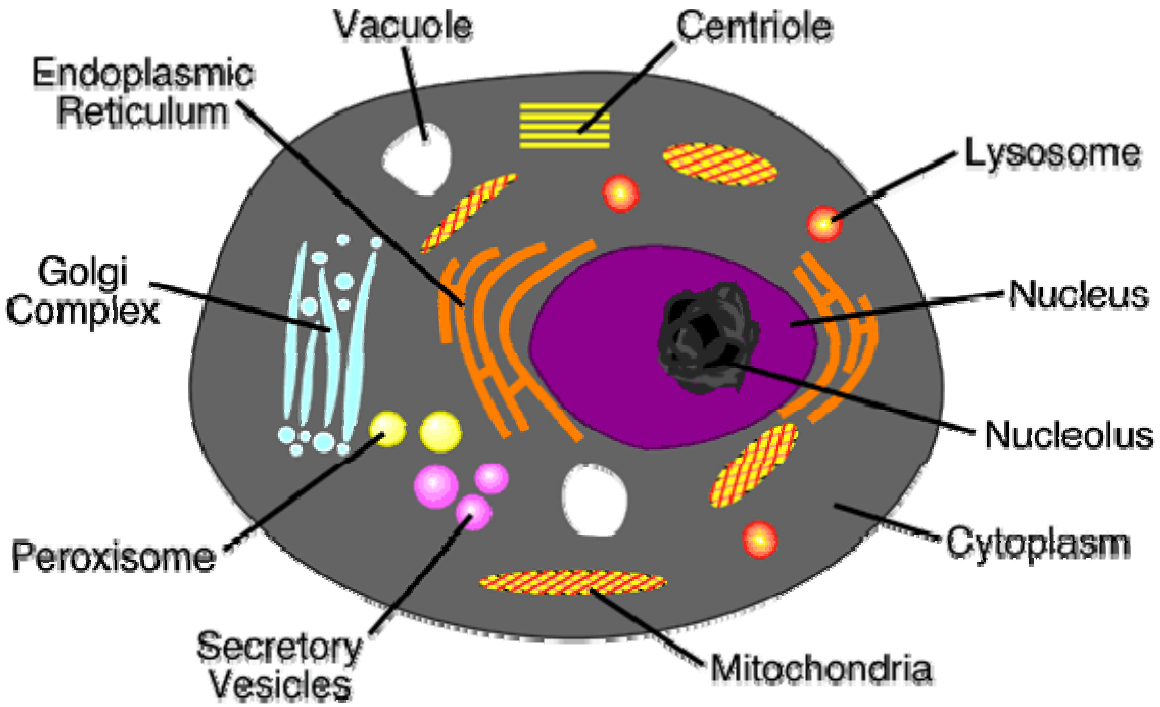

http://www.sciencehelpdesk.com/img/bg3_1/CellEukaryioticAnimal1.gif

營養生化學(0070210)

Nutritional biochemistry

保健營養學系三年級

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Nutrition and the Cells

Learning Objectives

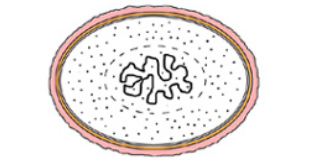
- **Components of typical cells (0.5 h)**
- **Cell structures and functions (1 h)**
- **Metabolism in the organelles (1 h)**
- **Metabolism in the liver (1.5 h)**

References

- **Gropper SS, Smith JL, Groff JL. Advanced Nutrition and Human Metabolism, 5th ed. Wadsworth: Belmont, 2009.**
- **Gropper SS, Smith JL, Groff JL. Advanced Nutrition and Human Metabolism, 4th ed. Wadsworth: Belmont, 2005.**
- **Linder MC. Nutritional Biochemistry and Metabolism: with Clinical Applications, 2nd ed. Elsevier: New York, 1991.**
- **Pike RL, Brown ML. Nutrition: An Integrated Approach, 3rd ed. MacMillan Publishing Company: New York, 1984.**
- **Wolfe SL. Molecular and Cellular Biology. Wadsworth: Belmont, 1993.**

Cell types

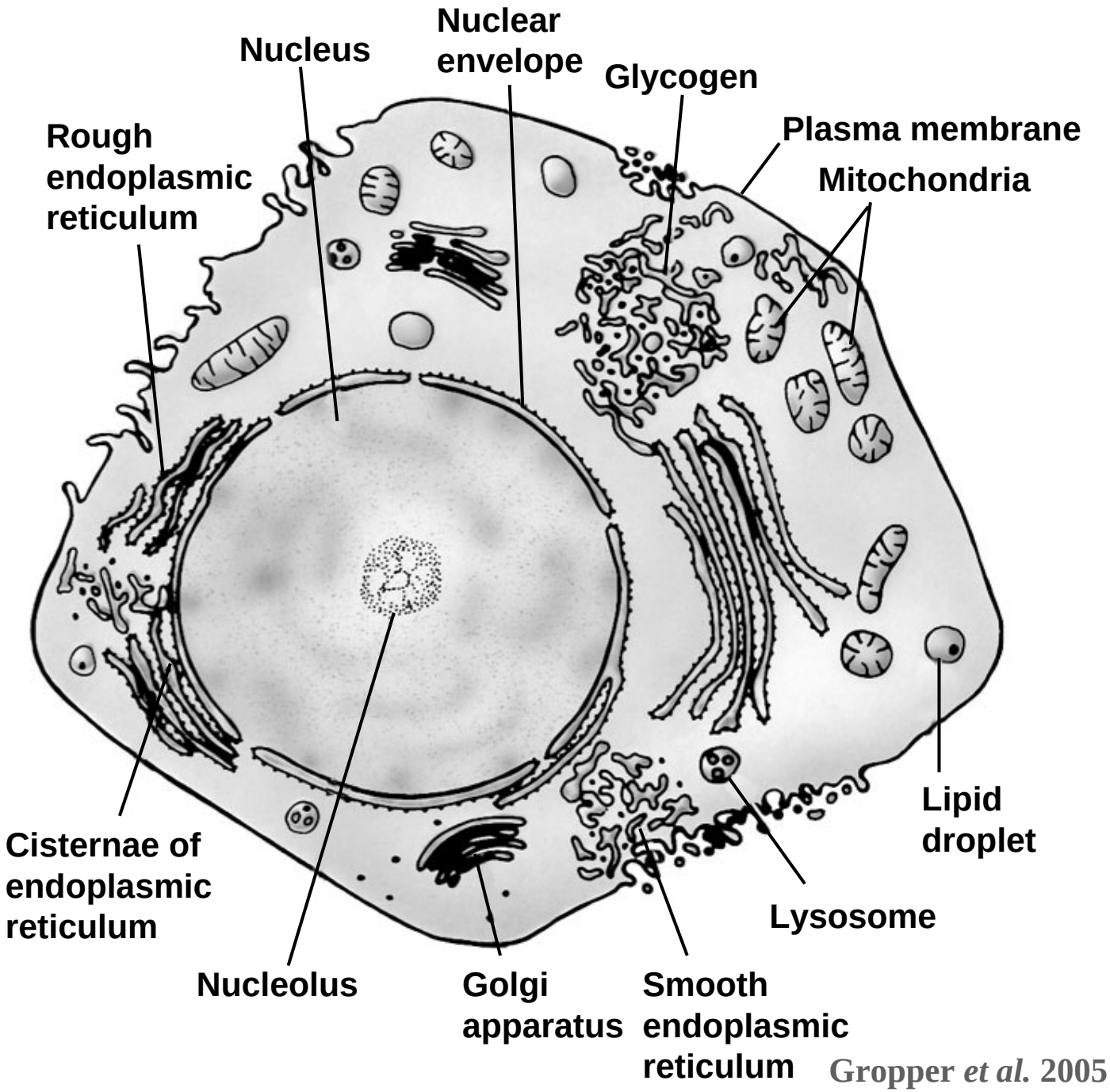
- **mono**cellular organisms: **pro**karyotic cells
- **multi**cellular organisms: **eu**karyotic cells



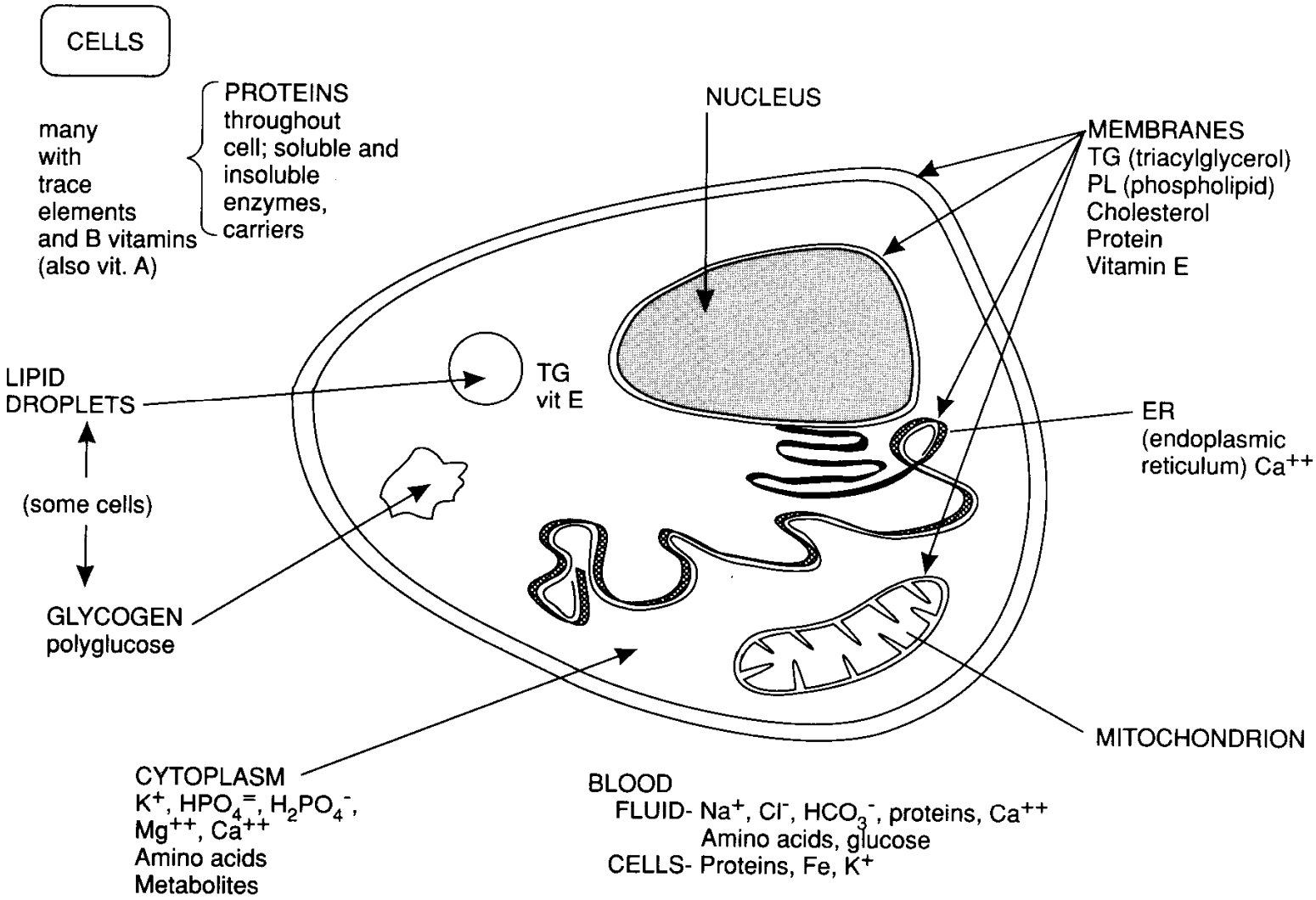
Prokaryotic Cell

Animal (Eukaryotic) Cell

http://www.cod.edu/PEOPLE/FACULTY/FANCHER/ProkEuk.htm



Gropper *et al.* 2005

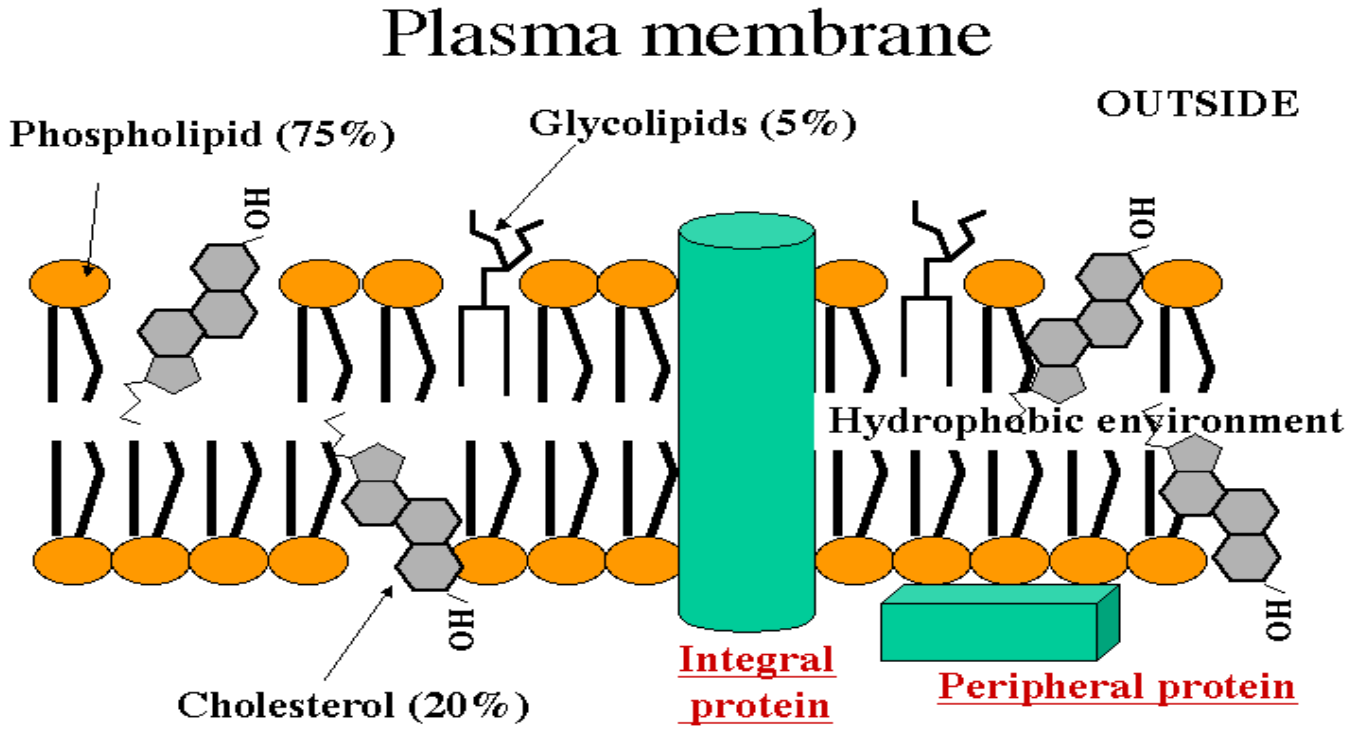


MEATS- MUSCLE rich in protein, fat, iron, Na^+, K^+, phosphate
LIVER rich in protein, iron, (fat) vitamins A, D, B12 folate, Na^+, K^+ etc.
FAT TISSUE rich in fat (triglyceride) (vit. E) (carotenes)
EGGS- rich in protein, vitamins, some trace elements, triglyceride, cholesterol
MILK- rich in protein, lactose, Ca^{++}, triglyceride

Linder 1991

Plasma membrane

- lipids
- proteins
- hold together by non-covalent interaction



http://www.ucl.ac.uk/~sjjgsca/CellMembraneComplex.gif

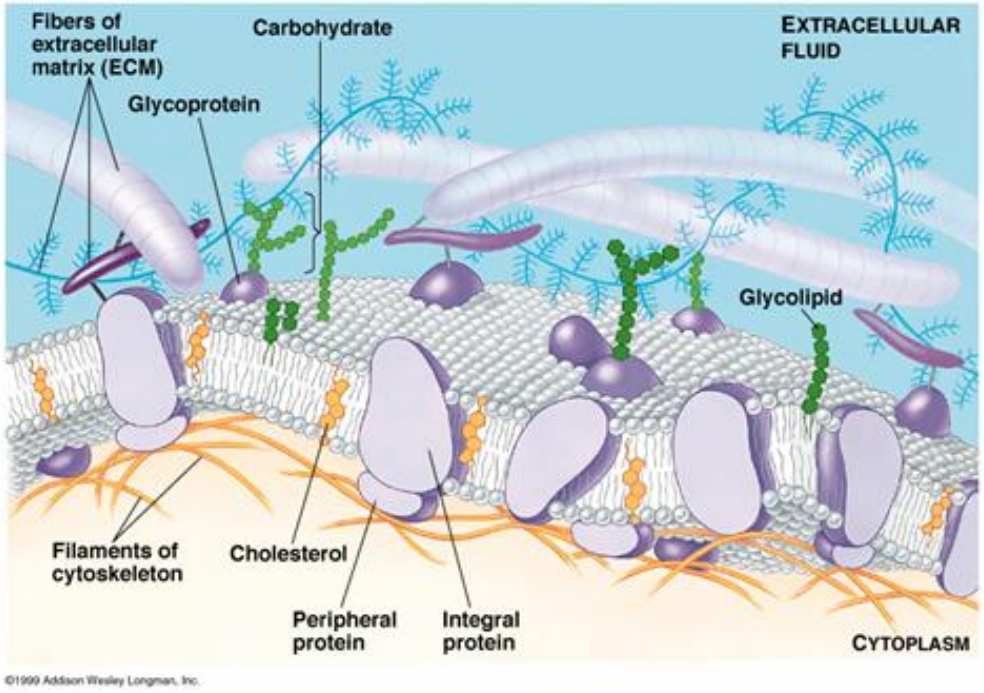
Membrane lipids

- **phospholipids**

  phosphoglycerides

  phosphingolipids (phosphate-containing sphingolipids)

- **cholesterol**



http://kentsimmons.uwinnipeg.ca/cm1504/Image127.gif

Phosphoglycerides

- **phosphoglycerides**

  glycerol + 2 fatty acid chains + 1 phosphate group

- **phosphate group links to**

  glycerol (phosphatidic acid)

  ethanolamine (phosphatidylethanolamine)

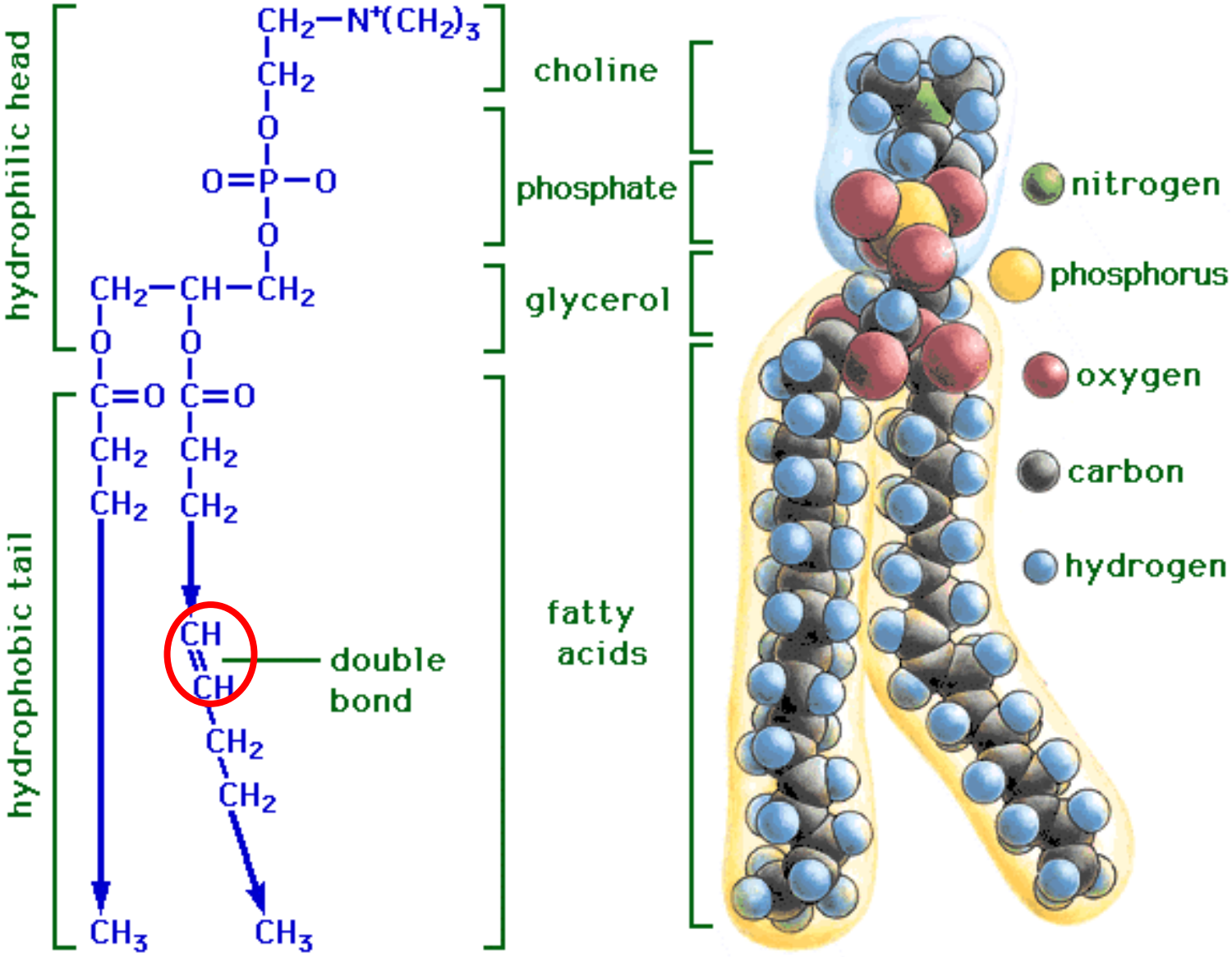
  choline (phosphatidylcholine; lecithin)

  serine (phosphatidylserine)

  threonine (phosphatidylthreonine)

  inositol (phosphatidylinositol)

Phosphoglycerides



phosphatidylcholine

http://cnx.org/content/m15254/latest/

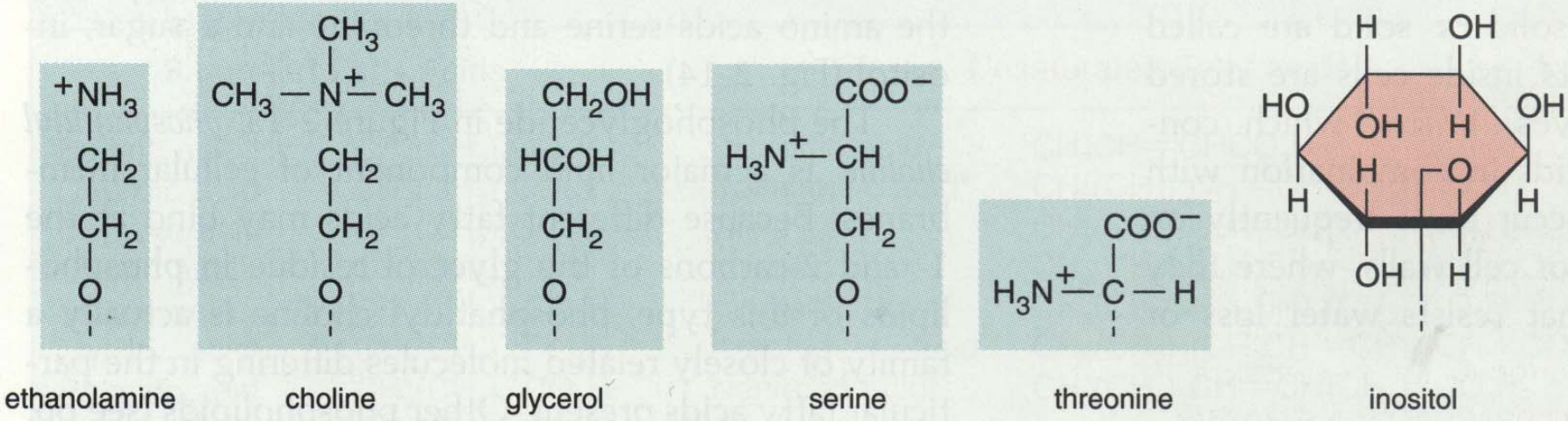


Figure 2-14 Organic subunits commonly linked to glycerol by a phosphate group in phospholipids. The site at which the subunit links to glycerol via a phosphate group is indicated by the dashed line.

Wolfe 1993

Phosphingolipids

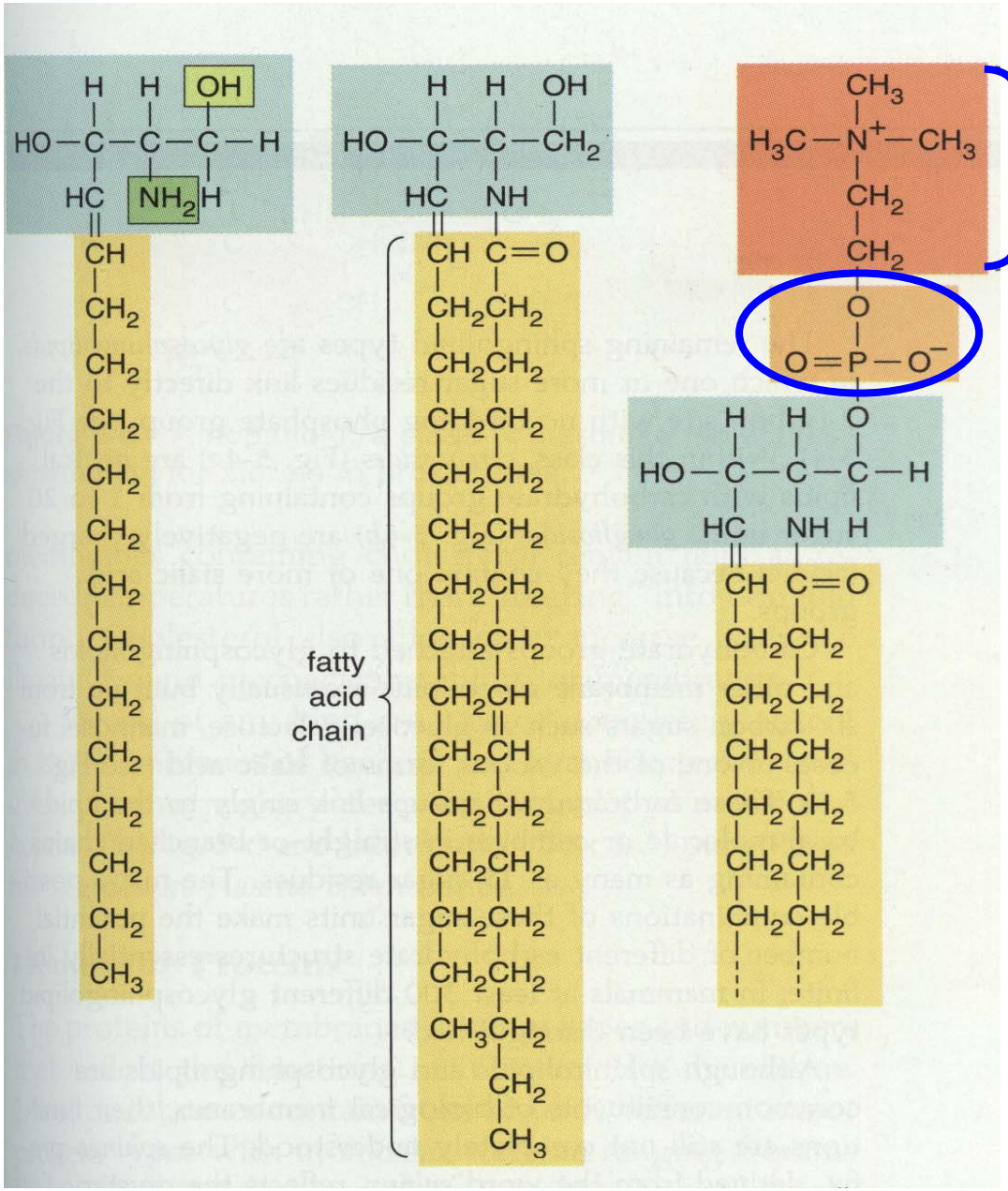
- **sphingolipids**

  built on a sphingosine backbone

- **phosphate-containing sphingolipids**

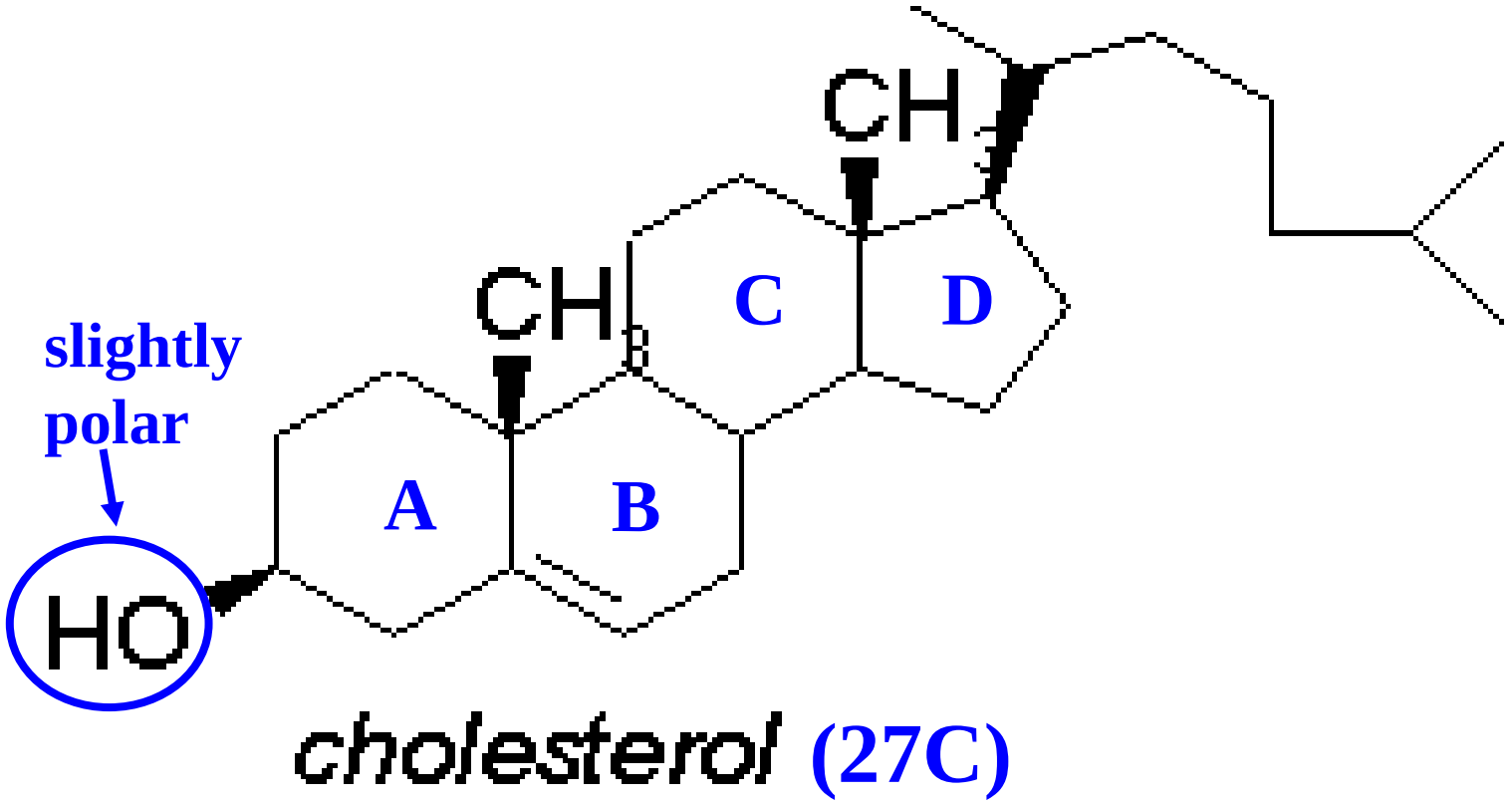
  sphingomyelin

Sphingolipids



Wolfe 1993

sphingosine ceramide sphingomyelin

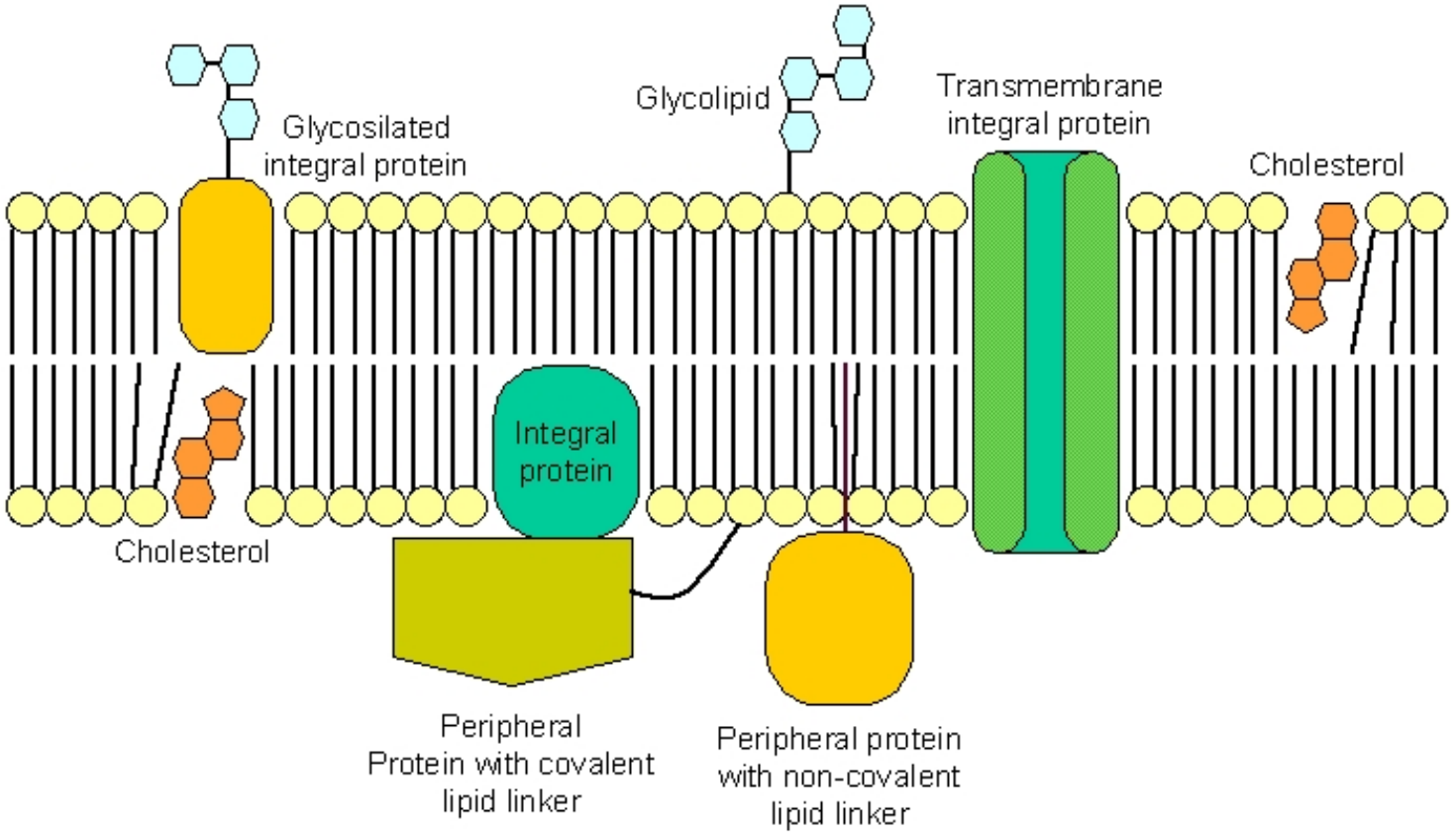


cholesterol **(27C)**

http://www.people.vcu.edu/~urdesai/ahlp.h1.gif

Membrane proteins

- **integral proteins**
- **peripheral proteins**



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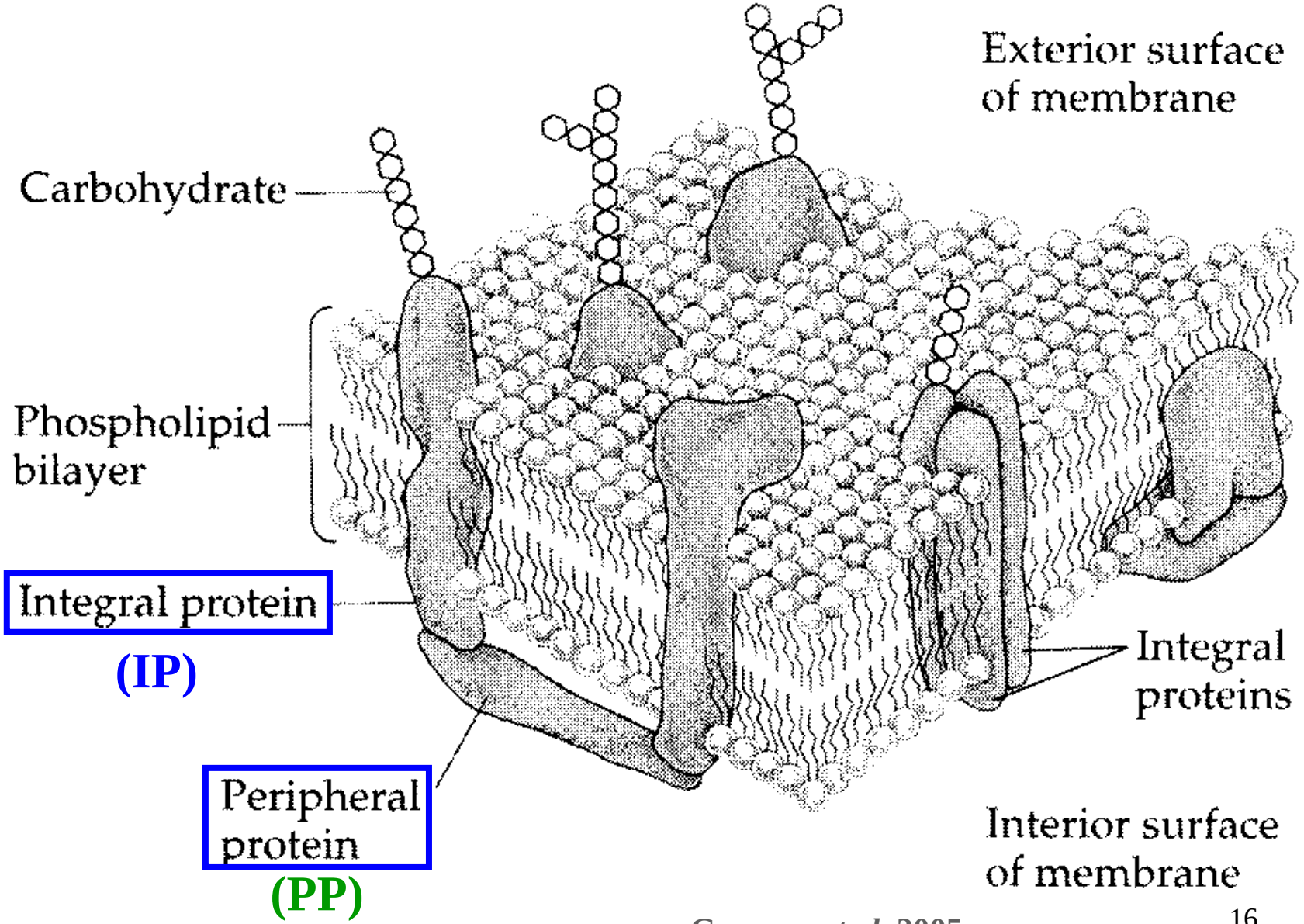
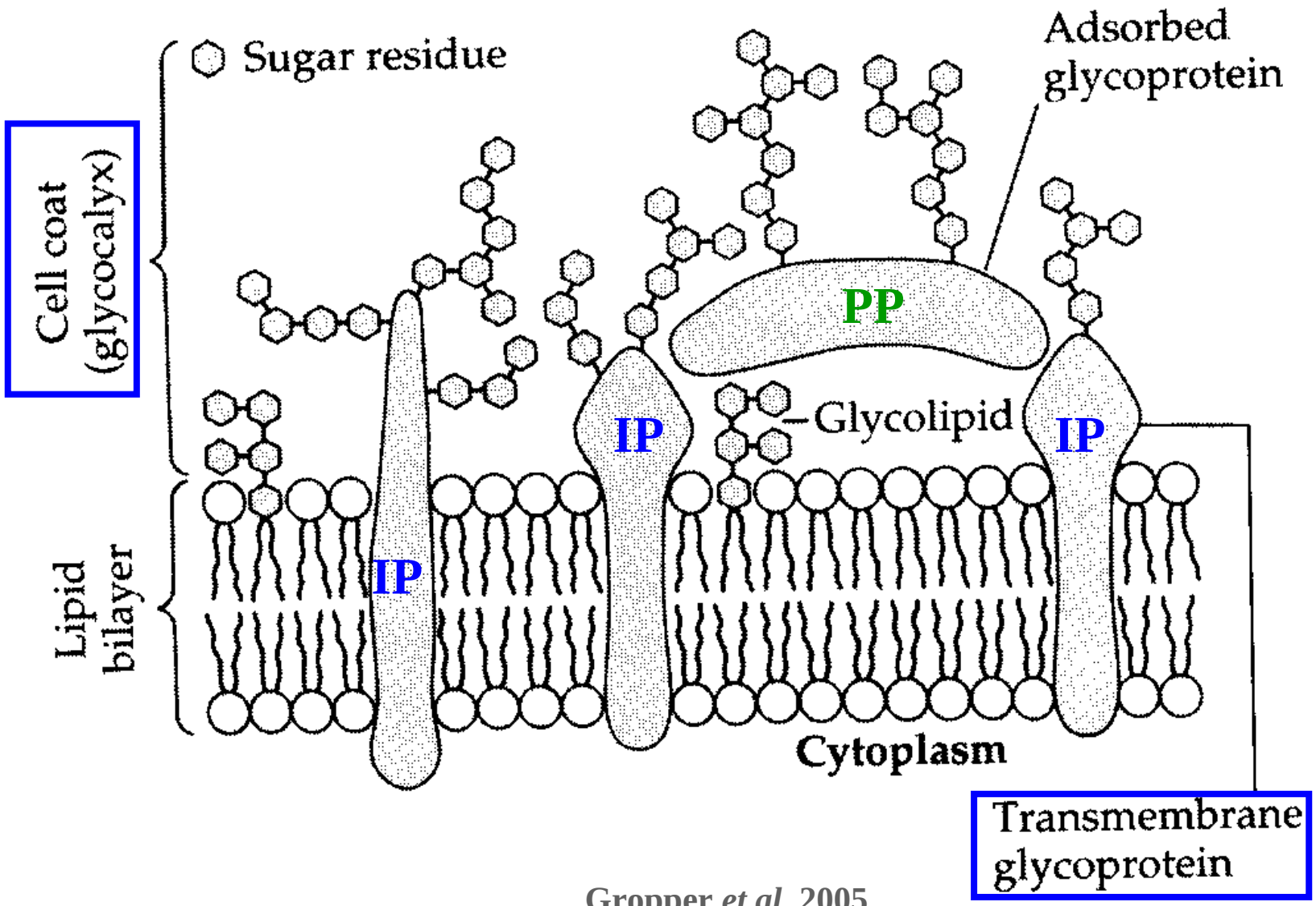
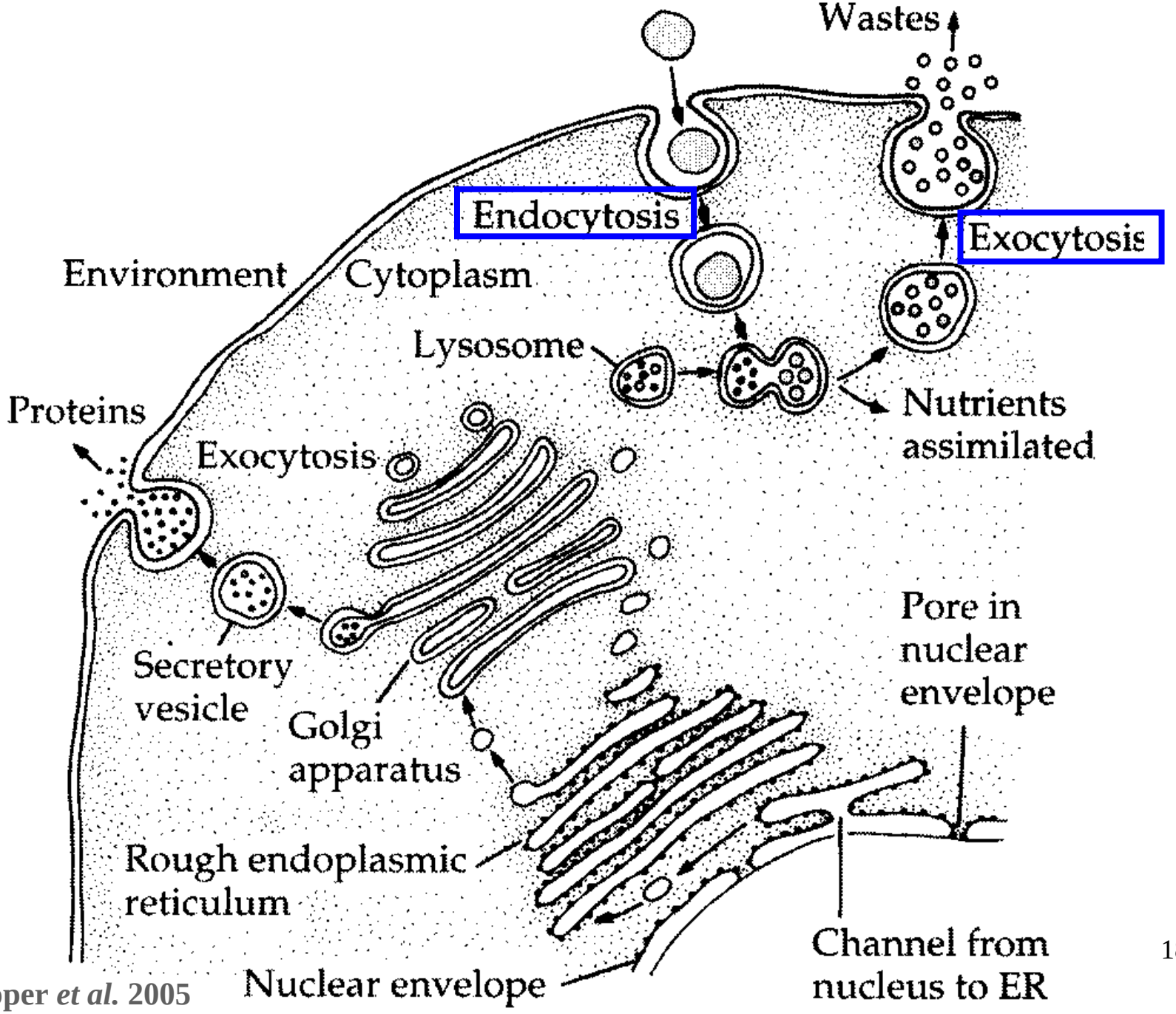


Gropper *et al.* 2005

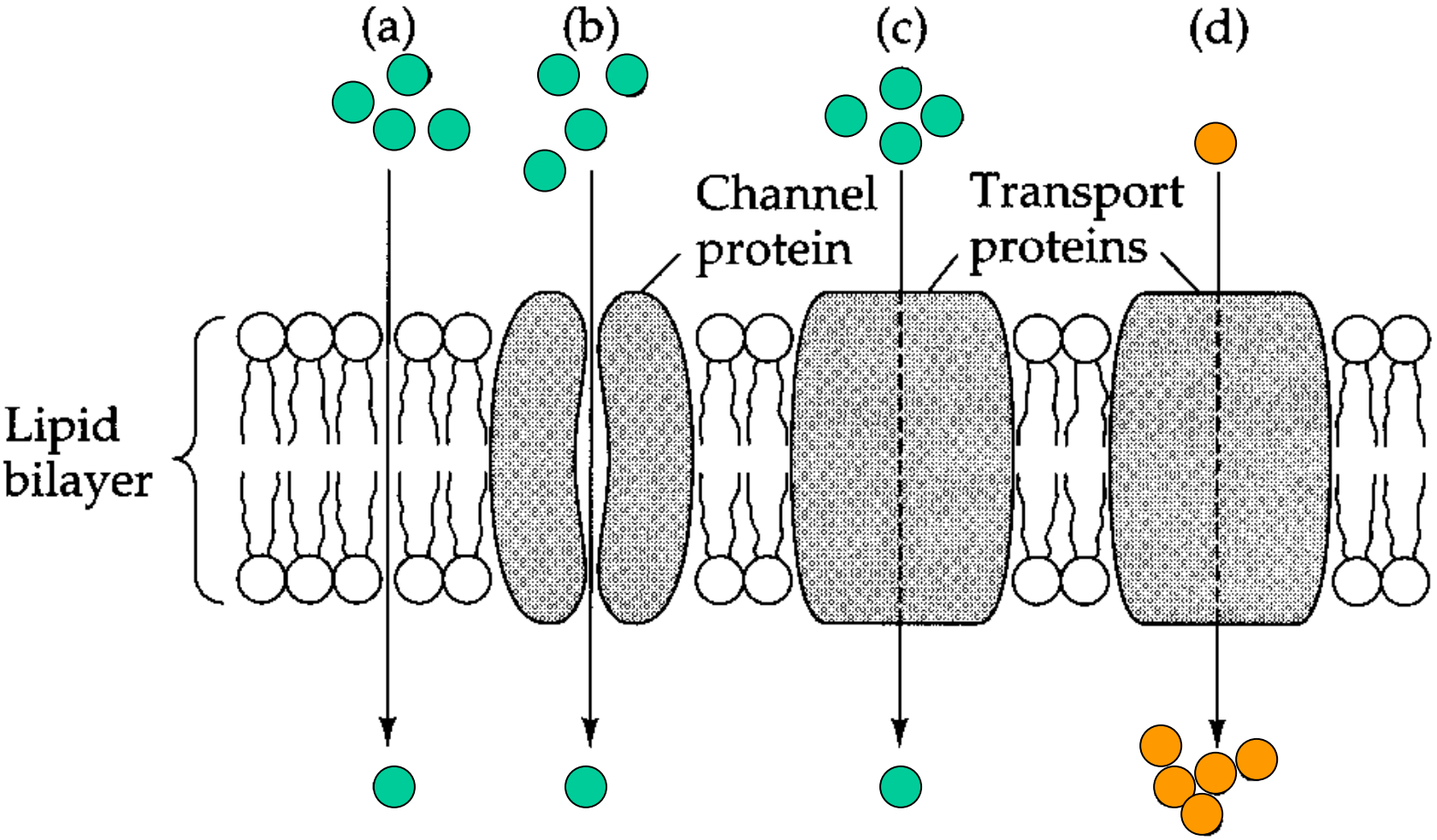


Gropper *et al.* 2005



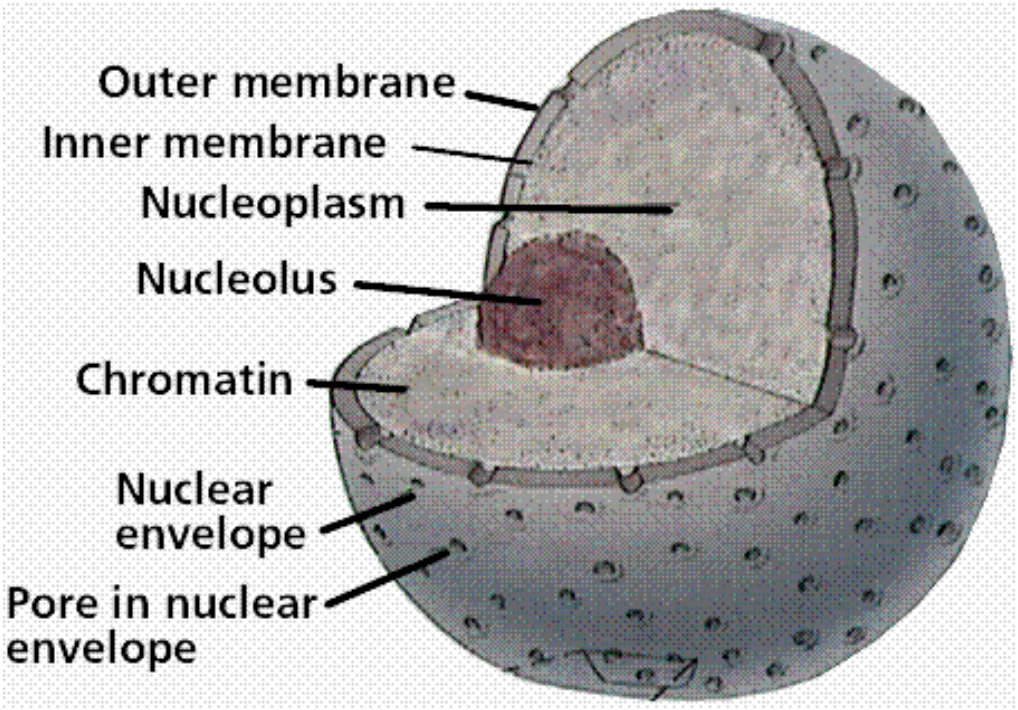
Gropper *et al.* 2005

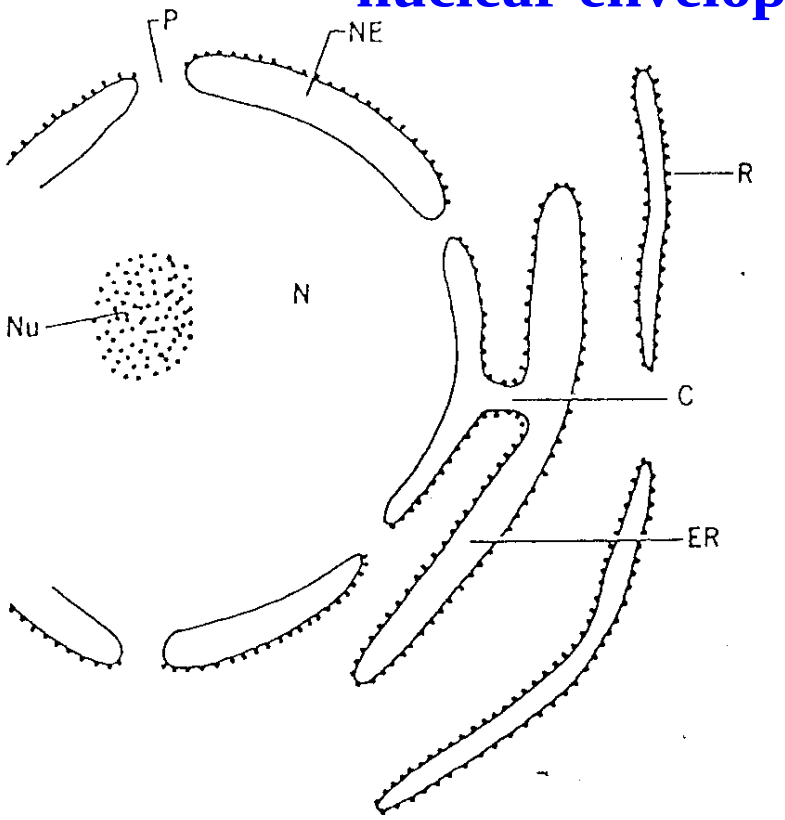
simple diffusion **channel diffusion** **facilitated diffusion** **active transport**



Gropper *et al.* 2005

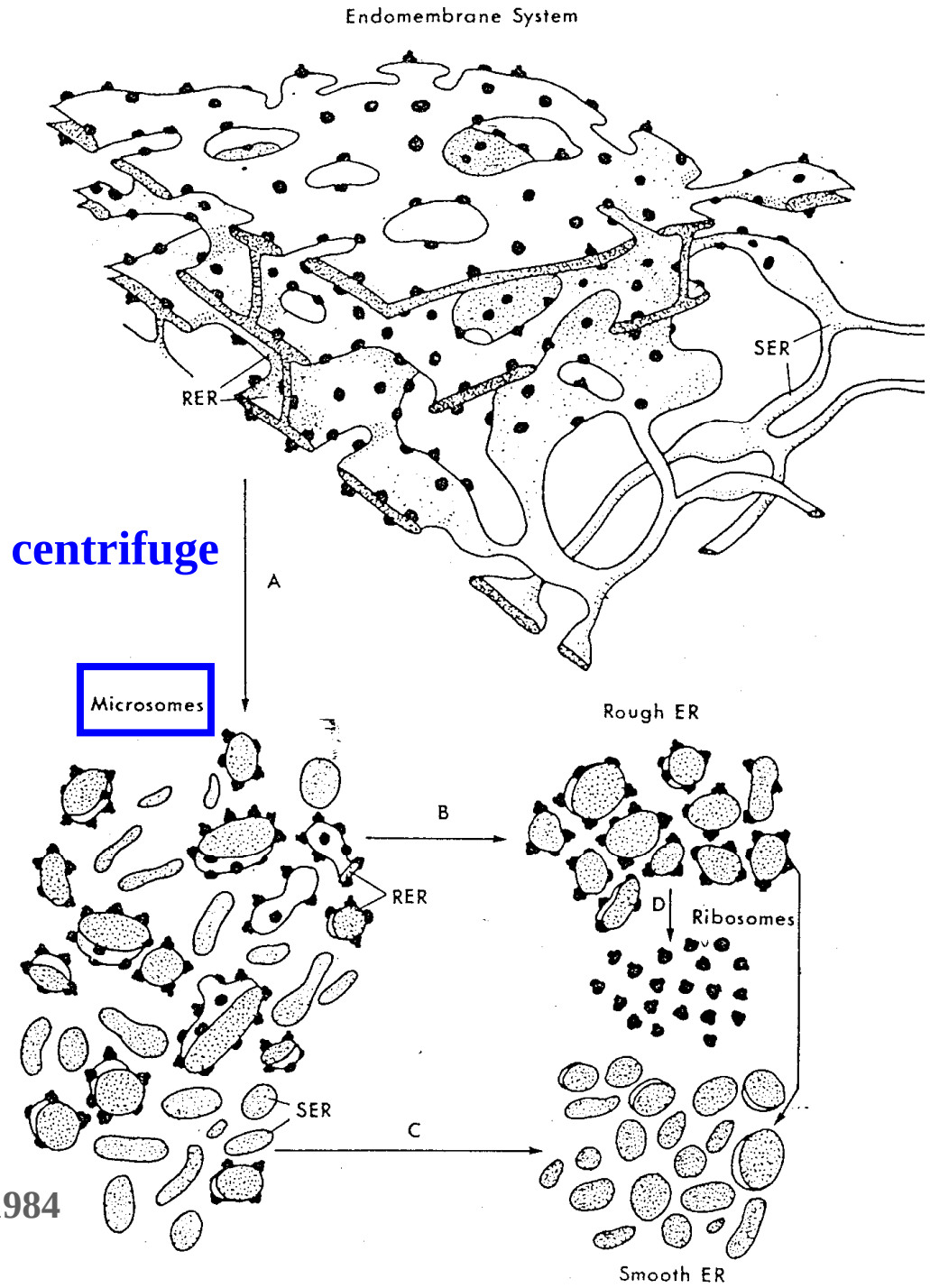
nuclear envelope





http://www.emc.maricopa.edu/faculty/farabee/BIOBK/nucleus_1.gif

Pike and Brown 1984



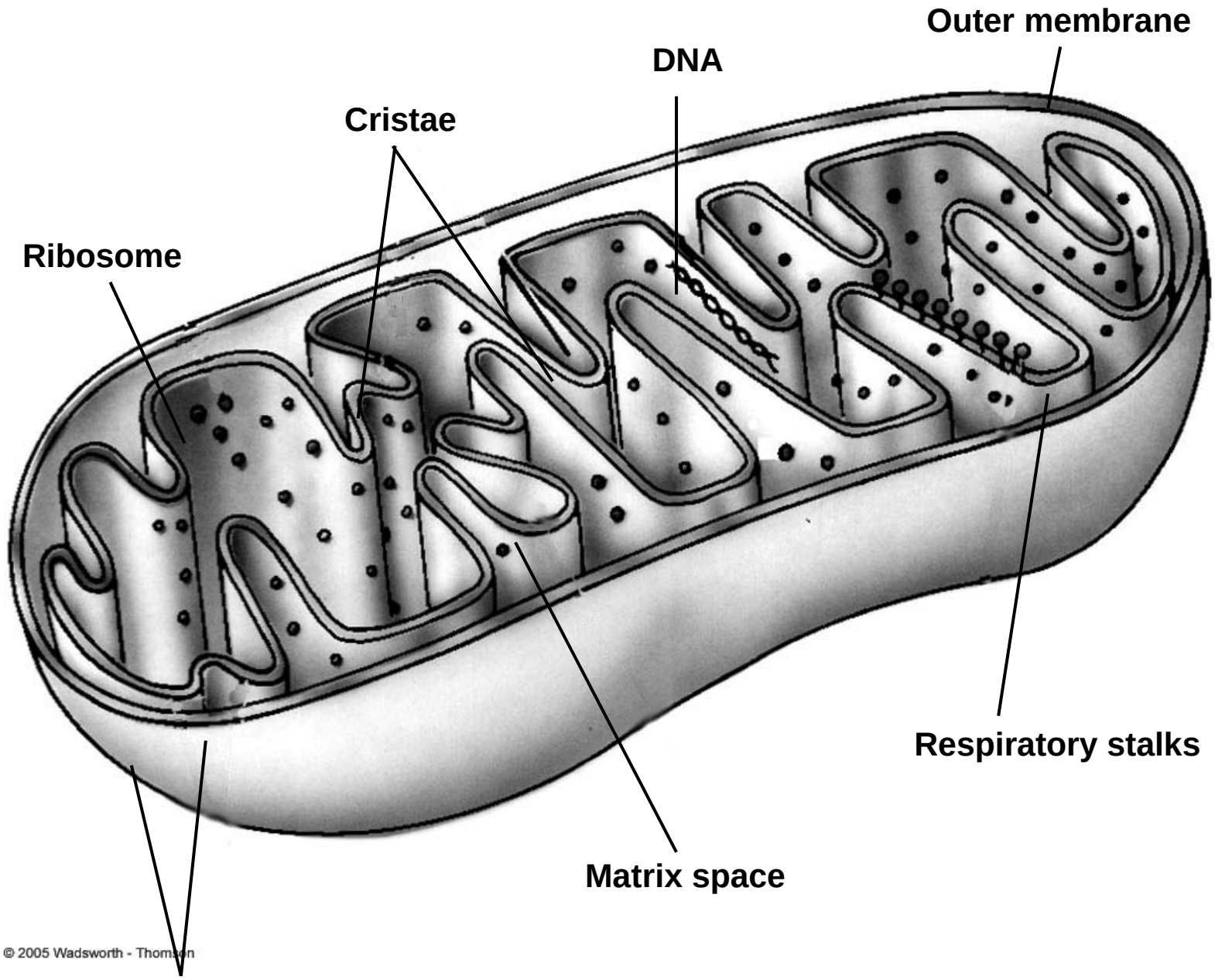
Pike and Brown 1984

Functions of ER

- **RER: protein synthesis in ribosomes**
- **SER: lipid and lipoprotein synthesis**
- **SER in the skeletal muscles: sarcoplasmic reticulum**

  calcium ATPase (or pump)
- **SER in the liver: a system for detoxification and metabolism of drugs**

  cytochrome P450 system



Gropper *et al.* 2005

Reactions in mitochondrial matrix

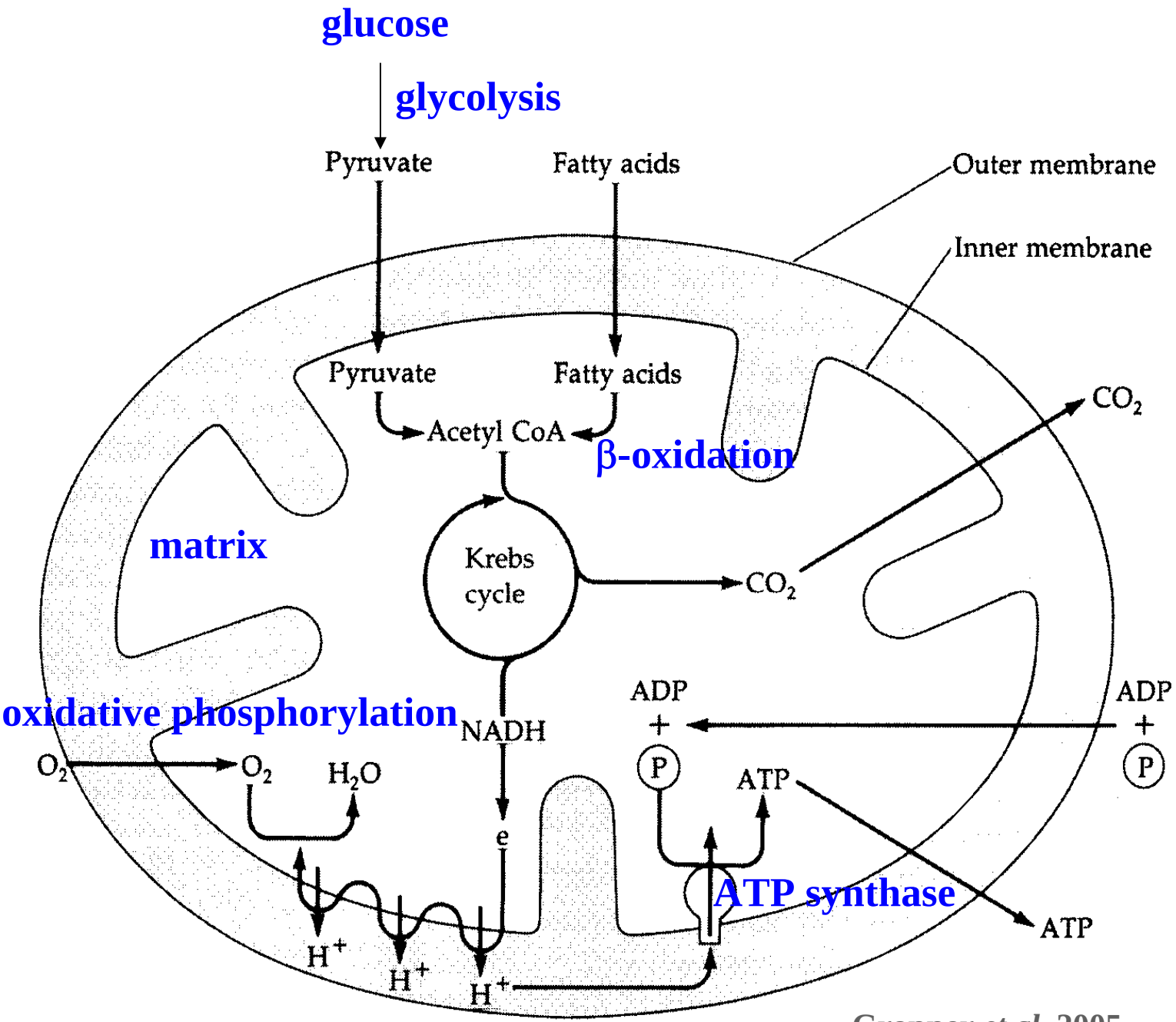
- **decarboxylation of pyruvate**

  pyruvate ⟶ acetyl CoA
- **Krebs (tricarboxylic acid, TCA) cycle**
- **transamination**
- **amino acid oxidation via TCA cycle**
- **Urea cycle (beginning)**
- **NEAA synthesis**
- **fatty acid oxidation**

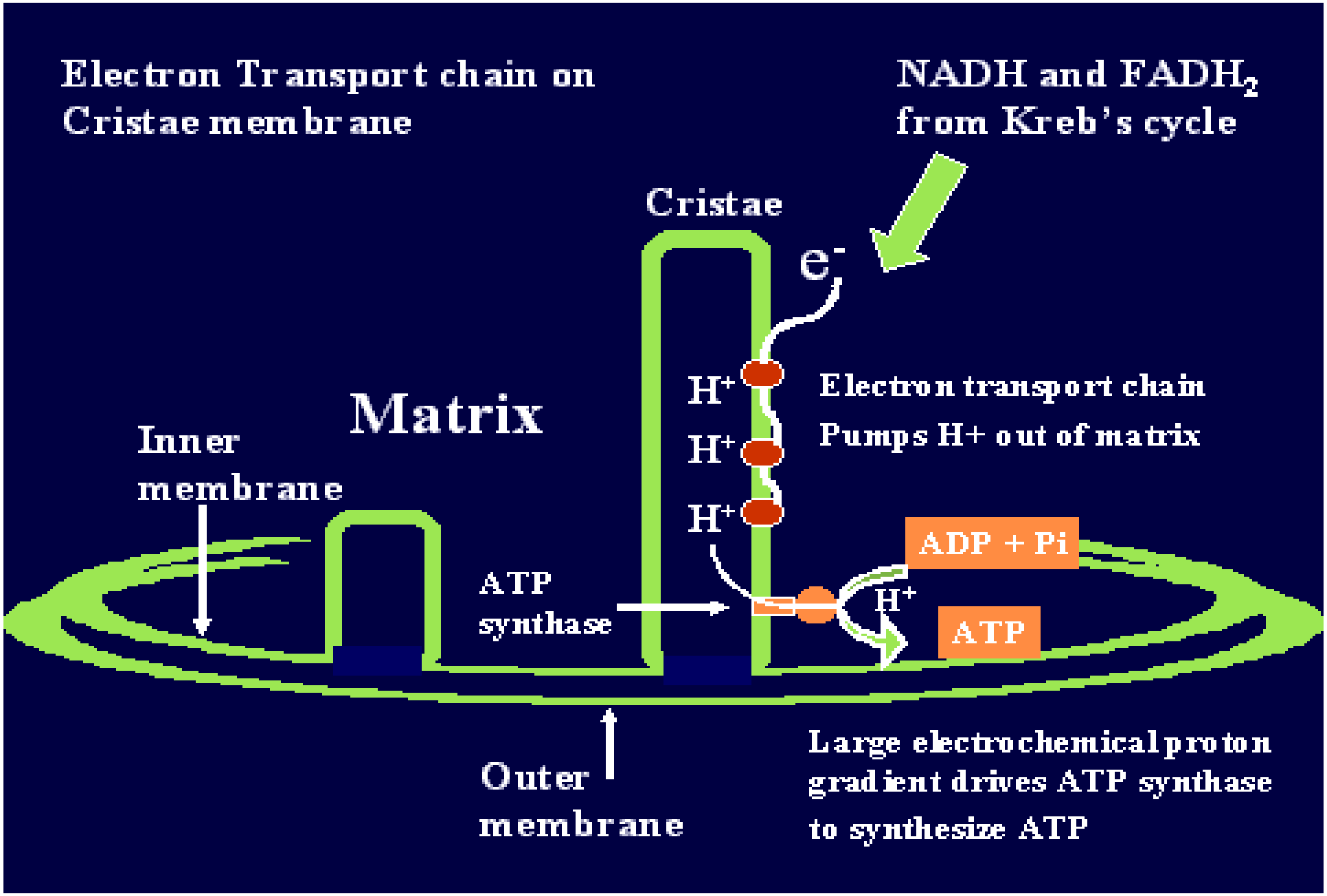
  fatty acid ⟶ acetyl CoA
- **polyamine synthesis**

Reactions in mitochondrial inner membrane

- **respiration**
- **electron transport chain and oxidative phosphorylation**

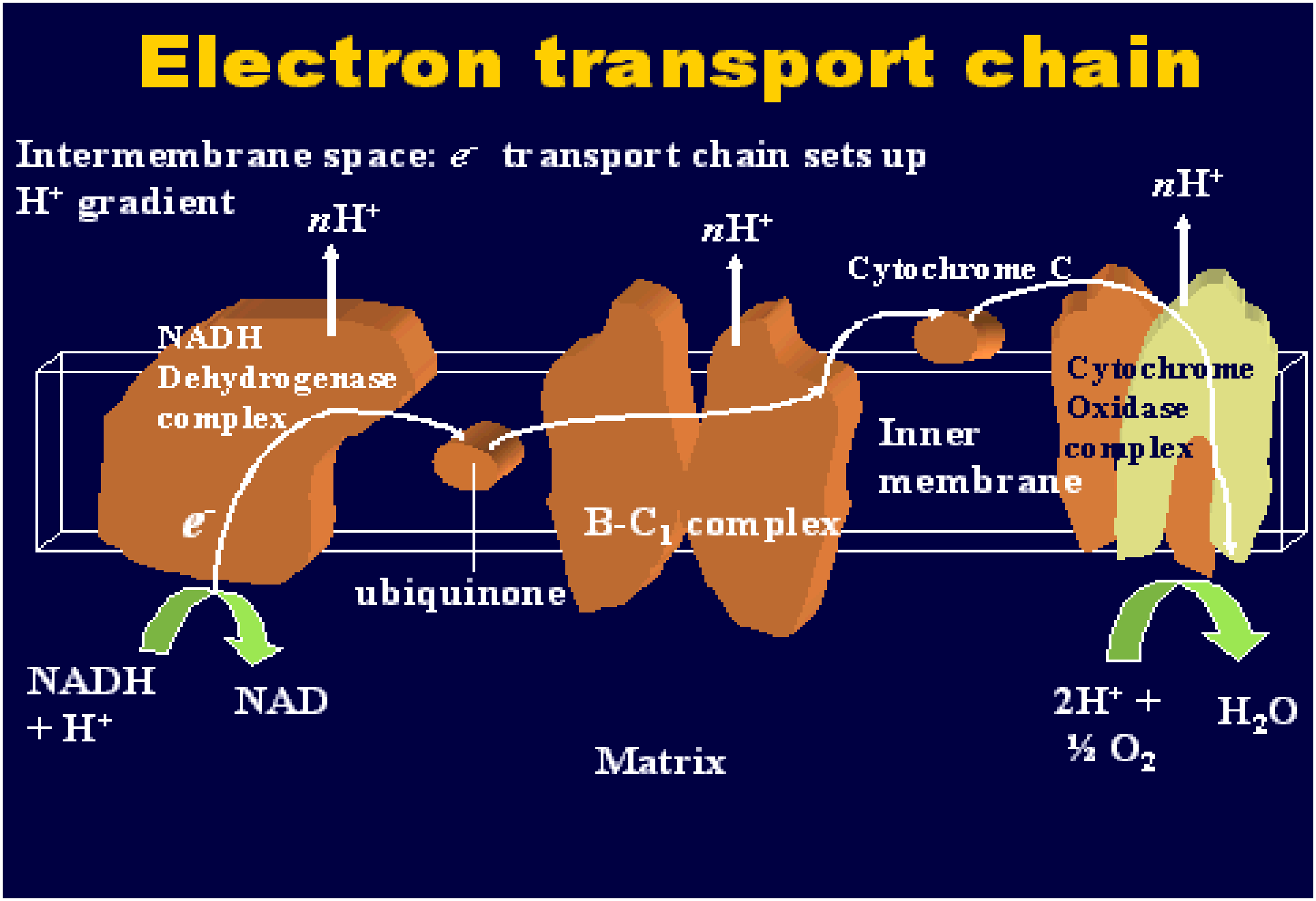


Gropper *et al.* 2005

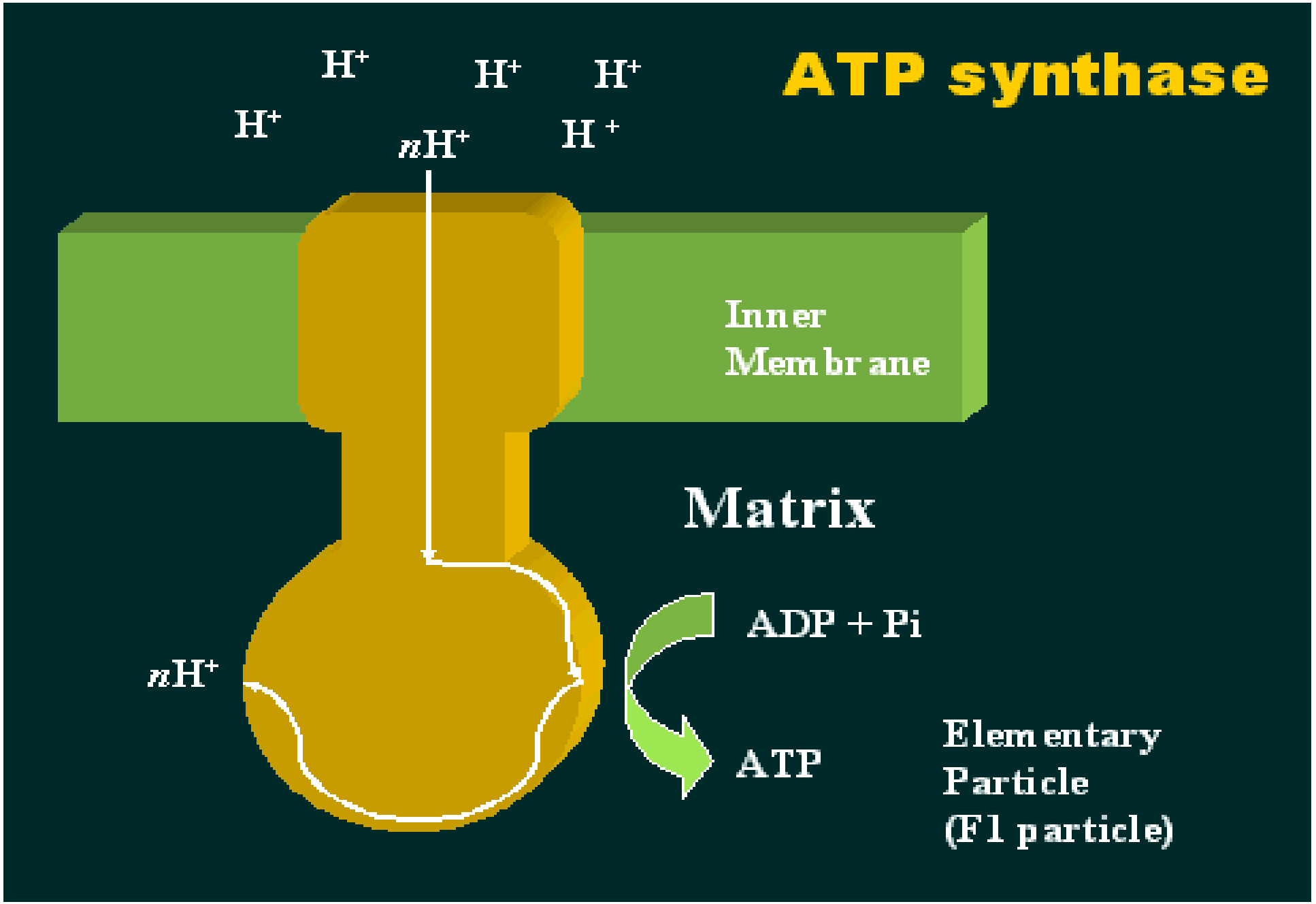


http://cellbio.utmb.edu/cellbio/mitochondria_1.htm

Electron transport chain



http://cellbio.utmb.edu/cellbio/mitochondria_1.htm



http://cellbio.utmb.edu/cellbio/mitochondria_1.htm

Functions of Golgi apparatus

- **package into zymogen granules**
- **carbohydrate group modification**
- **sorting different proteins into different vesicles**

Functions of lysosomes

- **abundant in macrophages and leukocytes**
- **present in greatest numbers in kidney cells**
- **contains hydrolytic enzymes**

  hydrolyze proteins, nucleic acids, polysaccharides, phospholipids
- **bone resorption (mineral removal)**

  lysosomes of osteoclasts promote dissolution of minerals and digest collagen

Dysfunctions of lysosomes

- **Type II glycogen storage disease (Pompe's disease)**

  missing lysosomal hydrolase (α-glucosidase)

  accumulation of glycogen in vacuoles

  glycogen can not be mobilized for metabolism

  proteolytic destruction of muscles

- **Rheumatoid arthritis**

  associated with incomplete cellular autolysis

  failure of lysosomal enzymes to perform their function of digesting dead cells and debris

  lysosomal enzymes released from cells of synovial lining

  infecting organisms to cause membrane and cartilage damage

Functions of peroxisomes

- contains catabolic **oxidative** enzymes
- absence of **acid phosphatase** (different from lysosomes)
- In plants and microorganisms: gluconeogenesis
- H_2O_2 metabolism

  $H_2O_2 \xrightarrow{\text{catalase}} H_2O + ½\ O_2$
- degradation of purines

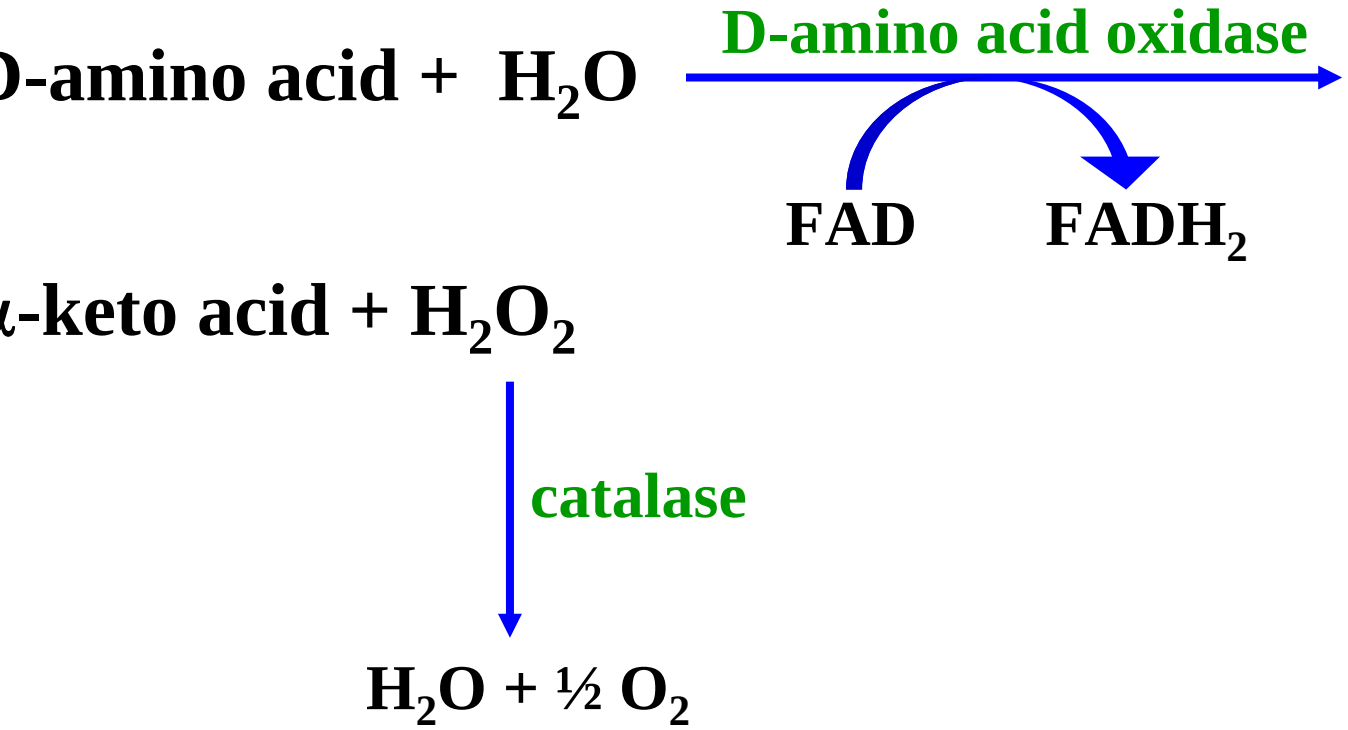
  urate oxidase, xanthine dehydrogenase
- oxidation of ethanol (detoxification)

  $CH_3\text{-}CH_2\text{-}OH + NAD^+ \xrightarrow{\text{alcohol dehydrogenase (ADH)}} CH_3\text{-}CHO + NADH + H^+$

  ethanol — acetaldehyde
- β-oxidation of unsaturated fatty acids

Functions of peroxisomes

- **deamination of D-amino acid**



Liver

- **processor and distributor in metabolism**
- **primarily responsible for the synthesis of urea, creatine, plasma proteins, triacylglycerol, phospholipids, and bile acids**
- **Blood enters liver: 65~75% from portal vein**

  25~35% from hepatic artery

Functions of liver

1. **Regulation of blood glucose level**

   maintenance of normal [blood glucose]

   rate of glucose entry into blood ≈ rate of glucose withdrawal

   withdraw glucose from the blood for synthesis of glycogen (glycogenesis) for storage

   supply glucose derived from its readily available store of glycogen through glycogenolysis

Functions of liver

- **Postabsorptive state**

  maintain blood glucose concentration: 80~100 mg/dL

  by glycogenolysis and gluconeogenesis

  i.e. overnight fasting glycogenolysis/gluconeogeneis (75% *vs* 25%)

  blood glucose in normal individuals: 60~160 mg/dL (remain constant)

  normal control of glycosylation to proteins: blood glucose < 180 mg/dL

  normal brain function requires ~ 6 g glucose/h

  which can be delivered only if arterial blood contains > 50 mg/dL

Glucose transporters (GLUT)

- **GLUT-1~GLUT-13**
- **GLUT-1: in most tissues during gestation**
- **GLUT-2: primarily in liver, intestine, and kidney, insulin-independent**
- **GLUT-3: in the intestine and neurons**
- **GLUT-4: in skeletal muscles, heart, and adipose tissue, insulin-sensitive**

Functions of liver

2. Gluconeogenesis

in liver and kidney during fasting or heavy exercise

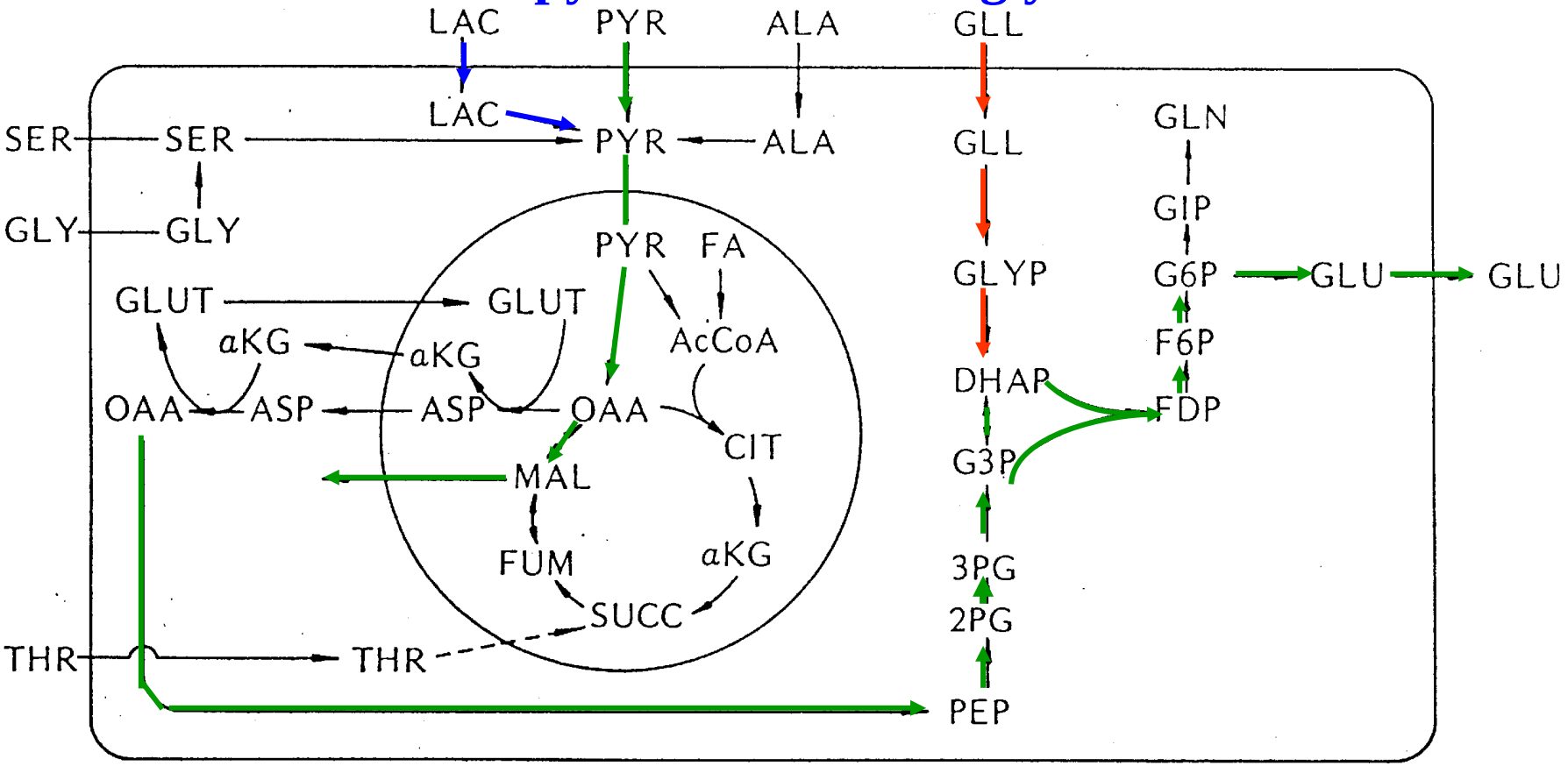
when carbohydrate intake is limited and body glycogen stores are depleted

sources: lactate (60%), glucogenic amino acids (25%), glycerol (10%), pyruvate (5%)

proves for recycling of lactate (Cori cycle) and glycerol accumulated in muscles

Gluconeogenesis

lactate pyruvate alanine glycerol



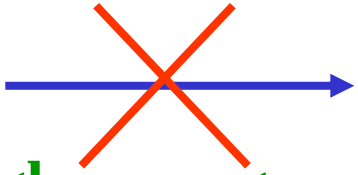
Pike and Brown 1984

Gluconeogenesis

- **in skeletal muscles and adipose tissue:**

  ∵ lack of glucose-6-phosphatase (G-6-Pase)

  glucose-6-phosphate  **glucose**

  lactate  **glucose**

Functions of liver

3. Cori cycle

- **oxygen supply is limiting (exercising muscles)**
- **in the absence of mitochondria (in RBC)**

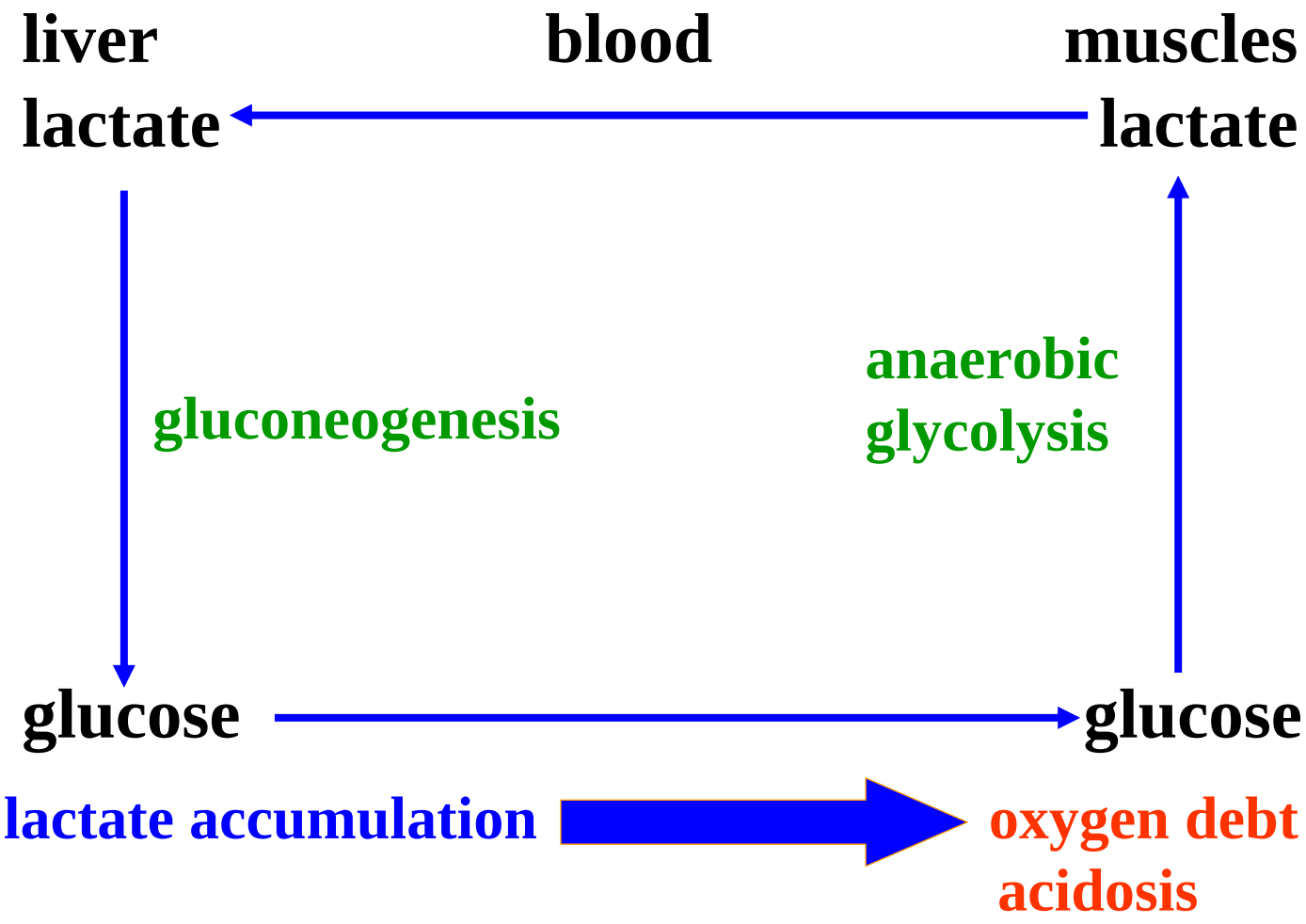
(1)early 12-h fasting: between liver and muscles, liver and RBC

(2)24~48-h fasting: between liver and RBC

(3)pregnancy: between liver and placenta

(4)heavy exercise: between liver and muscles

Cori cycle


liver
blood
muscles
lactate
lactate
gluconeogenesis
anaerobic
glycolysis
glucose
glucose
lactate accumulation
oxygen debt
acidosis

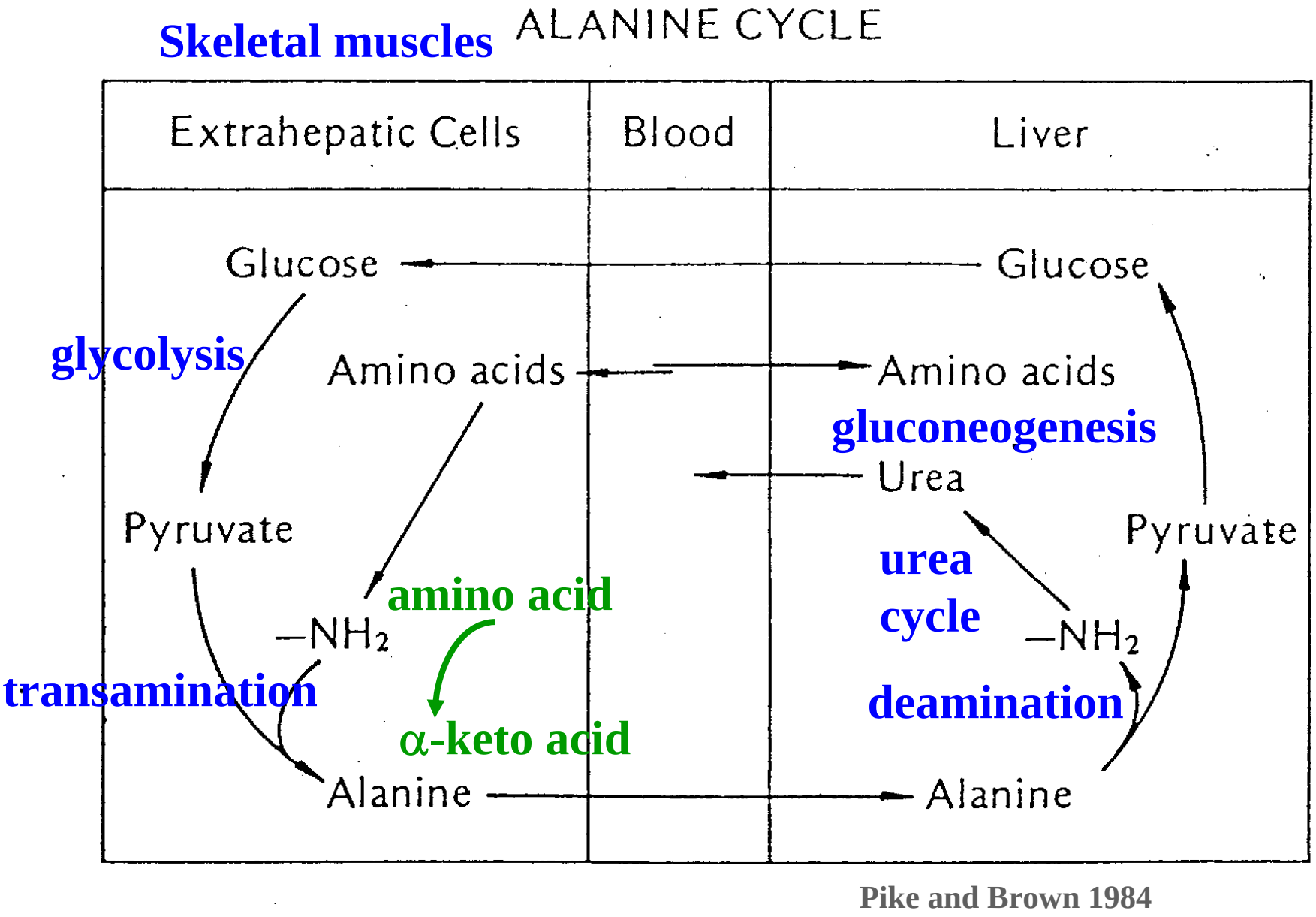
Functions of liver

4. Alanine cycle (glucose-alanine shuttle)

- **a mechanism for skeletal muscle to eliminate nitrogen while replenishing its energy supply**

(1) fasting

(2) exercise



Pike and Brown 1984

Functions of liver

5. Ketogenesis

- **as an important fuel for brain, heart, and skeletal muscles**

(1) starvation

(2) lack of carbohydrate (a very low carbohydrate diet)

(3)diabetes

→ high rate of fatty acid oxidation (↓ glucose ox.)

→accumulation of acetyl CoA (exceeds the capacity of TCA cycle)

Functions of liver

- **ketone bodies: acetoacetate**

  β-hydroxybutyrate

  acetone

- **occurs in liver mitochondria**
- **∵ fatty acids can not pass blood-brain barrier to brain**

  ∴ brain utilizes ketone bodies for fuel

Functions of liver

- **acetone is difficult to oxidize *in vivo***
- **if ↑↑ acetoacetate formed is faster than it can be oxidized**

  → ↑ [ketone bodies] in the blood

  → ketonemia
- **if blood level exceeds the renal threshold**

  → ketone bodies (H_2O-soluble) are excreted in urine

  → ketonuria
- **ketonemia + ketonuria → ketosis**

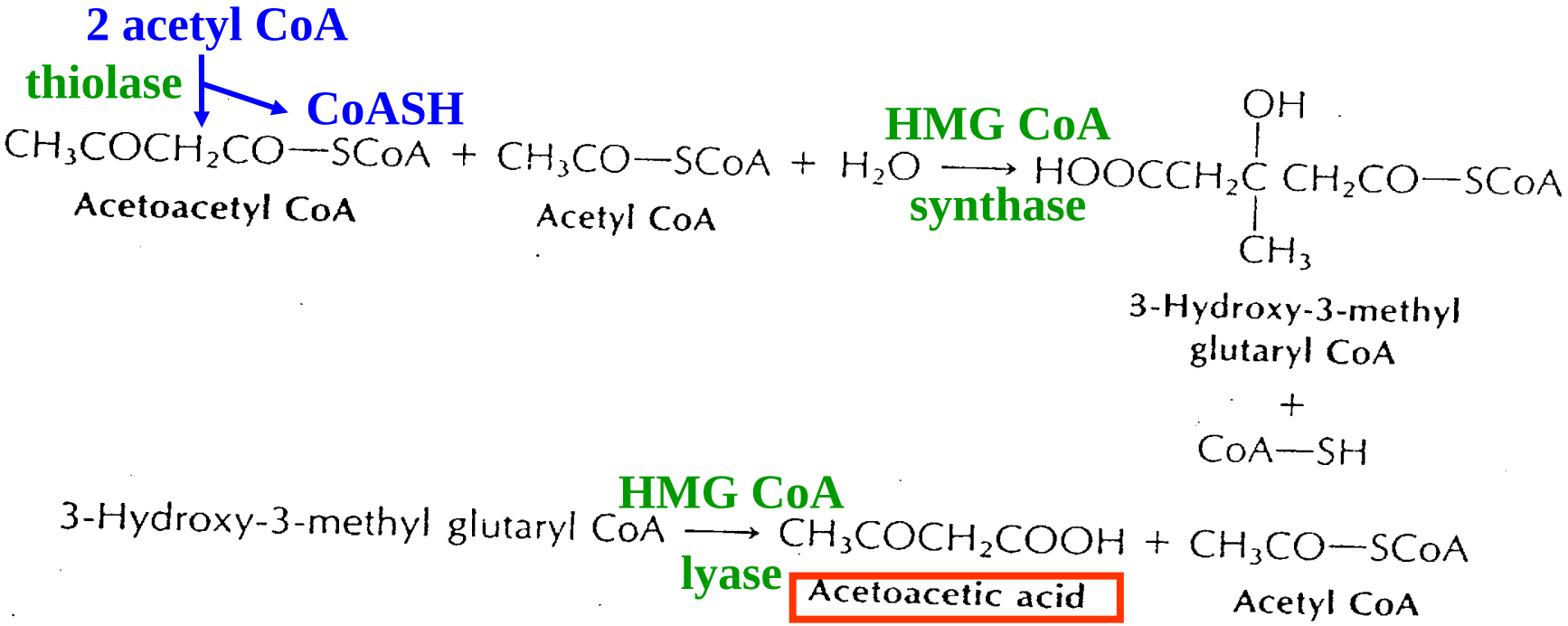
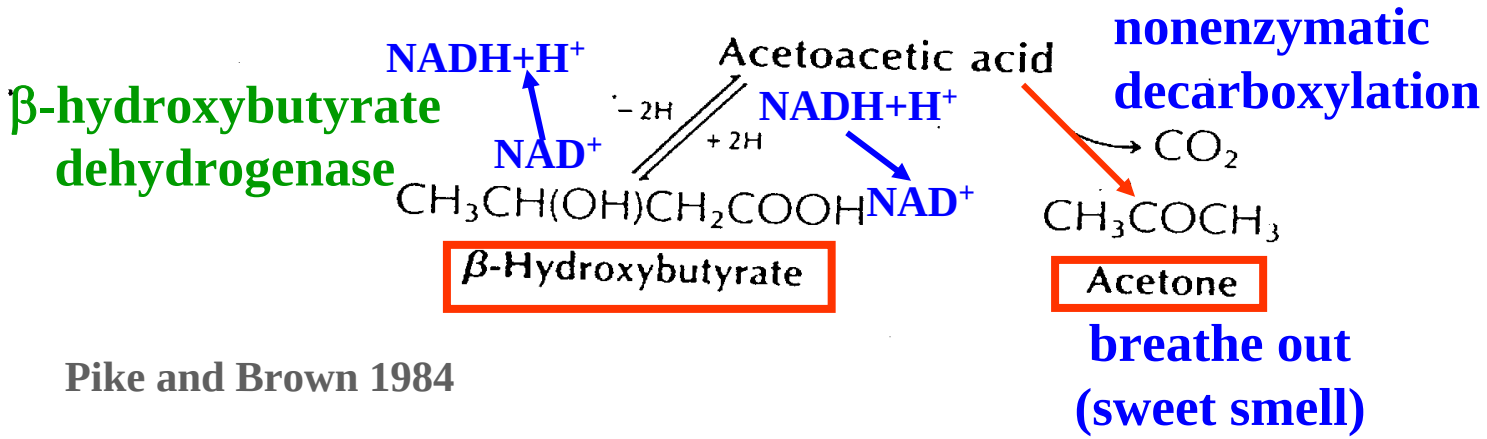


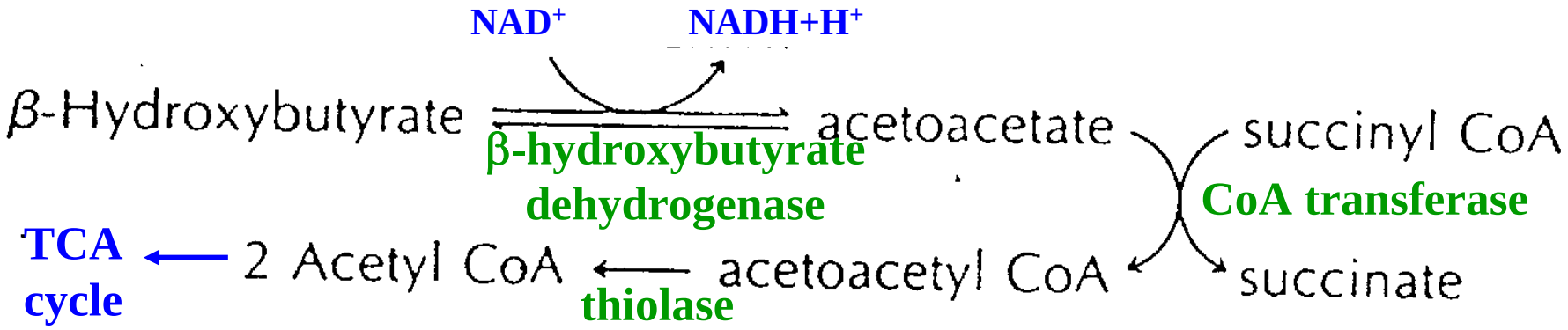
Figure 15.5 illustrates the pathway of ketogenesis in the liver cell. Acetoacetate, thus formed, may be reduced to form β-hydroxybutyrate in a reversible reaction or decarboxylated to form acetone.



Pike and Brown 1984

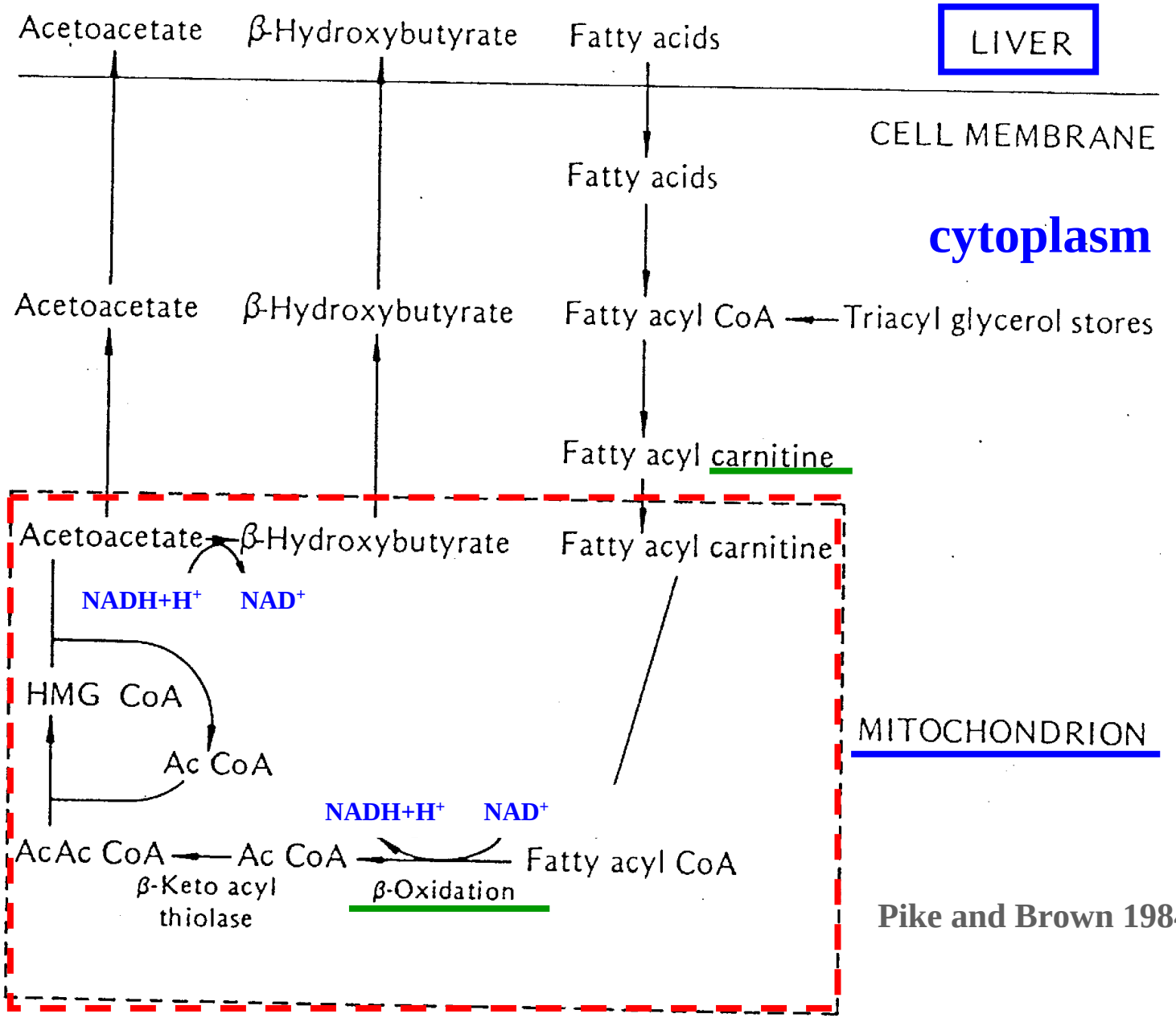
Utilization of ketone bodies

in extrahepatic cells (brain, heart, and skeletal muscles):



Pike and Brown 1984

Ketogenesis



Pike and Brown 1984

Functions of liver

6. Plasma protein synthesis

- albumin 150~250 mg/kg bw is synthesized daily in adult humans
- synthesis and release of one albumin: ~30 min
- during fasting and malnutrition: ↓ albumin synthesis

  malnutrition children: 100~148 mg albumin/kg/d

  well nourished children: 222~233 mg albumin /kg/d

Functions of liver

7. Creatine synthesis

- occurs in liver and kidney
- precursors: glycine, arginine, ornithine, methionine
- after synthesis, creatine is transported to muscles
- in muscles: creatine 

phosphocreatine

spontaneously

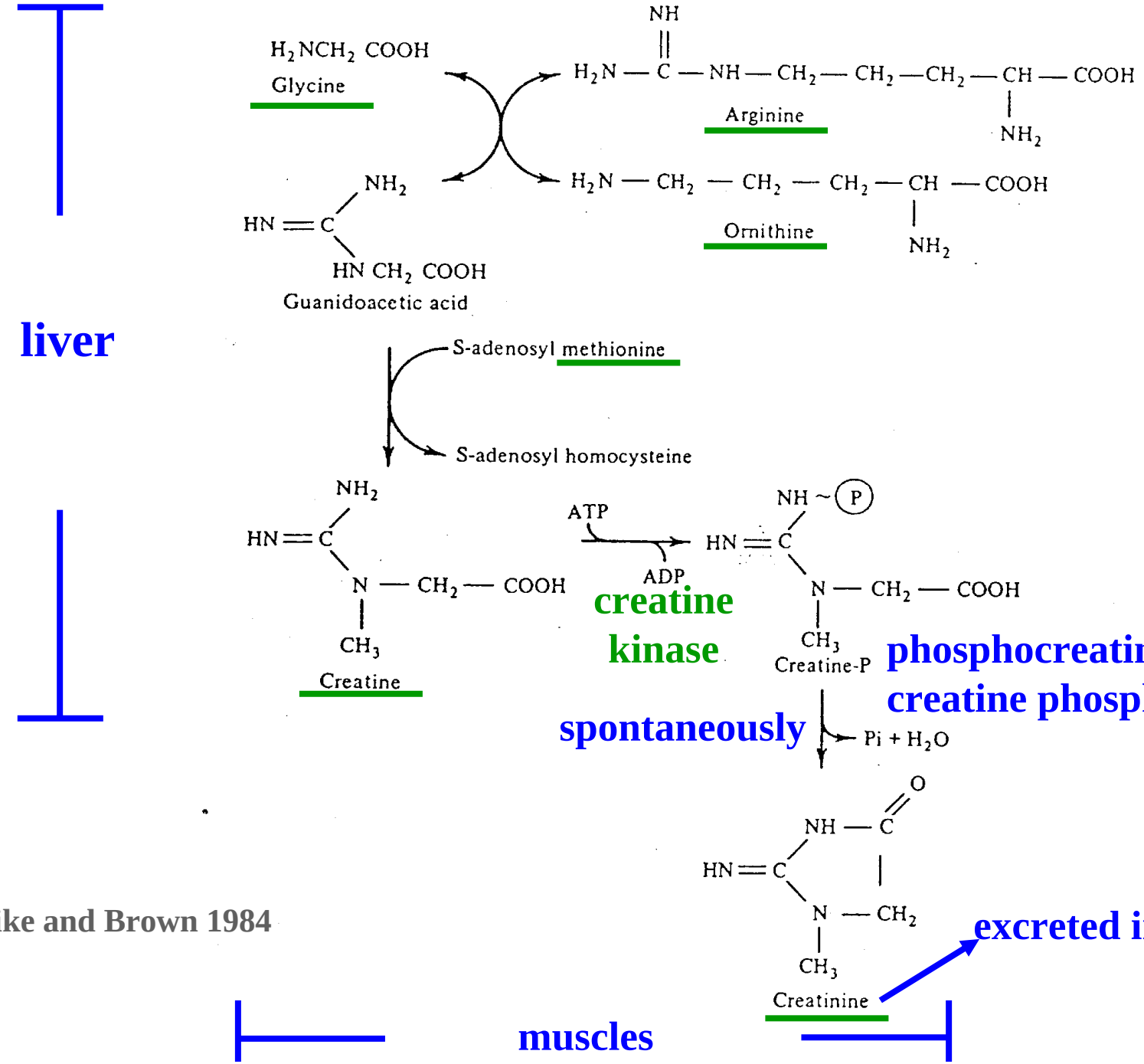
indicator of amount of existing muscle mass

creatinine

0.3~0.5% muscle mass (by wt)

can not be metabolized and is excreted in urine

creatinine clearance: estimates kidney function

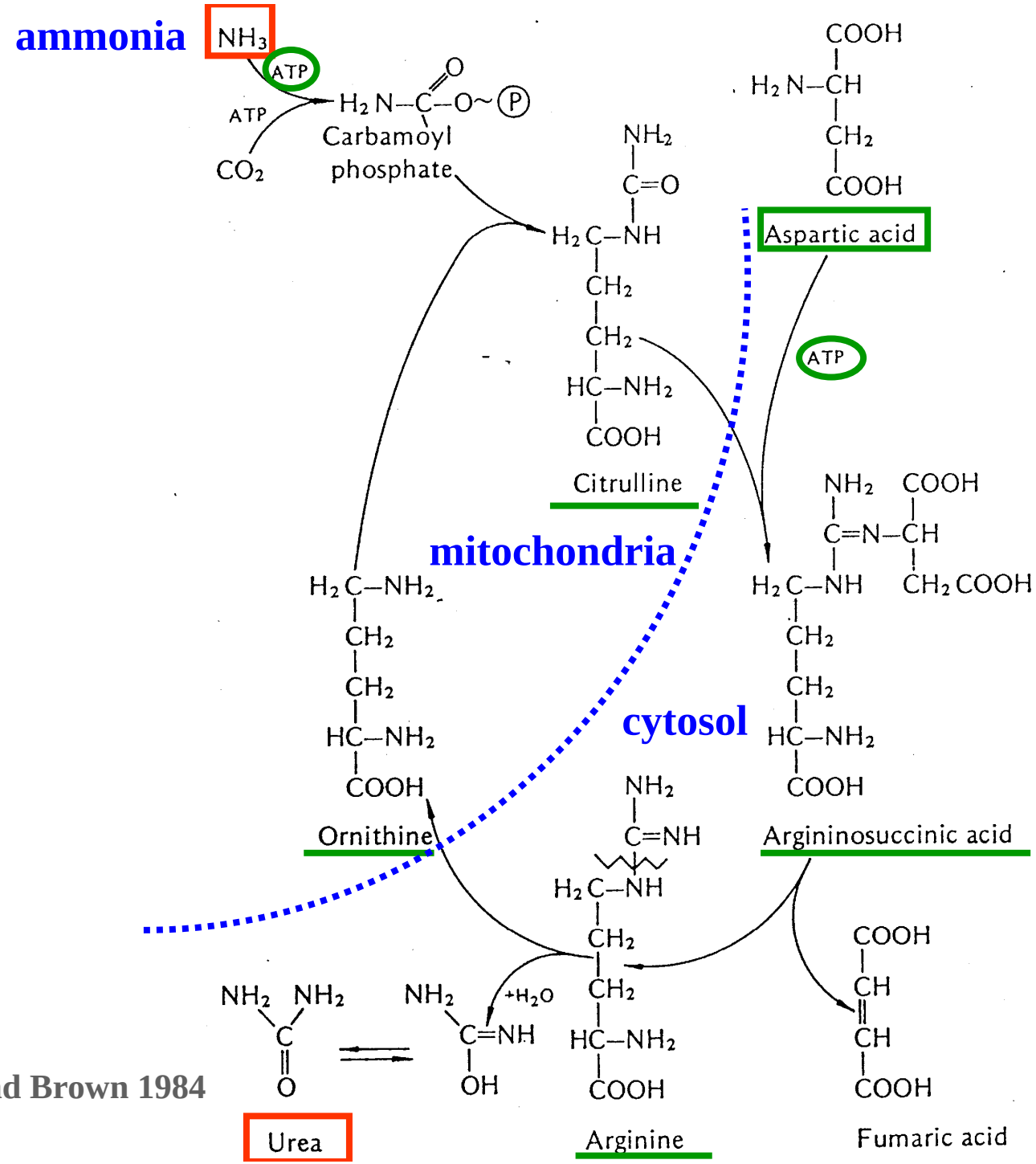


Pike and Brown 1984

Functions of liver

8. Urea synthesis (detoxication)

- occurs in liver, kidney, intestine
- disposal of ammonia arising from deamination and from absorbed ammonia synthesized by intestinal bacteria from urea and other sources
- glutamine serves as a major transport form for amino groups from peripheral tissues to liver



Pike and Brown 1984

Functions of liver

9. Plasma lipid synthesis

- **fatty acid synthesis**
- **plasma triacylglycerol, phospholipids, lipoproteins (VLDL, HDL)**

Functions of liver

10. Cholesterol synthesis and degradation

- **synthesis occurs in liver, adrenal cortex, skin, intestine, testis, aorta**
- **in cytoplasmic matrix**
- **rate-limiting enzyme: HMG CoA reductase**

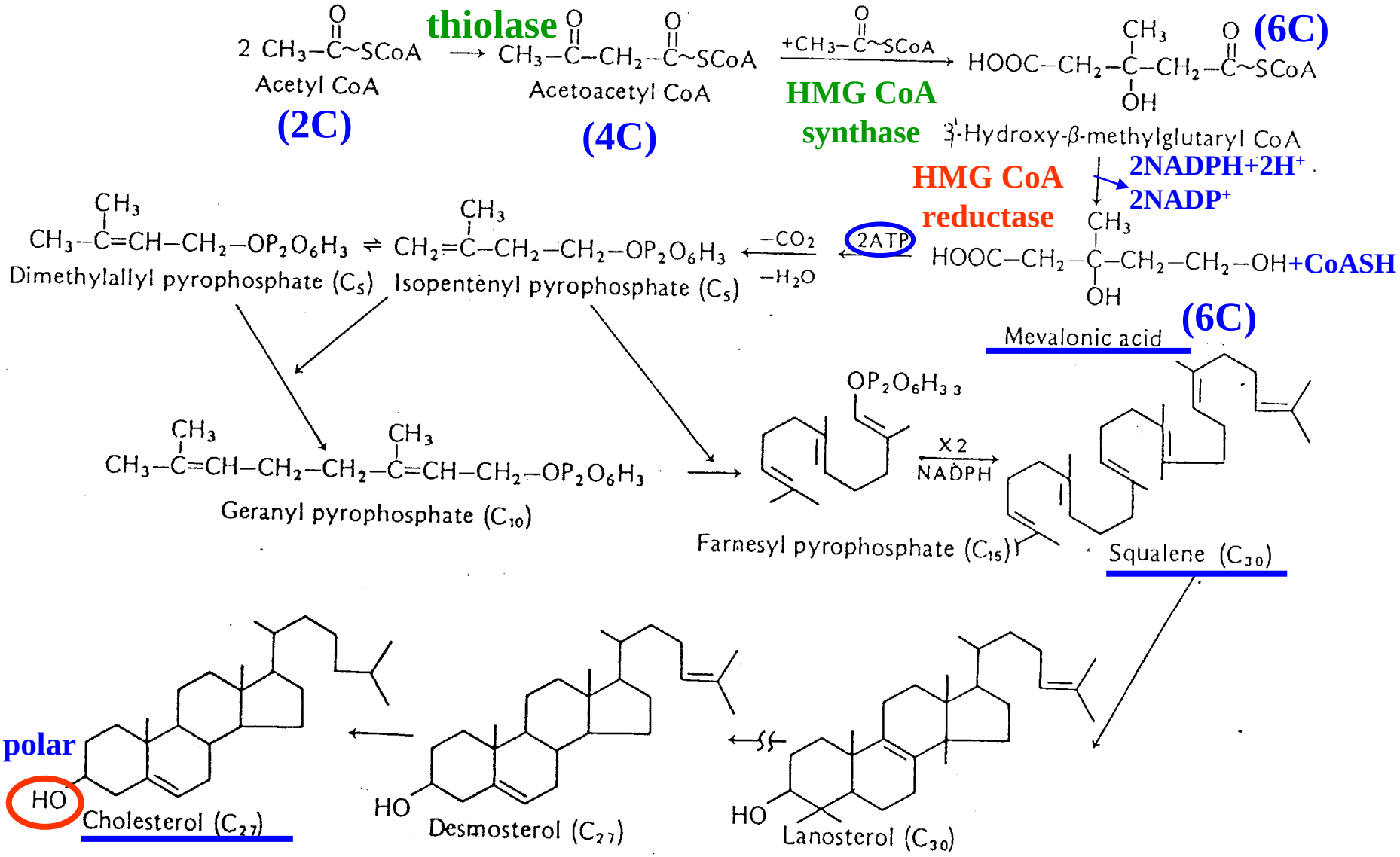


Figure 15.9
Biosynthesis of cholesterol.

Pike and Brown 1984

Functions of liver

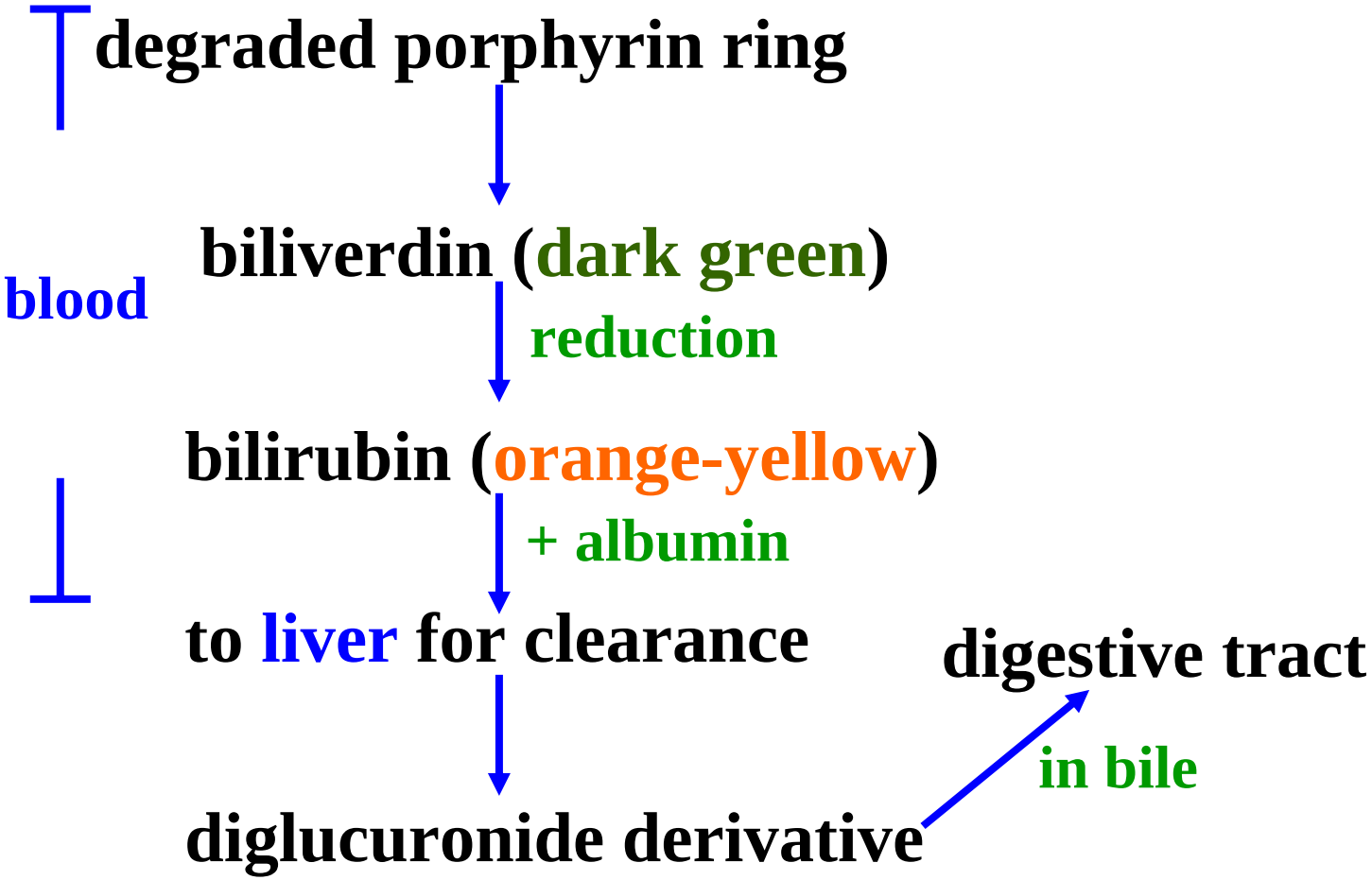
11. Bile acid synthesis

- **bile salts: promote solubilization of lipids and lipid-soluble materials for absorption through mucosal membrane**
- **primary (including conjugated) and secondary bile acids**

Functions of liver

12. Bile pigment formation

- derived from heme breakdown



Summary

- **Functions of organelles in eukaryotic cells are complicated.**
- **A variety of metabolic pathways occur in different organelles.**
- **Liver is responsible for a variety of synthesis, metabolism, and regulation.**