15.1 Industrial Products and the Microorganisms That Make Them

- *Industrial microbiology*
  - Uses microorganisms, typically grown on a large scale, to produce products or carry out chemical transformation
  - Originated with alcoholic fermentation processes
    - Later on, processes such as production of pharmaceuticals, food additives, enzymes, and chemicals were developed
  - Major organisms used are fungi and *Streptomyces*
  - Classic methods are used to select for high-yielding microbial variants

15.1 Industrial Products and the Microorganisms That Make Them

- Properties of a useful industrial microbe include
  - Produces spores or can be easily inoculated
  - Grows rapidly on a large scale in inexpensive medium
  - Produces desired product quickly
  - Should not be pathogenic
  - Amenable to genetic manipulation

15.1 Industrial Products and the Microorganisms That Make Them

- Microbial products of industrial interest include
  - Microbial cells
  - Enzymes
  - Antibiotics, steroids, alkaloids
  - Food additives
  - *Commodity chemicals*
    - Inexpensive chemicals produced in bulk
    - Include ethanol, citric acid, and many others

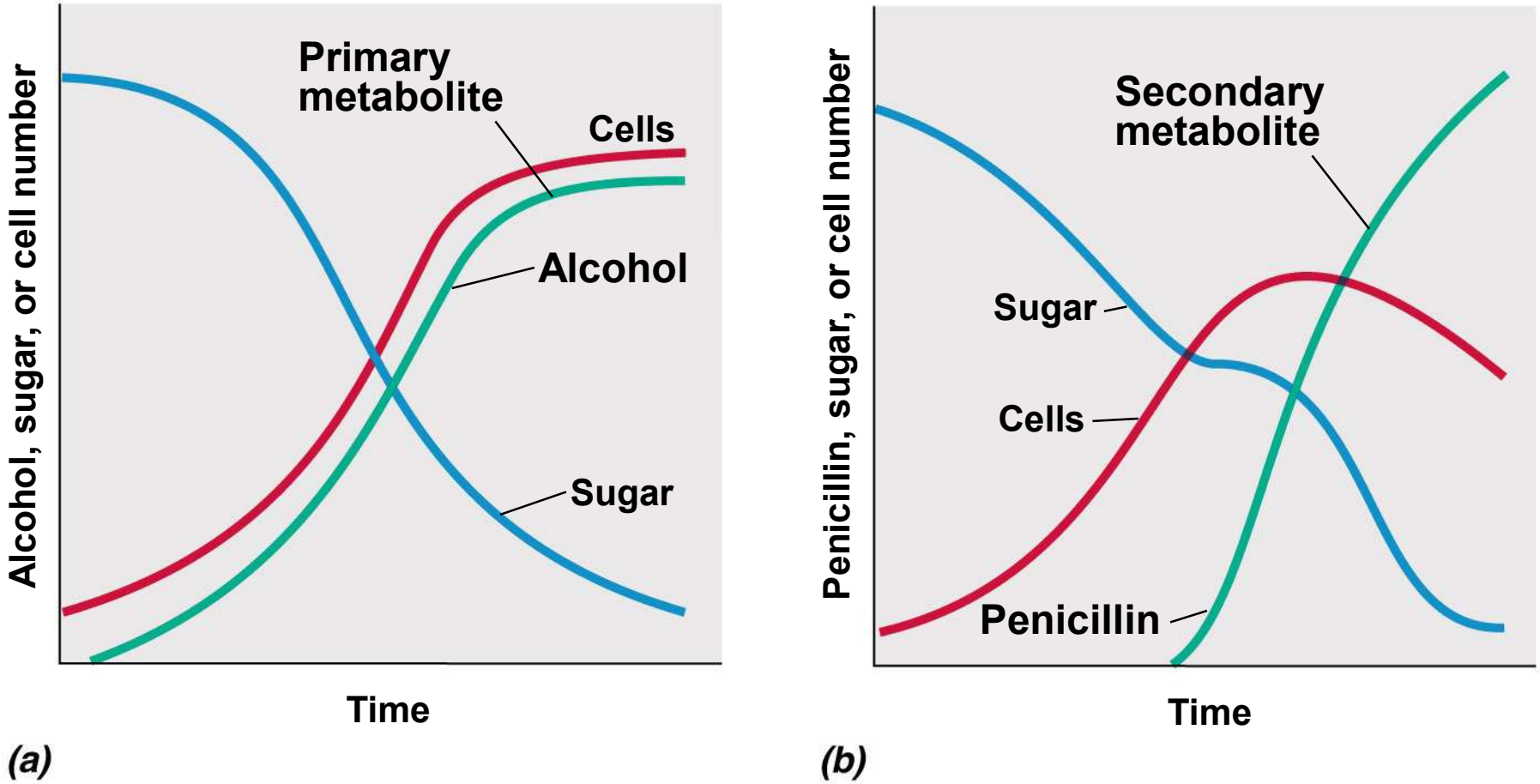
15.2 Production and Scale

- *Primary metabolite*
  - Produced during exponential growth
  - Example: alcohol
- *Secondary metabolite*
  - Produced during stationary phase

15.2 Production and Scale

- *Secondary metabolites*
  - Not essential for growth
  - Formation depends on growth conditions
  - Produced as a group of related compounds
  - Often significantly overproduced
  - Often produced by spore-forming microbes during sporulation

Figure 15.1



15.2 Production and Scale

- Secondary metabolites are often large organic molecules that require a large number of specific enzymatic steps for production
  - Synthesis of tetracycline requires at least 72 separate enzymatic steps
  - Starting materials arise from major biosynthetic pathways

15.2 Production and Scale

- *Fermentor* is where the microbiology process takes place (Figure 15.2a and b)
- Any large-scale reaction is referred to as a fermentation
  - Most are aerobic processes
- Fermentors vary in size from 5 to 500,000 liters
  - Aerobic and anaerobic fermentors
- Large-scale fermentors are almost always stainless steel
  - Impellers and spargers supply oxygen (Figure 15.2c)

Figure 15.2a

Queue Systems, Inc.

(a)

Figure 15.2b

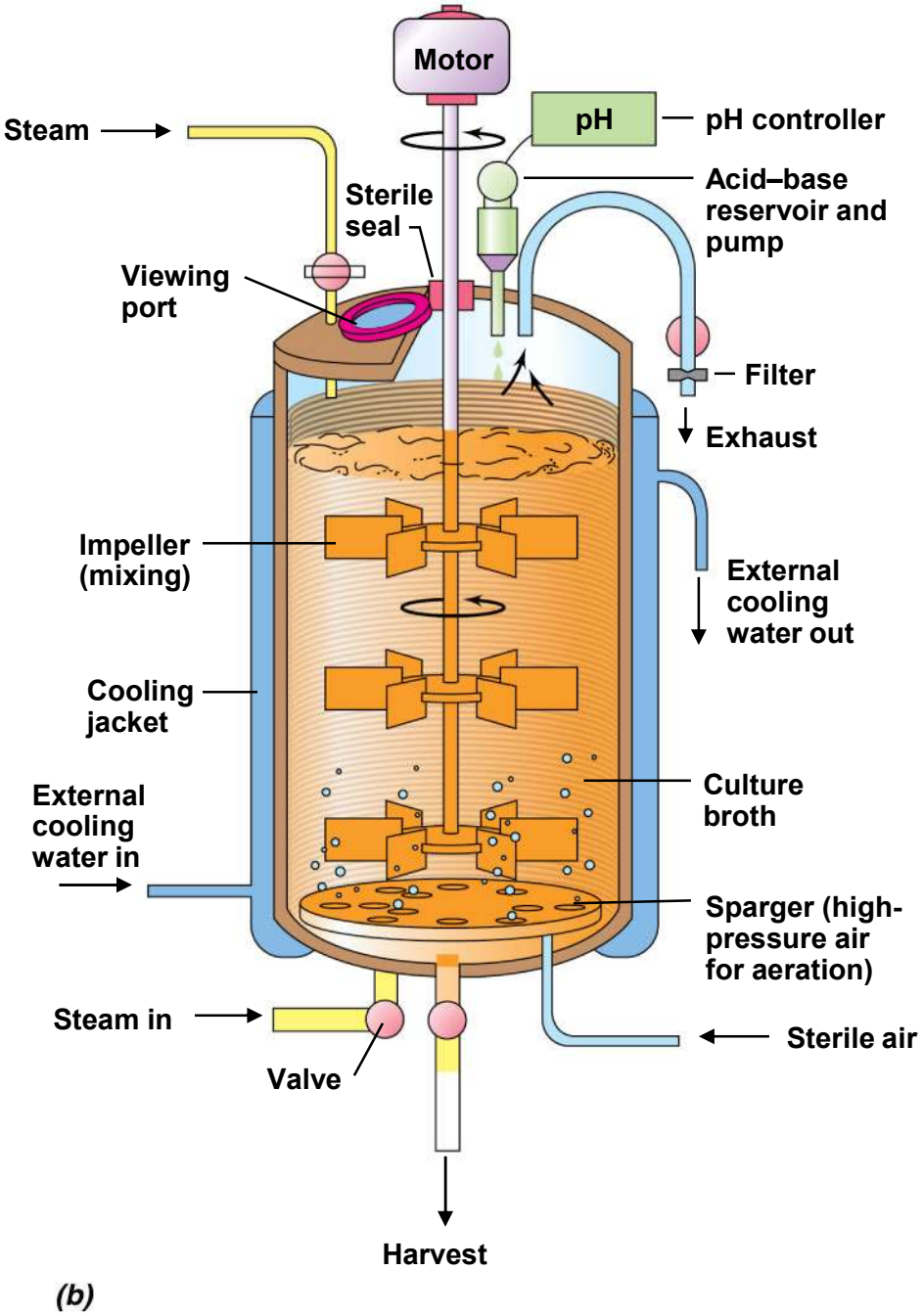


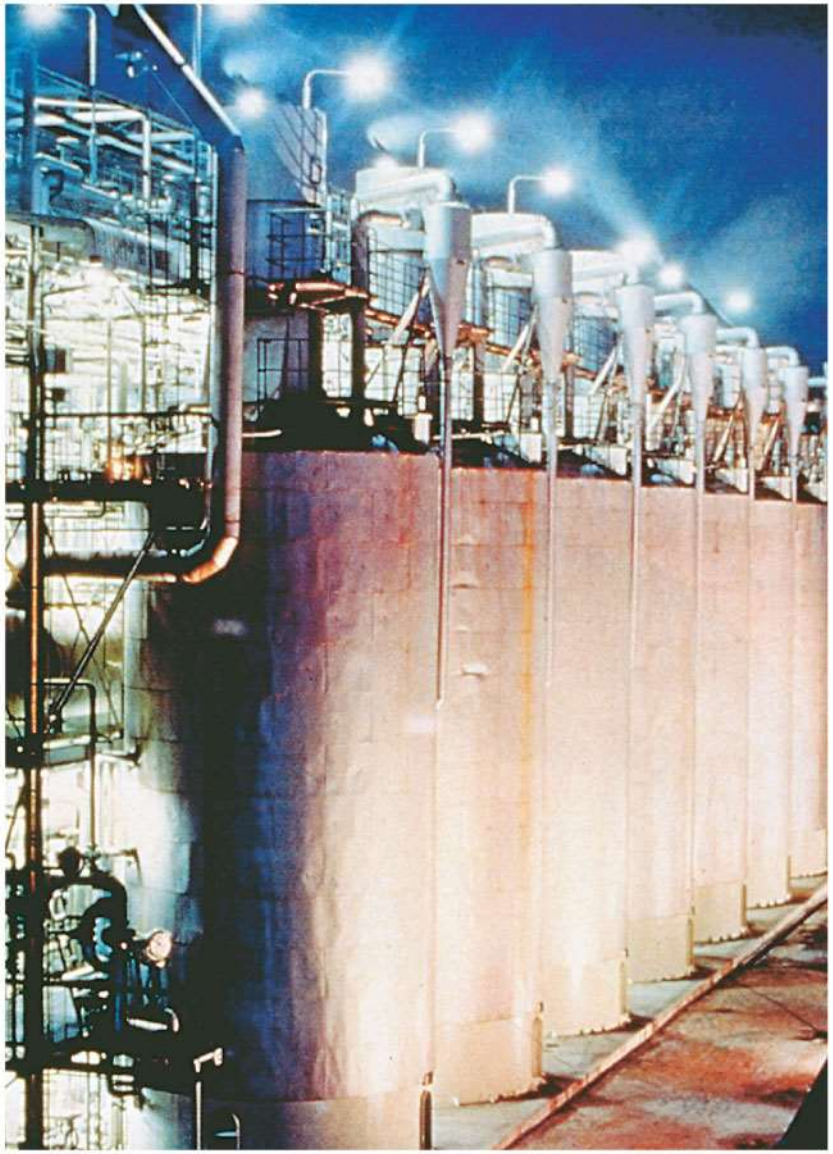
Figure 15.2c

(c)

Figure 15.3

Elmer L. Gaden, Jr.

(a)



Elmer L. Gaden, Jr.

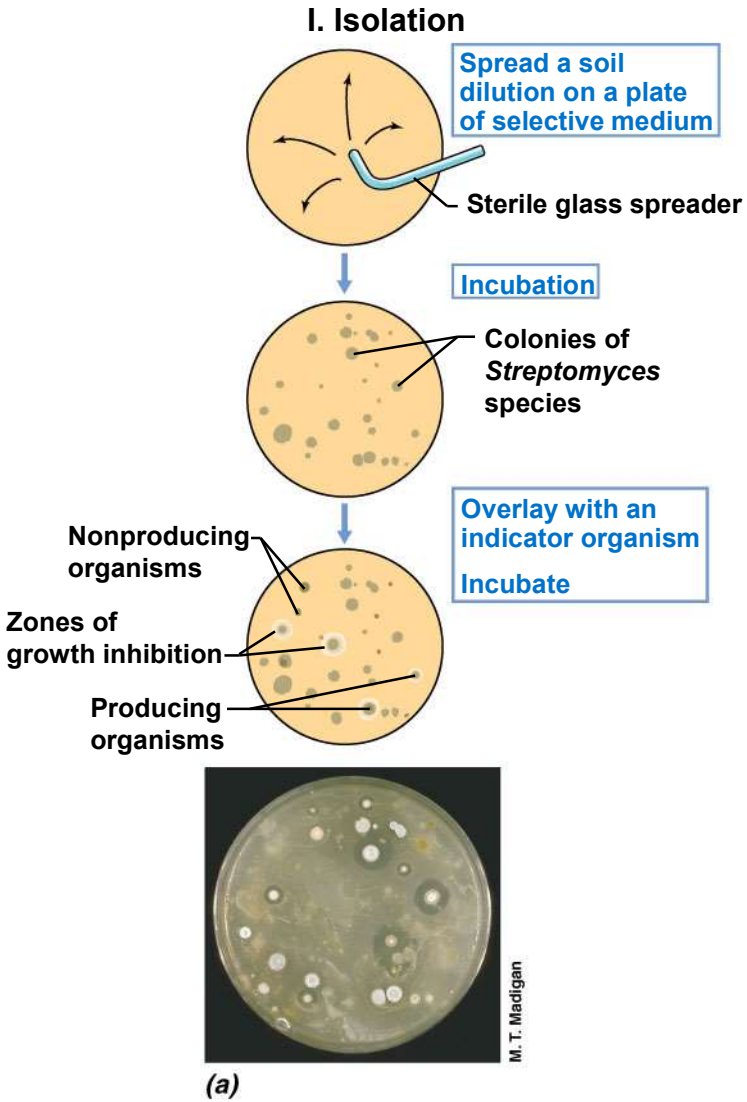
(b)

15.3 Antibiotics: Isolation, Yield, and Purification

- *Antibiotics*
  - Compounds that kill or inhibit the growth of other microbes
  - Typically secondary metabolites
  - Most antibiotics in clinical use are produced by filamentous fungi or actinomycetes
  - Still discovered by laboratory screening (Figure 15.4a)
    - Microbes are obtained from nature in pure culture
    - Assayed for products that inhibit growth of test bacteria

Animation: Isolation and Screening of Antibiotic Producers

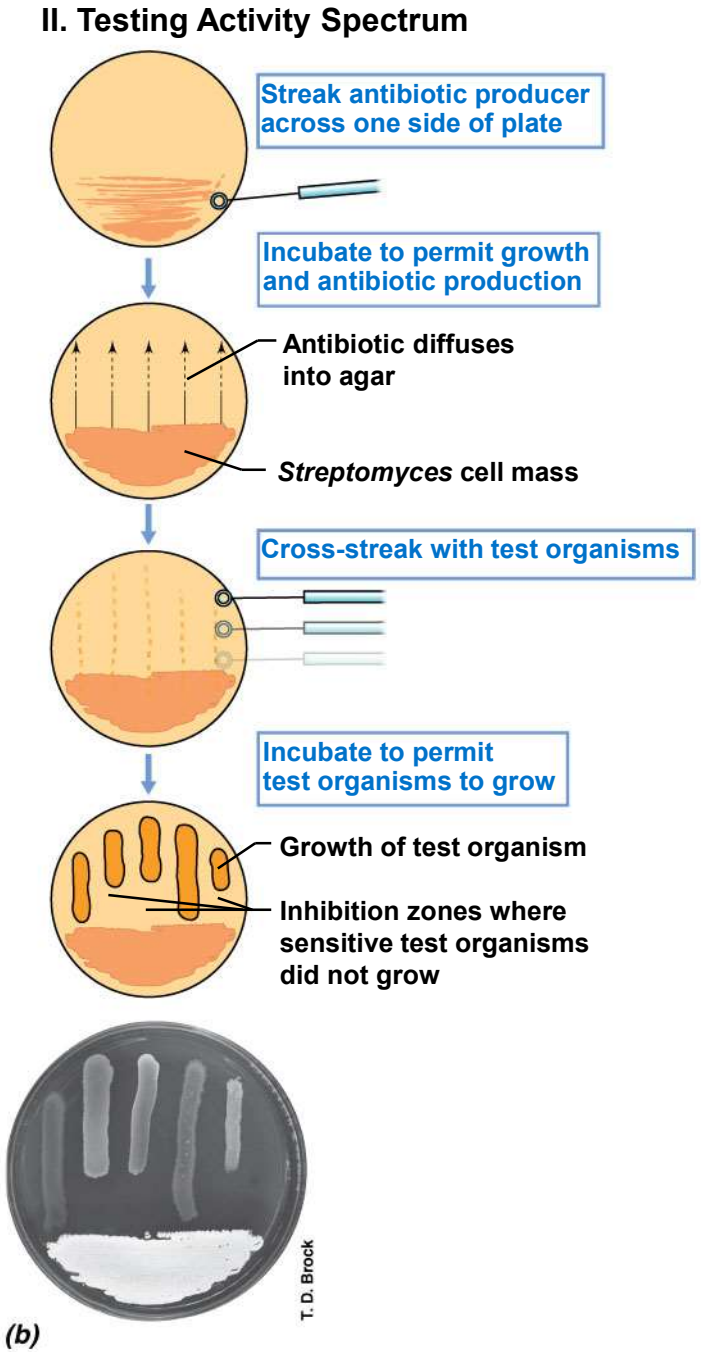
Figure 15.4a



15.3 Antibiotics: Isolation, Yield, and Purification

- *Cross-streak method* (Figure 15.4b)
  - Used to test new microbial isolates for antibiotic production
  - Most isolates produce known antibiotics
  - Most antibiotics fail toxicity and therapeutic tests in animals
  - Time and cost of developing a new antibiotic is approximately 15 years and $1 billion
    - Involves clinical trials and U.S. FDA approval
- Antibiotic purification and extraction often involves elaborate methods

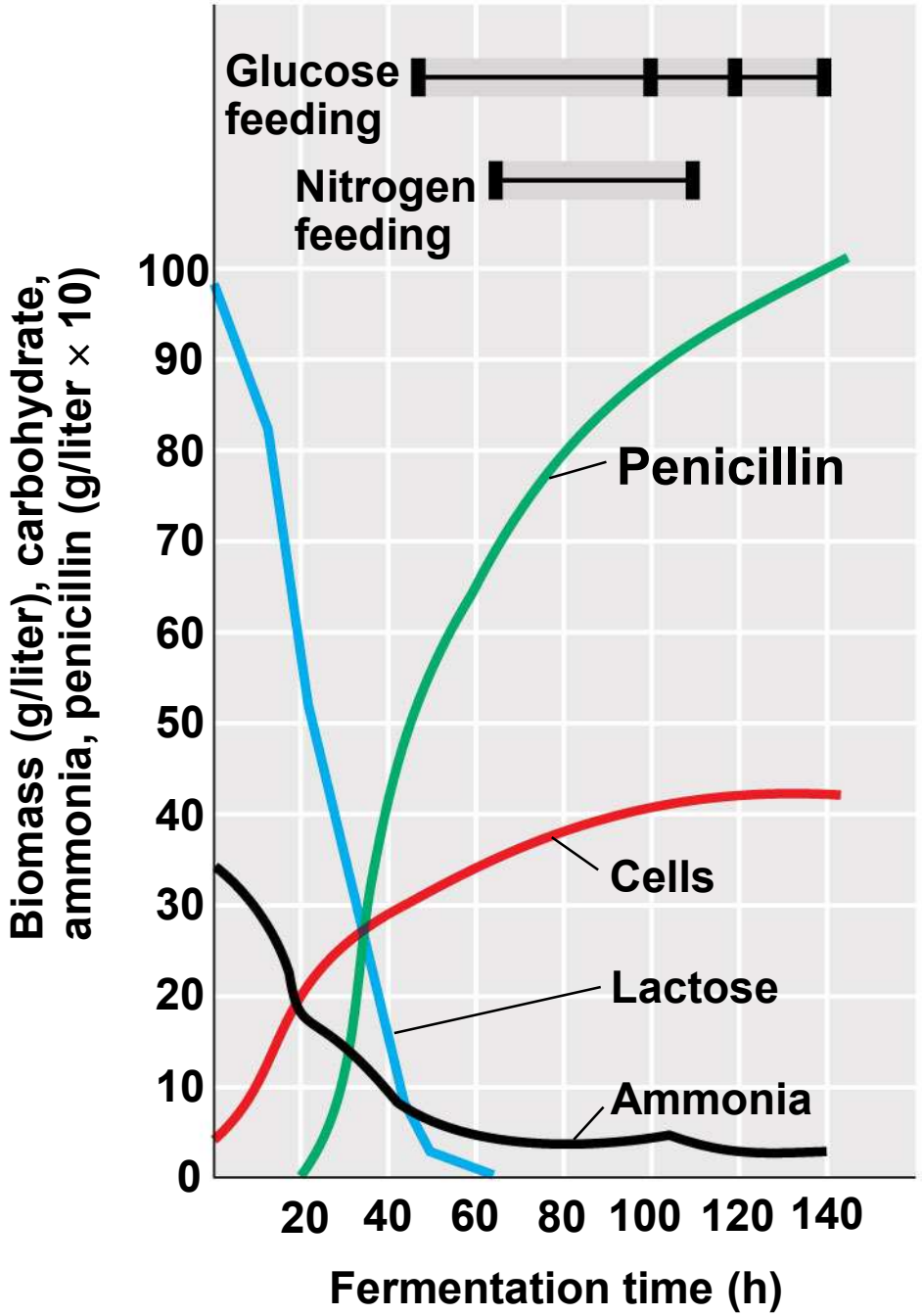
Figure 15.4b



15.4 Industrial Production of Penicillins and Tetracyclines

- Penicillins are *β-lactam antibiotics*
  - *Natural* and *biosynthetic penicillins* (Figure 15.5)
  - *Semisynthetic penicillins*
    - *Broad spectrum* of activity
- Penicillin production is typical of a secondary metabolite
  - Production only begins after near-exhaustion of carbon source (Figure 15.6)
  - High levels of glucose repress penicillin production

Figure 15.6



15.4 Industrial Production of Penicillins and Tetracyclines

- Biosynthesis of tetracycline has a large number of enzymatic steps
  - More than 72 intermediates
  - More than 300 genes involved!
  - Complex biosynthetic regulation (Figure 15.7)

15.5 Vitamins and Amino Acids

- Production of vitamins is second only to antibiotics in terms of total pharmaceutical sales
  - Vitamin B_{12} produced exclusively by microorganisms (Figure 15.8a)
    - Deficiency results in *pernicious anemia*
    - Cobalt is present in B_{12}
  - Riboflavin can also be produced by microbes (Figure 15.8b)

15.5 Vitamins and Amino Acids

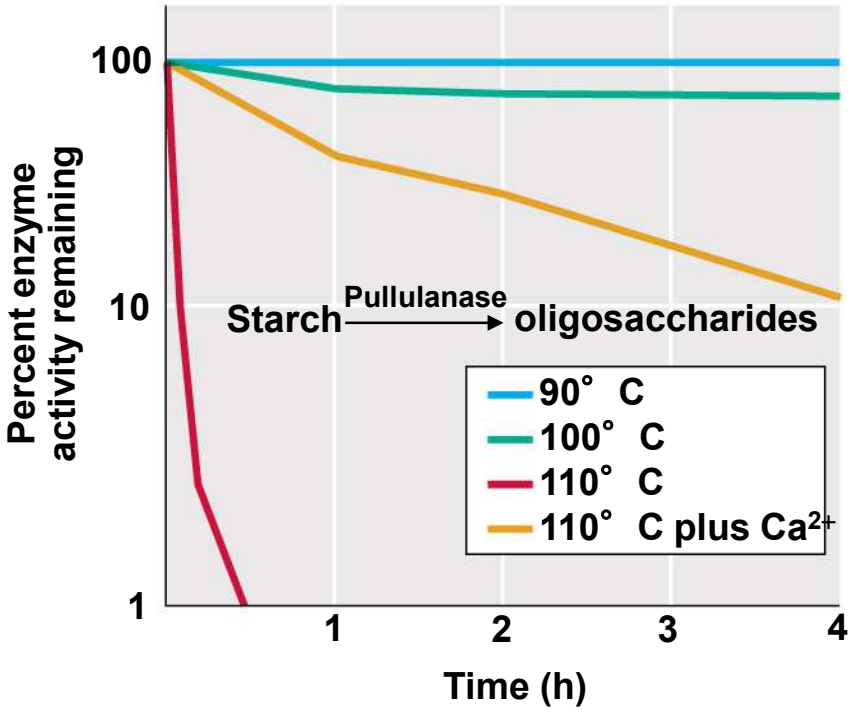
- *Amino acids*
  - Used as feed additives in the food industry
  - Used as nutritional supplements in nutraceutical industry
  - Used as starting materials in the chemical industry
  - Examples include
    - Glutamic acid (MSG)
    - Aspartic acid and phenylalanine (aspartame [NutraSweet])
    - Lysine (food additives; Figure 15.9)

15.6 Enzymes as Industrial Products

- Exoenzymes
  - Enzymes that are excreted into the medium instead of being held within the cell; they are extracellular
  - Can digest insoluble polymers such as cellulose, protein, and starch
- Enzymes are useful as industrial catalysts
  - Produce only one stereoisomer
  - High substrate specificity

Figure 15.10

(a)



(b)

III. Alcoholic Beverages and Biofuels

- 15.7 Wine
- 15.8 Brewing and Distilling
- 15.9 Biofuels

15.10 Wine

- Most wine is made from grapes
- Wine fermentation occurs in fermentors ranging in size from 200 to 200,000 liters
  - Fermentors are made of oak, cement, glass-lined steel, or stone (Figure 15.12b, c, and d)
- White wine is made from white grapes or red grapes that have had their skin removed (Figure 15.13)
- Red wine is aged for months or years
- White wine is often sold without aging

Figure 15.12b

(b)

The Christian Brothers Winery

Figure 15.12c

(c)

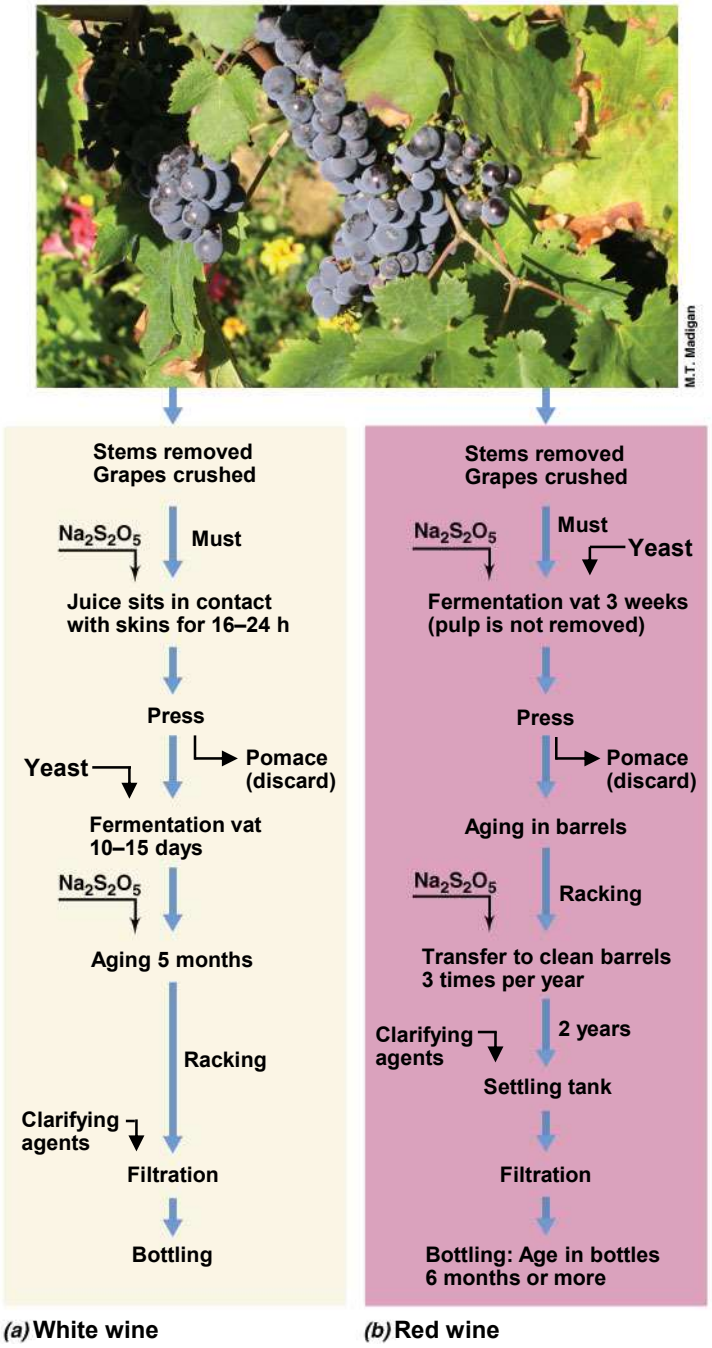
The Christian Brothers Winery

Figure 15.12d

(d)

M.T. Madigan

Figure 15.13



15.8 Brewing and Distilling

- *Brewing* is the term used to describe the manufacture of alcoholic beverages from malted grains (Figure 15.14)
- Yeast is used to produce beer
- Two main types of brewery yeast strains
  - *Top fermenting* — ales
  - *Bottom fermenting* — lagers

Figure 15.14

Busch Creative Services, Anheuser Busch Company

(a)

Busch Creative Services, Anheuser Busch Company

(b)

Busch Creative Services, Anheuser Busch Company

(c)

Busch Creative Services, Anheuser Busch Company

(d)

15.8 Brewing and Distilling

- *Distilled alcoholic beverages* are made by heating previously fermented liquid to a temperature that volatilizes most of the alcohol (Figure 15.16)
  - Whiskey, rum, brandy, vodka, gin
- >50,000,000,000 liters of ethanol are produced yearly for industrial purposes
  - Used as an industrial solvent and gasoline supplement

Figure 15.16

Barton Spear

15.9 Biofuels

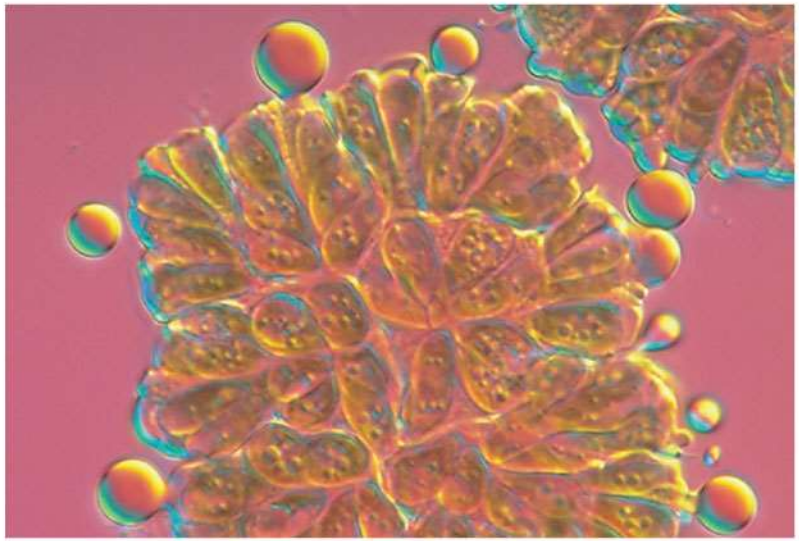
- Ethanol Biofuels
  - Ethanol is a major industrial commodity chemical
  - Over 60 billion liters of alcohol are produced yearly from the fermentation of feedstocks (Figure 15.17a and b)
  - Gasohol and E-85
- Petroleum Biofuels
  - Production of butanol
  - Synthesis of petroleum from green algae (Figure 15.17c)

Figure 15.17

Chris Standlee and DOE/NREL

(a)

(b)



Arthur Nonomura

(c)

IV. Products from Genetically Engineered Microorganisms

- 15.10 Expressing Mammalian Genes in Bacteria
- 15.11 Production of Genetically Engineered Somatotropin
- 15.12 Other Mammalian Proteins and Products
- 15.13 Genetically Engineered Vaccines
- 15.14 Mining Genomes
- 15.15 Engineering Metabolic Pathways

15.10 Expressing Mammalian Genes in Bacteria

- *Biotechnology*
  - Use of living organisms for industrial or commercial applications
- *Genetically modified organism (GMO)*
  - An organism whose genome has been altered
- Genetic engineering allows expression of eukaryotic genes in prokaryotes (e.g., insulin)
- This is achieved by
  - Cloning the gene via mRNA (Figure 15.18)
  - Finding the gene via the protein (Figure 15.19)