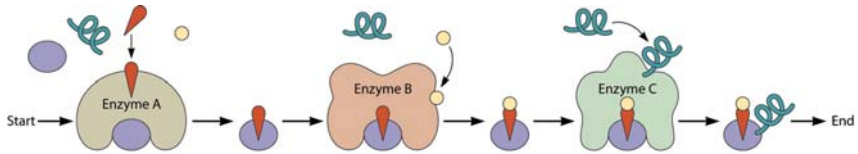
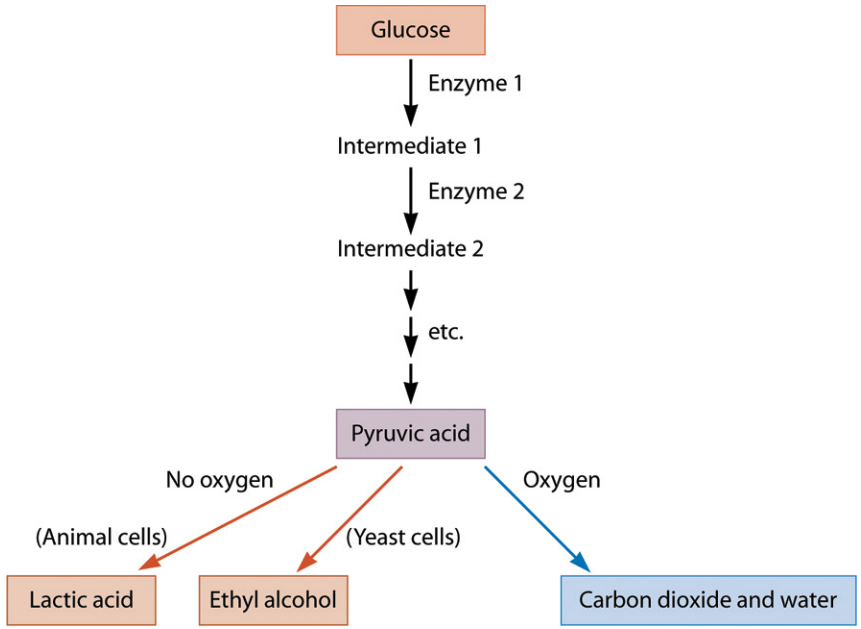
Chapter 6

Cell Metabolism

Metabolic Pathways

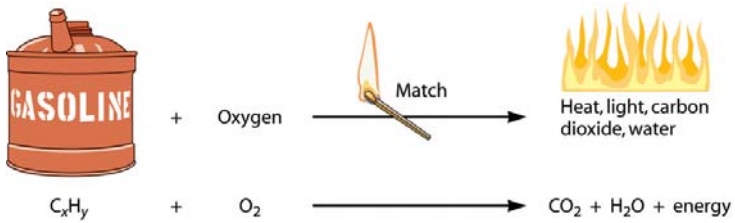
- Metabolic Pathways
  - Break down and manufacture molecules in a sequential set of reactions
  - Enzyme reaction: generate products from substrates
  - Networks of pathways : branch and converge
  - Similar metabolic pathways from bacteria to human



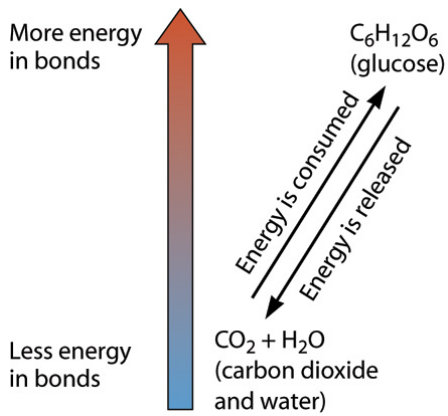


Catabolism and Anabolism

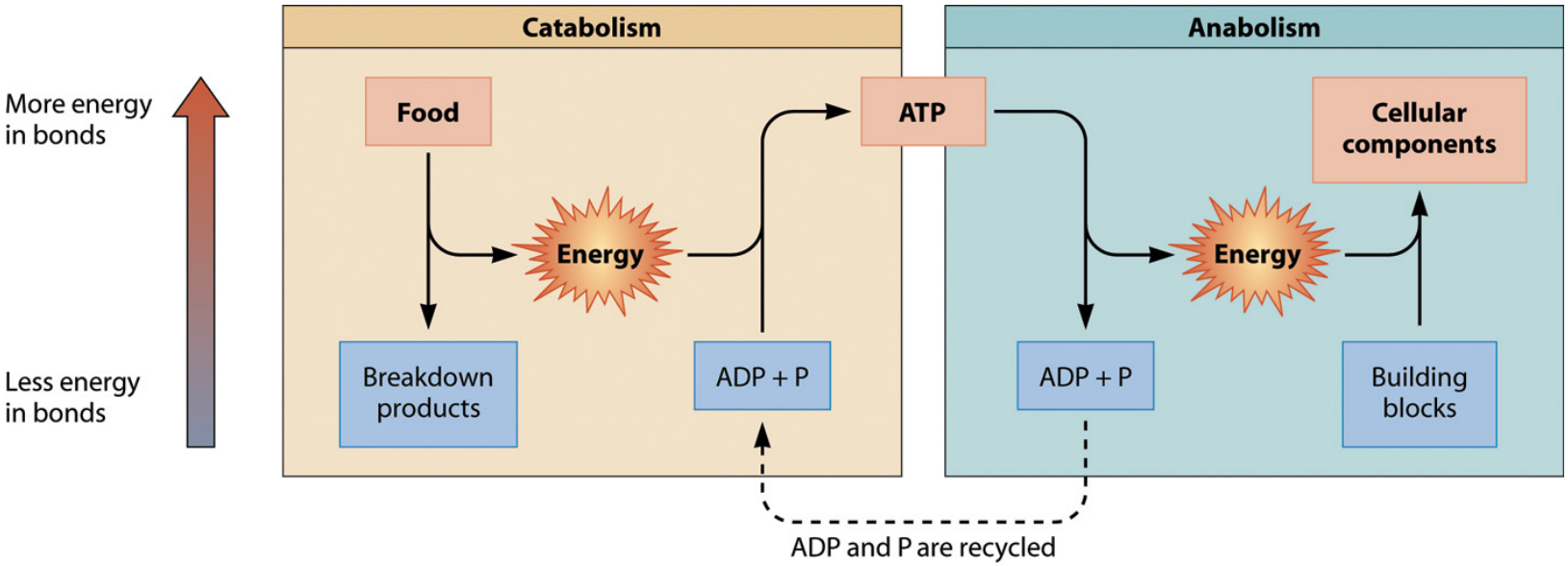
- Catabolism
  - Breaking down, Energy-yielding metabolism
  - Energy release from bond breakage
    - Burning of gasoline : high energy C-C, C-H bonds to lower energy C-O, H-O bonds
    - Burning of fat in human body : Enzymatic generation of molecules with lower E in bond



- Anabolism
  - Synthesis, Energy-requiring metabolism

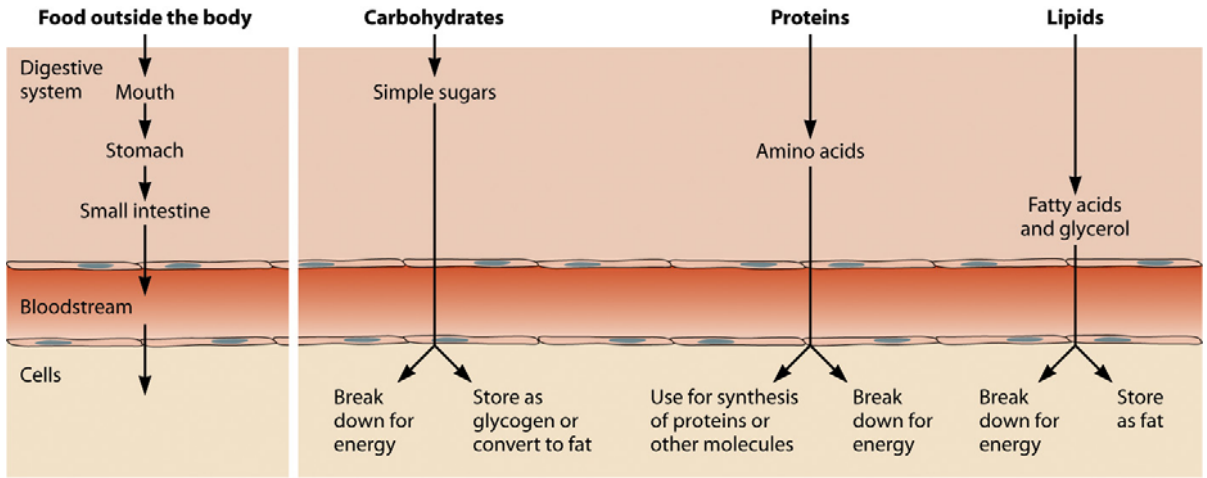


Catabolism and Anabolism



Catabolism of Food in Human Body

- Digestive system
  - Breaking down carbohydrates, lipids, and proteins into building blocks
  - Sugars
    - Used as E source immediately
    - Stored as glycogen for short term storage (liver, muscle) : 1 to 2 days
  - Fatty acids
    - Used as E source immediately
    - Stored as fats for long term storage (fat cells): 4-6 weeks
  - Amino acids
    - Used for protein synthesis, generation of other amino acids
    - E source

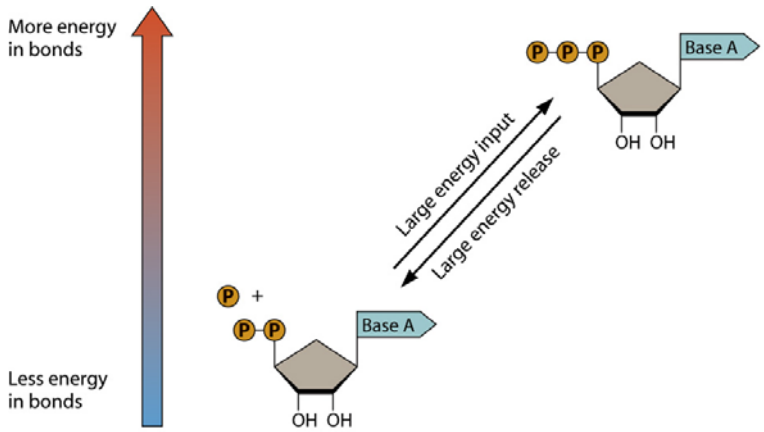


Catabolism of Glucose

- Glycolysis
  - From bacteria to animals
  - Glucose (C_6) to two pyruvic acid (C_3)
  - No O_2 is required
- Aerobic conditions
  - Conversion of pyruvic acid to CO_2 and acetyl coenzyme A (acetyl-CoA)
  - TCA (Krebs cycle)
    - Acetyl CoA → CO_2 + H_2O + NADH (temporary storage molecule)
- Anaerobic conditions
  - Fermentation
    - Generation of ethanol in yeast
    - Lactic acid synthesis in muscle

Electron Transport Pathway

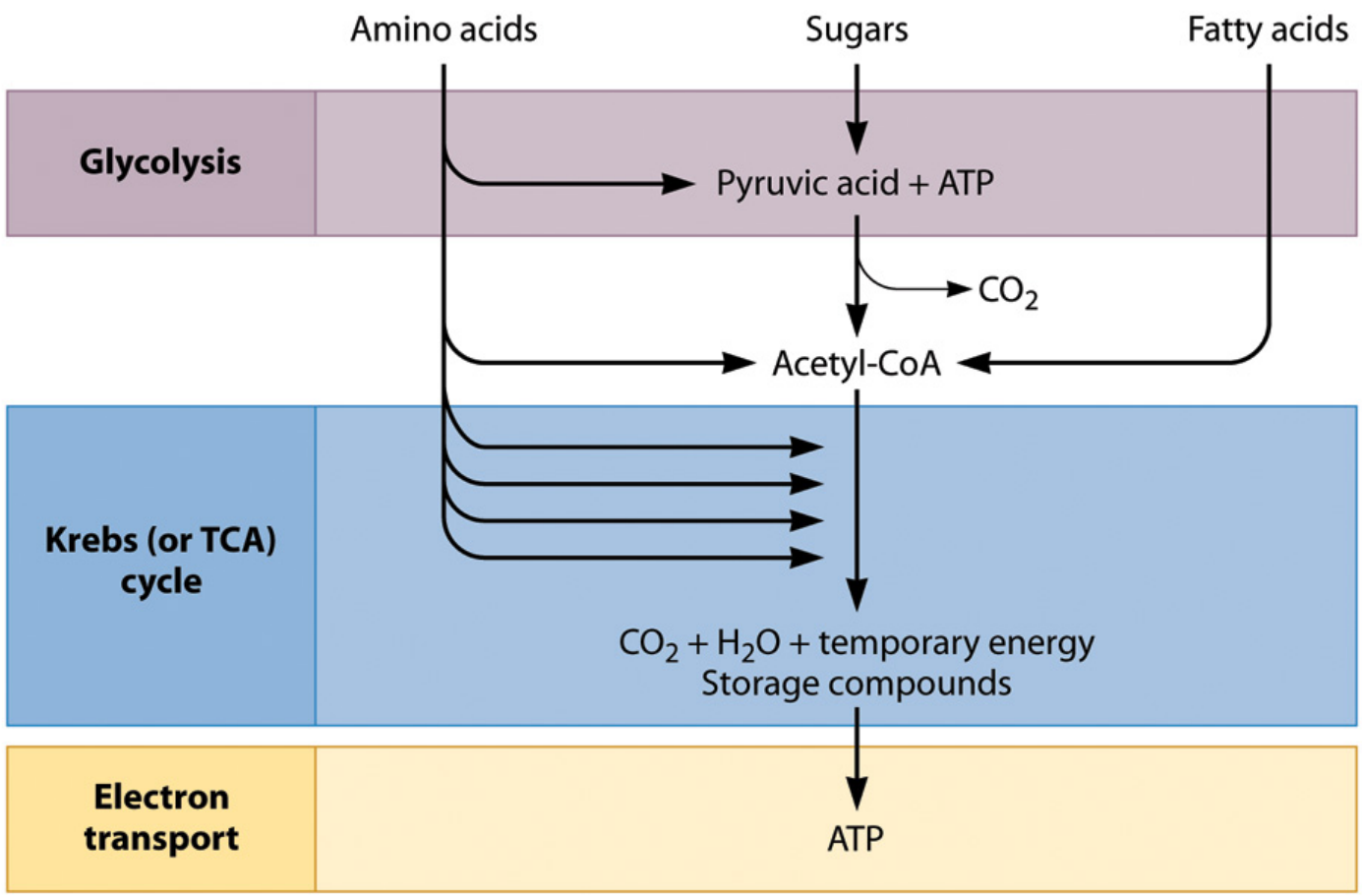
- Generation of ATP as E storage molecule
  - ATP : high E Phosphodiester bond
- Reduction of O_2 to H_2O
  - NADH + H+ + 3ADP + 3Pi + ½ O_2 → NAD^+ + 3ATP + H_2O
  - $FADH_2$ + 2 ADP + 2Pi + ½ O_2 → FAD + 2ATP + H_2O
- c.f. cyanide: blocking electron transport pathway



Net Reaction

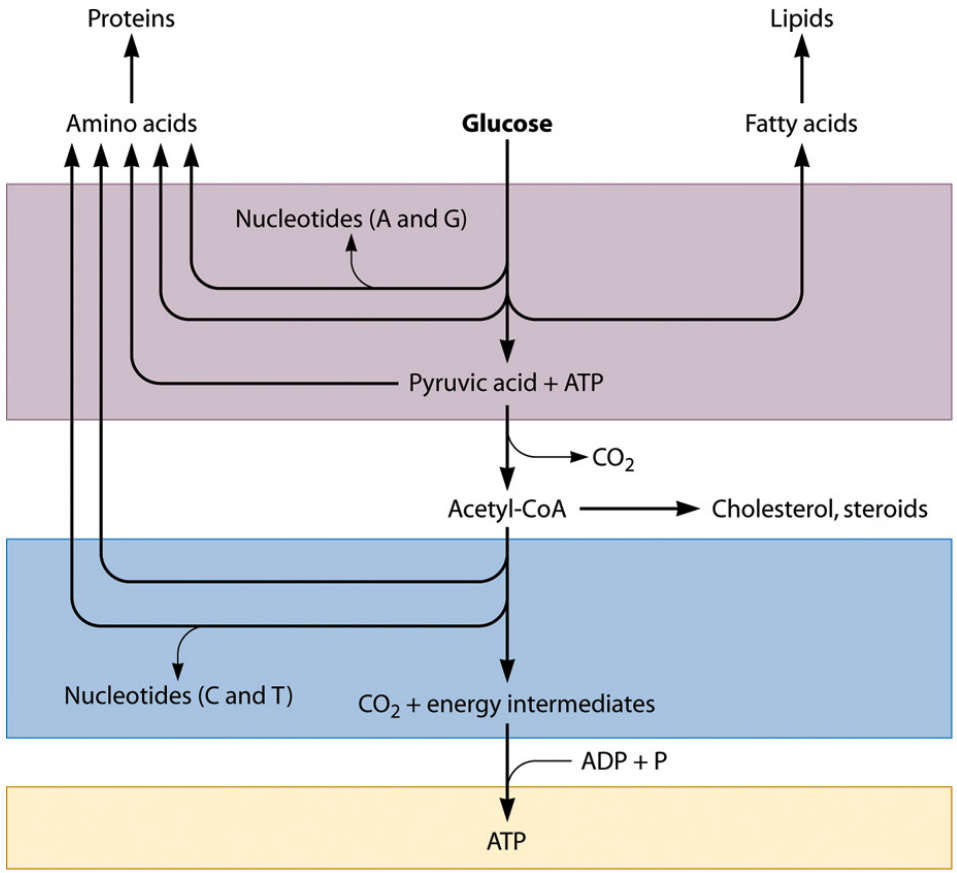
- Glycolysis
  - Glucose + 2ADP + 2Pi + $2NAD^+$ → 2 Pyruvate + 2ATP + 2NADH + $2H^+$ + 2 H_2O
- Fermentaion
  - 2 Pyruvate + 2NADH + $2H^+$ → 2 Lactase + $2NAD^+$
- TCA cycle
  - Pyruvate + 4 NAD^+ + FAD + ADP + pi + $2H_2O$ → 4 NADH + 4 H^+ + $FADH_2$ + ATP + 3 CO_2
- Glycolysis + fermentation : 2ATP
  - Glucose + 2ADP + 2Pi → 2 Lactase + 2ATP
- Glycolysis + TCA cycle : ~ 38 ATP
  - Glucose + 4ADP + 4Pi + $10NAD^+$ + 2 FAD + $4H_2O$ → 4 ATP + 10 NADH (30 ATP) + H^+ + 2 $FADH_2$ (4 ATP) + 6 CO_2

Catabolism of Other Nutrient



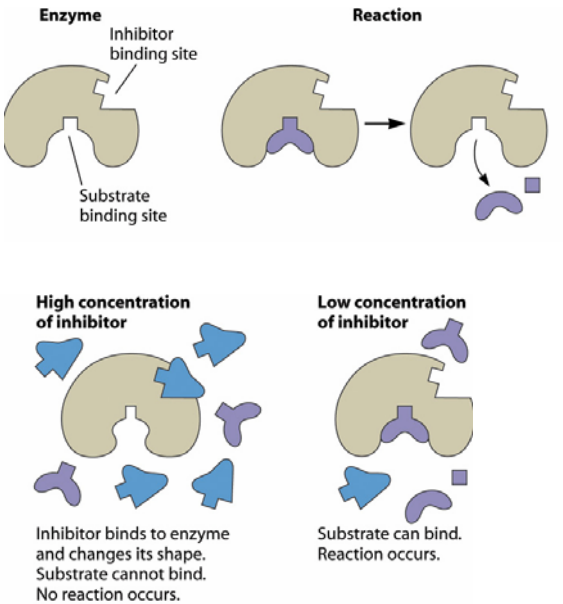
Anabolism

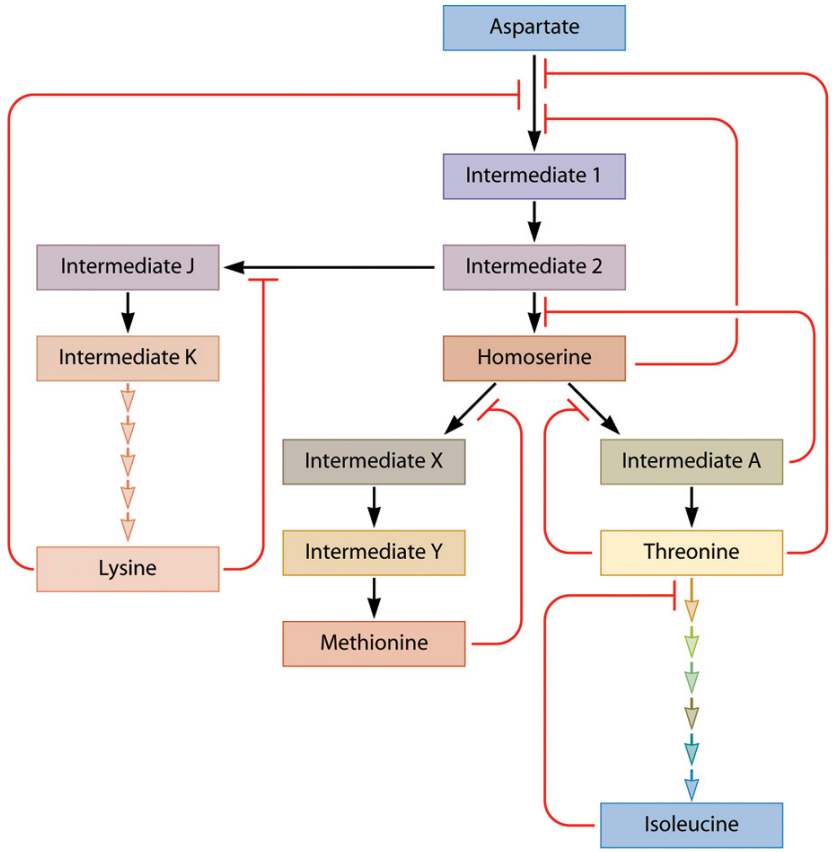
- Requirement
  - Energy: ATP
  - Chemical building blocks (intermediates of glucose breakdown)



Regulation of Metabolism

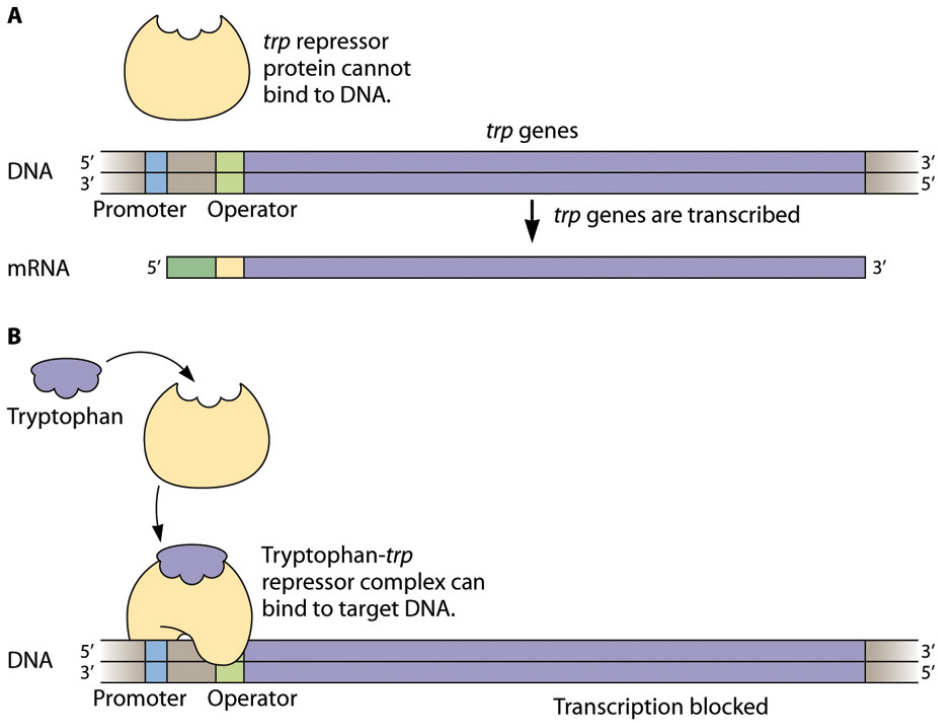
- Feedback Inhibition
  - Inhibition of enzyme activity by end product
  - e.g. amino acid synthesis





Regulation of Metabolism by Gene Expression

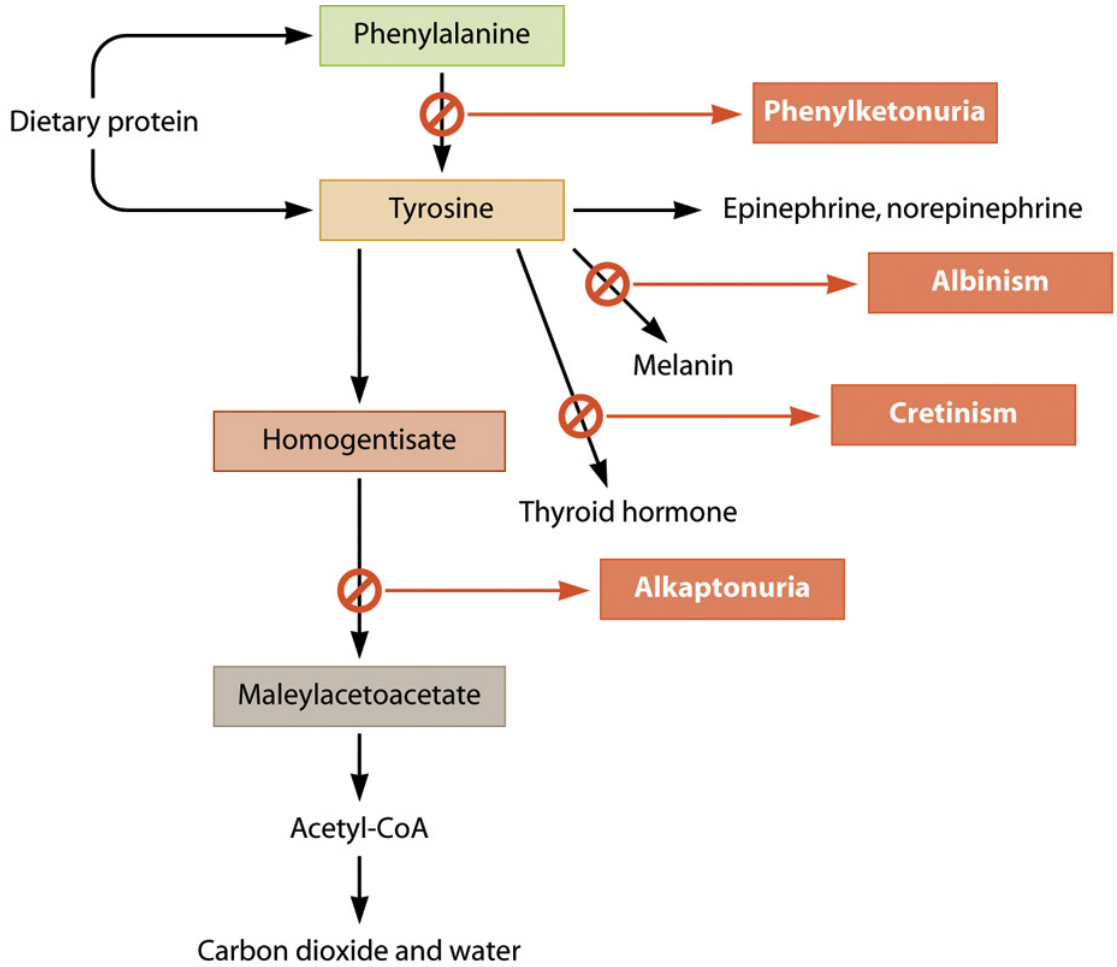
- Trp synthesis in *E.coli*
  - Turn off transcription of Trp genes in the presence of Trp
- Hormonal regulation in higher eukaryotes



Errors in Metabolism

- Enzyme defects and amino acid metabolism
  - Phenylketonuria (PKU)
    - Phenylalanine hydroxylase (PAH) defect
      - No conversion of phenylalanine to tyrosine
      - Production of phenylketones
      - Excretion of phenylalanine and phenylketones in the urine
      - Pehnylalanine inhibit normal development of nervous system
      - Treatment with controlled diet
  - Alkaptonuria
    - Defect in enzyme converting homogentisatate (HG) to maleylacetoacetate (MAA)
      - Oxidation of HG leads to black color → black urine
      - No serious effect
  - Albinism
    - Lacking enzyme converting tyrosine to melanin
  - Cretinism
    - Lacking enzyme converting tyrosine to thyroid hormone
    - Defect in growth and maturation of the skeletal and nervous systems

Diseases Related to the Defects in Phe Metabolism

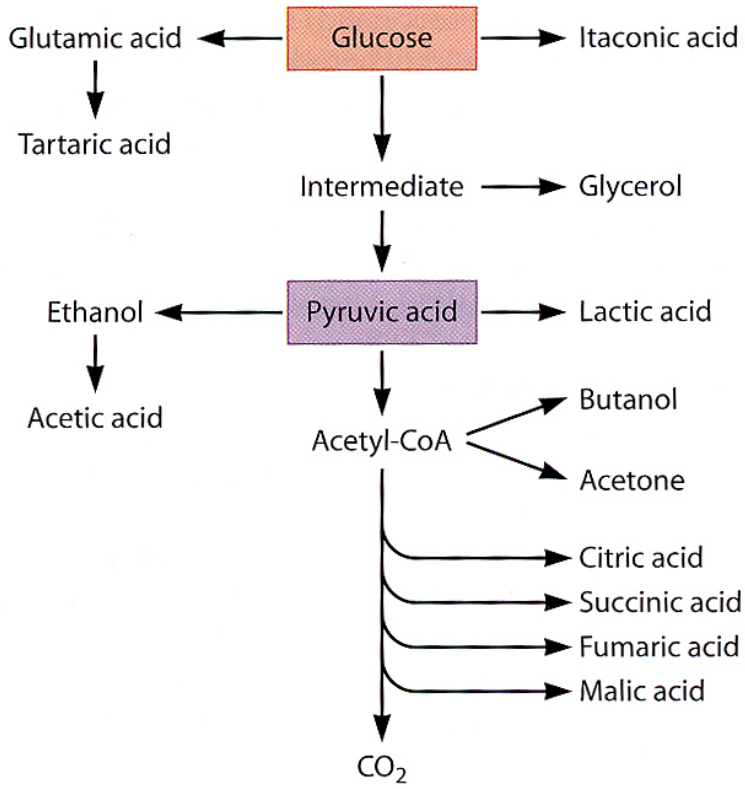


Biotechnology Applications

- Treatment of Metabolic Disorders
- Gaucher's disease
  - Problems
    - Defect in enzyme breaking down lipid glucocerebroside in RBC and WBC
    - Macrophage cannot break down glucocerebroside in engulfed blood cells
    - Accumulation of enlarged macrophage (Gaucher cell) in spleen, liver, and bone marrow, sometimes in nervous system
  - Treatments
    - Enzyme replacement of recombinant enzymes
    - Gene therapy

Using Microbial Metabolism

- Using enzymes for manufacturing (Biocatalyst)
  - Biotransformation
    - Whole cell reaction
    - e.g. production of fermented foods (wine, beer, cheese)
  - Reaction with isolated enzymes
- Bioremediation
  - Using microbes to degrade pollutants
  - e.g.oil-eating microbes



Generation of Useful Products from Microbial Metabolism

Table 6.1 Chemcials currently produced by microbial metabolism of glucose and their industrial applications

Chemical	Microbial source	Industrial uses
Ethanol	*Saccharomyces*	Industrial solvent, fuel, beverages
Acetic acid	*Acetobacter*	Industrial solvent, rubber, plastics, food acidulant[a] (vinegar)
Citric acid	*Aspergillus*	Food, pharmaceuticals, cosmetics, detergents
Gluconic acid	*Aspergillus*	Pharmaceuticals, food, detergent
Glycerol	*Saccharomyces*	Solvent, cosmetic preparations, soaps, antifreezes
Isopropanol	*Clostridium*	Industrial solvent, cosmetic preparations, antifreeze, inks
Acetone	*Clostridium*	Industrial solvent, intermediate in many chemical synthesis reactions
Lactic acid	*Lactobacillus, Streptococcus*	Food acidulant, fruit juice, soft drinks, dyeing, leather treatment, pharmaceuticals, plastics
Butanol	*Clostridium*	Industrial solvent, intermediate in many chemical synthesis reactions
Fumaric acid	*Rhizopus*	Intermediate in synthesis of synthetic resins, dyeing, acidulant, antioxidant
Succinic acid	*Rhizopus*	Manufacture of lacquers, dyes, and esters for perfumes
Malic acid	*Aspergillus*	Perfumes
Tartaric acid	*Acetobacter*	Acidulant, tanning, commercial esters for lacquers, printing
Itaconic acid	*Aspergillus*	Textiles, paper manufacture, paint

[a]An acidulant is a substance added to food or beverages to lower pH and to impart a tart, acid taste.

Table 6.2 Useful products from microbial metabolic pathways other than glucose metabolism

Type of product	Examples	Applications
Amino acid	Glutamic acid, phenylalanine, aspartic acid, lysine	Nutritional supplements, flavor enhancers, sweeteners
Carbohydrate	Dextran, xanthan gum	Food emulsifiers and thickeners, oil recovery
Vitamin	B_{12}, riboflavin, β-carotene	Nutritional supplements, pigments
Metabolic enzyme	Proteases, amylases, lipases	Detergents, sweeteners, brewing, cheese making, textiles, leather softening
Nucleotide	Guanosine, inosine	Flavor enhancers

Enzymes in manufacturing

- Invertase: soft-centered chocolate
- Cellulase: stone-washed jeans
- Amylase: reduced-calorie beer
  - Converting starch to sugars that yeast can use during brewing process
- Lipase, proteinases : laundry detergents