Coenzymes and Vitamins

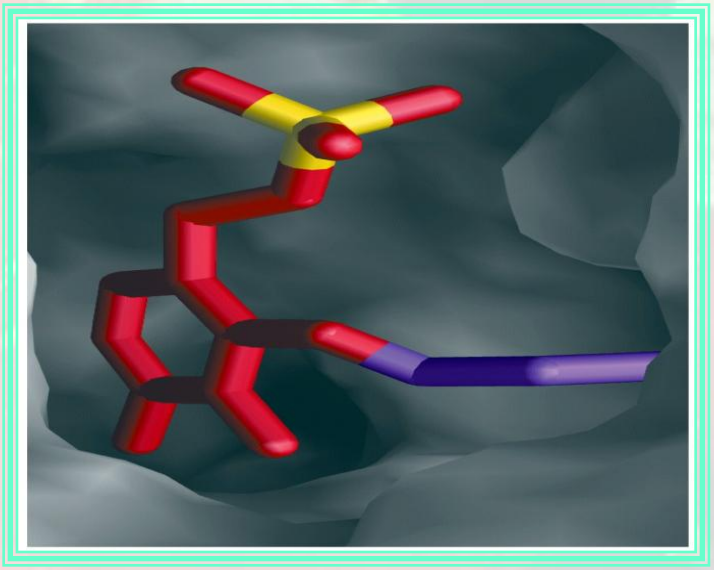
Dr.Sulieman Al-Khalil

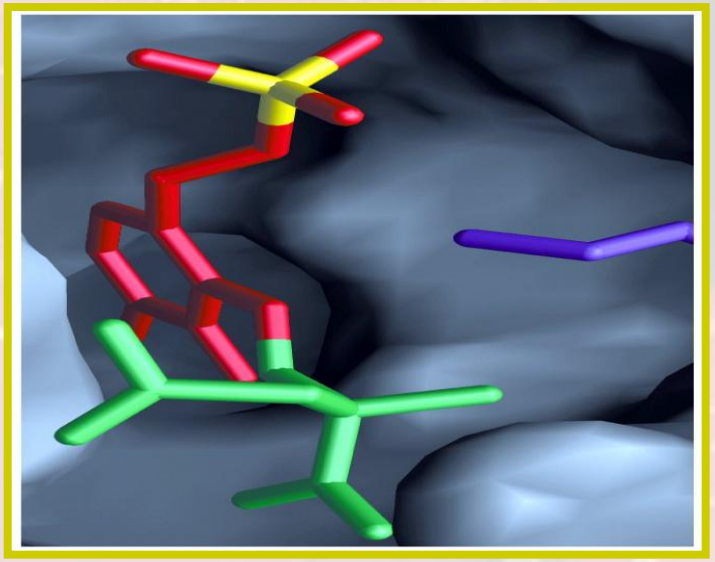
VITAMINS AND COENZYMES

Enzyme Vocabulary

cofactors

coenzymes





holoenzyme

apoenzyme

Introduction

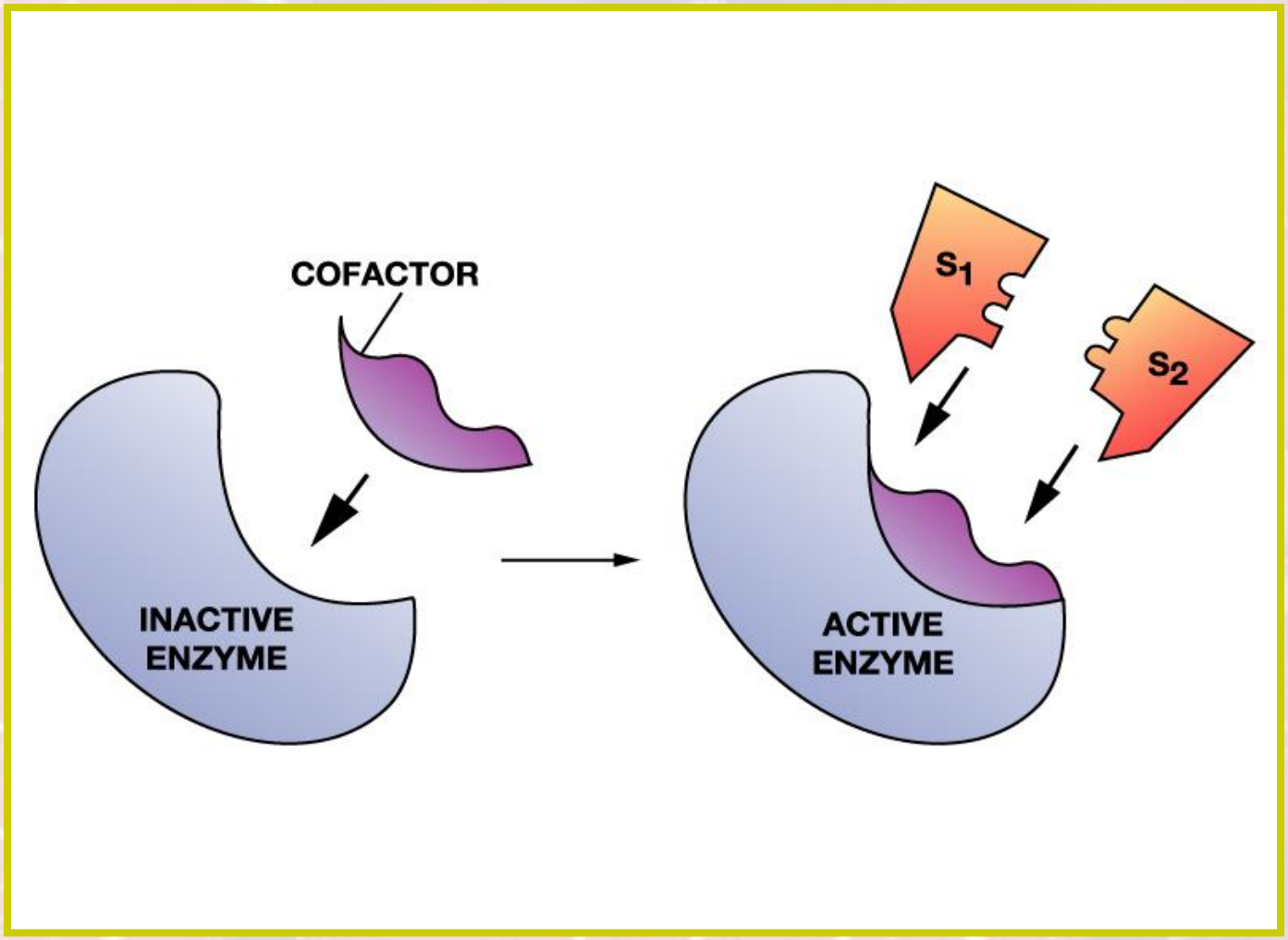
- Cofactors are inorganic, or non-protein organic molecules.
- Coenzymes are organic molecules that act as receptors and carriers for atoms/functional groups.
- Some enzymes require **cofactors** for activity

(1) **Essential ions** (mostly metal ions)

(2) **Coenzymes** (organic compounds)

vitamin + modification ---> coenzyme

Cofactors or Coenzymes



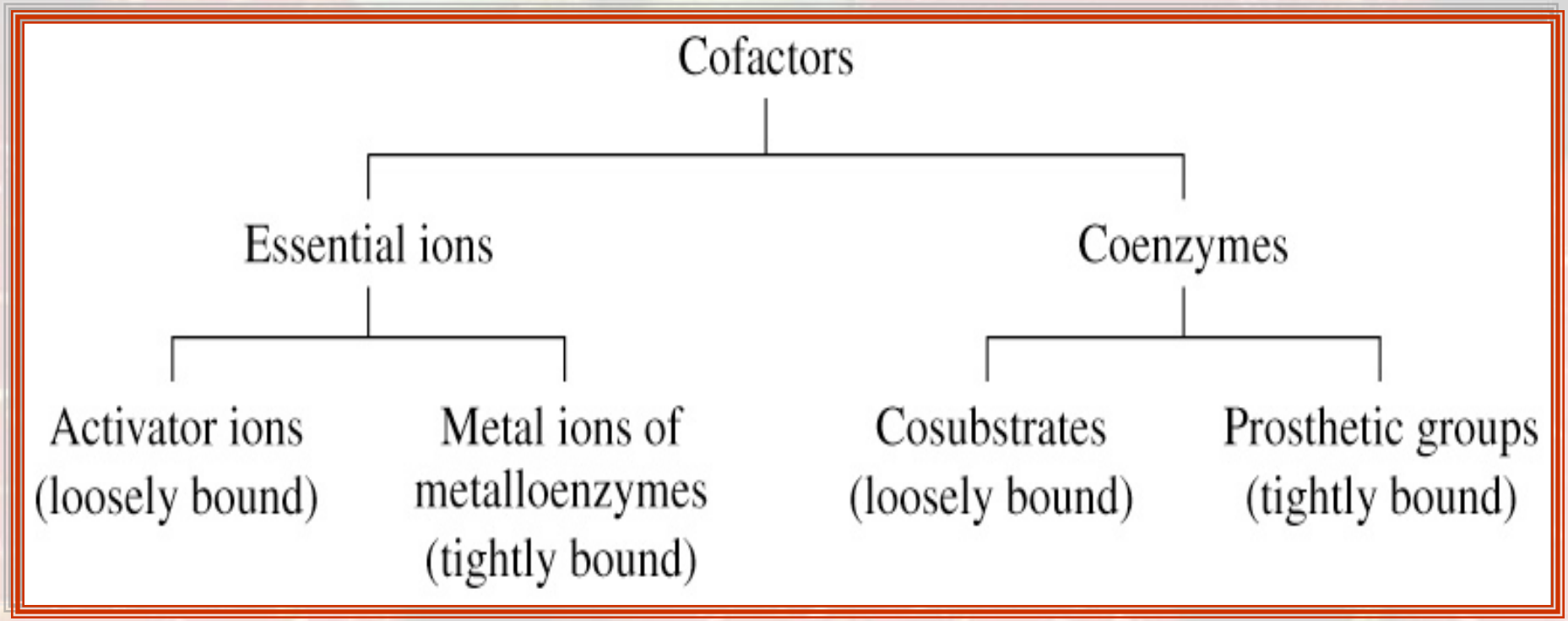
Apoenzyme + **Cofactor** → **Holoenzyme**

(protein only) (non-protein) (active)
(inactive)

- Coenzymes act as group-transfer reagents.
- Hydrogen, electrons, or other groups can be transferred.
- Larger mobile metabolic groups can be attached at the **reactive center** of the coenzyme.
- Coenzyme reactions can be organized by their types of substrates and mechanisms

Types of cofactors

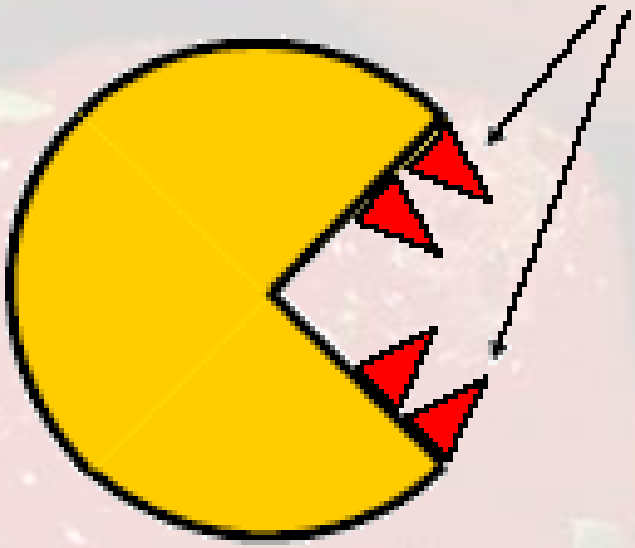
- A cofactor is a non-protein part of an enzyme



Cofactors

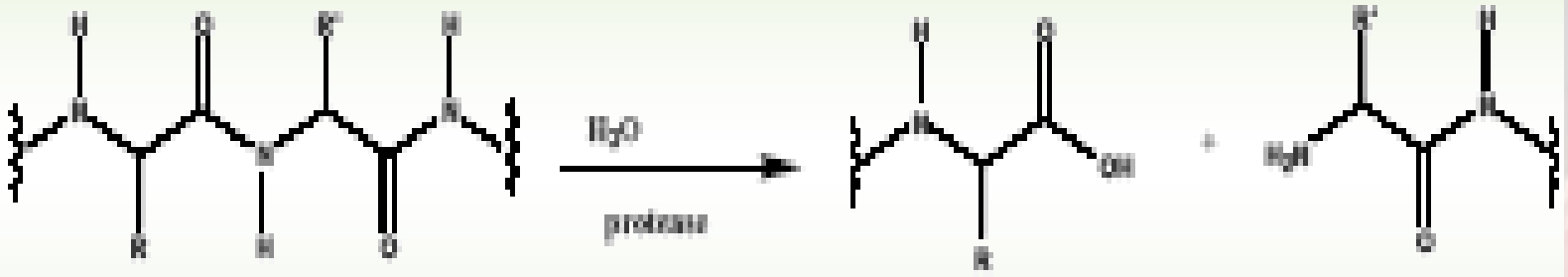
- provide "chemical teeth" for enzymes
- sometimes referred to as *coenzymes*
- enzymes: proteins with catalytic activity
  - simple enzymes: large protein (polypeptide) that catalyzes a reaction. The enzyme gets all the "tools" (chemical teeth) it needs from the amino acids. However, there are only 20 different amino acids
  - conjugated enzymes : *apoenzyme* + *cofactor* = *holoenzyme*

Some enzymes utilize cofactors



- Metals
- Coenzymes
  - Prosthetic groups
    - Heme
    - Thiamine (B_1), riboflavin (B_2), pyridoxine (B_6)
  - Transiently associated cofactors
    - ATP
    - NADH
    - $FADH_2$

EXAMPLE - Proteases:
Enzymes that cleave peptide bonds



Enzymes perform catalytic reactions such as hydrolysis; the side chains of amino acids participate in the reactions

Cofactors

- all water-soluble vitamins with the exception of vitamin C are converted/activated to cofactors
- only vitamin K of the fat-soluble vitamins is converted to a cofactor
- not all vitamins are cofactors; i.e., lipoic acid is not a vitamin
- cofactors may also act as carriers of specific functional groups such as methyl groups and acyl groups

Coenzyme Classification

- There are two classes of coenzymes

(1) **Cosubstrates** are altered during the reaction and regenerated by another enzyme

(2) **Prosthetic groups** remain bound to the enzyme during the reaction, and may be covalently or tightly bound to enzyme.

- **Classification of coenzymes in mammals**

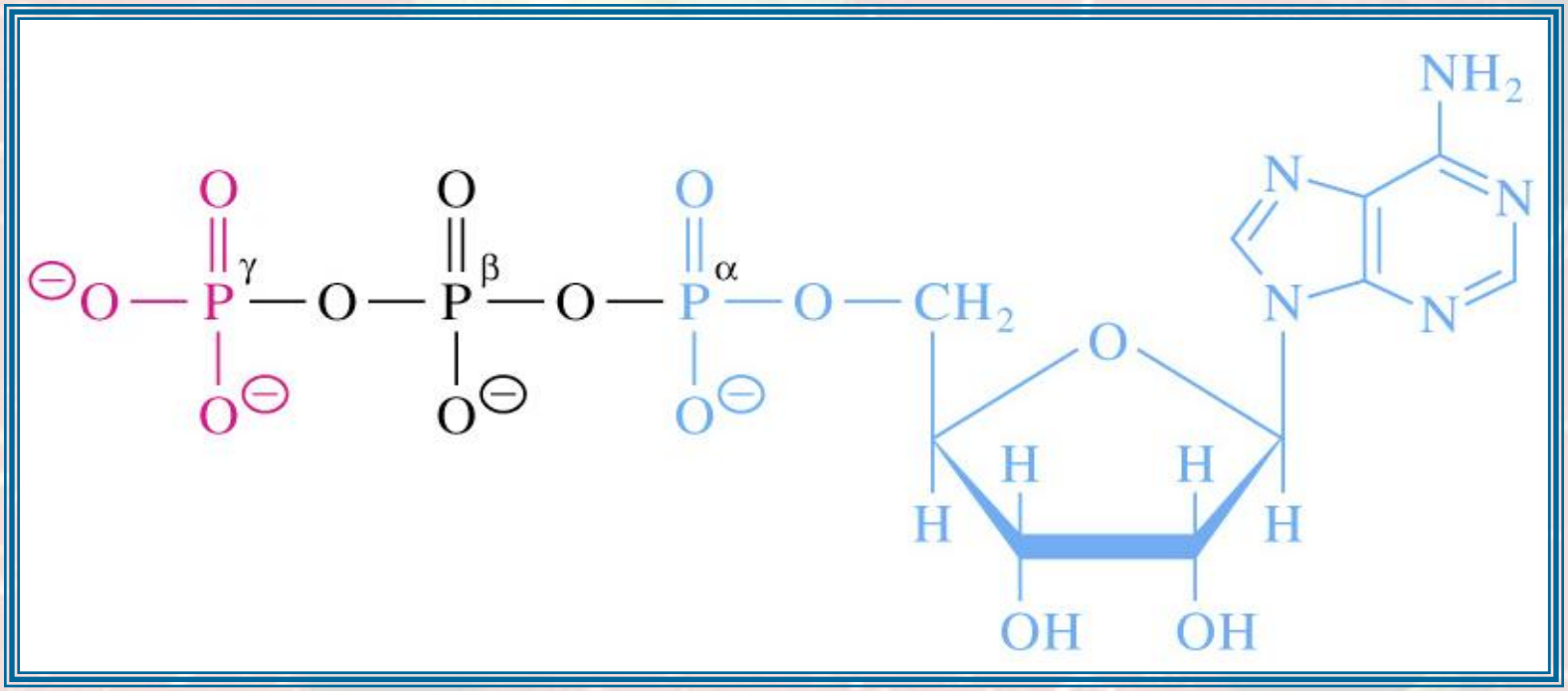
(A) **Metabolite coenzymes** - synthesized from common metabolites

(B) **Vitamin-derived coenzymes** - derivatives of vitamins (vitamins cannot be synthesized by mammals, but must be obtained as nutrients)

A. Metabolite Coenzymes

- Nucleoside triphosphates are examples

Fig 7.4 ATP



Coenzymes relevant for our course

Coenzyme	Vitamin	role
ATP	----------	Energy and phosphate transfer
NAD(P)	Niacin	Redox
FAD/FMN	Riboflavin (B_2)	Redox
Coenzyme A	Pantothenic acid (B_3)	Acyl transfer
TPP	Thiamine (B_1)	Transfer of 2 C
PLP	Pyridoxine (B_6)	Amino acids
Lipoamide	----------	Acyl transfer
Ubiquinone	----------	Electron carrier

Protein Coenzymes

Coenzyme	Prosthetic group	role
Fe-S proteins	Fe-S clusters	Electron carrier
Cytochromes a, b and c	Heme	Electron carrier

B. Vitamin-Derived Coenzymes and Nutrition

- Vitamins are required for coenzyme synthesis and must be obtained from nutrients.
- Animals rely on plants and microorganisms for vitamin sources (meat supplies vitamins also).
- Most vitamins must be enzymatically transformed to the coenzyme

Vitamin -----> Coenzyme

Vitamins and coenzymes

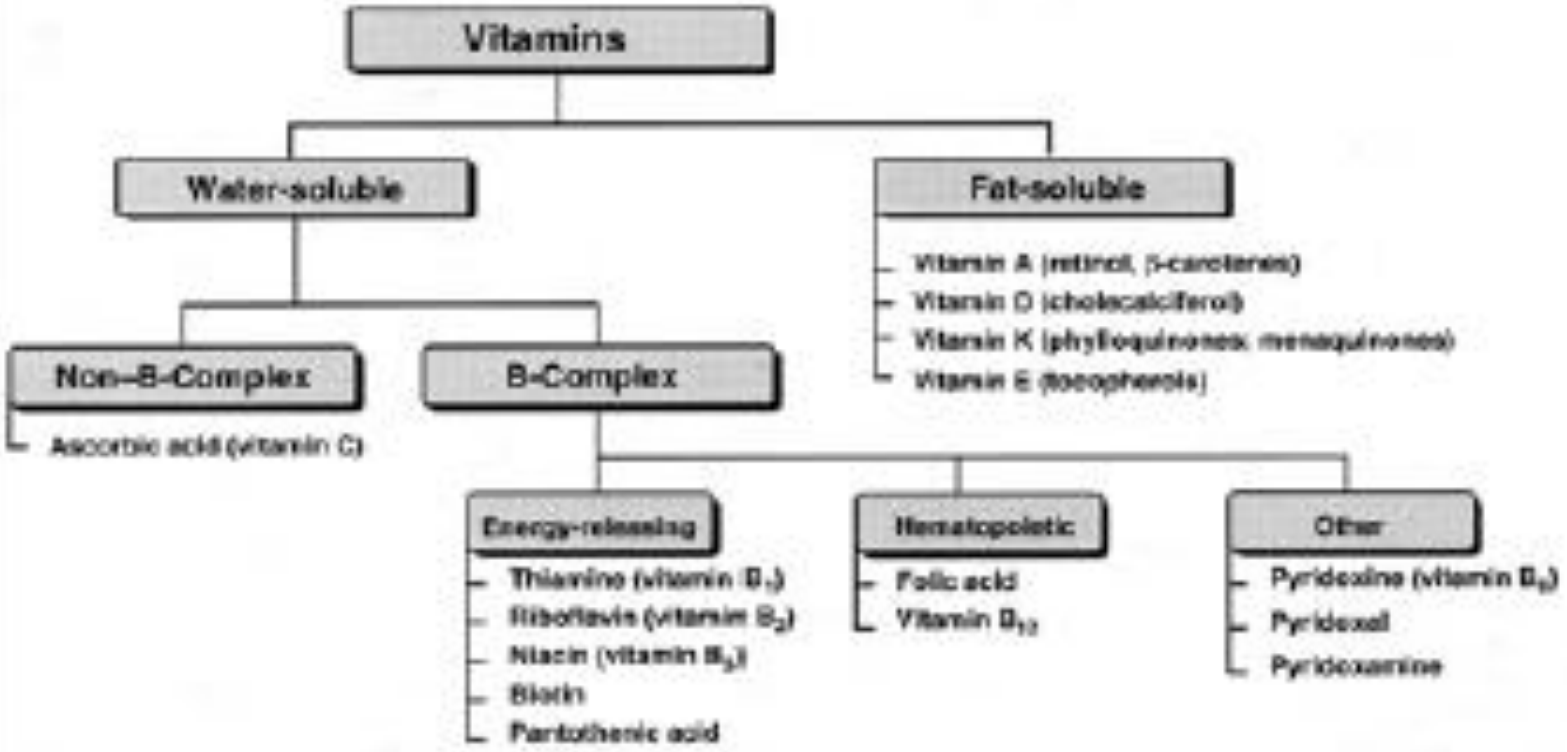
Vitamin	Coenzyme
Ascorbate (C)	none
Nicotinic acid	NAD^+, $NADP^+$
Riboflavin (B_2)	FMN, FAD
Pantothenate (B_3)	Coenzyme A
Pyridoxal (B_6)	Pyridoxal phosphate
Thiamine (B_1)	Thiamine pyrophosphate
Biotin	Biocytin
Folate	Tetrahydrofolate
Lipoic acid	Lipoamide
Cobalamin (B_{12})	Methylcobalamin
	5’-deoxyadenosyl cobal.

Cofactors and Coenzymes

Organic

Organic Cofactor	Vitamin	Function	Enzyme Class
NAD, NADP	Niacin	electron carrier	oxidoreductases
FAD	Riboflavin (B2)	electron carrier	oxidoreductases
Thiamin pyrophosphate	Thiamin (B1)	group transfer	oxidoreductases
Pyridoxal-5'-phosphate	Pyridoxine (B6)	group transfer	aminotransferases
Biocytin	Biotin	CO_2 transfer	carboxylases
Tetrahydrofolates	Folic acid	group transfer	one-carbon transfer
Coenzyme A	Pantothene	group transfer	Synthases
Lipoic acid	Lipoic acid	group transfer	oxidoreductases
Coenzyme Q	Ubiquinone	electron transfer	electron transport
Cobalamin	Vitamin B12	group transfer	mutases, methylases
Carnitine	Carnitine	group transfer	acyl group transport

There's a bunch of them



Nutritional Information per 150 g serving one medium)

Energy	109 Cal	460 Kj
Protein		3.7 g
Fat		0.2 g
Carbohydrate	23 g	

Percentage of Daily Recommended Intake

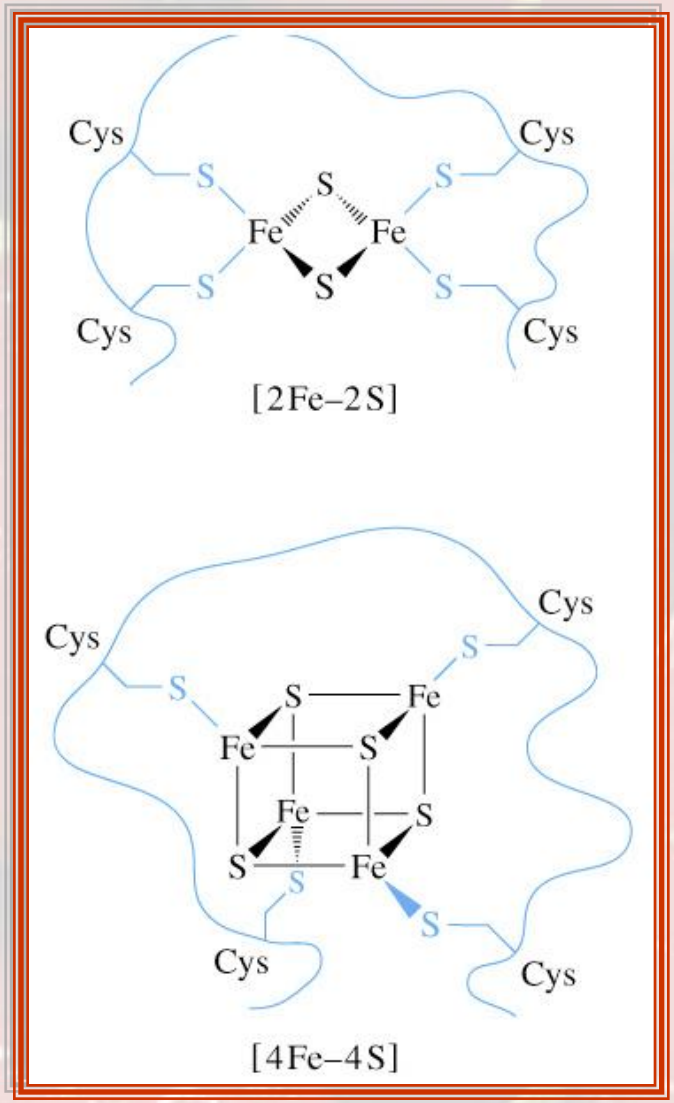
Vitamin C		45%
Thiamin		10%
Niacin	8%	
Vitamin B6		14%
Folacin	4%	
Pantothenic acid		6%
Phosphorous		6%
Magnesium		12%
Iron		9%

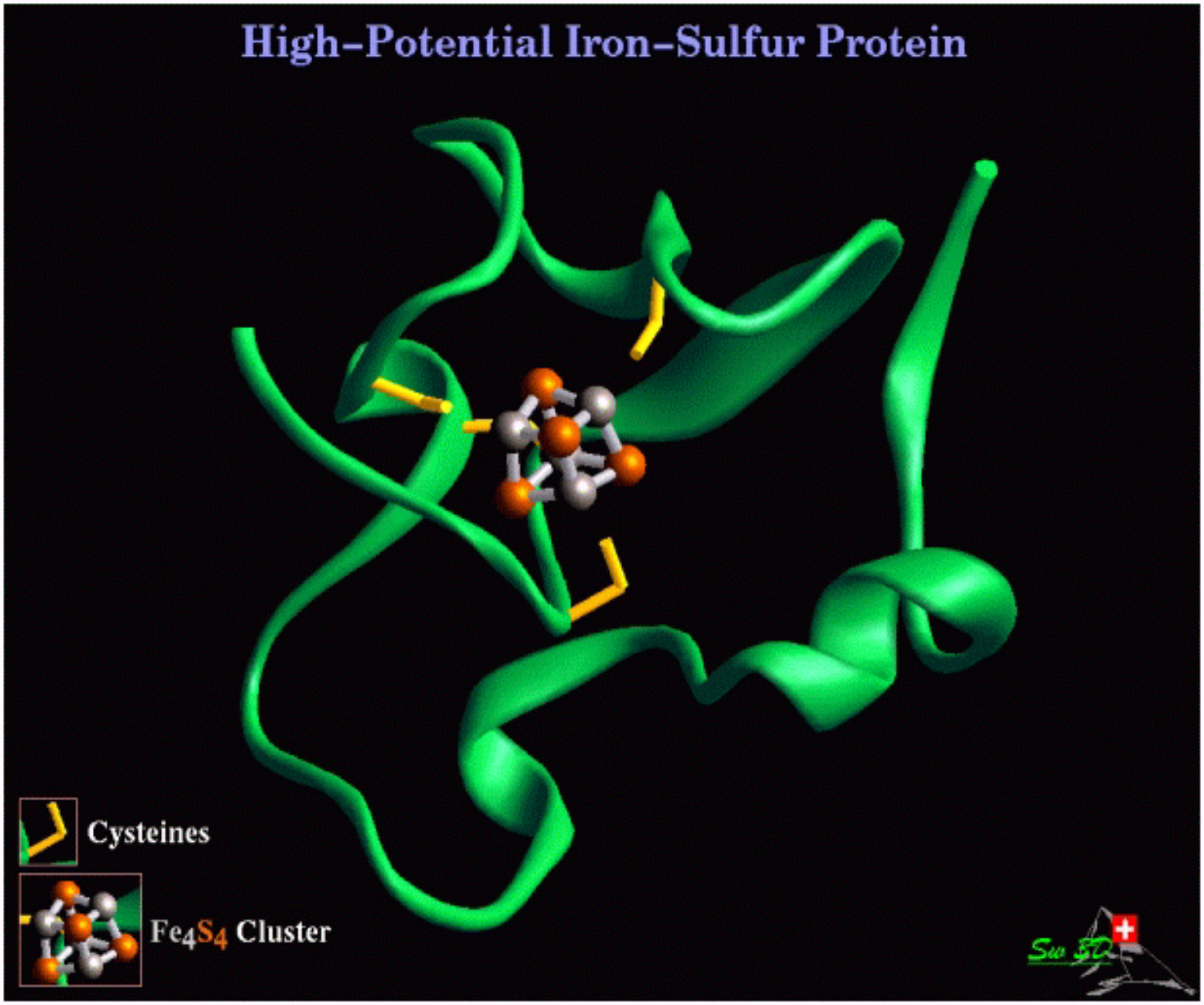
Protein Coenzymes

- **Protein coenzymes** (group-transfer proteins) contain a functional group as part of a protein or as a prosthetic group.
- Participate in:
  (1) Group-transfer reactions
  (2) Oxidation-reduction reactions where transferred group is a hydrogen or an electron.
- Metal ions, iron-sulfur clusters and heme groups are commonly found in these proteins

Iron-sulfur clusters

Iron atoms are complexed with an equal number of sulfide ions (S^{2-}) and with thiolate groups of Cys side chains

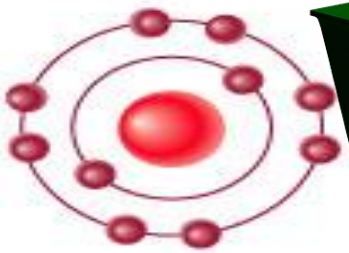



High-Potential Iron-Sulfur Protein
Cysteines
Fe4S4 Cluster

Vitamins: Vital Keys to Health

MAJOR ROLES OF VITAMINS

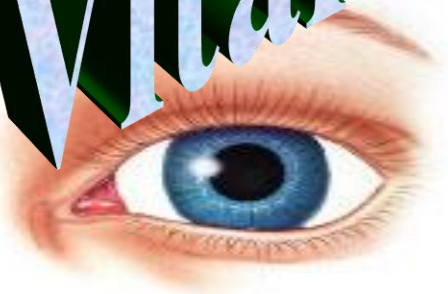
Antioxidants
Vitamin E
Vitamin C



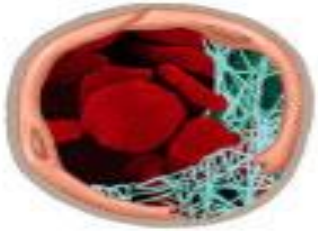
Coenzymes
The 8 B-vitamins

Bone hea
Vita

Vi



Blood clotting
Vitamin K



Reactions in biochemistry

- Five basic classes of chemical reactions
  - Oxidation-reduction: electron transfer
  - Group transfer reactions: coenzymes
  - Free radical reactions: prevent side reactions.
  - C-C bond making and breaking
  - Isomerizations, eliminations

LOOK to these Definitions of VITAMINS

What are Vitamins?

- That what's your name to age and diverse
- The vitamins are a chemically disparate group of substances whose only common feature is that they are required in small amounts for the normal functioning of the body, cannot be synthesized in the body and hence must be provided in the diet.
- Vitamins are those magical little co-factors (or their precursors) that can't be synthesized in our bodies from scratch …

Vitamins: Definition

- Organic compound found in foods
- Required in small amounts
- Required in the diet (essential)
- Proven to be required for health, growth, and reproduction
  - deficiency syndrome identified

“Vitamins”

- Vitamins are compounds essential to human health and must be obtained in the diet.
  - Hormone precursors:
    - Vitamin D
    - Vitamin A (retinol)
  - Redox cofactors/antioxidants:
    - Vitamin C (ascorbic acid)
    - Vitamin E (tocopherols)
    - Vitamin K (phylloquinone)
    - Vitamin B3 (Niacin)
    - Vitamin B2 (Riboflavin)
  - Group transfer agents:
    - Vitamin B6 (pyridoxine)
    - Vitamin B12 (Cobalmin)
    - Biotin
    - Folic acid
    - Pantothenic acid

Redox cofactors move electrons…

Directly as electrons

$$Cu^{2+} + O_2^{-} \rightleftharpoons Cu^{+} + O_2$$

As hydride ions (H-, 2 electrons; negative)

$$\text{Acetaldehyde} + NADH + H^{+} \rightleftharpoons NAD^{+} + \text{ethanol}$$

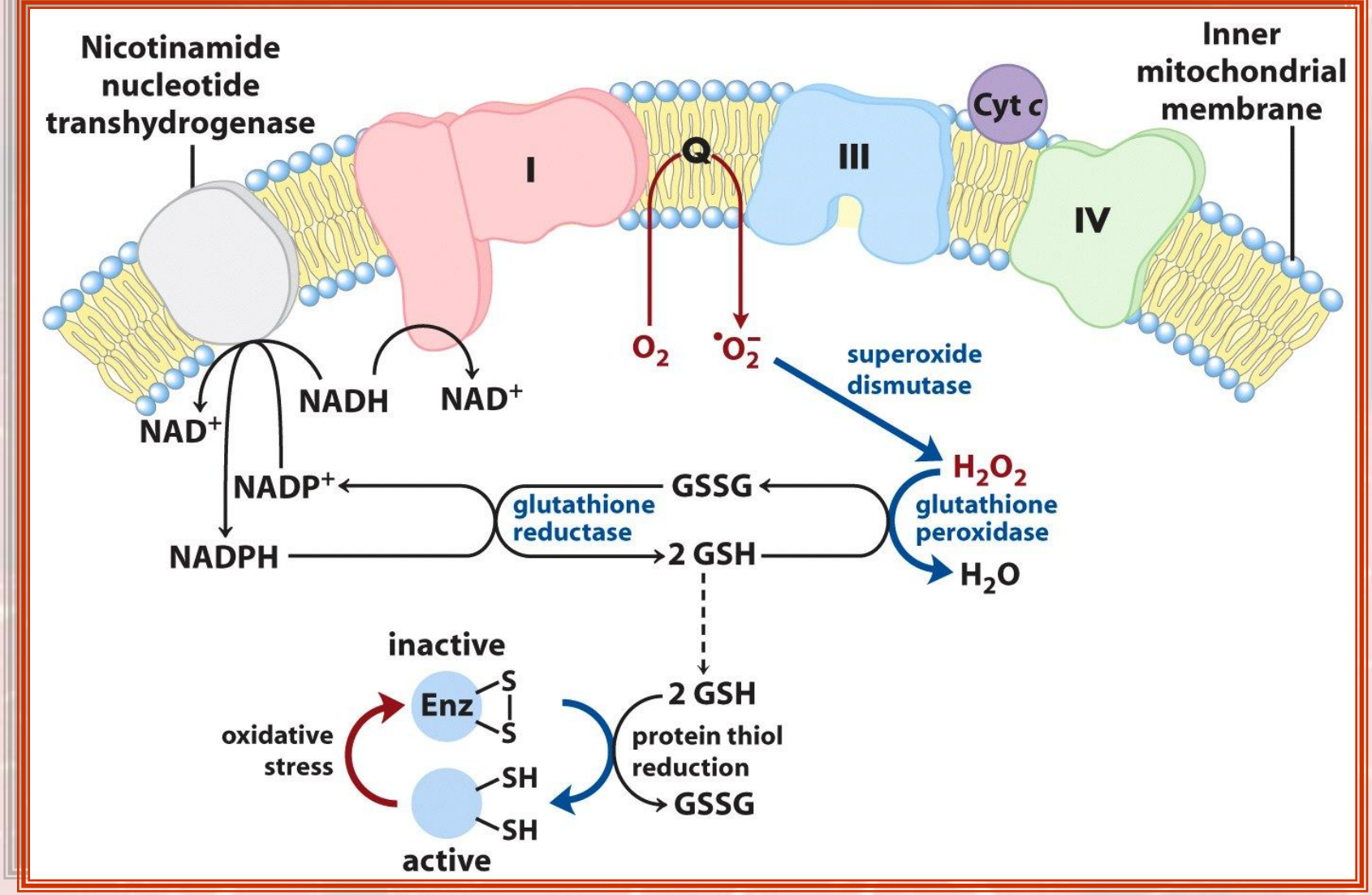
As hydrogen atoms ($H^{\cdot}$, 1 electron; neutral)

$$FADH_2 \rightleftharpoons FAD + 2\,e^{-} + 2\,H^{+}$$

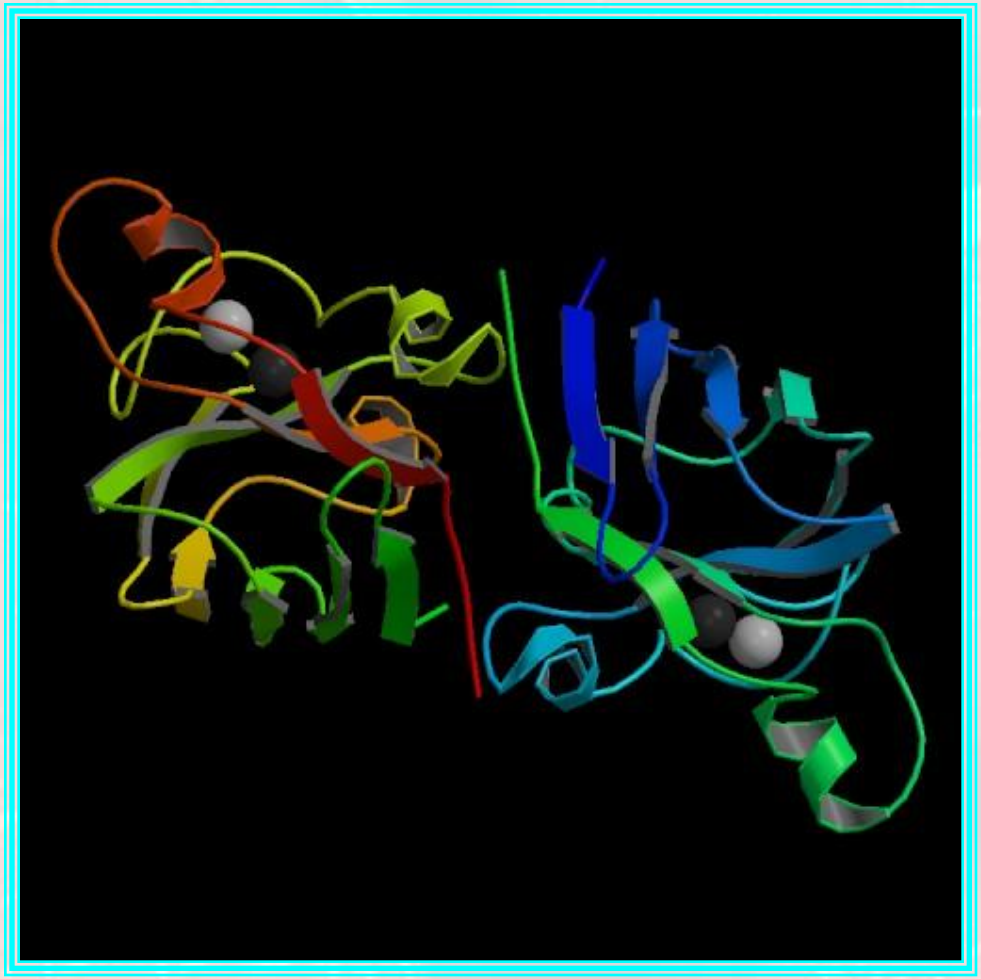
By directly combining with oxygen

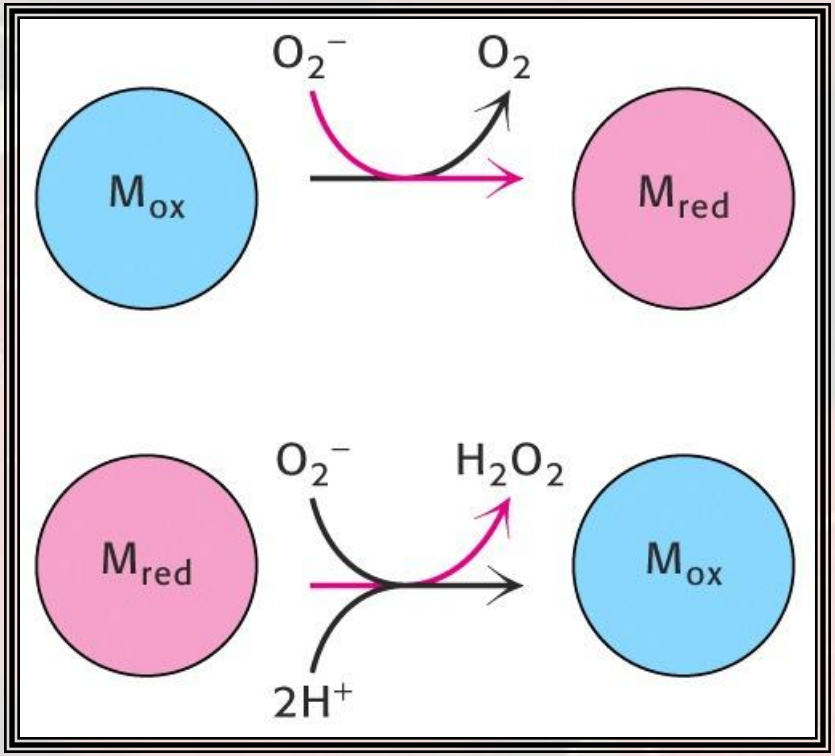
$$R\text{-}CH_3 + 1/2\ O_2 \rightleftharpoons R\text{-}CH_2\text{-}OH$$

… but sometimes redox reactions "misfire"



Remember Superoxide Dismutase?





Vitamin Nomenclature

- Fat soluble "A" & Water soluble "B"
- "Vital amines" = vitamines = vitamins
- Vitamin B "complex"
  - collection of water soluble vitamins that function as enzyme co-factors
- Vitamin C
- Vitamins D and E
- Bogus Vitamins

Understanding Vitamins

Fat-Soluble vs. Water-Soluble

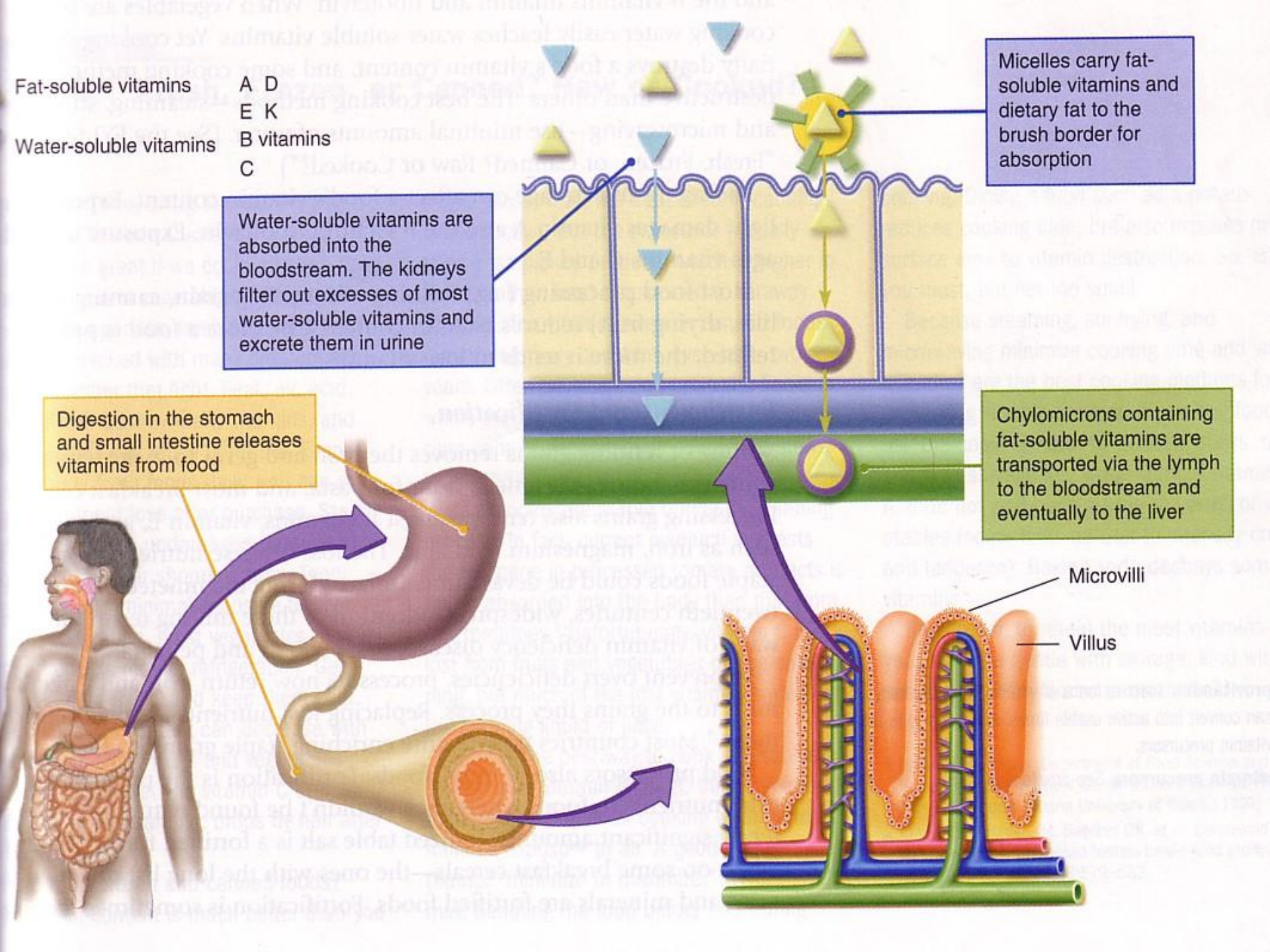
- Fat-soluble: vitamins A, D, E, K
  - Absorbed like fat, into lymphatic system
  - Stored in larger quantities
  - Less vulnerable to cooking losses
- Water-soluble: 8 B-vitamins, vitamin C
  - Absorbed into bloodstream
  - Stored in small amounts
  - Vulnerable to cooking losses

Fat and Water Soluble Vitamins

- Fat Soluble Vitamins (A, D, E, K)
  - Soluble in lipids and solvents
  - Excess stored and not excreted
  - Excess may be toxic
  - Deficiency slow to develop

Fat and Water Soluble Vitamins

- Water Soluble Vitamins
  - B vitamins, C
  - Soluble in water
  - excess excreted in urine, little stored
  - generally less toxic
  - deficiency develops quickly


Fat-soluble vitamins
A D
E K
Water-soluble vitamins
B vitamins
C
Micelles carry fat-soluble vitamins and dietary fat to the brush border for absorption
Water-soluble vitamins are absorbed into the bloodstream. The kidneys filter out excesses of most water-soluble vitamins and excrete them in urine
Digestion in the stomach and small intestine releases vitamins from food
Chylomicrons containing fat-soluble vitamins are transported via the lymph to the bloodstream and eventually to the liver
Microvilli
Villus

The Discovery of Vitamins

- The Vitamin Theory of Disease
  - Scurvy: Disease of sailors
    - Vitamin C deficiency
  - Beri-Beri: Disease of poor Asians
    - Thiamin deficiency
  - Rickets: Disease of poor Northern European children
    - Vitamin D deficiency
  - Pellagra: Disease of poor corn eating cultures
    - Niacin deficiency

General Functions of Vitamins

- Coenzymes or Cofactors
  - chemicals that assist enzymes to function as catalysts
    - B vitamins
    - Vitamin C, A, K