Does the information for how a protein will fold lie in its primary structure?

- How could we determine this?

Removal or inactivation of stabilizing forces unfolds (denatures) the protein to 1° structure, but no peptide bonds are broken

- All 2° and 3° structure is lost
- Almost always leads to loss of function
- Acids/bases, heat, detergents

If denaturing agent is removed, some proteins will resume properly folded 3D structure

- “instructions” are in 1° structure
Many proteins are **enzymes**: biological catalysts; they facilitate biological reactions

- This is necessary because most cellular reactions proceed at a very slow rate

Two broad categories of cellular reactions based on change in energy level (E):

- Reactions that **require** an input of energy
- Reactions that **release** energy upon completion

Reactions that require energy are called ________ or ________

- Linking together of smaller molecules into larger ones, such as condensation reactions of monomers to macromolecules

Reactions that release energy are called ________

- Break down larger molecules into smaller ones, such as the hydrolysis reactions of macromolecules to monomers
- Also referred to as ________ reactions
2 different meanings for the word *spontaneous*:

- Typical meaning: happens automatically
- Biology meaning: a reaction that *releases energy*, much of which is lost as heat

Catabolic (E-releasing) reactions require a certain amount of energy to get started

- **Energy of Activation**, or $E_a$
- Could come from heat, but why not?

### Standard Activation Energy Diagram:

- $[S] = $ energy level of substrate (reactants)
- $[P] = $ energy level of products
- $E_a = $ activation energy, which converts substrates into unstable transition states

$$\Delta G = \text{Free Energy of Reaction: difference in } E \text{ between reactants & products}$$
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Enzymes do not cause reactions to occur that would not eventually occur anyway; only speed up existing reactions

- Many enzymes ↑ reaction rates by several million times
- Some enzymes ↑ reaction rates by several trillion times

Example of enzyme catalyzed reaction:

- \(2\text{H}_2\text{O}_2 \leftrightarrow 2\text{H}_2\text{O} + \text{O}_2\)
  - platinum (inorganic catalyst) decreases \(E_a\) by 1/3rd
  - catalase (enzyme) decreases \(E_a\) by almost 90%!
Enzymes bind substrates with extremely high specificity into their ________ (usually just a few amino acids)

- Enzymes will most likely cause some conformational change in the substrate molecule(s), but they themselves usually change shape upon binding substrate
  - Called ___________

How does substrate binding to active site decrease $E_a$?

- Acting as a template for substrate orientation
- Stressing the substrate(s) and stabilizing the transition state
- Providing a favorable microenvironment
- Participating directly in the catalytic reaction

Very Important Point:

- If an enzyme accepts a group from a substrate, it must in turn donate that group to help form product
- ENZYMES ARE (ultimately) UNCHANGED BY THE REACTIONS THEY CATALYZE
Another Very Important Point:

- **ENZYMES DO NOT CHANGE THE EQUILIBRIUM OF REACTIONS**, they only make it easier (and therefore faster) to reach that equilibrium.

Because most enzymes are proteins, it follows that conditions that affect protein stability also affect enzyme activity.

- Enzymes have temperature and pH optima.
- Most tend to be:
Because most enzymes are proteins, it follows that conditions that affect protein stability also affect enzyme activity.

- Enzymes have temperature and pH optima.
- Most tend to be:

### Enzyme Inhibition

- $E + S \rightarrow [ES] \rightarrow E + P$
- $E + I \rightarrow [EI] \rightarrow E + P$
- Can be either reversible or irreversible.
- Reversible inhibition can be competitive or noncompetitive.
Irreversible Inhibitors

• Permanently bind to or modify active site; changing concentration of natural substrate or inhibitor has no effect
  - Nerve agents like sarin gas are irreversible inhibitors of acetylcholinesterase, which catalyzes termination of nerve impulses

• Tend to be molecules not typically encountered by that particular cell

Irreversible inhibition is a demonstration of the important point that enzymes must ultimately be unchanged if they are to be used over and over