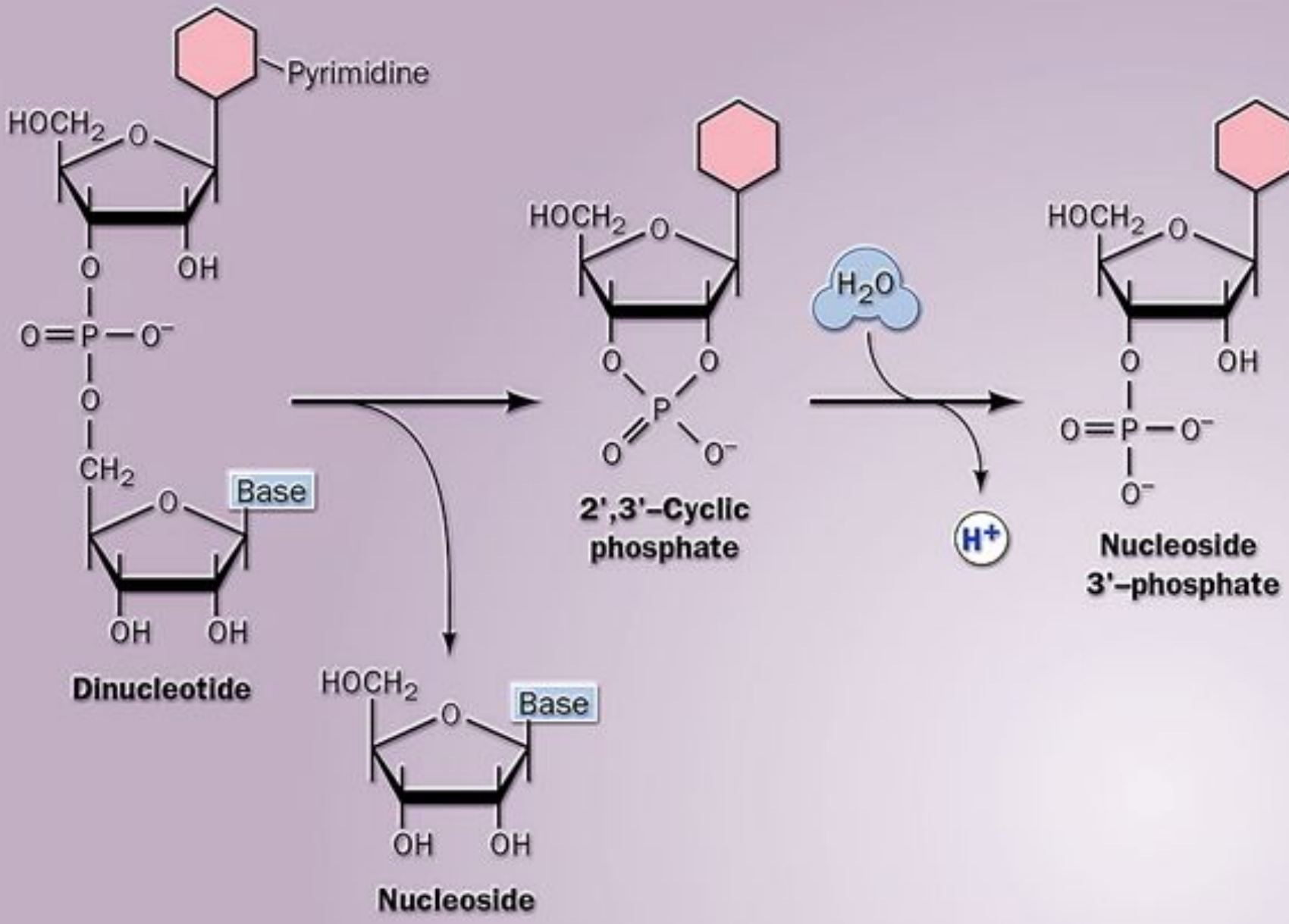
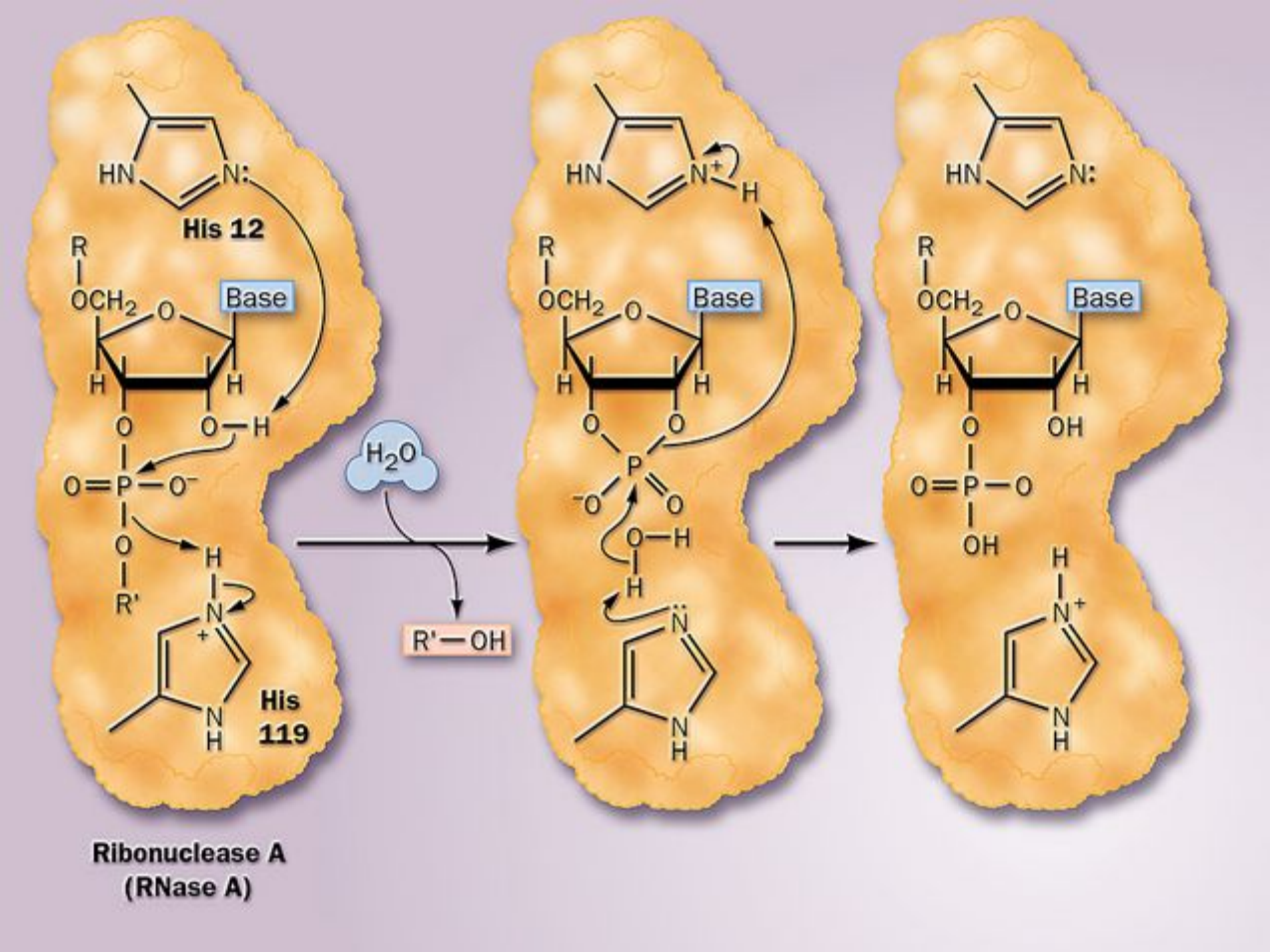
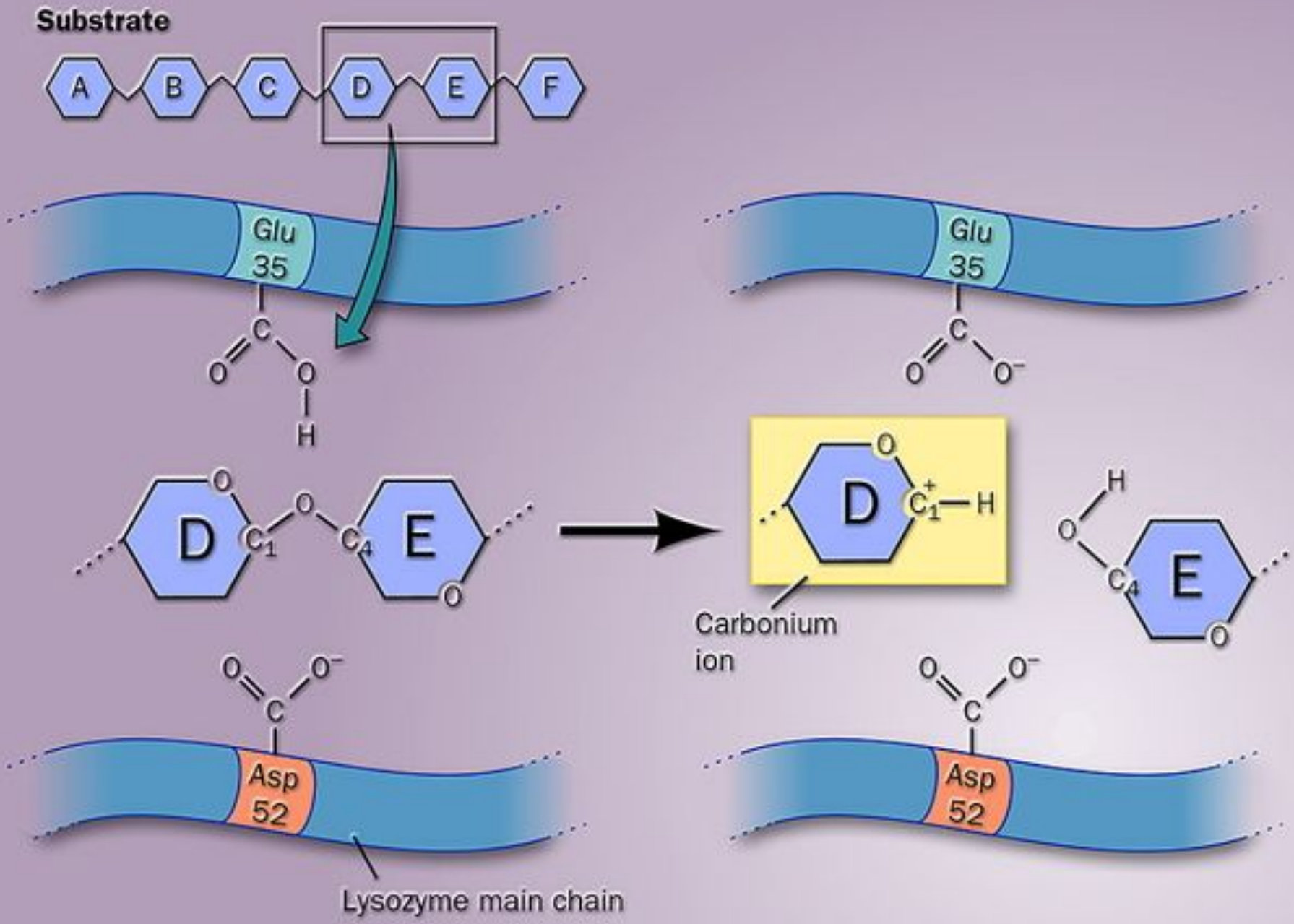
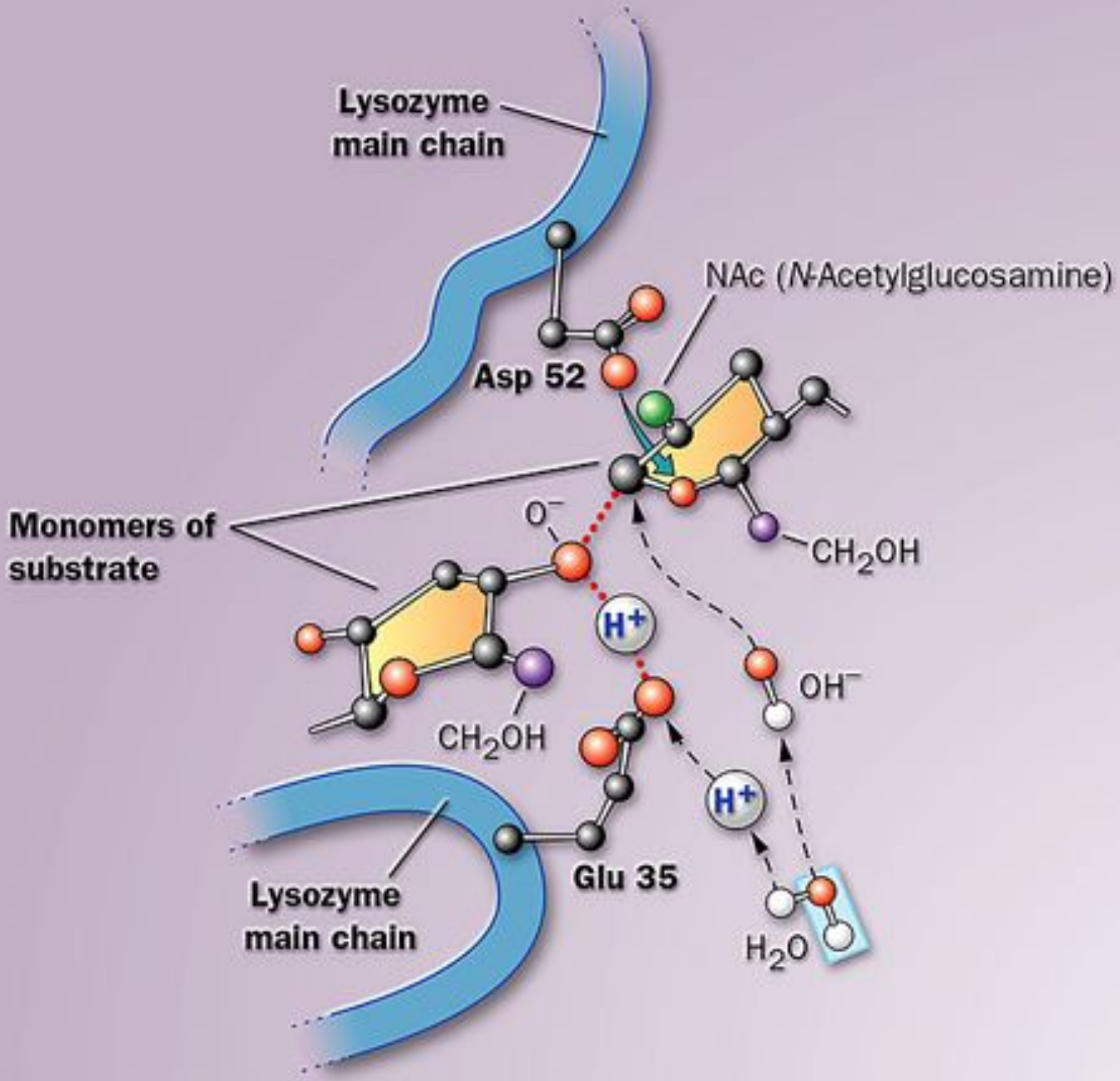
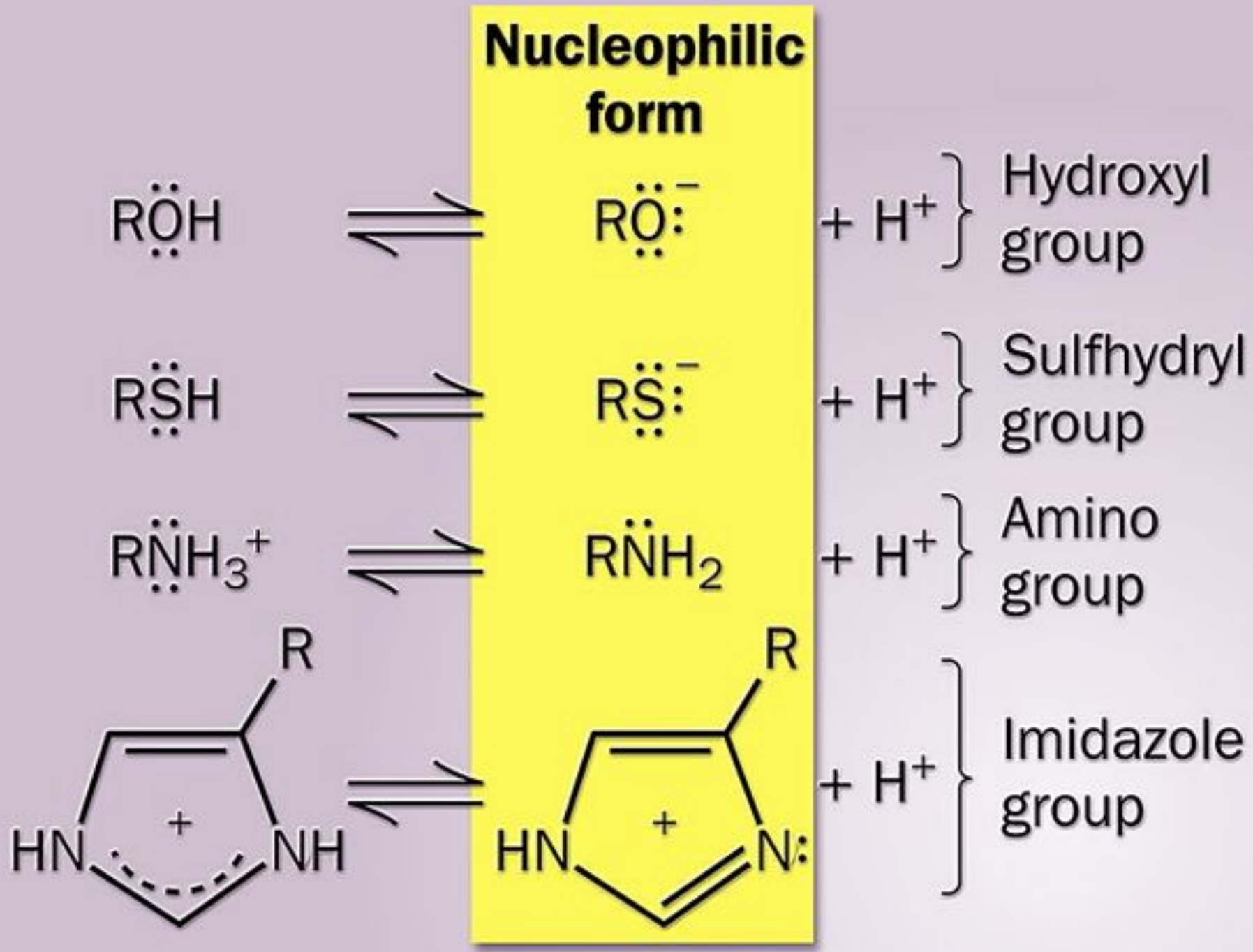
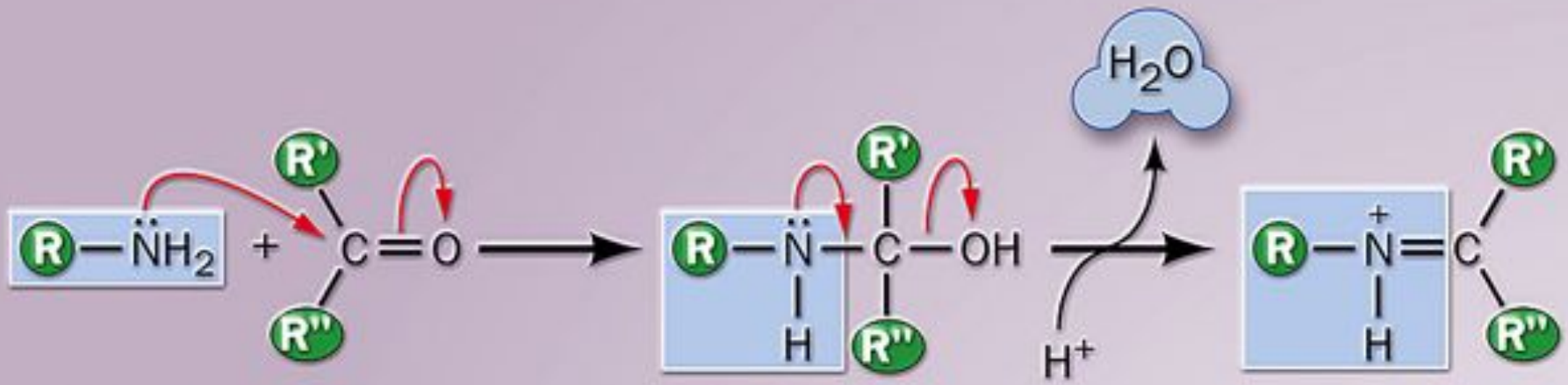

Pyrimidine
HOCH2
O
OH
O=P—O⁻
CH2
Base
OH
OH
Dinucleotide
2',3'–Cyclic phosphate
H2O
H+
Nucleoside 3'–phosphate
Nucleoside

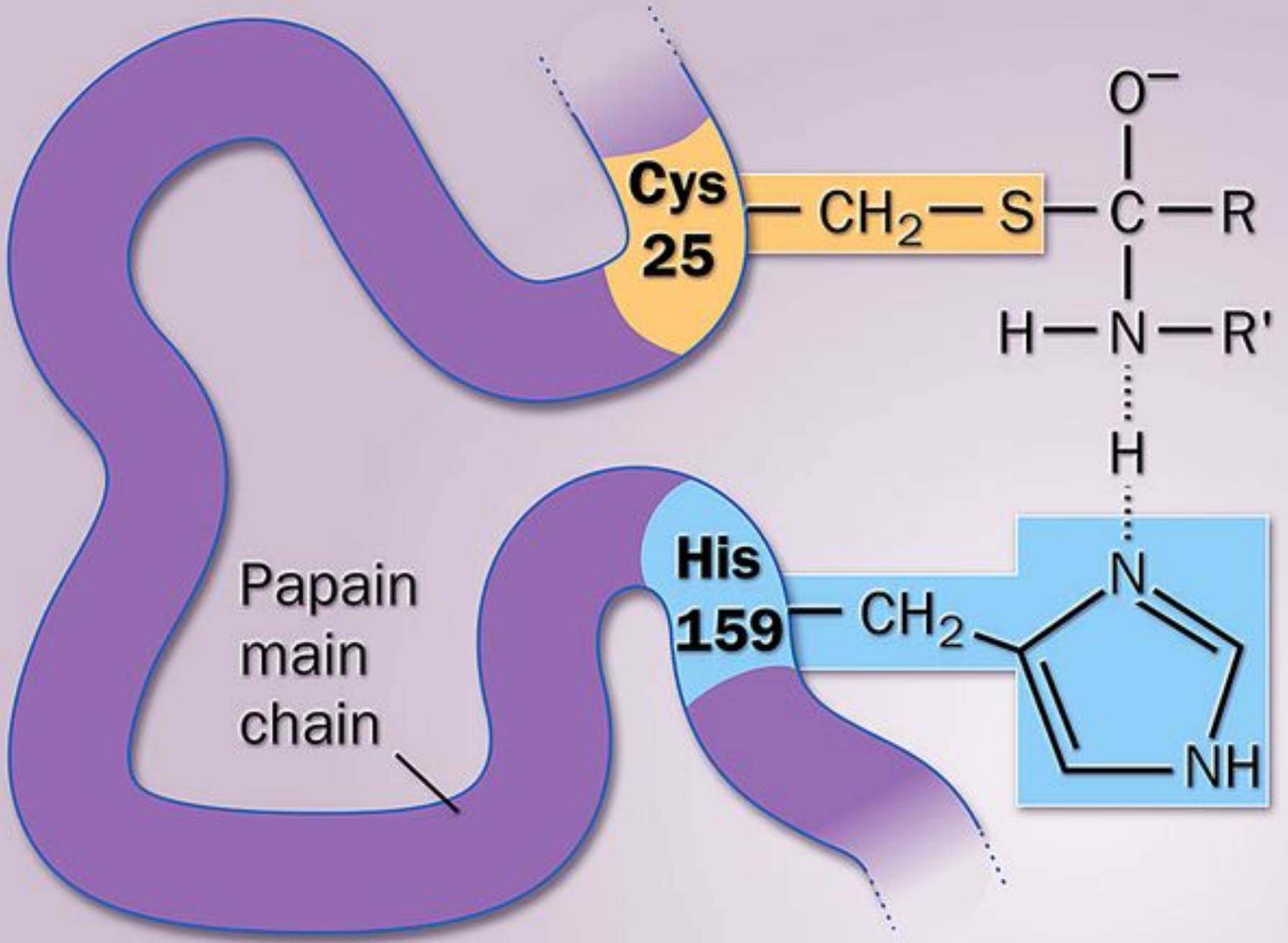

His 12
Base
H_2O
R'—OH
His 119
Ribonuclease A
(RNase A)

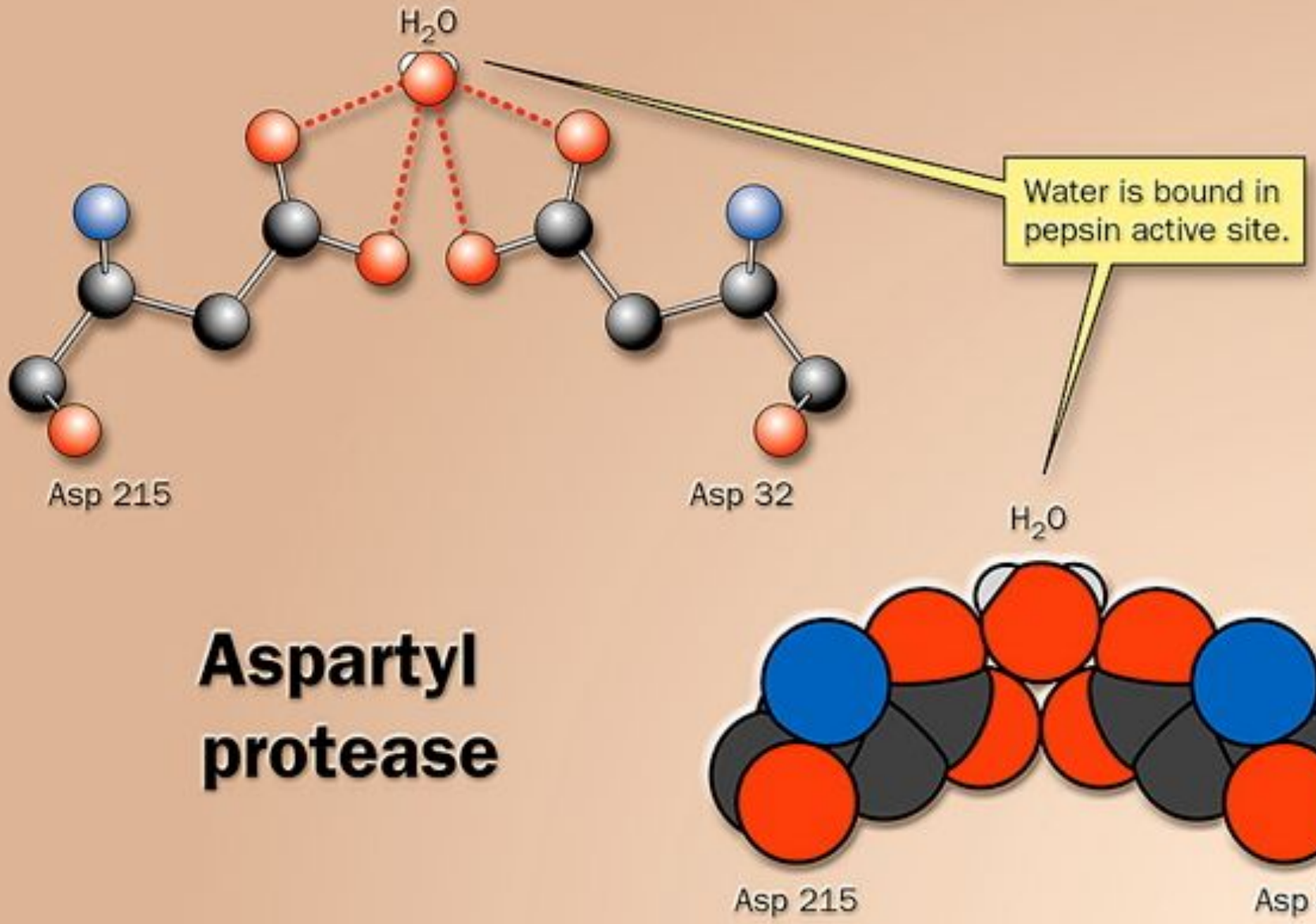

Substrate
A
B
C
D
E
F
Glu
35
Asp
52
Lysozyme main chain
Carbonium
ion


Lysozyme
main chain
NAc (N-Acetylglucosamine)
Asp 52
Monomers of
substrate
O⁻
CH2OH
H+
OH⁻
CH2OH
H+
Glu 35
Lysozyme
main chain
H2O

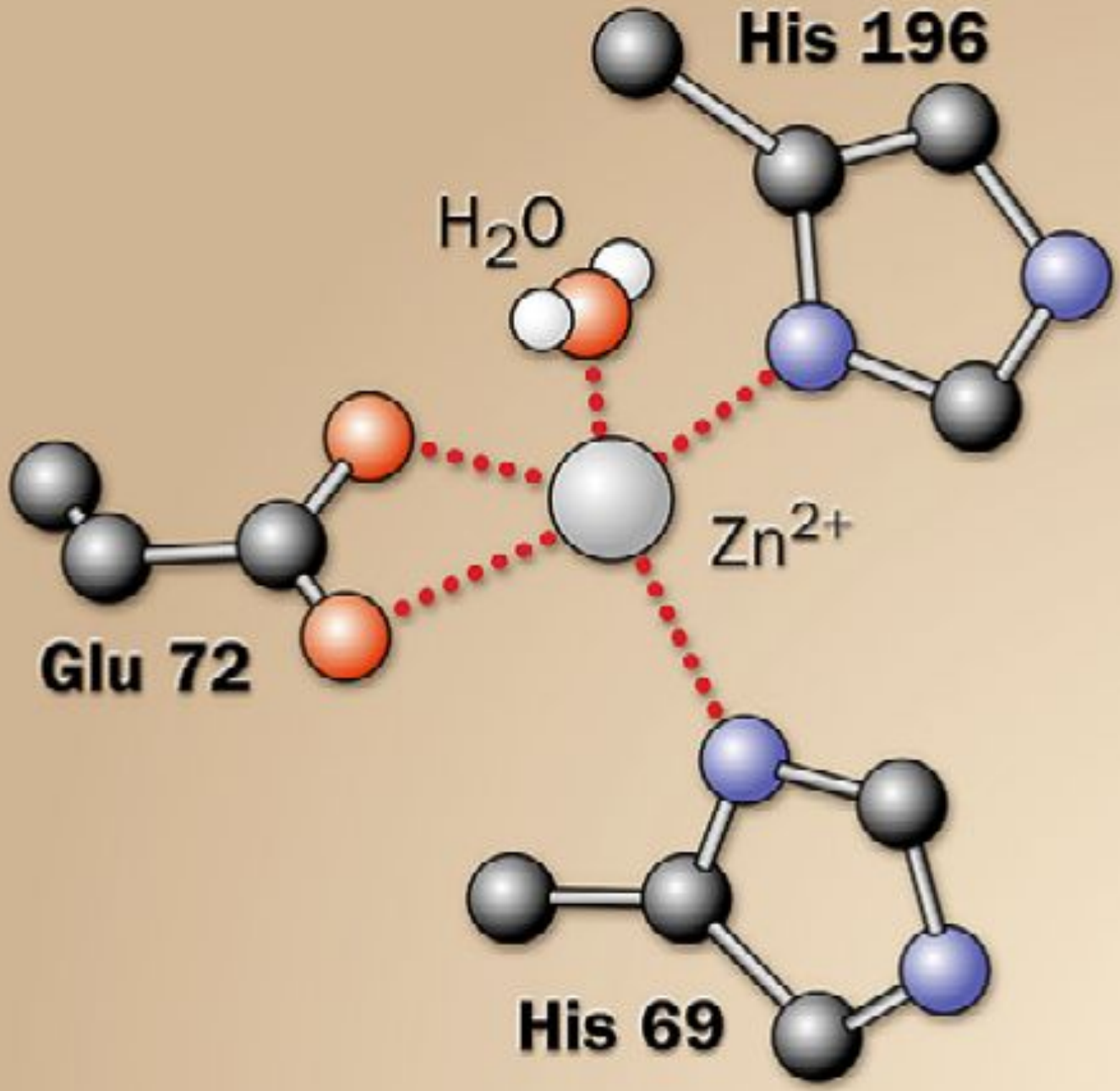

Nucleophilic form
ROH
RO:⁻
+ H⁺
Hydroxyl group
RSH
RS:⁻
+ H⁺
Sulfhydryl group
RNH3⁺
RNH2
+ H⁺
Amino group
R
HN
NH
R
HN
N:
+ H⁺
Imidazole group


R—NH2
+
R'
C=O
R"
R—N—C—OH
H
R'
R"
H2O
H+
R—N=C
H
R'
R"
Amine
Aldehyde or ketone
Carbinolamine intermediate
Imine


Cys
25
CH2
S
C
O−
R
H
N
R'
H
His
159
CH2
N
NH
Papain
main
chain

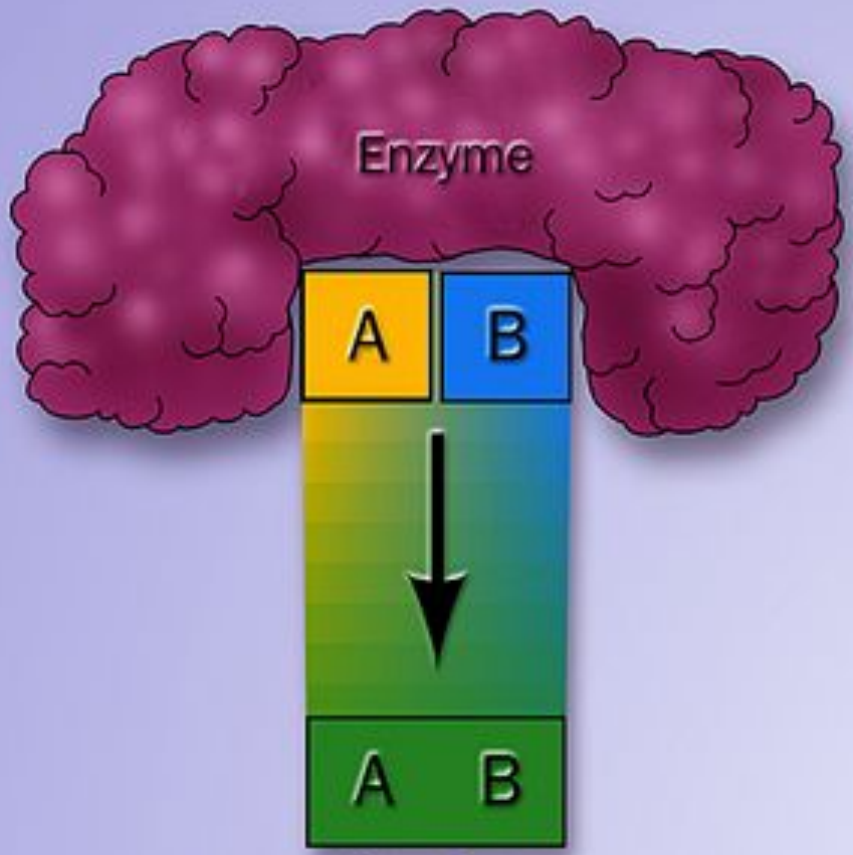


Aspartyl protease


His 196
H_2O
Zn^{2+}
Glu 72
His 69

Reactants are spatially separated

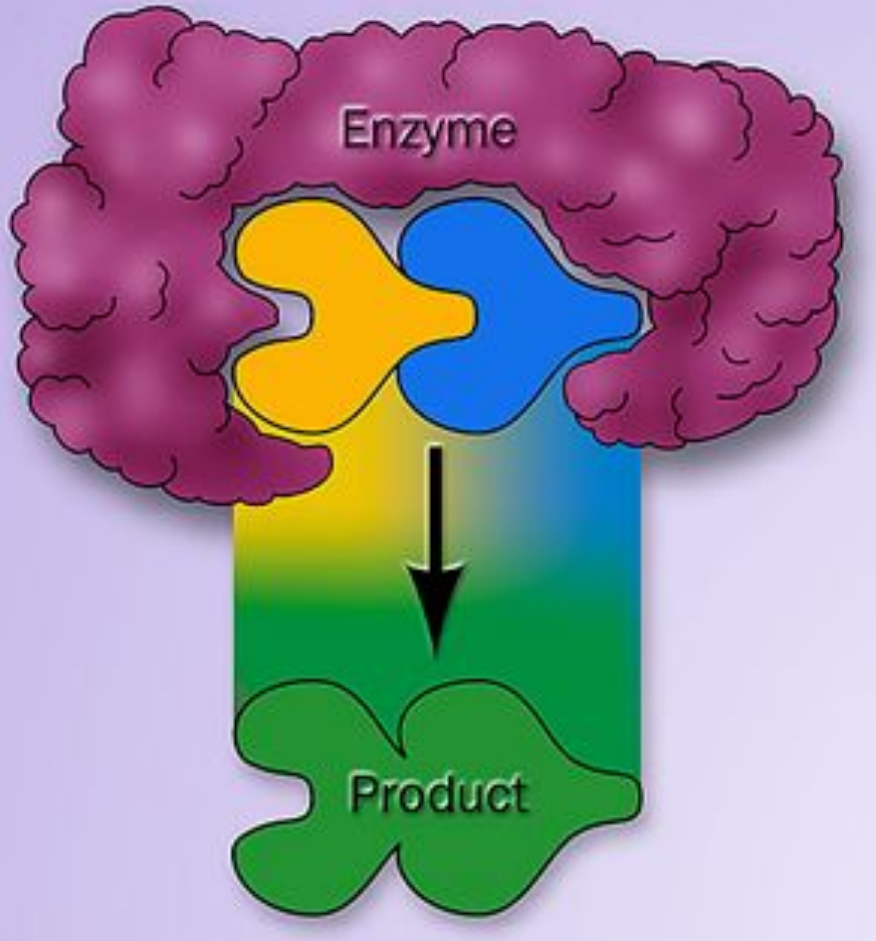
Enzyme brings reactants into proximity



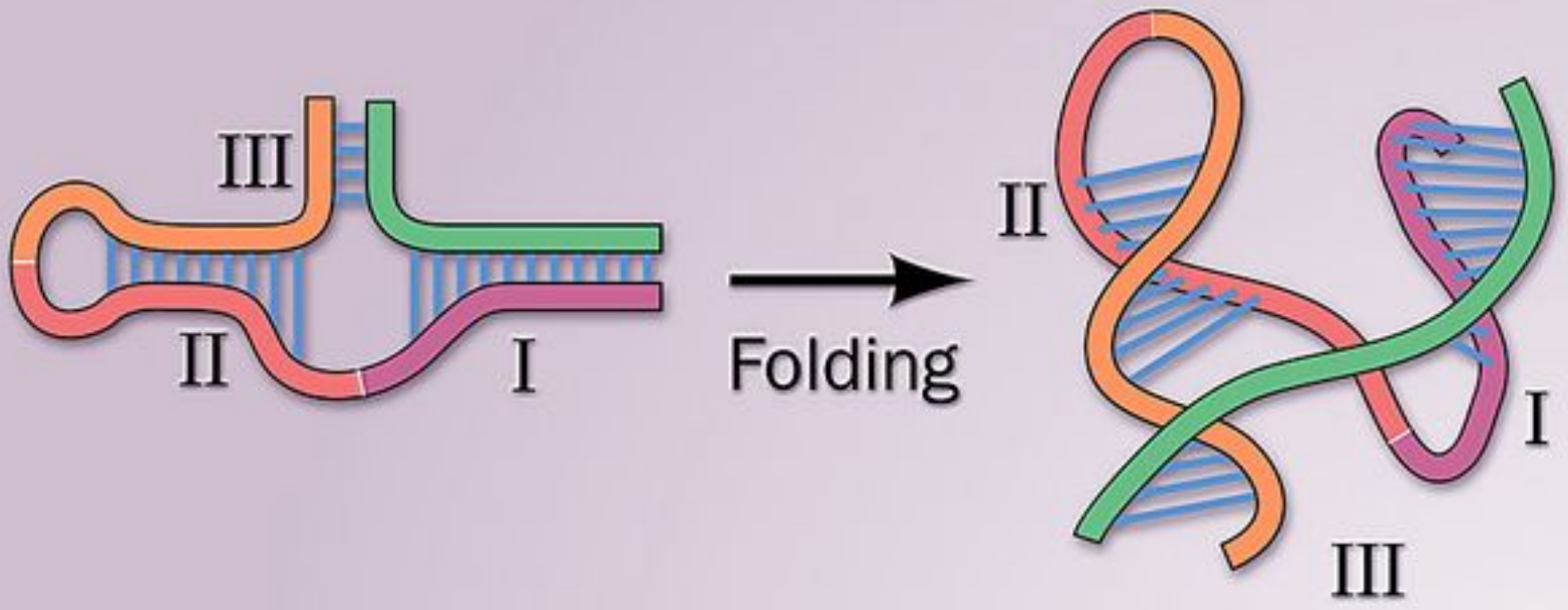
Transition to product occurs

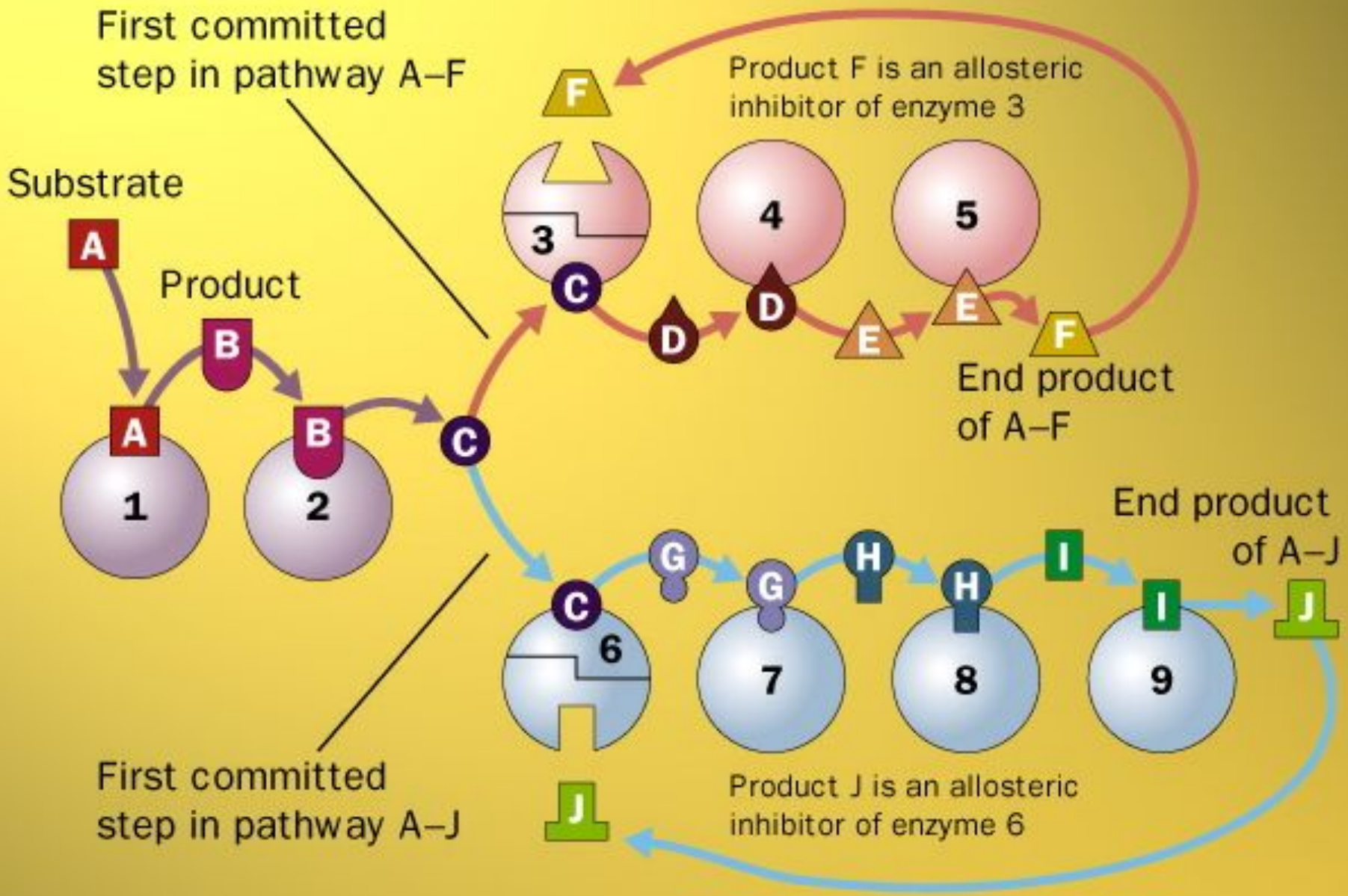
Reactants are not oriented for reaction

Enzyme orients reactants correctly



Transition to product occurs

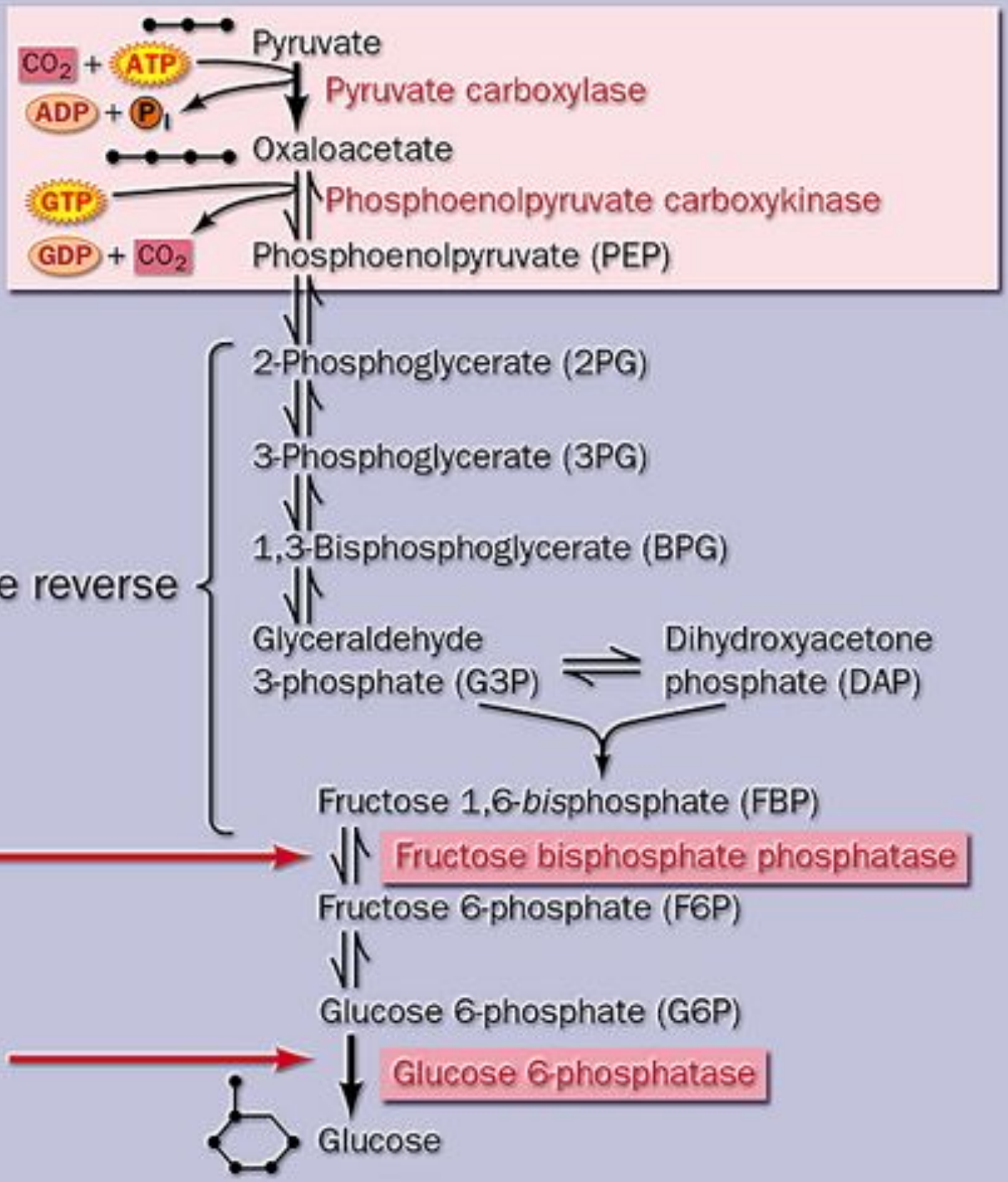

III
II
I
Folding
II
I
III

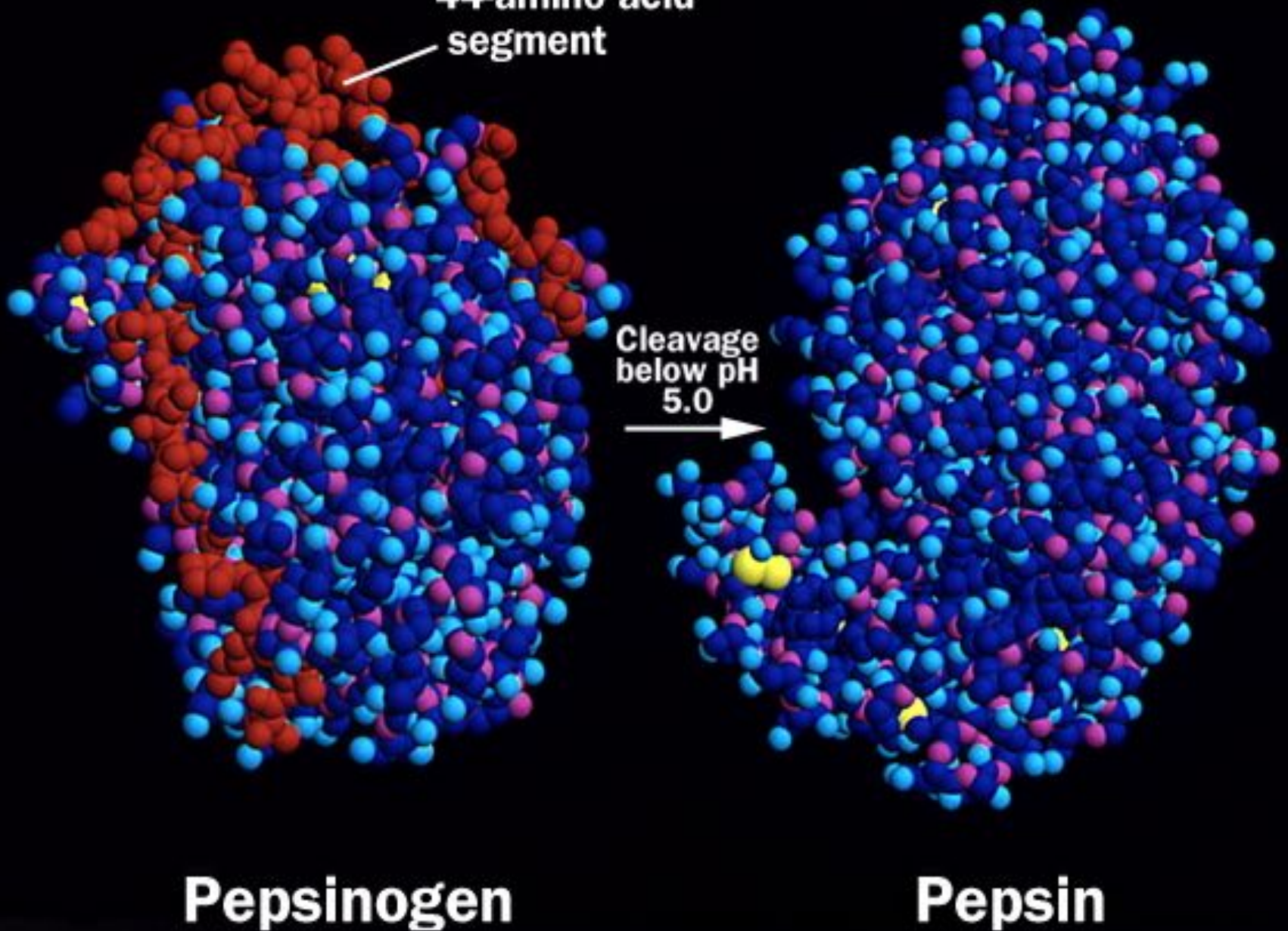


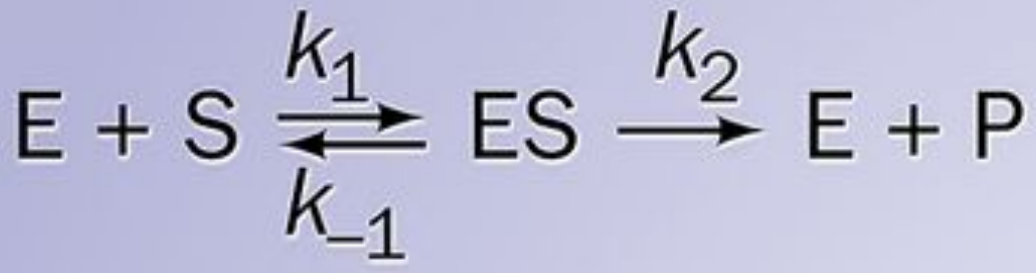
ALLOSTERIC INHIBITOR

GLUCONEOGENESIS

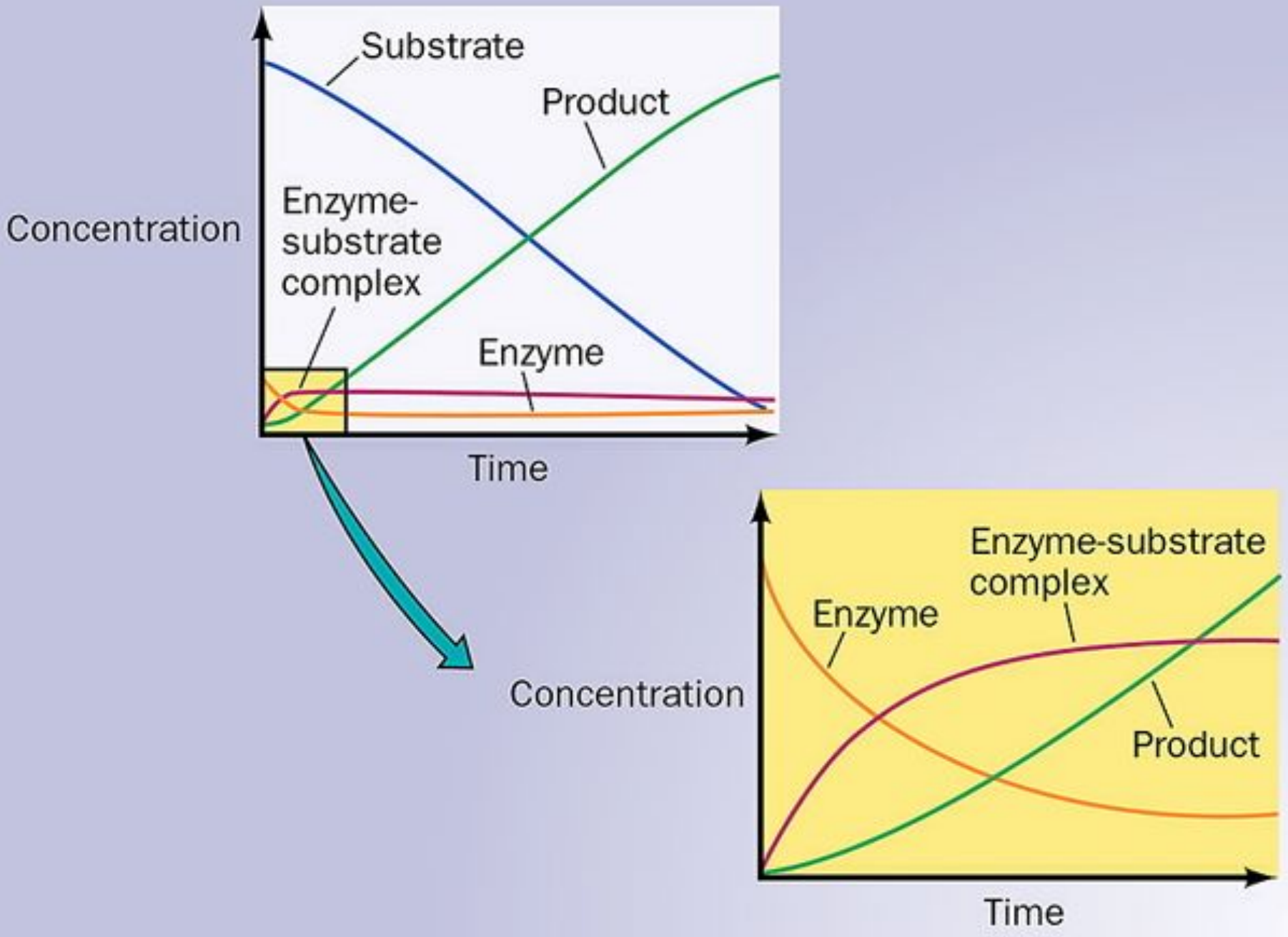
Not a reversal of glycolysis: differences are shown in boxes




44-amino acid segment
Cleavage below pH 5.0
Pepsinogen
Pepsin



Nonallosteric enzyme kinetics


Substrate
Product
Concentration
Enzyme-
substrate
complex
Enzyme
Time
Enzyme-substrate
complex
Enzyme
Concentration
Product
Time

$$\frac{\Delta[ES]}{\Delta t} = k_1[E][S]$$

Rate of formation of ES

$$-\frac{\Delta[ES]}{\Delta t} = k_{-1}[ES] + k_2[ES]$$

Rate of breakdown of ES

$$\frac{\Delta[ES]}{\Delta t} = -\frac{\Delta[ES]}{\Delta t}$$

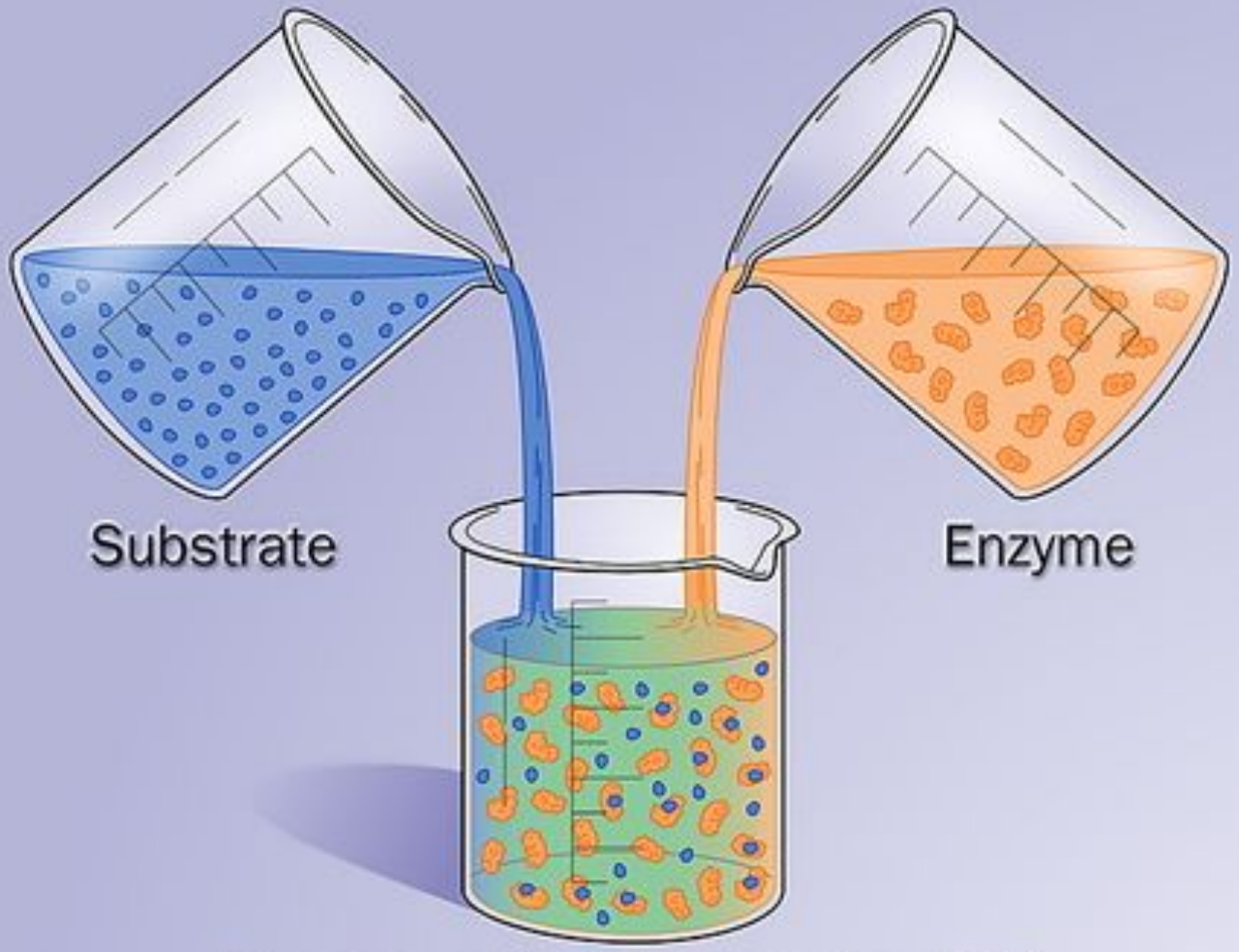
$$k_1[E][S] = k_{-1}[ES] + k_2[ES]$$

Steady state kinetics

Free enzyme concentration ([E])

$$[E] = [E]_0 - [ES]$$

$$\underbrace{k_1([E]_0 - [ES])[S]}_{\text{Formation of ES complex}} = \underbrace{k_{-1}[ES] + k_2[ES]}_{\text{Breakdown of ES complex}}$$



Enzyme–substrate complex (ES)
+ free enzyme (E)
+ unbound substrate

$$[E]_0 - [ES] = [E]$$

$$\underbrace{k_1([E]_0 - [ES])[S]}_{\text{Formation of ES complex}} = \underbrace{k_{-1}[ES] + k_2[ES]}_{\text{Breakdown of ES complex}}$$

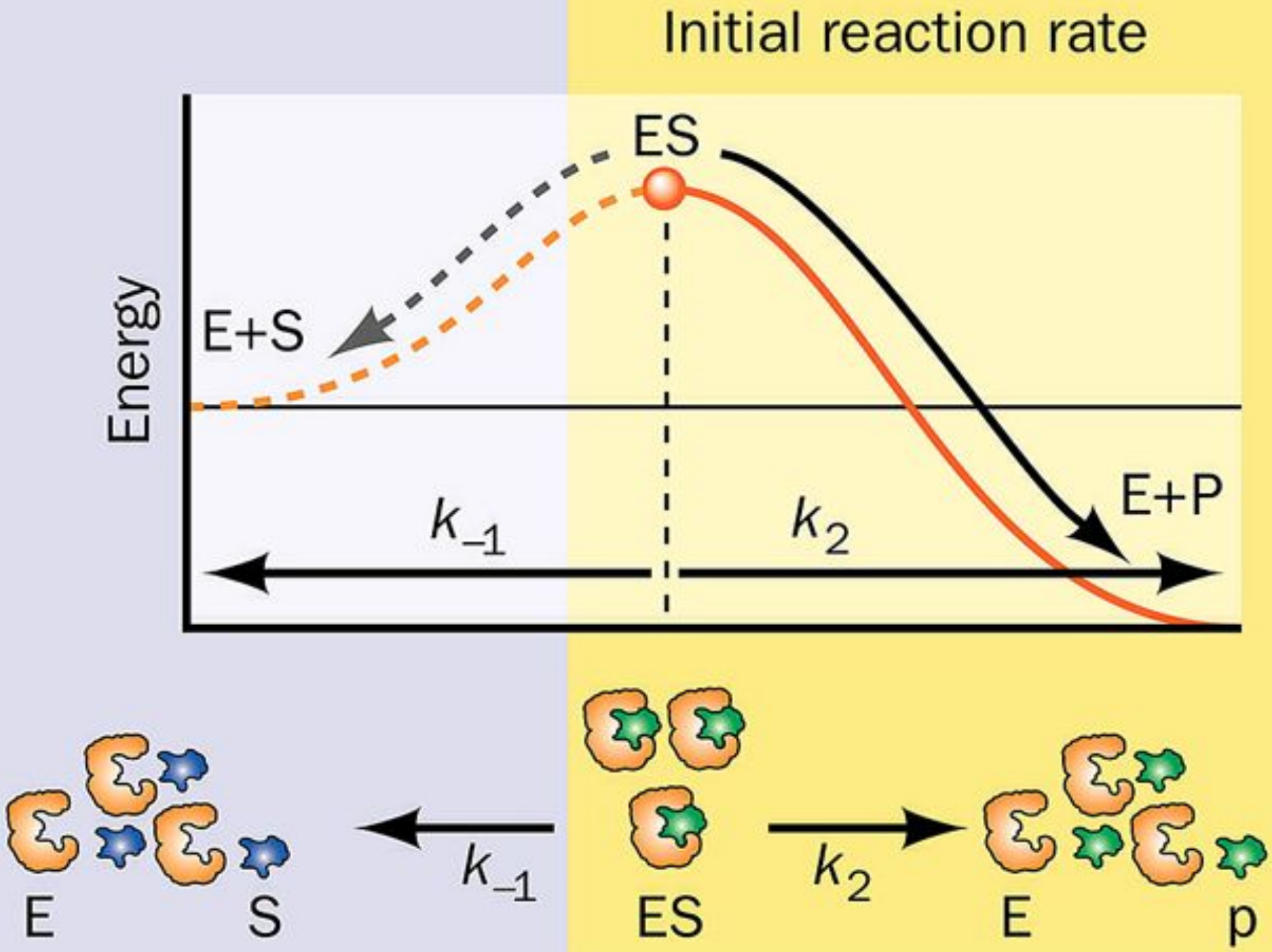
$$\frac{([E]_0 - [ES])[S]}{[ES]} = \frac{k_{-1} + k_2}{k_1} = K_m$$

The Michaelis constant (K_m)

$$V_{init} = k_2[ES] \text{ and } [ES] = \frac{[E]_0[S]}{K_M + [S]}$$

$$V_{init} = \frac{k_2[E]_0[S]}{K_M + [S]}$$

Initial reaction rate


Initial reaction rate
ES
Energy
E+S
E+P
k_{-1}
k_2
E
S
k_{-1}
ES
k_2
E
p

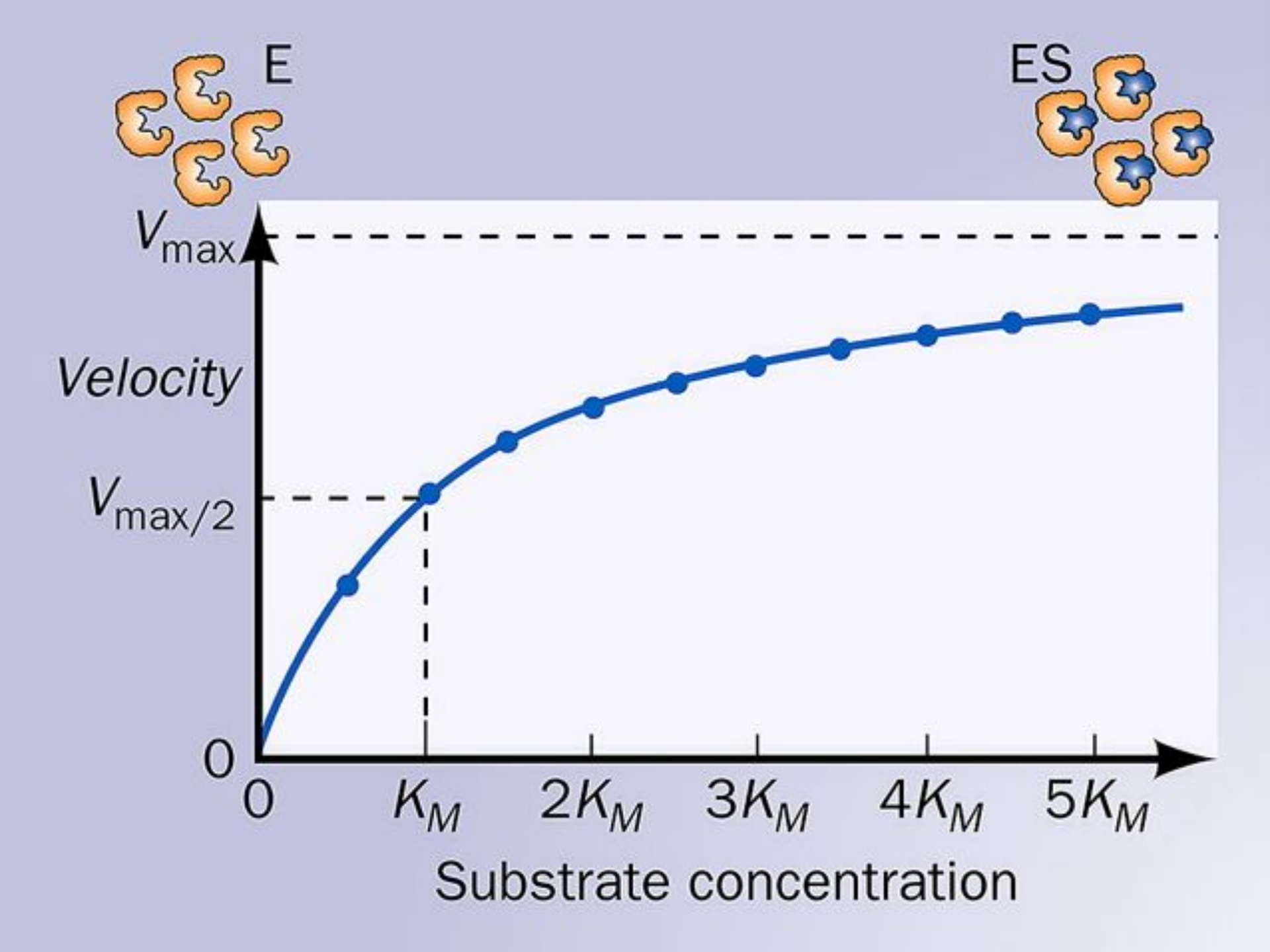
Enzyme-substrate complex

Total enzyme

$$[ES] = [E]_0$$

$$V_{init} = V_{max} = k_2[E]_0$$

Maximum reaction rate


E
ES
V_{max}
Velocity
$V_{max/2}$
0
0
K_M
$2K_M$
$3K_M$
$4K_M$
$5K_M$
Substrate concentration

$$V_{init} = \frac{k_2[E]_0[S]}{K_M + [S]}$$

$$V_{init} = \frac{V_{max}[S]}{K_M + [S]}$$

Michaelis-Menten Equation

Michaelis-Menten equation

$$V = \frac{V_{max}[S]}{K_M + [S]}$$

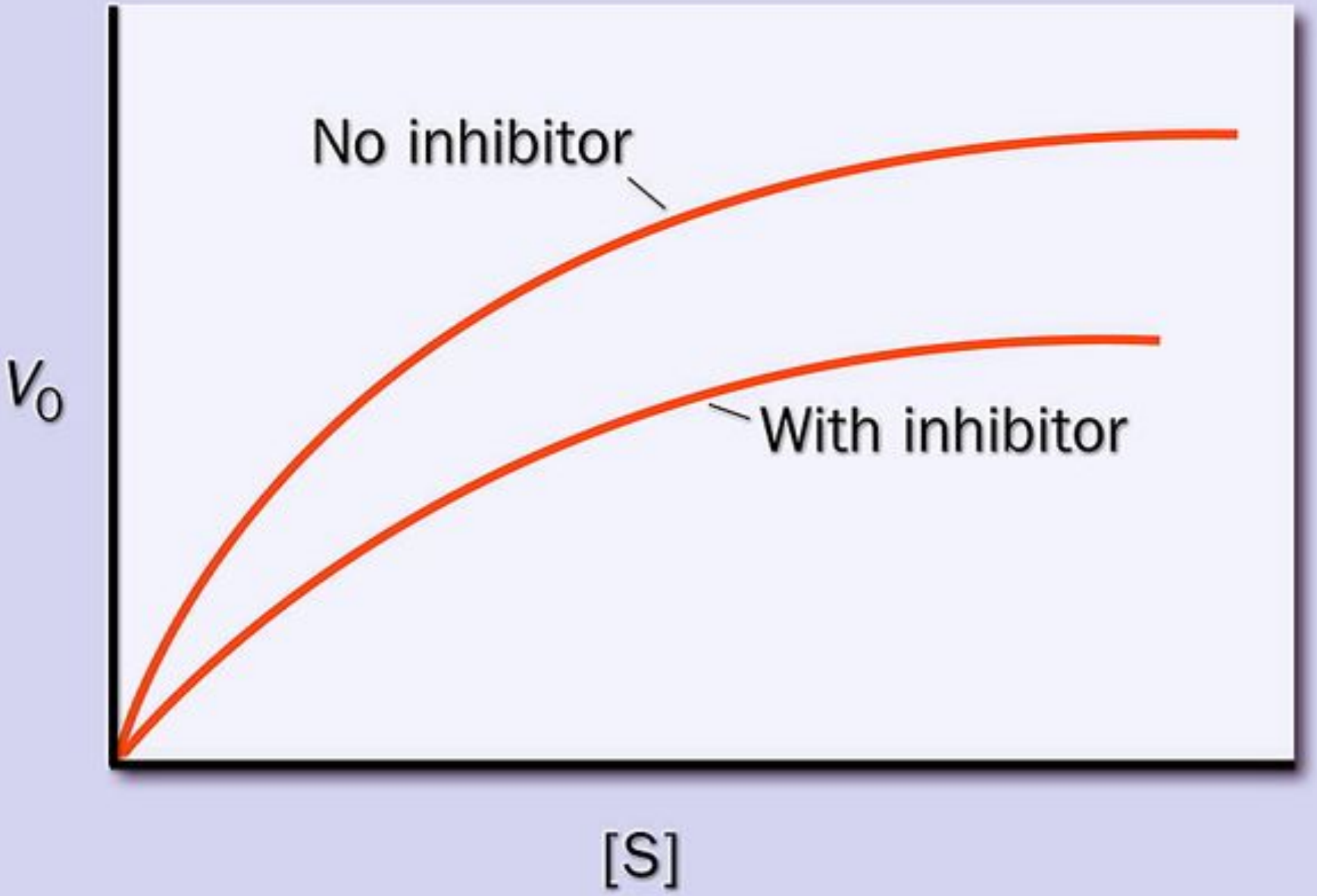
Take the reciprocal of both sides

$$\frac{1}{V} = \frac{K_M + [S]}{V_{max}[S]}$$

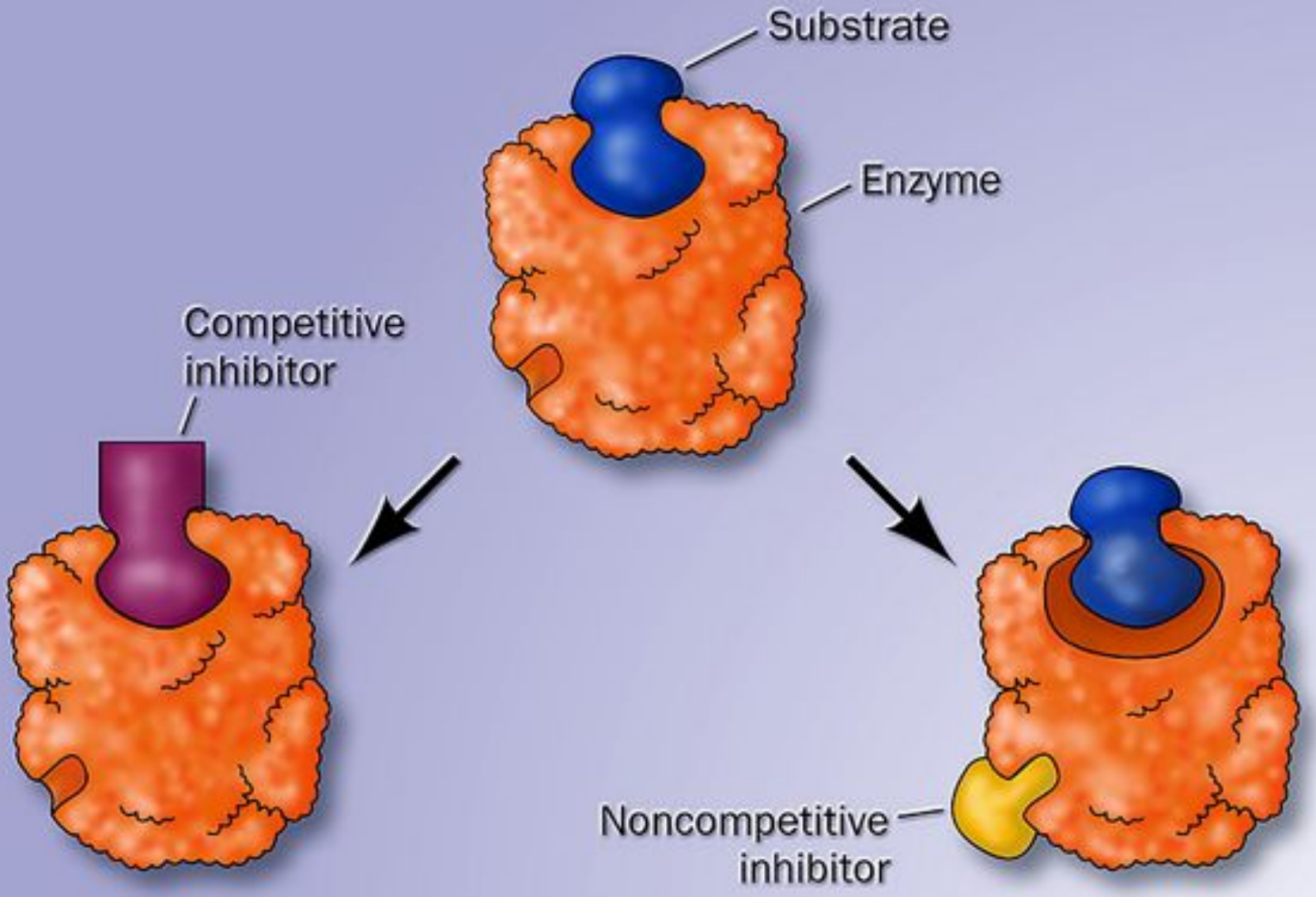
$$\frac{1}{V} = \frac{K_M}{V_{max}[S]} + \frac{[S]}{V_{max}[S]}$$

$$\frac{1}{V} = \frac{K_M}{V_{max}} \frac{1}{[S]} + \frac{1}{V_{max}}$$

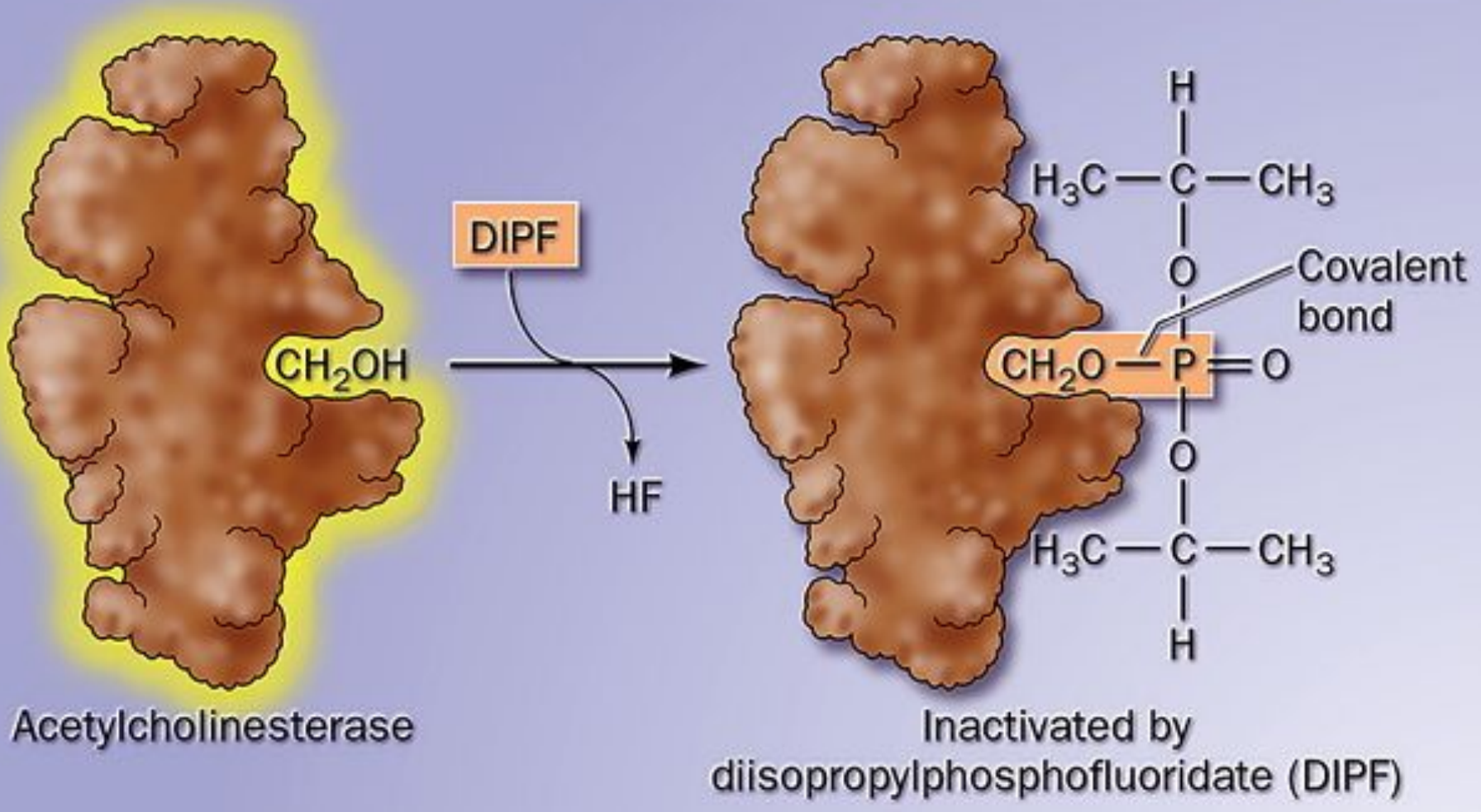
$$y = mx + b$$


No inhibitor
With inhibitor
V_0
[S]

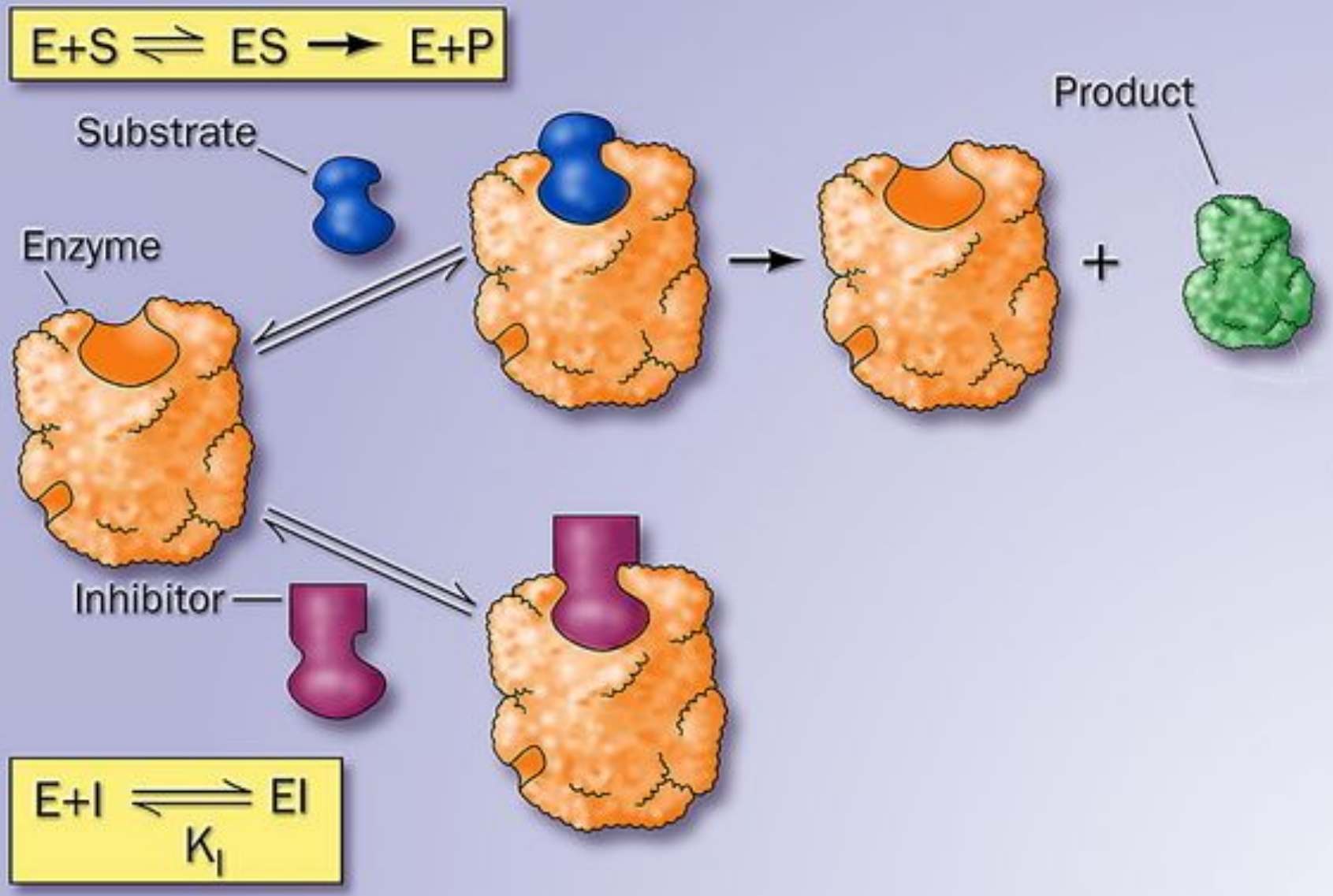
Competitive and Noncompetitive Inhibitors

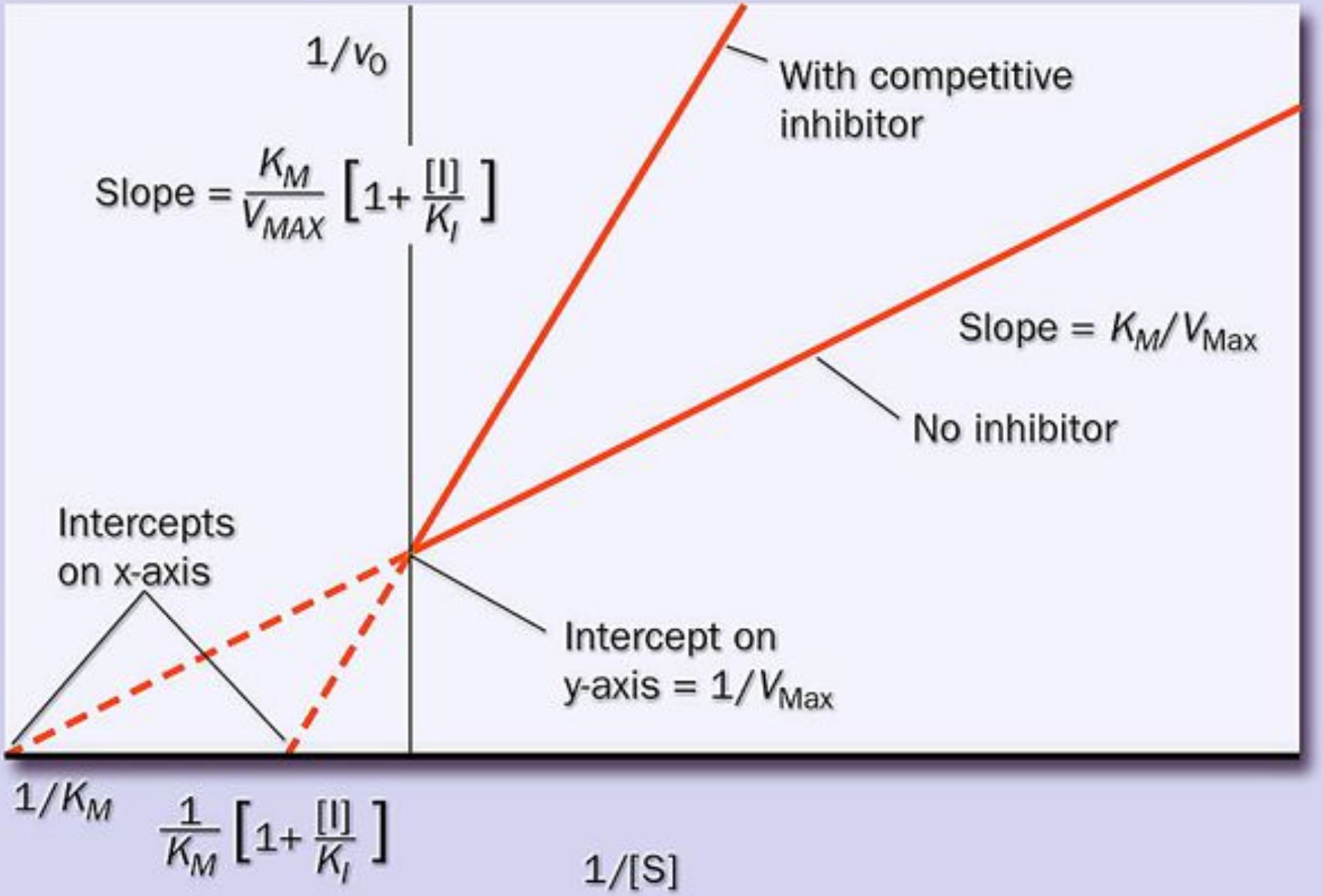


Inactivation of Acetylcholinesterase by DIPF

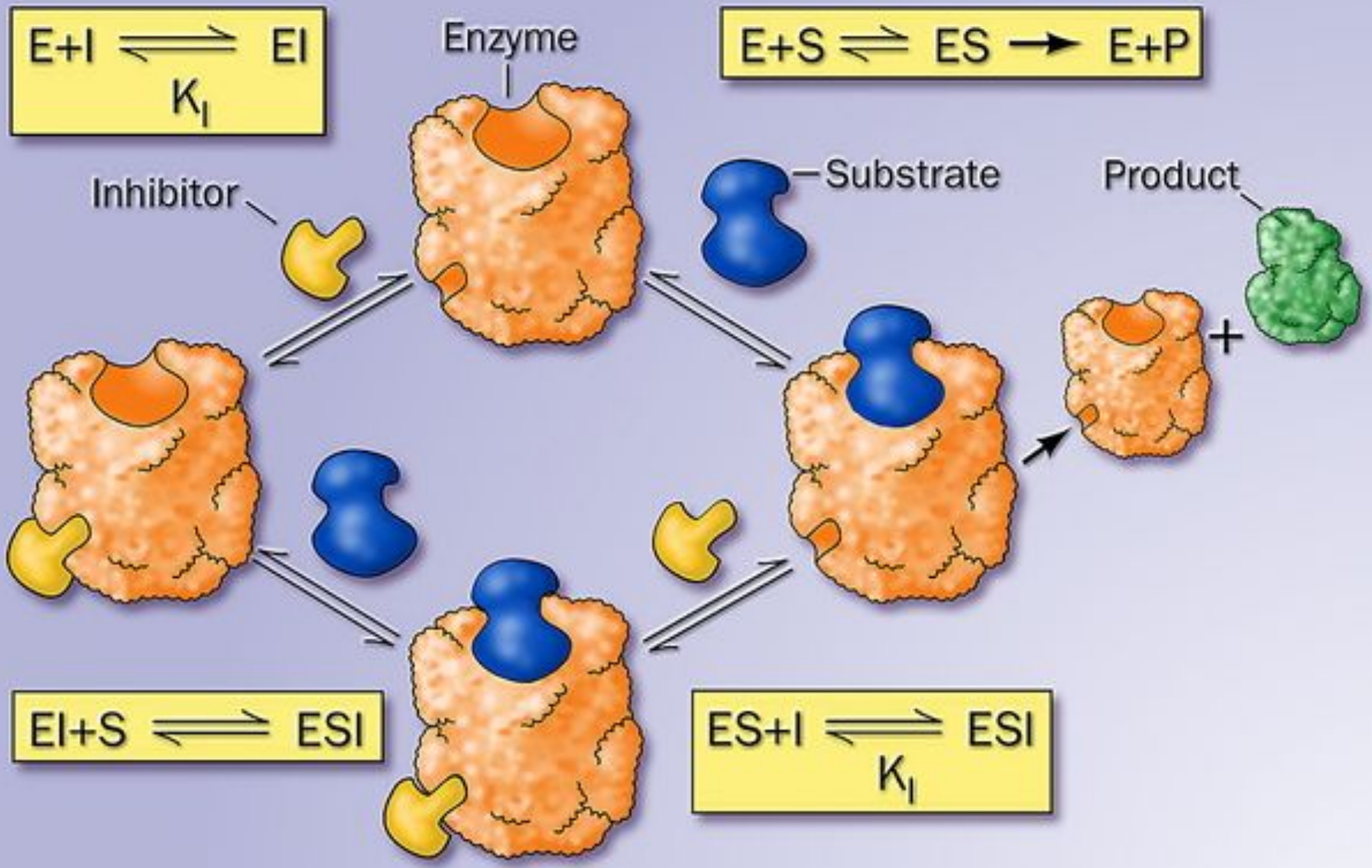


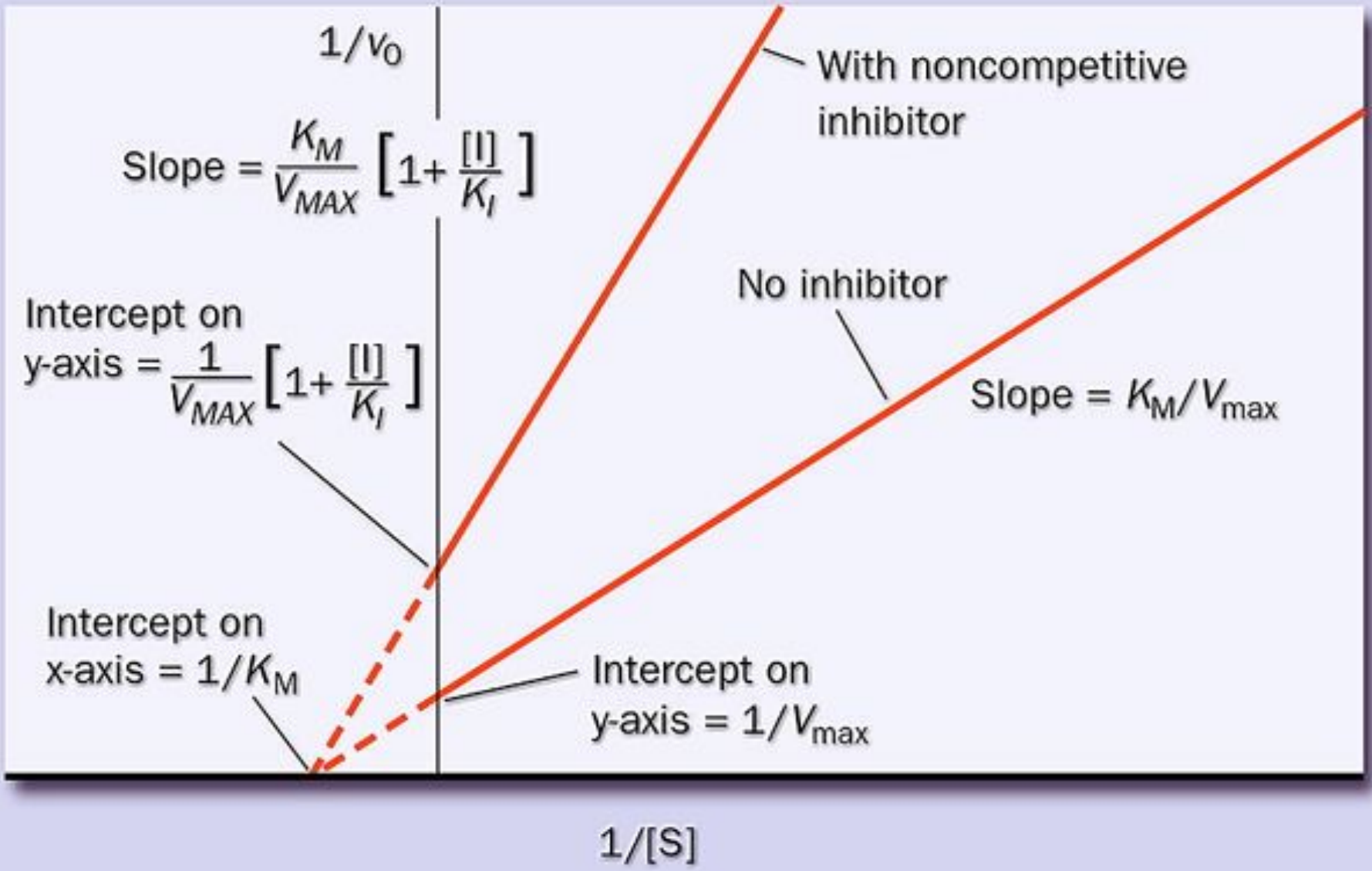
Competitive Inhibition



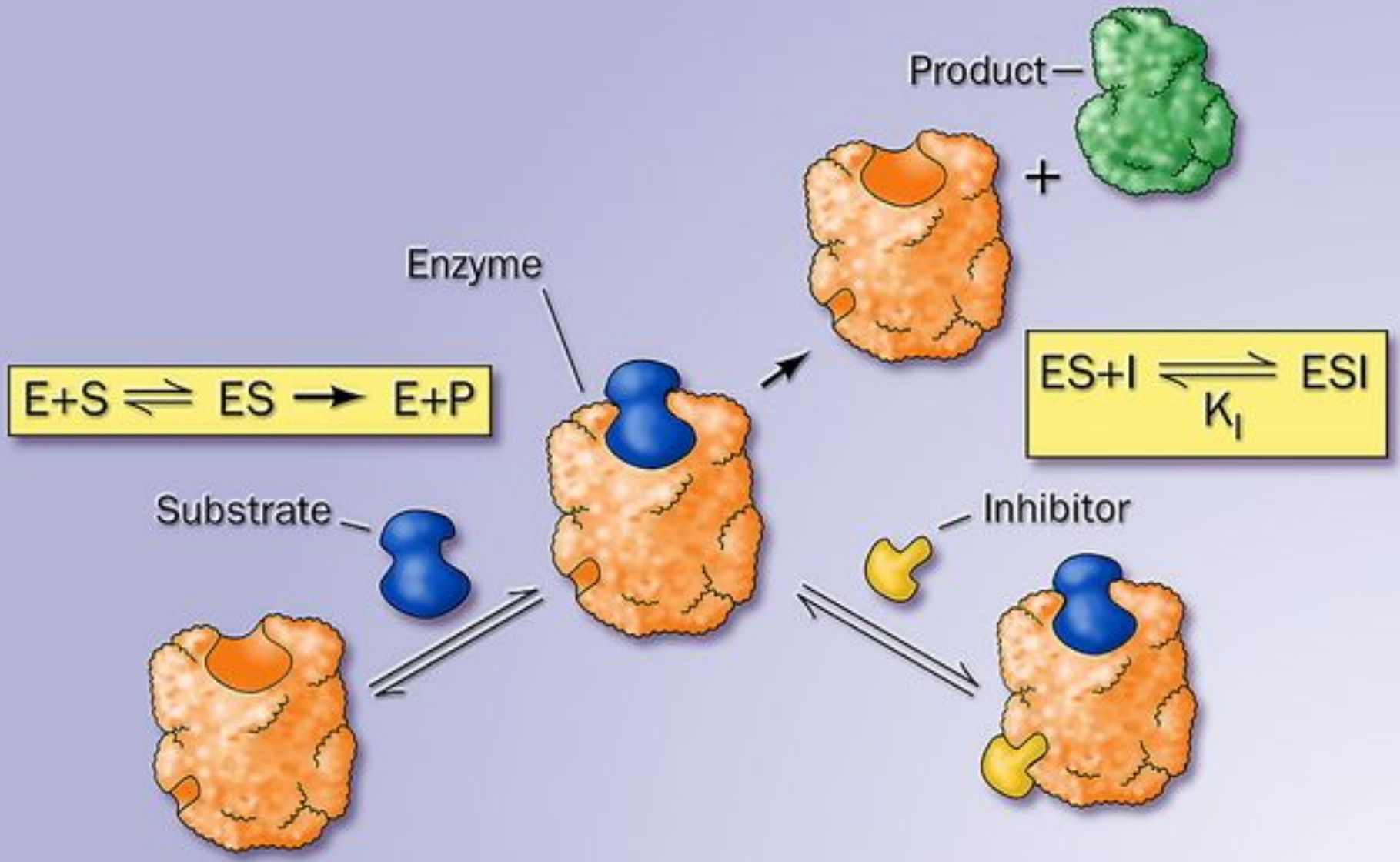

1/v_0
With competitive inhibitor
Slope = $\frac{K_M}{V_{MAX}}\left[1+\frac{[I]}{K_I}\right]$
Slope = K_M/V_{Max}
No inhibitor
Intercepts on x-axis
Intercept on y-axis = $1/V_{Max}$
$-1/K_M$
$-\frac{1}{K_M}\left[1+\frac{[I]}{K_I}\right]$
1/[S]

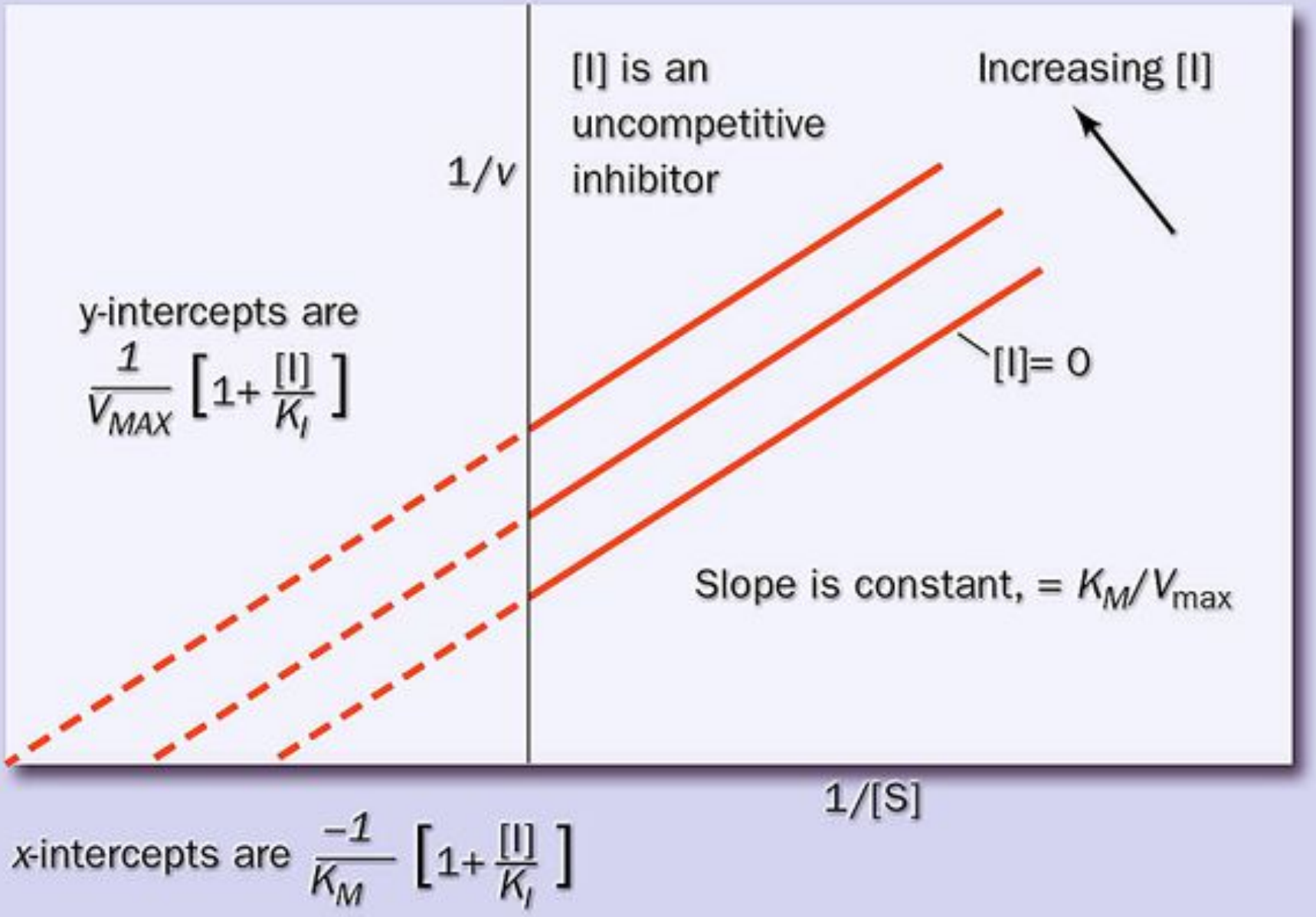
Noncompetitive Inhibition

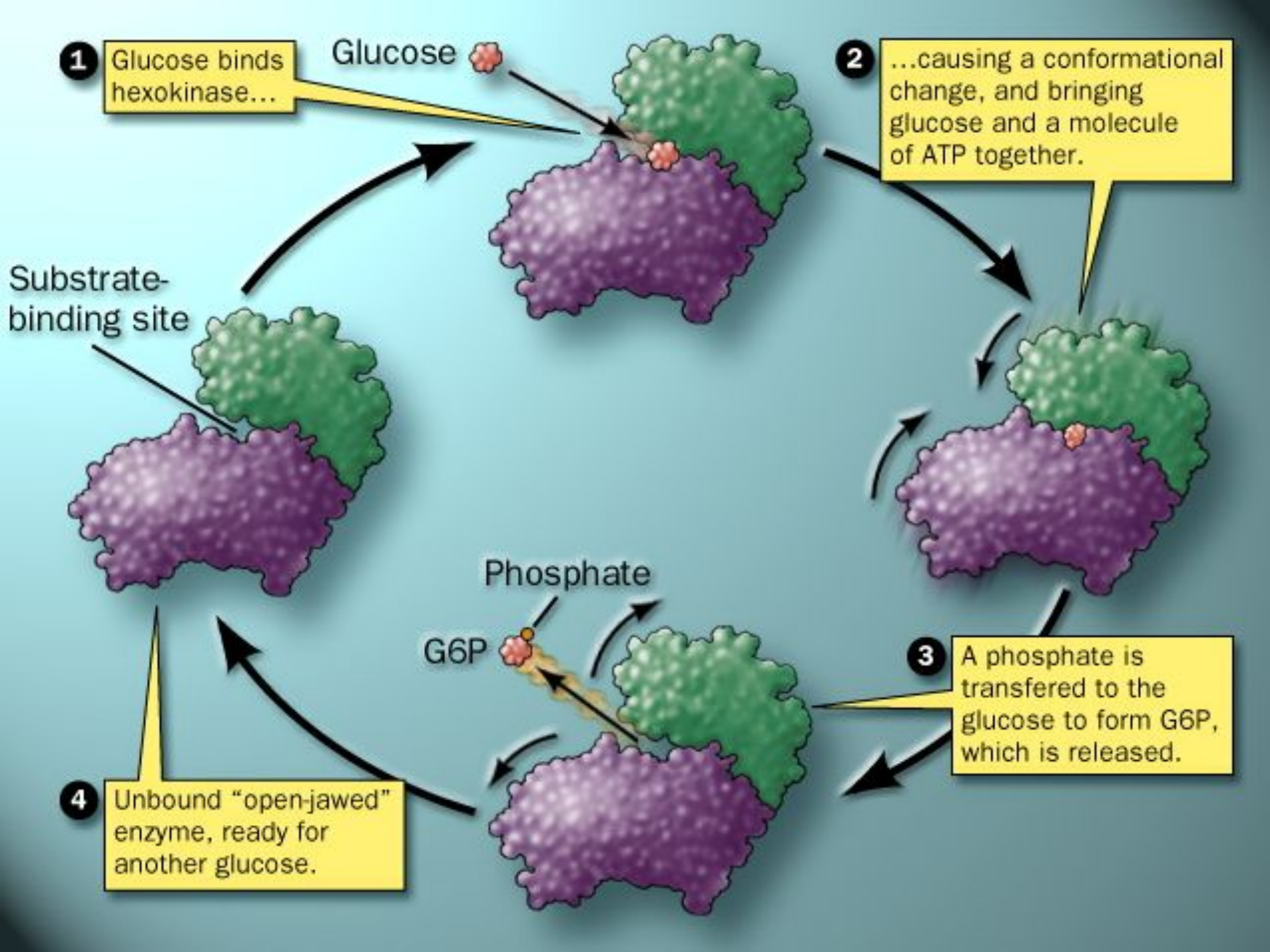


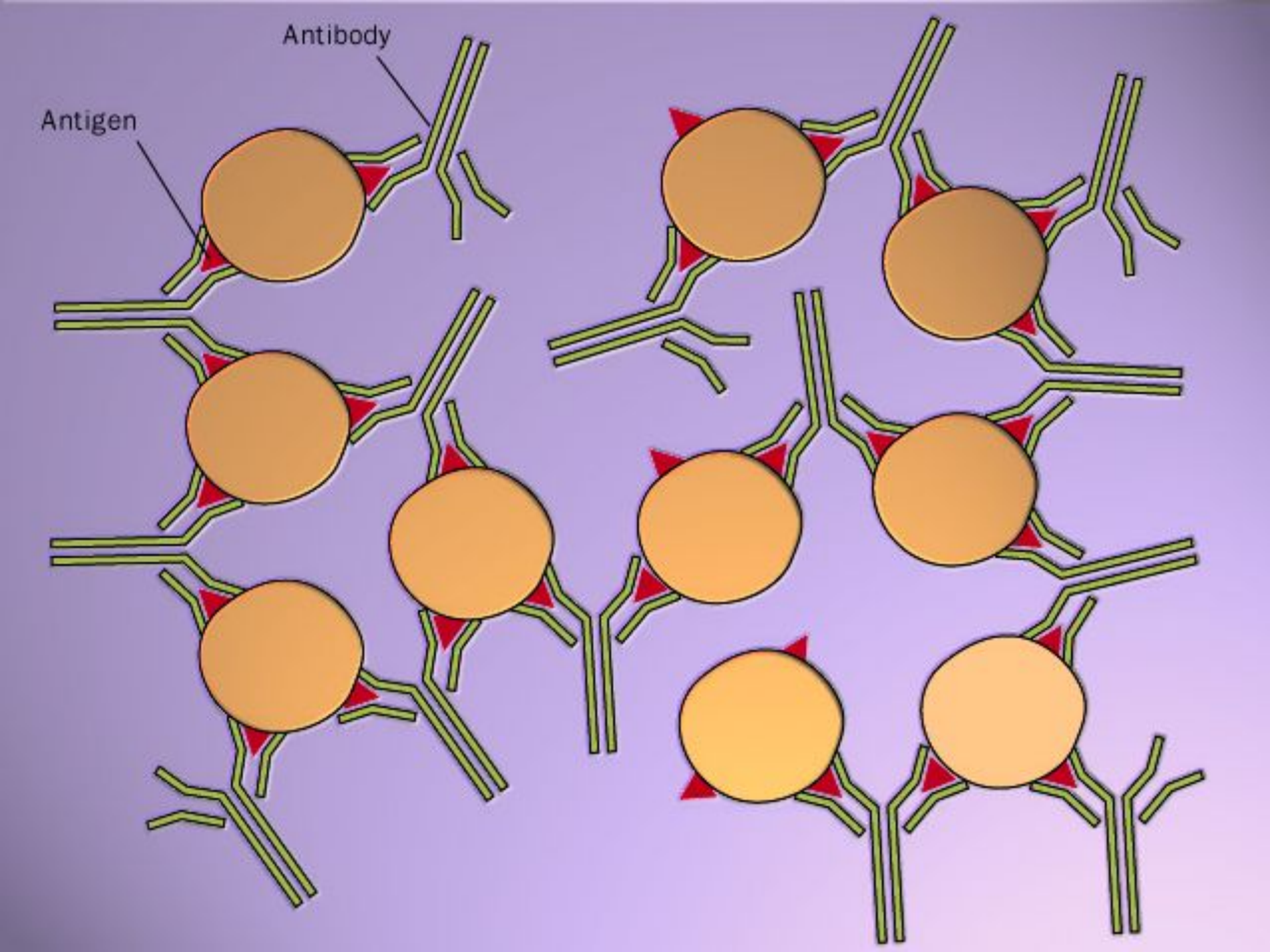

1/v0
With noncompetitive inhibitor
Slope = KM/VMAX [1+ [I]/KI]
No inhibitor
Intercept on y-axis = 1/VMAX [1+ [I]/KI]
Slope = KM/Vmax
Intercept on x-axis = 1/KM
Intercept on y-axis = 1/Vmax
1/[S]

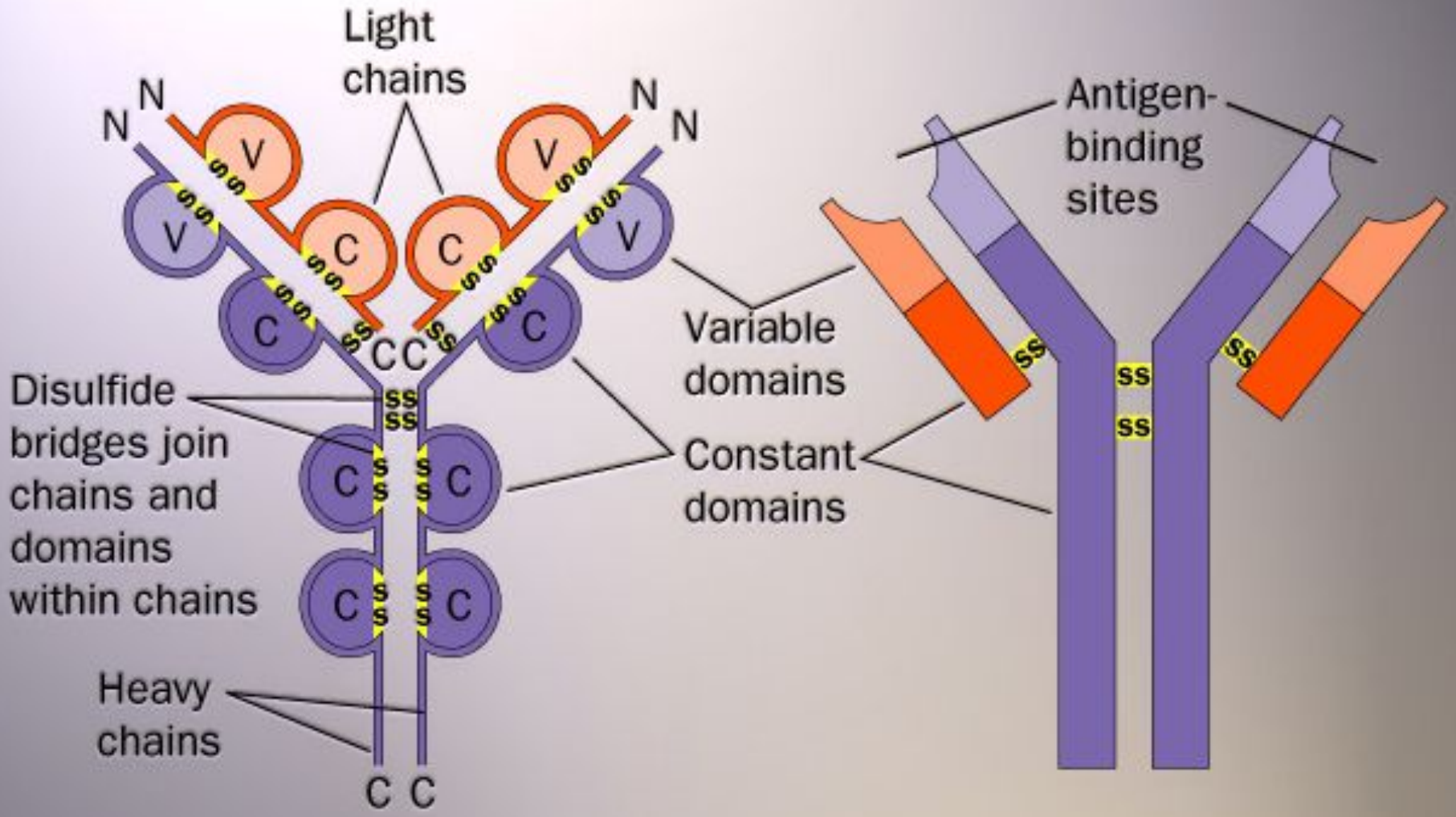
Uncompetitive Inhibition




[I] is an uncompetitive inhibitor
Increasing [I]
1/v
y-intercepts are $\frac{1}{V_{MAX}}\left[1+\frac{[I]}{K_I}\right]$
[I]= 0
Slope is constant, = K_M/V_{max}
1/[S]
x-intercepts are $\frac{-1}{K_M}\left[1+\frac{[I]}{K_I}\right]$


1
Glucose binds hexokinase…
Glucose
2
…causing a conformational change, and bringing glucose and a molecule of ATP together.
Substrate-binding site
Phosphate
G6P
3
A phosphate is transfered to the glucose to form G6P, which is released.
4
Unbound “open-jawed” enzyme, ready for another glucose.


Antibody
Antigen

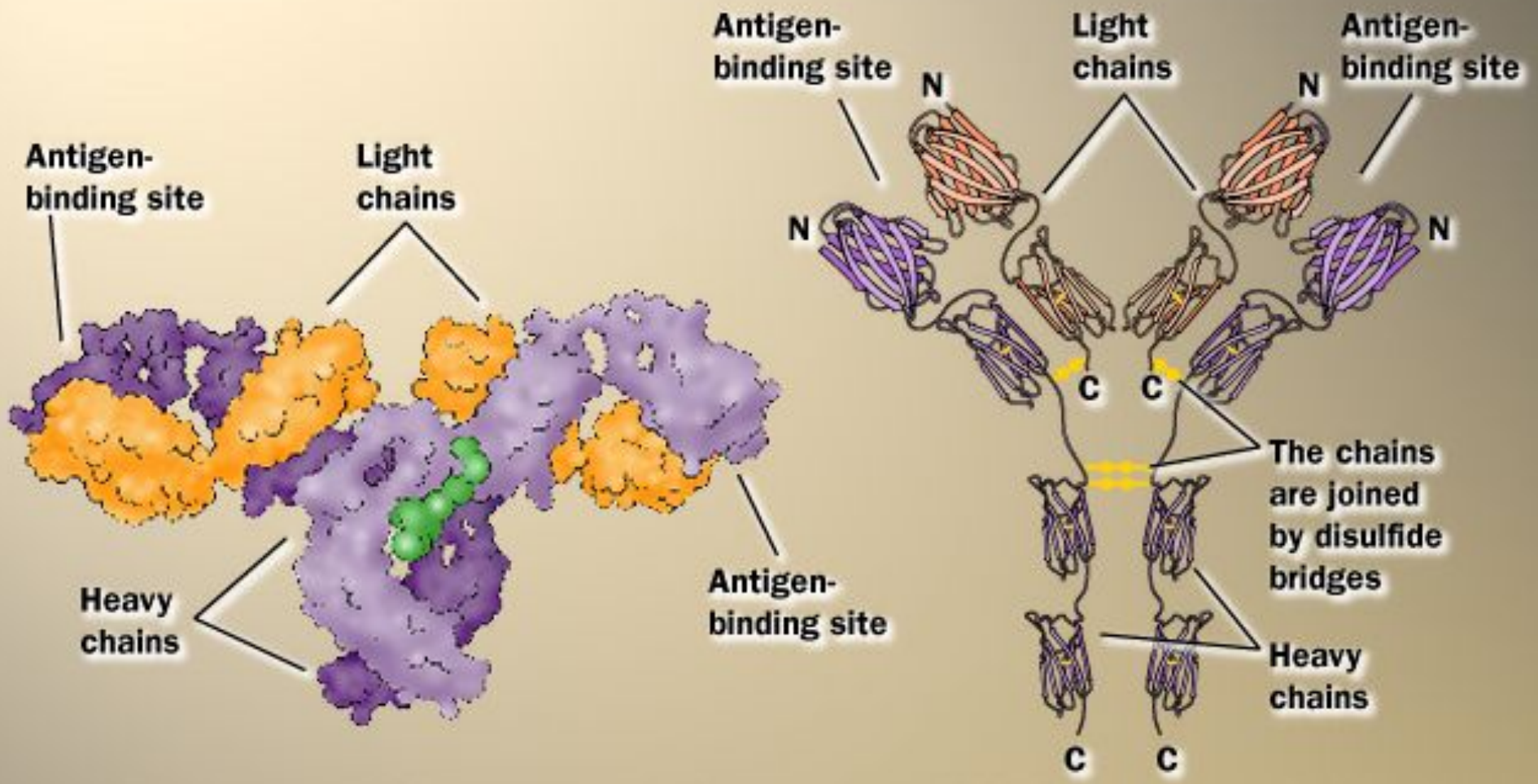


Domain model

Showing globular constant (C) and variable (V) domains

"Y" model

Emphasizes the antigen-binding site

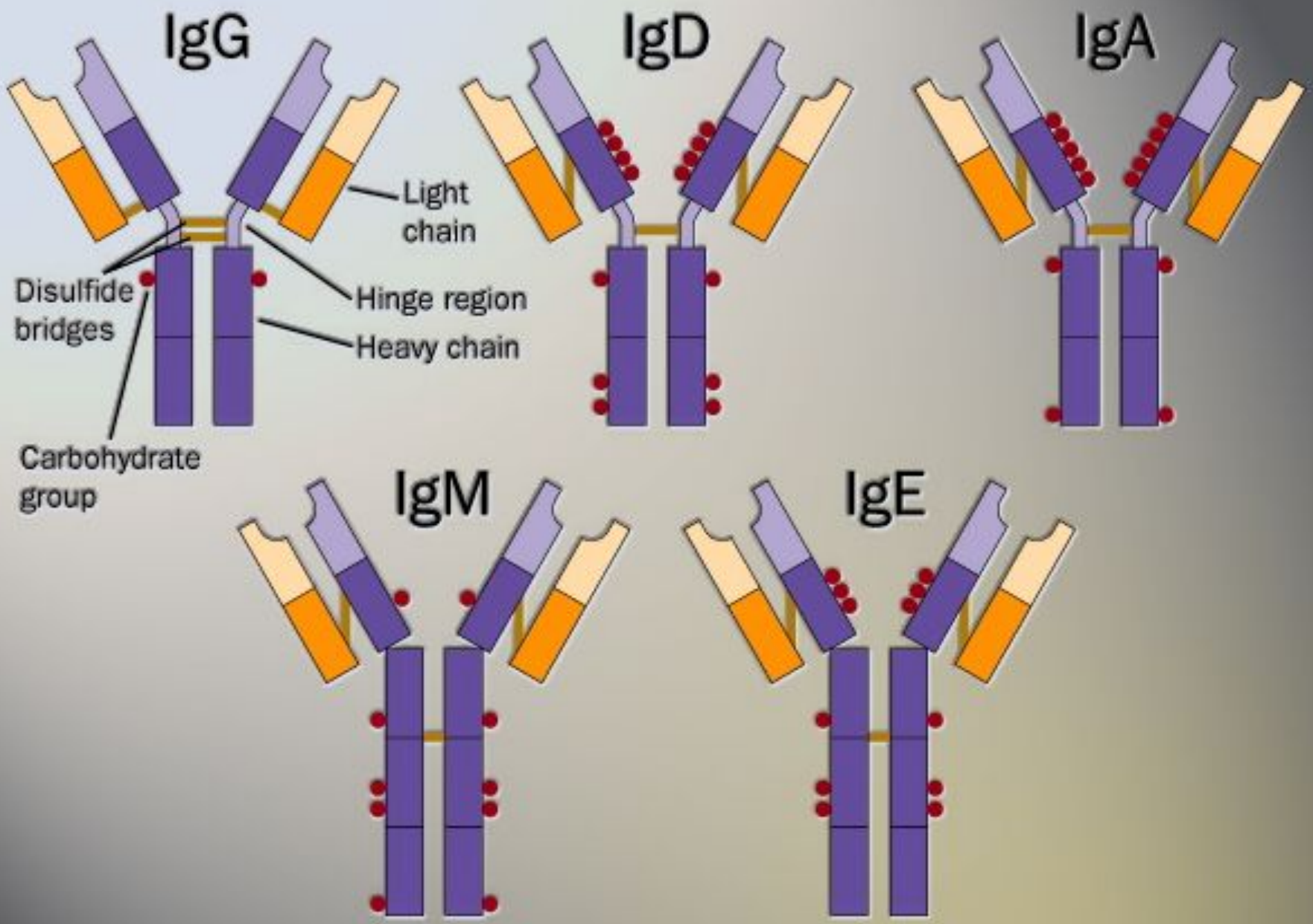


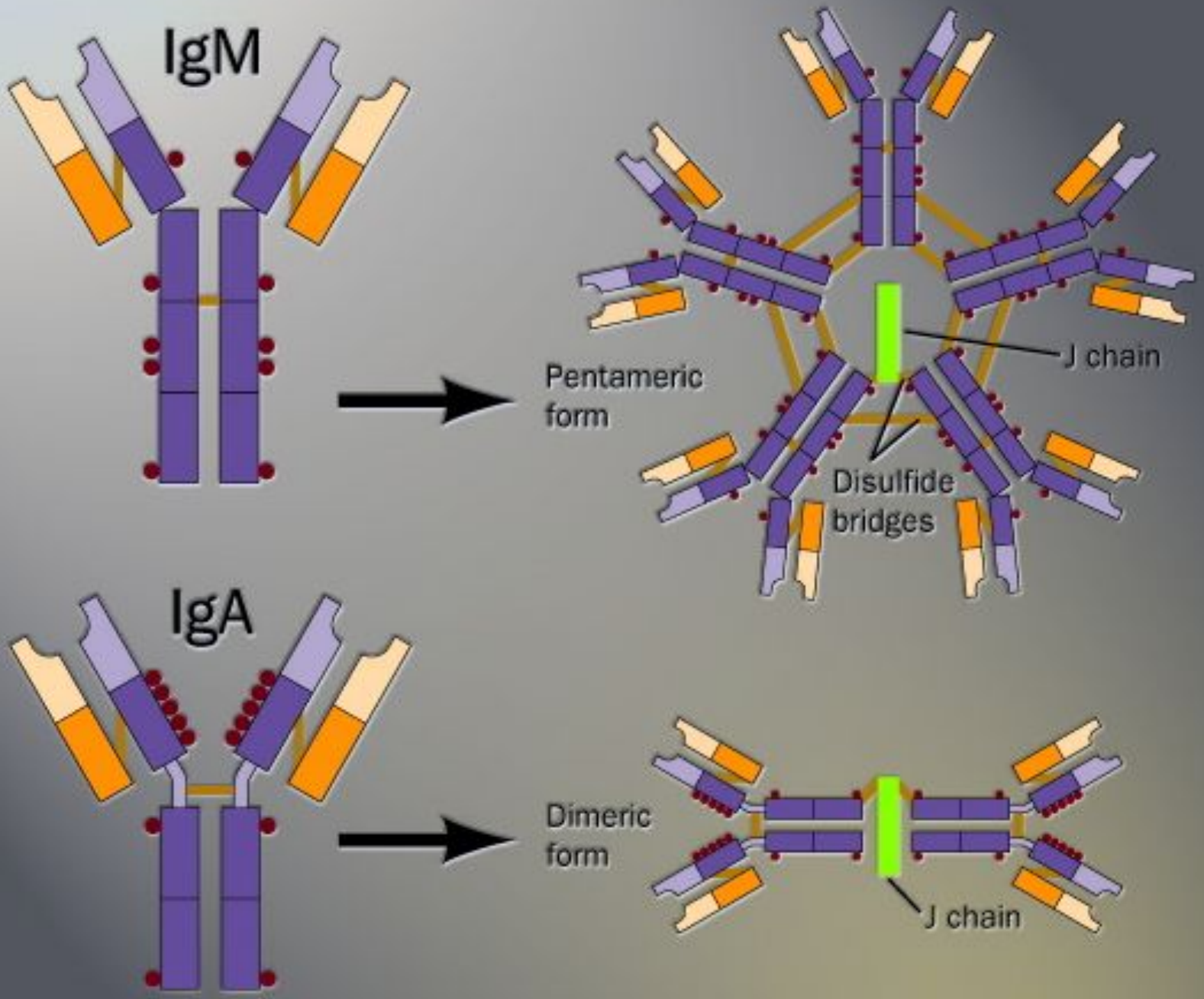
Space-filling model

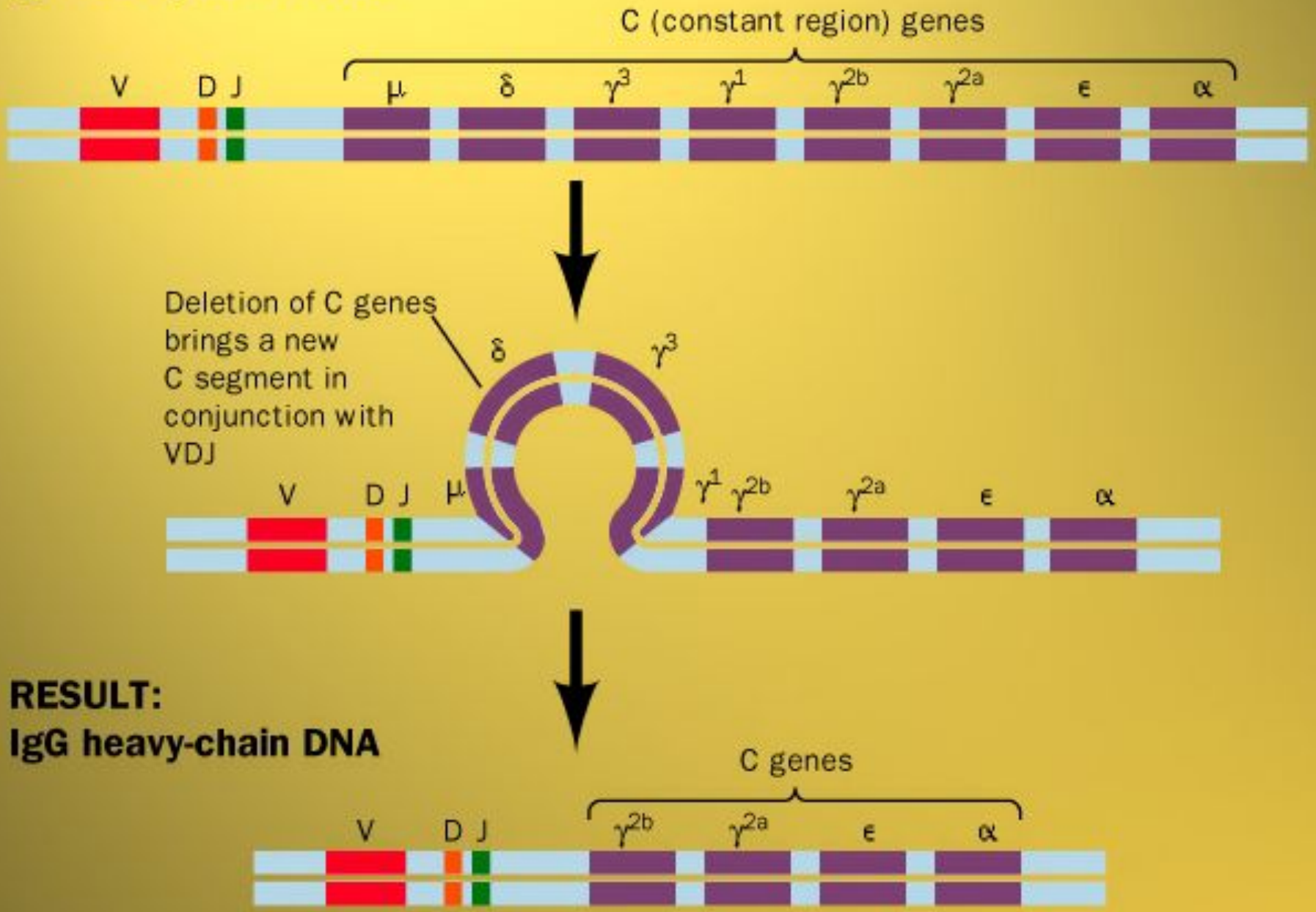
The heavy chain and light chains twist around each other

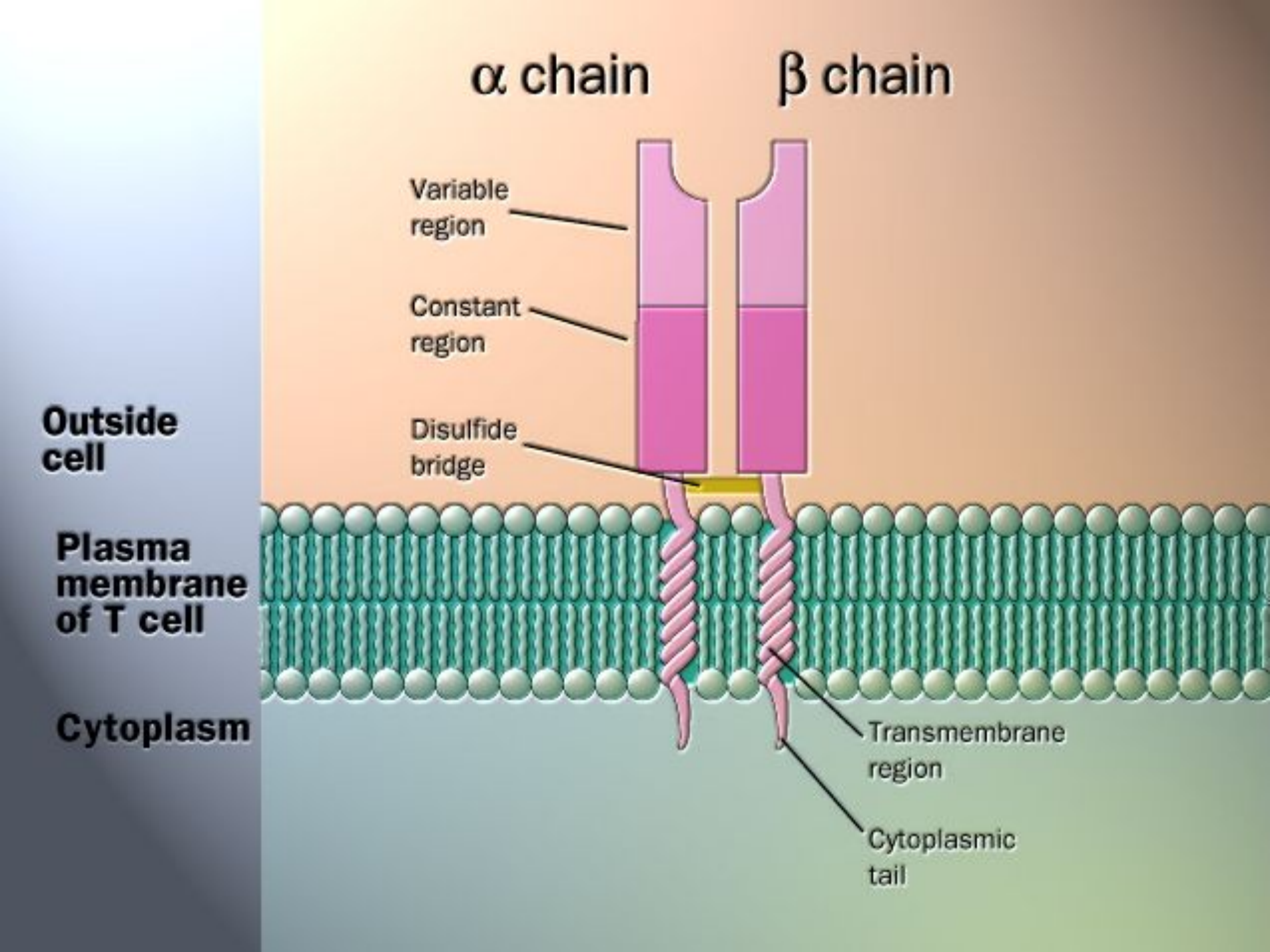
Ribbon model

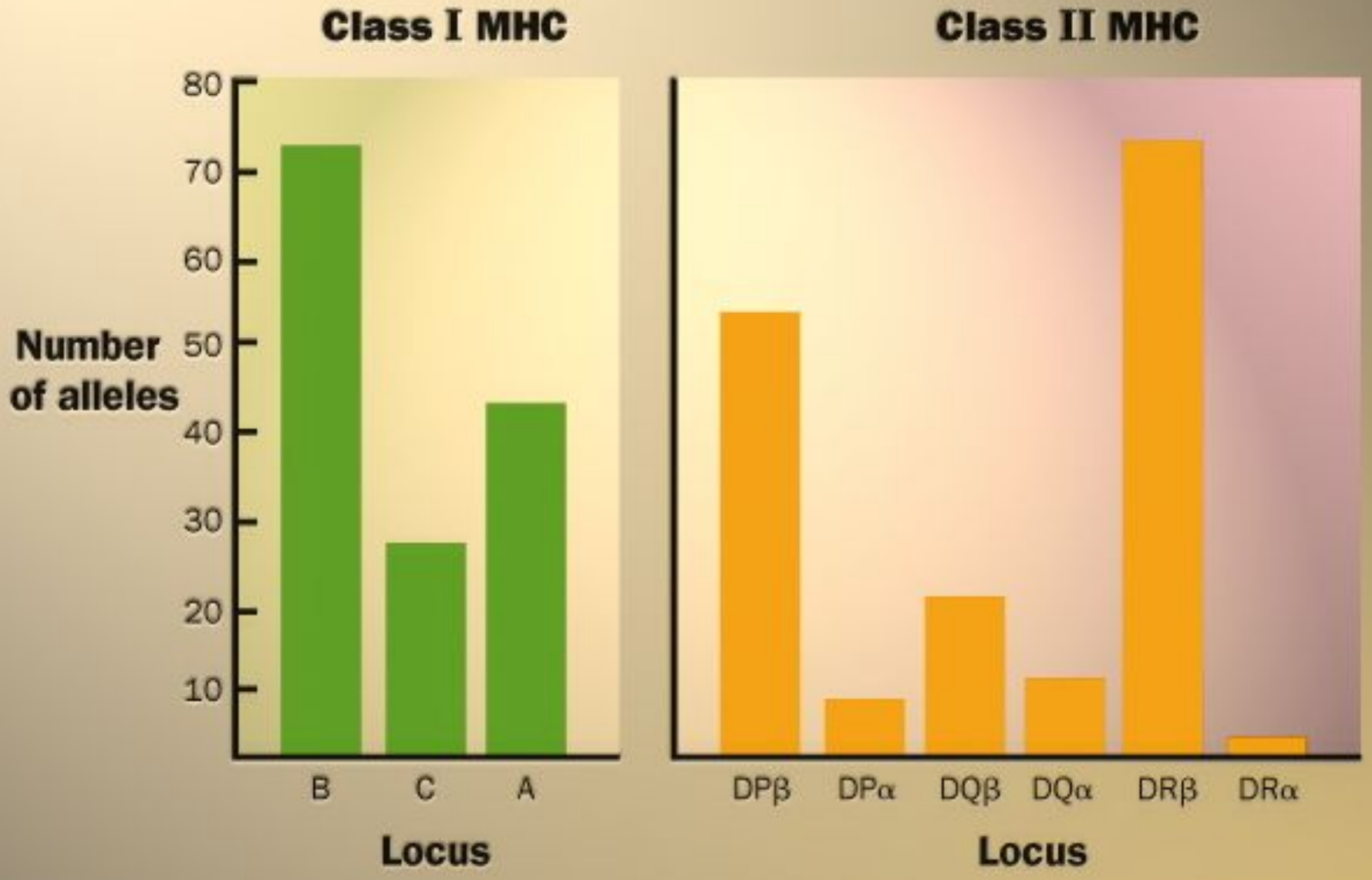
This model shows domains of β-sheets arranged like barrels ("β-barrels")

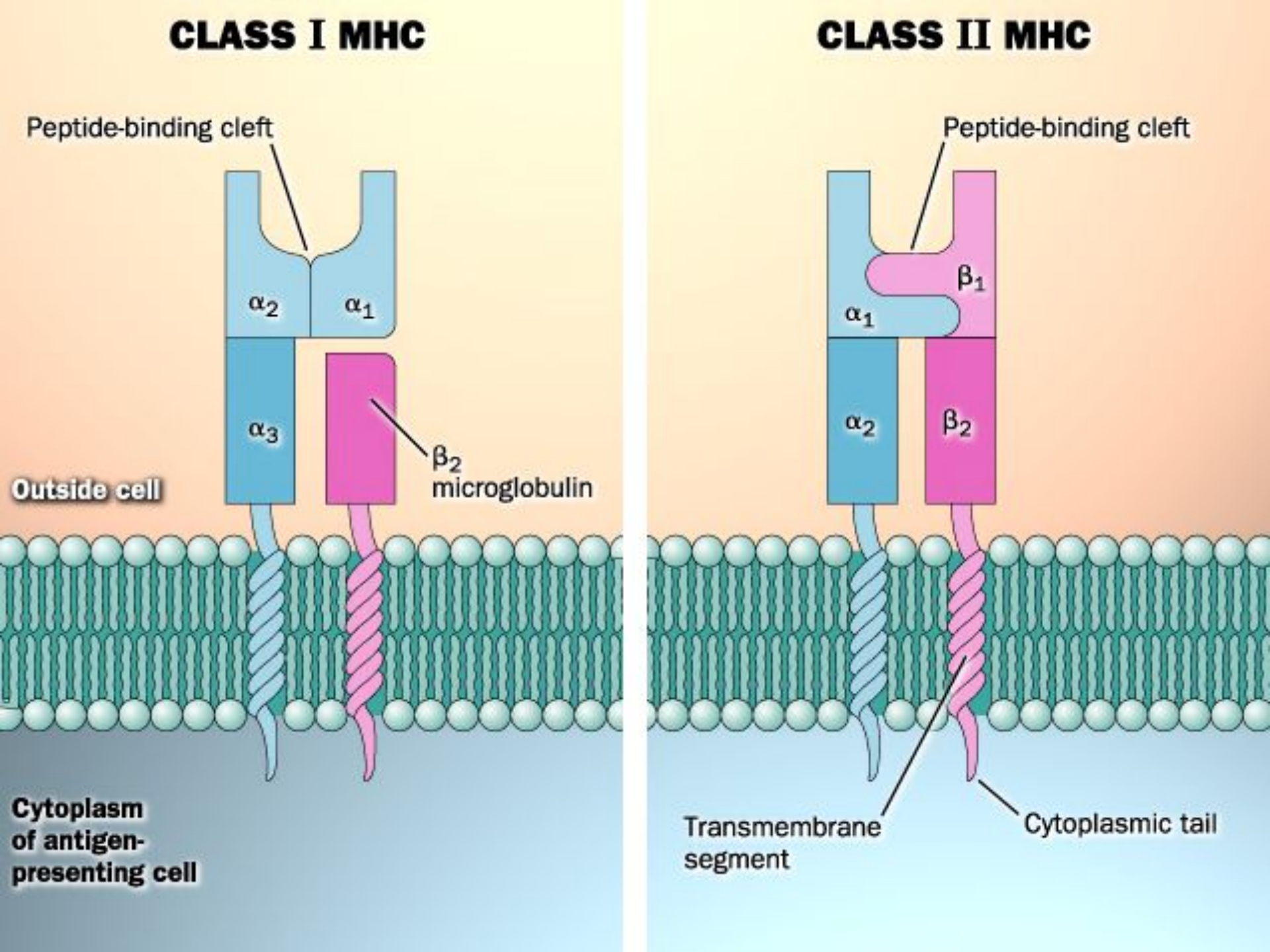

IgG
Light chain
Disulfide bridges
Hinge region
Heavy chain
Carbohydrate group
IgD
IgA
IgM
IgE

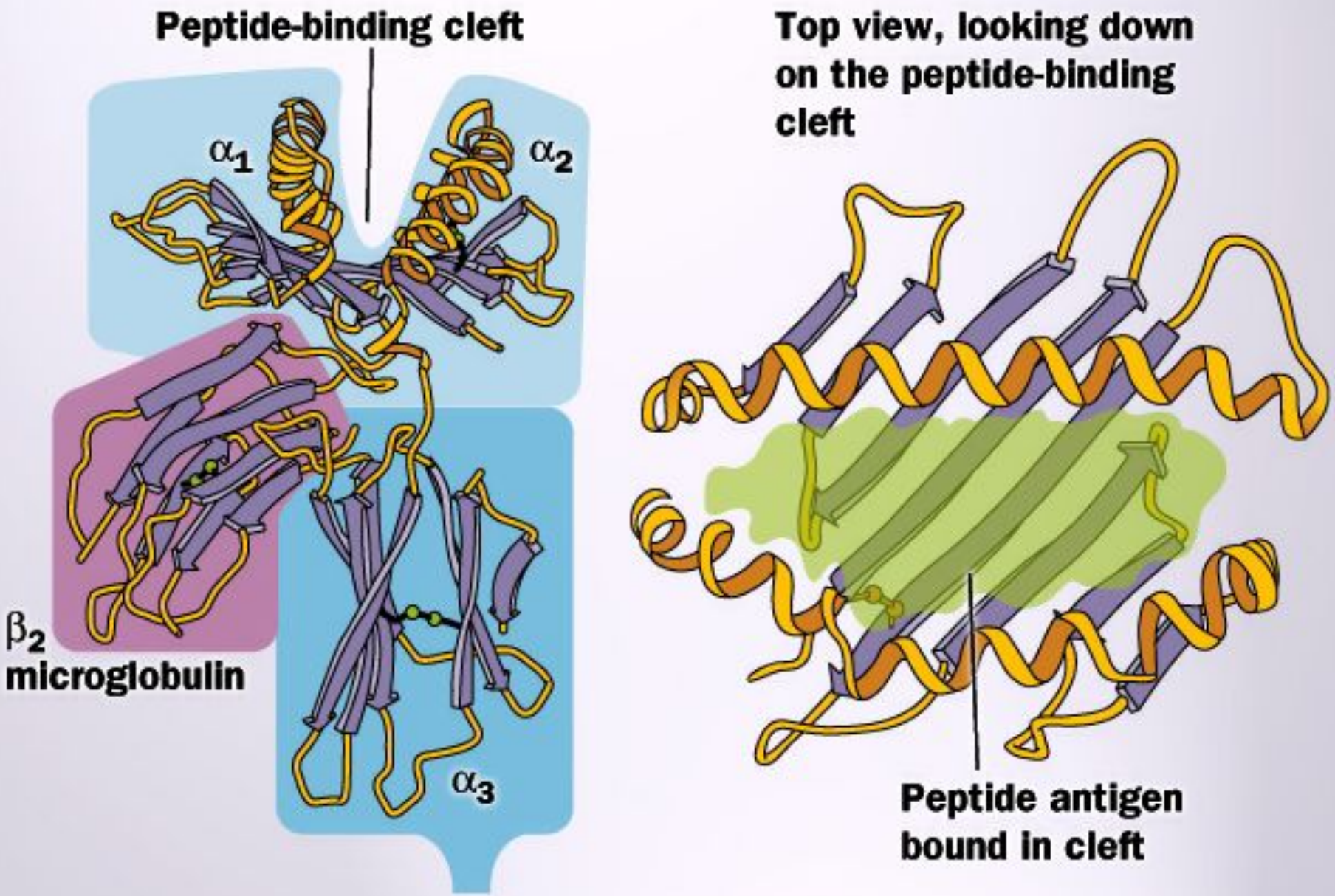

IgM
Pentameric form
J chain
Disulfide bridges
IgA
Dimeric form
J chain


IgM heavy-chain DNA
C (constant region) genes
V
D J
μ
δ
γ3
γ1
γ2b
γ2a
ε
α
Deletion of C genes brings a new C segment in conjunction with VDJ
δ
γ3
V
D J
μ
γ1
γ2b
γ2a
ε
α
RESULT:
IgG heavy-chain DNA
C genes
V
D J
γ2b
γ2a
ε
α

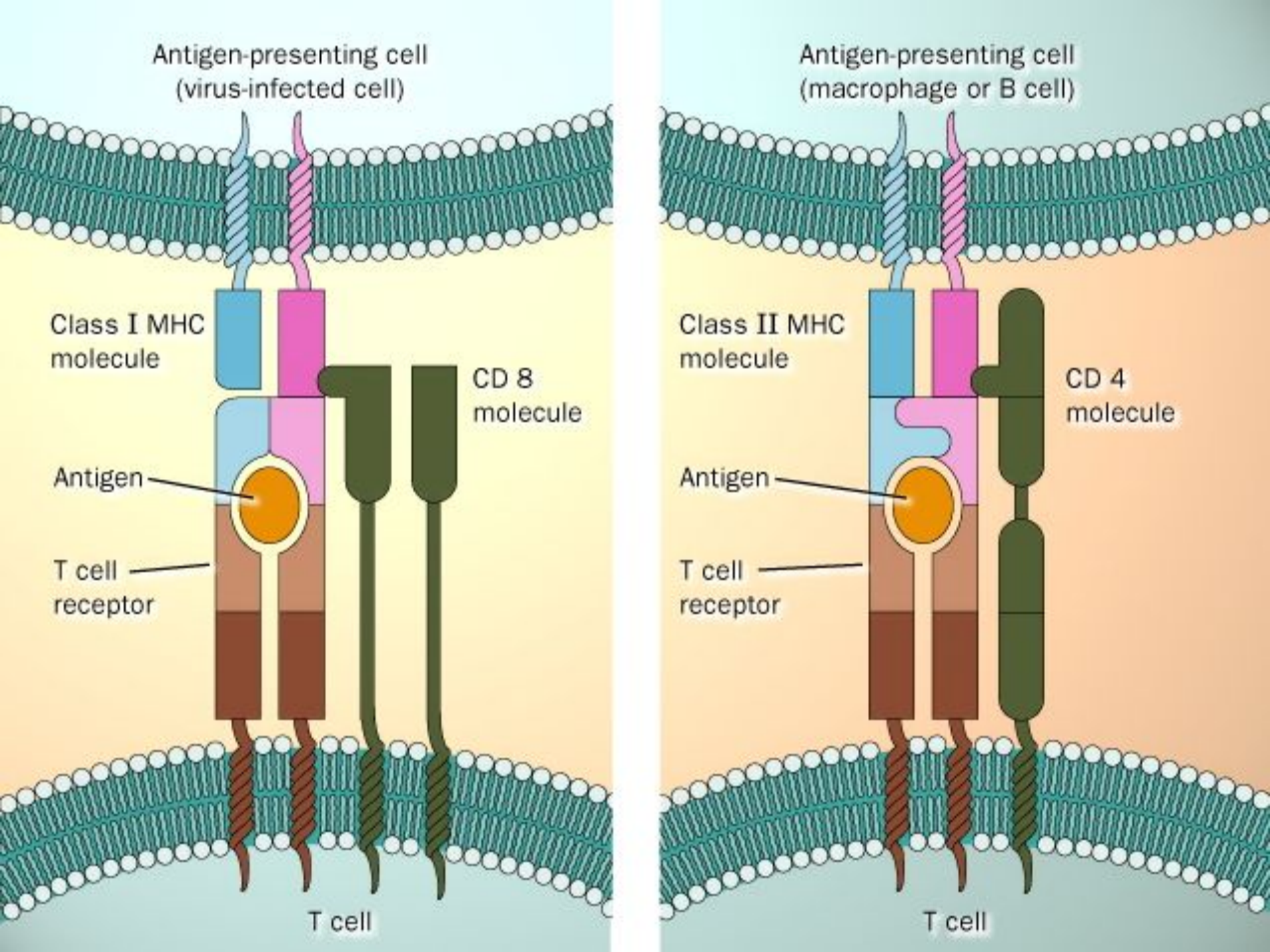

α chain
β chain
Variable region
Constant region
Disulfide bridge
Outside cell
Plasma membrane of T cell
Cytoplasm
Transmembrane region
Cytoplasmic tail

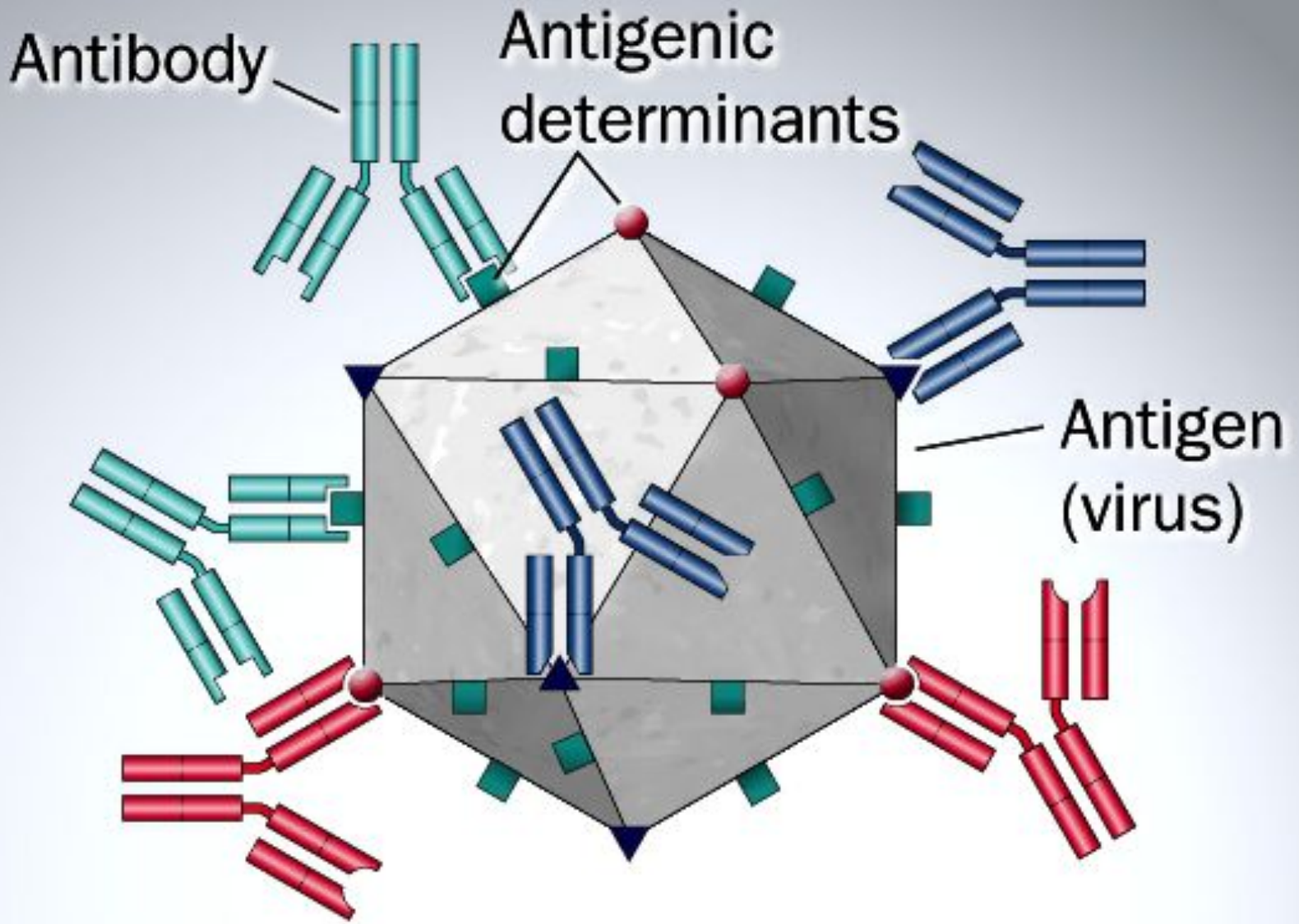

Class I MHC
Class II MHC
Number of alleles
80
70
60
50
40
30
20
10
B
C
A
Locus
DPβ
DPα
DQβ
DQα
DRβ
DRα
Locus


CLASS I MHC
Peptide-binding cleft
α2
α1
α3
β2 microglobulin
Outside cell
Cytoplasm of antigen-presenting cell
CLASS II MHC
Peptide-binding cleft
β1
α1
α2
β2
Transmembrane segment
Cytoplasmic tail

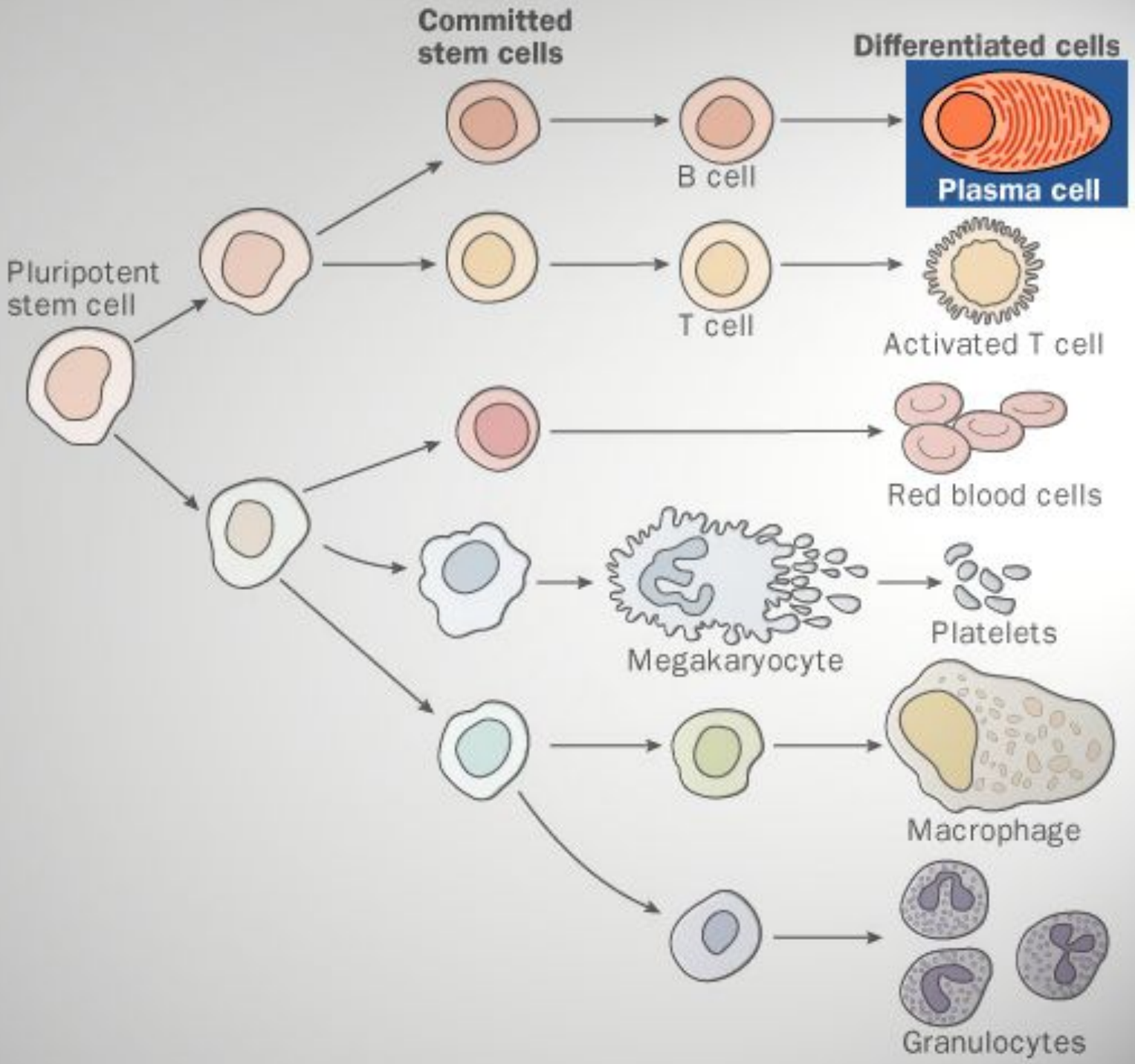

Peptide-binding cleft
α_1
α_2
β_2 microglobulin
α_3
Top view, looking down on the peptide-binding cleft
Peptide antigen bound in cleft

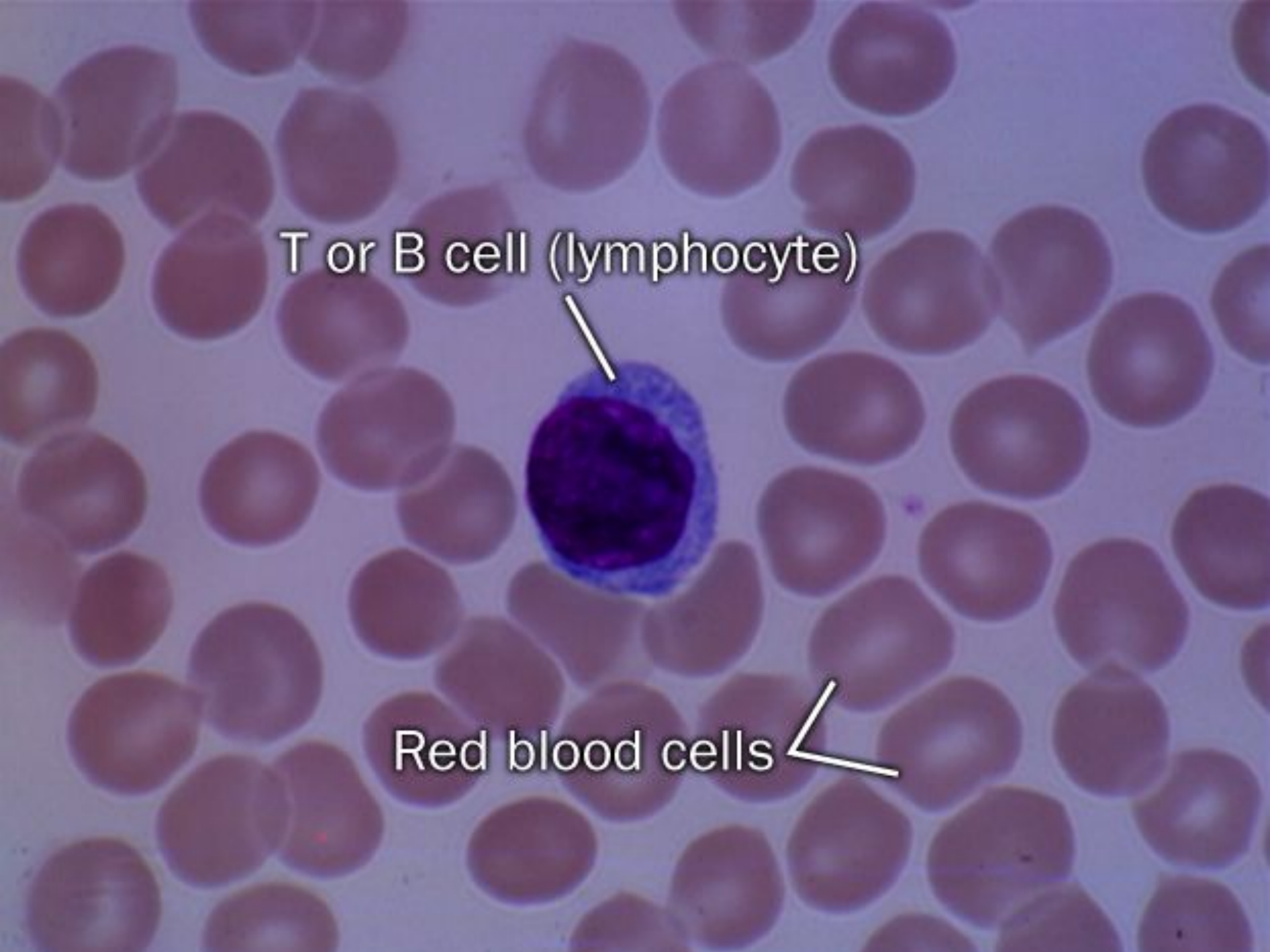
Class I MHC

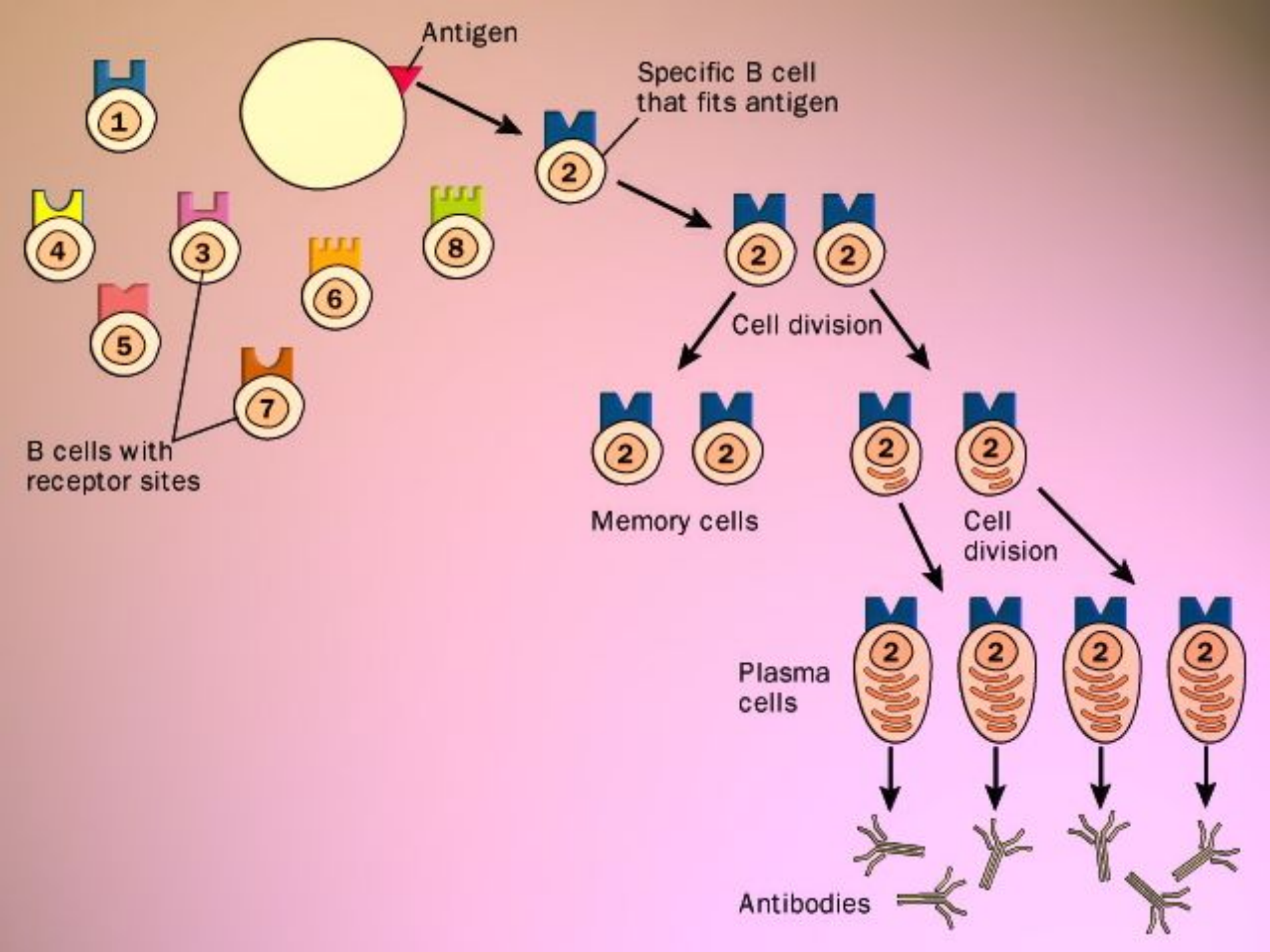

Antigen-presenting cell
(virus-infected cell)
Class I MHC
molecule
CD 8
molecule
Antigen
T cell
receptor
T cell
Antigen-presenting cell
(macrophage or B cell)
Class II MHC
molecule
CD 4
molecule
Antigen
T cell
receptor
T cell

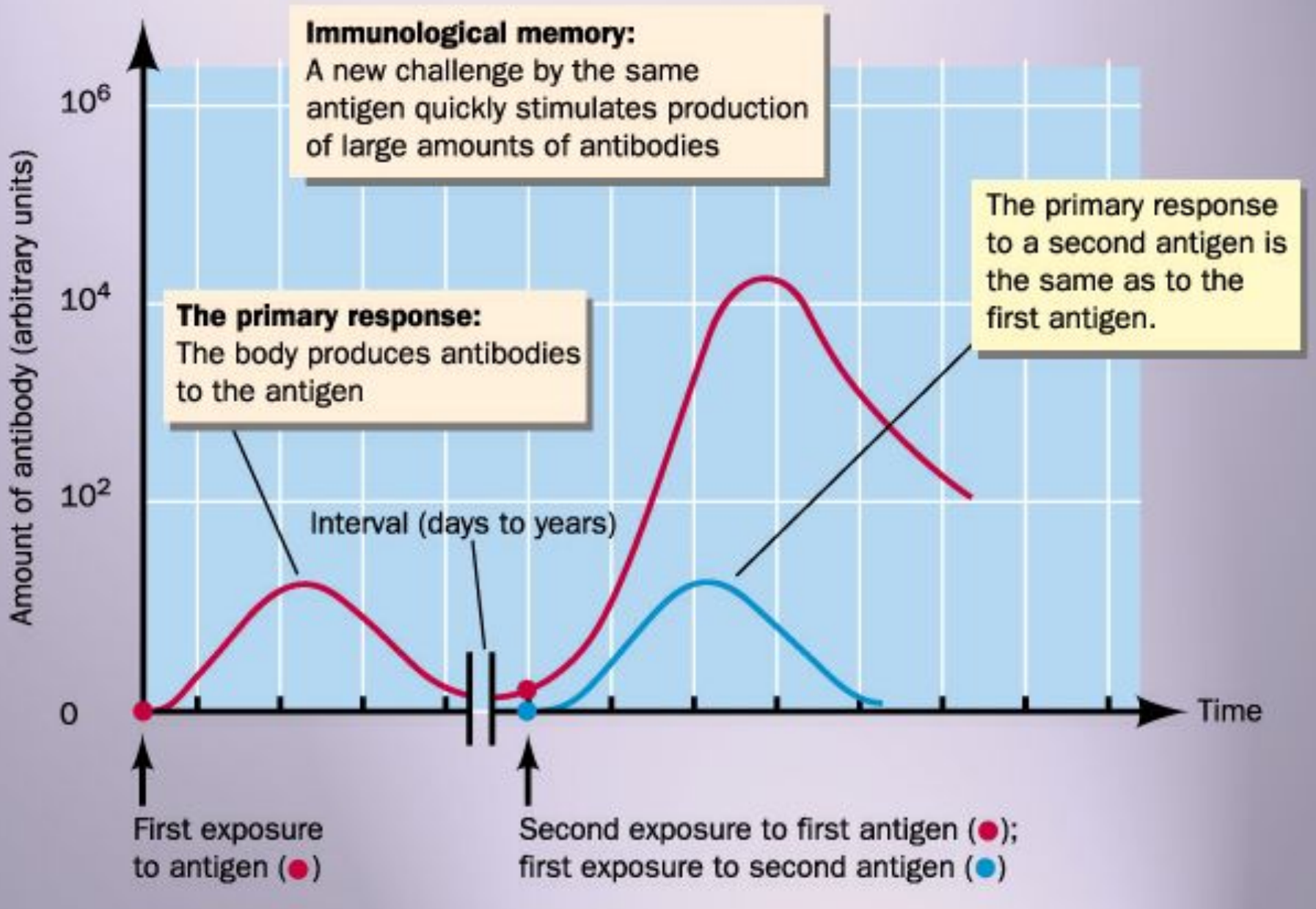


An antigen may have more than one determinant, each binding a specific antibody molecule


Committed stem cells
Differentiated cells
B cell
Plasma cell
Pluripotent stem cell
T cell
Activated T cell
Red blood cells
Megakaryocyte
Platelets
Macrophage
Granulocytes


T or B cell (lymphocyte)
Red blood cells


Antigen
Specific B cell
that fits antigen
1
2
3
4
5
6
7
8
B cells with
receptor sites
Cell division
Memory cells
Cell
division
Plasma
cells
Antibodies


Immunological memory:
A new challenge by the same antigen quickly stimulates production of large amounts of antibodies
The primary response:
The body produces antibodies to the antigen
The primary response to a second antigen is the same as to the first antigen.
Amount of antibody (arbitrary units)
10^6
10^4
10^2
0
Interval (days to years)
Time
First exposure to antigen (●)
Second exposure to first antigen (●); first exposure to second antigen (●)