

# Enzyme Structure

From a biochemical point of view, enzymes are proteins with catalytic properties. According to the structure, we distinguish monomers, enzymes remaining from one chain and enzymes with an oligomeric structure, which are composed of multiple subunits. Some enzymes can combine to form multienzyme complexes.

## Enzyme function and structure

### Enzyme

- is a globular protein (exception – catalytically acting RNA molecules = ribozymes)
- accelerates reaction by at least 6 orders of magnitude
- during reaction – not consumed or permanently altered

### Structure and interaction

- ES-complex – non-binding interactions (H bridges, Van der Waals forces, hydrophobic interactions, electrostatic forces)
  - active site (6–12 amino acid residues (AMK)) – depression, hydrophobic character; multimeric enzyme – at the interface of subunits
1. binding groups – aromatic rings (Phe, Tyr), associated with substrate ← hydrophobic groups
  2. catalytic groups – carboxyls of dicarboxylic (acidic) AMK, OH serine, carbonyl oxygens, His, Arg, catal. Reaction ← polar structure
- Lock and key theory
  - Theory of induced adaptation – dynamics during recognition

## 7 enzyme classes

1. Oxidoreductases
2. Transferases
3. Hydrolases
4. Lyases
5. Isomerases
6. Ligases
7. Translogases

File:String, enzyme.jpg

- \* 1 string
- \* 1 string – several domains with the same enz. specificity
- \* 1 string – several domains with different specificity
- \* multienzyme complex – quaternary structure, subunits NOT connected forged. bonds, different specificity, 1 input substrate – each processes it differently, e.g. fatty acid synthase, highly economical

### Oxidoreductases

- Catalyze redox reactions
- They transfer  $H^+$  or O, or just  $e^-$  from one substance to another
- Dehydrogenase, oxidase, oxygenase, hydroxylase

### Transferases

- Transmits functional groups
- Usually, the name of the transferred groups – aminotransferases, transglycosylases, transmethyases
- Hexokinase does not reflect the name of the functional group

### Hydrolases

- Catalyse hydrolytic reactions
- Breaks down substrate at the input of  $H_2O$ ; covalent bonds C-O, C-C, C-N, ...
- Are distinguished by cleaved substrate into peptidases (proteases), lipases, esterases, glycosides, and others

### Lyases

- cleaves C-C, C-O or C-N; without input  $H_2O$  = non-hydrolytic
- Aldolase, decarboxylation -R
- Participating syntheses are called SYNTHASES – they don't need ATP!!

### Isomerases

- Catalyse isomerization reactions; catalyse geometric or structural changes within a single molecule
- Subclasses – cis-trans isomerases, epimerases, mutases, racemases

### Ligases

- Combine 2 compounds to form C-O bonds; C-N; C-C; C-S
- Energy consumption from current ATP splitting
- SYNTHETASES – alternative name, consume ATP!!

## Translocases

- Membrane enzymes that ensure the active transport of substances using the energy released by their catalysed chemical reaction

The most common are 1), 2) and 3).

## Cofactors

- are low molecular weight organic compounds necessary for enzyme activity (or ions – e.g., Zn in carboxypeptidase)
- enzyme/substrate binding is short-lived, easily dissociates and is reversible
- e.g., ATP, metal ions – enzymes activated by metal ions (other than metalloenzymes)

## Coenzymes

- are "recyclable shuttles – group carriers"
- transfer of substrates from the site of synthesis to the place of use, the substrate is stabilized during binding (eg H)
- some coenzymes contain adenine, ribose, phosphate group AMP/ADP
- Also transmitted:
  - methyl groups (folates)
  - acyl groups (coenzyme A)
  - oligosaccharides (dolichol)

## Prosthetic groups

- are bound both covalently and non-covalently
- e.g. pyridoxal phosphate, FMN, FAD, thiamine diphosphate (thiamine pyrophosphate, FPP), biotin, ions of some metals – Co, Cu, Mg, Mn, Zn
- metalloenzymes – 1/3 of all enzymes
  - have tightly bound metal ions
    - are tightly bound to the enzyme
    - participates in redox reactions during the formation of complex compounds (e.g. heme, Fe-S clusters)
    - facilitate establishment and orientation S
    - are for the formation of a covalent bond in the reaction intermediate (Co<sup>2+</sup> ions in coenzyme B12)
    - interact with the substrate with the intention of transforming it into more electrophilic (poorer in E<sup>-</sup>/less nucleophilic (richer in E<sup>-</sup>))

## Derivatives of vit. B

Many coenzymes, cofactors and prosthetic groups are derivatives of vit. B.  
These are:

- nicotinamide (vit. PP, B<sub>3</sub>, niacin) – coenzyme NAD, NADP (redox reaction)
- riboflavin (B<sub>2</sub>) - FMN, FAD (redox reaction)
- pantothenic acid (B<sub>5</sub>) – precursor of coenzyme A (acyl group transporter)
- thiamine (B<sub>1</sub>) – in the form of pyrophosphate (diphosphate) (decarboxylation of α-oxo acids)
- acid. foliar (B<sub>9</sub>, folate) and cobalide coenzymes (B<sub>12</sub>) – (transfer of single-carbon residues)

## Enzyme surface

- contain an allosteric site ← allosteric enzymes (enzymes that easily alter conformation under the influence of effectors),
- also determinant groups = epitopes → immune characteristics,
- but also places weighing poisons and pharmaceuticals.

## Proenzyme (=zymogen)

- The protease cleaves off a part → asset unmasking. places

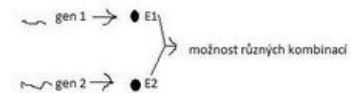
## Multiple forms of enzymes = isoforms of enzymes

- have identical names but different forms
- also the same specificity

- have different size, structure, different number of el. charges (→ separation in ELFO), temperature resistance, immune properties
- and subsequently the formation of multiple forms of enzymes – proteolytic cleavage of varying depths

## Isoenzymes

- differences are genetically determined (determined by different but closely related genes)
- subunits can hybridize
- e.g. lactate dehydrogenase = LDH – tetramer, produces 5 isoenzymes (subunits H-heart and M-muscle)



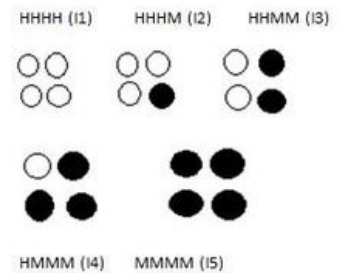
Isoenzymes

## Practical medicine

### Diagnostic and prognostic aid

Enzymes are part of all bb. and body fluids:

- **compartmentations:** mitochondria – cytochrome oxidases, lysosome – acid phosphatase, cytosol – glycolysis enzymes → uneven distribution of enzymes in B.
- **tissue differences:** prostate – acid phosphatase, liver – glutamate dehydrogenase, muscle – creatine kinase isoenzyme
- **secretory enzymes** (less)
- **Intracellular enzymes** (metabolic functions only in b.) – damage to bb. enzymes get into body fluids ← their activity is determined (muscle enzymes – released even after strenuous exercise)
- **isoenzymes** – tissue localization



5 LDH isoenzymes

### Use in practice:

- enzyme determination of blood glucose using glucose oxidase (unlike chemical processes, structurally similar blood-reducing substances – e.g. glucuronate – are not captured)
- amylase in the blood indicates acute pancreatitis (cave parotitis); alkaline phosphatase gets into the blood in various bone diseases, obstructive liver diseases; lactate dehydrogenase isoenzyme 5 indicates liver diseases; Acid phosphatase indicates prostate cancer metastases
- "diagnostic window" = the time that elapses before the marker gets into the blood in sufficient concentration – the finding may be false negative (myocardial infarction up to two hours)
- diagnosis of myocardial infarction (MI), where we monitor:
  - aspartate aminotransferase (AST), alanine aminotransferase (ALT) – slow onset, not specific for MI
  - lactate dehydrogenase (LDH) – isoenzymes ← electrophoretic determined; disadvantage! – releases slowly
  - Creatine kinase (CK) – 3 isoenzymes: CK-MM (skeletal muscle), CK-BB (brain), CK-MB (heart and skeletal muscle)
- CK-MB – discovery within 4–6 hours, peak 24 hours, normal within 48–72 hours
  - troponin – complex of 3 proteins

determination of cardiac troponins I and T concentration rises after 2–6 hours, remains elevated for 4–10 days even damage other than IM increases its concentration

- restriction endonucleases – RFLP
- thermostable DNA polymerase – PCR

## Treatment, examples

- missing digestive enzyme products can be substituted
- proteolytic enzymes – for bloodless removal of dead tissue deposits/fibrin
- Liposome – incorporation of the enzyme into artificially prepared lipoprotein particles and thus facilitated transfer into the cell
- enzyme therapy – acid-resistant tablets (proteolytic enzymes) – taken by mouth
- many drugs – enzyme inhibitors
  - statin drugs → inhibition of 3-hydroxy-3-methylglutaryl-CoA-reductase (decreased cholesterol production)
  - angiotensin-converting enzyme inhibition → decreased angiotensin II concentration (vasoconstrictor) → treatment of hypertension
  - $\beta$ -lactam resistance = bacteria produce  $\beta$ -lactamases → hydrolysis of the functional  $\beta$ -lactam ring in penicillin and related drugs → simultaneous administration of  $\beta$ -lactamase inhibitor and  $\beta$ -lactam antibiotics
  - Transformation of prodrugs (inactive drugs) → biol. active drugs

## References

**Related articles**

- [Enzymes](#)
- [Coenzymes](#)

**References**

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