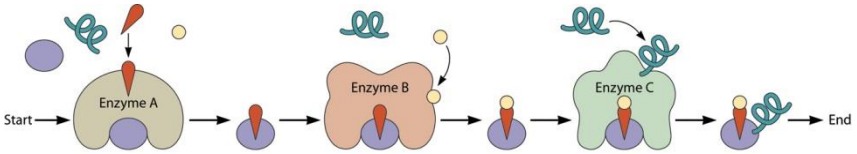
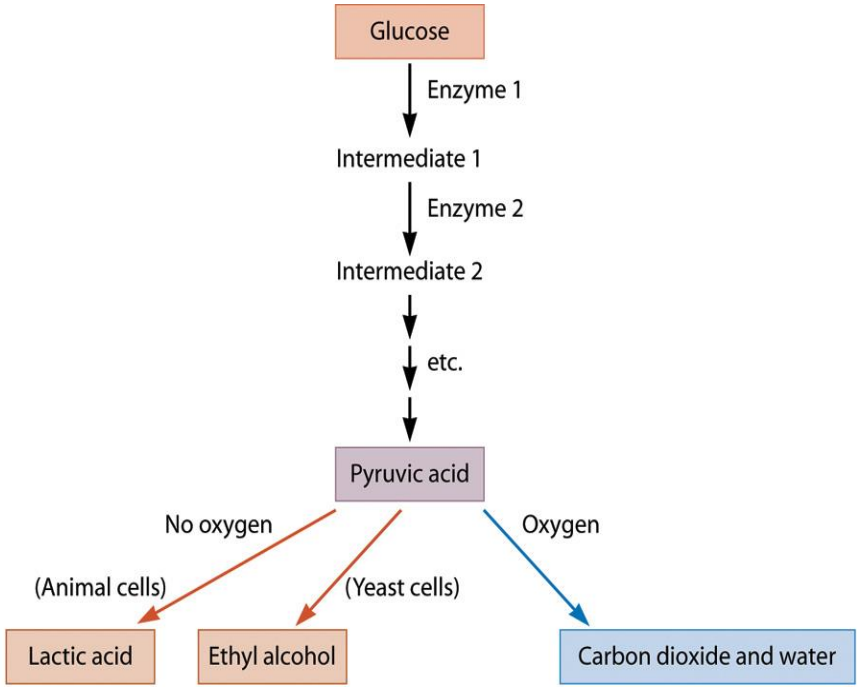
Chapter 6

Cell Metabolism

Metabolic Pathways

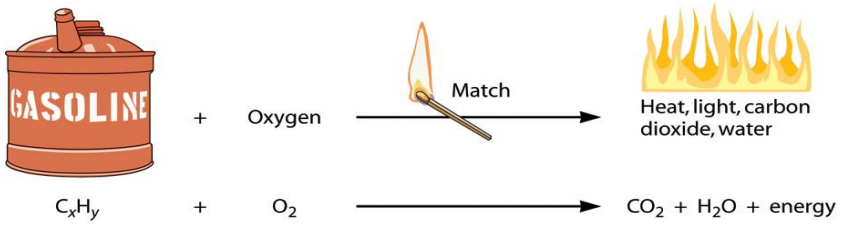
- Metabolic Pathways
  - Break down and manufacture molecules in a sequential set of reactions
  - Enzyme reaction: generate products from substrates
  - Networks of pathways : branch and converge
  - Similar metabolic pathways from bacteria to human



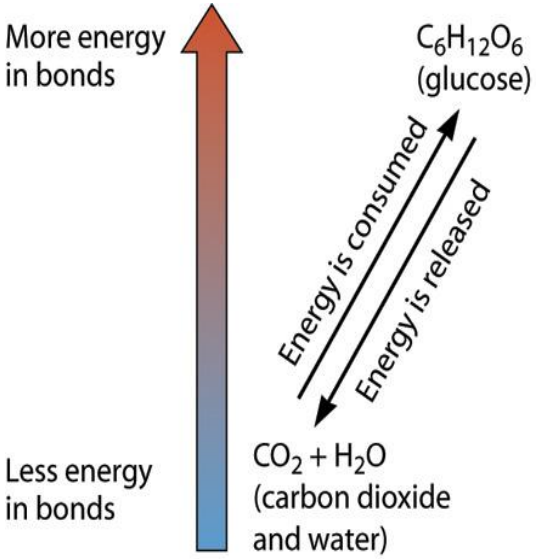


Catabolism and Anabolism

- Catabolism
  - Breaking down, Energy-yielding metabolism
  - Energy release from bond breakage
    - Burning of gasoline
      - high E C-C, C-H bonds to lower E C-O, H-O bonds



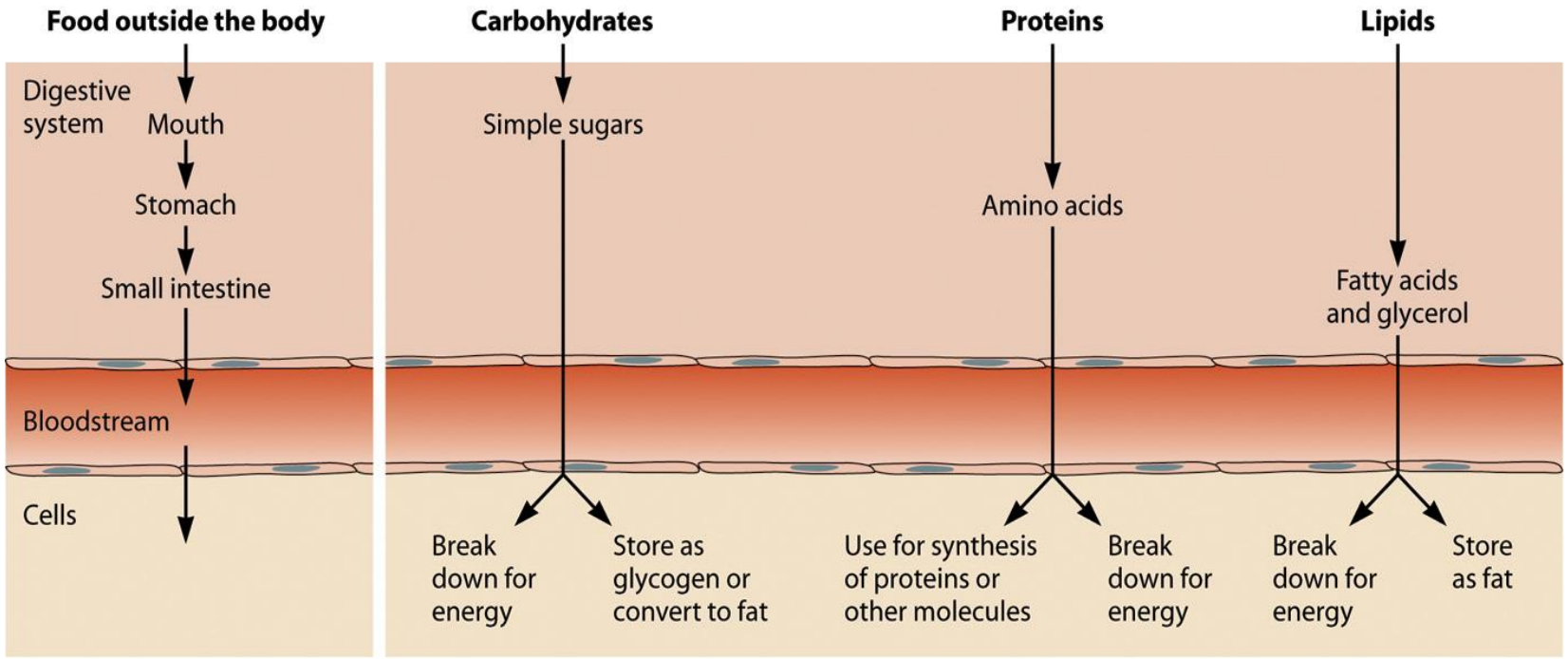
    - Burning of fat in human body
      - Enzymatic generation of molecules with lower E in bond
- Anabolism
  - Synthesis, Energy-requiring metabolism



Catabolism of Food in Human Body

- Digestive system
  - Breaking down carbohydrates, lipids, and proteins into building blocks
  - Sugars
    - Used for quick E
    - If excess, stored as glycogen for short term storage (E for1 to 2 days)
  - Fatty acids
    - Used for quick E
    - If not necessary, stored as fat (fat droplets in fat cells) for long term storage (E for 4-6 weeks)
  - Amino acids
    - Can be also used for E (but not the primary fate)
    - Used for protein synthesis and generation of other amino acids

Catabolism in Animals



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 etc.

BOX 6.1 *The exercise burn and a metabolic branch point*

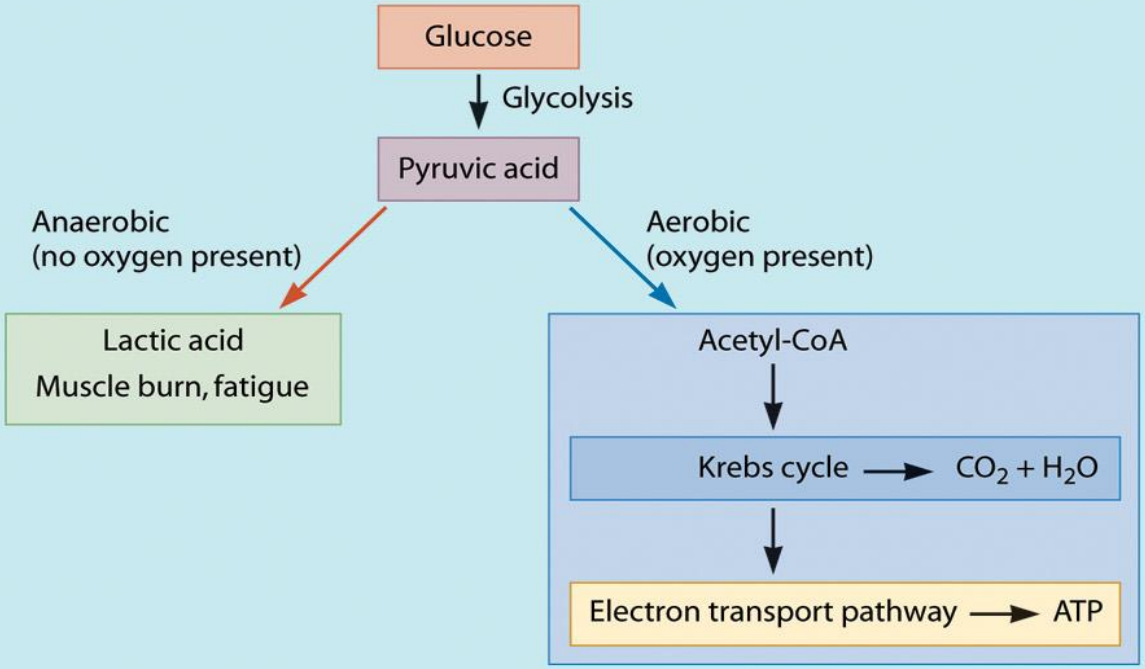
Have you ever exercised until you felt your muscles burn? The burning is a direct result of a branch point in the metabolic pathway for breaking down glucose and other substrate molecules.

When you exercise, your muscles need a lot of energy. Exercising muscle cells break down lots of glucose—muscles even have their own glycogen stores for just such situations. Breaking down glucose to carbon dioxide and water requires another input: oxygen. When your muscles are working hard, you are breathing harder, and your heart is beating faster to supply your muscles with extra oxygen to power all that glucose catabolism. Sometimes, though, you cannot get enough oxygen to your muscles. You might be putting extraordinary demands on isolated muscles, as when you lift weights, or demanding output from your entire body that exceeds your capacity to supply oxygen via breathing and blood circulation, as when you sprint for a while.

When your muscles can't get enough oxygen, the normal catabolism of glucose to carbon dioxide and water cannot happen. Look at the figure. When oxygen is present, pyruvic acid is converted into acetyl-CoA and on to carbon dioxide and water. This step is actually a metabolic branch point. If oxygen is not present, your muscle cells do something different with the pyruvic acid. They have another enzyme that converts it into a three-carbon compound called lactic acid. When lactic acid builds up in your muscles, you feel that burning sensation.

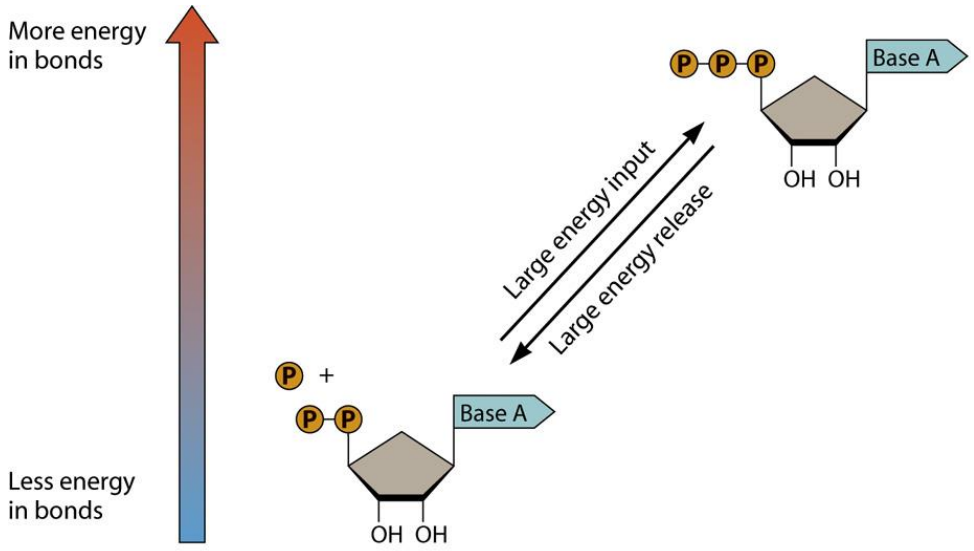
The lactic acid burn is a sign that your muscles are working anaerobically (without oxygen). You've probably heard of aerobic exercise. The word aerobic means with oxygen. Aerobic exercise by definition causes you to breathe hard, but your breathing can keep up with your muscles' need for oxygen. That means you can sustain the exercise for longer periods of time. Because you are breathing harder and your heart is beating faster than usual during aerobic exercise, sustained exercise of this kind can strengthen your heart.

Metabolism and muscle burn.

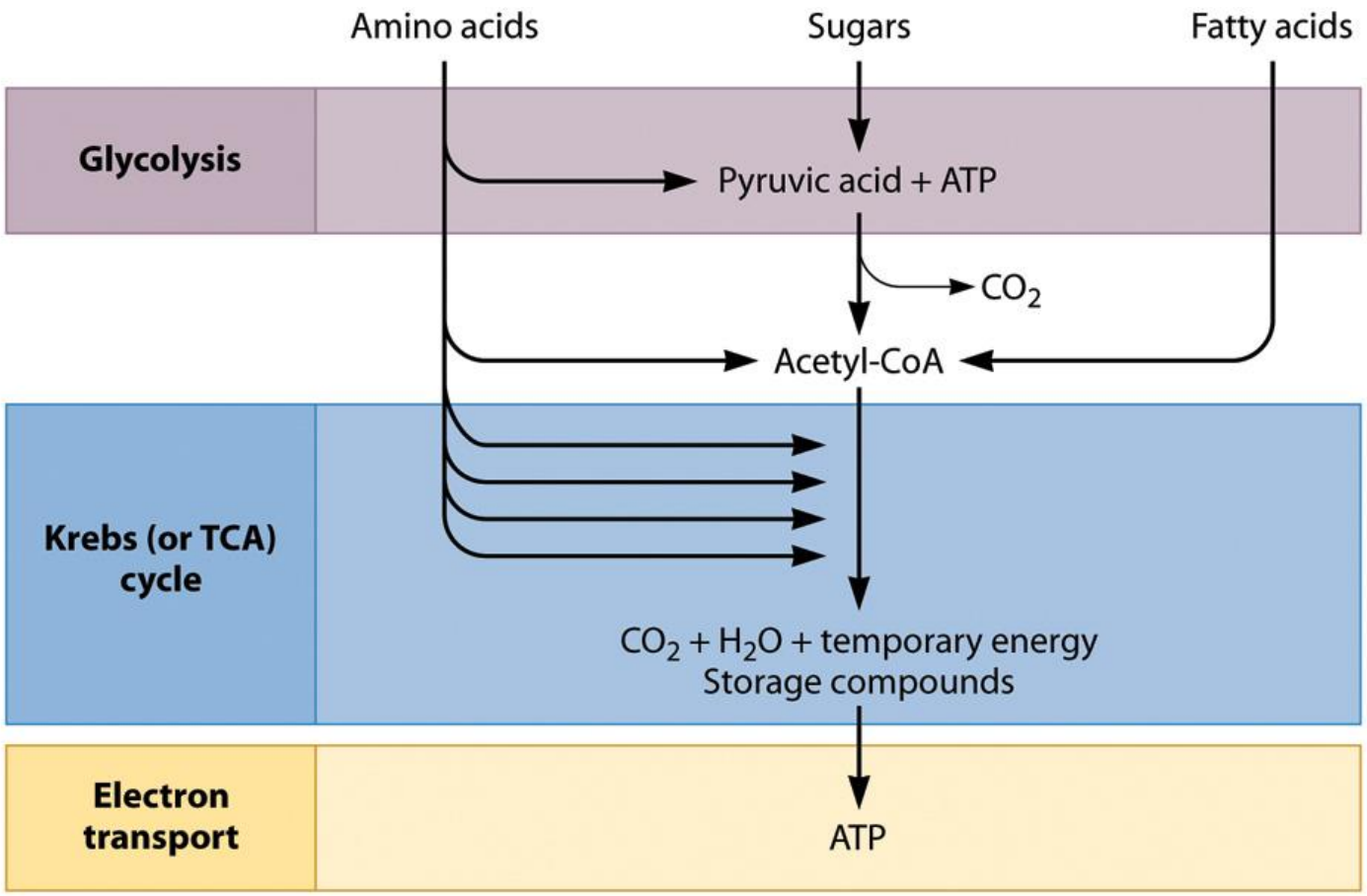


Electron Transport Pathway

- Generation of ATP as E storage molecule
  - ATP : high E phosphodiester bond
- Reduction of O_2 to H_2O
  c.f. cyanide: blocking electron transport pathway

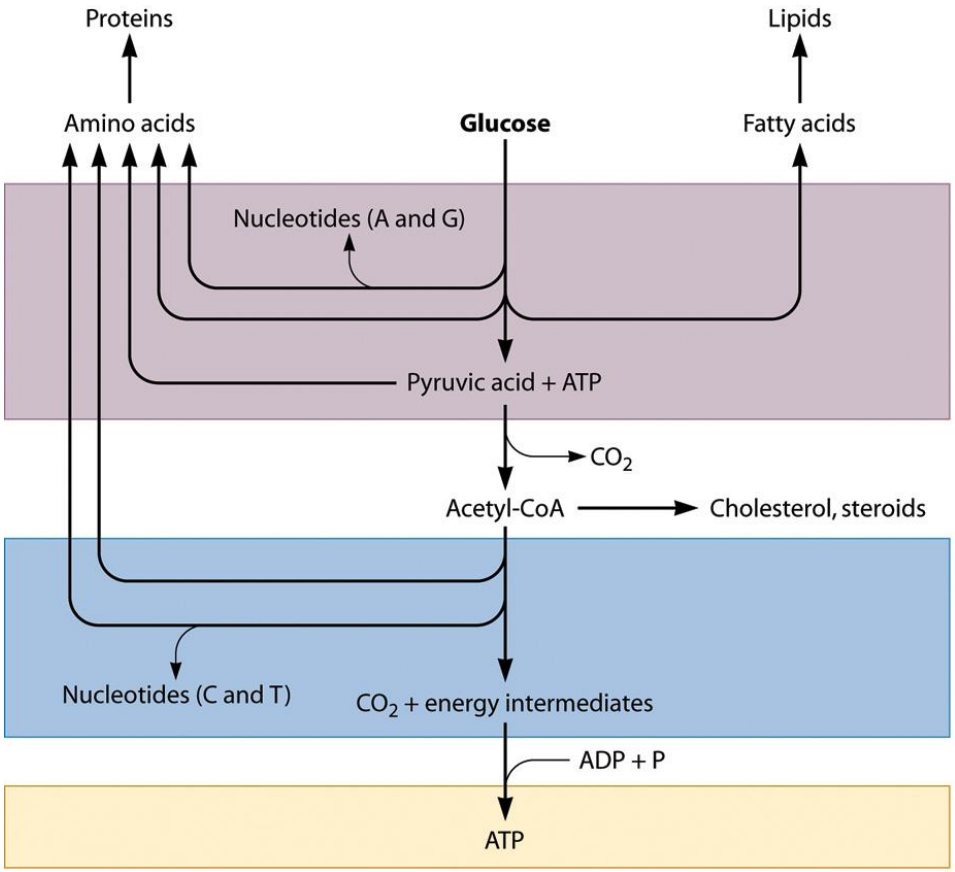


Catabolism of Other Nutrient



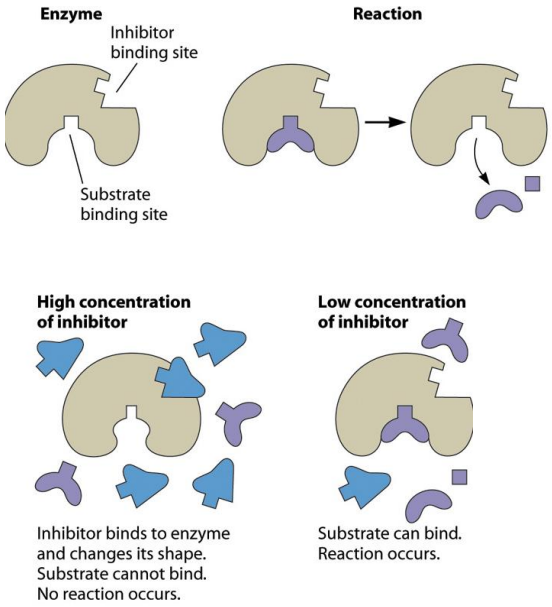
Anabolism

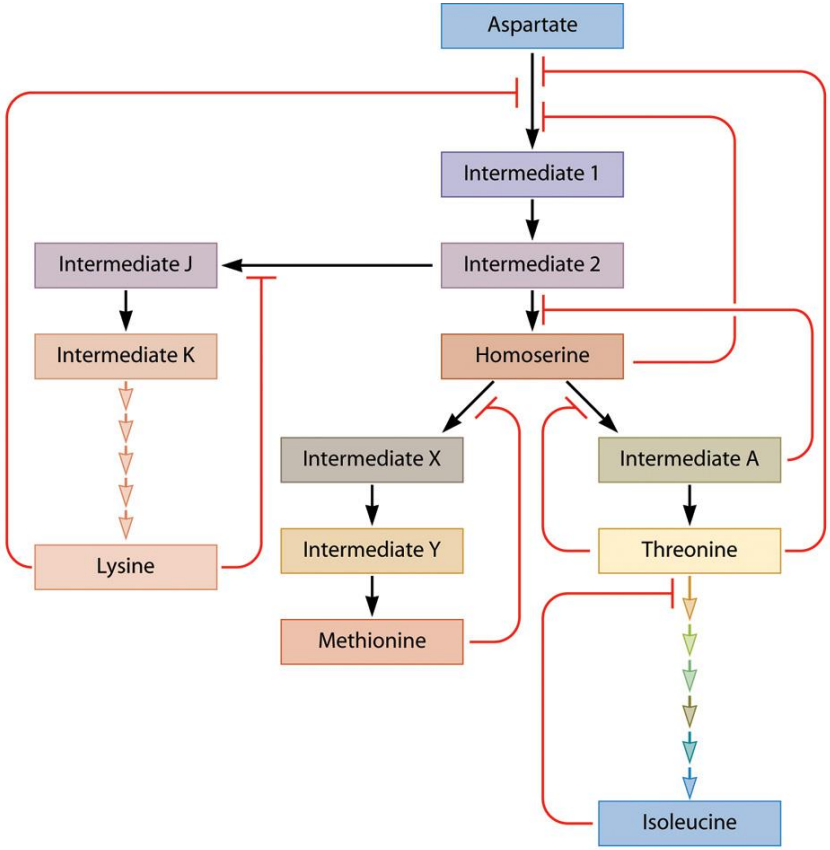
- Requirement
  - Energy: ATP
  - Chemical building blocks (intermediates of glucose breakdown)



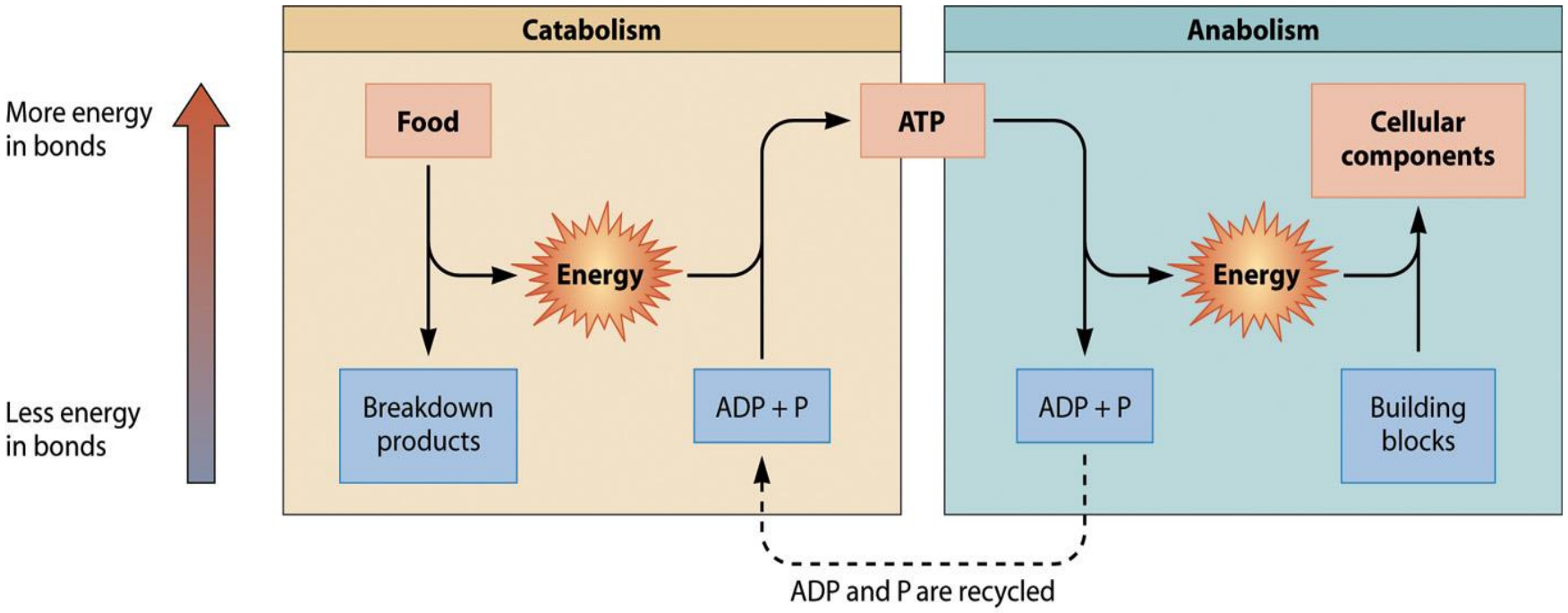
Regulation of Metabolism

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



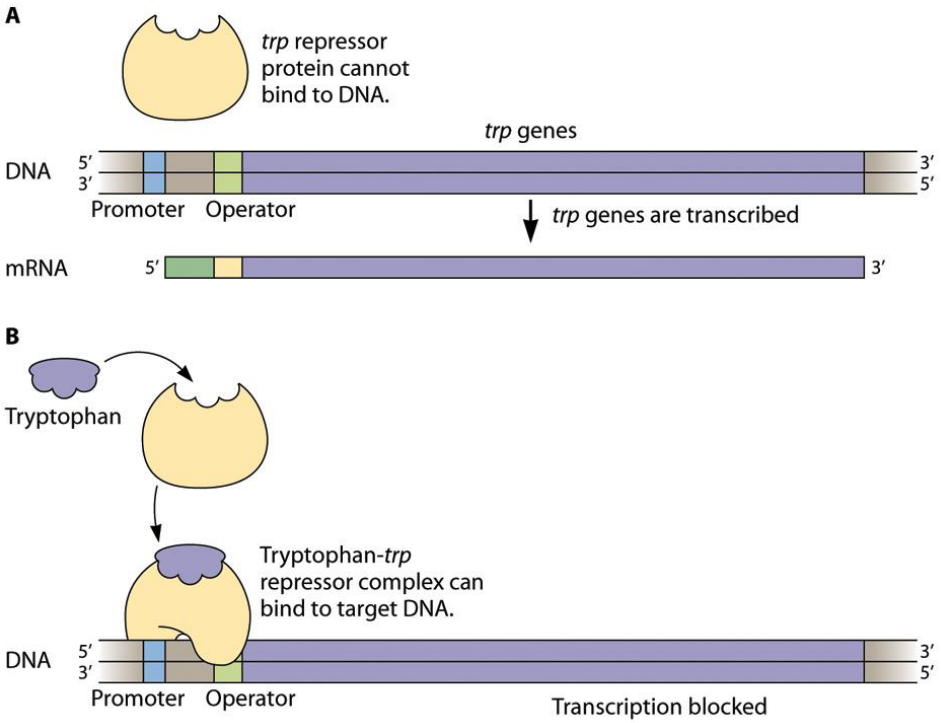


Catabolism & Anabolism

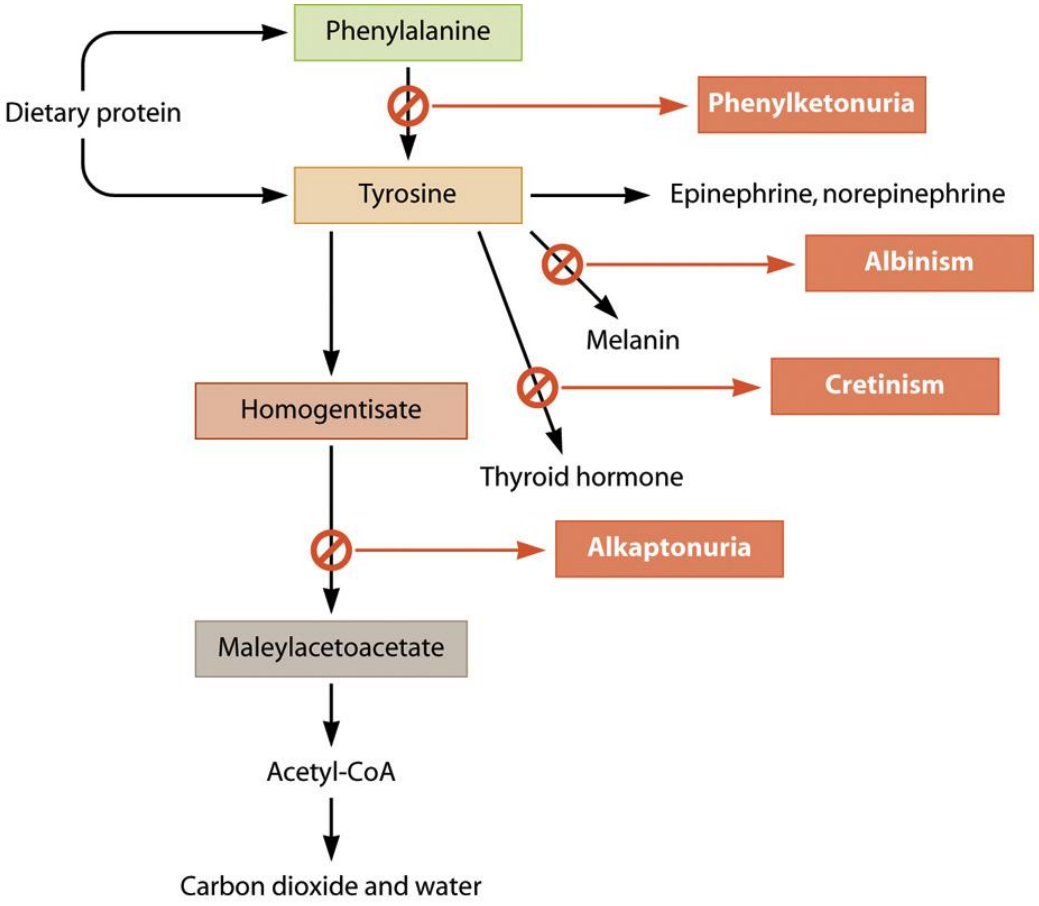


Regulation of Metabolism by Gene Expression

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



Errors in Metabolism



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

Diet drink
--- warning
"Phenylketonurics: contains phenylalanine"
--- Aspartame(NutraSweet): Asp-Phe

  - Alkaptonuria
    - Defect in enzyme converting homogentisate (HG) to maleylacetoacetate (MAA)
      - Oxydation 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

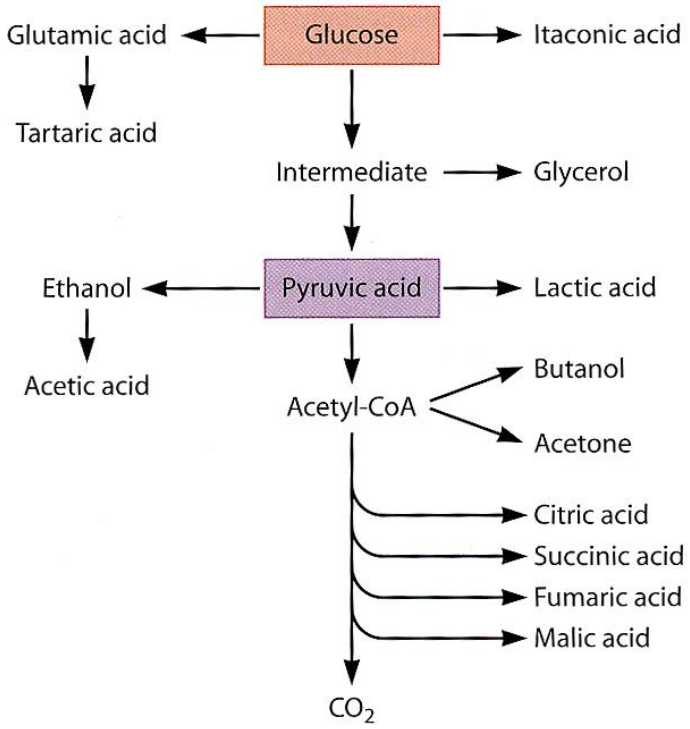
Biotechnology Applications

- Treatment of Metabolic Disorders
- Gaucher's disease (pronounced go-shay)
  - Problems
    - Defect in enzyme breaking down glucocerebroside (lipid) in RBC and WBC
    - Accumulation of enlarged macrophage (Gaucher cell) in spleen, liver, and bone marrow
  - 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



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

Application of Microbial Metabolism

- Bioremediation
  - Using microbes to degrade pollutants
  - e.g. Oil-eating microbes
- Enzymes in manufacturing
  - Invertase: soft-centered chocolate
  - Cellulase: stone-washed jeans
  - Amylase: reduced-calorie beer
  - Lipase, proteinases : laundry detergents