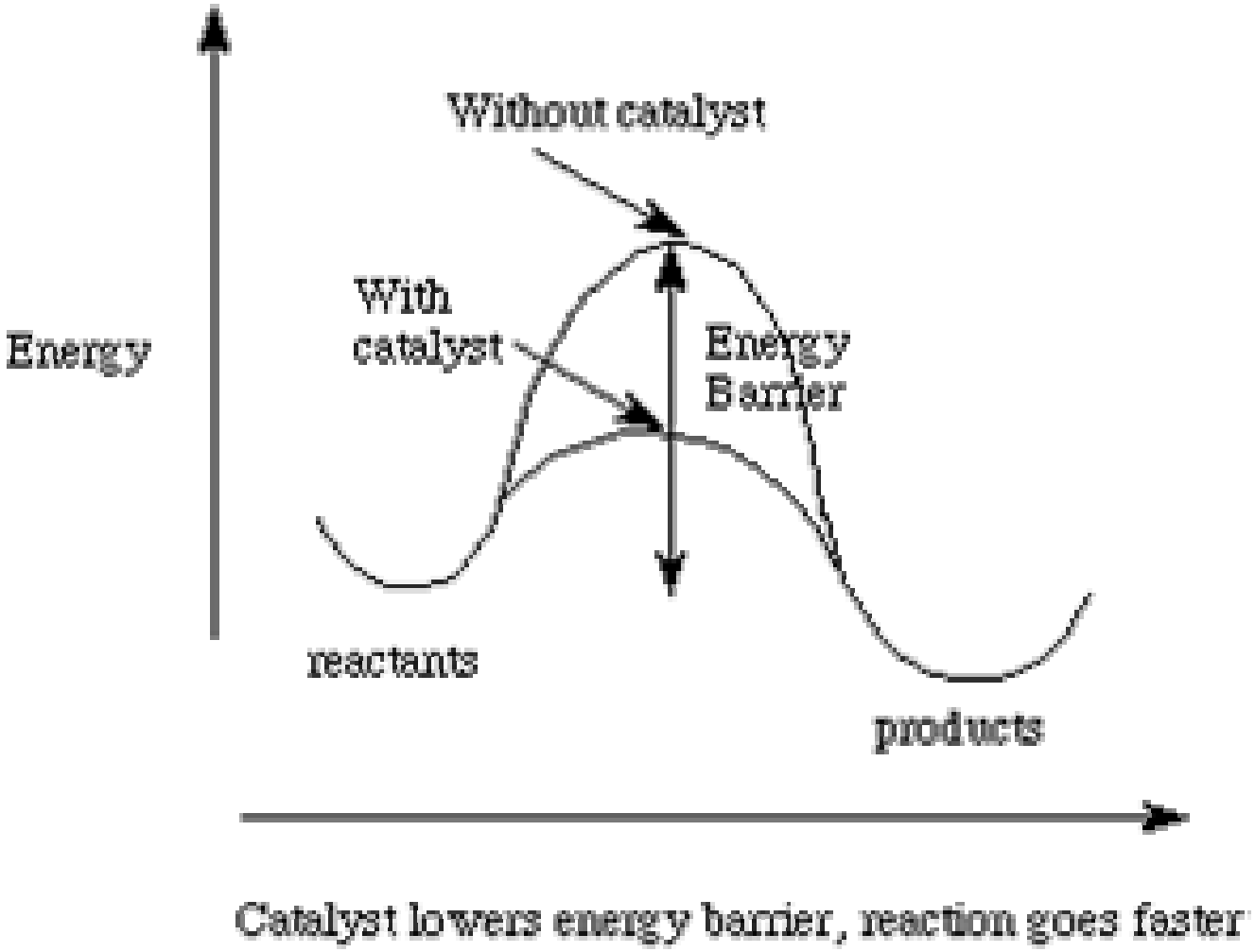
Introduction to Enzymology

- Functional Properties
- Nomenclature
- Enzyme specificity
- Enzyme regulation

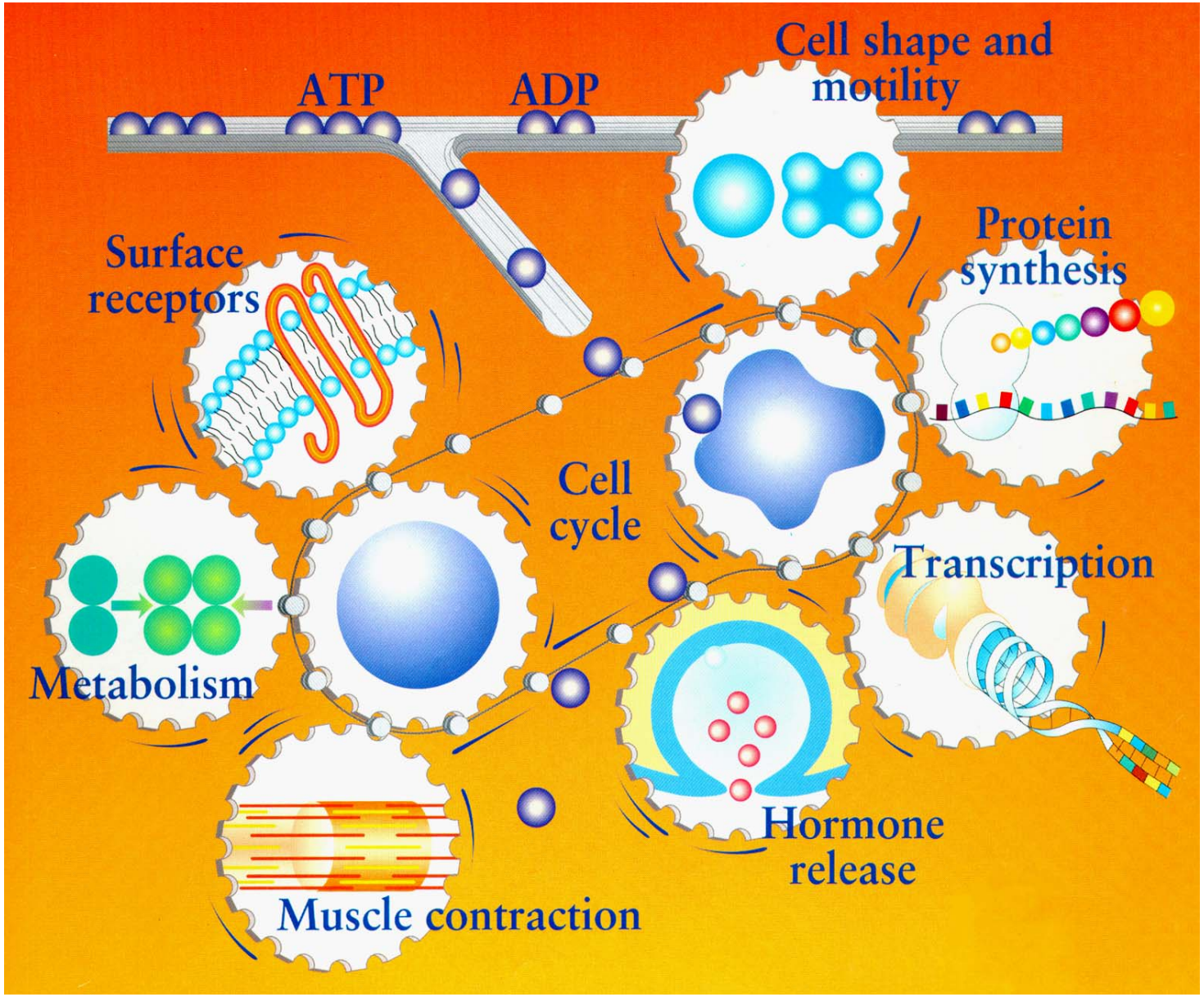
Introduction to Enzymology



Enzymes - Biological catalysts

- By definition a Catalyst :
  - Accelerates the **rate** of chemical reactions
  - Capable of performing multiple reactions (recycled)
  - Final distribution of reactants and products governed by equilibrium properties
- Enzymes are biological catalysts
  - Proteins, (a few RNA exceptions)
  - Orders of magnitude faster than chemical catalysts
  - Act under mild conditions (temperature and pressure)
  - Highly Specific
  - Tightly Regulated

Enzymes are critical for every aspect of cellular life



Enzyme Properties

- Vital for chemical reactions to occur in the cell (the breaking, forming and rearranging of bonds on a **substrate (reactant)**)

- Modified substrate (now a **product**) often performs a different task

- Consequence:
  - Transformation of energy and matter in the cell
  - Cell-cell and intracellular communication
  - Allows for cellular homeostasis to persist

Enzyme Nomenclature

Superfamilies:

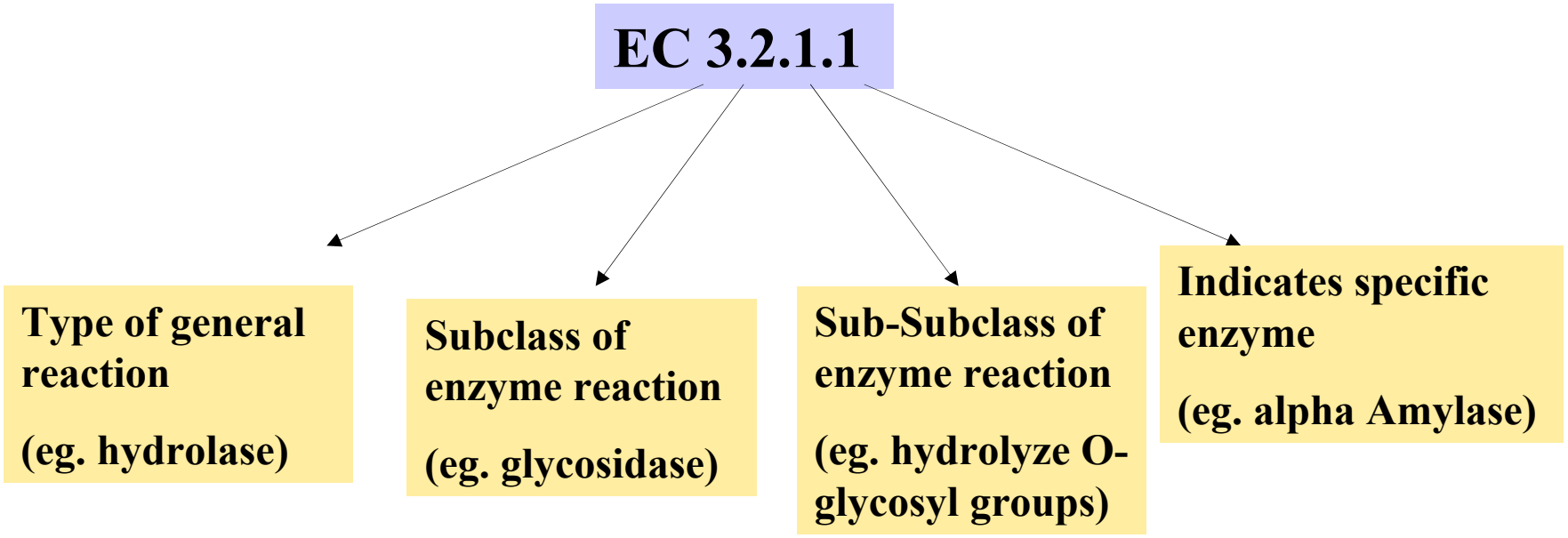
EC 1.1.3.4

- Transferases
  - Transfer functional groups between molecules
- Oxidoreductases
  - Transfer electrons (RedOx reactions)
- Hydrolases
  - Break bonds by adding H2O
- Lyases
  - Elimination reactions to form double bonds
- Isomerases
  - Intramolecular rearangements
- Ligases
  - Join molecules with new bonds

Enzyme Nomenclature

Enzymes can be classified using a numbering system defined by the *Enzyme Commission*.

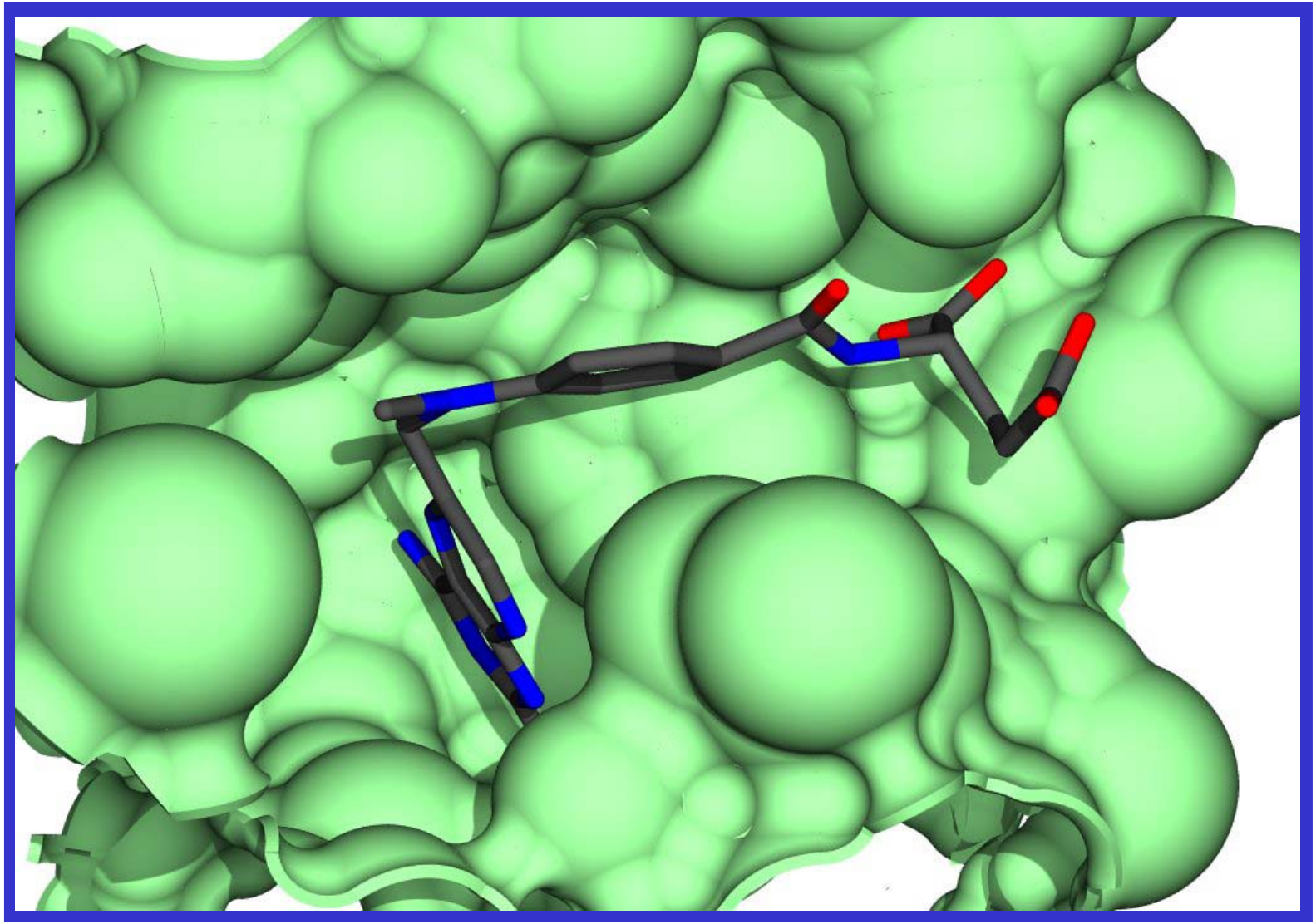
This system consists of a four digit number which classifies based on the type of reaction the enzyme catalyzes



Enzyme Specificity

- The active site of an enzyme dictates specificity
  - Tend to be specific for one type of chemical group
  - Substrates have to interact in stereospecific manner (fit)
  - Substrates have to bind relatively well (affinity)
    - H-bonds, electrostatics, hydrophobicity
  - Substrates have to react
    - bonds to be broken or formed have to have proper reactivity
    - Substances that fit and bind but don't react are inhibitors

Stereospecificity of Enzymes



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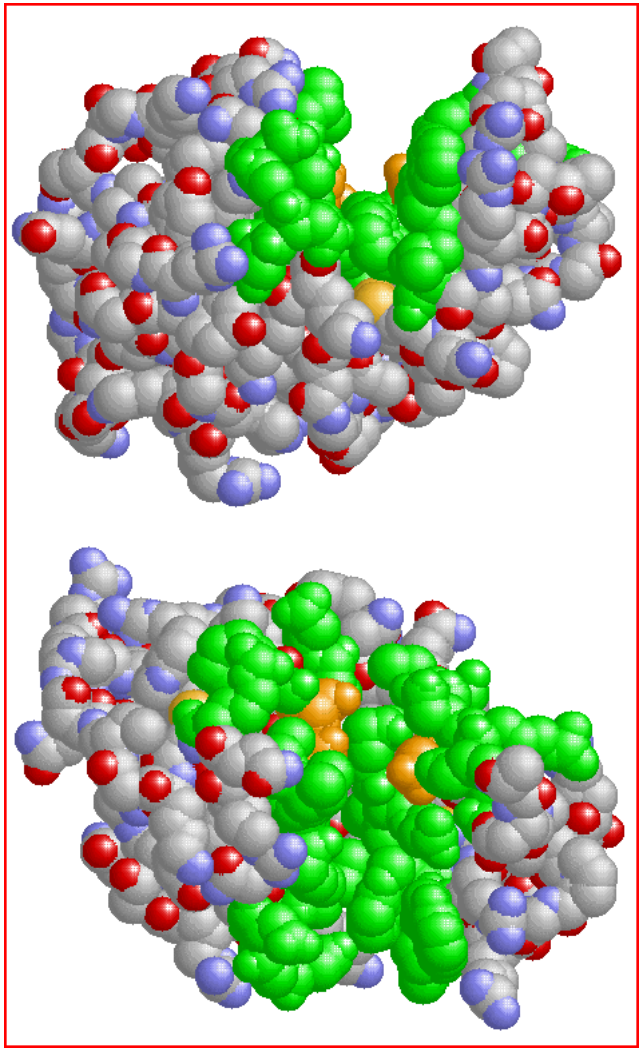
Enzyme Active Sites

Lysozyme active site: Green shows substrate contacts and orange are catalytic residues

Active site complements structure of substrate

Contain amino acids that function in substrate binding, chemical catalysis, and product release



Enzyme Three Dimensional Structure

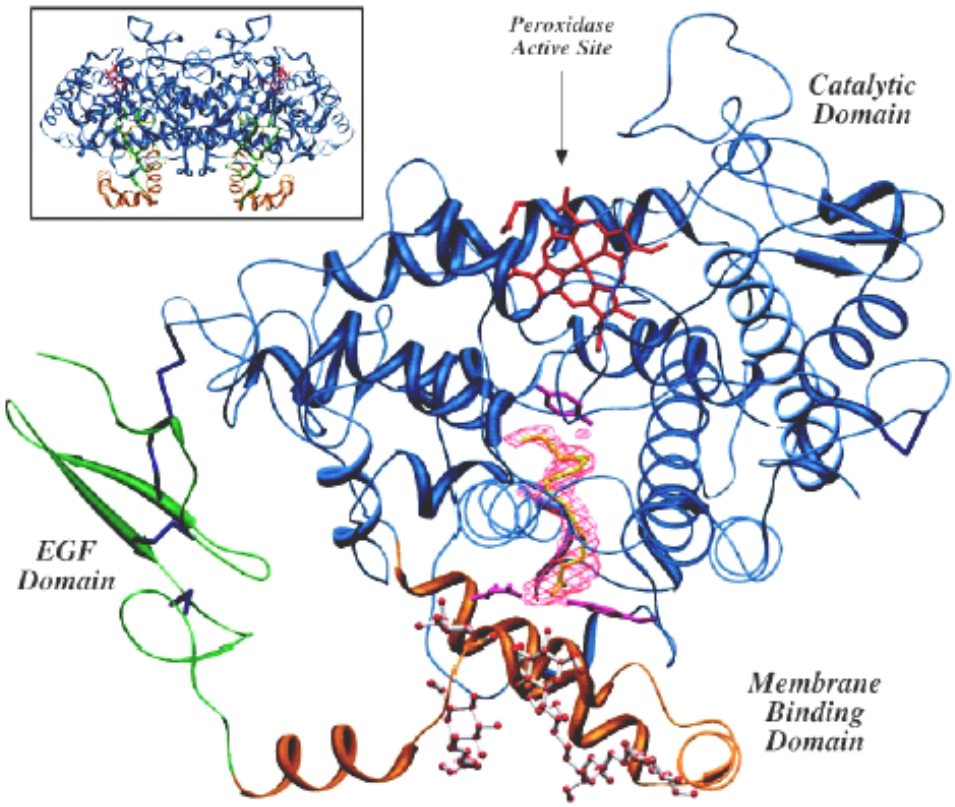
X-ray crystallography (also NMR); physical methods to solve structure of enzymes

Conformation with or without substrate provides functional/biological information

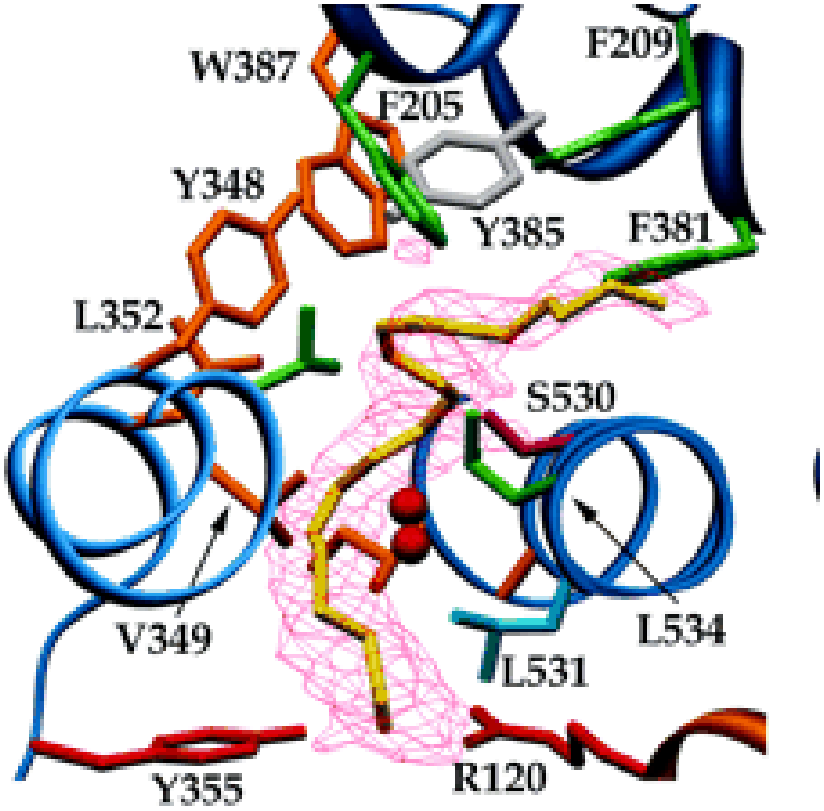
Used to identify amino acids involved in catalysis

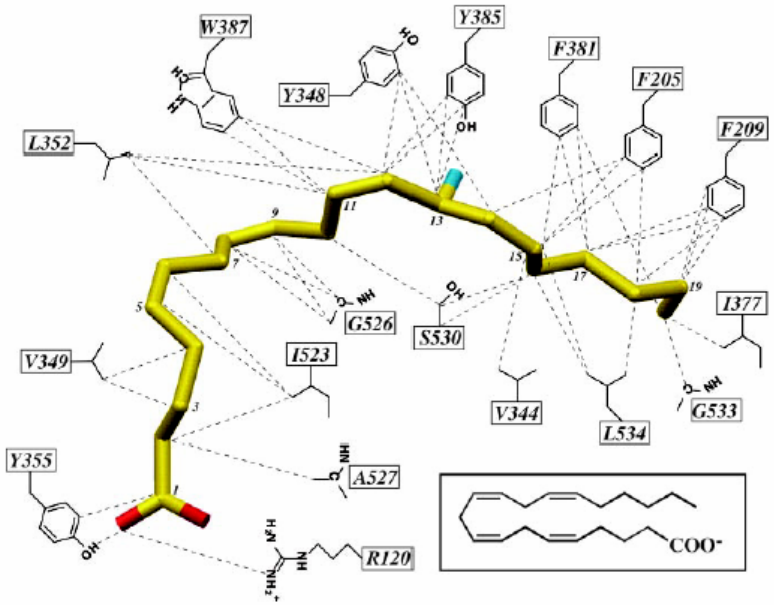
Example: Prostaglandin Synthase I with arachidonic acid

PGHS (COX) target of aspirin



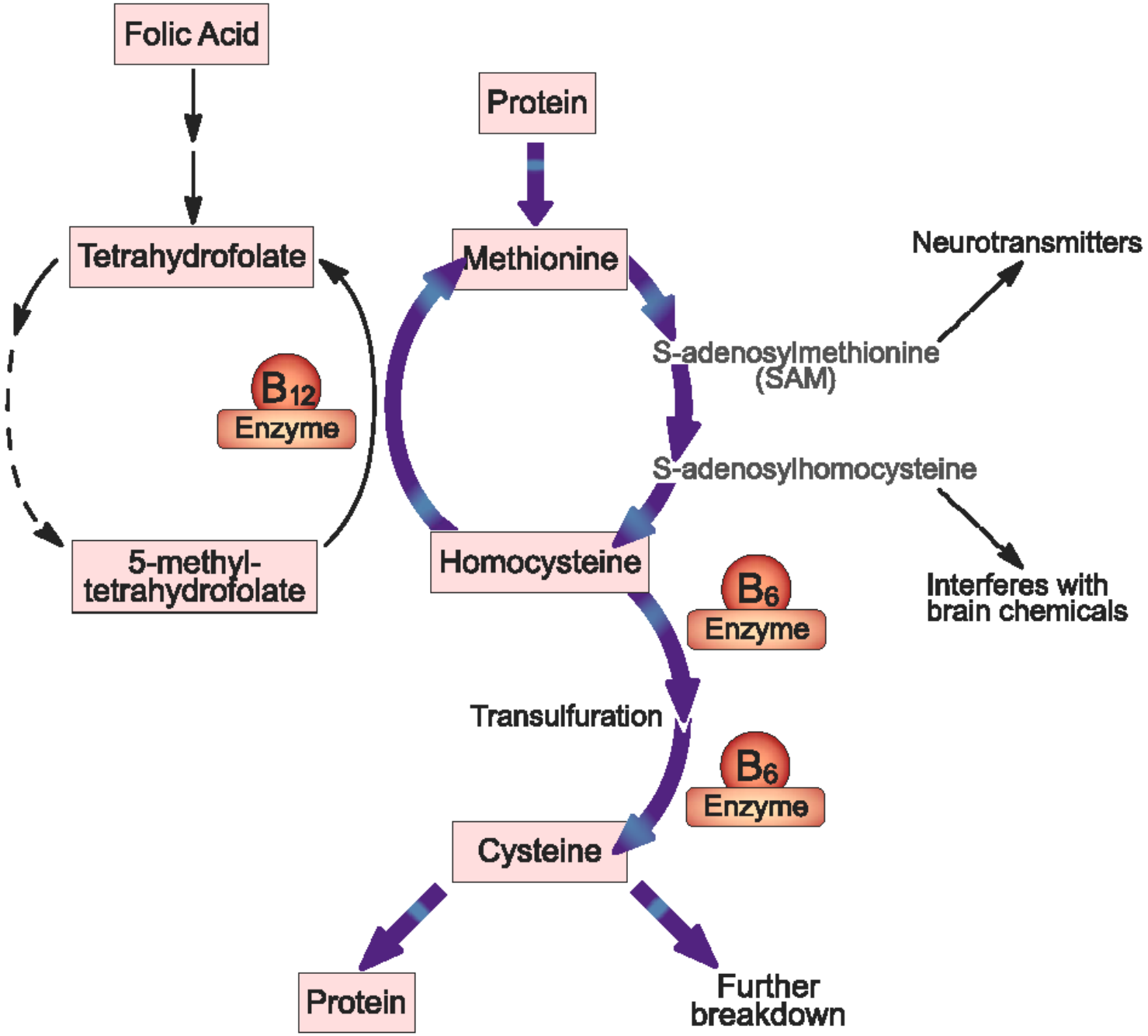
Enzyme Three Dimensional Structure





Enzyme Regulation

- Enzymes are tightly regulated light switches
- Unregulated enzymes become constitutively active or inactive (light is always on or off)
- Unregulated enzyme activity disrupts cell homeostasis and often lead to disease states.


Folic Acid
Protein
Tetrahydrofolate
Methionine
Neurotransmitters
S-adenosylmethionine
(SAM)
B12
Enzyme
S-adenosylhomocysteine
5-methyl-
tetrahydrofolate
Homocysteine
B6
Enzyme
Interferes with
brain chemicals
Transulfuration
B6
Enzyme
Cysteine
Protein
Further
breakdown

Summary

- **Enzymes are biological catalysts vital for cellular life**
- **Their activities are carefully orchestrated and highly specific**
- **A multitude of different families of enzymes exist allowing for a diverse array of chemical catalysis to occur in the cell**

Next class:

Chemical catalysis:

Transition state theory

Hammond's Postulate

Principles of catalysis