone melting* or *refining*, which relies on selective distribution of impurities between a liquid and a solid phase. It involves moving a molten zone slowly through an ingot by moving the heater or drawing the ingot past the heater. Single crystals of very high-purity silicon are produced by this method.

Sublimation is the transfer of a species from the solid to the gaseous state without formation of an intermediate liquid phase. Examples are separation of sulfur from impurities, purification of benzoic acid, and freeze-drying of foods. The reverse process, *desublimation*, (16), is practiced in the recovery of phthalic anhydride from gaseous reactor effluent. A common application of sublimation is the use of dry ice as a refrigerant for storing ice cream, vegetables, and other perishables. The sublimed gas, unlike water, does not puddle.

Liquid–solid extraction, *leaching*, (17), is used in the metallurgical, natural product, and food industries. To promote rapid solute diffusion out of the solid and into the liquid solvent, particle size of the solid is usually reduced.

The major difference between solid–liquid and liquid–liquid systems is the difficulty of transporting the solid (often as slurry or a wet cake) from stage to stage. In the pharmaceutical, food, and natural product industries, countercurrent solid transport is provided by complicated mechanical devices.

In adsorptive-bubble separation methods, surface-active material collects at solution interfaces. If the (very thin) surface layer is collected, partial solute removal from the solution is achieved. In ore flotation processes, solid particles migrate through a liquid and attach to rising gas bubbles, thus floating out of solution. In *foam fractionation*, (18), a natural or chelate-induced surface activity causes a solute to migrate to rising bubbles and is thus removed as foam.

The equipment symbols shown in Table 1.1 correspond to the simplest configuration for each operation. More complex versions are frequently desirable. For example, a more complex version of the reboiled absorber, Operation (5) in Table 1.1, is shown in Figure 1.7. It has two feeds, an intercooler, a side stream, and both an interreboiler and a bottoms reboiler. Design procedures must handle such complex equipment. Also, it is possible to conduct chemical reactions simultaneously with separation operations. Siirola [6] describes the evolution of a commercial process for producing methyl acetate by esterification. The process is conducted in a single column in an integrated process that involves three reaction zones and three separation zones.

§1.4 SEPARATIONS BY BARRIERS

Use of microporous and nonporous membranes as semipermeable barriers for selective separations is gaining adherents. Membranes are fabricated mainly from natural fibers and synthetic polymers, but also from ceramics and metals. Membranes are fabricated into flat sheets, tubes, hollow fibers, or spiral-wound sheets, and incorporated into commercial

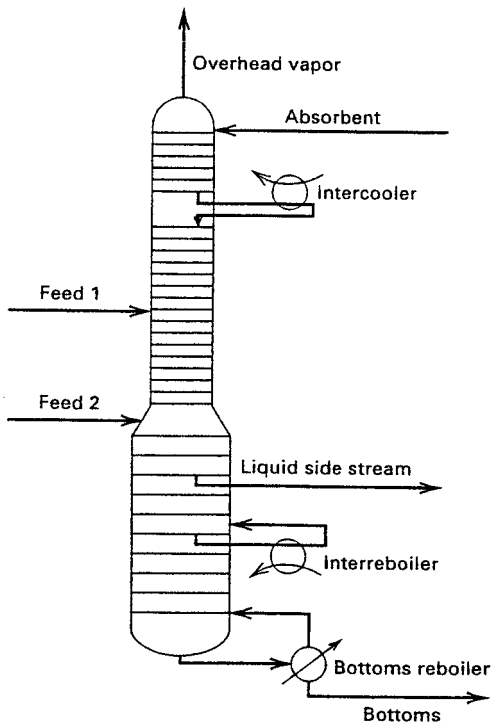


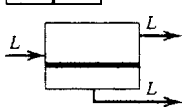
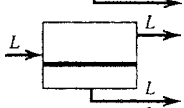
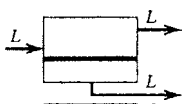
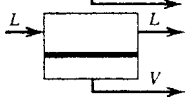
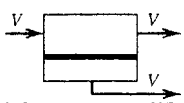
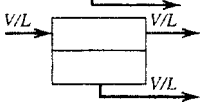
Figure 1.7 Complex reboiled absorber.

modules or cartridges. For microporous membranes, separation is effected by rate of species diffusion through the pores; for nonporous membranes, separation is controlled by differences in solubility in the membrane and rate of species diffusion. The most complex and selective membranes are found in the trillions of cells in the human body.

Table 1.2 lists membrane-separation operations. *Osmosis*, Operation (1), involves transfer, by a concentration gradient, of a solvent through a membrane into a mixture of solute and solvent. The membrane is almost impermeable to the solute. In *reverse osmosis*, (2), transport of solvent in the opposite direction is effected by imposing a pressure, higher than the osmotic pressure, on the feed side. Using a nonporous membrane, reverse osmosis desalts brackish water commercially. *Dialysis*, (3), is the transport by a concentration gradient of small solute molecules, sometimes called crystalloids, through a porous membrane. The molecules unable to pass through the membrane are small, insoluble, nondiffusible particles.

Microporous membranes selectively allow small solute molecules and/or solvents to pass through the membrane, while preventing large dissolved molecules and suspended solids from passing through. *Microfiltration*, (4), refers to the retention of molecules from 0.02 to 10 μm. *Ultrafiltration*, (5), refers to the retention of molecules that range from 1 to

Table 1.2 Separation Operations Based on a Barrier

Separation Operation	Symbol[a]	Initial or Feed Phase	Separating Agent	Industrial Example[b]
Osmosis (1)		Liquid	Nonporous membrane	—
Reverse osmosis* (2)		Liquid	Nonporous membrane with pressure gradient	Desalinization of sea water
Dialysis* (3)		Liquid	Porous membrane with pressure gradient	Recovery of caustic from hemicellulose
Microfiltration* (4)		Liquid	Microporous membrane with pressure gradient	Removal of bacteria from drinking water
Ultrafiltration* (5)		Liquid	Microporous membrane with pressure gradient	Separation of whey from cheese
Pervaporation* (6)		Liquid	Nonporous membrane with pressure gradient	Separation of azeotropic mixtures
Gas permeation* (7)		Vapor	Nonporous membrane with pressure gradient	Hydrogen enrichment
Liquid membrane (8)		Vapor and/or liquid	Liquid membrane with pressure gradient	Removal of hydrogen sulfide

*Design procedures are fairly well accepted.

[a]Single units are shown. Multiple units can be cascaded.

[b]Details of examples may be found in *Kirk-Othmer Encyclopedia of Chemical Technology*, 5th ed., John Wiley & Sons, New York (2004–2007).

20 nm. To retain molecules down to 0.1 nm, nonporous membranes can be used in *hyperfiltration.*

To achieve high purities, reverse osmosis requires high pressures. Alternatively, *pervaporation*, (6), wherein the species transported through the nonporous membrane is evaporated, can be used. This method, which is used to separate azeotropic mixtures, uses much lower pressures than reverse osmosis, but the heat of vaporization must be supplied.

Separation of gases by selective *gas permeation*, (7), using a pressure driving force is a process that was first used in the 1940s with porous fluorocarbon barriers to separate $^{235}UF_6$ and $^{238}UF_6$. It required enormous amounts of electric power. Today, centrifuges are used to achieve enrichment more economically. Nonporous polymer membranes are employed to enrich mixtures containing H_2, recover hydrocarbons from gas streams, and produce O_2-enriched air.

Liquid membranes, (8), only a few molecules thick, can be formed from surfactant-containing mixtures at the interface between two fluid phases. With liquid membranes, aromatic/paraffinic hydrocarbons can be separated. Alternatively, a liquid membrane can be formed by imbibing the micropores with liquids doped with additives to facilitate transport of solutes such as CO_2 and H_2S.

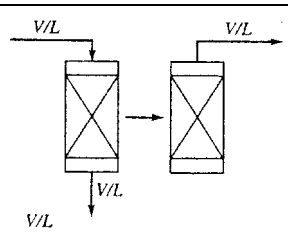
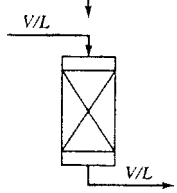
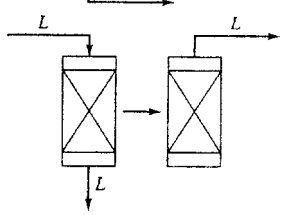
§1.5 SEPARATIONS BY SOLID AGENTS

Separations that use solid agents are listed in Table 1.3. The solid, in the form of a granular material or packing, is the adsorbent itself, or it acts as an inert support for a thin layer of adsorbent by selective adsorption or chemical reaction with species in the feed. Adsorption is confined to the surface of the solid adsorbent, unlike absorption, which occurs throughout the absorbent. The active separating agent eventually becomes saturated with solute and must be regenerated or replaced. Such separations are often conducted batchwise or semicontinuously. However, equipment is available to simulate continuous operation.

Adsorption, Operation (1) in Table 1.3, is used to remove species in low concentrations and is followed by desorption to regenerate the adsorbents, which include activated carbon, aluminum oxide, silica gel, and synthetic sodium or calcium aluminosilicate zeolites (molecular sieves). The sieves are crystalline and have pore openings of fixed dimensions, making them very selective. Equipment consists of a cylindrical vessel packed with a bed of solid adsorbent particles through which the gas or liquid flows. Because regeneration is conducted periodically, two or more vessels are used, one desorbing while the other(s) adsorb(s), as indicated in Table 1.3. If the vessel is vertical, gas flow is best employed downward. With upward flow, jiggling can cause particle attrition, pressure-drop increase, and loss of material. However, for liquid mixtures, upward flow achieves better flow distribution. Regeneration occurs by one of four methods: (1) vaporization of the adsorbate with a hot purge gas (*thermal-swing adsorption*), (2) reduction of pressure to vaporize the adsorbate (*pressure-swing adsorption*), (3) inert purge stripping without change in temperature or pressure, and (4) displacement desorption by a fluid containing a more strongly adsorbed species.

Chromatography, Operation (2) in Table 1.3, separates gas or liquid mixtures by passing them through a packed bed. The bed may be solid particles (gas–solid chromatography)

Table 1.3 Separation Operations Based on a Solid Agent

Separation Operation	Symbol[a]	Initial or Feed Phase	Separating Agent	Industrial Example[b]
Adsorption* (1)		Vapor or liquid	Solid adsorbent	Purification of *p*-xylene
Chromatography* (2)		Vapor or liquid	Solid adsorbent or liquid adsorbent on a solid support	Separation and purification of proteins from complex mixtures. Separation of xylene isomers and ethylbenzene
Ion exchange* (3)		Liquid	Resin with ion-active sites	Demineralization of water

*Design procedures are fairly well accepted.

[a]Single units are shown. Multiple units can be cascaded.

[b]Details of examples may be found in *Kirk-Othmer Encyclopedia of Chemical Technology*, 5th ed., John Wiley & Sons, New York (2004–2007).

or a solid–inert support coated with a viscous liquid (gas–liquid chromatography). Because of selective adsorption on the solid surface, or absorption into liquid absorbents followed by desorption, components move through the bed at different rates, thus effecting the separation. In *affinity chromatography*, a macromolecule (a *ligate*) is selectively adsorbed by a *ligand* (e.g., an ammonia molecule in a coordination compound) covalently bonded to a solid-support particle. Ligand–ligate pairs include inhibitors–enzymes, antigens–antibodies, and antibodies–proteins. Chromatography is widely used in bioseparations.

Ion exchange, (3), resembles adsorption in that solid particles are used and regenerated. However, a chemical reaction is involved. In water softening, an organic or inorganic polymer in its sodium form removes calcium ions by a calcium–sodium exchange. After prolonged use, the (spent) polymer, saturated with calcium, is regenerated by contact with a concentrated salt solution.

§1.6 SEPARATIONS BY EXTERNAL FIELD OR GRADIENT

External fields can take advantage of differing degrees of response of molecules and ions to force fields. Table 1.4 lists common techniques and combinations.

Centrifugation, Operation (1) in Table 1.4, establishes a pressure field that separates fluid mixtures according to molecular weight. It is used to separate $^{235}UF_6$ from $^{238}UF_6$, and large polymer molecules according to molecular weight.

If a temperature gradient is applied to a homogeneous solution, concentration gradients are established, and *thermal diffusion*, (2), is induced. This process has been used to enhance separation of isotopes in permeation processes.

Water contains 0.000149 atom fraction of deuterium. When it is decomposed by *electrolysis*, (3), into H_2 and O_2, the deuterium concentration in the hydrogen is lower than it was in the water. Until 1953, this process was the only source of heavy water (D_2O), used to moderate the speed of nuclear reactions. In *electrodialysis*, (4), cation- and anion-permeable membranes carry a fixed charge, thus preventing migration of species of like charge. This phenomenon is applied in seawater desalination. A related process is *electrophoresis*, (5), which exploits the different migration velocities of charged colloidal or suspended species in an electric field. Positively charged species, such as dyes, hydroxide sols, and colloids, migrate to the cathode, while most small, suspended, negatively charged particles go to the anode. By changing from an acidic to a basic condition, migration direction can be changed, particularly for proteins. Electrophoresis is thus a versatile method for separating biochemicals.

Another separation technique for biochemicals and heterogeneous mixtures of micromolecular and colloidal materials is *field-flow fractionation*, (6). An electrical or magnetic field or thermal gradient is established perpendicular to a laminar-flow field. Components of the mixture travel in the flow direction at different velocities, so a separation is achieved. A related device is a small-particle collector where the particles are charged and then collected on oppositely charged metal plates.

§1.7 COMPONENT RECOVERIES AND PRODUCT PURITIES

If no chemical reaction occurs and the process operates in a continuous, steady-state fashion, then for each component i, in a mixture of C components, the molar (or mass) flow rate in the feed, $n_i^{(F)}$, equals the sum of the product molar (or mass) flow rates, $n_i^{(p)}$, for that component in the N product phases, p. Thus, referring to Figure 1.5,

$$n_i^{(F)} = \sum_{p=1}^{N} n_i^{(p)} = n_i^{(1)} + n_i^{(2)} + \cdots + n_i^{(N-1)} + n_i^{(N)} \qquad (1\text{-}1)$$

To solve (1-1) for values of $n_i^{(p)}$ from specified values of $n_i^{(F)}$, an additional $N - 1$ independent expressions involving $n_i^{(p)}$ are required. This gives a total of NC equations in NC unknowns. If a single-phase feed containing C components is separated into N products, $C(N - 1)$ additional expressions are needed. If more than one stream is fed to the separation process, $n_i^{(F)}$is the summation for all feeds.

§1.7.1 Split Fractions and Split Ratios

Chemical plants are designed and operated to meet specifications given as *component recoveries* and *product purities*. In Figure 1.8, the feed is the bottoms product from a reboiled absorber used to deethanize—i.e., remove ethane and lighter components from—a mixture of petroleum refinery gases and liquids. The separation process of choice, shown in Figure 1.8, is a sequence of three multistage distillation columns, where feed components are rank-listed by decreasing volatility, and hydrocarbons heavier (i.e., of greater

Table 1.4 Separation Operations by Applied Field or Gradient

Separation Operation	Initial or Feed Phase	Force Field or Gradient	Industrial Example[a]
Centrifugation (1)	Vapor or liquid	Centrifugal force field	Separation of uranium isotopes
Thermal diffusion (2)	Vapor or liquid	Thermal gradient	Separation of chlorine isotopes
Electrolysis (3)	Liquid	Electrical force field	Concentration of heavy water
Electrodialysis (4)	Liquid	Electrical force field and membrane	Desalinization of sea water
Electrophoresis (5)	Liquid	Electrical force field	Recovery of hemicelluloses
Field-flow fractionation (6)	Liquid	Laminar flow in force field	—

[a]Details of examples may be found in *Kirk-Othmer Encyclopedia of Chemical Technology*, 5th ed., John Wiley & Sons, New York (2004–2007).

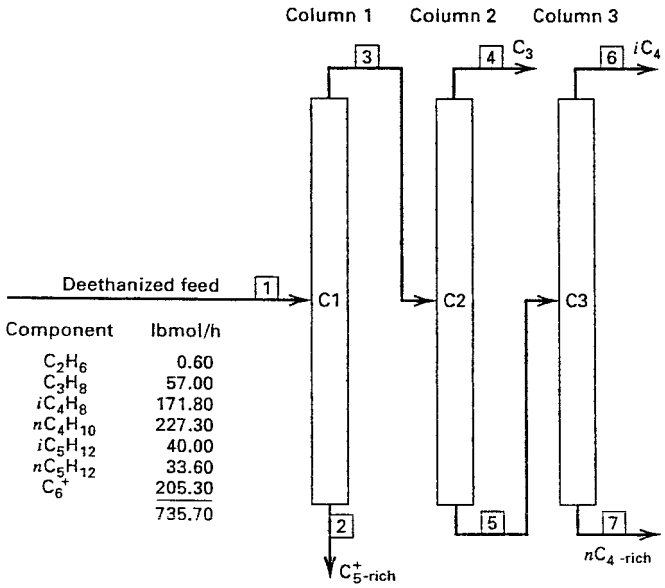


Figure 1.8 Hydrocarbon recovery process.

molecular weight) than *n*-pentane, and in the hexane (C_6)-to-undecane (C_{11}) range, are lumped together in a C_6^+ fraction. The three distillation columns of Figure 1.8 separate the feed into four products: a C_5^+-rich bottoms, a C_3-rich distillate, an iC_4-rich distillate, and an nC_4-rich bottoms. For each column, feed components are partitioned between the overhead and the bottoms according to a *split fraction* or *split ratio* that depends on (1) the component thermodynamic and transport properties, (2) the number of stages, and (3) the vapor and liquid flows through the column. The *split fraction*, SF, for component i in separator k is the fraction found in the first product:

$$\boxed{\mathrm{SF}_{i,k} = \frac{n_{i,k}^{(1)}}{n_{i,k}^{(F)}}} \qquad (1\text{-}2)$$

where $n^{(1)}$ and $n^{(F)}$ refer to component flow rates in the first product and feed. Alternatively, a *split ratio*, SR, between two products is

$$\boxed{\mathrm{SR}_{i,k} = \frac{n_{i,k}^{(1)}}{n_{i,k}^{(2)}} = \frac{\mathrm{SF}_{i,k}}{\left(1 - \mathrm{SF}_{i,k}\right)}} \qquad (1\text{-}3)$$

where $n^{(2)}$ refers to a component flow rate in the second product.

If the process shown in Figure 1.8 operates with the material balance of Table 1.5, the computed split fractions and split ratios are given in Table 1.6. In Table 1.5, it is seen that only two of the products are relatively pure: C_3 overhead from Column C2 and iC_4 overhead from Column C3. Molar purity of C_3 in Column C2 overhead is (54.80/56.00), or 97.86%, while the iC_4 purity is (162.50/175.50), or 92.59% iC_4. The nC_4 bottoms from Column C3 has an nC_4 purity of (215.80/270.00), or 79.93%.

Each column is designed to make a split between two adjacent key components in the feed, whose components are ordered in decreasing volatility. As seen by the horizontal lines in Table 1.6, the key splits are nC_4H_{10}/iC_5H_{12}, C_3H_8/iC_4H_{10}, and iC_4H_{10}/nC_4H_{10} for Columns C1, C2, and C3, respectively. From Table 1.6, we see that splits are sharp (SF $>$ 0.95 for the light key and SF $<$ 0.05 for the heavy key), except for Column C1, where the heavy-key split (iC_5H_{12}) is not sharp and ultimately causes the nC_4-rich bottoms to be impure in nC_4, even though the key-component split in the third column is sharp.

In Table 1.6, for each column we see that SF and SR decrease as volatility decreases, and SF may be a better degree-of-separation indicator than SR because SF is bounded between 0 and 1, while SR can range from 0 to a large value.

Two other measures of success can be applied to each column or to the entire process. One is the *percent recovery* of a designated product. These values are listed in the last column of Table 1.6. The recoveries are high (>95%), except for the pentane isomers. Another measure is *product purity*. Purities were computed for all except the C_5^+-rich product, which is [(11.90 + 16.10 + 205.30)/234.10], or 99.66% pure with respect to pentanes and heavier products. Such a product is a *multicomponent product*, an example of which is gasoline.

Impurity and impurity levels are included in *specifications* for chemicals in commerce. The computed product purity of

Table 1.5 Operating Material Balance for Hydrocarbon Recovery Process

	lbmol/h in Stream						
Component	1 Feed to C1	2 C_5^+-rich	3 Feed to C2	4 C_3	5 Feed to C3	6 iC_4	7 nC_4-rich
C_2H_6	0.60	0.00	0.60	0.60	0.00	0.00	0.00
C_3H_8	57.00	0.00	57.00	54.80	2.20	2.20	0.00
iC_4H_{10}	171.80	0.10	171.70	0.60	171.10	162.50	8.60
nC_4H_{10}	227.30	0.70	226.60	0.00	226.60	10.80	215.80
iC_5H_{12}	40.00	11.90	28.10	0.00	28.10	0.00	28.10
nC_5H_{12}	33.60	16.10	17.50	0.00	17.50	0.00	17.50
C_6^+	205.30	205.30	0.00	0.00	0.00	0.00	0.00
Total	735.60	234.10	501.50	56.00	445.50	175.50	270.00

Table 1.6 Computed Split Fractions (SF) and Split Ratios (SR) for Hydrocarbon Recovery Process

	Column 1		Column 2		Column 3		
Component	SF	SR	SF	SR	SF	SR	Overall Percent Recovery
C_2H_6	1.00	Large	1.00	Large	—	—	100
C_3H_8	1.00	Large	0.9614	24.91	1.00	Large	96.14
iC_4H_{10}	0.9994	1,717	0.0035	0.0035	0.9497	18.90	94.59
nC_4H_{10}	0.9969	323.7	0.00	0.00	0.0477	0.0501	94.94
iC_5H_{12}	0.7025	2.361	0.00	0.00	0.00	0.00	29.75
nC_5H_{12}	0.5208	1.087	0.00	0.00	0.00	0.00	47.92
C_6^+	0.00	Small	—	—	—	—	100

the three products for the process in Figure 1.8 is given in Table 1.7, where the values are compared to the specified maximum allowable percentages of impurities set by the govenment or trade associations. The C_5^+ fraction is not included because it is an intermediate. From Table 1.7, it is seen that two products easily meet specifications, while the iC_4 product barely meets its specification.

§1.7.2 Purity and Composition Designations

The product purities in Table 1.7 are given in mol%, a designation usually restricted to gas mixtures for which vol% is equivalent to mol%. Alternatively, *mole fractions* can be used. For liquids, purities are more often specified in wt% or *mass fraction* (ω). To meet environmental regulations, small amounts of impurities in gas, liquid, and solid streams are often specified in *parts of solute per million parts* (ppm) or *parts of solute per billion parts* (ppb), where if a gas, the parts are moles or volumes; if a liquid or solid, the parts are mass or weight. For aqueous solutions, especially those containing acids and bases, common designations for composition are *molarity* (M), or molar concentration in moles of solute per liter of solution (m/L); millimoles per liter (mM/L); *molality* (m) in moles of solute per kilogram of solvent; or *normality* (N) in number of equivalent weights of solute per liter of solution. *Concentrations* (*c*) in mixtures can be in units of moles or mass per volume (i.e., mol/L, g/L, lbmol/ft^3, and lb/ft^3). For some chemical products, an attribute such as color may be used in place of a purity in terms of composition. For biochemical processes, a biological *activity* specification is added for bioproducts such as pharmaceuticals, as discussed in §1.9.

§1.7.3 Separation Sequences

The three-column recovery process shown in Figure 1.8 is only one of five alternative sequences of distillation operations that can separate the feed into the four products when each column has a single feed and produces an overhead product and a bottoms product. For example, consider a hydrocarbon feed that consists, in order of decreasing volatility, of propane (C_3), isobutane (iC_4), *n*-butane (nC_4), isopentane (iC_5), and *n*-pentane (nC_5). A sequence of distillation columns is to be used to separate the feed into three nearly pure products of C_3, iC_4, and nC_4; and one multicomponent product of iC_5 and nC_5. The five alternative sequences are shown in Figure 1.9.

If only two products are desired, only a single column is required. For three final products, there are two alternative sequences. As the number of final products increases, the number of alternative sequences grows rapidly, as shown in Table 1.8.

Methods for determining the optimal sequence from the possible alternatives are discussed by Seider et al. [7]. For initial screening, the following heuristics are useful and easy to apply, and do not require column design or cost estimation:

Table 1.7 Comparison of Calculated Product Purities with Specifications

	mol% in Product					
	Propane		Isobutane		Normal Butane	
Component	Data	Spec	Data	Spec	Data	Spec
C_2H_6	1.07	5 max	0	—	0	—
C_3H_8	97.86	93 min	1.25	3 max	0	1 max
iC_4H_{10}	1.07	2 min	92.60	92 min	83.11	80 min
nC_4H_{10}	0	—	6.15	7 max		
C_5^+	0	—	0	—	16.89	20 max
Total	100.00		100.00		100.00	

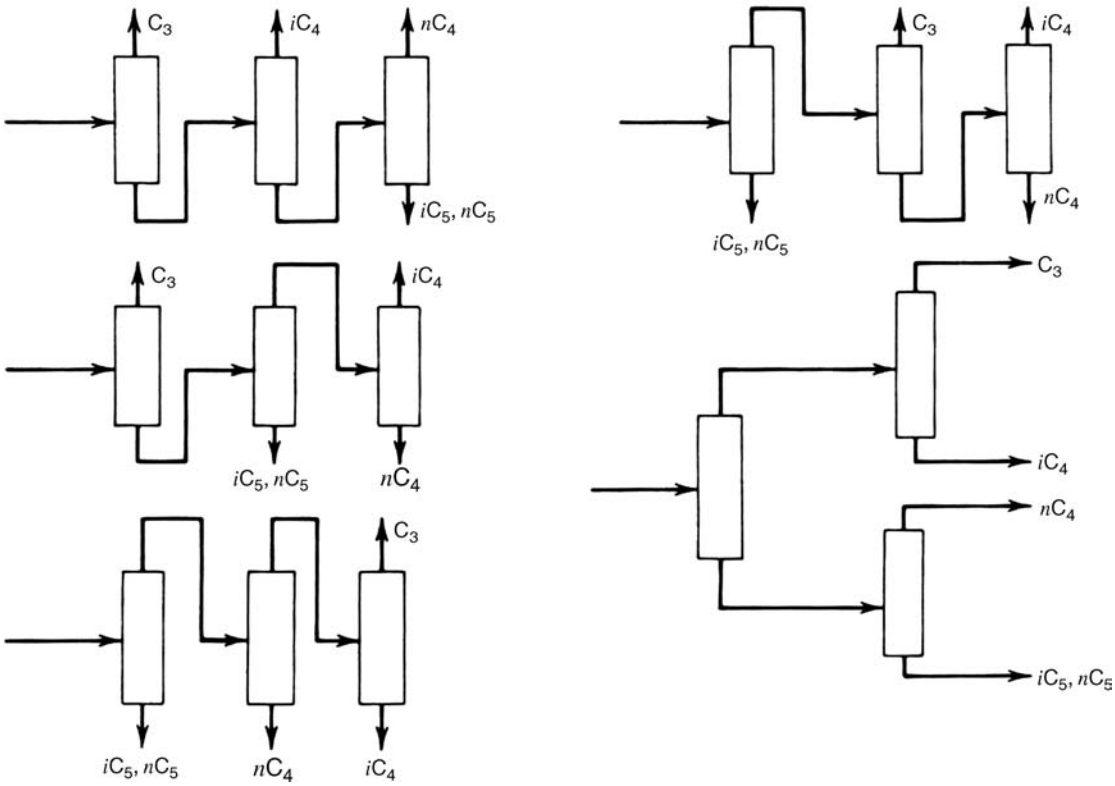


Figure 1.9 Distillation sequences to produce four products.

1. Remove unstable, corrosive, or chemically reactive components early in the sequence.
2. Remove final products one by one as overhead distillates.
3. Remove, early in the sequence, those components of greatest molar percentage in the feed.
4. Make the most difficult separations in the absence of the other components.
5. Leave for later in the sequence those separations that produce final products of the highest purities.
6. Select the sequence that favors near-equimolar amounts of overhead and bottoms in each column.

Unfortunately, these heuristics sometimes conflict with each other, and thus a clear choice is not always possible. Heuristic 1 should always be applied if applicable. The most common industrial sequence is that of Heuristic 2. When energy costs are high, Heuristic 6 is favored. When one of the separations, such as the separation of isomers, is particularly difficult, Heuristic 4 is usually applied. Seider et al. [7] present more rigorous methods, which do require column design and costing to determine the optimal sequence. They also consider complex sequences that include separators of different types and complexities.

Table 1.8 Number of Alternative Distillation Sequences

Number of Final Products	Number of Columns	Number of Alternative Sequences
2	1	1
3	2	2
4	3	5
5	4	14
6	5	42

EXAMPLE 1.2 Selection of a separation sequence using heuristics.

A distillation sequence produces the same four final products from the same five components in Figure 1.9. The molar percentages in the feed are C_3 (5.0%), iC_4 (15%), nC_4 (25%), iC_5 (20%), and nC_5 (35%). The most difficult separation by far is that between the isomers, iC_4 and nC_4. Use the heuristics to determine the best sequence(s). All products are to be of high purity.

Solution

Heuristic 1 does not apply. Heuristic 2 favors taking C_3, iC_4, and nC_4 as overheads in Columns 1, 2, and 3, respectively, with the iC_5, nC_5 multicomponent product taken as the bottoms in Column 3, as in Sequence 1 in Figure 1.9. Heuristic 3 favors the removal of the iC_5, nC_5 multicomponent product (55% of the feed) in Column 1, as in Sequences 3 and 4. Heuristic 4 favors the separation of iC_4 from nC_4 in Column 3, as in Sequences 2 and 4. Heuristics 3 and 4 can be combined, with C_3 taken as overhead in Column 2 as in Sequence 4. Heuristic 5 does not apply. Heuristic 6 favors taking the multicomponent product as bottoms in Column 1 (45/55 mole split), nC_4 as bottoms in Column 2 (20/25 mole split), and C_3 as overhead, with iC_4 as bottoms in Column 3 as in Sequence 3. Thus, the heuristics lead to four possible sequences as being most favorable.

However, because of the large percentage of the iC_5/nC_5 multicomponent product in the feed, and the difficulty of the separation between iC_4 and nC_4, the best of the four favored sequences is Sequence 4, based on Heuristics 3 and 4.

§1.8 SEPARATION FACTOR

Some separation operations in Table 1.1 are incapable of making a sharp split between key components and can effect the desired recovery of only a single component. Examples are Operations 1, 2, 6, 7, 8, 9, 11, 13, 14, 15, 16, and 17. For these, either a single separation stage is utilized, as in Operations 1, 2, 13, 14, 15, 16, and 17, or the feed enters at one end (not near the middle) of a multistage separator, as in Operations 6, 7, 8, 9, and 11. The split ratio (SR), split fraction (SF), recovery, or purity that can be achieved for the single key component depends on a number of factors. For the simplest case of a single separation stage, these factors include: (1) the relative molar amounts of the two phases leaving the separator and (2) thermodynamic, mass transport, and other component properties. For multistage separators, additional factors are the number of stages and their configurations. The relationships involving these factors are unique to each type of separator, and are discussed in detail in Chapters 5 and 6.

If the feed enters near the middle of the column as in distillation (discussed in Chapter 7), it has both enriching and stripping sections, and it is often possible to achieve a sharp separation between two key components. The enriching section purifies the light key and the stripping section purifies the heavy key. Examples are Operations 3, 4, 5, 10, and 12 in Table 1.1. For these, a measure of the relative degree of separation between two key components, i and j, is the *separation factor* or *power*, SP, defined in terms of the component splits as measured by the compositions of the two products, (1) and (2):

$$\boxed{\mathrm{SP}_{i,j} = \frac{C_i^{(1)}/C_i^{(2)}}{C_j^{(1)}/C_j^{(2)}}} \tag{1-4}$$

where C is some measure of composition. SP is readily converted to the following forms in terms of split fractions or split ratios:

$$\mathrm{SP}_{i,j} = \frac{\mathrm{SR}_i}{\mathrm{SR}_j} \tag{1-5}$$

$$\mathrm{SP}_{i,j} = \frac{\mathrm{SF}_i/\mathrm{SF}_j}{(1-\mathrm{SF}_i)/(1-\mathrm{SF}_j)} \tag{1-6}$$

Achievable values of SP depend on the number of stages and the properties of components i and j. In general, components i and j and products 1 and 2 are selected so that $\mathrm{SP}_{i,j} > 1.0$. Then, a large value corresponds to a relatively high degree of separation or separation factor, and a small value close to 1.0 corresponds to a low degree of separation factor. For example, if SP = 10,000 and $\mathrm{SR}_i = 1/\mathrm{SR}_j$, then, from (1-5), $\mathrm{SR}_i = 100$ and $\mathrm{SR}_j = 0.01$, corresponding to a sharp separation. However, if SP = 9 and $\mathrm{SR}_i = 1/\mathrm{SR}_j$, then $\mathrm{SR}_j = 3$ and $\mathrm{SR}_j = 1/3$, corresponding to a nonsharp separation.

Table 1.9 Key Component Separation Factors for Hydrocarbon Recovery Process

Key-Component Split	Column	Separation Factor, SP
nC_4H_{10}/iC_5H_{12}	C1	137.1
C_3H_{10}/iC_4H_{10}	C2	7103
iC_4H_{10}/nC_4H_{10}	C3	377.6

For the process of Figure 1.8, the values of SP in Table 1.9 are computed from Table 1.5 or 1.6 for the main split in each separator. The SP in Column C1 is small because the split for the heavy key, iC_5H_{12}, is not sharp. The largest SP occurs in Column C2, where the separation is relatively easy because of the large volatility difference. Much more difficult is the butane-isomer split in Column C3, where only a moderately sharp split is achieved.

Component flows and recoveries are easily calculated, while split ratios and purities are more difficult, as shown in the following example.

EXAMPLE 1.3 Using recovery and purity specifications.

A feed, F, of 100 kmol/h of air containing 21 mol% O_2 and 79 mol% N_2 is to be partially separated by a membrane unit according to each of four sets of specifications. Compute the amounts, in kmol/h, and compositions, in mol%, of the two products (retentate, R, and permeate, P). The membrane is more permeable to O_2.

Case 1: 50% recovery of O_2 to the permeate and 87.5% recovery of N_2 to the retentate.

Case 2: 50% recovery of O_2 to the permeate and 50 mol% purity of O_2 in the permeate.

Case 3: 85 mol% purity of N_2 in the retentate and 50 mol% purity of O_2 in the permeate.

Case 4: 85 mol% purity of N_2 in the retentate and a split ratio of O_2 in the permeate to the retentate equal to 1.1.

Solution

The feed is

$$n_{O_2}^{(F)} = 0.21(100) = 21\ \mathrm{kmol/h}$$
$$n_{N_2}^{(F)} = 0.79(100) = 79\ \mathrm{kmol/h}$$

Case 1: Because two recoveries are given:

$$n_{O_2}^{(P)} = 0.50(21) = 10.5\ \mathrm{kmol/h}$$
$$n_{N_2}^{(R)} = 0.875(79) = 69.1\ \mathrm{kmol/h}$$
$$n_{O_2}^{(R)} = 21 - 10.5 = 10.5\ \mathrm{kmol/h}$$
$$n_{N_2}^{(P)} = 79 - 69.1 = 9.9\ \mathrm{kmol/h}$$

Case 2: O_2 recovery is given; the product distribution is:

$$n_{O_2}^{(P)} = 0.50(21) = 10.5\ \mathrm{kmol/h}$$
$$n_{O_2}^{(R)} = 21 - 10.5 = 10.5\ \mathrm{kmol/h}$$

Using the fractional purity of O_2 in the permeate, the total permeate is

$$n^{(P)} = 10.5/0.5 = 21\text{kmol/h}$$

By a total permeate material balance,

$$n_{N_2}^{(P)} = 21 - 10.5 = 10.5\,\text{kmol/h}$$

By an overall N_2 material balance,

$$n_{N_2}^{(R)} = 79 - 10.5 = 68.5\,\text{kmol/h}$$

Case 3: Two material-balance equations, one for each component, can be written.
For nitrogen, with a fractional purity of $1.00 - 0.50 = 0.50$ in the permeate,

$$n_{N_2} = 0.85n^{(R)} + 0.50n^{(P)} = 79\,\text{kmol/h} \quad (1)$$

For oxygen, with a fractional purity of $1.00 - 0.85 = 0.15$ in the retentate,

$$n_{O_2} = 0.50n^{(P)} + 0.15n^{(R)} = 21\,\text{kmol/h} \quad (2)$$

Solving (1) and (2) simultaneously for the total products gives

$$n^{(P)} = 17.1\,\text{kmol/h}, \quad n^{(R)} = 82.9\,\text{kmol/h}$$

Therefore, the component flow rates are

$$n_{N_2}^{(R)} = 0.85(82.9) = 70.5\,\text{kmol/h}$$
$$n_{O_2}^{(R)} = 82.9 - 70.5 = 12.4\,\text{kmol/h}$$
$$n_{O_2}^{(P)} = 0.50(17.1) = 8.6\,\text{kmol/h}$$
$$n_{N_2}^{(P)} = 17.1 - 8.6 = 8.5\,\text{kmol/h}$$

Case 4: First compute the O_2 flow rates using the split ratio and an overall O_2 material balance,

$$\frac{n_{O_2}^{(P)}}{n_{O_2}^{(R)}} = 1.1, \quad 21 = n_{O_2}^{(P)} + n_{O_2}^{(R)}$$

Solving these two equations simultaneously gives

$$n_{O_2}^{(R)} = 10\,\text{kmol/h}, \quad n_{O_2}^{(P)} = 21 - 10 = 11\,\text{kmol/h}$$

Since the retentate contains 85 mol% N_2 and, therefore, 15 mol% O_2, the flow rates for N_2 are

$$n_{N_2}^{(R)} = \frac{85}{15}(10) = 56.7\,\text{kmol/h}$$
$$n_{N_2}^{(P)} = 79 - 56.7 = 22.3\,\text{kmol/h}$$

§1.9 INTRODUCTION TO BIOSEPARATIONS

Bioproducts are products extracted from plants, animals, and microorganisms to sustain life and promote health, support agriculture and chemical enterprises, and diagnose and remedy disease. From the bread, beer, and wine produced by ancient civilizations using fermented yeast, the separation and purification of biological products (bioproducts) have grown in commercial significance to include process-scale recovery of antibiotics from mold, which began in the 1940s, and isolation of recombinant DNA and proteins from transformed bacteria in biotechnology protocols initiated in the 1970s. Bioproducts used in pharmaceutical, agrichemical, and biotechnology market sectors—excluding commodity foods, beverages, and biofuels—accounted for an estimated $28.2 billion in sales in 2005, with an average annual growth rate of 12% that projects to $50 billion in sales by 2010.

§1.9.1 Bioproducts

To identify features that allow selection and specification of processes to separate bioproducts from other *biological species*[1] of a host cell, it is useful to classify biological species by their complexity and size as *small molecules*, *biopolymers*, and *cellular particulates* (as shown in Column 1 of Table 1.10), and to further categorize each type of species by name in Column 2, according to its biochemistry and function within a biological host in Column 3.

Small molecules include *primary metabolites*, which are synthesized during the primary phase of cell growth by sets of enzyme-catalyzed biochemical reactions referred to as *metabolic pathways*. Energy from organic nutrients fuels these pathways to support cell growth and relatively rapid reproduction. Primary metabolites include organic commodity chemicals, amino acids, mono- and disaccharides, and vitamins. *Secondary metabolites* are small molecules produced in a subsequent stationary phase, in which growth and reproduction slows or stops. Secondary metabolites include more complex molecules such as antibiotics, steroids, phytochemicals, and cytotoxins. Small molecules range in complexity and size from H_2 (2 daltons, Da), produced by cyanobacteria, to vitamin B-12 (1355 Da) or vancomycin antibiotic (1449 Da), whose synthesis originally occurred in bacteria.

Amino acid and monosaccharide metabolites are building blocks for higher-molecular-weight **biopolymers,** from which cells are constituted. Biopolymers provide mechanical strength, chemical inertness, and permeability; and store energy and information. They include *proteins*, *polysaccharides*, *nucleic acids*, and *lipids*.

Cellular particulates include cells and cell derivatives such as *extracts* and *hydrolysates* as well as subcellular components.

Proteins, the most abundant biopolymers in cells, are long, linear sequences of 20 naturally occurring amino acids, covalently linked end-to-end by peptide bonds, with molecular weights ranging from 10,000 Da to 100,000 Da. Their structure is often helical, with an overall shape ranging from globular to sheet-like, with loops and folds as determined largely by attraction between oppositely charged groups on the amino acid chain and by hydrogen bonding. Proteins participate in storage, transport, defense, regulation, inhibition, and catalysis. The first products of biotechnology were biocatalytic proteins that initiated or inhibited specific biological cascades [8]. These included hormones, thrombolytic agents, clotting factors, and

[1]The term "biological species" as used in this book is not to be confused with the word "species," a taxonomic unit used in biology for the classification of living and fossil organisms, which also includes genus, family, order, class, phylum, kingdom, and domain.

Table 1.10 Products of Bioseparations

Biological Species Classification	Types of Species	Examples
Small Molecules		
Primary metabolites	Gases, organic alcohols, ketones	H_2, CO_2, ethanol (biofuels, beverages), isopropanol, butanol (solvent), acetone
	Organic acids	Acetic acid (vinegar), lactic acid, propionic acid, citric acid, glutamic acid (MSG flavor)
	Amino acids	Lysine, phenylalanine, glycine
	Monosaccharides	Aldehydes: D-glucose, D-ribose; Ketones: D-fructose (in corn syrup)
	Disaccharides	Sucrose, lactose, maltose
	Vitamins	Fat soluble: A, E, and C (ascorbic acid); Water soluble: B, D, niacin, folic acid
Secondary metabolites	Antibiotics	Penicillin, streptomycin, gentamycin
	Steroids	Cholesterol, cortisone, estrogen derivatives
	Hormones	Insulin, human grown
	Phytochemicals	Resveratrol® (anti-aging agent)
	Cytotoxins	Taxol® (anti-cancer)
Biopolymers		
Proteins	Enzymes	Trypsin, ribonuclease, polymerase, cellulase, whey protein, soy protein, industrial enzymes (detergents)
	Hormones	Insulin, growth hormone, cytokines, erythropoietin
	Transport	Hemoglobin, β_1-lipoprotein
	Thrombolysis/clotting	Tissue plasminogen activator, Factor VIII
	Immune agents	α-interferon, interferon β-1a, hepatitis B vaccine
	Antibodies	Herceptin®, Rituxan®, Remicade®, Enbrel®
Polysaccharides		Dextrans (thickeners); alginate, gellan, pullulan (edible films); xanthan (food additive)
Nucleic acids		Gene vectors, antisense oligonucleotides, small interfering RNA, plasmids, ribozymes
Lipids		Glycerol (sweetener), prostaglandins
Virus		Retrovirus, adenovirus, adeno-associated virus (gene vectors), vaccines
Cellular Particulates		
Cells	Eubacteria	*Bacillus thuringensis* (insecticide)
	Eukaryotes	*Saccharomyces cerevisia* (baker's yeast), diatoms, single cell protein (SCP)
	Archae	Methanogens (waste treatment), acidophiles
Cell extracts and hydrolysates		Yeast extract, soy extract, animal tissue extract, soy hydrolysate, whey hydrolysate
Cell components		Inclusion bodies, ribosomes, liposomes, hormone granules

immune agents. Recently, bioproduction of monoclonal antibodies for pharmaceutical applications has grown in significance. Monoclonal antibodies are proteins that bind with high specificity and affinity to particles recognized as foreign to a host organism. Monoclonal antibodies have been introduced to treat breast cancer (Herceptin®), B-cell lymphoma (Rituxan®), and rheumatoid arthritis (Remicade® and Enbrel®).

Carbohydrates are mono- or polysaccharides with the general formula $(CH_2O)_n$, $n \geq 3$, photosynthesized from CO_2. They primarily store energy as cellulose and starch in plants, and as glycogen in animals. *Monosaccharides* ($3 \leq n \leq 9$) are aldehydes or ketones. Condensing two monosaccharides forms a *disaccharide*, like sucrose (α-D-glucose plus β-D-fructose), lactose (β-D-glucose plus β-D-galactose) from milk or whey, or maltose, which is hydrolyzed from germinating cereals like barley. *Polysaccharides* form by condensing >2 monosaccharides. They include the starches amylase and amylopectin, which are partially hydrolyzed to yield glucose and dextrin, and cellulose, a long, unbranched D-glucose chain that resists enzymatic hydrolysis.

Nucleic acids are linear polymers of *nucleotides*, which are nitrogenous bases covalently bonded to a pentose sugar attached to one or more phosphate groups. They preserve the genetic inheritance of the cell and control its development, growth, and function by regulated translation of proteins. Linear deoxyribonucleic acid (DNA) is *transcribed* by polymerase into messenger ribonucleic acid (mRNA) during cell growth and metabolism. mRNA provides a template on which polypeptide sequences are formed (i.e., *translated*) by amino acids transported to the ribosome by transfer RNA (tRNA). Plasmids are circular, double-stranded DNA

segments used to introduce genes into cells using recombinant DNA (rDNA), a process called genetic engineering.

Lipids are comprised primarily of *fatty acids*, which are straight-chain aliphatic hydrocarbons terminated by a hydrophilic carboxyl group with the formula $CH_3—(CH_2)_n—COOH$, where $12 \leq n \leq 20$ is typical. Lipids form membrane bilayers, provide reservoirs of fuel (e.g., fats), and mediate biological activity (e.g., phosopholipids, steroids). Fats are esters of fatty acids with glycerol, $C_3H_5(OH)_3$, a sweetener and preservative. Biodiesel produced by caustic transesterification of fats using caustic methanol or ethanol yields 1 kg of crude glycerol for every 9 kg of biodiesel. *Steroids* like cholesterol and cortisone are cyclical hydrocarbons that penetrate nonpolar cell membranes, bind to and modify intracellular proteins, and thus act as hormone regulators of mammalian development and metabolism.

Viruses are protein shells containing DNA or RNA genes that replicate inside a host such as a bacterium (e.g., bacteriophages) or a plant or mammalian cell. Viral *vectors* may be used to move genetic material into host cells in a process called *transfection*. Transfection is used in *gene therapy* to introduce nucleic acid that complements a mutated or inactive gene of a cell. Transfection also allows *heterologous* protein production (i.e., from one product to another) by a nonnative host cell via rDNA methods. Viruses may be inactivated for use as vaccines to stimulate a prophylactic humoral immune response.

Cellular particulates include cells themselves, crude cell *extracts* and cell *hydrolysates*, as well as subcellular components. Cells are mostly *aerobes* that require oxygen to grow and metabolize. *Anaerobes* are inhibited by oxygen, while *facultative anaerobes*, like yeast, can switch metabolic pathways to grow with or without O_2. As shown in Figure 1.10, *eukaryotic* cells have a nuclear membrane envelope around genetic material. Eukaryotes are single-celled organisms and multicelled systems consisting of fungi (yeasts and molds), algae, protists, animals, and plants. Their DNA is associated with small proteins to form chromosomes. Eukaryotic cells contain specialized *organelles* (i.e., membrane-enclosed domains). Plant cell walls consist of cellulose fibers embedded in pectin aggregates. Animal cells have only a sterol-containing cytoplasmic membrane, which makes them shear-sensitive and fragile. *Prokaryotic* cells, as shown in Figure 1.11, lack a nuclear membrane and organelles like mitochondria or endoplasmic reticulum. Prokaryotes are classified as *eubacteria* or *archae.* Eubacteria are single cells that double in size, mass, and number in 20 minutes to several hours. Most eubacteria are categorized as gram-negative or gram-positive using a dye method. *Gram-negative* bacteria have an outer membrane supported by *peptidoglycan* (i.e., cross-linked polysaccharides and amino acids) that is separated from an inner (*cytoplasmic*) membrane. *Gram-positive* bacteria lack an outer membrane (and more easily secrete protein) but have a rigid cell wall (~200 Å) of multiple peptidoglycan layers.

§1.9.2 Bioseparation Features

Several features are unique to removal of contaminant biological species and recovery of bioproducts. These features distinguish the specification and operation of bioseparation equipment and process trains from traditional chemical engineering unit operations. Criteria for selecting a bioseparation method are based on the ability of the method to differentiate the targeted bioproduct from contaminants based on physical property differences, as well as its capacity to accommodate the following six features of bioproducts.

Activity: Small primary and secondary metabolites are uniquely defined by a chemical composition and structure that are quantifiable by precise analytical methods (e.g., spectroscopic, physical, and chemical assays). In contrast, biopolymers and cellular particulates are valued for their *activity* in biological systems. Proteins, for example, act in enzyme catalysis and cell regulatory roles. Plasmid DNA or virus is valued as a vector (i.e., delivery vehicle of genetic information into target cells). Biological activity is a function of the assembly of the biopolymer, which results in a complex structure and surface functionality, as well as the presence of organic or inorganic *prosthetic groups.* A subset of particular structural features may be analyzable by spectroscopic, microscopic, or physicochemical assays. Surrogate in vitro assays that approximate biological conditions *in vivo* may provide a limited measure of activity. For biological products, whose origin and characteristics are complex, the manufacturing process itself defines the product.

Complexity: Raw feedstocks containing biological products are complex mixtures of cells and their constituent biomolecules as well as residual species from the cell's native environment. The latter may include *macro-* and *micronutrients* from media used to culture cells in vitro, woody material from harvested fauna, or tissues from mammalian extracts. Bioproducts themselves range from simple, for primary metabolites such as organic alcohols or acids, to complex, for infectious virus particles composed of polymeric proteins and nucleic acids. To recover a target species from a complex matrix of biological species usually requires a series of complementary separation operations that rely on differences in size, density, solubility, charge, hydrophobicity, diffusivity, or volatility to distinguish bioproducts from contaminating host components.

Lability: Susceptibility of biological species to phase change, temperature, solvents or exogenous chemicals, and mechanical shear is determined by bond energies, which maintain native configuration, reaction rates of enzymes and cofactors present in the feedstock, and biocolloid interactions. Small organic alcohols, ketones, and acids maintained by high-energy covalent bonds can resist substantial variations in thermodynamic state. But careful control of solution conditions (e.g., pH buffering, ionic strength, temperature) and suppression of enzymatic reactions (e.g., actions of proteases, nucleases, and lipases) are required to maintain biological activity of polypeptides, polynucleotides, and polysaccharides. Surfactants and organic solvents may

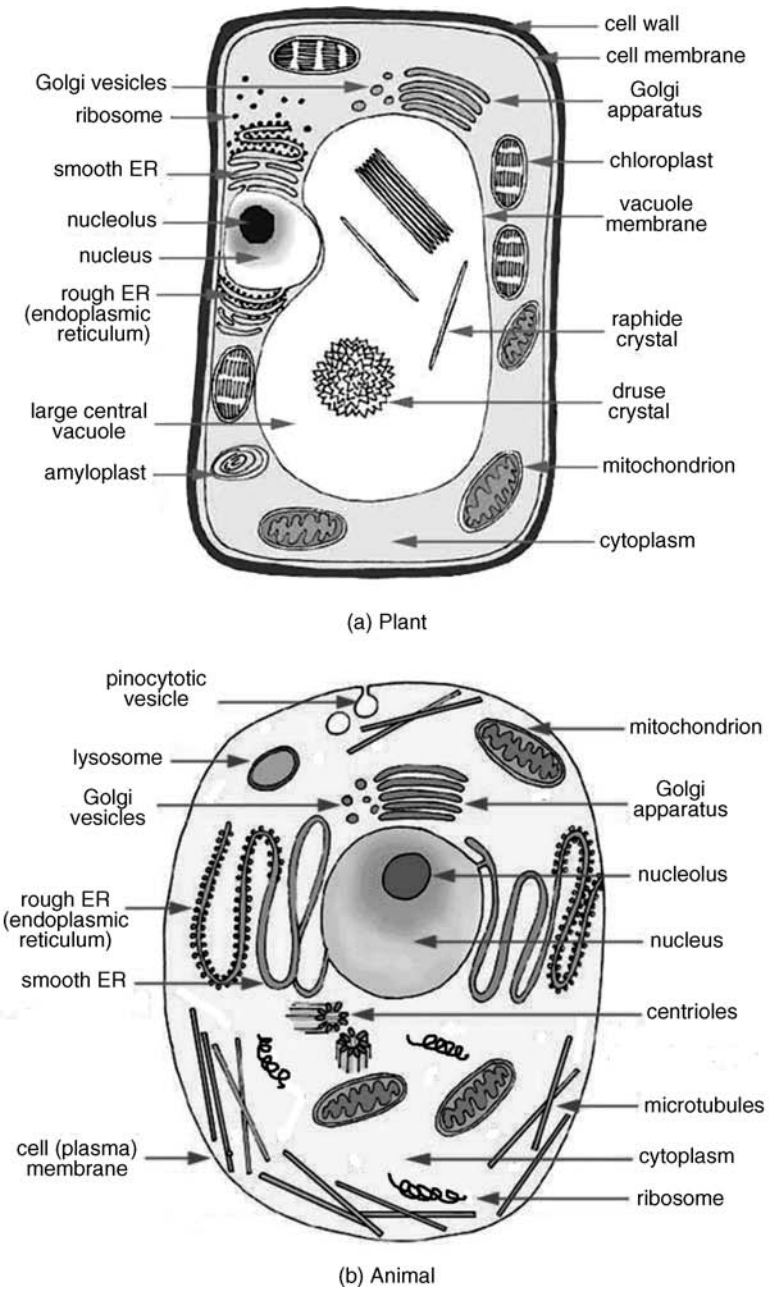


Figure 1.10 Typical eukaryotic cells.

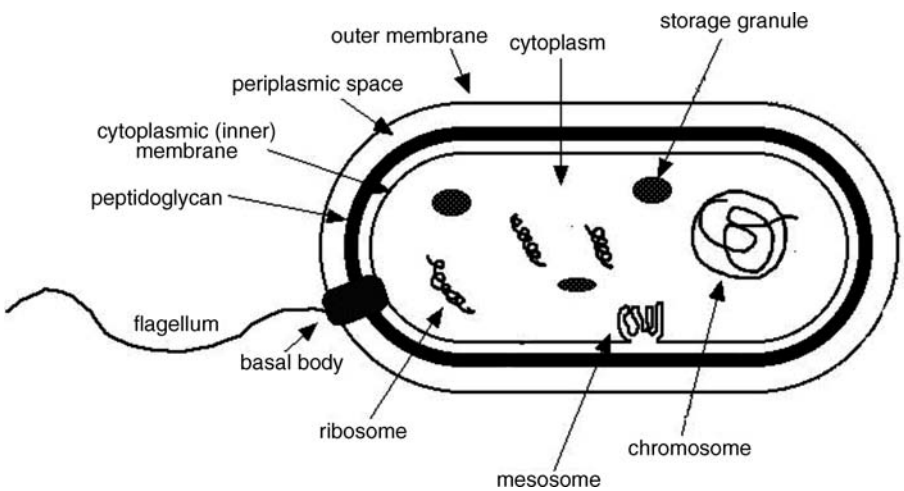


Figure 1.11 Typical prokaryotic bacterial cell.

disrupt weaker hydrophobic bonds that maintain native configuration of proteins. Fluid–solid or gas–liquid interfaces that absorb dissolved biopolymers may unfold, inactivate, and aggregate biopolymers, particularly when mechanical shear is present.

Process scale: Small primary metabolites may be commodity chemicals with market demands of tons per year. Market requirements for larger biopolymers, proteins in particular, are typically 1 to 10 kg/yr in rDNA hosts. The hosts are usually Chinese Hamster Ovary (CHO) cells, *Escherichia coli* bacteria, and yeast. CHO cells are cultured in batch volumes of 8,000–25,000 liters and yield protein titers of about 1 to 3 g/L. Antibodies are required in quantities of approximately 1,000 kg/yr. Production in transgenic milk, which can yield up to 10 g/L, is being evaluated to satisfy higher demand for antibodies. The initially low concentration of bioproducts in aqueous fermentation and cell culture feeds, as illustrated in Figure 1.12, results in excess water, which is removed early in the bioprocess train to reduce equipment size and improve process economics.

Purity: The mass of host-cell proteins (HCP), product variants, DNA, viruses, endotoxins, resin and membrane leachables, and small molecules is limited in biotechnology products for therapeutic and prophylactic application.

The Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration (FDA) approves HCP limits established by the manufacturer after review of process capability and safety testing in toxicology and clinical trials. The World Health Organization (WHO) sets DNA levels at $\leq$ 10 μg per dose. Less than one virus particle per 10^6 doses is allowed in rDNA-derived protein products. Sterility of final products is ensured by sterile filtration of the final product as well as by controlling microbial contaminant levels throughout the process.

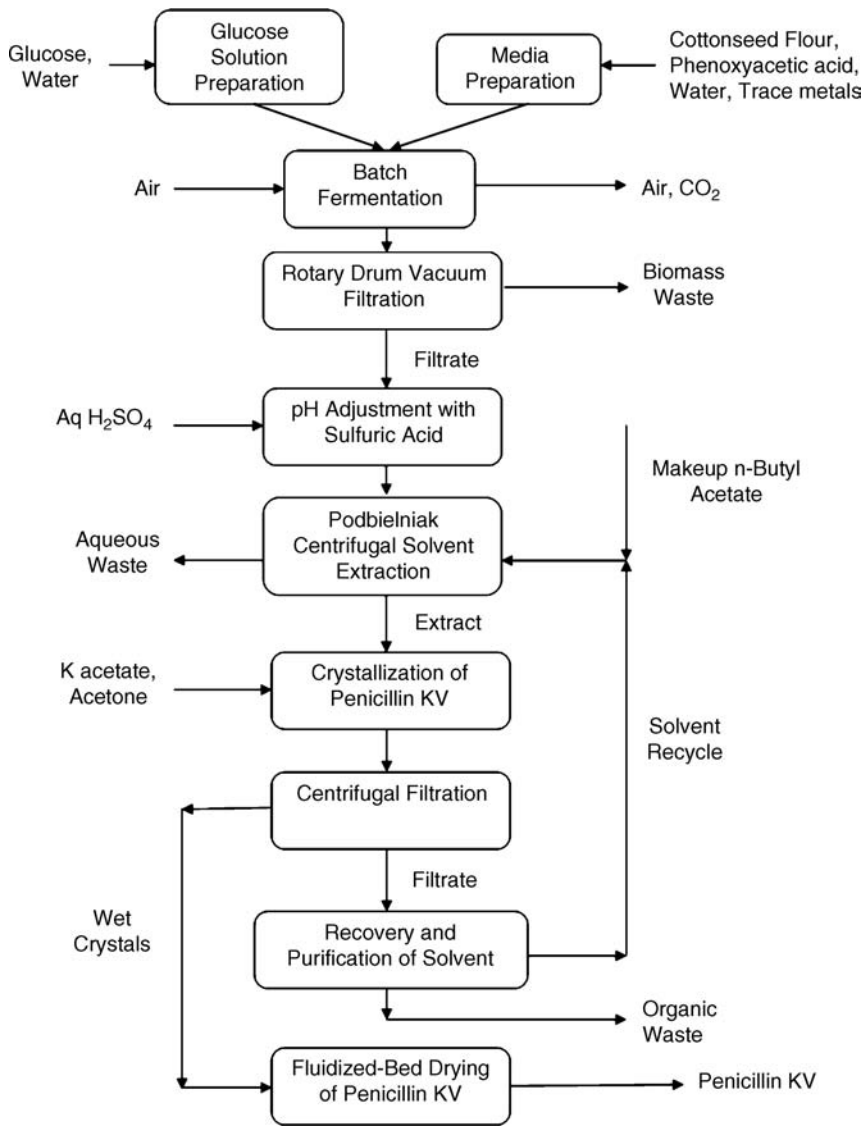


Figure 1.12 Block-Flow Diagram for Penicillin KV Process.

Approval and Manufacturing: The FDA ensures safety and efficacy of bioproducts used in human diagnostic, prophylactic, and therapeutic applications. They review clinical trial data as well as manufacturing process information, eventually approving approximately 1 in 10 candidates for introduction into the market as an *investigational new drug* (IND). Manufacture of drugs under current good manufacturing practices (cGMP) considers facility design and layout, equipment and procedures including operation, cleaning and sterilization documented by standard operating procedures (SOPs), analysis in labs that satisfy good laboratory practices (GLP), personnel training, control of raw materials and cultures, and handling of product. Drug manufacturing processes must be validated to assure that product reproducibly meets predetermined specifications and quality characteristics that ensure biological activity, purity, quality, and safety.

Bioseparation synthesis: Bioprocesses are required to economically and reliably recover purified bioproducts from chemical and biological species in complex cell matrices in quantities sufficient to meet market demands. Beginning with a raw cellular source: (1) cellular particulates are recovered or retained by sedimentation or filtration; (2) biopolymers are usually purified by filtration, adsorption, extraction, or precipitation; and (3) small biomolecules are often recovered by extraction. Economics, documentation, consideration of genetic engineering, and ordering of process steps are key features of bioseparation synthesis.

Bioprocess economics: Large-scale recovery operations must be efficient, since the cost of recovering biomolecules and treating aqueous, organic, and solid wastes can dominate total product manufacturing costs. Inefficient processes consume inordinate volumes of expensive solvent, which must be recovered and recycled, or disposed of. Costs resulting from solvent tankage and consumption during downstream recovery represent a significant fraction of biological-recovery costs. Development of a typical pharmaceutical bioproduct cost $400 million in 1996 and required 14 years—6.5 years from initial discovery through preclinical testing and another 7.5 years for clinical trials in human volunteers.

Bioprocess documentation: The reliability of process equipment must be well-documented to merit approval from governmental regulatory agencies. Such approval is important to meet cGMP quality standards and purity requirements for recovered biological agents, particularly those in prophylactic and therapeutic applications, which require approval by subdivisions of the FDA, including the CBER.

Genetic engineering: Conventional bioproduct-recovery processes can be enhanced via genetic engineering by fusing proteins to active species or intracellular insertion of active DNA to stimulate *in vivo* production of desired proteins. *Fusion proteins* consist of a target protein attached to an affinity peptide tag such as histidine hexamer, which binds transition metals (e.g., nickel, zinc, and copper) immobilized on sorptive or filtration surfaces. Incorporating purification considerations into early upstream cell culture manufacturing decisions can help streamline purification.

§1.9.3 Bioseparation Steps

A series of bioseparation steps are commonly required upstream of the bioreactor (e.g., filtration of incoming gases and culture media), after the bioreactor (i.e., *downstream* or *recovery processes*), and during (e.g., centrifugal removal of spent media) fermentation and cell culture operations. A general sequence of biorecovery steps is designed to remove solvent, insolubles (e.g., particle removal), unrelated soluble species, and similar species. A nondenaturing protein-recovery process, for example, consists of consecutive steps of *extraction*, *clarification*, *concentration*, *fractionation*, and *purification*. The performance of each purification step is characterized in terms of product *purity*, *activity*, and *recovery*, which are evaluated by:

$$\text{purity} = \frac{\text{bioproduct mass}}{\text{bioproduct mass} + \text{impurities mass}}$$

$$\text{activity} = \frac{\text{units of biological activity}}{\text{bioproduct mass}}$$

$$\text{yield} = \frac{\text{bioproduct mass recovered}}{\text{bioproduct mass in feed}}$$

Recovery yields of the final product can range from about 20% to 60–70% of the initial molecule present in the feed stream. Some clarification of raw fermentation or cell-culture feed streams prior is usually required to analyze their bioproduct content, which makes accurate assessment of recovery yields difficult. It is particularly important to preserve biological activity during the bioseparation steps by maintaining the structure or assembly of the bioproduct.

Table 1.11 classifies common bioseparation operations according to their *type*, *purpose*, and illustrative *species removed*. Subsequent chapters in this book discuss these bioseparation operations in detail.

Following this subsection, the production of penicillin KV is summarized to illustrate integration of several bioseparation operations into a sequence of steps. Modeling of the penicillin process as well as processes to produce citric acid, pyruvic acid, cysing, riboflavin, cyclodextrin, recombinant human serum albumin, recombinant human insulin, monoclonal antibodies, antitrypsin, and plasmid DNA are discussed by Heinzle et al. [18].

Extraction of cells from fermentation or cell culture broths by removing excess water occurs in a harvest step. Extraction of soluble biological species from these cellular extracts, which contain unexcreted product, occurs by homogenization, which renders the product soluble and accessible to solid–fluid and solute–solute separations. Lysis (breaking up) of whole cells by enzymatic degradation, ultrasonication, Gaulin-press homogenization, or milling releases and solubilizes intracellular enzymes.

Table 1.11 Synthesis of Bioseparation Sequences

Separation Operation	Purpose	Species Removed
Homogenization	**Extract** target from cells	
Cell disruption		
Fluid–Solid Separations	**Reduce volume**	Solvent
Flocculation	**Clarify** target species	Culture media
Precipitation/Centrifugation		Fermentation broth
Crystallization		Insolubles
Extraction		Host-cell debris
Filtration		Aggregates
Evaporation/Drying		
Solute–Solute Separations	**Fractionate** target species	Unrelated Solutes
Chromatography		Small metabolites
Extraction		Proteins
Crystallization		Lipids
Tangential-flow filtration		Nucleic acids
		Carbohydrates
	Purify target species	Related Solutes
		Truncated/misfolded
		Oligomers
Fluid–Solid Separations	**Formulation (Polishing)**	
Precipitation/Centrifugation	Preserve target species	Buffers
Crystallization	Prepare for injection	Solutions
Filtration		
Evaporation/Drying		

Clarification of solid cell debris, nucleic acids, and insoluble proteins by centrifugal precipitation or membrane filtration decreases fouling in later process steps. Selective precipitation is effected by adding salt, organic solvent, detergent, or polymers such as polyethyleneimine and polyethylene glycol to the buffered cell lysate. Size-selective membrane microfiltration may also be used to remove cell debris, colloidal or suspended solids, or virus particles from the clarified lysate. Ultrafiltration, tangential-flow filtration, hollow fibers, and asymmetrical membrane filtration are commonly used membrane-based configurations for clarification. Incompletely clarified lysate has been shown to foul dead-end stacked-membrane adsorbers, in concentrations as low as 5%.

Concentration reduces the volume of total material that must be processed, thereby improving process economics. Extraction of cells from media during harvest involves concentration, or solvent removal. Diafiltration of clarified extract into an appropriate buffer prepares the solution for concentration via filtration. Alternatively, the targeted product may be concentrated by batch adsorption onto a solid resin. The bioproduct of interest and contaminants with similar physical properties are removed by an eluting solvent. Microfiltration to clarify lysate and concentrate by adsorption has been performed simultaneously using a spiral-wound membrane adsorber.

Fractionation of the targeted product usually requires one or more complementary separation processes to distinguish between the product and the contaminants based on differences in their physicochemical features. As examples, filtration, batch adsorption, isoelectric focusing, and isotachophoresis are methods used to separate biological macromolecules based on differences in size, mass, isoelectric point, charge density, and hydrophobicity, respectively. Additional complementary separation steps are often necessary to fractionate the product from any number of similar contaminants. Due to its high specificity, adsorption using affinity, ion exchange, hydrophobic interaction, and reversed-phase chemistries is widely used to fractionate product mixtures.

Purification of the concentrated, fractionated product from closely related variants occurs by a high-resolution technique prior to final formulation and packaging of pharmaceutical bioproducts. Purification often requires differential absorption in an adsorptive column that contains a large number of theoretical stages or plates to attain the required purity. Batch electrophoresis achieves high protein resolution at laboratory scale, while production-scale, continuous apparatus for electrophoresis must be cooled to minimize ohmic heating of bioproducts. Crystallization is preferred, where possible, as a final purification step prior to formulation and packaging. Counterflow resolution of closely related species has also been used.

Formulation: The dosage form of a pharmaceutical bioproduct results from *formulating* the bioactive material by adding *excipients* such as stabilizers (e.g., reducing compounds, polymers), tablet solid diluents (e.g., gums, PEG, oils), liquid diluent (e.g., water for injection, WFI), or

adjuvant (e.g., alum) to support activity, provide stability during storage, and provide deliverability at final concentration.

EXAMPLE 1.4 Using properties to select bioseparations

Proteins, nucleic acids, and viral gene vectors are current pharmaceutical products. Identify five physical and biochemical properties of these biological species by which they could be distinguished in a bioseparation. Identify a separation operation that could be used to selectively remove or retain each species from a mixture of the other two. Summarize important considerations that might constrain the bioseparation operating parameters.

Solution

Properties that could allow separation are density, size, solubility, charge, and hydrophobicity. Separation operations that could be considered are: CsCl gradient ultracentrifugation (UC), which selectively retains viral vectors from proteins and nucleic acids, based primarily on density; ultrafiltration (UF), which is commonly used to size-selectively remove nucleic acids enzymatically digested by nuclease (e.g., Benzonase^{TM}) from proteins and viral vectors; and ion-exchange adsorption (IEX), which is used to selectively remove proteins and/or nucleic acids from viral suspensions (or vice versa). Some important considerations in UC, UF, and IEX are maintaining temperature ($\sim$4°C), water activity (i.e., ionic strength), pH to preserve virus stability, proper material selection to limit biological reactivity of equipment surfaces in order to prevent protein denaturation or virus disassembly, and aseptic operating procedures to prevent batch contamination.

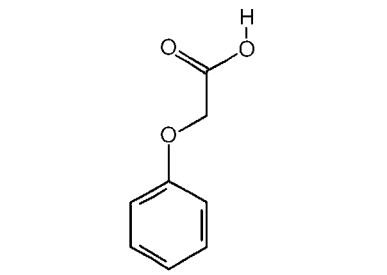
Many industrial chemical separation processes introduced in earlier sections of this chapter have been adapted for use in bioproduct separation and purification. Specialized needs for adaptation arise from features unique to recovery of biological species. *Complex* biological feedstocks must often be processed at moderate temperatures, with low shear and minimal gas–liquid interface creation, in order to maintain *activity* of *labile* biological species. Steps in a recovery sequence to remove biological species from the feed milieu, whose complexity and size range broadly, are often determined by unique cell characteristics. For example, extracellular secretion of product may eliminate the need for cell disruption. High *activity* of biological species allows market demand to be satisfied at *process scales* suited to batch operation. Manufacturing process validation required to ensure *purity* of biopharmaceutical products necessitates batch, rather than continuous, operation. Batchwise expansion of seed inoculums in fermented or cultured cell hosts is also conducive to batch bioseparations in downstream processing. The value per gram of biopharmaceutical products relative to commodity chemicals is higher due to the higher specific activity of the former in vivo. This permits cost-effective use of high-resolution chromatography or other specialized operations that may be cost-prohibitive for commodity chemical processes.

§1.9.4 Bioprocess Example: Penicillin

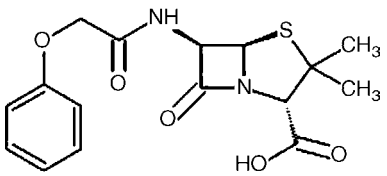
In the chemical industry, a unit operation such as distillation or liquid–liquid extraction adds pennies to the sale price of an average product. For a 40 cents/lb commodity chemical, the component separation costs do not generally account for more than 10–15% of the manufacturing cost. An entirely different economic scenario exists in the bioproduct industry. For example, in the manufacture of tissue plasminogen activator (tPA), a blood clot dissolver, Datar et al., as discussed by Shuler and Kargi [9], enumerate 16 processing steps when the bacterium *E. coli* is the cell culture. Manufacturing costs for this process are $22,000/g, and it takes a $70.9 million investment to build a plant to produce 11 kg/yr of product. Purified product yields are only 2.8%. Drug prices must also include recovery of an average $400 million cost of development within the product's lifetime. Furthermore, product lifetimes are usually shorter than the nominal 20-year patent life of a new drug, since investigational new drug (IND) approval typically occurs years after patent approval. Although some therapeutic proteins sell for $100,000,000/kg, this is an extreme case; more efficient tPA processes using CHO cell cultures have separation costs averaging $10,000/g.

A more mature, larger-scale operation is the manufacture of penicillin, the first modern antibiotic for the treatment of bacterial infections caused by gram-positive organisms. Penicillin typically sells for about $15/kg and has a market of approximately $4.5 billion/yr. Here, the processing costs represent about 60% of the total manufacturing costs, which are still much higher than those in the chemical industry. Regulatory burden to manufacture and market a drug is significantly higher than it is for a petrochemical product. Figure 1.12 is a block-flow diagram for the manufacture of penicillin, a secondary metabolite secreted by the common mold *Penicillium notatum*, which, as Alexander Fleming serendipitously observed in September 1928 in St. Mary's Hospital in London, prevents growth of the bacterium *Staphylococcus aureus* on a nutrient surface [2]. Motivated to replace sulfa drugs in World War II, Howard Florey and colleagues cultured and extracted this delicate, fragile, and unstable product to demonstrate its effectiveness. Merck, Pfizer, Squibb, and USDA Northern Regional Research Laboratory in Peoria, Illinois, undertook purification of the product in broths with original titers of only 0.001 g/L using a submerged tank process. Vessel sizes grew to 10,000 gal to produce penicillin for 100,000 patients per year by the end of World War II. Ultraviolet irradiation of *Penicillium* spores has since produced mutants of the original strain, with increased penicillin yields up to 50 g/L.

The process shown in Figure 1.12 is one of many that produces 1,850,000 kg/yr of the potassium salt of penicillin V by the fermentation of phenoxyacetic acid (a side-chain precursor), aqueous glucose, and cottonseed flour in the presence of trace metals and air. The structures of phenoxyacetic acid and penicillin V are shown in Figure 1.13. *Upstream processing* includes preparation of culture medias. It is followed, after fermentation, by *downstream processing* consisting of a



Phenoxyacetic acid



Penicillin V

Figure 1.13 Structure of penicillin V and its precursor.

number of bioseparation steps to recover and purify the penicillin and the *n*-butyl acetate, a recycled solvent used to extract the penicillin. A total of 20 steps are involved, some batch, some semicontinuous, and some continuous. Only the main steps are shown in Figure 1.12.

One upstream processing step, at 25°C, mixes the feed media, consisting of cottonseed flour, phenoxyacetic acid, water, and trace metals. The other step mixes glucose with water. These two feeds are sent to one of 10 batch fermentation vessels.

In the fermentation step, the penicillin product yield is 55 g/L, which is a dramatic improvement over the earliest yield of 0.001 g/L. Fermentation temperature is controlled at 28°C, vigorous aeration and agitation is required, and the fermentation reaction residence time is 142 hours (almost 6 days), which would be intolerable in the chemical industry. The fermentation effluent consists, by weight, of 79.3% water; 9.3% intracellular water; 1.4% unreacted cottonseed flour, phenoxyacetic acid, glucose, and trace metals; 4.5% mycelia (biomass); and only 5.5% penicillin V.

The spent mycelia (biomass), is removed using a rotary-drum vacuum filter, resulting in (following washing with water) a filter cake of 20 wt% solids and 3% of the penicillin entering the filter. Prior to the solvent-extraction step, the filtrate, which is now 6.1% penicillin V, is cooled to 2°C to minimize chemical or enzymatic product degradation, and its pH is adjusted to between 2.5 and 3.0 by adding a 10 wt% aqueous solution of sulfuric acid to enhance the penicillin partition coefficient for its removal by solvent extraction, which is extremely sensitive to pH. This important adjustment, which is common to many bioprocesses, is considered in detail in §2.9.1.

Solvent extraction is conducted in a Podbielniak centrifugal extractor (POD), which provides a very short residence time, further minimizing product degradation. The solvent is *n*-butyl acetate, which selectively dissolves penicillin V. The extract is 38.7% penicillin V and 61.2% solvent, while the raffinate contains almost all of the other chemicals in the filtrate, including 99.99% of the water. Unfortunately, 1.6% of the penicillin is lost to the raffinate.

Following solvent extraction, potassium acetate and acetone are added to promote the crystallization of the potassium salt of penicillin V (penicillin KV). A basket centrifuge with water washing then produces a crystal cake containing only 5 wt% moisture. Approximately 4% of the penicillin is lost in the crystallization and centrifugal filtration steps. The crystals are dried to a moisture content of 0.05 wt% in a fluidized-bed dryer. Not shown in Figure 1.12 are subsequent finishing steps to produce, if desired, 250 and 500 mg tablets, which may contain small amounts of lactose, magnesium stearate, povidone, starch, stearic acid, and other inactive ingredients. The filtrate from the centrifugal filtration step contains 71 wt% solvent *n*-butyl acetate, which must be recovered for recycle to the solvent extraction step. This is accomplished in the separation and purification step, which may involve distillation, adsorption, three-liquid-phase extraction, and/or solvent sublation (an adsorption-bubble technique). The penicillin process produces a number of waste streams—e.g., wastewater containing *n*-butyl acetate—that require further processing, which is not shown in Figure 1.12.

Overall, the process has only a 20% yield of penicillin V from the starting ingredients. The annual production rate is achieved by processing 480 batches that produce 3,850 kg each of the potassium salt, with a batch processing time of 212 hours. It is no wonder that bioprocesses, which involve (1) research and development costs, (2) regulatory burden, (3) fermentation residence times of days, (4) reactor effluents that are dilute in the product, and (5) multiple downstream bioseparation steps, many of which are difficult, result in high-cost biopharmaceutical products.

Alternative process steps such as direct penicillin recovery from the fermentation broth by adsorption on activated carbon, or crystallization of penicillin from amyl or butyl acetate without a water extraction, are described in the literature. Industrial processes and process conditions are proprietary, so published flowsheets and descriptions are not complete or authoritative.

Commercially, penicillin V and another form, G, are also sold as intermediates or converted, using the enzyme penicillin acylase, to 6-APA (6-aminopenicillic acid), which is further processed to make semisynthetic penicillin derivatives. Another medicinal product for treating people who are allergic to penicillin is produced by subjecting the penicillin to the enzyme penicillinase.

§1.10 SELECTION OF FEASIBLE SEPARATIONS

Only an introduction to the separation-selection process is given here. A detailed treatment is given in Chapter 8 of Seider, Seader, Lewin, and Widagdo [7]. Key factors in the selection are listed in Table 1.12. These deal with feed and product conditions, property differences, characteristics of

Table 1.12 Factors That Influence the Selection of Feasible Separation Operations

A. Feed conditions
- **1.** Composition, particularly of species to be recovered or separated
- **2.** Flow rate
- **3.** Temperature
- **4.** Pressure
- **5.** Phase state (solid, liquid, or gas)

B. Product conditions
- **1.** Required purities
- **2.** Temperatures
- **3.** Pressures
- **4.** Phases

C. Property differences that may be exploited
- **1.** Molecular
- **2.** Thermodynamic
- **3.** Transport

D. Characteristics of separation operation
- **1.** Ease of scale-up
- **2.** Ease of staging
- **3.** Temperature, pressure, and phase-state requirements
- **4.** Physical size limitations
- **5.** Energy requirements

E. Economics
- **1.** Capital costs
- **2.** Operating costs

the candidate separation operations, and economics.The most important feed conditions are composition and flow rate, because the other conditions (temperature, pressure, and phase) can be altered to fit a particular operation. However, feed vaporization, condensation of a vapor feed, or compression of a vapor feed can add significant energy costs to chemical processes. Some separations, such as those based on the use of barriers or solid agents, perform best on dilute feeds. The most important product conditions are purities because the other conditions listed can be altered by energy transfer after the separation is achieved.

Sherwood, Pigford, and Wilke [11], Dwyer [12], and Keller [13] have shown that the cost of recovering and purifying a chemical depends strongly on its concentration in the feed. Keller's correlation, Figure 1.14, shows that the more dilute the feed, the higher the product price. The five highest priced and most dilute in Figure 1.14 are all proteins.

When a very pure product is required, large differences in volatility or solubility or significant numbers of stages are needed for chemicals in commerce. For biochemicals, especially proteins, very expensive separation methods may be required. Accurate molecular and bulk thermodynamic and transport properties are also required. Data and estimation methods for the properties of chemicals in commerce are given by Poling, Prausnitz, and O'Connell [14], Daubert and Danner [15], and others.

A survey by Keller [13], Figure 1.15, shows that the degree to which a separation operation is technologically mature correlates with its commercial use. Operations based on

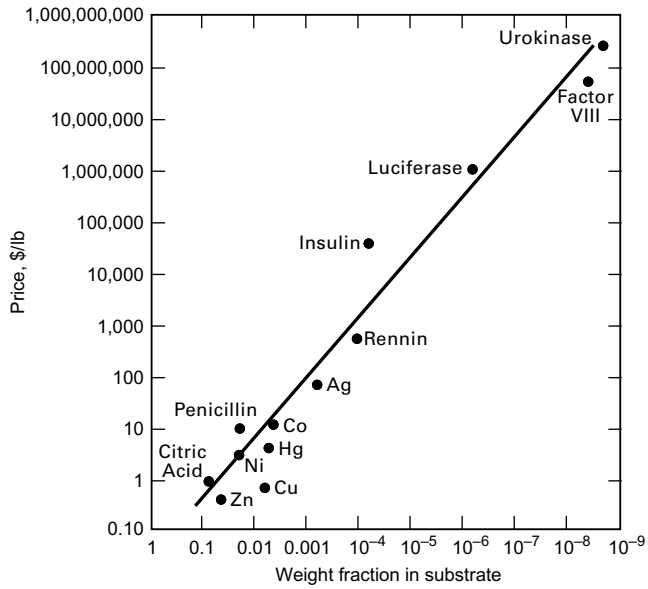


Figure 1.14 Effect of concentration of product in feed material on price [13].

barriers are more expensive than operations based on the use of a solid agent or the creation or addition of a phase. All separation equipment is limited to a maximum size. For capacities requiring a larger size, parallel units must be provided. Except for size constraints or fabrication problems, capacity of a single unit can be doubled, for an additional investment cost of about 60%. If two parallel units are installed, the additional investment is 100%. Table 1.13 lists operations ranked according to ease of scale-up. Those ranked near the top are frequently designed without the need for pilot-plant or laboratory data provided that neither the process nor the final product is new and equipment is guaranteed by vendors. For new processes, it is never certain that product specifications will be met. If there is a potential impurity, possibility of corrosion, or other uncertainties such as

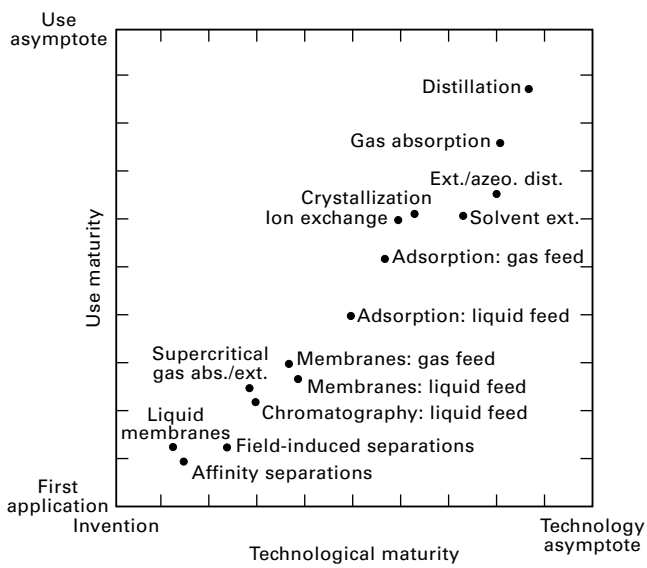


Figure 1.15 Technological and use maturities of separation processes [13].

Table 1.13 Ease of Scale-up of the Most Common Separation Operations

Operation in Decreasing Ease of Scale-up	Ease of Staging	Need for Parallel Units
Distillation	Easy	No need
Absorption	Easy	No need
Extractive and azeotropic distillation	Easy	No need
Liquid–liquid extraction	Easy	Sometimes
Membranes	Repressurization required between stages	Almost always
Adsorption	Easy	Only for regeneration cycle
Crystallization	Not easy	Sometimes
Drying	Not convenient	Sometimes

product degradation or undesirable agglomeration, a pilot-plant is necessary. Operations near the middle usually require laboratory data, while those near the bottom require pilot-plant tests.

Included in Table 1.13 is an indication of the ease of providing multiple stages and whether parallel units may be required. Maximum equipment size is determined by height limitations, and shipping constraints unless field fabrication is possible and economical. The selection of separation techniques for both homogeneous and heterogeneous phases, with many examples, is given by Woods [16]. Ultimately, the process having the lowest operating, maintenance, and capital costs is selected, provided it is controllable, safe, nonpolluting, and capable of producing products that meet specifications.

EXAMPLE 1.5 Feasible separation alternatives.

Propylene and propane are among the light hydrocarbons produced by cracking heavy petroleum fractions. Propane is valuable as a fuel and in liquefied natural gas (LPG), and as a feedstock for producing propylene and ethylene. Propylene is used to make acrylonitrile for synthetic rubber, isopropyl alcohol, cumene, propylene oxide, and polypropylene. Although propylene and propane have close boiling points, they are traditionally separated by distillation. From Figure 1.16, it is seen that a large number of stages is needed and that the reflux and boilup flows are large. Accordingly, attention has been given to replacement of distillation with a more economical and less energy-intensive process. Based on the factors in Table 1.12, the characteristics in Table 1.13, and the list of species properties given at the end of §1.2, propose alternatives to Figure 1.16.

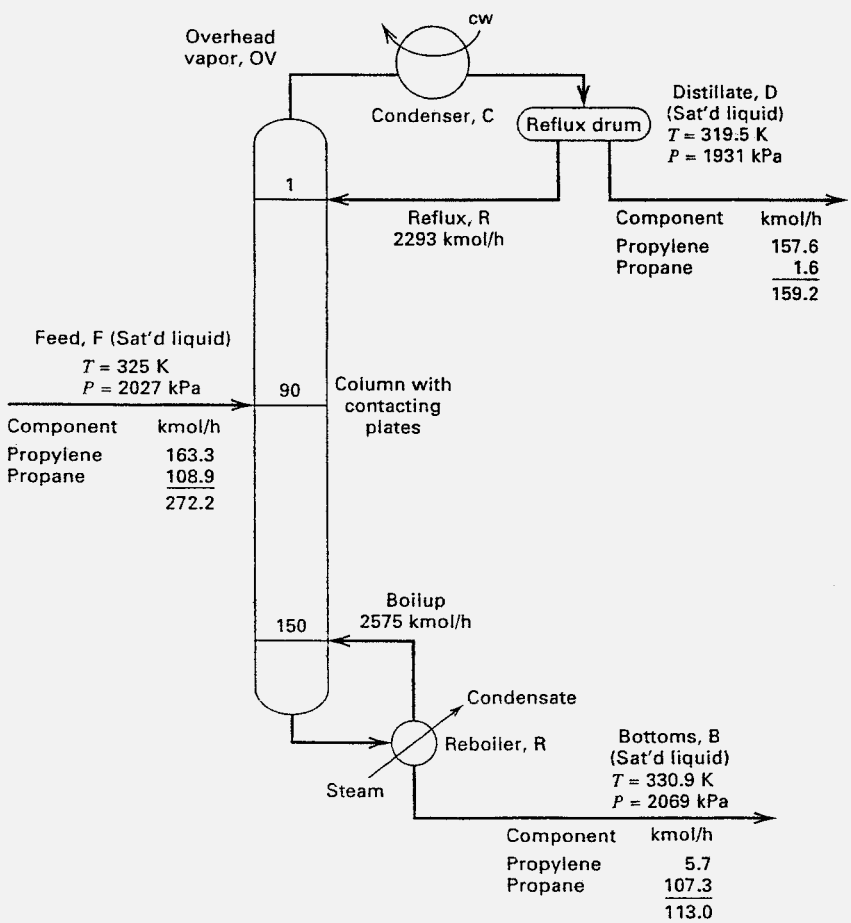


Figure 1.16 Distillation of a propylene–propane mixture.

Solution

First, verify that the component feed and product flows in Figure 1.16 satisfy (1-1), the conservation of mass. Table 1.14 compares properties taken mainly from Daubert and Danner [15]. The only listed property that might be exploited is the dipole moment. Because of the asymmetric location of the double bond in propylene, its dipole moment is significantly greater than that of propane, making propylene a weakly polar compound. Operations that can exploit this difference are:

1. Extractive distillation with a polar solvent such as furfural or an aliphatic nitrile that will reduce the volatility of propylene (Ref.: U.S. Patent 2,588,056, March 4, 1952).
2. Adsorption with silica gel or a zeolite that selectively adsorbs propylene [Ref.: *J.Am. Chem. Soc*, **72**, 1153–1157 (1950)].
3. Facilitated transport membranes using impregnated silver nitrate to carry propylene selectively through the membrane [Ref.: *Recent Developments in Separation Science*, Vol. IX, 173–195 (1986)].

Table 1.14 Comparison of Properties for Example 1.5

Property	Propylene	Propane
Molecular weight	42.081	44.096
van der Waals volume, m^3/kmol	0.03408	0.03757
van der Waals area, m^2/kmol $\times 10^{-8}$	5.060	5.590
Acentric factor	0.142	0.152
Dipole moment, debyes	0.4	0.0
Radius of gyration, m $\times 10^{10}$	2.254	2.431
Normal melting point, K	87.9	85.5
Normal boiling point, K	225.4	231.1
Critical temperature, K	364.8	369.8
Critical pressure, MPa	4.61	4.25

SUMMARY

1. Industrial chemical processes include equipment for separating chemicals in the process feed(s) and/or species produced in reactors within the process.
2. More than 25 different separation operations are commercially important.
3. The extent of separation achievable by a separation operation depends on the differences in species properties.
4. The more widely used separation operations involve transfer of species between two phases, one of which is created by energy transfer or the reduction of pressure, or by introduction as an MSA.
5. Less commonly used operations are based on the use of a barrier, solid agent, or force field to cause species to diffuse at different rates and/or to be selectively absorbed or adsorbed.
6. Separation operations are subject to the conservation of mass. The degree of separation is measured by a split fraction, SF, given by (1-2), and/or a split ratio, SR, given by (1-3).
7. For a train of separators, component recoveries and product purities are of prime importance and are related by material balances to individual SF and/or SR values.
8. Some operations, such as absorption, are capable of only a specified degree of separation for one component. Other operations, such as distillation, can effect a sharp split between two components.
9. The degree of component separation by a particular operation is indicated by a separation factor, SP, given by (1-4) and related to SF and SR values by (1-5) and (1-6).
10. Bioseparations use knowledge of cell components, structures, and functions to economically purify byproducts for use in agrichemical, pharmaceutical, and biotechnology markets.
11. For specified feed(s) and products, the best separation process must be selected from among a number of candidates. The choice depends on factors listed in Table 1.12. The cost of purifying a chemical depends on its concentration in the feed. The extent of industrial use of a separation operation depends on its technological maturity.

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STUDY QUESTIONS

1.1. What are the two key process operations in chemical engineering?

1.2. What are the main auxiliary process operations in chemical engineering?

1.3. What are the five basic separation techniques, and what do they all have in common?

1.4. Why is mass transfer a major factor in separation processes?

1.5. What limits the extent to which the separation of a mixture can be achieved?

1.6. What is the most common method used to separate two fluid phases?

1.7. What is the difference between an ESA and an MSA? Give three disadvantages of using an MSA.

1.8. What is the most widely used industrial separation operation?

1.9. What is the difference between adsorption and absorption?

1.10. The degree of separation in a separation operation is often specified in terms of component recoveries and/or product purities. How do these two differ?

1.11. What is a key component?

1.12. What is a multicomponent product?

1.13. What are the three types of bioproducts and how do they differ?

1.14. Identify the major objectives of the steps in a biopurification process.

1.15. Give examples of separation operations used for the steps in a bioprocess.

EXERCISES

Section 1.1

1.1. Fluorocarbons process.

Shreve's Chemical Process Industries, 5th edition, by George T. Austin (McGraw-Hill, New York, 1984), contains process descriptions, flow diagrams, and technical data for commercial processes. For each of the fluorocarbons processes on pages 353–355, draw a block-flow diagram of the reaction and separation steps and describe the process in terms of just those steps, giving attention to the chemicals formed in the reactor and separator.

Section 1.2

1.2. Mixing vs. separation.

Explain, using thermodynamic principles, why mixing pure chemicals to form a homogeneous mixture is a spontaneous process, while separation of that mixture into its pure species is not.

1.3. Separation of a mixture requires energy.

Explain, using the laws of thermodynamics, why the separation of a mixture into pure species or other mixtures of differing compositions requires energy to be transferred to the mixture or a degradation of its energy.

Section 1.3

1.4. Use of an ESA or an MSA.

Compare the advantages and disadvantages of making separations using an ESA versus using an MSA.

1.5. Producing ethers from olefins and alcohols.

Hydrocarbon Processing published a petroleum-refining handbook in November 1990, with process-flow diagrams and data for commercial processes. For the ethers process on page 128, list the separation operations of the type given in Table 1.1 and indicate what chemical(s) is (are) being separated.

1.6. Conversion of propylene to butene-2s.

Hydrocarbon Processing published a petrochemical handbook in March 1991, with process-flow diagrams and data for commercial processes. For the butene-2 process on page 144, list the separation operations of the type given in Table 1.1 and indicate what chemical(s) is (are) being separated.

Section 1.4

1.7. Use of osmosis.

Explain why osmosis is not an industrial separation operation.

1.8. Osmotic pressure for recovering water from sea water.

The osmotic pressure, π, of sea water is given by $\pi = RTc/M$, where c is the concentration of the dissolved salts (solutes) in g/cm^3 and M is the average molecular weight of the solutes as ions. If pure water is to be recovered from sea water at 298 K and containing 0.035 g of salts/cm^3 of sea water and $M = 31.5$, what is the minimum required pressure difference across the membrane in kPa?

1.9. Use of a liquid membrane.

A liquid membrane of aqueous ferrous ethylenediaminetetraacetic acid, maintained between two sets of microporous, hydrophobic, hollow fibers packed in a permeator cell, can selectively and continuously remove sulfur dioxide and nitrogen oxides from the flue gas of power plants. Prepare a drawing of a device to carry out such a separation. Show locations of inlet and outlet streams, the arrangement of the hollow fibers, and a method for handling the membrane

liquid. Should the membrane liquid be left in the cell or circulated? Is a sweep fluid needed to remove the oxides?

Section 1.5

1.10. Differences in separation methods.

Explain the differences, if any, between adsorption and gas–solid chromatography.

1.11. Flow distribution in a separator.

In gas–liquid chromatography, is it essential that the gas flow through the packed tube be plug flow?

Section 1.6

1.12. Electrical charge for small particles.

In electrophoresis, explain why most small, suspended particles are negatively charged.

1.13. Flow field in field-flow fractionation.

In field-flow fractionation, could a turbulent-flow field be used? Why or why not?

Section 1.7

1.14. Material balance for a distillation sequence.

The feed to Column C3 in Figure 1.8 is given in Table 1.5. The separation is to be altered to produce a distillate of 95 mol% pure isobutane with a recovery (SF) in the distillate of 96%. Because of the sharp separation in Column C3 between iC$_4$ and nC$_4$, assume all propane goes to the distillate and all C$_5$'s go to the bottoms.

(a) Compute the flow rates in lbmol/h of each component in each of the two products leaving Column C3.

(b) What is the percent purity of the *n*-butane bottoms product?

(c) If the isobutane purity in the distillate is fixed at 95%, what % recovery of isobutane in the distillate will maximize the % purity of normal butane in the bottoms product?

1.15. Material balance for a distillation sequence.

Five hundred kmol/h of liquid alcohols containing, by moles, 40% methanol (M), 35% ethanol (E), 15% isopropanol (IP), and 10% normal propanol (NP) are distilled in two distillation columns. The distillate from the first column is 98% pure M with a 96% recovery of M. The distillate from the second is 92% pure E with a 95% recovery of E from the process feed. Assume no propanols in the distillate from Column C1, no M in the bottoms from Column C2, and no NP in the distillate from Column C2.

(a) Assuming negligible propanols in the distillate from the first column, compute the flow rates in kmol/h of each component in each feed, distillate, and bottoms. Draw a labeled block-flow diagram. Include the material balances in a table like Table 1.5.

(b) Compute the mol% purity of the propanol mixture leaving as bottoms from the second column.

(c) If the recovery of ethanol is fixed at 95%, what is the maximum mol% purity of the ethanol in the distillate from the second column?

(d) If instead, the purity of the ethanol is fixed at 92%, what is the maximum recovery of ethanol (based on the process feed)?

1.16. Pervaporation to separate ethanol and benzene.

Ethanol and benzene are separated in a network of distillation and membrane separation steps. In one step, a near-azeotropic liquid mixture of 8,000 kg/h of 23 wt% ethanol in benzene is fed to a pervaporation membrane consisting of an ionomeric film of perfluorosulfonic polymer cast on a Teflon support. The membrane is selective for ethanol, so the vapor permeate contains 60 wt% ethanol, while the non-permeate liquid contains 90 wt% benzene.

(a) Draw a flow diagram of the pervaporation step using symbols from Table 1.2, and include all process information.

(b) Compute the component flow rates in kg/h in the feed stream and in the product streams, and enter these results into the diagram.

(c) What operation could be used to purify the vapor permeate?

Section 1.8

1.17. Recovery of hydrogen by gas permeation.

The Prism gas permeation process developed by the Monsanto Company is selective for hydrogen when using hollow-fiber membranes made of silicone-coated polysulphone. A gas at 16.7 MPa and 40°C, and containing in kmol/h: 42.4 H_2, 7.0 CH_4, and 0.5 N_2 is separated into a nonpermeate gas at 16.2 MPa and a permeate gas at 4.56 MPa.

(a) If the membrane is nonpermeable to nitrogen; the Prism membrane separation factor (SP), on a mole basis for hydrogen relative to methane, is 34.13; and the split fraction (SF) for hydrogen to the permeate gas is 0.6038, calculate the flow of each component and the total flow of non-permeate and permeate gas.

(b) Compute the mol% purity of the hydrogen in the permeate gas.

(c) Using a heat-capacity ratio, γ, of 1.4, estimate the outlet temperatures of the exiting streams, assuming the ideal gas law, reversible expansions, and no heat transfer between gas streams.

(d) Draw a process-flow diagram and include pressure, temperature, and component flow rates.

1.18. Nitrogen injection to recover natural gas.

Nitrogen is injected into oil wells to increase the recovery of crude oil (enhanced oil recovery). It mixes with the natural gas that is produced along with the oil. The nitrogen must then be separated from the natural gas. A total of 170,000 SCFH (based on 60°F and 14.7 psia) of natural gas containing 18% N_2, 75% CH_4, and 7% C_2H_6 at 100°F and 800 psia is to be processed so that it contains less than 3 mol% nitrogen in a two-step process: (1) membrane separation with a nonporous glassy polyimide membrane, followed by (2) pressure-swing adsorption using molecular sieves highly selective for $N_2\left(SP_{N_2,CH_4} = 16\right)$ and completely impermeable to ethane. The pressure-swing adsorption step selectively adsorbs methane, giving 97% pure methane in the adsorbate, with an 85% recovery of CH_4 fed to the adsorber. The non-permeate (retentate) gas from the membrane step and adsorbate from the pressure-swing adsorption step are combined to give a methane stream that contains 3.0 mol% N_2. The pressure drop across the membrane is 760 psi. The permeate at 20°F is compressed to 275 psia and cooled to 100°F before entering the adsorption step. The adsorbate, which exits the adsorber during regeneration at 100°F and 15 psia, is compressed to 800 psia and cooled to 100°F before being combined with non-permeate gas to give the final pipeline natural gas.

(a) Draw a flow diagram of the process using appropriate symbols. Include compressors and heat exchangers. Label the diagram with the data given and number all streams.

(b) Compute component flow rates of N_2, CH_4, and C_2H_6 in lbmol/h in all streams and create a material-balance table similar to Table 1.5.

1.19. Distillation sequences.

The feed stream in the table below is to be separated into four nearly pure products. None of the components is corrosive and, based on the boiling points, none of the three separations is difficult. As seen in Figure 1.9, five distillation sequences are possible. (a) Determine a suitable sequence of three columns using the heuristics of §1.7. (b) If a fifth component were added to give five products, Table 1.8 indicates that 14 alternative distillation sequences are possible. Draw, in a manner similar to Figure 1.9, all 14 of these sequences.

Component	Feed rate, kmol/h	Normal boiling point, K
Methane	19	112
Benzene	263	353
Toluene	85	384
Ethylbenzene	23	409

Section 1.9

1.20. Bioproduct separations.

Current and future pharmaceutical products of biotechnology include proteins, nucleic acids, and viral gene vectors. Example 1.4 identified five physical and biochemical features of these biological species by which they could be distinguished in a bioseparation; identified a bioseparation operation that could be used to selectively remove or retain each species from a mixture of the other two; and summarized important considerations in maintaining the activity of each species that would constrain the operating parameters of each bioseparation. Extend that example by listing the purity requirements for FDA approval of each of these three purified species as a parenteral product, which is one that is introduced into a human organism by intravenous, subcutaneous, intramuscular, or intramedullary injection.

1.21. Separation processes for bioproducts from *E. coli*.

Recombinant protein production from *E. coli* resulted in the first products from biotechnology. (a) List the primary structures and components of *E. coli* that must be removed from a fermentation broth to purify a heterologous protein product (one that differs from any protein normally found in the organism in question) expressed for pharmaceutical use. (b) Identify a sequence of steps to purify a conjugate heterologous protein (a compound comprised of a protein molecule and an attached non-protein prosthetic group such as a carbohydrate) that remained soluble in cell paste. (c) Identify a separation operation for each step in the process and list one alternative for each step. (d) Summarize important considerations in establishing operating procedures to preserve the activity of the protein. (e) Suppose net yield in each step in your process was 80%. Determine the overall yield of the process and the scale of operation required to produce 100 kg per year of the protein at a titer of 1 g/L.

1.22. Purification process for adeno-associated viral vector.

An AAV viral gene vector must be purified from an anchorage-dependent cell line. Repeat Exercise 1.21 to develop a purification process for this vector.

Section 1.10

1.23. Separation of a mixture of ethylbenzene and xylenes.

Mixtures of ethylbenzene (EB) and the three isomers (ortho, meta, and para) of xylene are available in petroleum refineries.

(a) Based on differences in boiling points, verify that the separation between *meta*-xylene (MX) and *para*-xylene (PX) by distillation is more difficult than the separations between EB and PX, and MX and *ortho*-xylene (OX).

(b) Prepare a list of properties for MX and PX similar to Table 1.14. Which property differences might be the best ones to exploit in order to separate a mixture of these two xylenes?

(c) Explain why melt crystallization and adsorption are used commercially to separate MX and PX.

1.24. Separation of ethyl alcohol and water.

When an ethanol–water mixture is distilled at ambient pressure, the products are a distillate of near-azeotropic composition (89.4 mol % ethanol) and a bottoms of nearly pure water. Based on differences in certain properties of ethanol and water, explain how the following operations might be able to recover pure ethanol from the distillate: (a) Extractive distillation. (b) Azeotropic distillation. (c) Liquid–liquid extraction. (d) Crystallization. (e) Pervaporation. (f) Adsorption.

1.25. Removal of ammonia from water.

A stream of 7,000 kmol/h of water and 3,000 parts per million (ppm) by weight of ammonia at 350 K and 1 bar is to be processed to remove 90% of the ammonia. What type of separation would you use? If it involves an MSA, propose one.

1.26. Separation by a distillation sequence.

A light-hydrocarbon feed stream contains 45.4 kmol/h of propane, 136.1 kmol/h of isobutane, 226.8 kmol/h of *n*-butane, 181.4 kmol/h of isopentane, and 317.4 kmol/h of *n*-pentane. This stream is to be separated by a sequence of three distillation columns into four products: (1) propane-rich, (2) isobutane-rich, (3) *n*-butane-rich, and (4) combined pentanes-rich. The first-column distillate is the propane-rich product; the distillate from Column 2 is the isobutane-rich product; the distillate from Column 3 is the *n*-butane-rich product; and the combined pentanes are the Column 3 bottoms. The recovery of the main component in each product is 98%. For example, 98% of the propane in the process feed stream appears in the propane-rich product.

(a) Draw a process-flow diagram similar to Figure 1.8.

(b) Complete a material balance for each column and summarize the results in a table similar to Table 1.5. To complete the balance, you must make assumptions about the flow rates of: (1) isobutane in the distillates for Columns 1 and 3 and (2) *n*-butane in the distillates for Columns 1 and 2, consistent with the specified recoveries. Assume that there is no propane in the distillate from Column 3 and no pentanes in the distillate from Column 2.

(c) Calculate the mol% purities of the products and summarize your results as in Table 1.7, but without the specifications.

1.27. Removing organic pollutants from wastewater.

The need to remove organic pollutants from wastewater is common to many industrial processes. Separation methods to be considered are: (1) adsorption, (2) distillation, (3) liquid–liquid extraction, (4) membrane separation, (5) stripping with air, and (6) stripping with steam. Discuss the advantages and disadvantages of each method. Consider the fate of the organic material.

1.28. Removal of VOCs from a waste gas stream.

Many waste gas streams contain volatile organic compounds (VOCs), which must be removed. Recovery of the VOCs may be accomplished by (1) absorption, (2) adsorption, (3) condensation, (4) freezing, (5) membrane separation, or (6) catalytic oxidation. Discuss the pros and cons of each method, paying particular attention to the fate of the VOC. For the case of a stream containing 3 mol% acetone in air, draw a flow diagram for a process based on

absorption. Choose a reasonable absorbent and include in your process a means to recover the acetone and recycle the absorbent.

1.29. Separation of air into nitrogen and oxygen.

Describe three methods suitable for the separation of air into nitrogen and oxygen.

1.30. Separation of an azeotrope.

What methods can be used to separate azeotropic mixtures of water and an organic chemical such as ethanol?

1.31. Recovery of magnesium sulfate from an aqueous stream.

An aqueous stream contains 5% by weight magnesium sulfate. Devise a process, and a process-flow diagram, for the production of dry magnesium sulfate heptahydrate crystals from this stream.

1.32. Separation of a mixture of acetic acid and water.

Explain why the separation of a stream containing 10 wt% acetic acid in water might be more economical by liquid–liquid extraction with ethyl acetate than by distillation.

1.33. Separation of an aqueous solution of bioproducts.

Clostridium beijerinckii is a gram-positive, rod-shaped, motile bacterium. Its BA101 strain can ferment starch from corn to a mixture of acetone (A), *n*-butanol (B), and ethanol (E) at 37°C under anaerobic conditions, with a yield of more than 99%. Typically, the molar ratio of bioproducts is 3(A):6(B):1(E). When a semidefined fermentation medium containing glucose or maltodextrin supplemented with sodium acetate is used, production at a titer of up to 33 g of bioproducts per liter of water in the broth is possible. After removal of solid biomass from the broth by centrifugation, the remaining liquid is distilled in a sequence of distillation columns to recover: (1) acetone with a maximum of 10% water; (2) ethanol with a maximum of 10% water; (3) *n*-butanol (99.5% purity with a maximum of 0.5% water); and (4) water (W), which can be recycled to the fermentation reactor. If the four products distill according to their normal boiling points in °C of 56.5 (A), 117 (B), 78.4 (E), and 100 (W), devise a suitable distillation sequence using the heuristics of §1.7.3.

Answers to Selected Exercises

Chapter 1
1.8 2,750 kPa
1.14(b) 80.8%
1.15(b) 96.08%
1.17(b) 98.8%

Chapter 2
2.1 2,060 kJ/h
2.2 924,000 Btu/h
2.3(e) 3.05%
2.4(b) 4,883,000 Btu/h
2.7(b) 0.00257
2.13 427 kg/m^3

Chapter 3
3.2 991 lb/day
3.4(a) 2,260 h
3.8(a) 1.91×10^{-7} mol/s-cm^2
3.14 0.218 cm
3.17 2.1×10^{-5} cm^2/s
3.20(c) 169,500 h
3.23 54 h
3.24(a) 3.4×10^{-5} cm^2/s
3.27 4.4 cm
3.29(a) 2.54×10^{-4} kmol/s-m^2
3.30 3.73 m
3.31(d) 380 s
3.33 3.44×10^{-5} kmol/s-m^2
3.36(b) 4.08 s
3.38(b) 1.24×10^{-4} mol/s-cm^2-atm

Chapter 4
4.1(c) $4C + 10$
4.3(d) $C + 3$
4.11 4
4.12(b) 196 kJ/kg of feed
4.27 126 psia
4.31 211°F
4.37(c) 65% of nC$_8$
4.39(a) −61°F
4.46(a) 4.4 kg, **(b)** 504 kg
4.55 2,500 lb/h of crystals
4.57 3,333 kg/h of crystals
4.60 3,800 kg added water
4.65 99.96%
4.67 97.73%
4.71(a) 3,565 kg/h

Chapter 5
5.4(b) 98.8%
5.8(c) 85.5%
5.9(e) 13.1 g
5.10(b) 74.3%, **(e)** 100%
5.11(d) 1,748 kg
5.14(b) 7,169 kg/h
5.15(b) 2,766 kg/h
5.17 165 lbmol/h
5.23 Need 5 more specs
5.29 Need 5 more specs
5.31 $N_D = 19$
5.33(c) $2(N + M) + C + 16$
5.35(c) $2(N + M) + C + 15$

Chapter 6
6.7(a) 1.74
6.9(b) 9–10 stages
6.11 0.005 ppm DCA
6.16(b) 375,000 gpm
6.18 3.56 ft
6.20(b) 0.23 psi/tray
6.21(c) 76%
6.23(d) 6.4%
6.27(b) 2.53 m
6.33 1.61 ft^3
6.35(b) 3.57
6.37(a) 1.70, **(b)** 0.01736,
(c) 7.5, **(d)** 8.7, **(e)** 16 ft

Chapter 7
7.9(a) 90.4%, **(c)** 8
7.13(b) 10 + reboiler
7.14 0.90 and 0.28 for benzene
7.15(b) 43.16 kmol/h
7.21 8 + reboiler
7.23 20 stages + reboiler, feed at 17 from top
7.25 63.49 kmol
7.27 9–10 trays + reboiler
7.29(d) 26 plates + reboiler
7.31(b) 4 + reboiler
7.33(c) 8
7.35 32 + reboiler, feeds at 17 and 27 from the top
7.39 102 + reboiler
7.41(d) 77.4%
7.47(a) 14.7 and 21.2 ft
7.51(c) 42.5 ft, **(d)** 32 ft
7.53(a) 3.8 ft, **(e)** 0.11 psia

Chapter 8
8.11(a) 233 kg/h, **(b)** 5
8.13 2.5 stages
8.15 5 stages

8.17 5 stages
8.23(b) 64 kg/h, **(c)** 142,000 kg/h
8.27(a) 1.66
8.29 139,000 lb/h
8.31(a) 0.32 mm, **(c)** 1,234 ft^2/ft^3
8.33(a) 81 rpm, **(b)** 5.6 Hp,
(c) 0.53 mm, **(d)** 2,080 ft^2/ft^3,
(e) 0.202 ft/h, **(f)** 26.3, **(h)** 96.8%

Chapter 9
9.4 28.3 stages
9.5(a) 7.1, **(b)** 5.3, **(c)** 2.3
9.7 8.4 stages
9.11 272.8 kmol/h reflux rate
9.17(c) 1.175, **(e)** 6 or 7 from top
9.24 65 kmol/h

Chapter 10
10.4 0.3674, 0.2939, 0.1917
10.5 −16.67, −33.333, −33.333, −33.333, −33.333
10.9(a) 1.0, 4.0
10.10(a) 0.2994, 0.9030
10.12 $x_1 = -2.62161$, $x_2 = 3.72971$
10.21 Stage 8 or 9
10.23 Reb. duty = 1,014,000 Btu/h
10.25 Cond. duty = 1,002,000 Btu/h
10.27 Reb. duty = 3,495,000 Btu/h
10.33 14.00
10.41 Reb. duty = 4,470,000 Btu/h
10.43 5 to 6 stages

Chapter 11
11.9 57 stages, 70 mol/s solvent, 7 ft diam. for extractive colm.
11.16 100 stages, 115 kmol/h methanol, $R = 10$

Chapter 12
12.17(a) 15, **(b)** 20 trays
12.18(a) 24, feed to stage 20 from the condenser
12.19 23 m above, 4 m below

Chapter 13
13.1(b) 29.9 wt% distilled
13.3 57.9 moles
13.7 2.14 h
13.9 0, 0.571 isopropanol
13.10 35 lbmol
13.11 0.549 kmol distilled
13.13(a) 9 stages
13.15(a) 7.28 h
13.16(a) 4.60 h
13.23 0.695 and 0.498 for A
13.27(a) 22.8 h, **(b)** 50.6 lbmol
13.30 26, 8, 26, 40 kmol
13.31 26.6, 48.4, 25 kmol

Chapter 14
14.3 48,800 m^2, 281 kmol/h
14.5 2 mm
14.7 41,700 m^3/m^2-day
14.11 Case 1, 195 m^2/stage, permeate = 60 lbmol/h
14.14 545 m^2, 65% recovery
14.16 73 amp/m^2, 25.6 amp
14.18 75% recovery for Des. 2
14.20 548,000 ft^2
14.22 197,000 ft^2 for crossflow
14.24 EtOH permeance = 4.62×10^{-5} kmol/h-m^2-mm Hg
14.30 141 cartridges/stage

Chapter 15
15.1(a) 0.369 cm^3/g, **(b)** 2.5 g/cm^3, 47.6 angstroms
15.3(b) 0.87
15.4 52.1 m^2/g
15.5 5.35 meq/g
15.13(b) 0.15
15.15 4,170 kg dry resin
15.16 0.0741 m/s and 170.1 J/m^2-s-K
15.19 0.0054 cm^2/s
15.22 0.045, 0.24, 2×10^{-5}
15.26(a) 0.66 g/L, **(b)** 12.2 h
15.27(c) 1,845 h
15.29 13.8 days
15.30 279 days
15.31 679 min ideal, 451 min actual, 2.6 ft
15.32 84 cannisters
15.39(a) 21,850 kg/h, **(b)** 10
15.41 660 s, 1,732 s

Chapter 16
16.2(c) 130,600 kg/d water
16.3 90.44% recovery
16.4 10 stages total
16.5(a) 88.54%, **(b)** 76.6%
16.6 2 washing stages
16.12 42.2 minutes
16.15 17.9 h

Chapter 17
17.1(a) 0.696, **(b)** 0.727
17.5 0.579, 0.911, 0.132, 0.272 mm
17.9 1,442 lb/h
17.10 1,320 lb/h
17.11 1,490 lb/h, 44.6 tons/day
17.12 0.512
17.13 257°F
17.17 1.007
17.22 87 m^2
17.23(a) 4.84 tons/h, **(c)** 43 units
17.24(a) 1,777 kg/h, **(b)** 1.22 mm
17.25(c) 4.96 m^3
17.26(f) 3.9×10^{10} crystals/h
17.27(b) 0.0647 micron/s
17.29(c) 0.705 micron
17.34 0.0079
17.36 1,350 tubes, 14.2 h
17.37 101°C, 93%
17.39(a) 44°F, **(e)** 29,100 lb/h
17.41(c) 330 ft^2 each

Chapter 18
18.15(a) 0.0158 lb/lb, **(d)** 1.22%
18.16(a) 127.5°F, **(c)** 3.69%,
(e) 2.262 lb/lb, **(i)** 1.73 psia
18.17(a) 0.048 mol/mol, **(c)** 44.3%,
(d) 41.7%, **(e)** 10.4 ft^3/lb
18.18(a) 0.041 atm, **(c)** 22.2% **(d)** 0.037
18.19 0.21 lb/lb, 112°F, 118°F, 1.908
18.21(a) 151°F, **(d)** 158°F
18.23 2.48 lb/lb
18.25(a) 0.194 lb/lb, **(c)** 0.425 lb/lb
18.27(d) 70.9 h
18.29(b) 0.154 h
18.31 530 minutes
18.33(d) 1.8×10^{-6} cm^2/s
18.36(c) 30,200 Btu/h
18.37(a) 13.6, **(c)** 832
18.39(c) 1,782 lb/h
18.41 18.1% average
18.43 11.5 ft diameter

Chapter 19
19.1(b) 0.0839 m/s
19.3 5.5 μm for yeast
19.5 4.4 ft
19.7 43 s
19.9 88.7% of particles
19.12 42 ft^2
19.13(a) 114 ft^2
19.16 26.9 minutes
19.17 27.2 m^2
19.19 0.29 gpm
19.21 83.7% for $W = 1$
19.23 1.30 M

Index