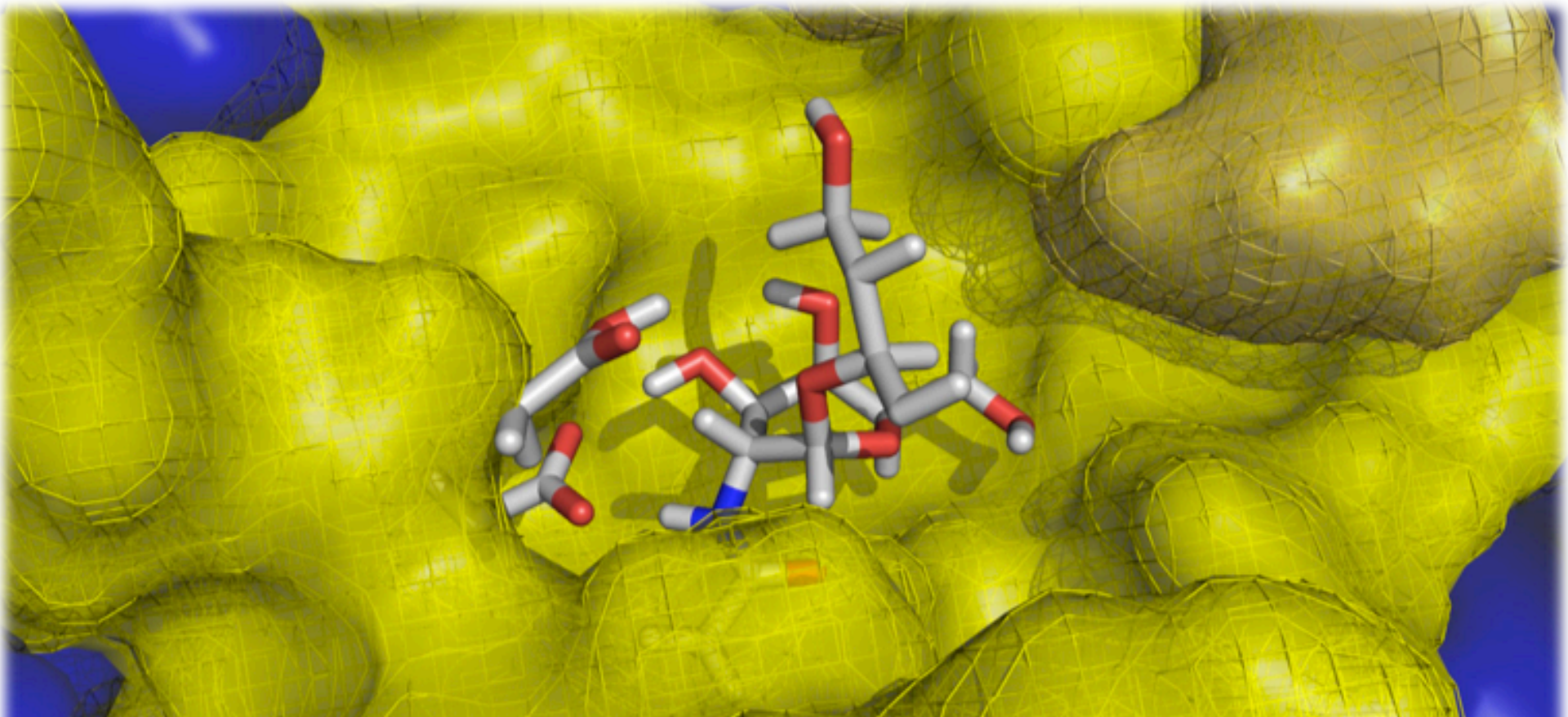


# Basics About Enzyme Catalysis

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# Catalyst



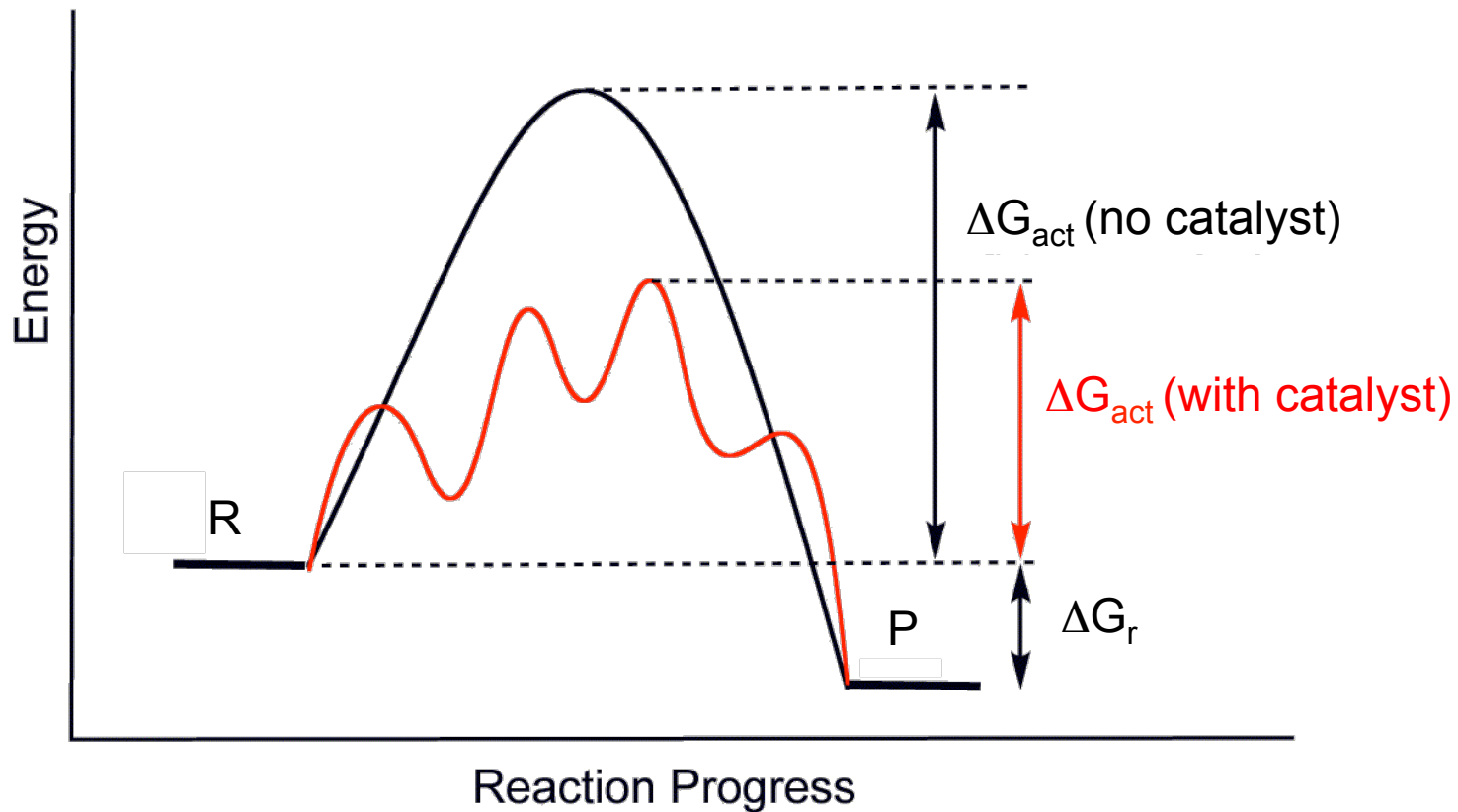
A catalyst is a substance that increases the rate of a chemical reaction

The catalyst does not change the extent of the reaction

The catalyst is not consumed or is fully regenerated in the reaction

# Catalyst

The catalyst changes the mechanism for another one with a lower rate-limiting step



# Enzymes



Biocatalysts that accelerates chemical reaction to a rate compatible with life

Macromolecules, mostly (**but not always**) proteins

Intermediate between homogenous and heterogeneous catalysts.

Strictly speaking soluble enzymes are homogeneous and membrane bound enzymes are heterogeneous catalysts.

# Enzyme Classification

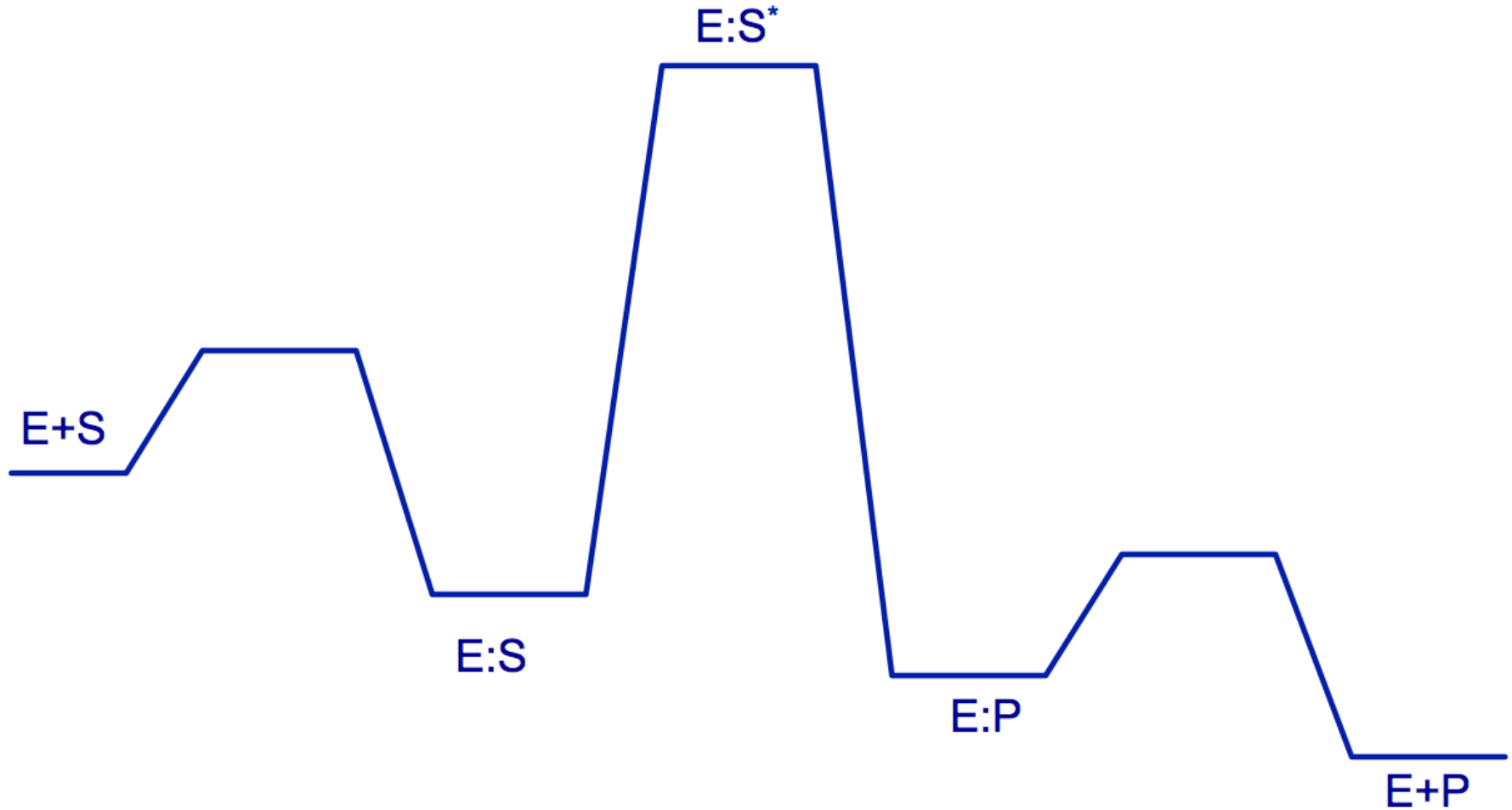


there are six major classes of enzymes

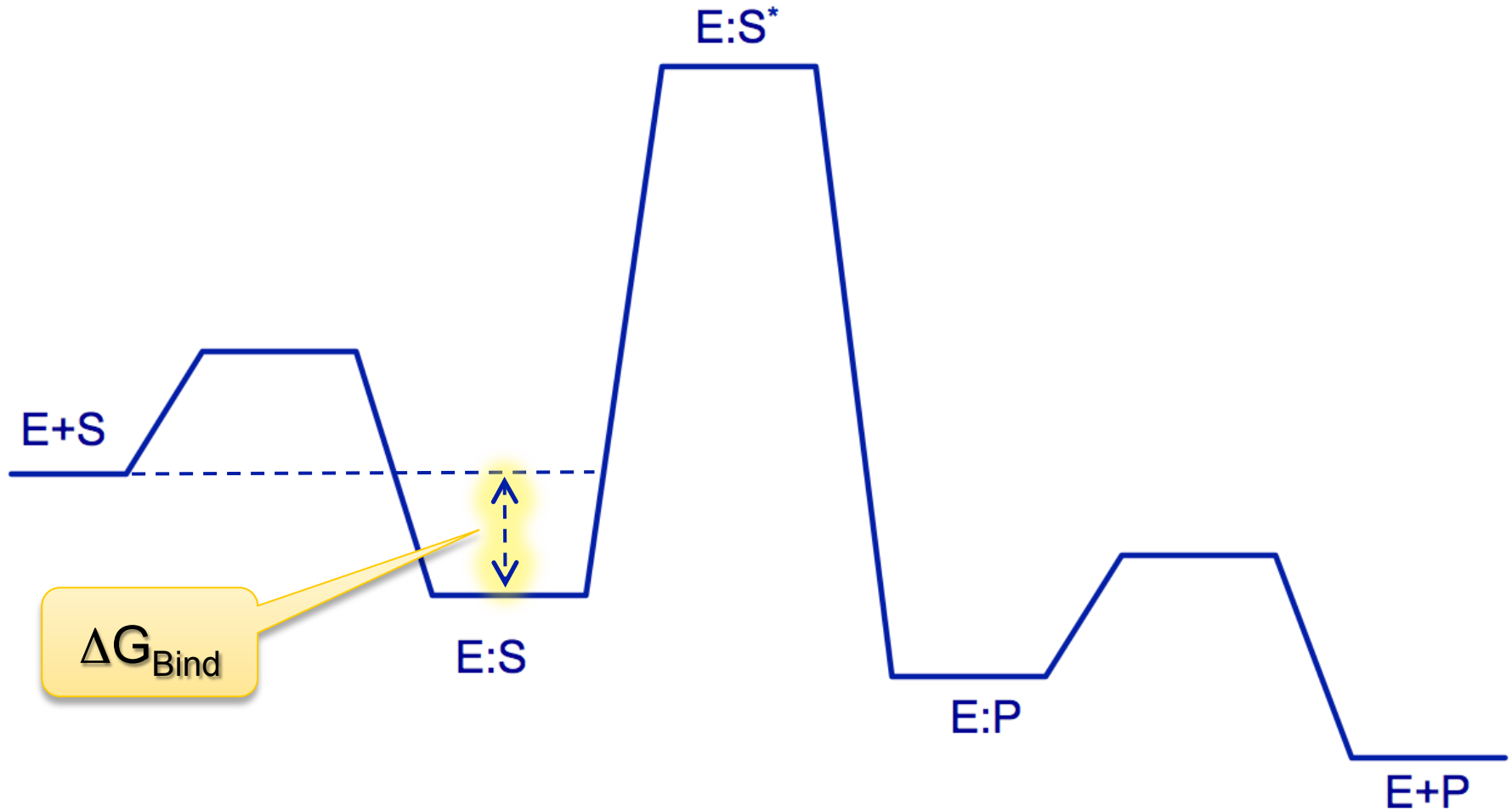
| Class              | Type of reaction  | Example                                      |
|--------------------|---|--|
| 1. Oxidoreductases | Oxidation-reduction   | Lactate dehydrogenase                        |
| 2. Transferases    | Group transfer  | Nucleoside monophosphate kinase (NMP kinase) |
| 3. Hydrolases      | Hydrolysis reactions (transfer of functional groups to water) | Chymotrypsin                                 |
| 4. Lyases          | Addition or removal of groups to form double bonds            | Fumarase                                     |
| 5. Isomerases      | Isomerization (intramolecular group transfer)                 | Triose phosphate isomerase                   |
| 6. Ligases         | Ligation of two substrates at the expense of ATP hydrolysis   | Aminoacyl-tRNA synthetase                    |

classification & nomenclature of enzymes- Enzyme Commission (EC), 1964

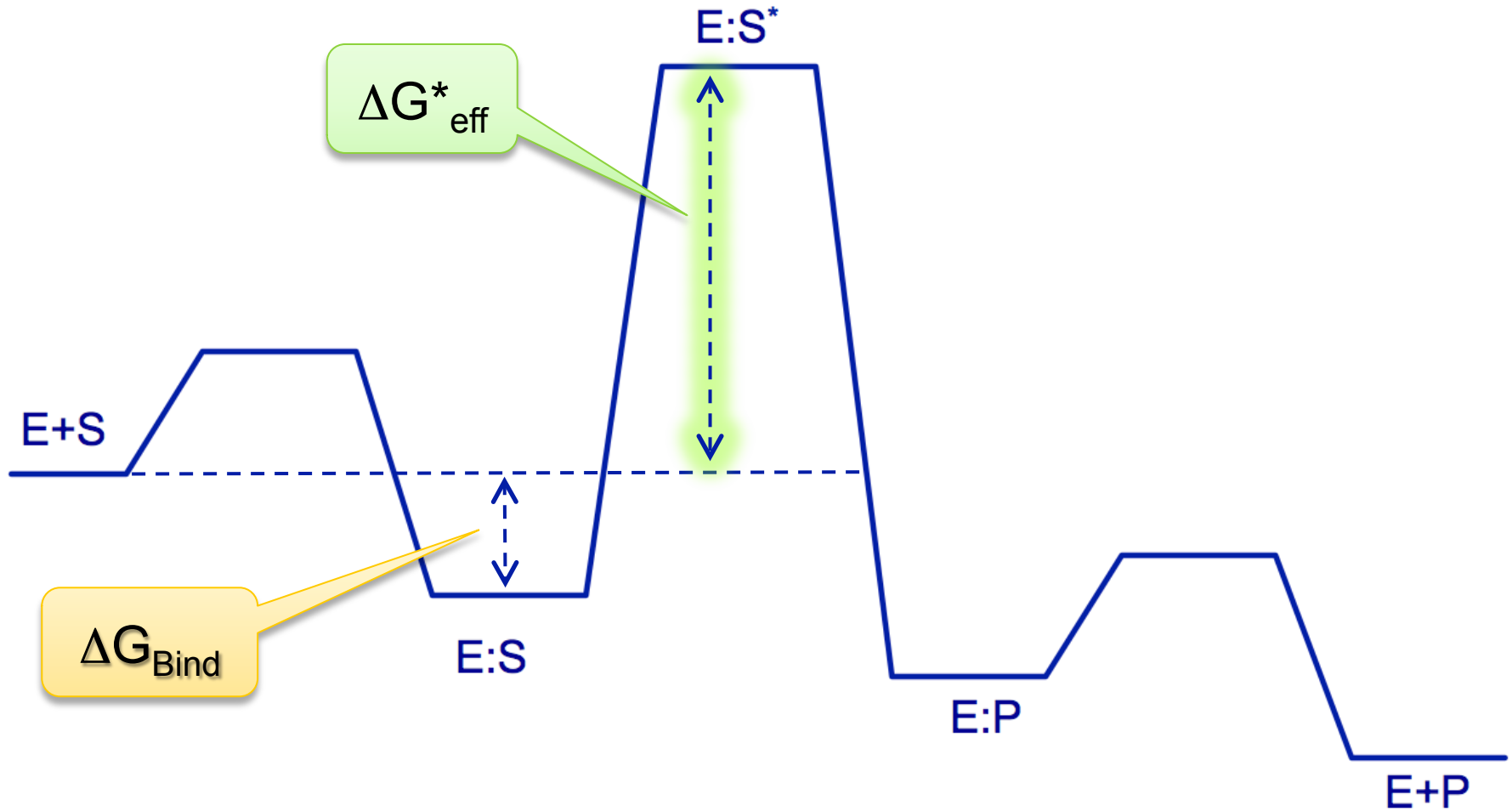
# PES for a Typical Enzymatic Reaction



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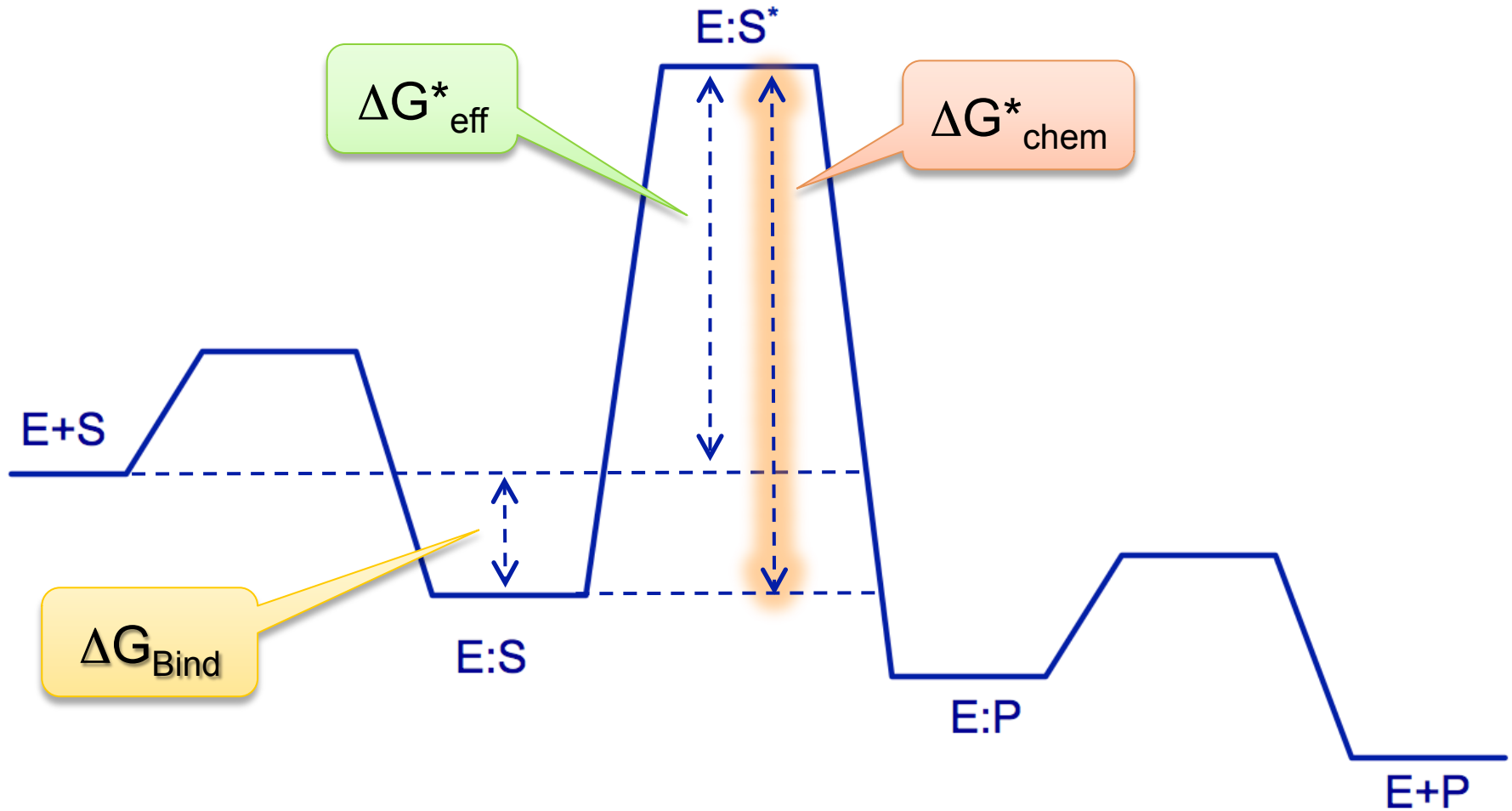


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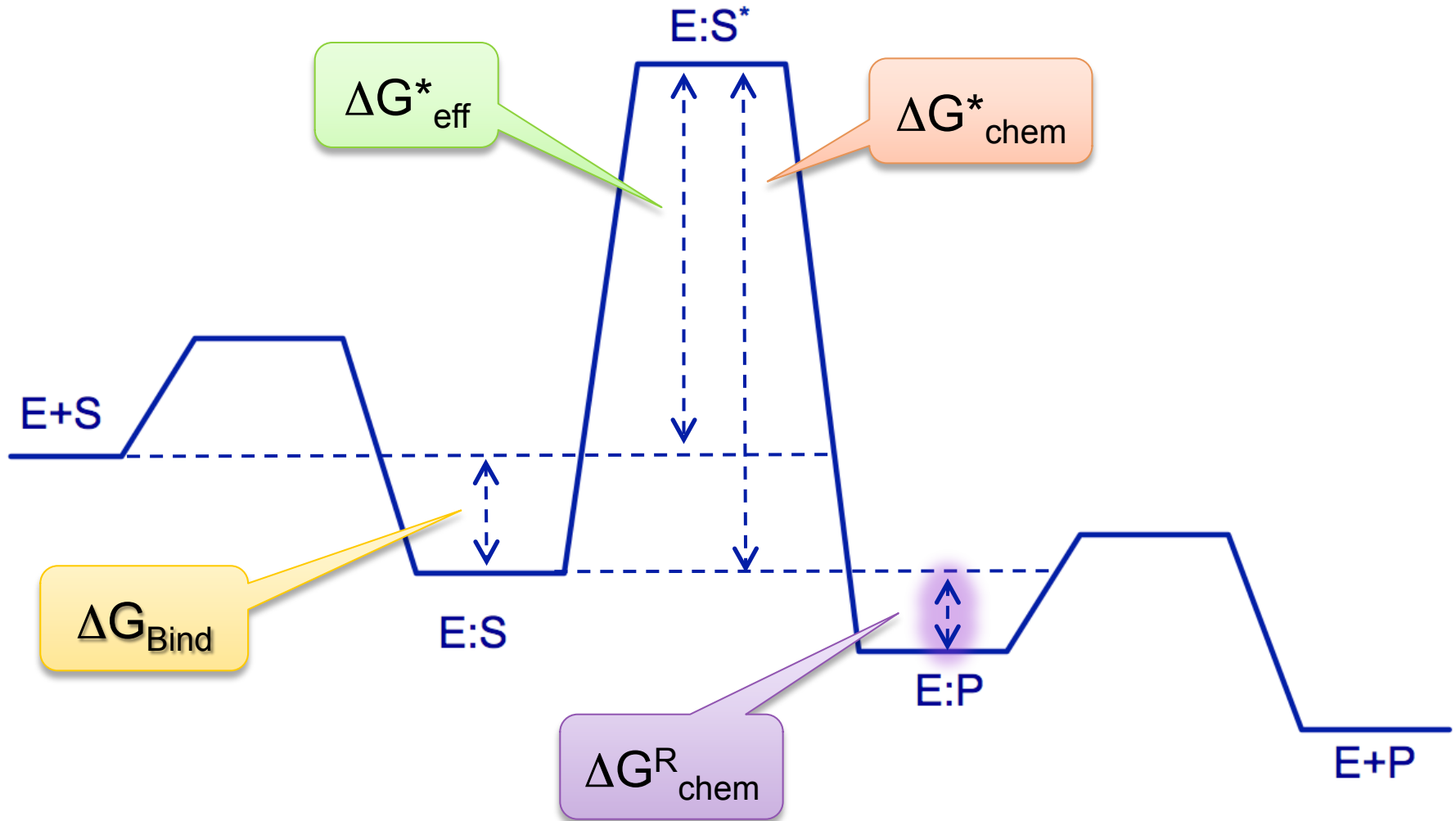




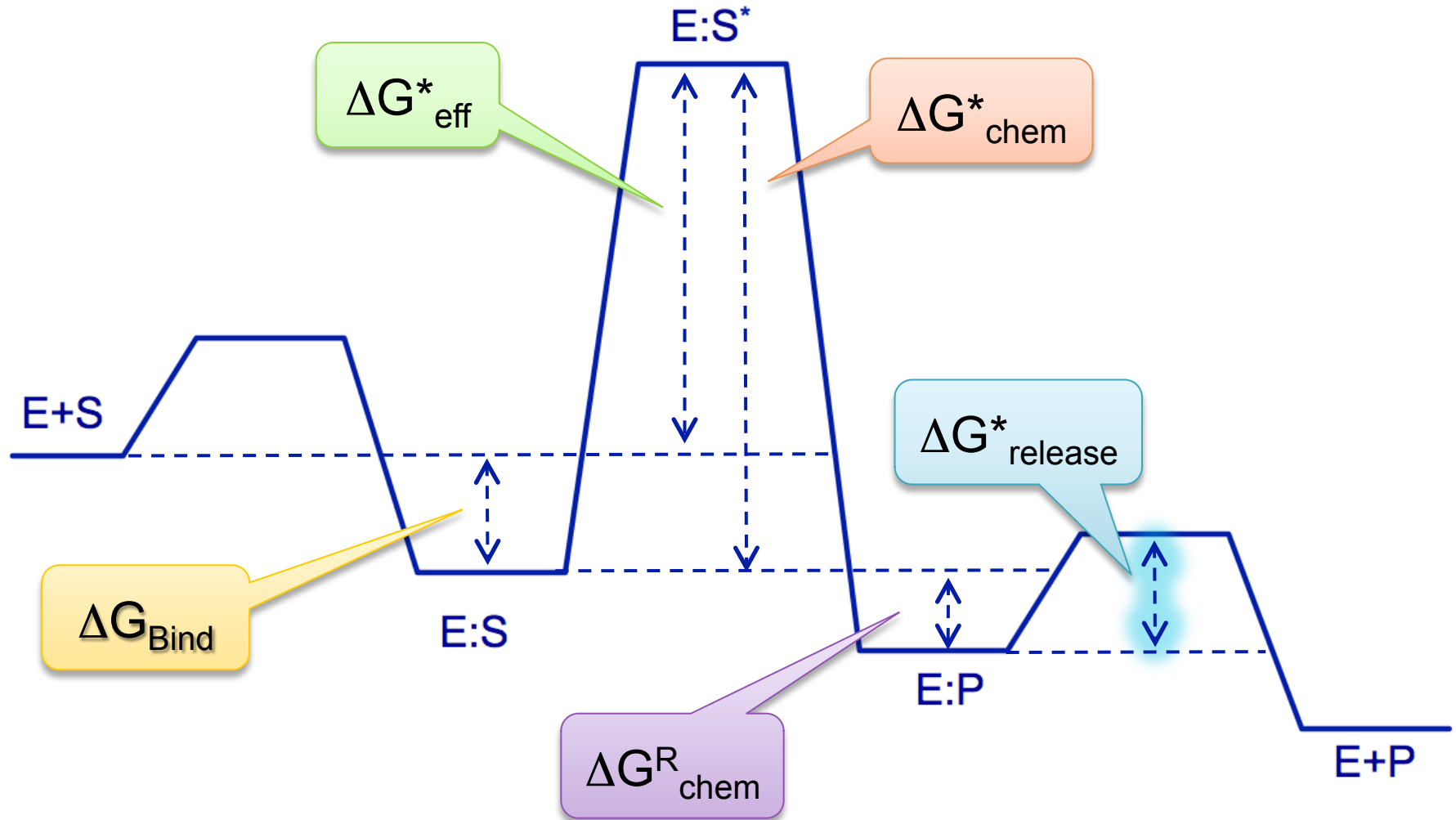
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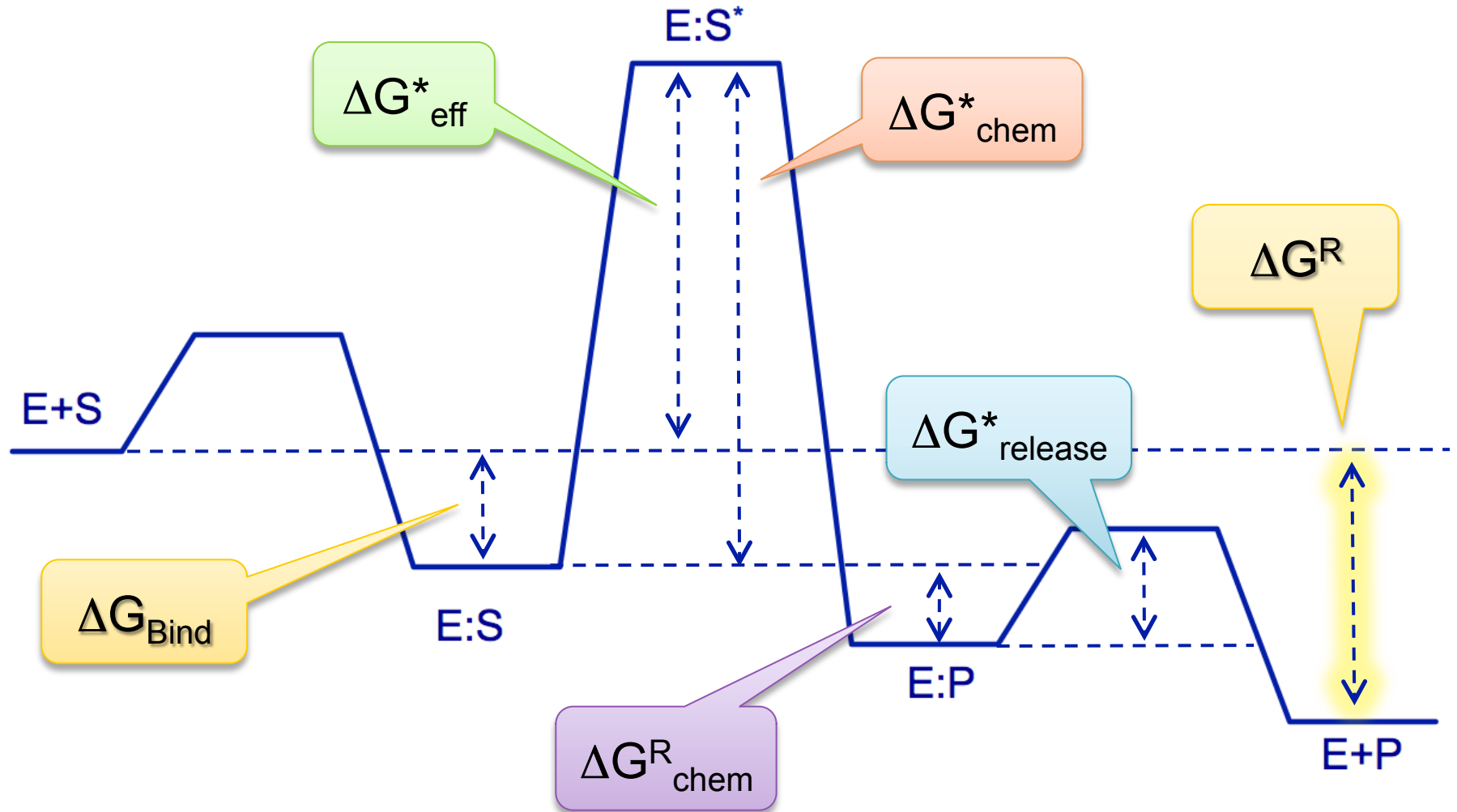
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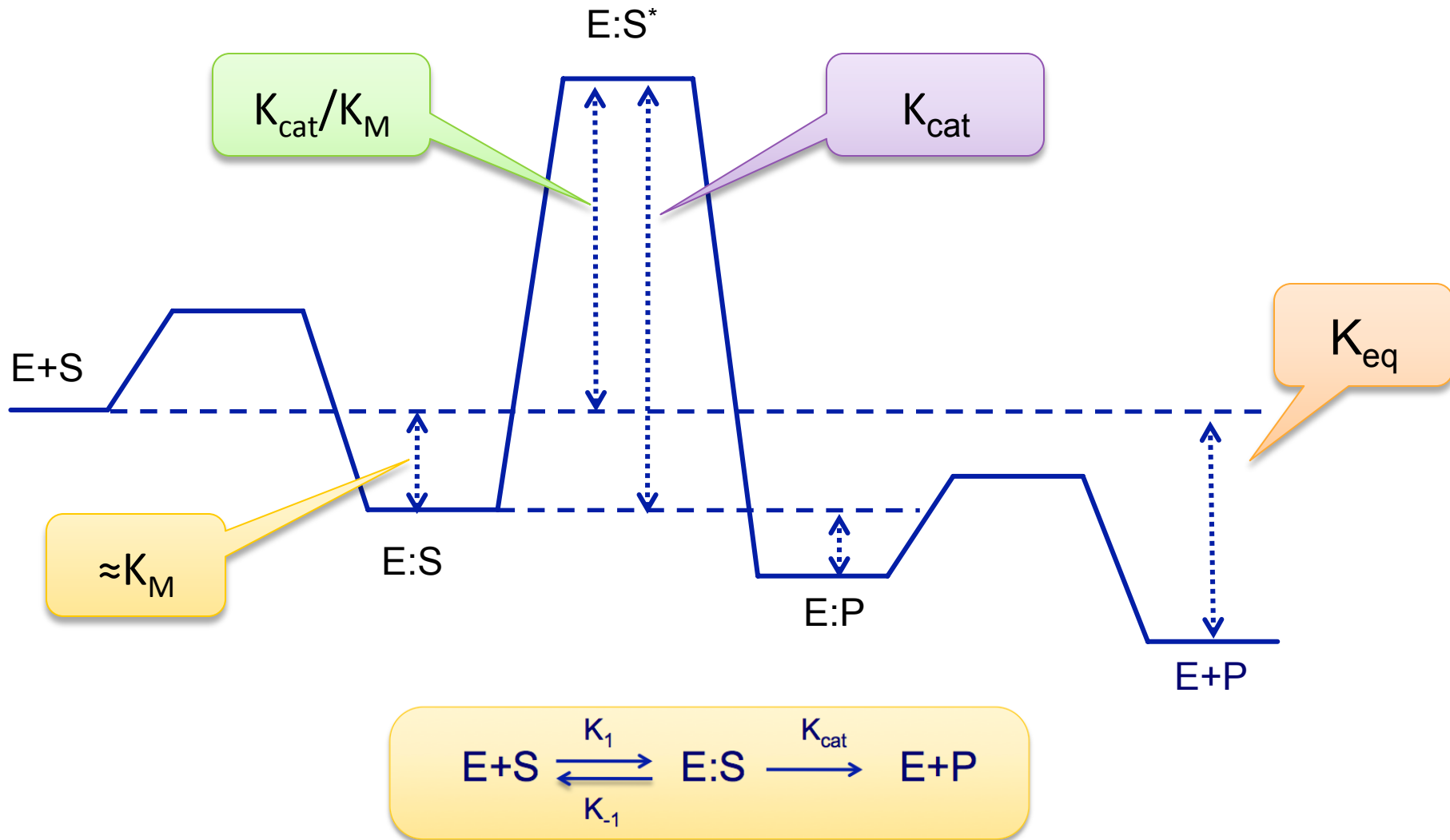
# PES for a Typical Enzymatic Reaction



# PES for a Typical Enzymatic Reaction



# Equilibrium and rate constants



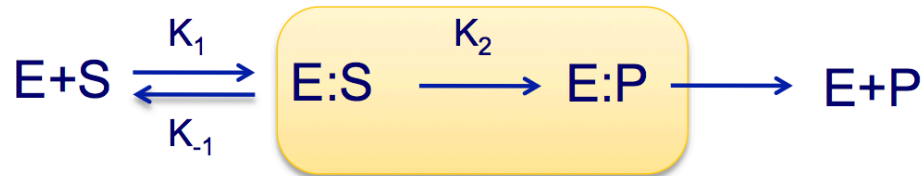
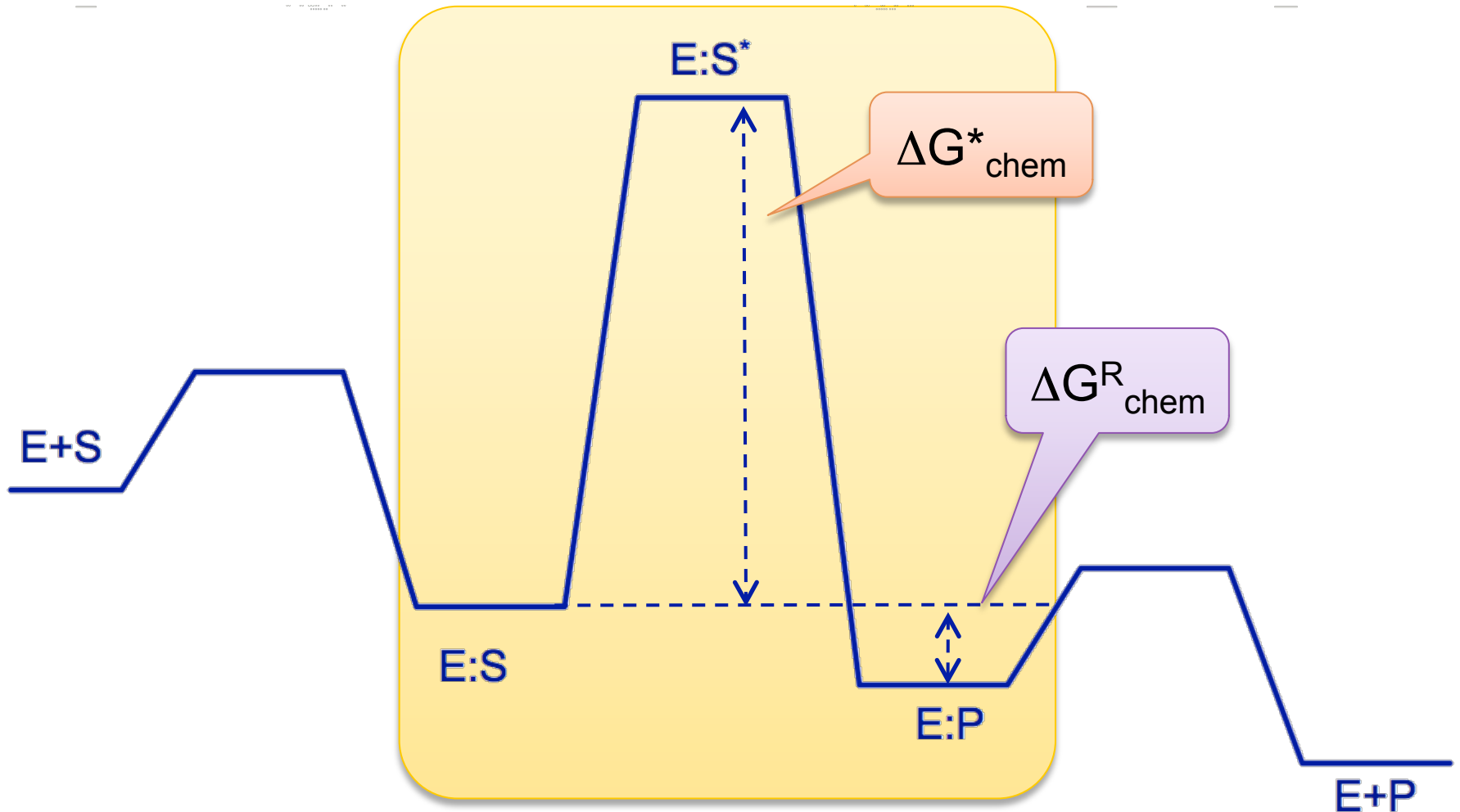
# The enormous catalytic power of enzymes

## rate enhancement by selected enzymes

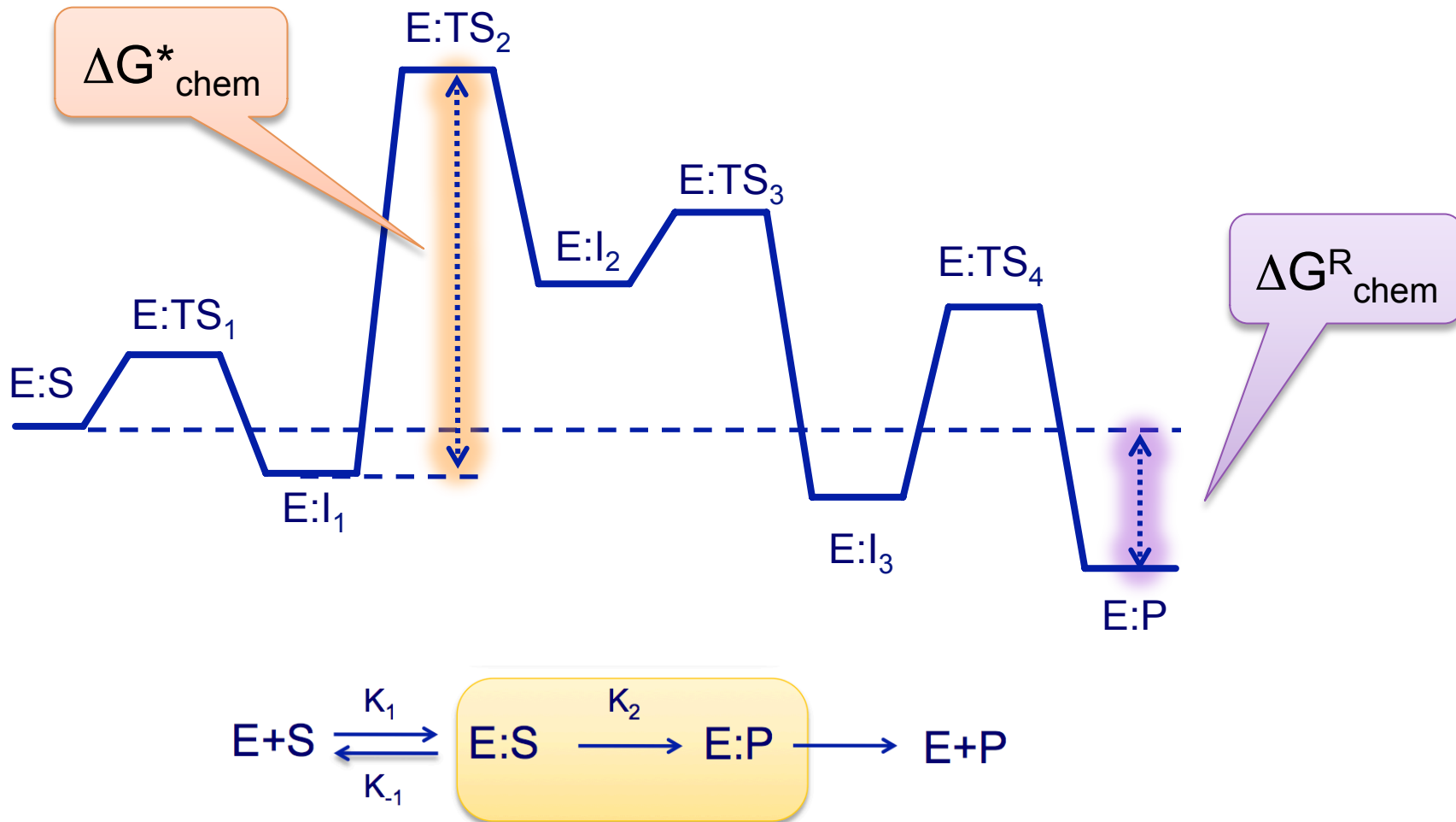
| Enzyme                     | Nonenzymatic half-life | Uncatalyzed rate ( $k_{\text{un}} \text{ s}^{-1}$ ) | Catalyzed rate ( $k_{\text{cat}} \text{ s}^{-1}$ ) | Rate enhancement ( $k_{\text{cat}}/k_{\text{un}}$ ) |
|----------------------------|------------------------|---|--|---|
| OMP decarboxylase          | 78,000,000 years       | $2.8 \times 10^{-16}$                               | 39   | $1.4 \times 10^{17}$                                |
| Staphylococcal nuclease    | 130,000 years          | $1.7 \times 10^{-13}$                               | 95   | $5.6 \times 10^{14}$                                |
| AMP nucleosidase           | 69,000 years           | $1.0 \times 10^{-11}$                               | 60   | $6.0 \times 10^{12}$                                |
| Carboxypeptidase A         | 7.3 years              | $3.0 \times 10^{-9}$                                | 578  | $1.9 \times 10^{11}$                                |
| Ketosteroid isomerase      | 7 weeks                | $1.7 \times 10^{-7}$                                | 66,000   | $3.9 \times 10^{11}$                                |
| Triose phosphate isomerase | 1.9 days               | $4.3 \times 10^{-6}$                                | 4,300  | $1.0 \times 10^9$                                   |
| Chorismate mutase          | 7.4 hours              | $2.6 \times 10^{-5}$                                | 50   | $1.9 \times 10^6$                                   |
| Carbonic anhydrase         | 5 seconds              | $1.3 \times 10^{-1}$                                | $1 \times 10^6$                                    | $7.7 \times 10^6$                                   |

enzymes are able to speed up chemical reactions in an order of magnitude of  $10^6$  to  $10^{20}$

# What we usually do with a computer?



# The chemical reaction usually consists in many elementary steps





# Finding out a catalytic mechanism: The method



Characterize the geometry and the energy of the reactants

# Finding out a catalytic mechanism: The method



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Formulate an hypothesis for the mechanism of reaction

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All other data matches the experimental values?



YES

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All other data matches the experimental values?

There are viable alternatives for the chemical mechanism?



YES



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Formulate an hypothesis for the mechanism of reaction

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All other data matches the experimental values?

There are viable alternatives for the chemical mechanism?



YES

# Finding out a catalytic mechanism: The method

Characterize the geometry and the energy of the reactants

Formulate hypotheses for the mechanism of reaction

Characterize the geometry and the energy of all TSs and Int.

The rate constants matches the experimental values?

All other data matches the experimental values?

There are no viable alternatives for the chemical mechanism?

Problem solved



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