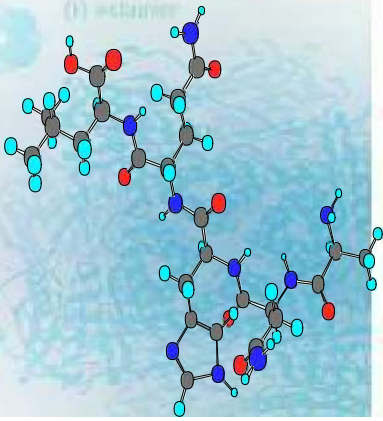
Protein

第5章
蛋白质结构与功能的关系及进化



一、蛋白质分子结构与功能的关系

蛋白质一级结构是空间结构和生物功能的基础，一级结构决定空间结构，但一级结构并非是决定空间结构唯一因素，空间结构是生物活性的直接体现者.

1、蛋白质一级结构与功能的关系

（一）、一级结构与生物进化

（二）、一级结构与分子病

2、蛋白质高级结构与功能的关系

1、蛋白质一级结构与功能的关系

（一） 同源蛋白质一级结构的种属差异与生物进化

同源蛋白质：是指在不同生物体中行使相同或相似功能的蛋白质。

同源蛋白质的特点：

① 同源蛋白质的氨基酸序列具有明显的相似性（序列同源性）

② **同源蛋白中的一级结构中有许多位置的氨基酸对所有种属来说都是相同的，称为不变残基，不变残基高度保守，是必需的。**

除不变残基以外，其它位置的氨基酸对不同的种属有很大变化，称可变残基，可变残基中，个别氨基酸的变化不影响蛋白质的功能，可用于判断生物体间亲缘关系的远近。

③多肽链长度相同或相近

如：血红蛋白在不同的脊椎动物中都具有输送氧气的功能，细胞色素C在所有的生物中都是电子传递链的组分。

通过比较同源蛋白质的氨基酸序列的差异可以研究不同物种间的亲源关系和进化。

亲源关系越远，同源蛋白的氨基酸顺序差异就越大。

（1）胰岛素

- 来自不同动物的胰岛素绝大多数由51个氨基酸组成，其排列顺序大体相同，但也有细微差异。
- 有22个氨基酸残基位置始终不变：A．B链上6个Cys 不变，其余相同的氨基酸多数为非极性侧链，对稳定蛋白质的空间结构起重要作用。
- 其它可变氨基酸对稳定蛋白质的空间结构作用不大，但对免疫反应起作用。
- 猪与人接近，而狗则与人不同，因此可用猪的胰岛素治疗人的糖尿病。

（2） 细胞色素C

分子量：13000左右

氨基酸残基：104个左右，单链。

- 其中有35个氨基酸残基是不变的（特别是14、17位的Cys, 18位的His和80位的Met、48位的Tyr和59位的Trp都是不变的位置，对保证细胞色素 C 的功能起关键作用）。
- 可变残基可能随着进化而变异，而且不同种属的细胞色素 C氨基酸差异数与种属之间的亲缘关系相关。亲缘关系相近者，氨基酸差异少，反之则多（进化树）

人与黑猩猩　　0

人与猴　　1

人与狗　　11

人与酵母　　44

（二）、一级结构与分子病

分子病是指蛋白质分子一级结构的氨基酸排列顺序与正常有所不同的遗传病。是由于遗传基因突变导致蛋白质分子中氨基酸残基被更换所造成的。

例**1** 镰刀型贫血病

●患者血红细胞合成了一种不正常的血红蛋白（**Hb-S**）

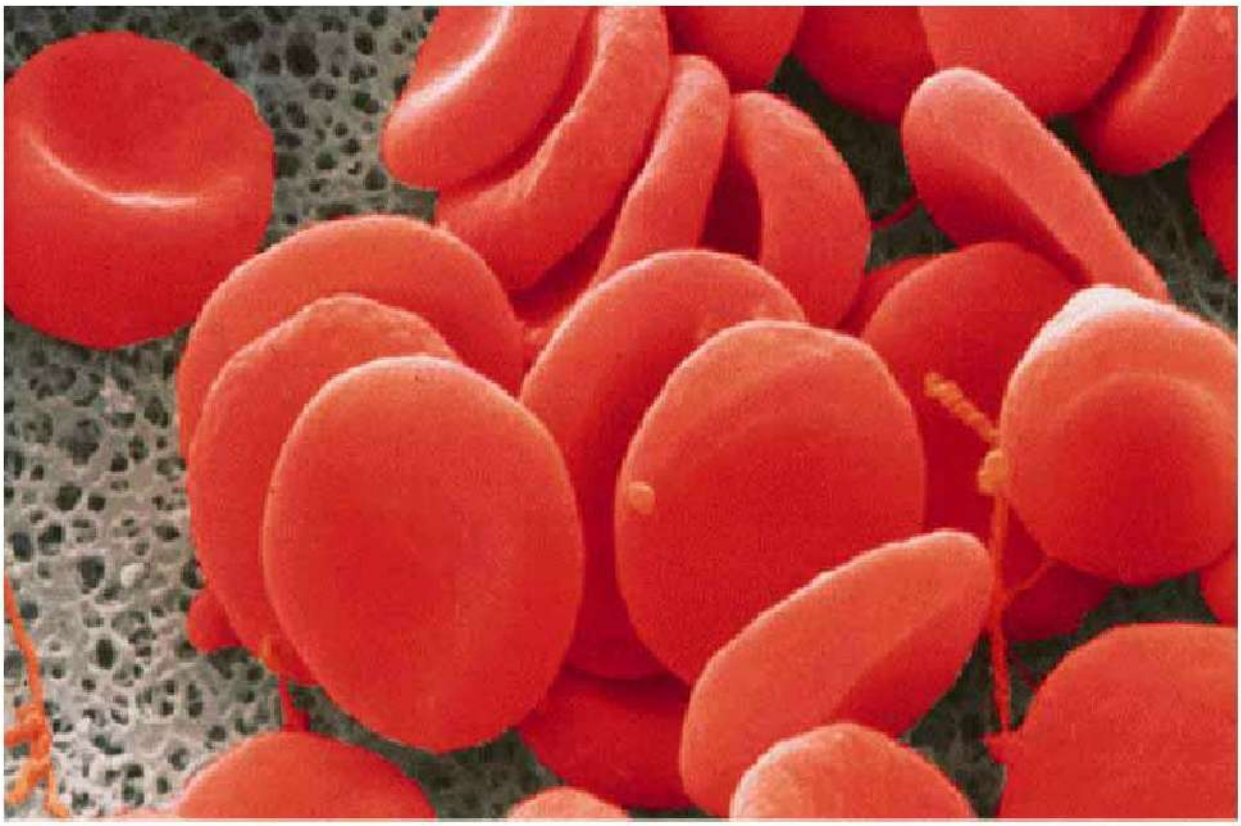
●它与正常的血红蛋白（**Hb-A**）的差别：仅仅在于β链的**N-**末端第**6**位残基发生了变化

●（**Hb-A**）第**6**位残基是极性谷氨酸残基，（**Hb-S**）中换成了非极性的缬氨酸残基

●使血红蛋白细胞收缩成镰刀形，输氧能力下降，易发生溶血

●这说明了蛋白质分子结构与功能关系的高度统一性

(b)


(a)
2 μm

例：镰刀形红细胞贫血

HbA β 肽链

N-val · his · leu · thr · pro · glu · glu · · · · ·C(146)

HbS β 肽链

N-val · his · leu · thr · pro · val · glu · · · · ·C(146)

这种由蛋白质分子发生变异所导致的疾病，称为“分子病”。

2．蛋白质的构象与功能的关系

别构效应：又称变构效应，是指寡聚蛋白与配基结合，改变蛋白质构象，导致蛋白质生物活性改变的现象.它是细胞内最简单的调节方式.

例：血红蛋白的别构效应

- 一个亚基与氧结合后，引起该亚基构象改变
- 进而引起另三个亚基的构象改变
- 整个分子构象改变
- 与氧的结合能力增加

蛋白质构象改变与疾病

蛋白质构象疾病：若蛋白质的折叠发生错误，尽管其一级结构不变，但蛋白质的构象发生改变，仍可影响其功能，严重时可导致疾病发生。

蛋白质构象改变导致疾病的机理：有些蛋白质错误折叠后相互聚集，常形成抗蛋白水解酶的淀粉样纤维沉淀，产生毒性而致病，表现为蛋白质淀粉样纤维沉淀的病理改变。

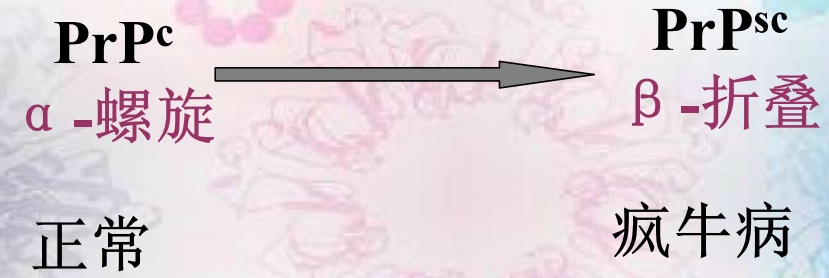
这类疾病包括：老年痴呆症、疯牛病、人纹状体脊髓变性病、亨停顿舞蹈病等。

疯牛病中的蛋白质构象改变

疯牛病是由朊病毒蛋白(prion protein, PrP)引起的一组人和动物神经退行性病变。

正常的**PrP**富含α-螺旋，称为**PrP^{c}**。

PrP^{c}在某种未知蛋白质的作用下可转变成全为β-折叠的**PrP^{sc}**，从而致病。

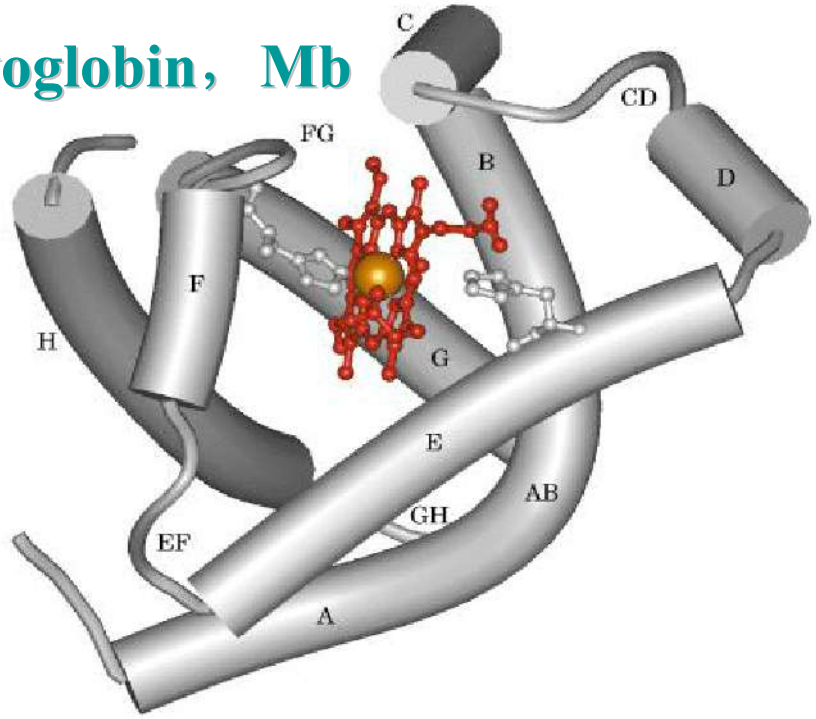


- 结构与功能举例如下：

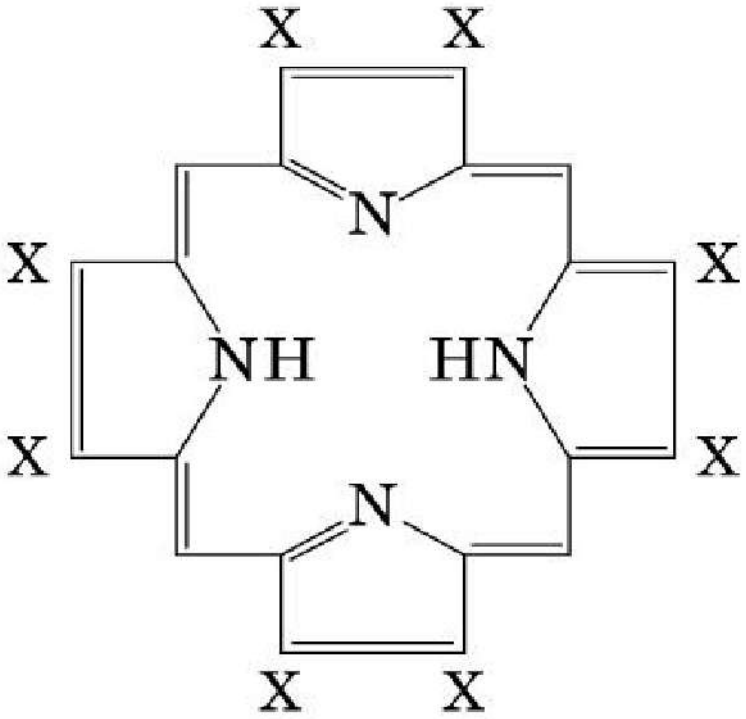
二、肌红蛋白的结构和功能

（一）三级结构

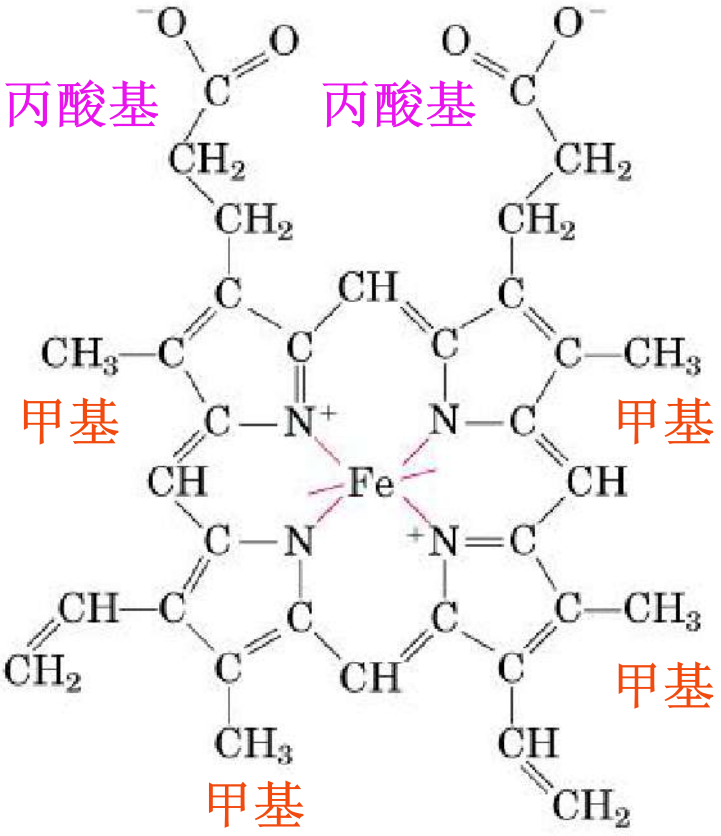
myoglobin，Mb



（二）辅基

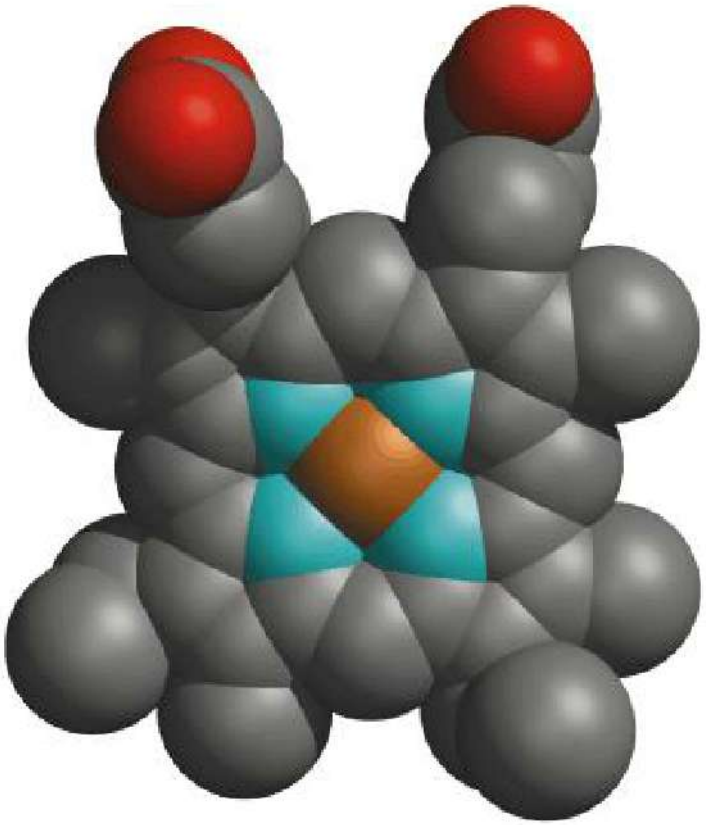


(a)

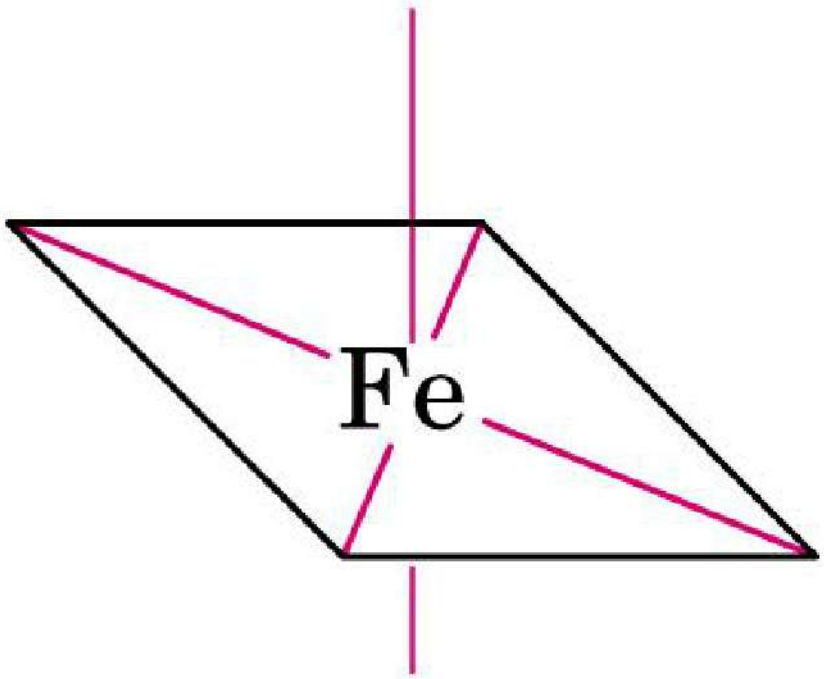


(b)

血红素

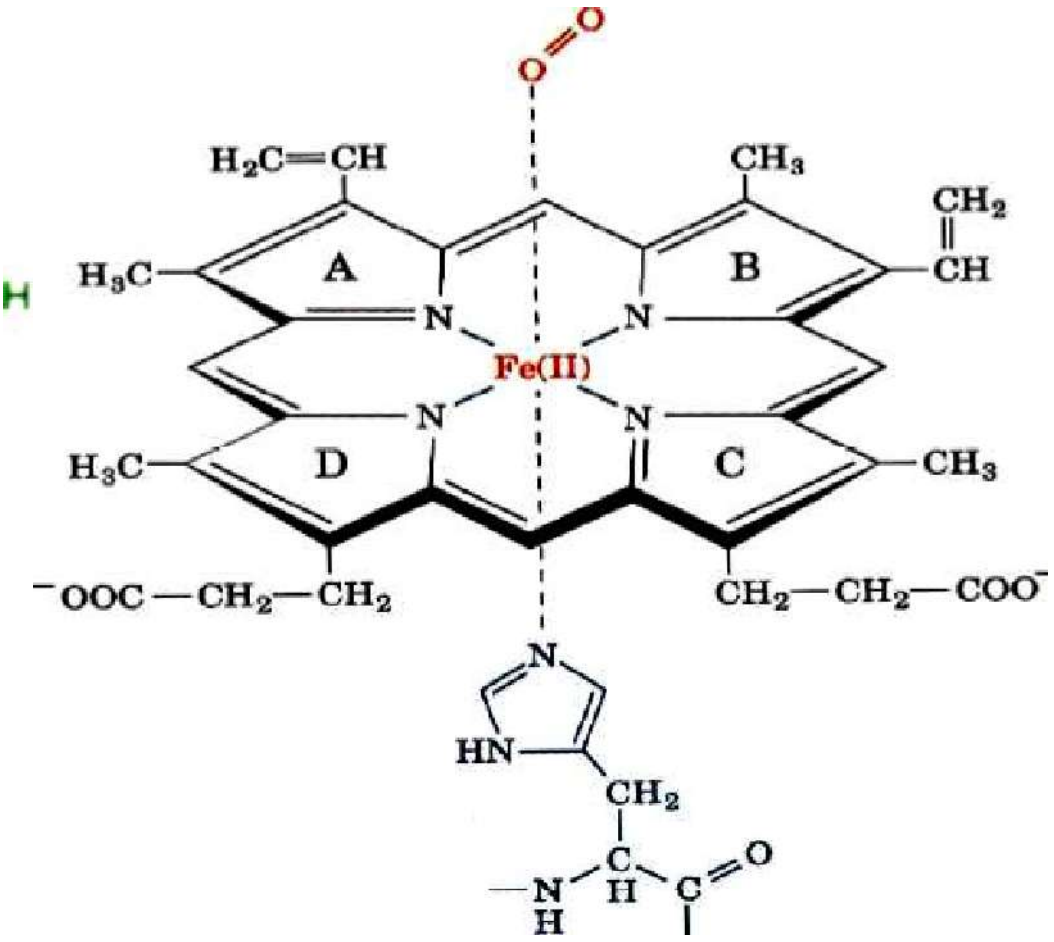


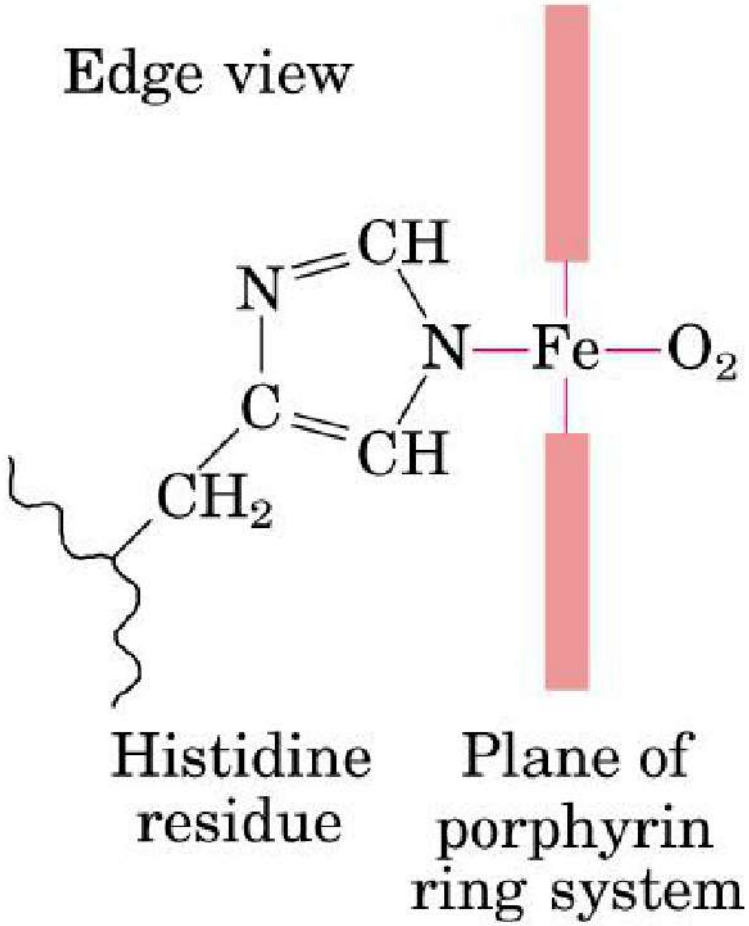
(c)

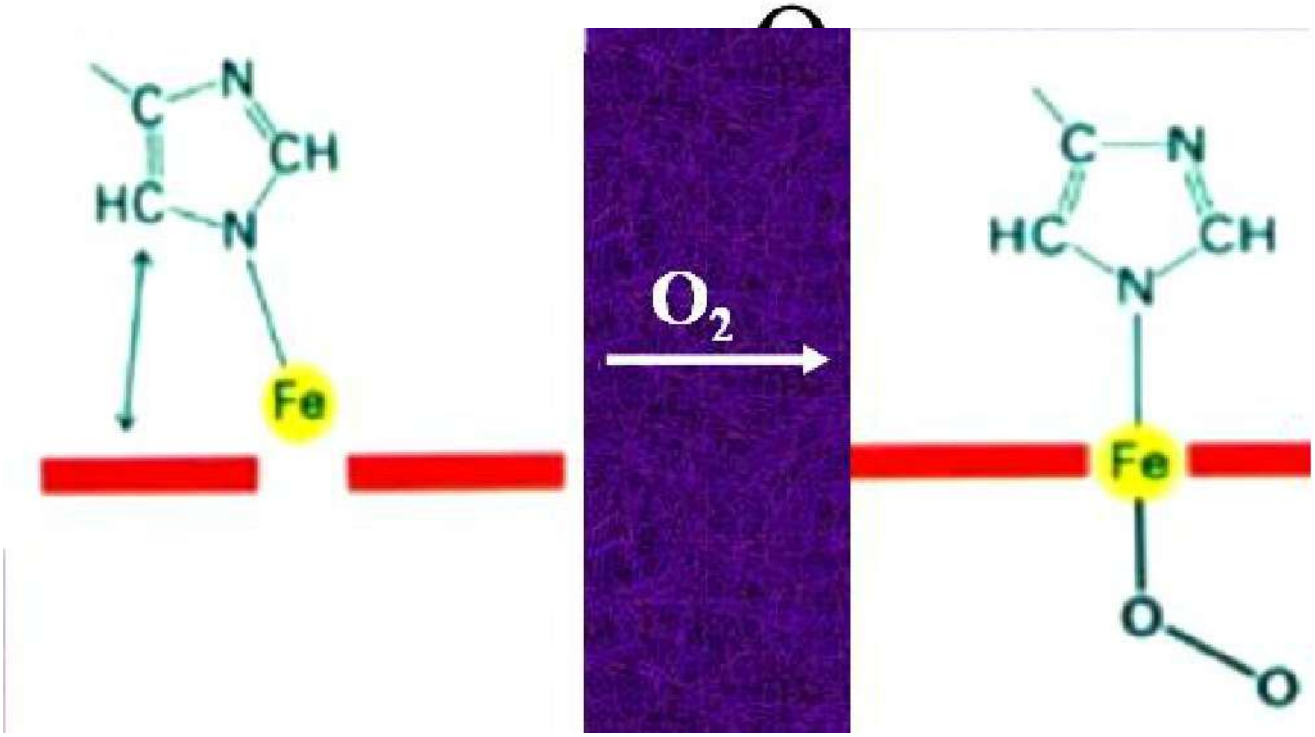


(d)

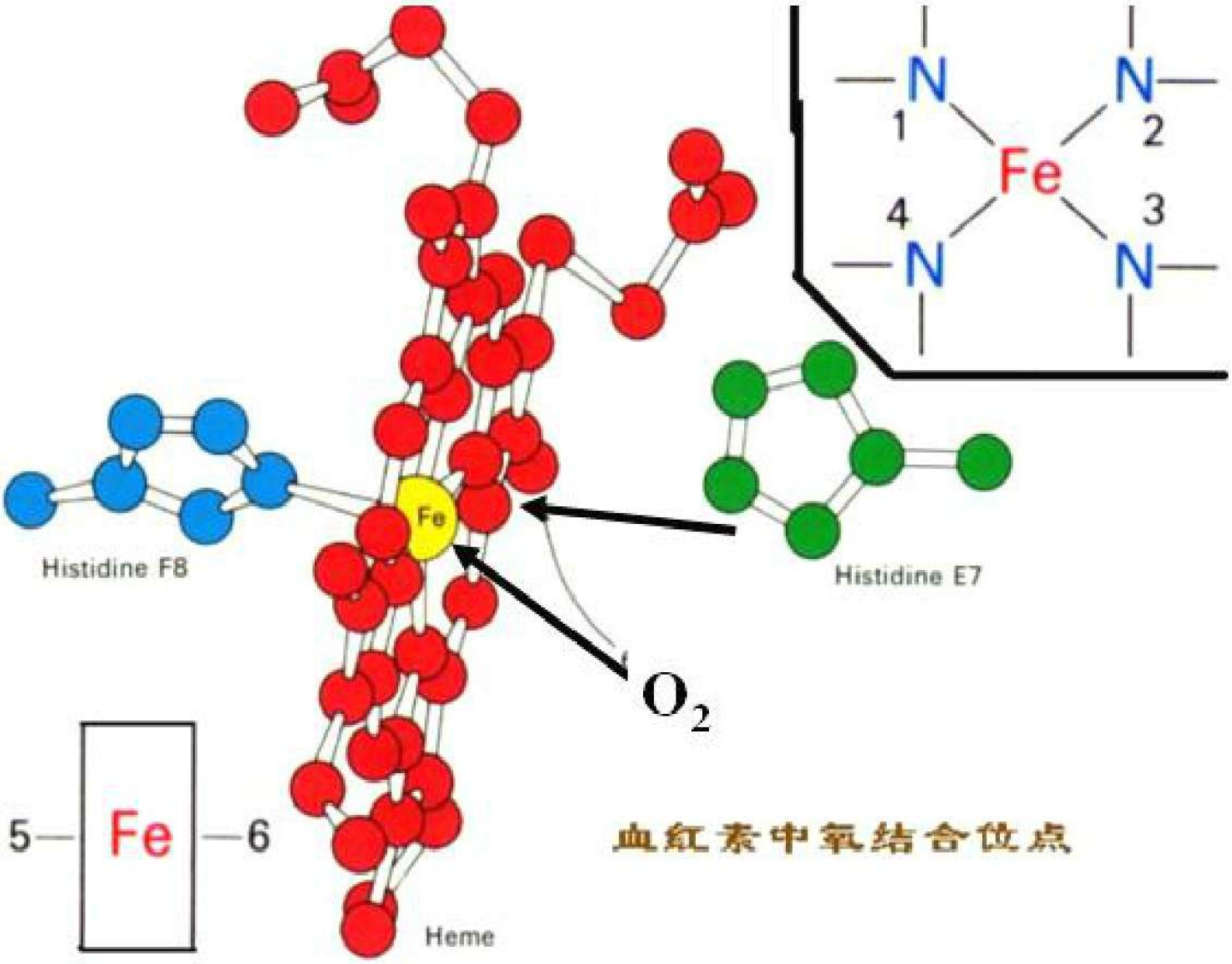
（三）O_2与Mb的结合


O=O
H2C=CH
CH3
CH2
CH
H3C
A
B
N
N
Fe(II)
N
N
H3C
D
C
CH3
−OOC—CH2—CH2
CH2—CH2—COO−
N
HN
CH2
C
H
C
O
N
H

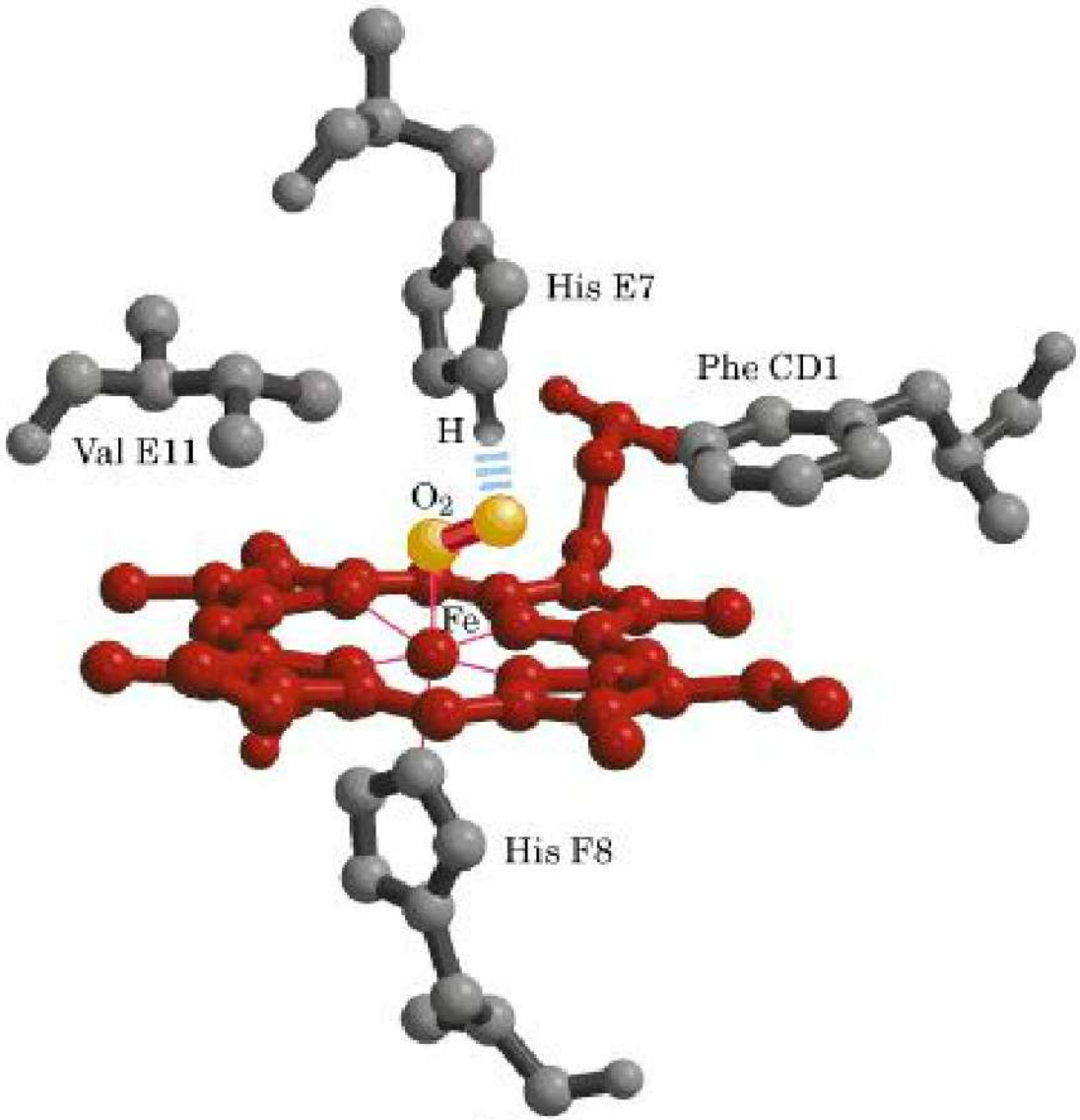

Edge view
CH
N
N
Fe
O2
C
CH
CH2
Histidine residue
Plane of porphyrin ring system



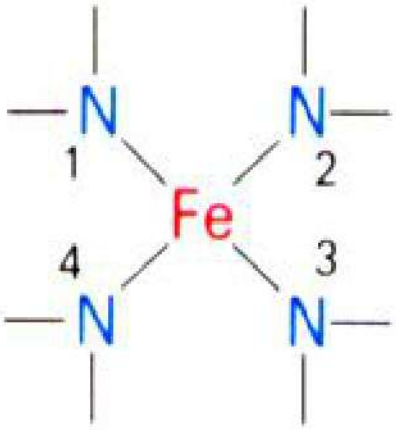
(a)

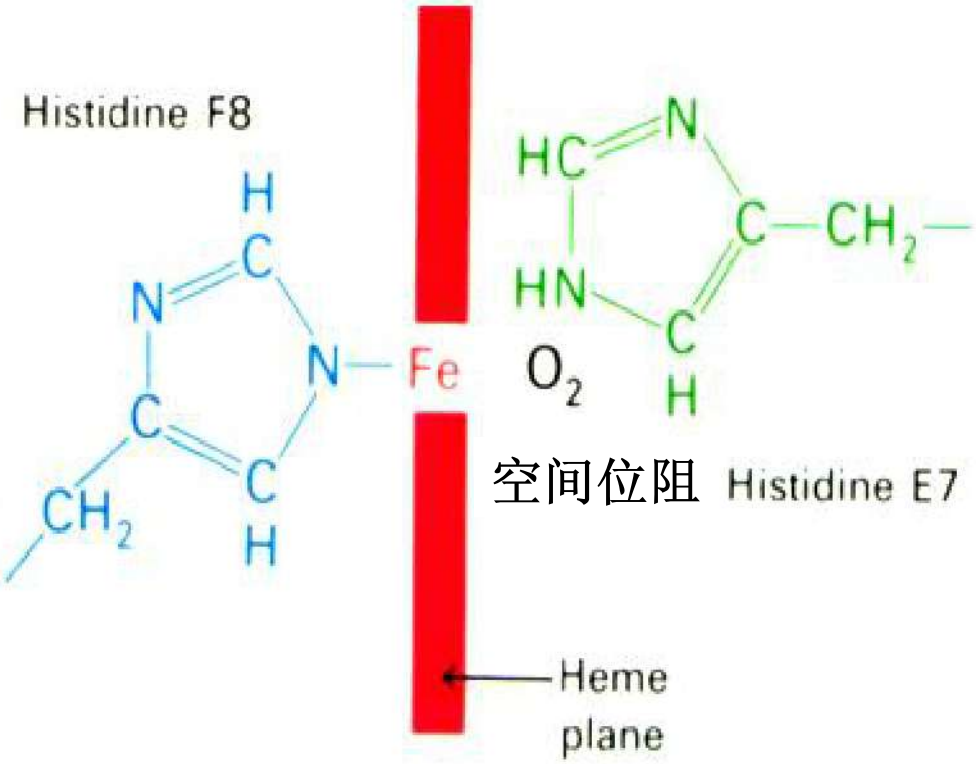


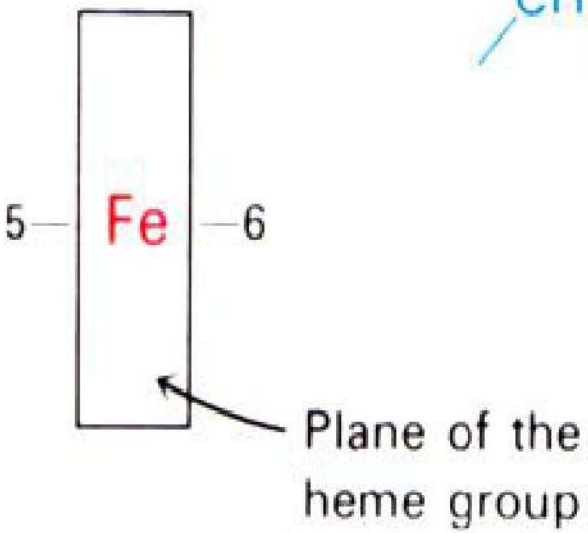
血红素中氧结合位点



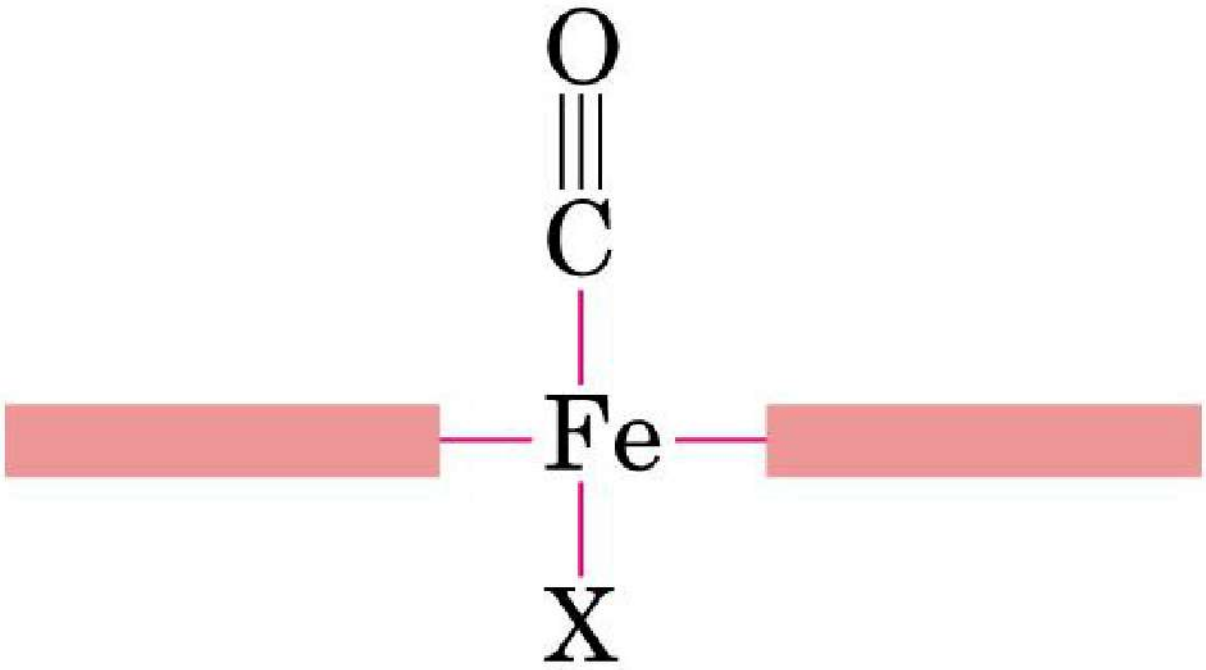
(c)







血红素中铁原子的六个连键



(b)

（四）Mb的氧结合曲线

$$MbO_2 \rightleftharpoons Mb + O_2$$

氧合Mb　　去氧Mb

$$K = \frac{[Mb]\,[O_2]}{[MbO_2]} \rightarrow \frac{[MbO_2]}{[Mb]} = \frac{[O_2]}{K}$$

氧合Mb与去氧Mb的浓度比与氧浓度成正比

- 氧分数饱和度（**fractional satuation**）

氧合肌红蛋白分子数

$$Y = \frac{[MbO_2]}{[MbO_2]+[Mb]} \qquad Y = \frac{[O_2]}{[O_2]+K}$$

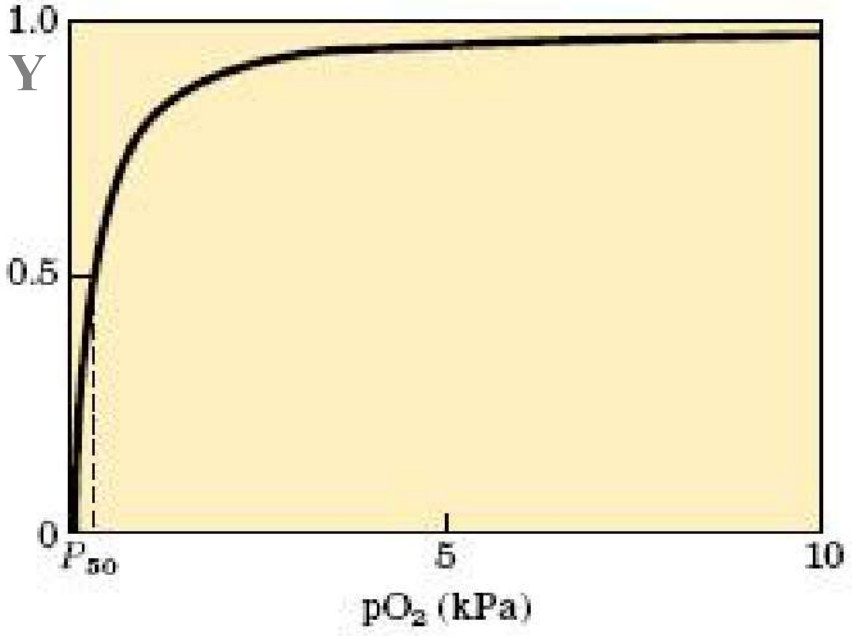
肌红蛋白分子总数

$$Y = \frac{p(O_2)}{p(O_2)+K}$$

$$Y = \frac{p(O_2)}{p(O_2) + K}$$

- *Y*=1　　Mb被氧完全饱和
- *Y*=0.5　　$p(O_2)=K=P_{50}$

P_{50}：Mb被氧半饱和时的氧分压



Mb氧结合/解离曲线

$$Y = \frac{p(O_2)}{p(O_2) + K} \quad \Rightarrow \quad \frac{1}{Y} = 1 + \frac{K}{p(O_2)}$$

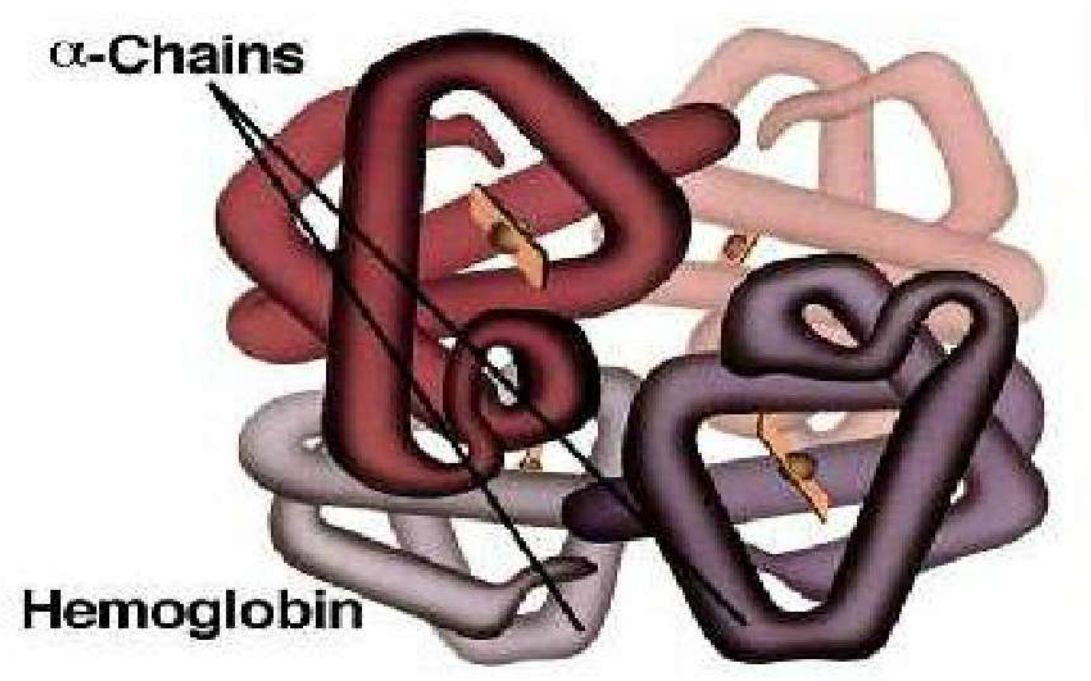
$$\frac{K}{p(O_2)} = \frac{1}{Y} - 1 = \frac{1 - Y}{Y}$$

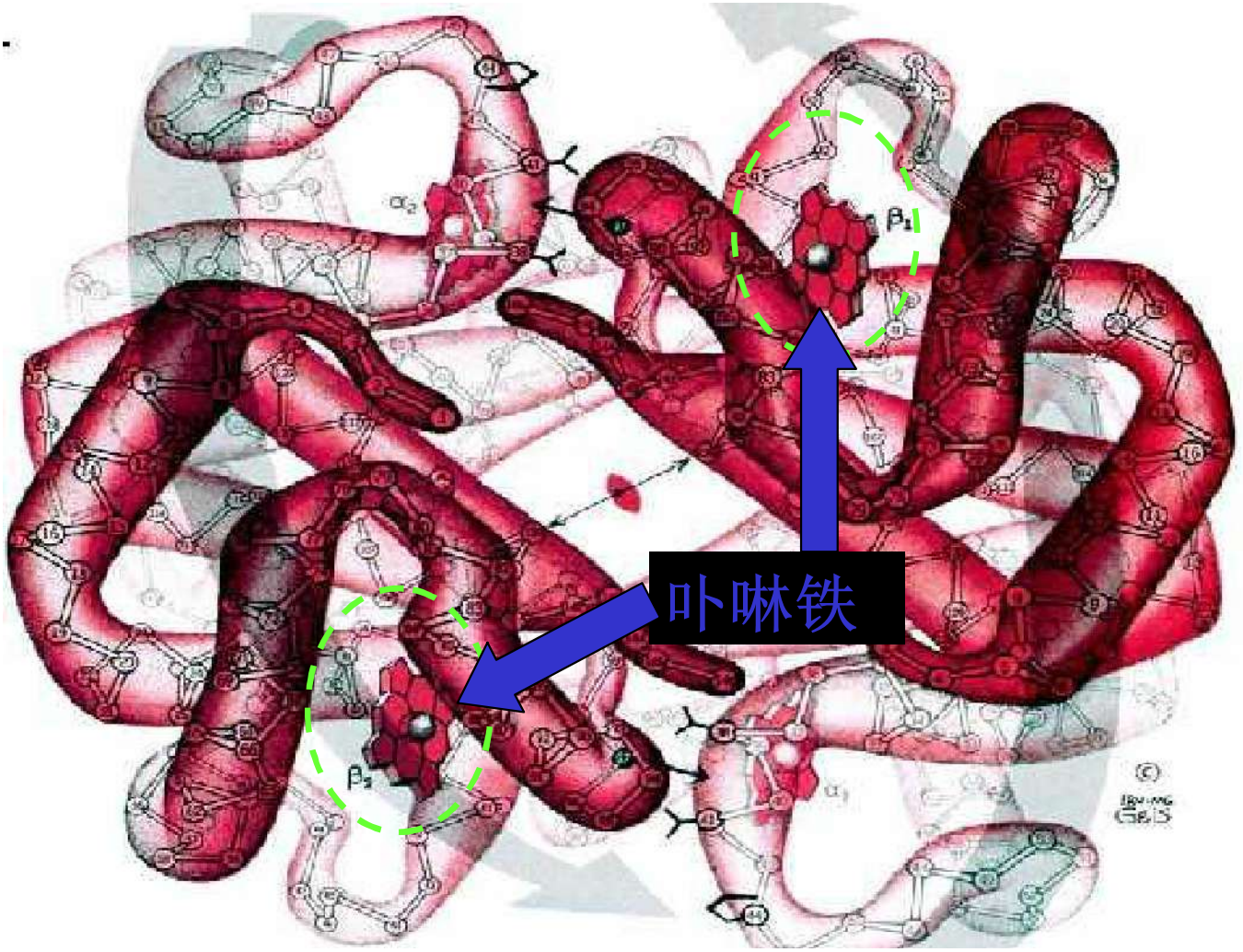
$$\log\left(\frac{Y}{1 - Y}\right) = \log p(O_2) - \log K$$

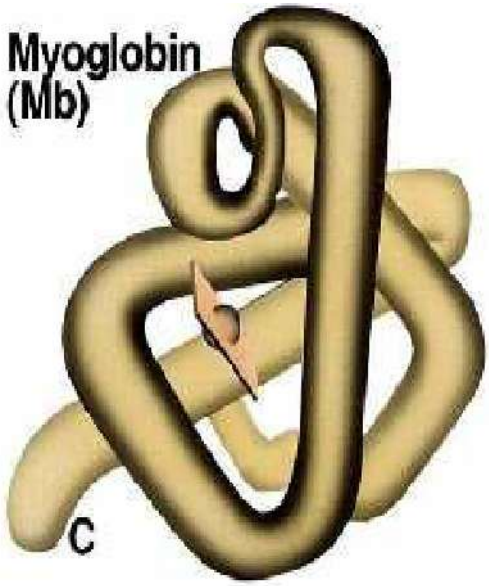
Hill图

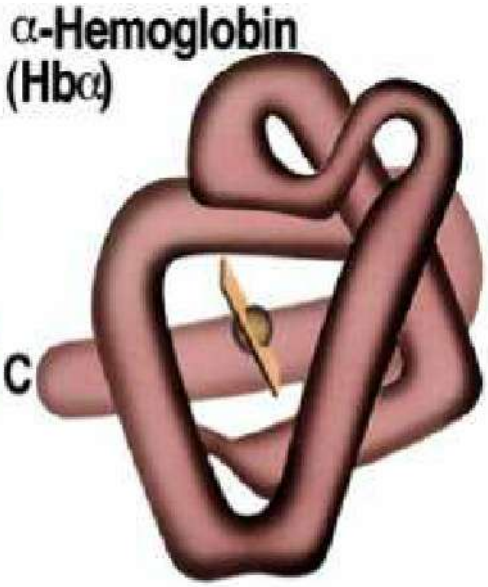
三、血红蛋白的结构和功能（hemoglobin，Hb）

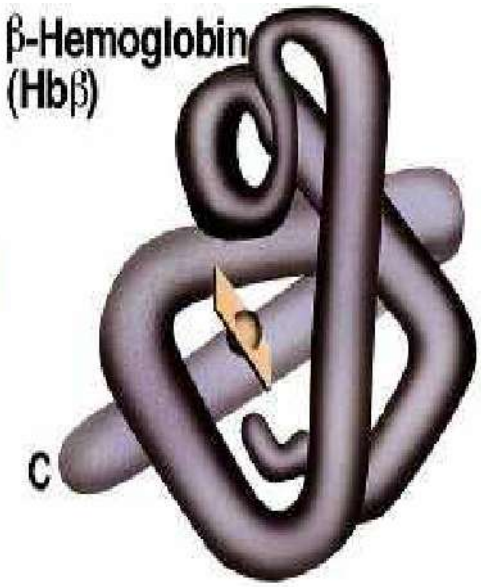
1、结构：α_1、α_2、β_1、β_2亚基



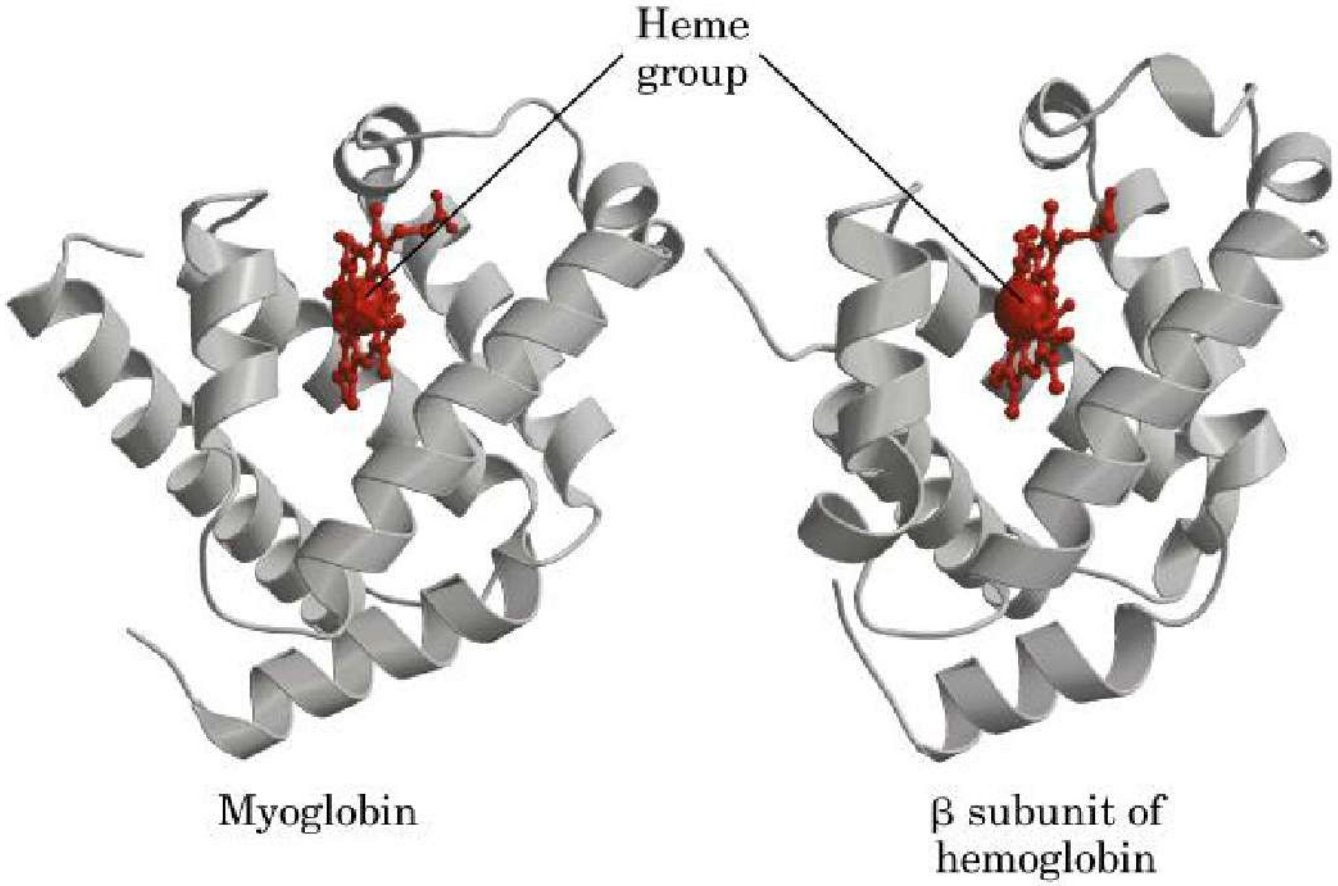

卟啉铁

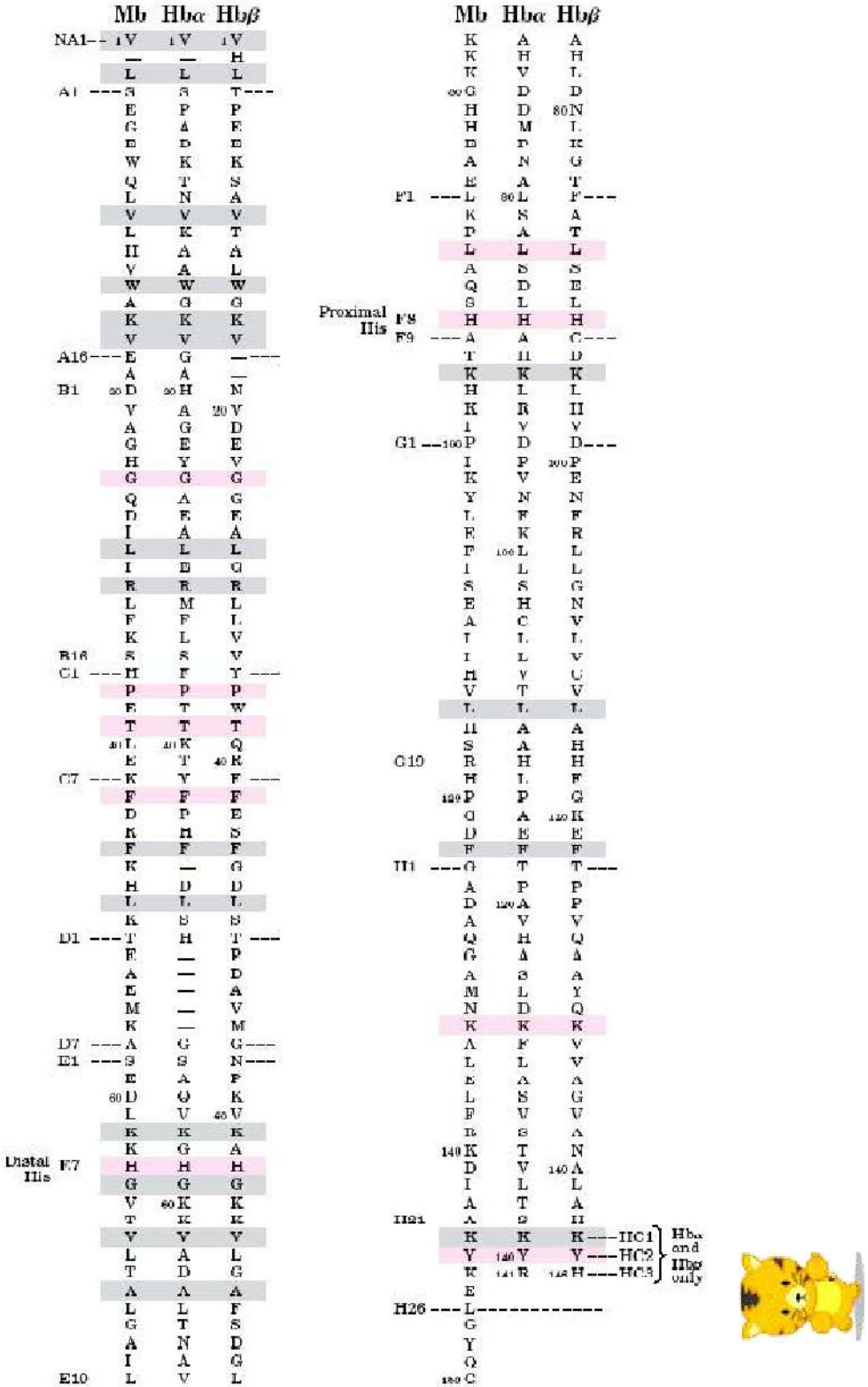




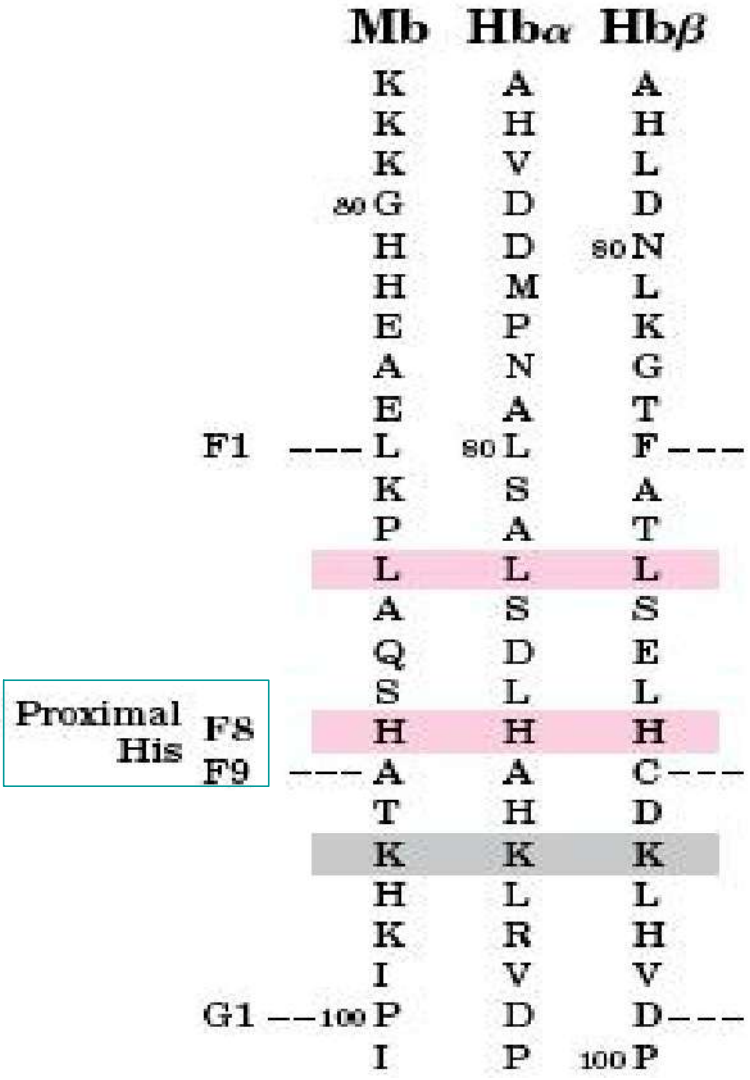


- *肌红蛋白*　　*血红蛋白α*　　*血红蛋白β*


Heme
group
Myoglobin
β subunit of
hemoglobin


Mb Hbα Hbβ
NA1 1 V 1 V 1 V
— — H
L L L
A1 3 S S T
E P P
G A E
E D E
W K K
Q T S
L N A
V V V
L K T
H A A
V A L
W W W
A G G
K K K
V V V
A16 E G —
A A —
B1 D H N
V A V
A G D
G E E
H Y V
G G G
Q A G
D E E
I A A
L L L
I D G
R R R
L M L
F F L
K L V
B16 S S V
C1 H F Y
P P P
E T W
T T T
L K Q
E T K
C7 K Y F
F F F
D P E
K H S
F F F
K — G
H D D
L L L
K S S
D1 T H T
F —
A —
E —
M —
K —
D7 A G G
E1 S S N
E A F
D Q K
L V V
K K K
K G A
Distal His F7 H H H
G G G
V K K
T K K
V V V
L A L
T D G
A A A
L L F
G T S
A N D
I A G
E10 L V L
Proximal His F8 H H H
F9 A A C
T H D
K K K
H L L
K R H
I V V
G1 P D D
I P P
K V E
Y N N
L F F
E K R
F L L
I L L
S S G
E H N
A C V
T I. I.
I L V
H V C
V T V
L L L
H A A
S A H
G10 R H H
H I. F
P P G
Q A K
D E E
F F F
H1 G T T
A P P
D A P
A V V
Q H Q
G A A
A S A
M L Y
N D Q
K K K
A F V
L L V
E A A
L S G
F V V
R S A
K T N
D V A
I L L
A T A
H121 A S H
K K K HC1
V V HC2
K R H HC3
E
H26 L
G
Y
Q
C
Hbα and Hbβ only

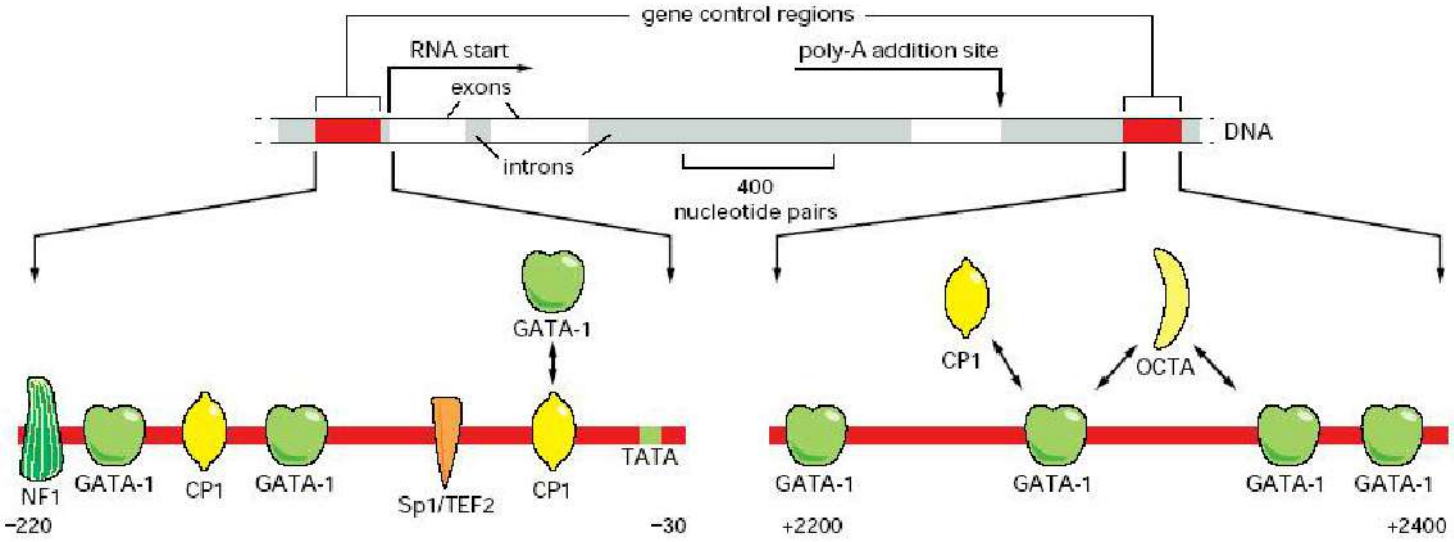
	Mb	Hbα	Hbβ
	E	—	A
	M	—	V
	K	—	M
D7 ---	A	G	G ---
E1 ---	S	S	N ---
	E	A	P
60	D	Q	K
	L	V	60 V
	K	K	K
	K	G	A
Distal His E7	H	H	H
	G	G	G
	V	60 K	K
	T	K	K
	V	V	V
	L	A	L
	T	D	G
	A	A	A
	L	L	F
	G	T	S
	A	N	D
	I	A	G
E19 ---	L	V	L ---


Mb
Hbα
Hbβ
F1
Proximal His
F8
F9
G1
80
100

肌红蛋白 / 血红蛋白α / 血红蛋白β

- AA序列大不相同，结构相似
- 结构决定功能（载氧）

2、血红蛋白的分类　HbA1　HbA2



（二）氧结合引起的Hb的构象变化

变构

脱氧血红蛋白 ⟷ 氧合血红蛋白

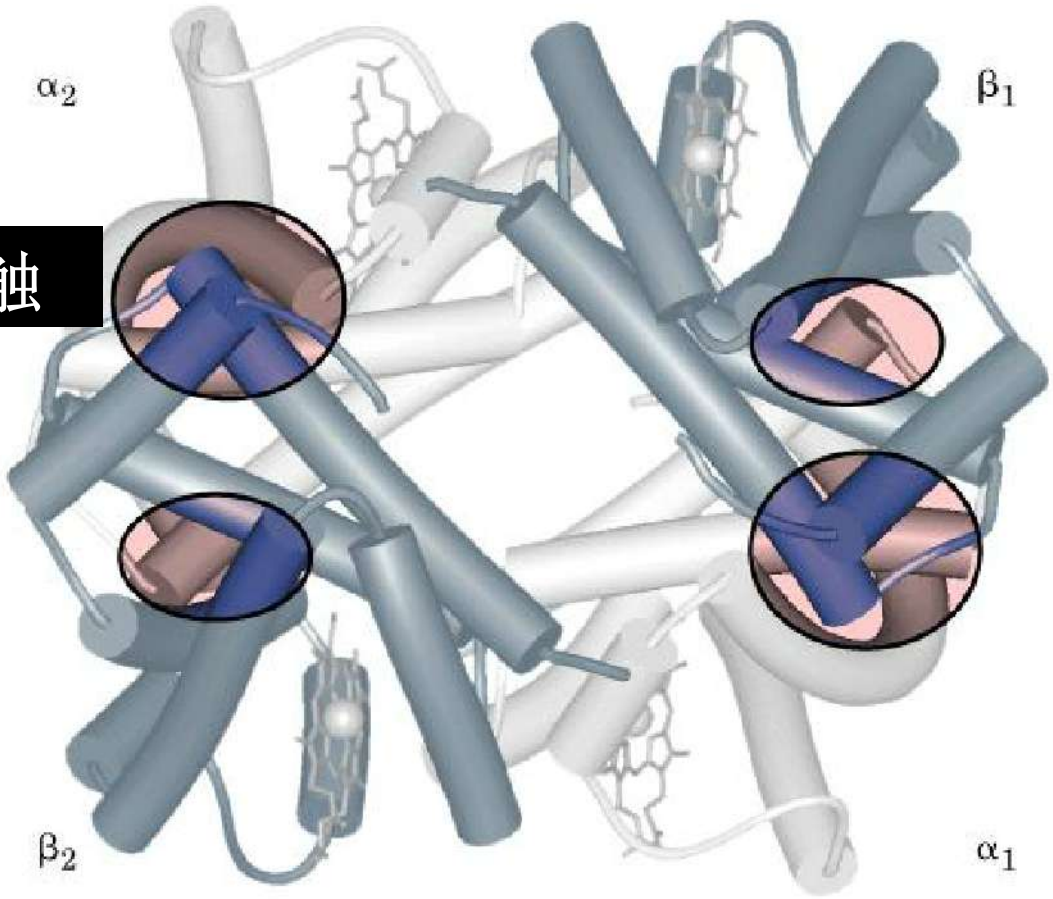
对氧的亲和力低 ⟷ 对氧的亲和力高

1、氧合作用改变Hb四级结构

滑动接触

$\alpha_2\beta_1$

$\alpha_1\beta_2$

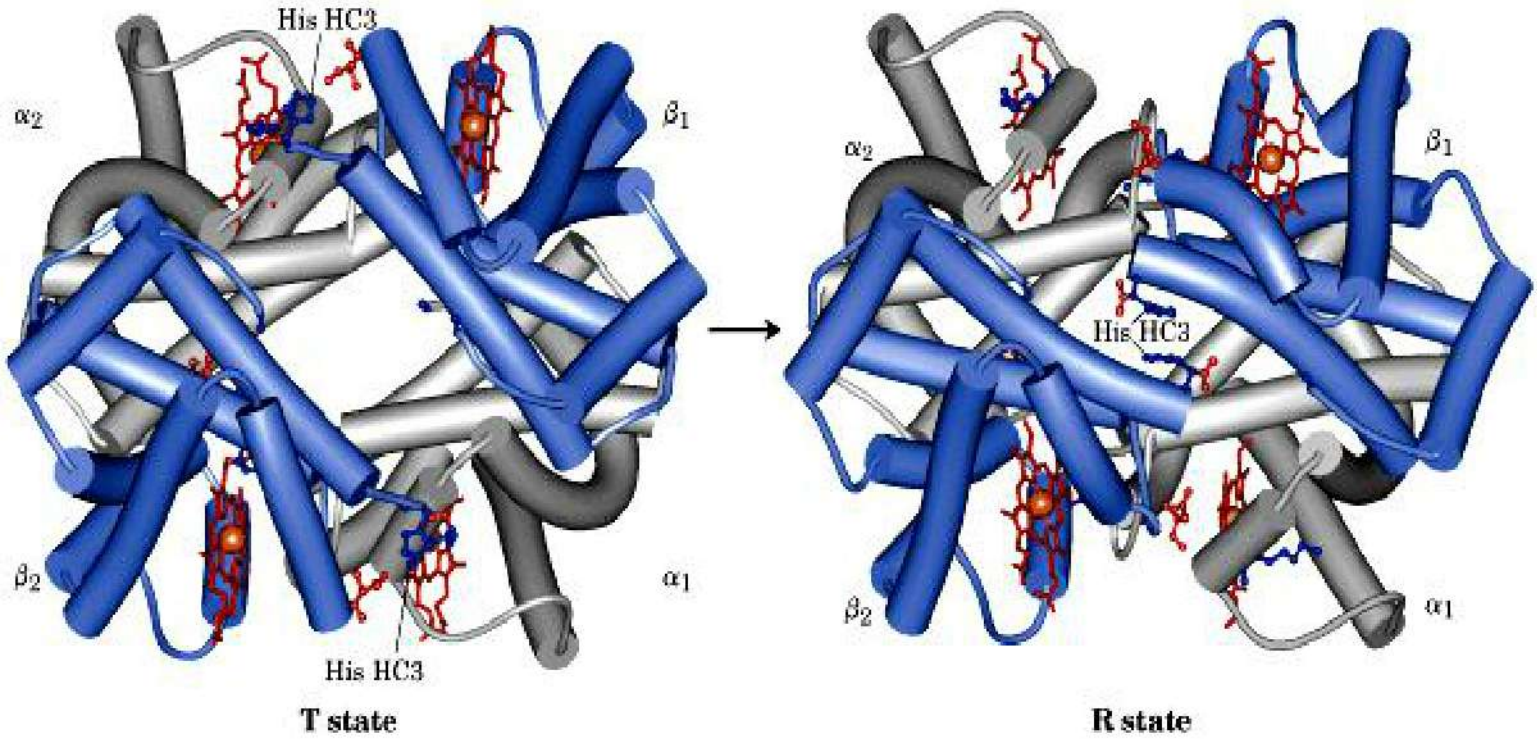


装配接触

$\alpha_2\beta_2$

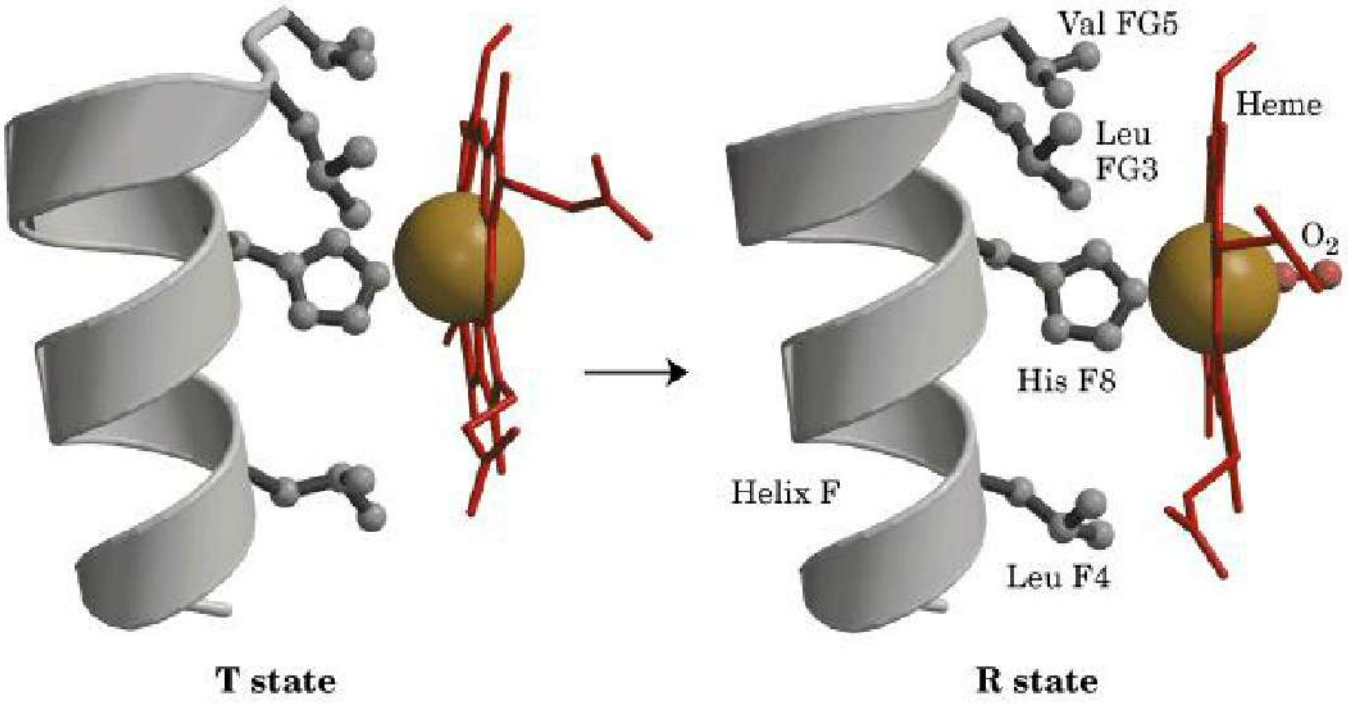
$\alpha_1\beta_1$

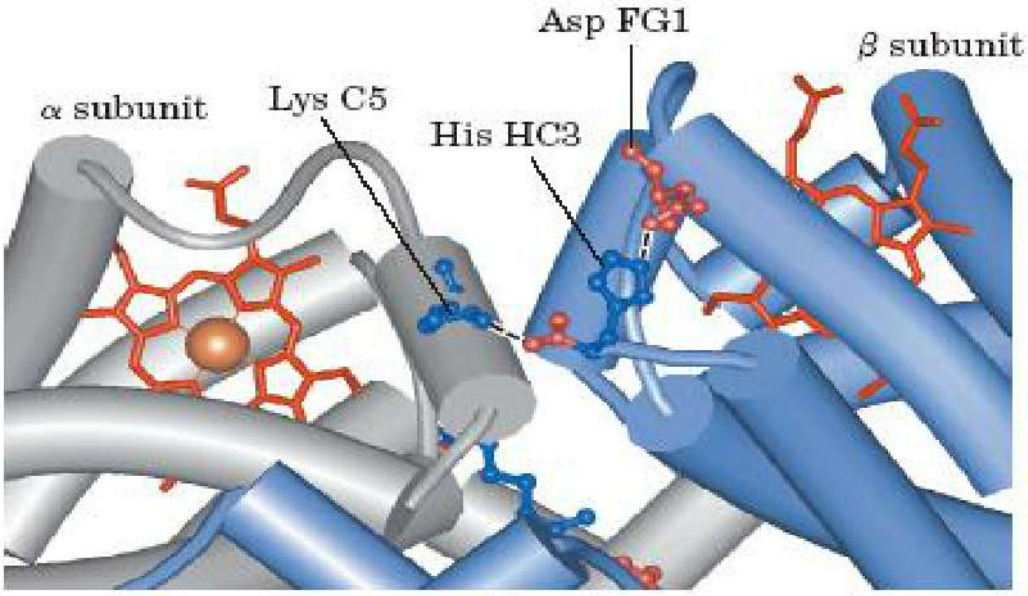
2、Hb的两种不同构象态



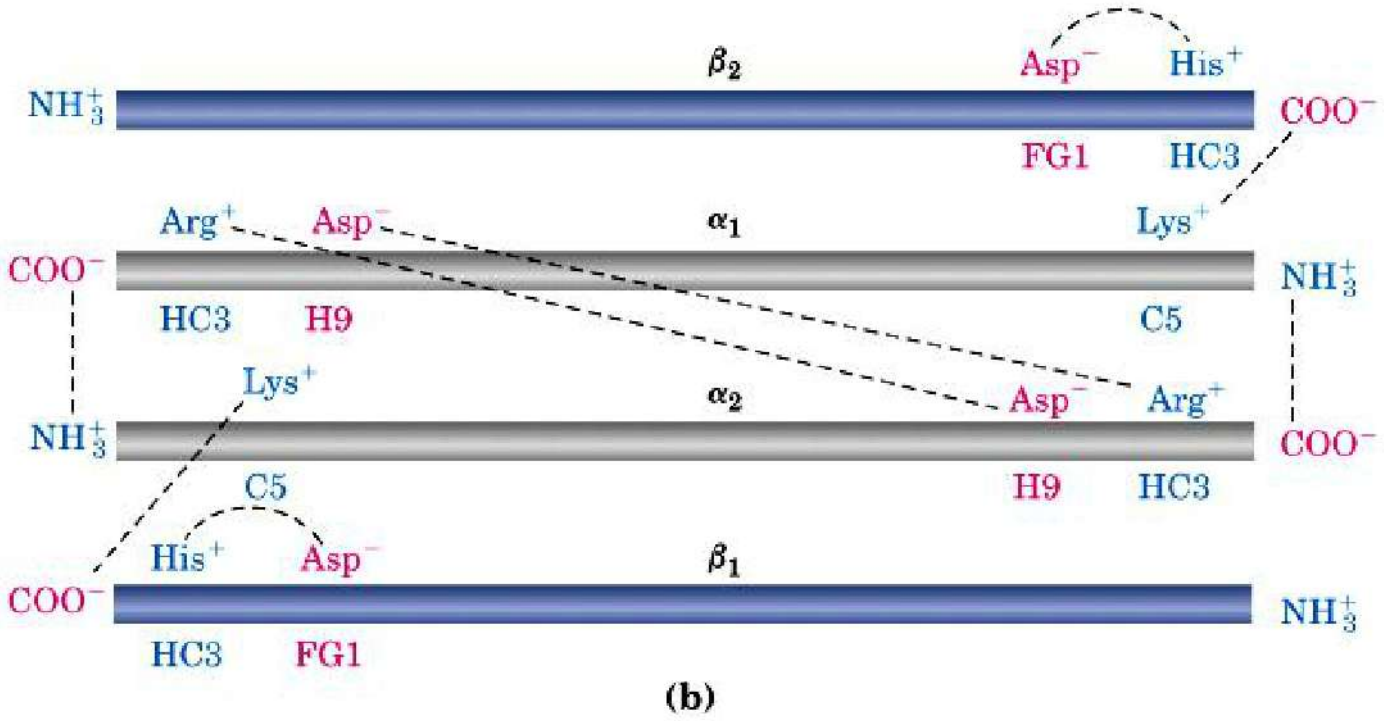
tense state

relaxed state


Val FG5
Heme
Leu
FG3
O_2
His F8
Helix F
Leu F4
T state
R state



(a)



(b)

- T 型血红蛋白肽链之间的8个盐桥
- α β链C末端有Tyr-OH可与C=O形成氢键

（三）Hb氧结合曲线

对于具有n个结合位点的蛋白P:

$$P + nL \rightleftharpoons PL_n$$

$$K = \frac{[P][L]^n}{[PL_n]} \qquad Y = \frac{[PL_n]}{[PL_n]+[P]}$$

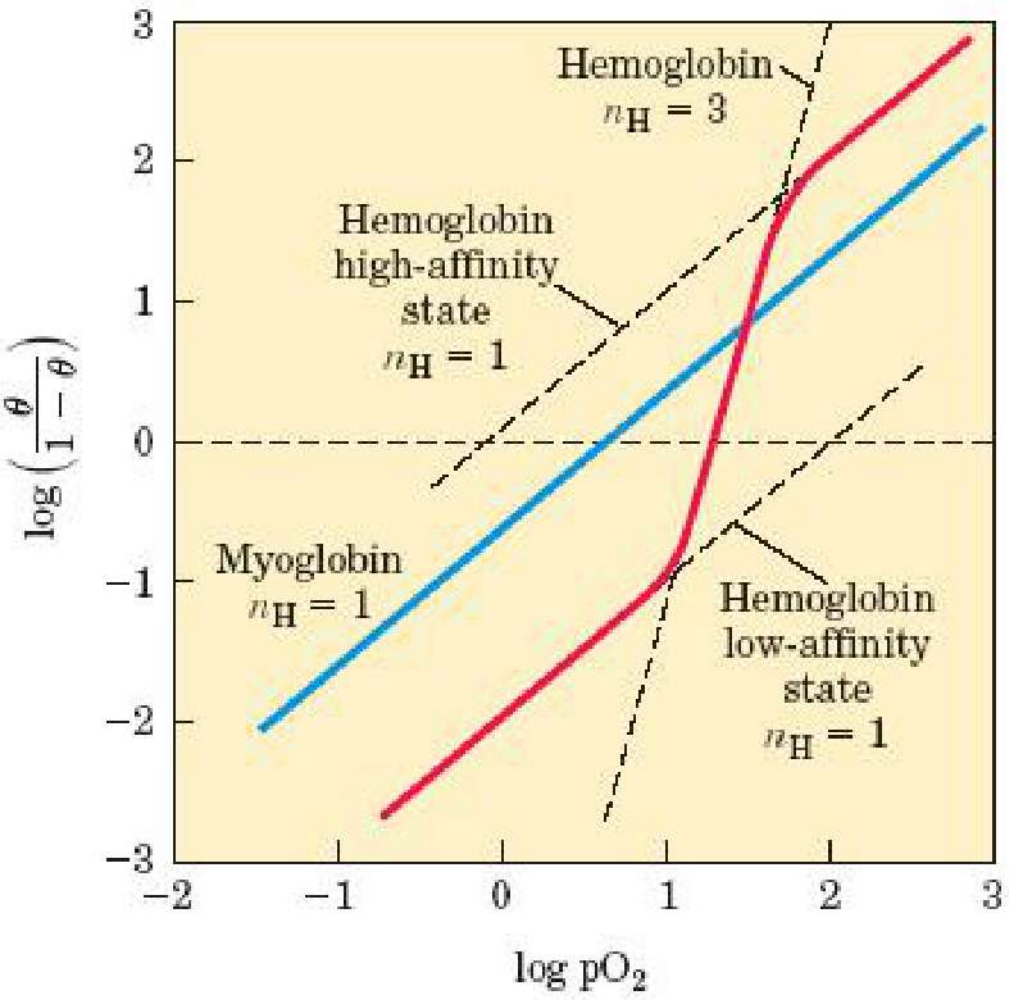
$$Y = \frac{[L]^n}{[L]^n + K} \qquad Y = \frac{p^4(O_2)}{p^4(O_2) + K}$$

$$Y = \frac{p^{4}(O_2)}{p^{4}(O_2) + K}$$

$$\frac{Y}{1 - Y} = \frac{p^{4}(O_2)}{K}$$

$$\log \frac{Y}{1 - Y} = \log \frac{p^{n}(O_2)}{K} = n \log p_{(O_2)} - \log K$$

Hill 方程

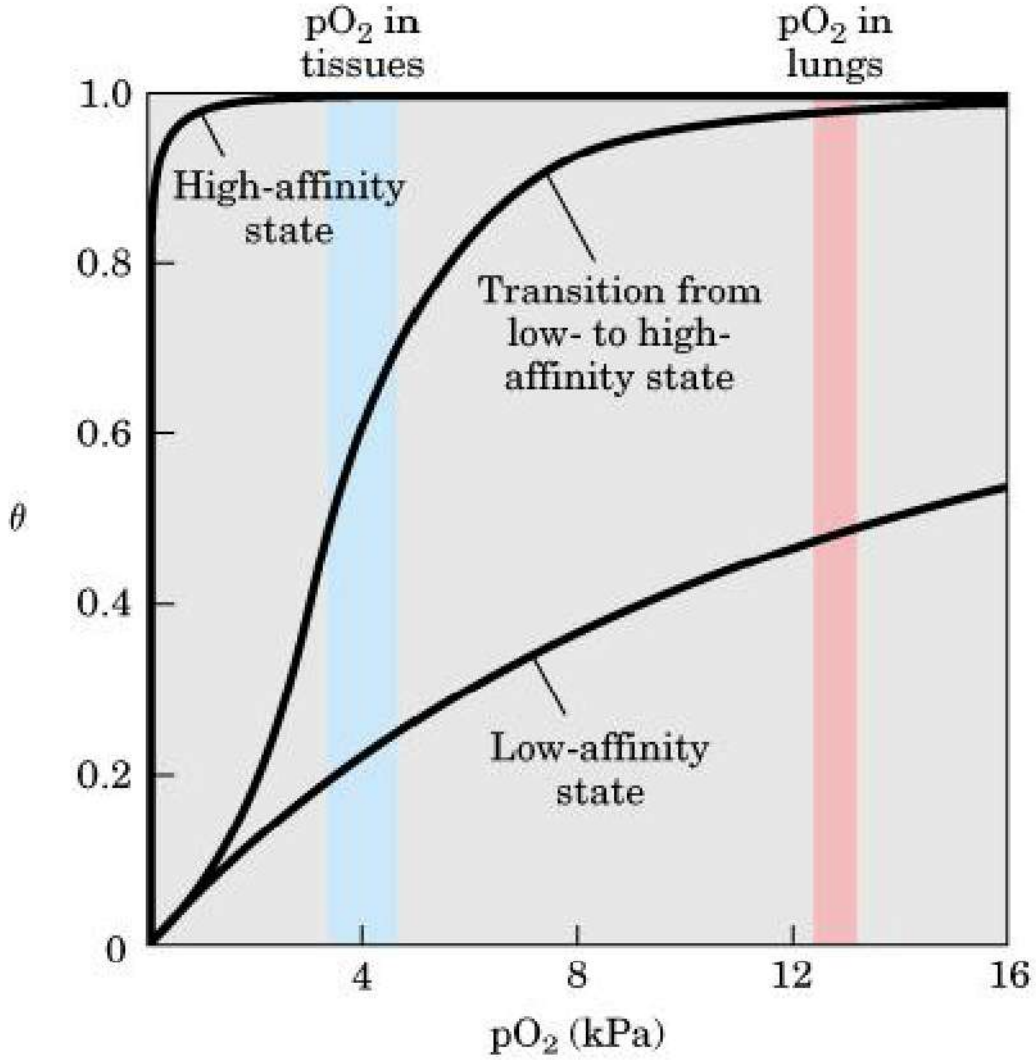


nH = 1
非协同

nH ＞1
正协同

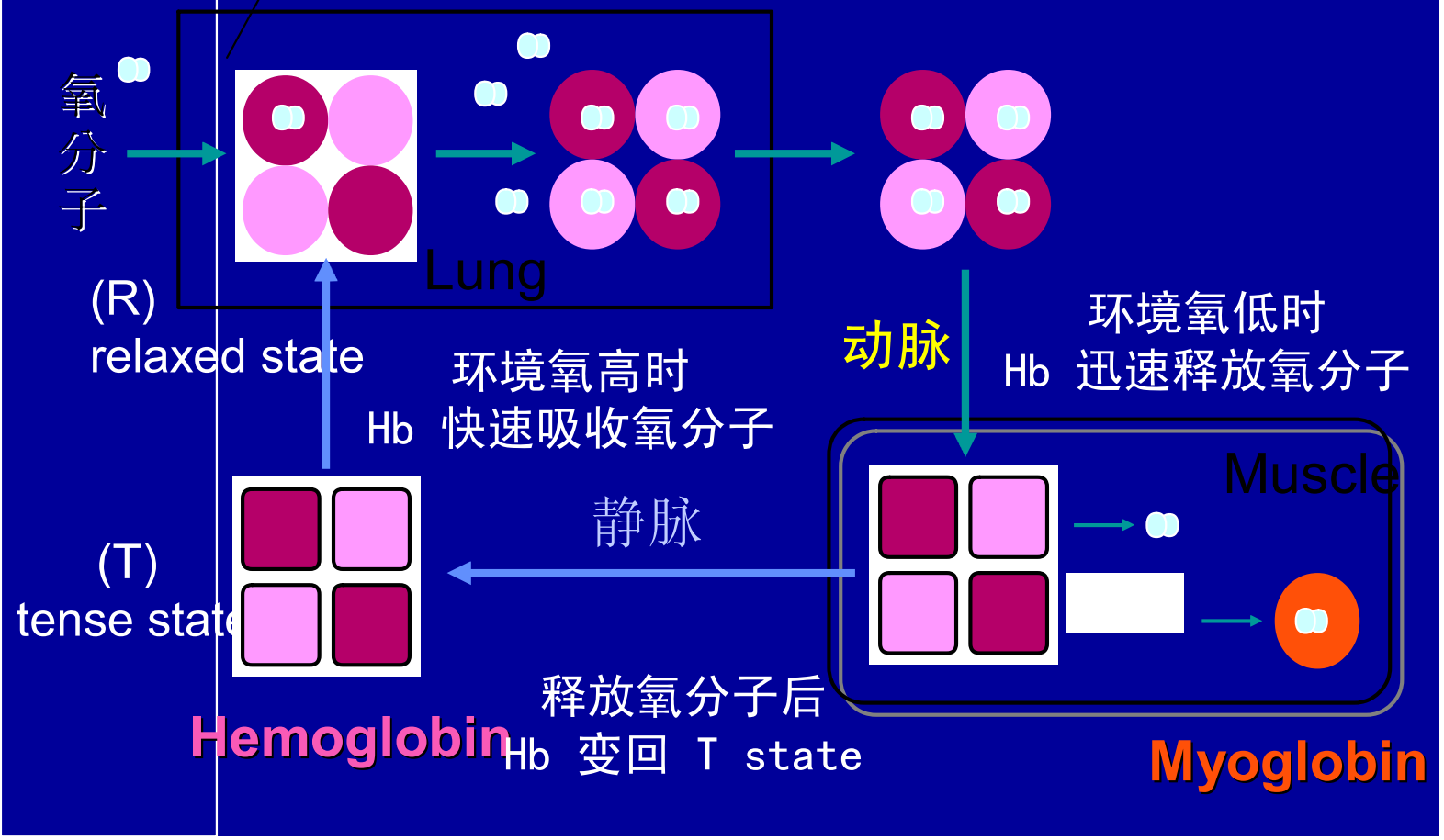
nH =n
完全协同

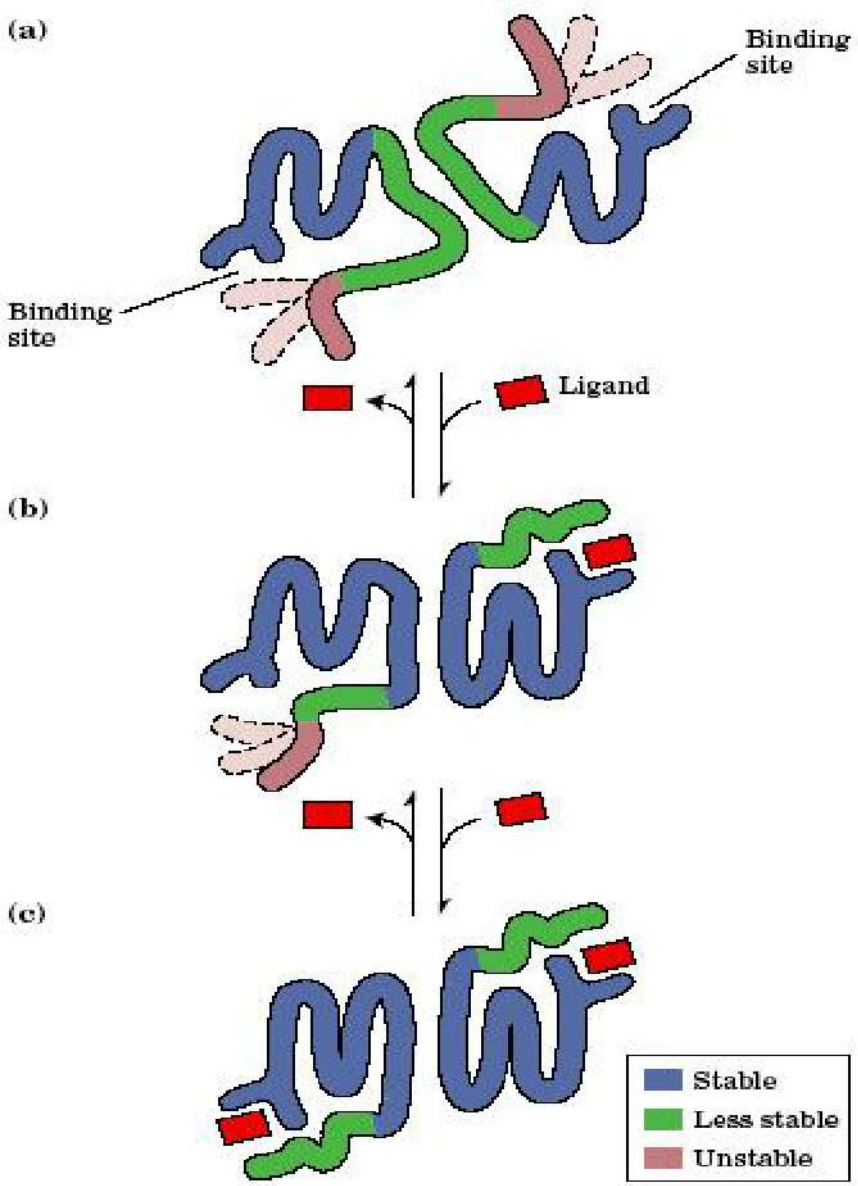
Hill 系数与配体的结合


pO_2 in tissues
pO_2 in lungs
1.0
0.8
0.6
0.4
0.2
0
θ
High-affinity state
Transition from low- to high-affinity state
Low-affinity state
4
8
12
16
pO_2 (kPa)

血中氧分子的运送：

任何一个亚基接受氧分子后，会增进其它亚基吸附氧分子的能力




(a)
Binding site
Binding site
Ligand
(b)
(c)
Stable
Less stable
Unstable

（四）Hb结合氧的调节

1、 H^+、CO_2促进O_2的释放

碳酸酐酶

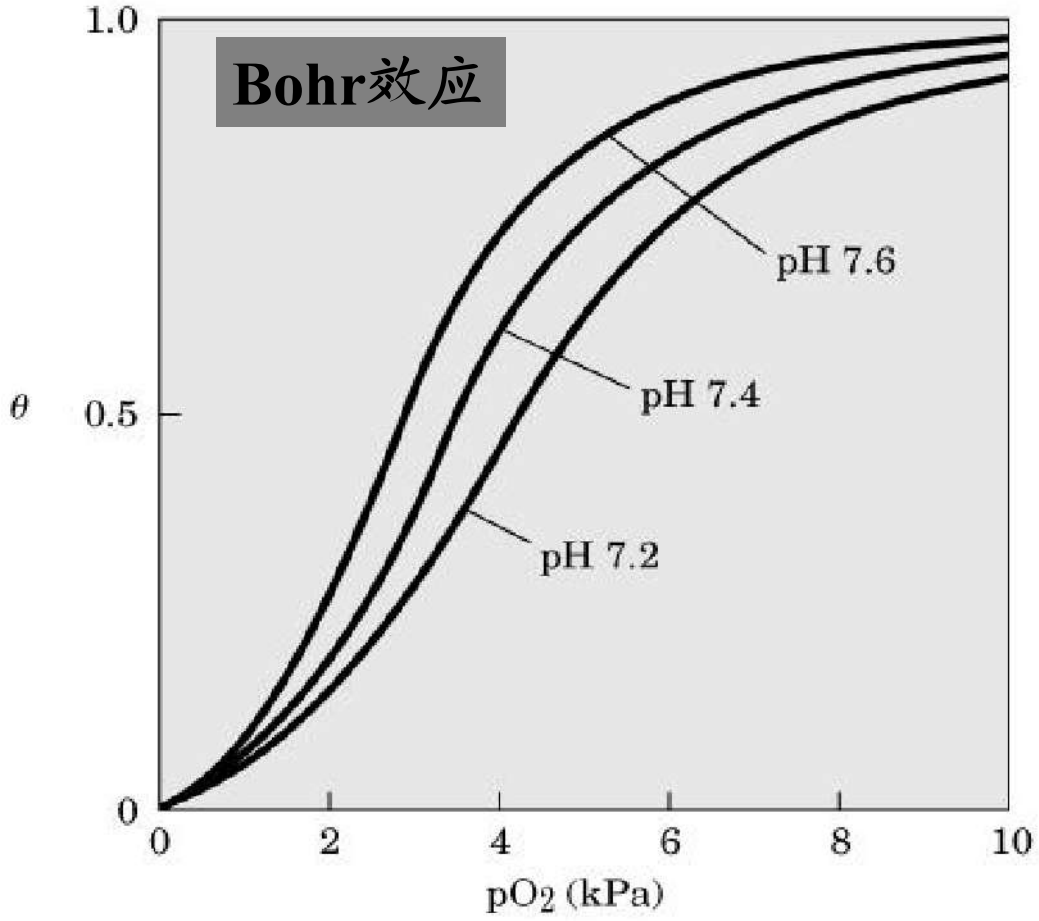
$$CO_2 + H_2O \rightleftharpoons H^+ + HCO_3^-$$

$$HbO_2 + H^+ \rightleftharpoons HbH^+ + O_2$$

H^+—Hb氧合的拮抗物

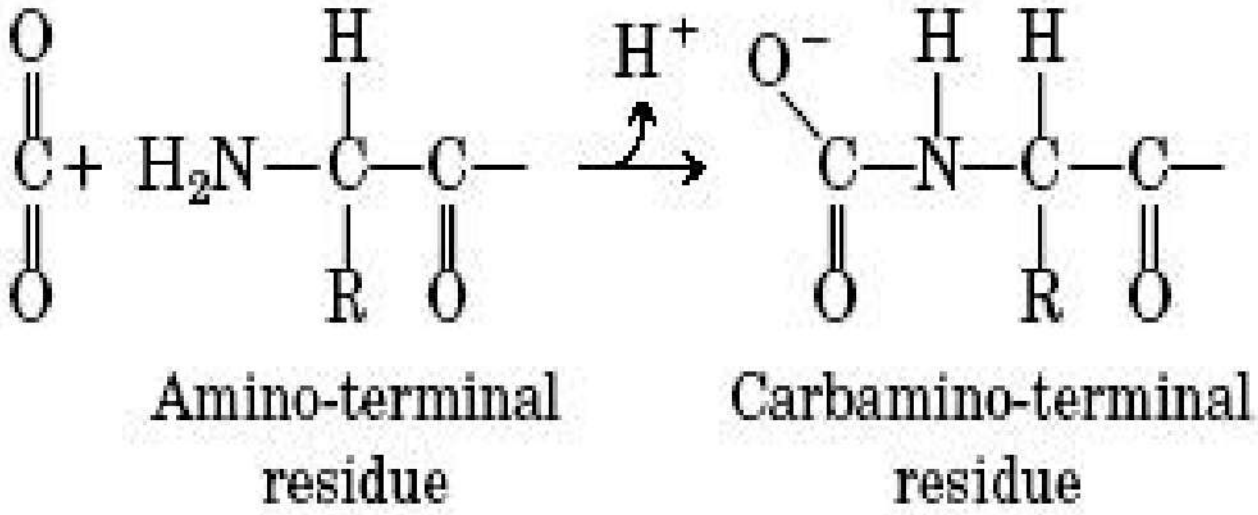
pH降低时：促进氧的释放

缓冲血液pH



在氧分压不变时，低**pH**能促进更多的氧释放

CO_2与Hb的结合

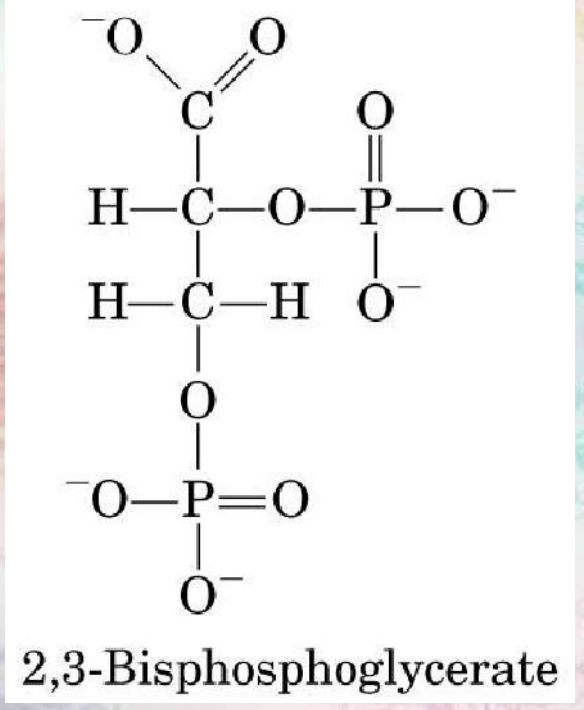


释放的H^+有助于Bohr效应

氨甲酸可形成额外的盐桥：稳定T态

促进氧的释放

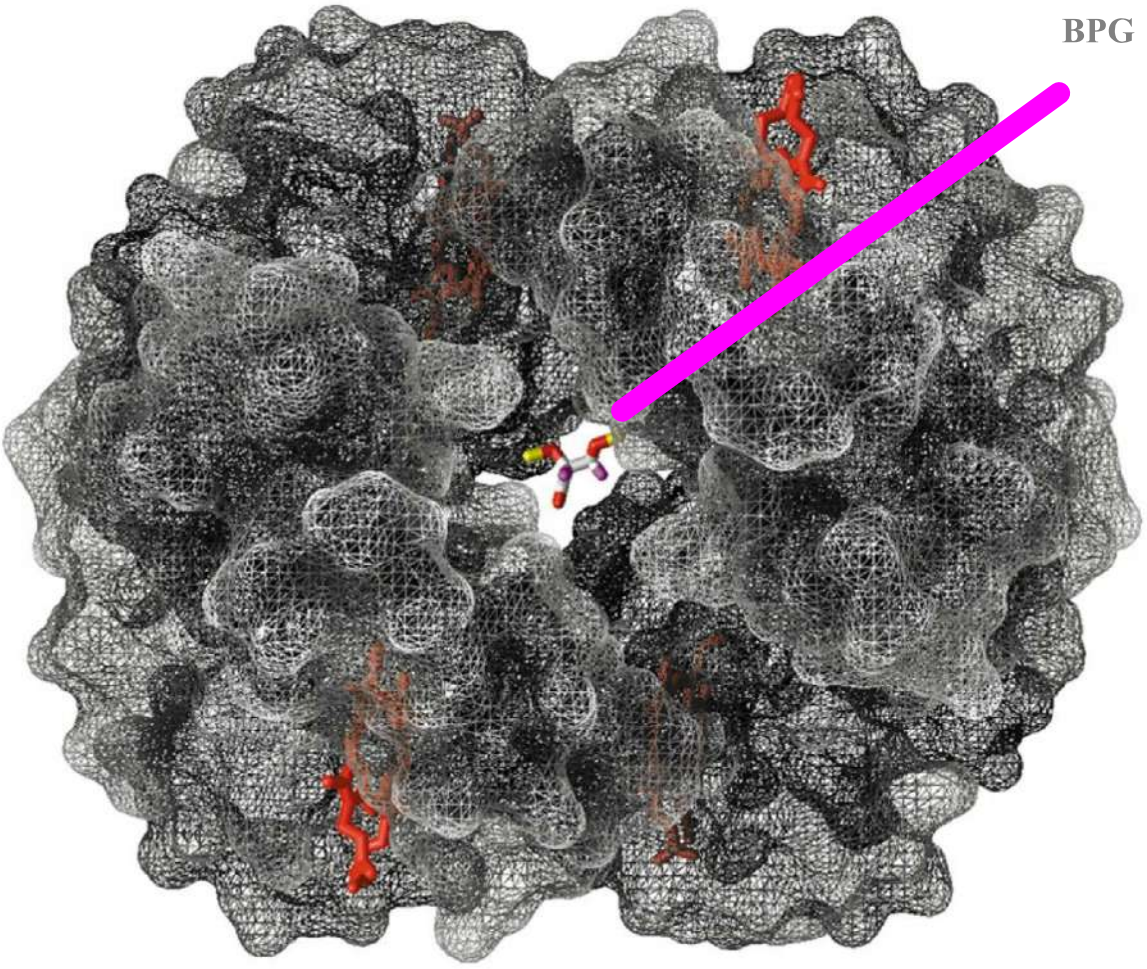
2、BPG降低Hb对氧的亲和力



Hb四聚体只有一个BPG结合部位

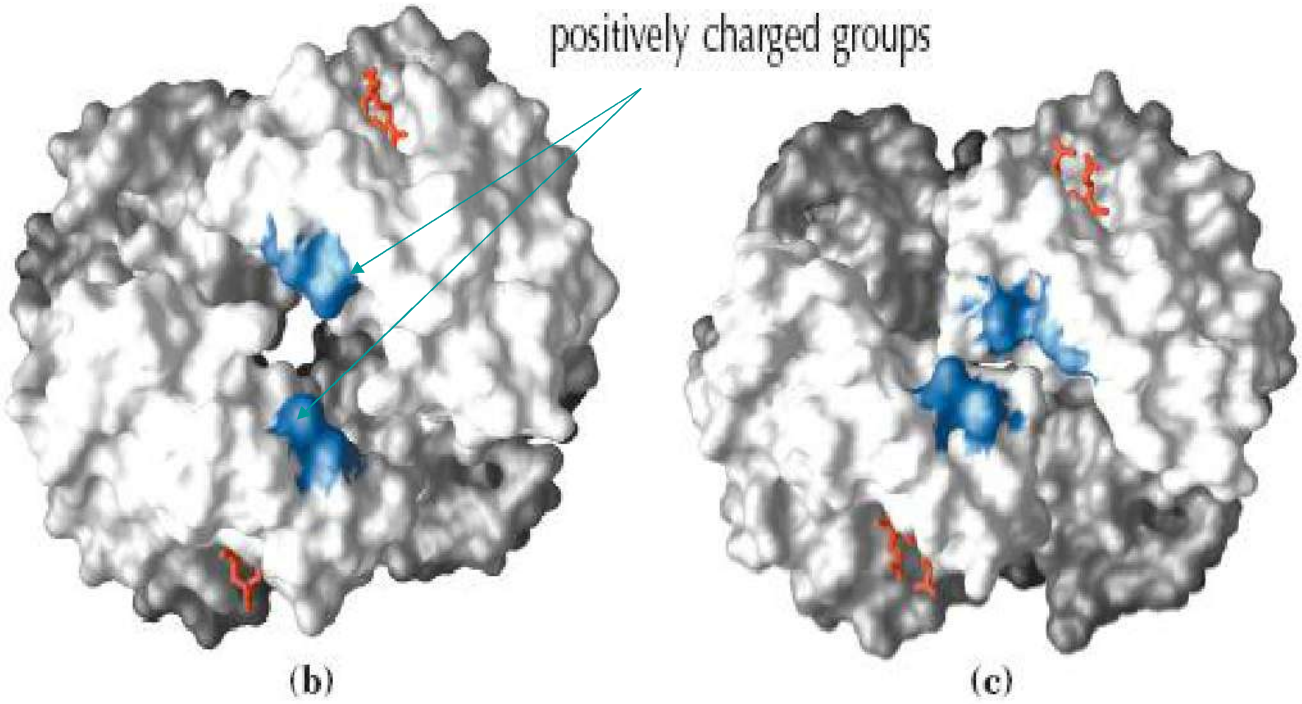
—4个亚基缔合形成的中央空穴内

2，3 - 二磷酸甘油酸——Hb异促别构调节的效应物

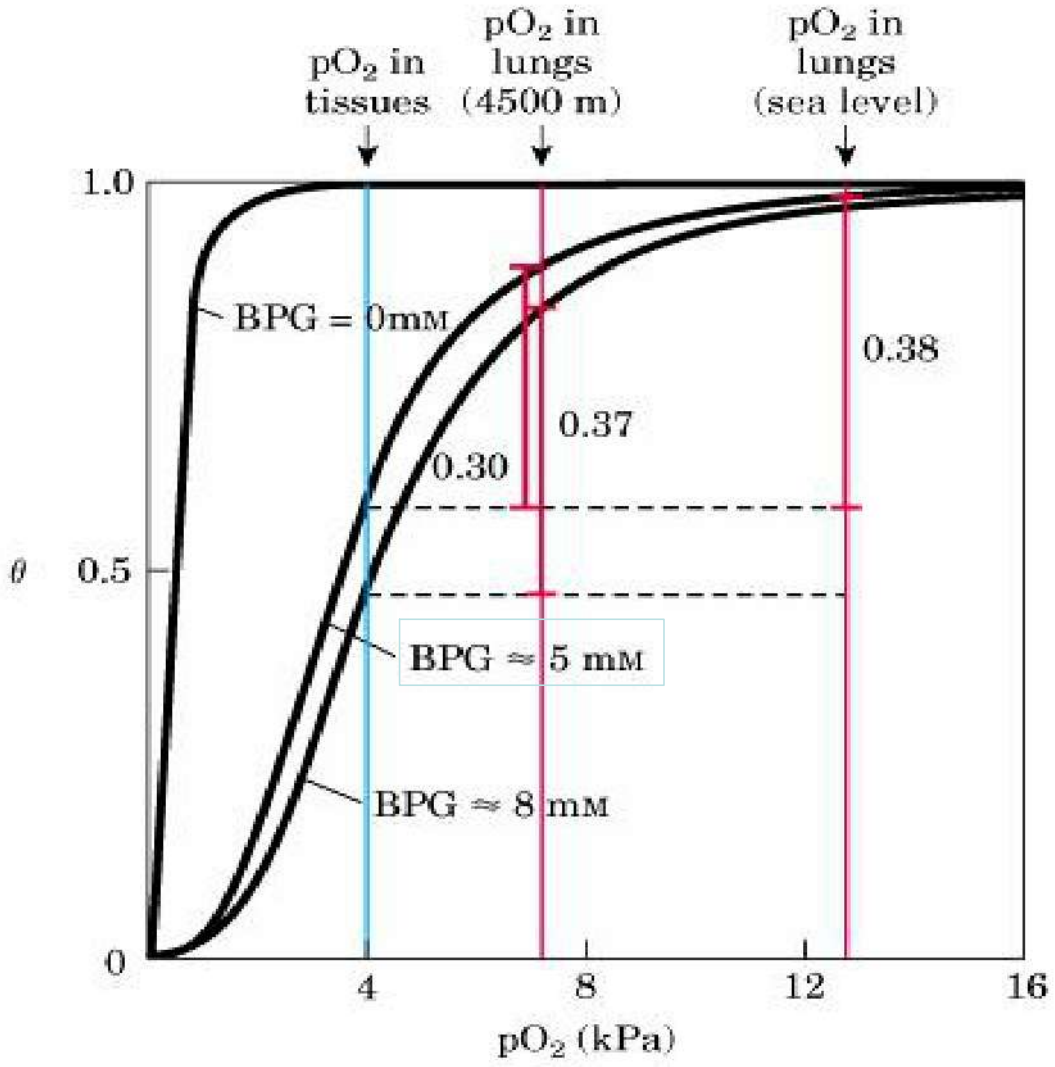


(a)

离子键稳定T态



$$HbBPG + O_2 \rightleftharpoons HbO_2 + BPG$$


pO_2 in tissues
pO_2 in lungs (4500 m)
pO_2 in lungs (sea level)
1.0
0.5
0
θ
BPG = 0mM
BPG ≈ 5 mM
BPG ≈ 8 mM
0.38
0.37
0.30
4
8
12
16
pO_2 (kPa)

氧合Hb中央空穴太小，容纳不了BPG,

BPG对R态Hb亲和力的大小顺序为：

$HbO_2 > Hb(O_2)_2 > Hb(O_2)_3$

BPG与$Hb(O_2)_4$不结合

hemoglobin fetal HbF ($\alpha_2\gamma_2$)

对氧的亲和力比成人高

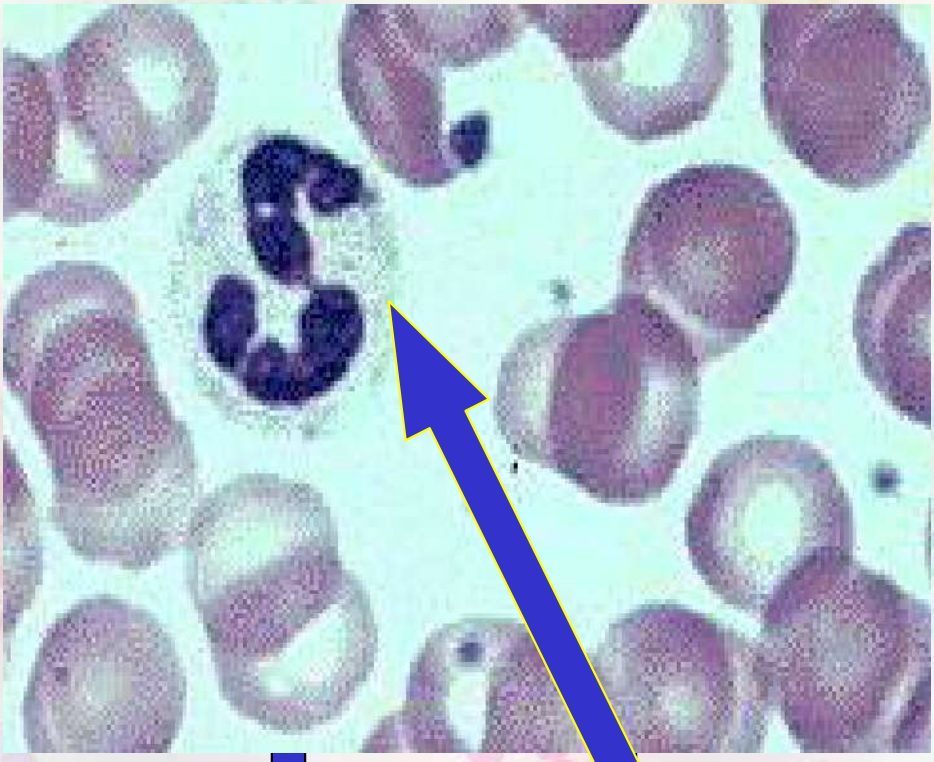
——Ser取代His

与BPG结合能力减弱

四、血红蛋白分子病

分子病：由于基因突变，导致蛋白质中氨基酸种类发生变化，并引起功能降低或丧失。

镰刀型贫血症（**sickle-cell anemia**）



- 镰刀状贫血病—血液中大量出现镰刀红细胞，患者因此缺氧窒息

- 它是最早认识的一种分子病
- 死亡率极高
- 由于遗传基因突变导致血红蛋白分子结构突变

- *正常细胞　镰刀形细胞*

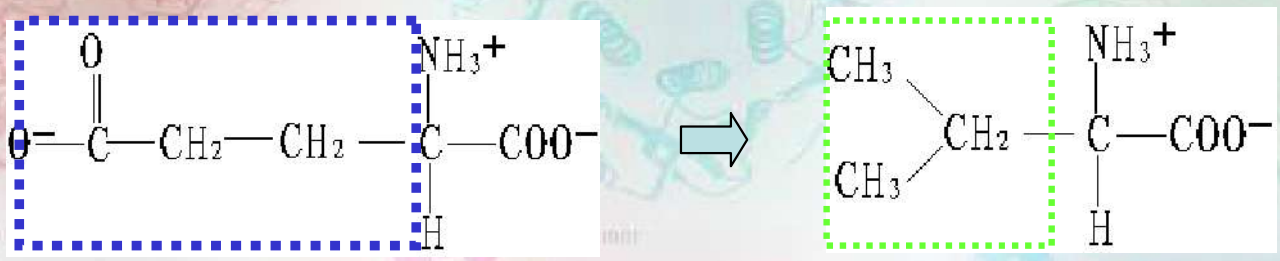
N

正常型 **---Val-His-Leu-Thr-Pro-Glu-Lys ---**

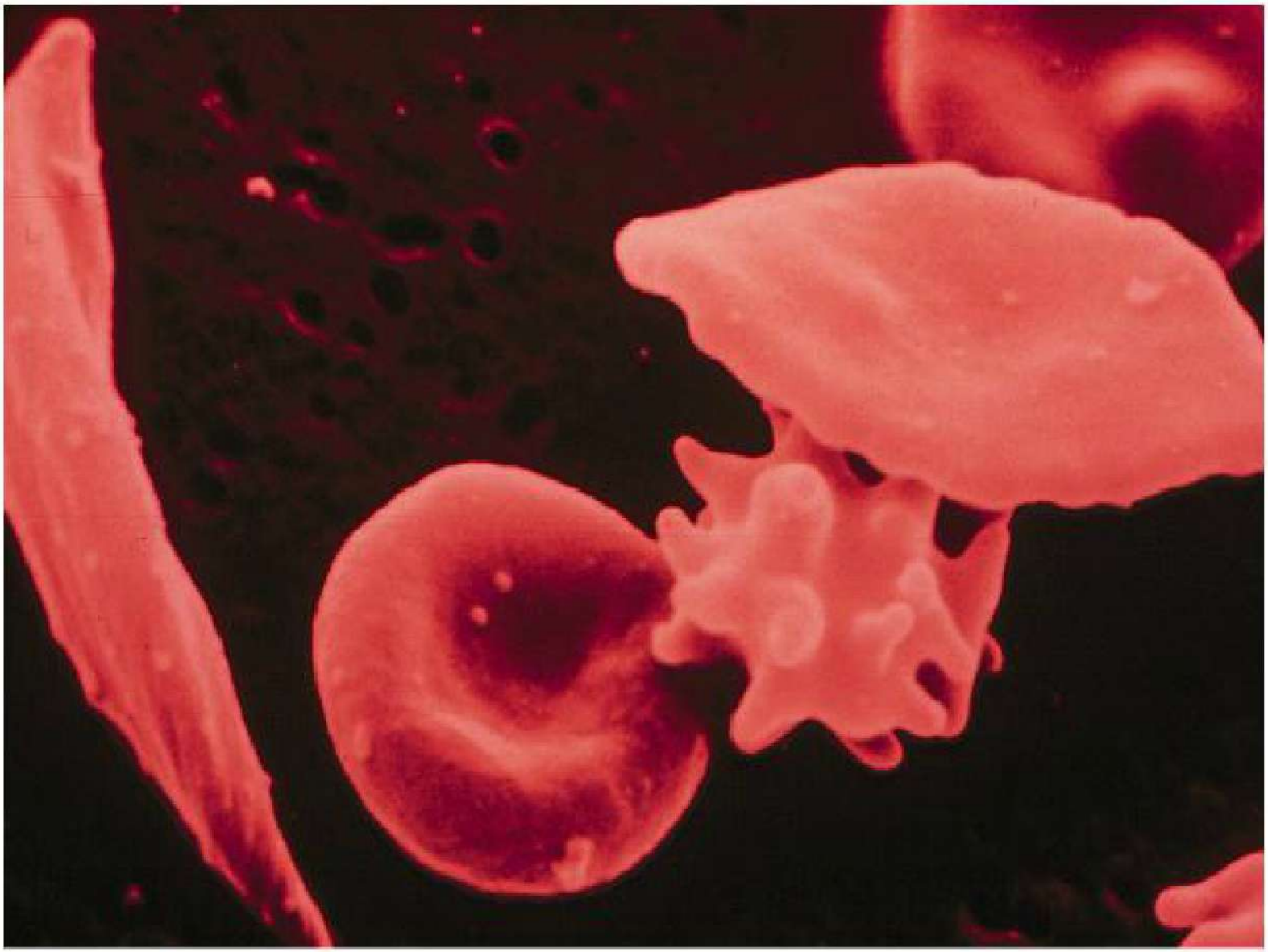
β链 *谷氨酸*

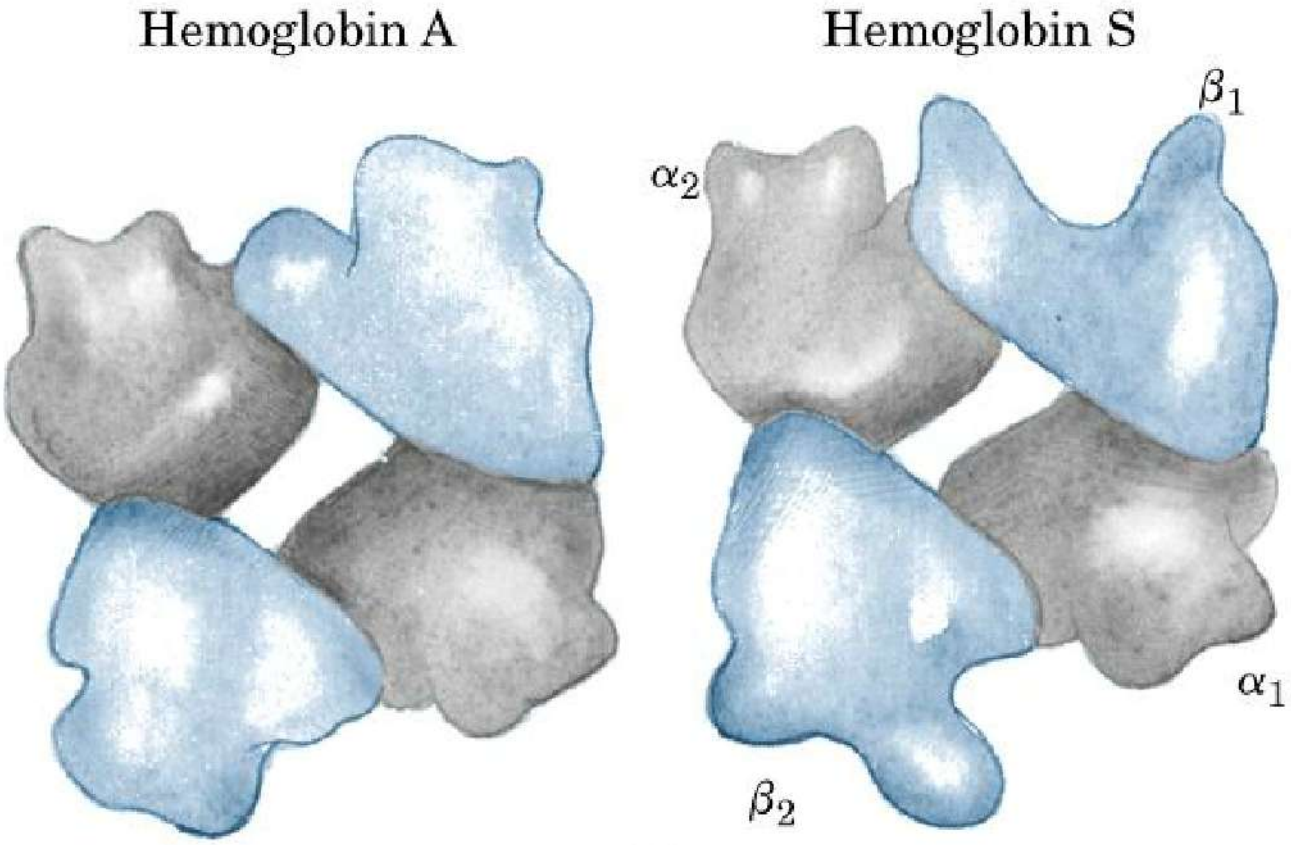
镰刀型 **---Val-His-Leu-Thr-Pro-Val-Lys ---**

β链 *缬氨酸*

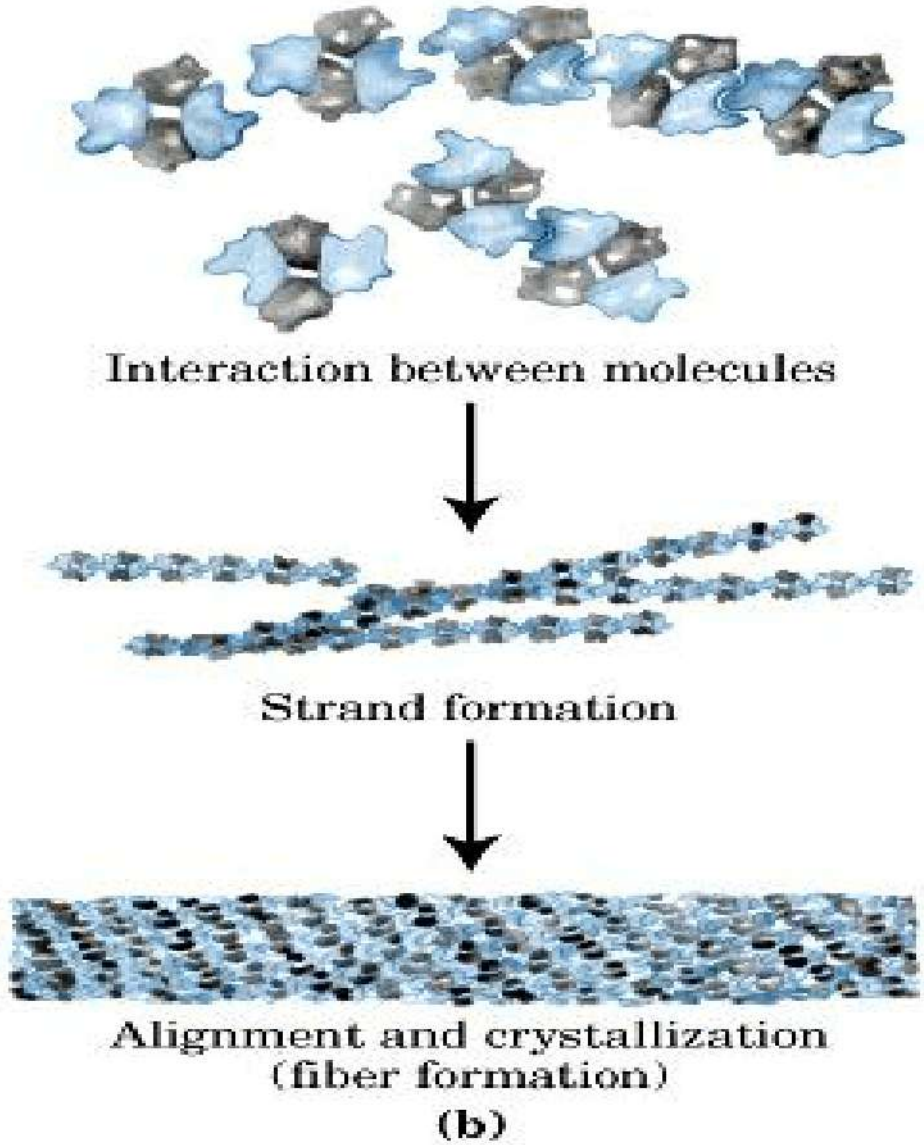


（极性） （非极性）



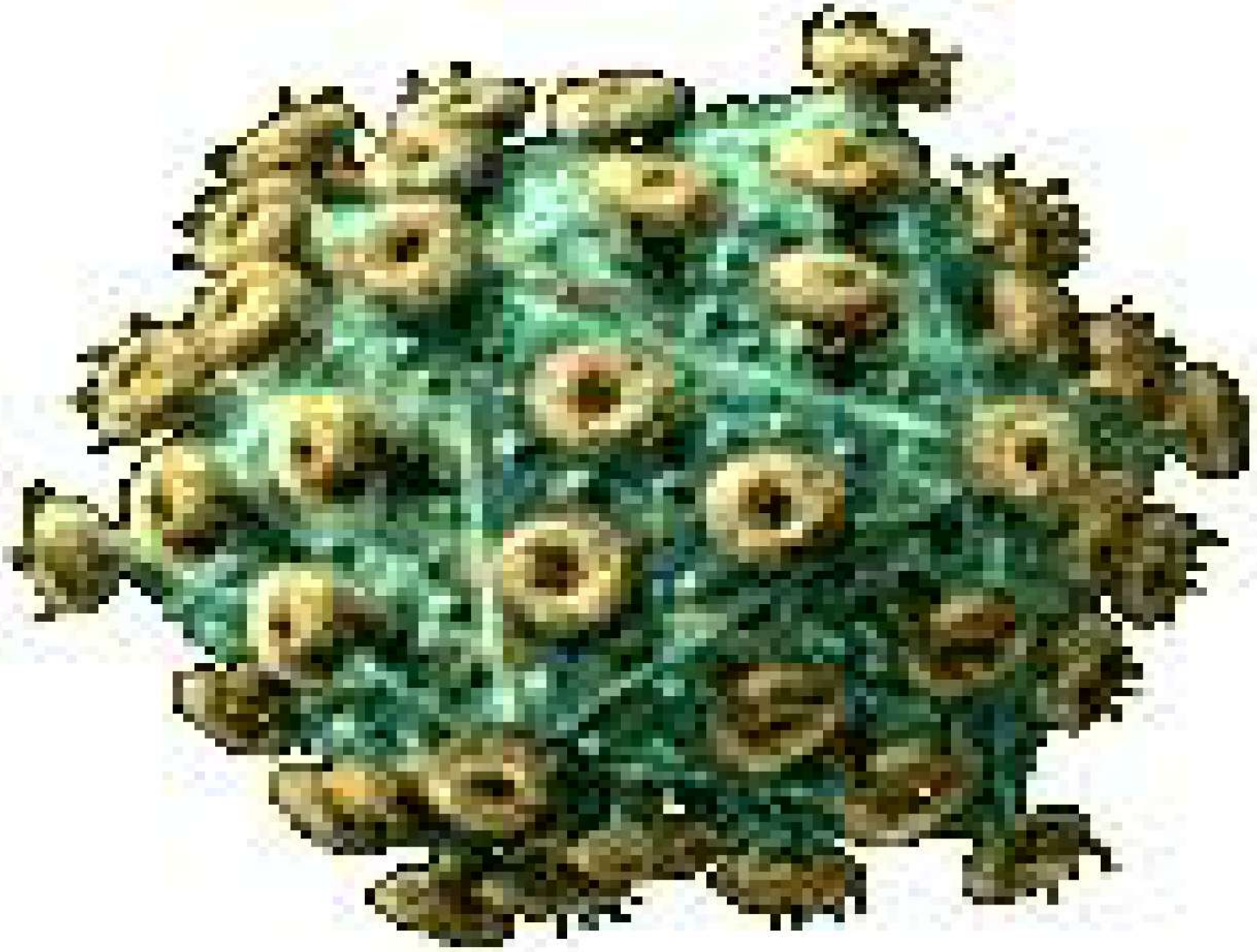


(a)


Interaction between molecules
Strand formation
Alignment and crystallization
(fiber formation)

(b)

五、与免疫有关的蛋白质



（一）体内参与免疫反应的淋巴细胞

T 淋巴细胞　　胸腺　　细胞免疫

B 淋巴细胞　　骨髓　　体液免疫

抗体

巨噬细胞

table 7–2

Some Types of Leukocytes Associated with the Immune System

Cell type	Function
Macrophages	Ingest large particles and cells by phagocytosis
B lymphocytes (B cells)	Produce and secrete antibodies
T lymphocytes (T cells)	
Cytotoxic (killer) T cells (T_C)	Interact with infected host cells through receptors on T-cell surface
Helper T cells (T_H)	Interact with macrophages and secrete cytokines (interleukins) that stimulate T_C, T_H, and B cells to proliferate.

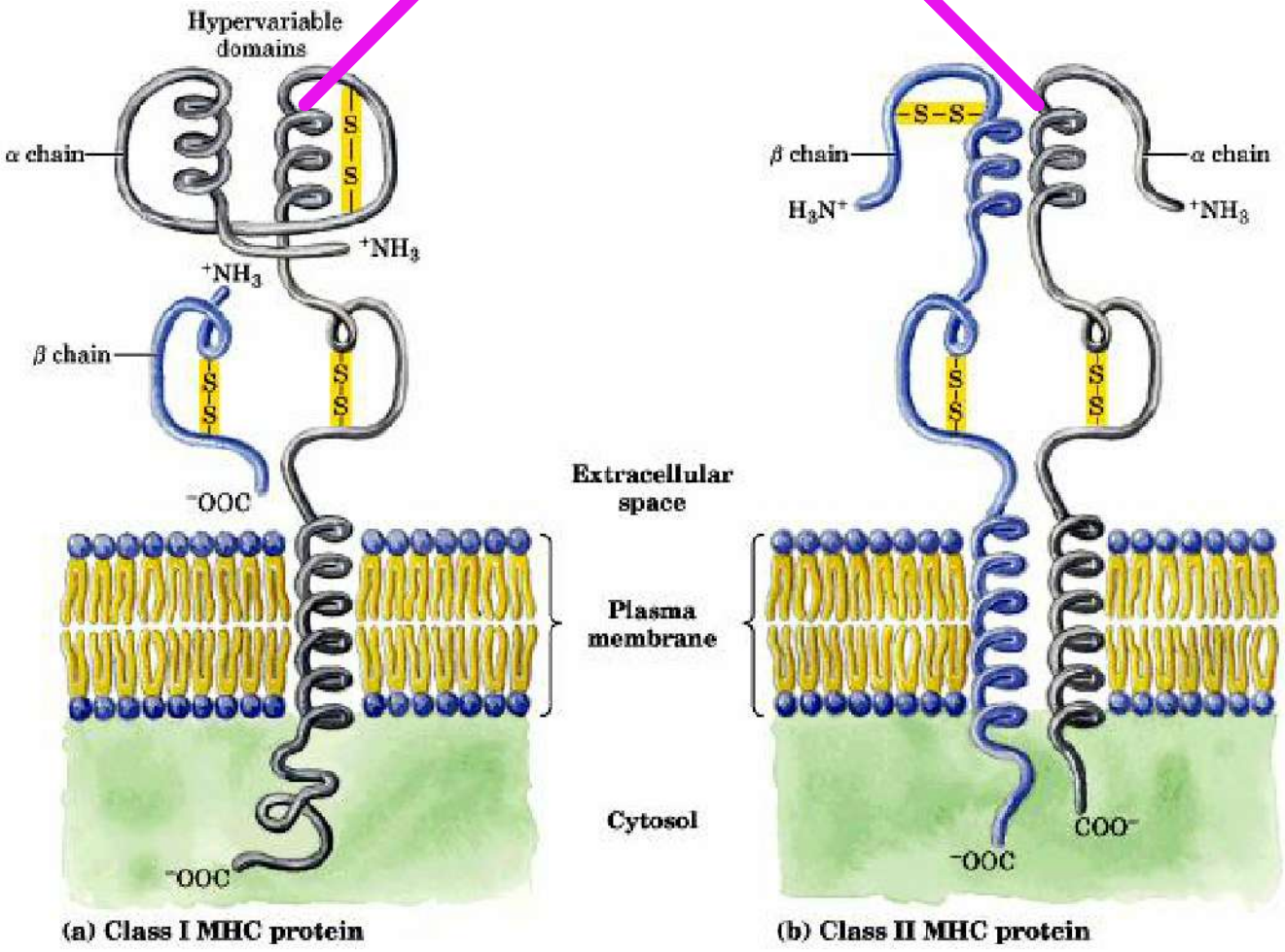
（二）与免疫有关的蛋白

1、主要组织相容性复合体

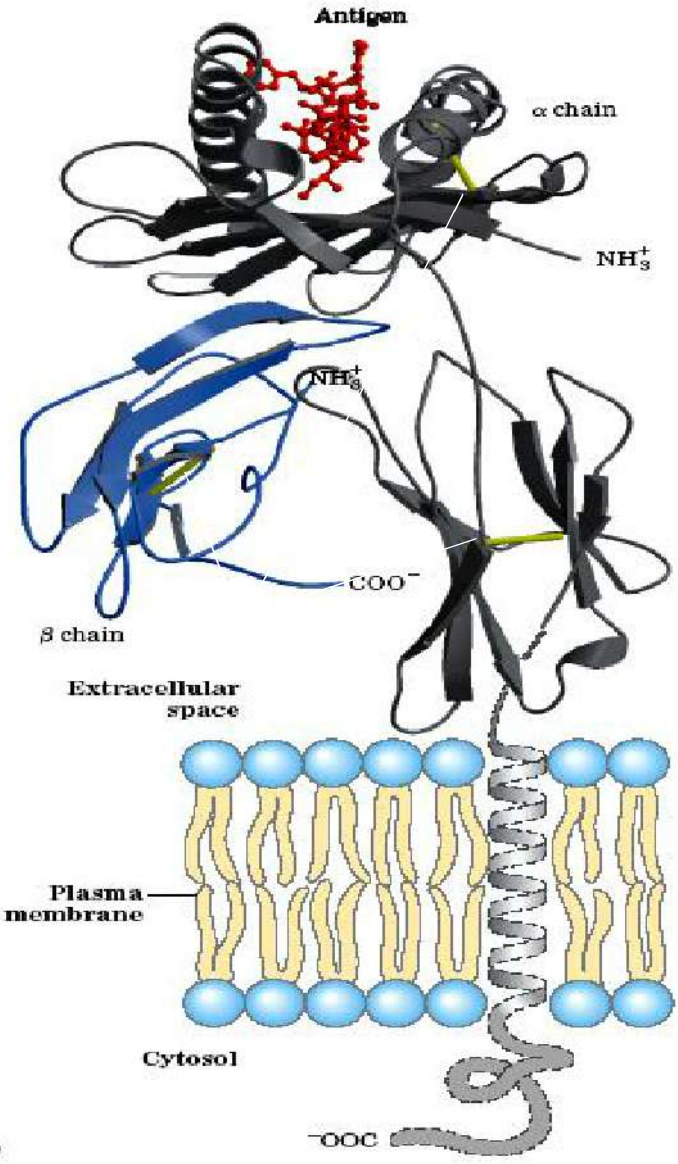
（major histocompatibility complex， MHC ）

——膜蛋白、呈递抗原给T细胞

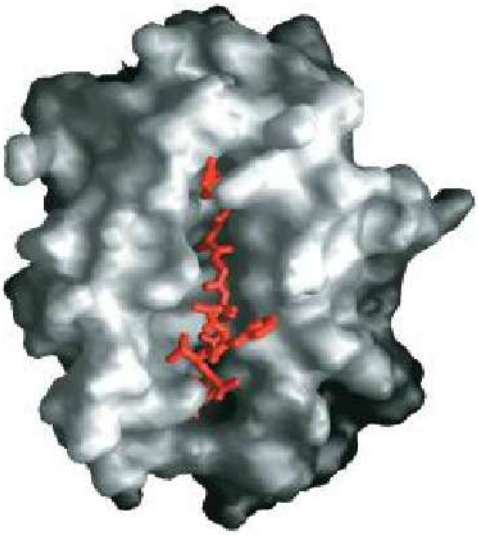
结合抗原肽的裂隙


Hypervariable domains
α chain
β chain
+NH3
+NH3
+NH3
S–S
S–S
S–S
⁻OOC
⁻OOC
Extracellular space
Plasma membrane
Cytosol
(a) Class I MHC protein
β chain
α chain
H3N+
+NH3
–S–S–
S–S
S–S
COO⁻
⁻OOC
(b) Class II MHC protein

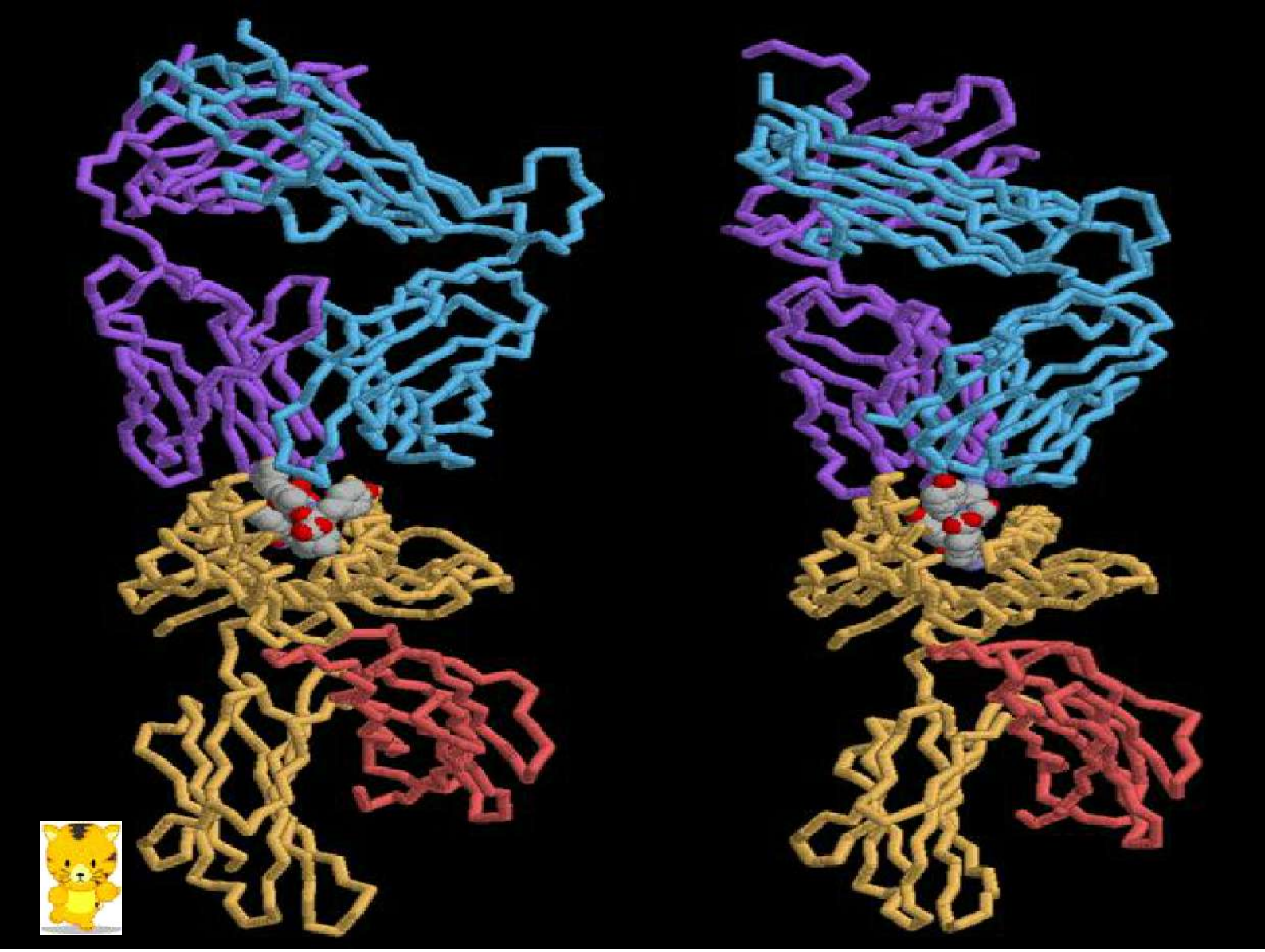
人：MHC Ⅰ

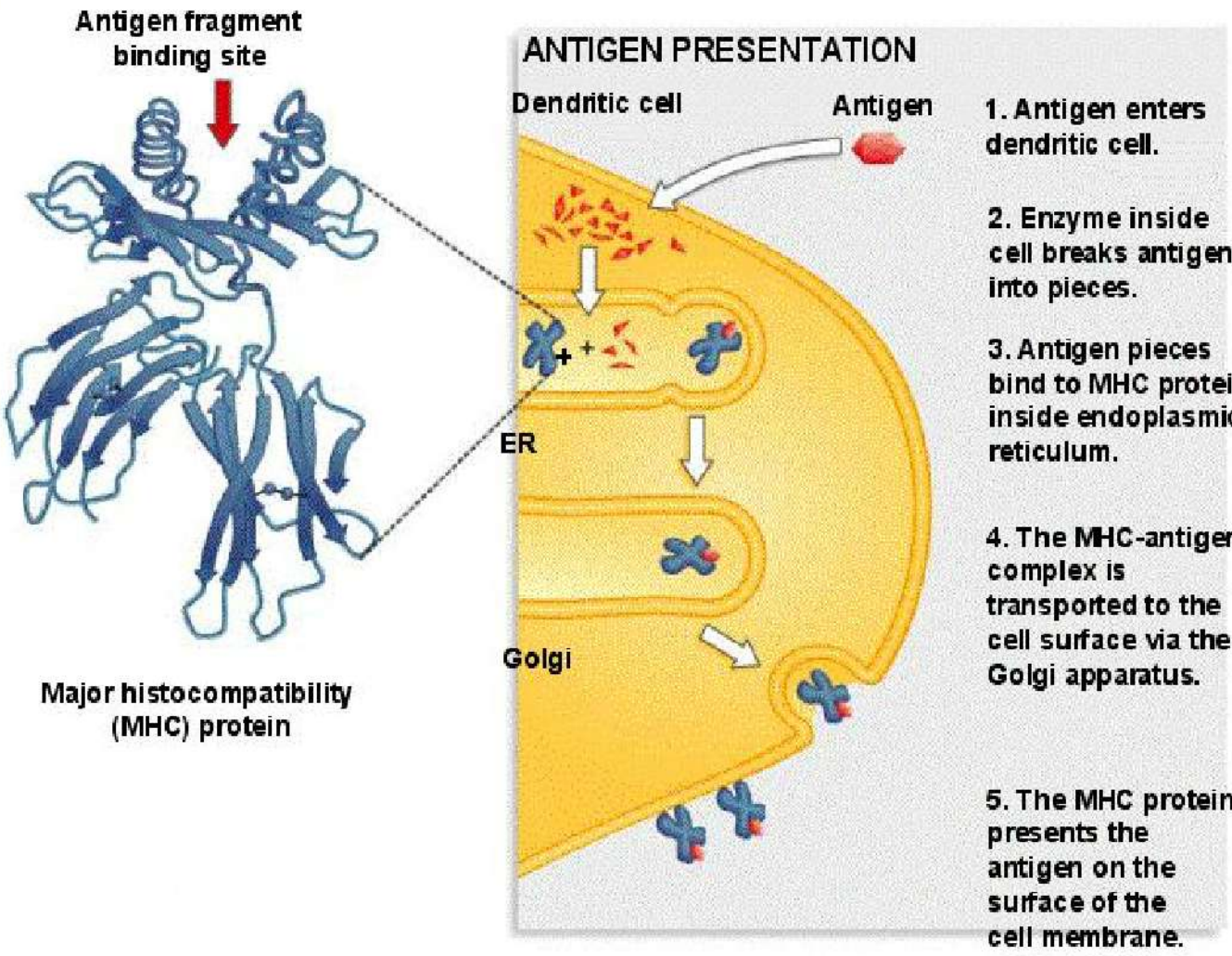

Antigen
α chain
NH_3^+
NH_3^+
COO^-
β chain
Extracellular space
Plasma membrane
Cytosol
^-OOC

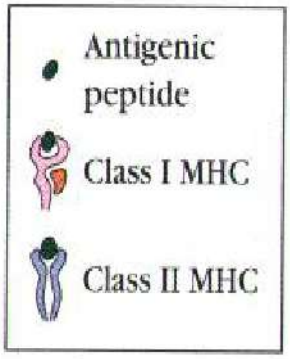
(a)

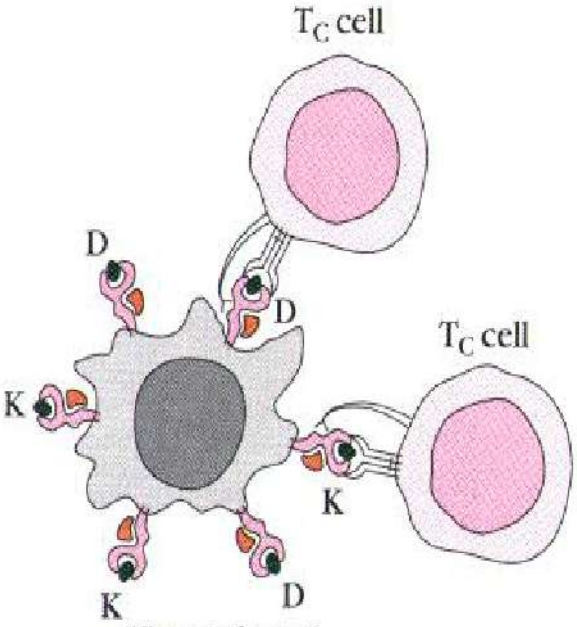


(b)

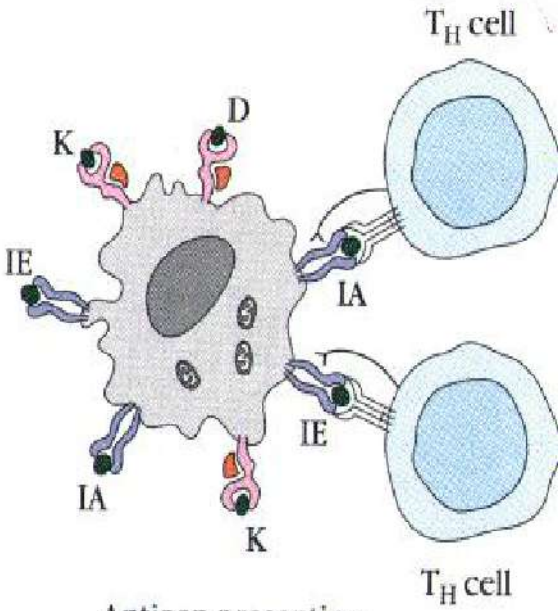



Antigen fragment binding site
Major histocompatibility (MHC) protein
ANTIGEN PRESENTATION
Dendritic cell
Antigen
ER
Golgi
1. Antigen enters dendritic cell.
2. Enzyme inside cell breaks antigen into pieces.
3. Antigen pieces bind to MHC protein inside endoplasmic reticulum.
4. The MHC-antigen complex is transported to the cell surface via the Golgi apparatus.
5. The MHC protein presents the antigen on the surface of the cell membrane.

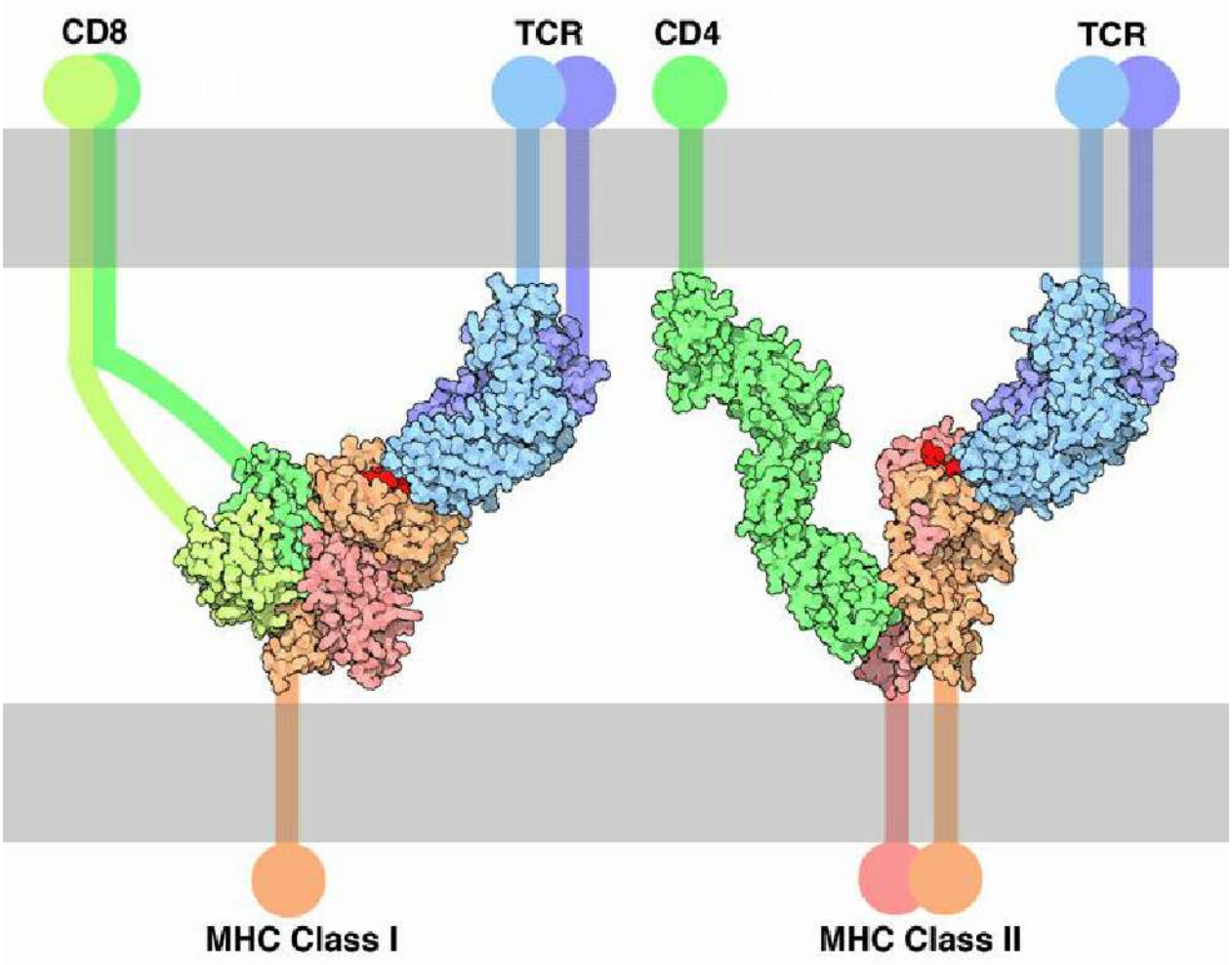


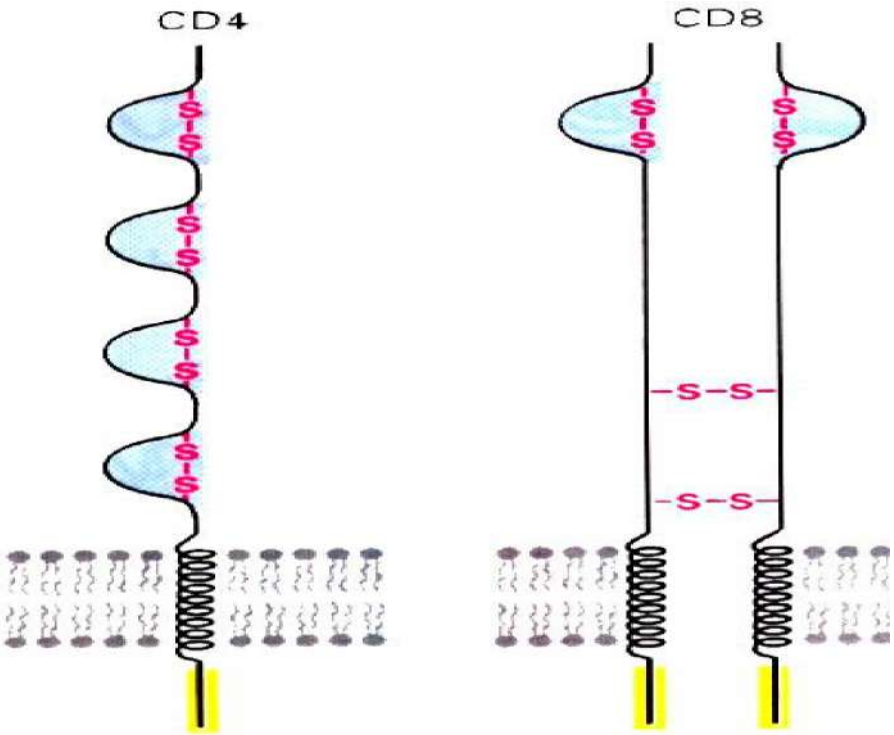


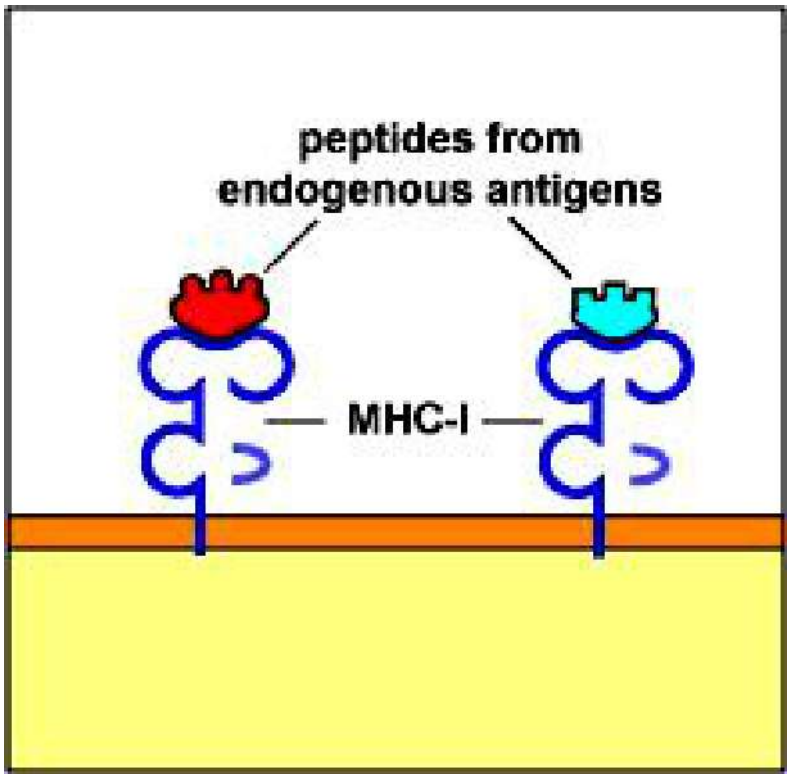
Virus-infected mouse cell



Antigen-presenting mouse cell

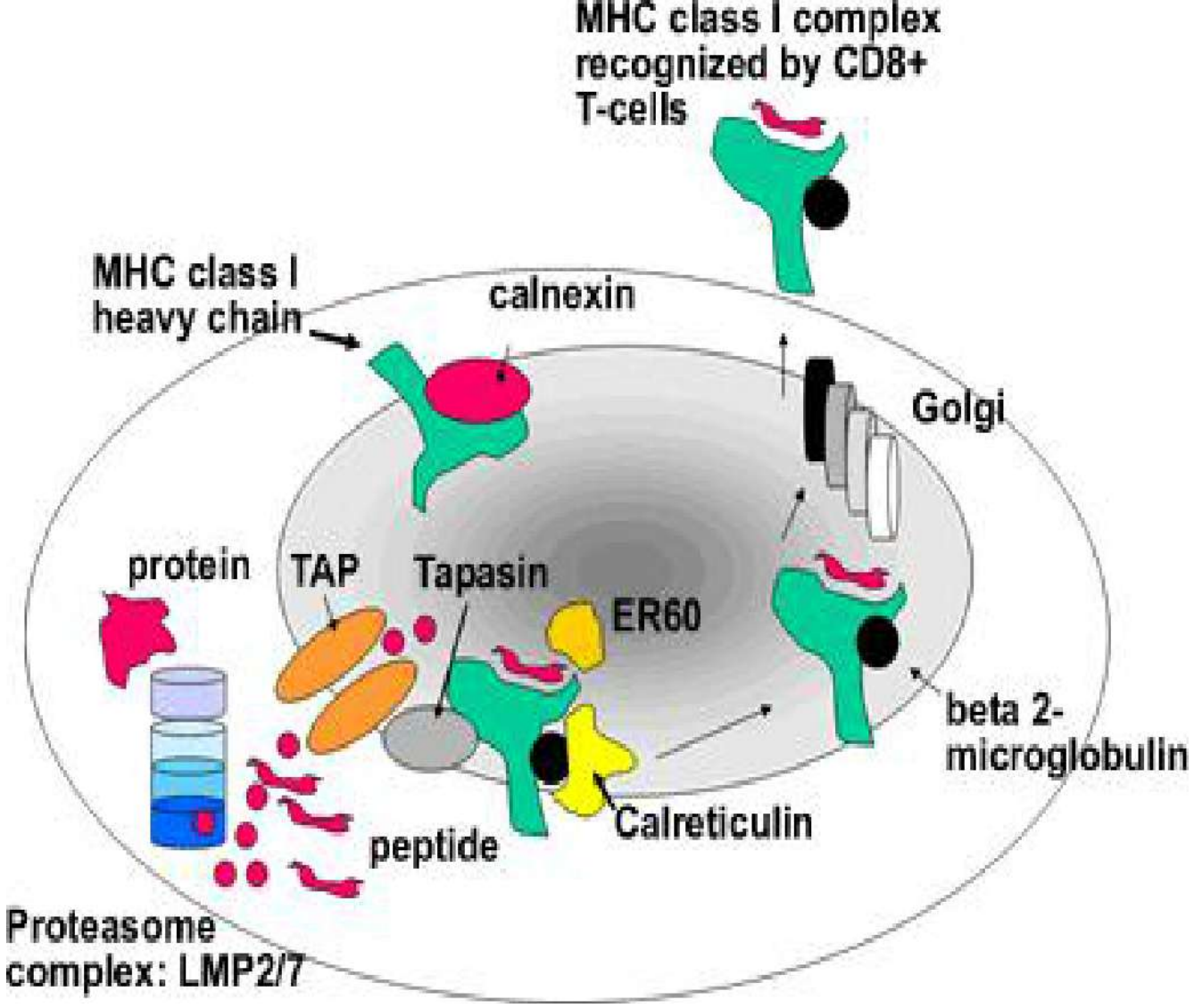

CD8
TCR
CD4
TCR
MHC Class I
MHC Class II

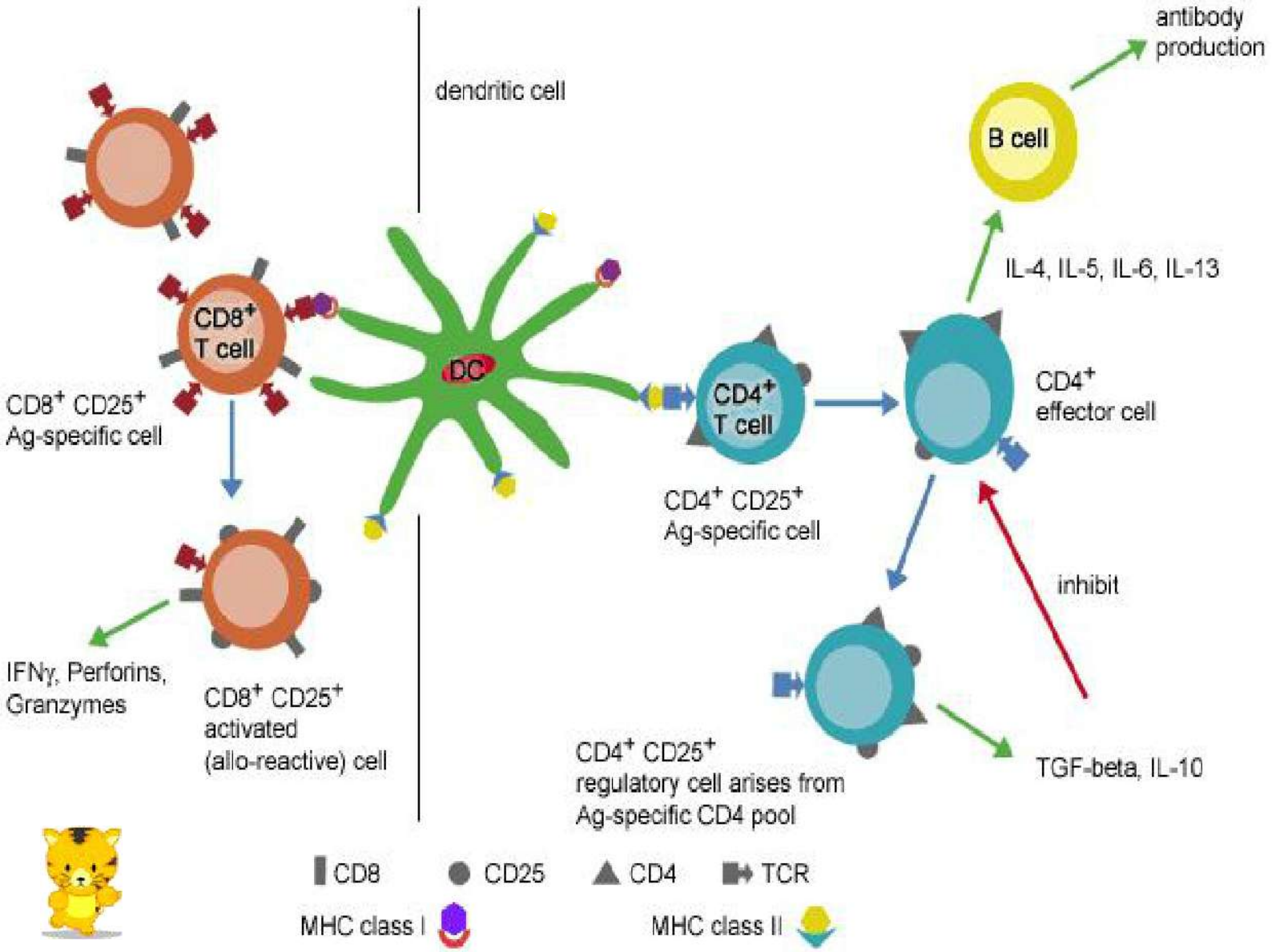

CD4
CD8
S-S
S-S
S-S
S-S
S-S
S-S
S-S
S-S
S-S



存在于：几乎所有的脊椎动物细胞表面

结合并展示：细胞内随机发生的蛋白降解及更新衍生来的肽


MHC class I complex
recognized by CD8+
T-cells
MHC class I
heavy chain
calnexin
Golgi
protein
TAP
Tapasin
ER60
beta 2-
microglobulin
Calreticulin
peptide
Proteasome
complex: LMP2/7


antibody production
dendritic cell
B cell
IL-4, IL-5, IL-6, IL-13
CD8+ T cell
DC
CD4+ T cell
CD4+ effector cell
CD8+ CD25+ Ag-specific cell
CD4+ CD25+ Ag-specific cell
inhibit
IFNγ, Perforins, Granzymes
CD8+ CD25+ activated (allo-reactive) cell
CD4+ CD25+ regulatory cell arises from Ag-specific CD4 pool
TGF-beta, IL-10
CD8
CD25
CD4
TCR
MHC class I
MHC class II

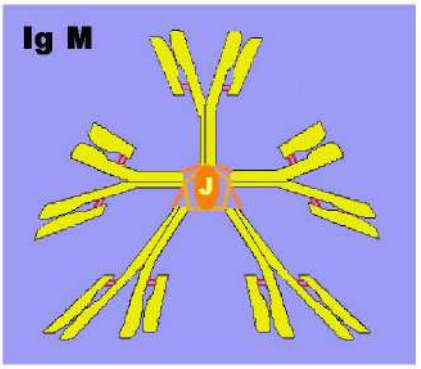
2、免疫球蛋白（immunoglobulin）

——可溶性血清糖蛋白

（1）分类

A、IgA：存在于身体的分泌物中

B、IgD：存在于B细胞表面



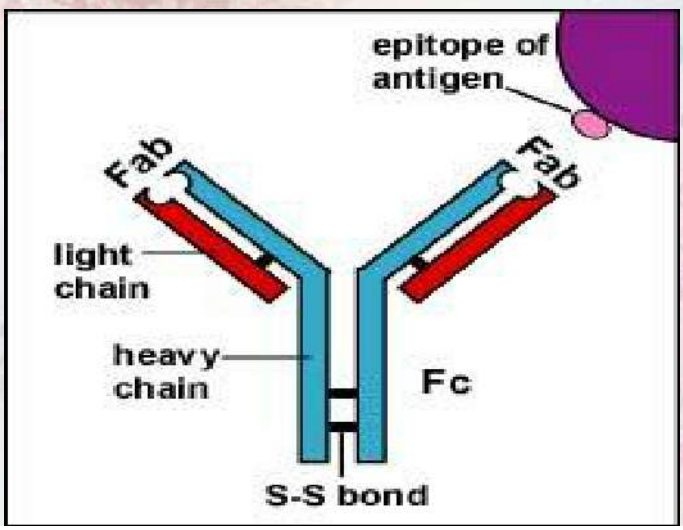
C、IgE：与过敏反应有关

D、IgM：初次免疫反应初期产生

E、IgG：体内最多的一类

（2）结构特点

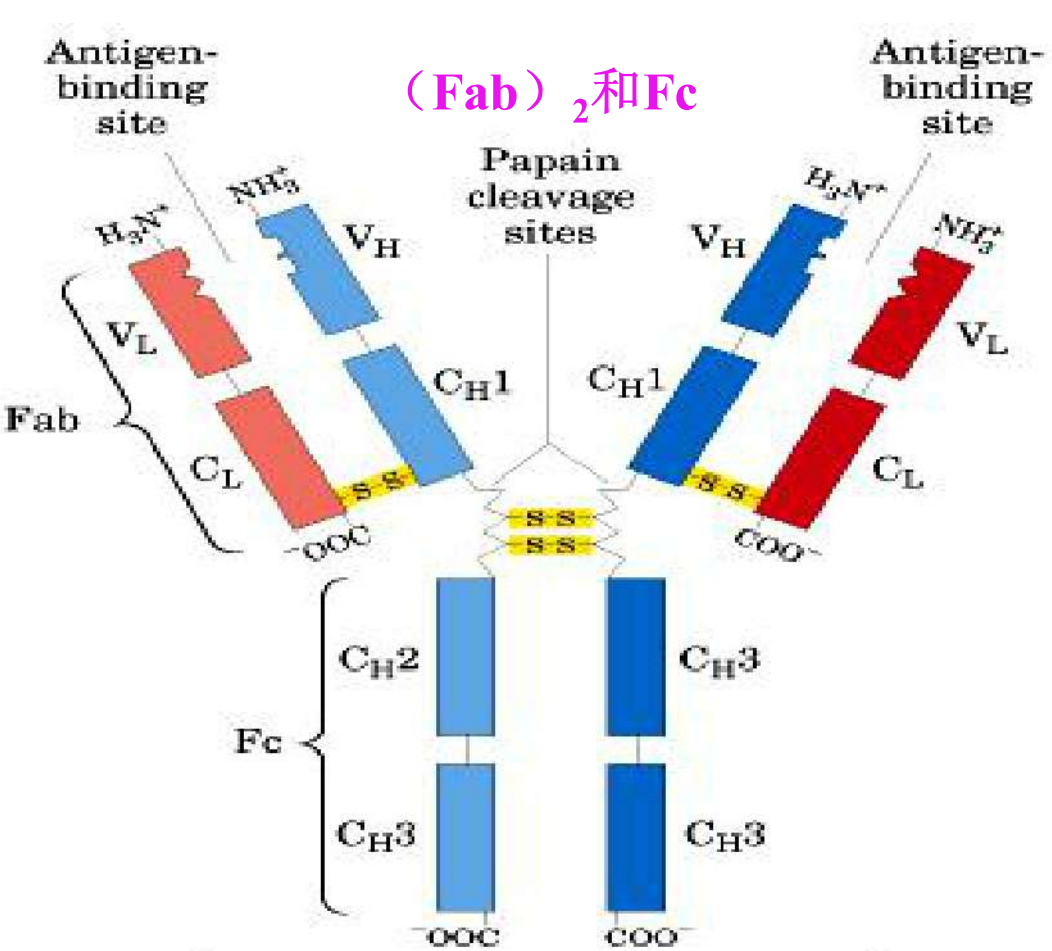
- 两条轻链（L）、两条重链（H）
- 每条链都有可变区（V）、恒定区（C）
- 可变区都在N端



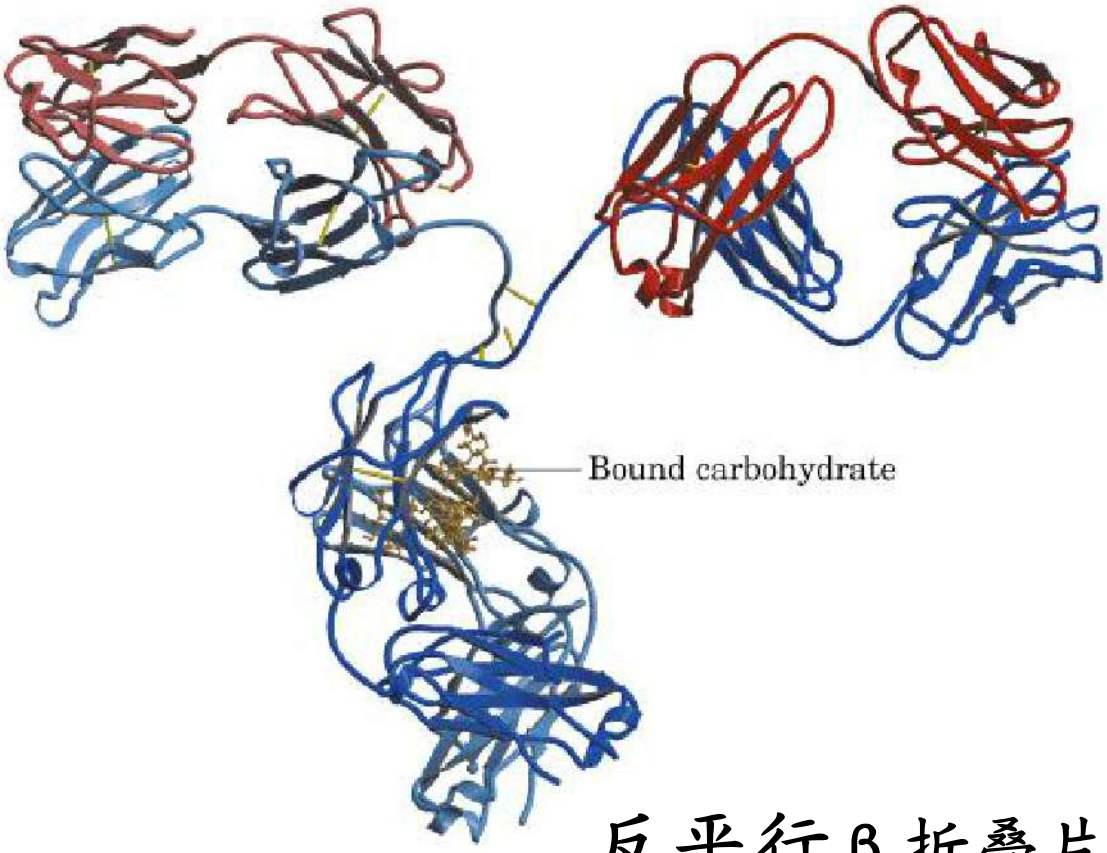
Fab：Fragment antigen binding

Fc： Fragment crystallizable

（Fab）$_2$和Fc

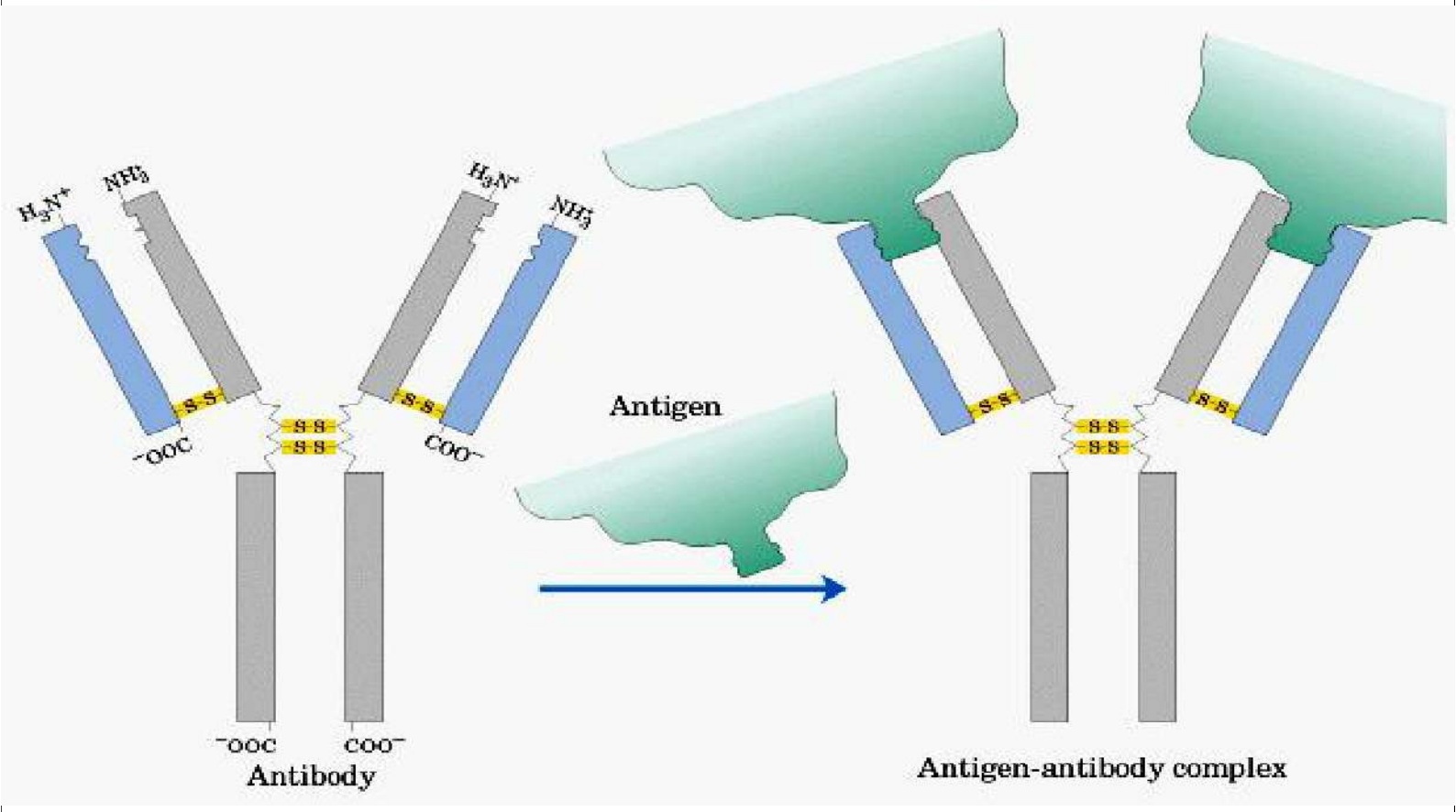

Antigen-binding site
Antigen-binding site
Papain cleavage sites
H_3N^+
NH_3^+
V_H
V_L
C_H1
C_L
Fab
S-S
^-OOC
COO^-
C_H2
C_H3
Fc
C = constant domain
V = variable domain
H, L = heavy, light chains

(a)

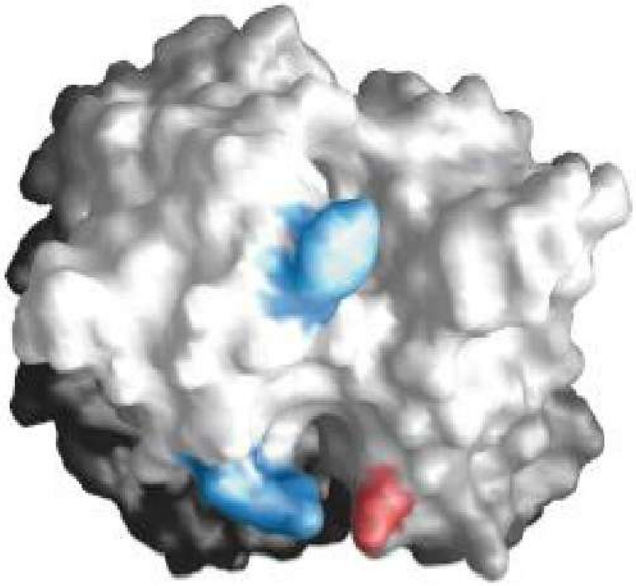


(b)

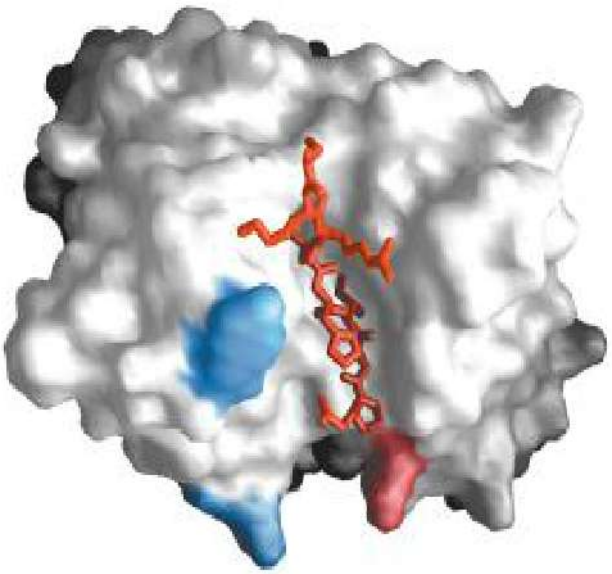
反平行β折疊片


Antigen
Antibody
Antigen-antibody complex

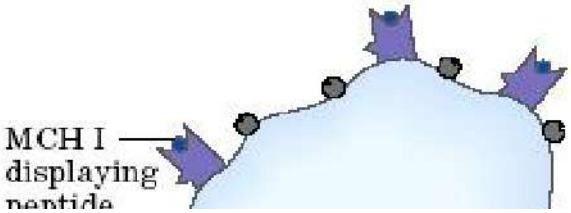
Fab与抗原的结合



(a) Conformation with no antigen bound

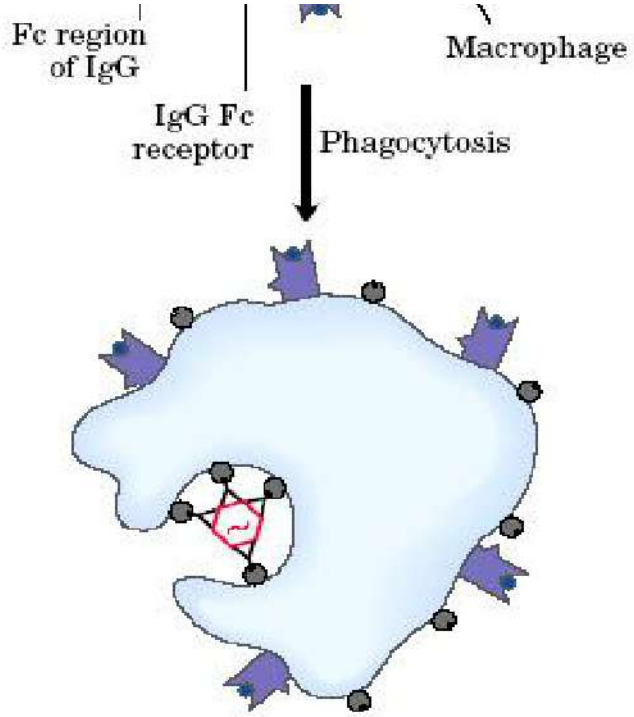


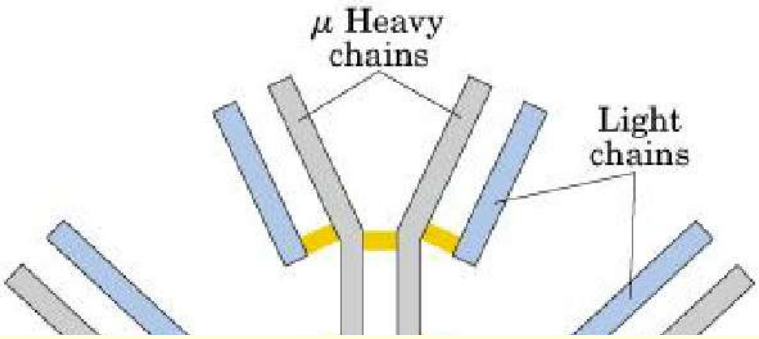
(c) Antigen bound (shown)

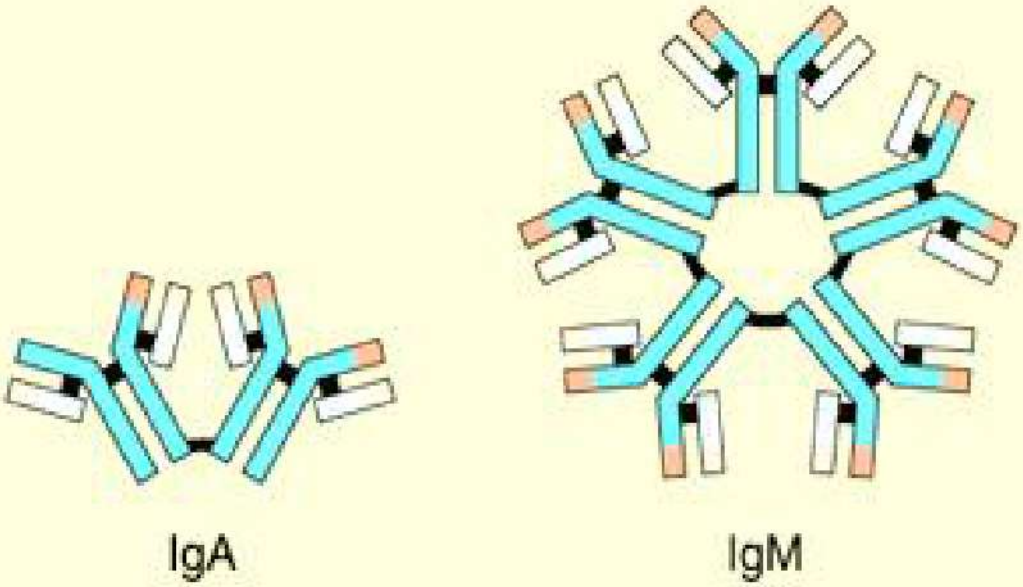


IgG是血液中参与免疫反应的最主要的抗体

IgG + 抗原 ⟶ 巨噬细胞结合、吞噬



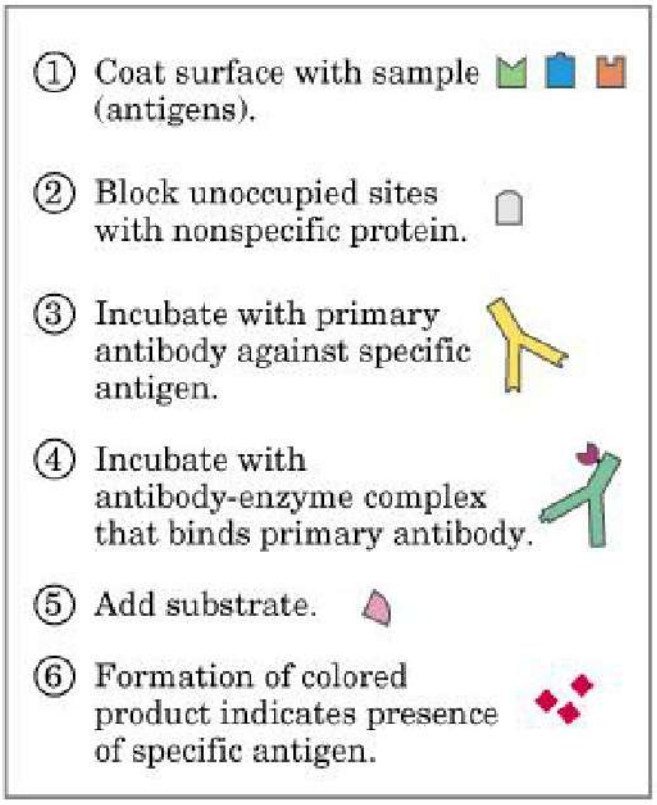


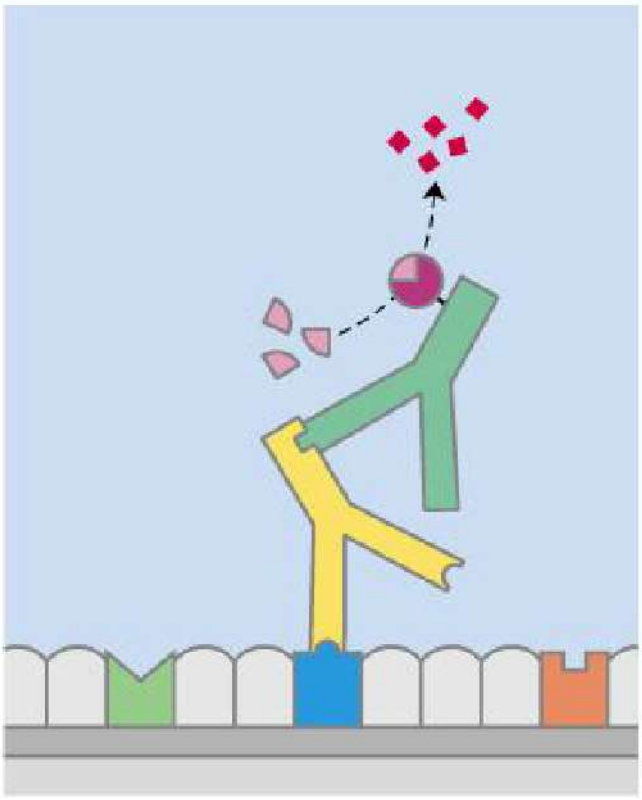


IgA

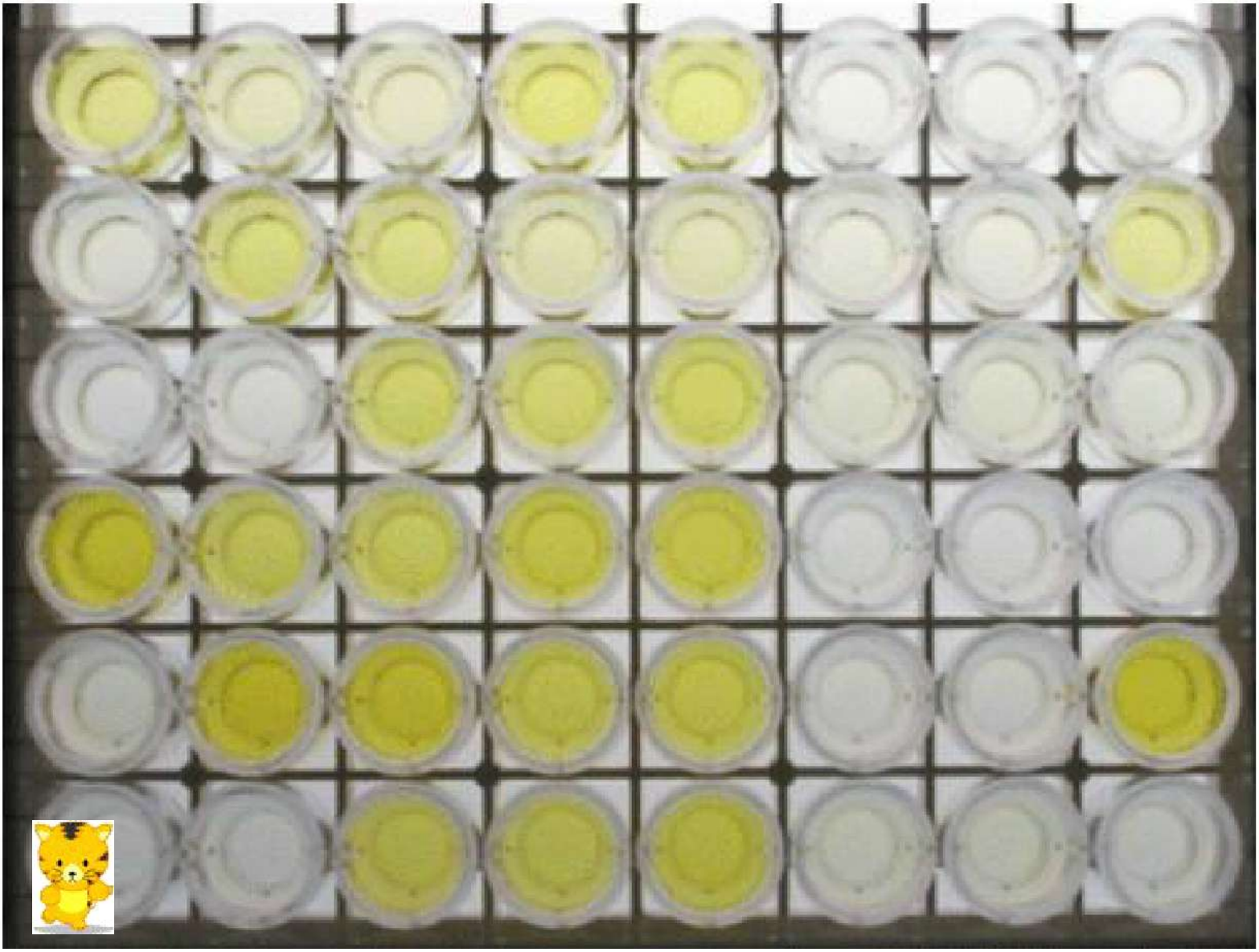
IgM

（3）基于抗原-抗体反应的生化分析方法

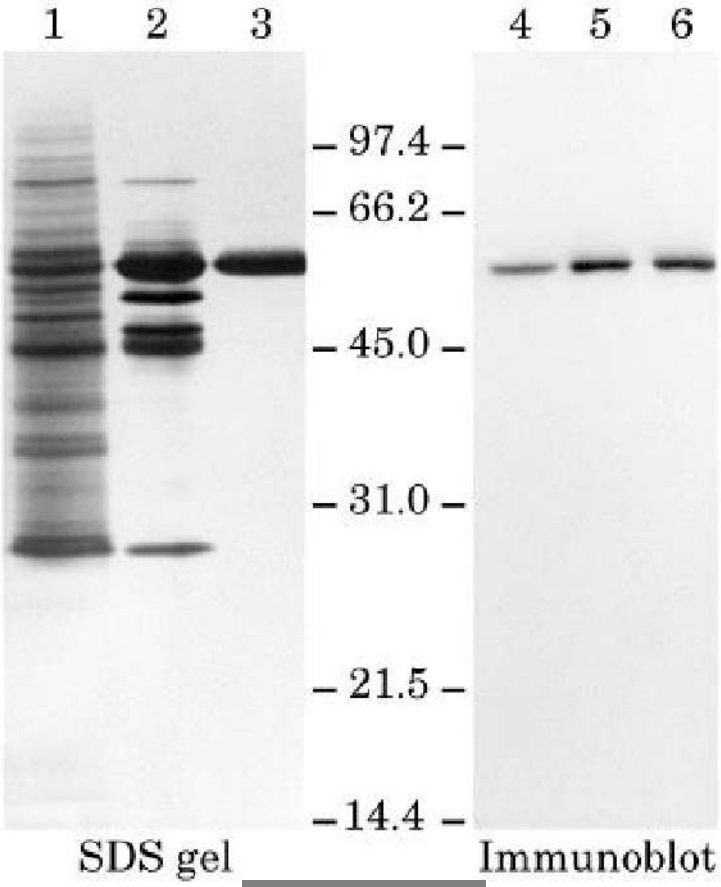




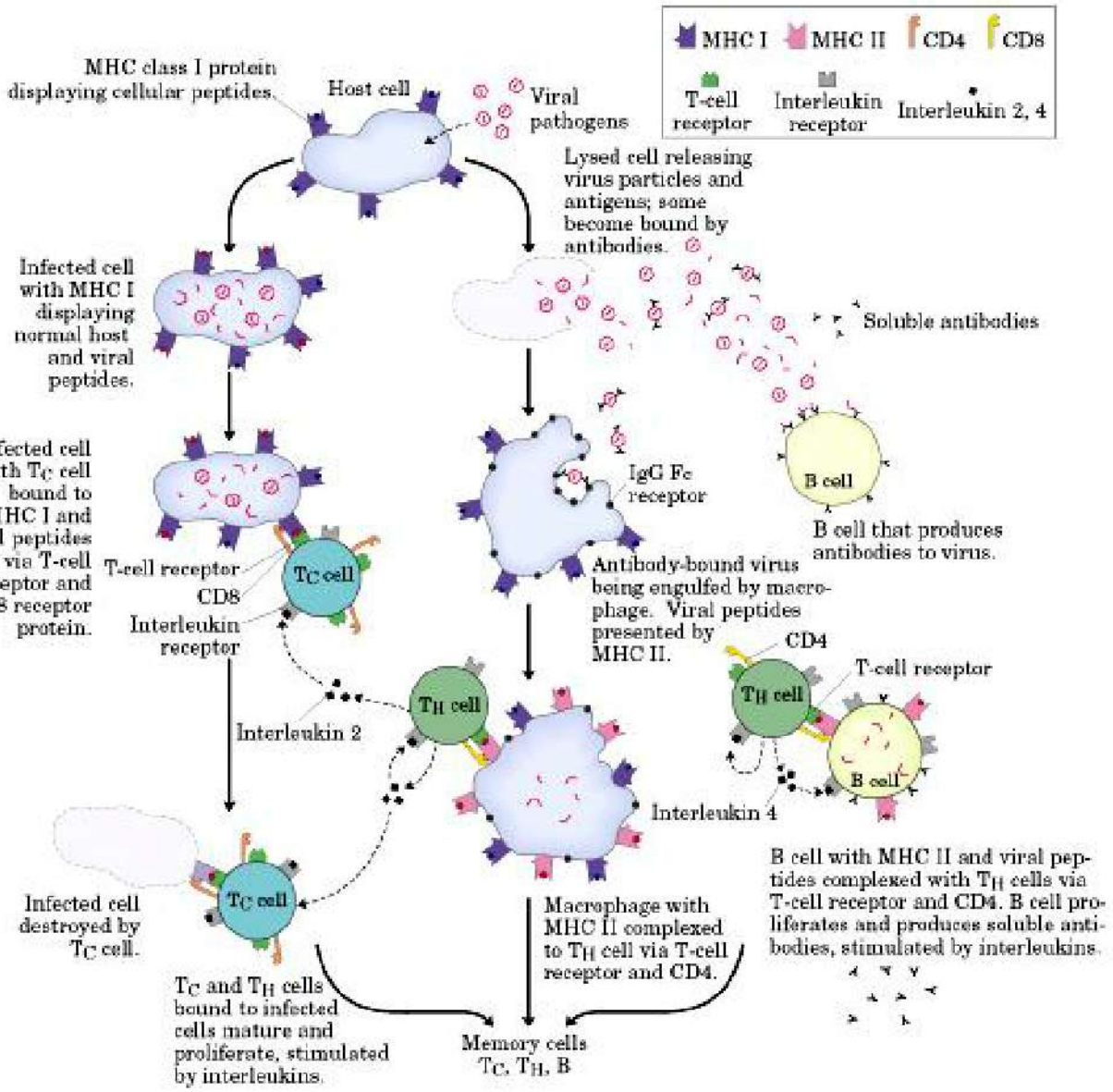
ELISA



样品纯化 前　后

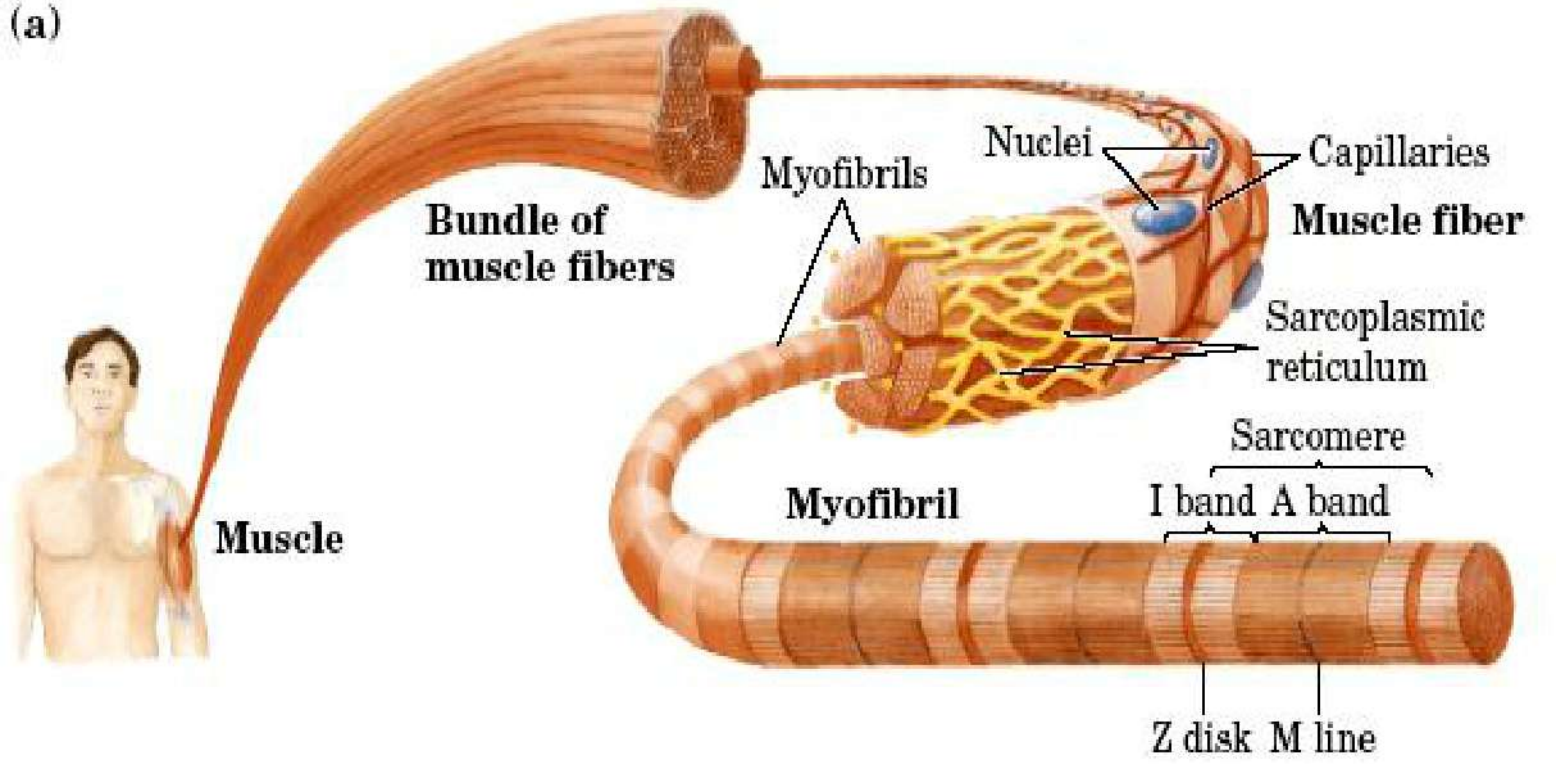


免疫印迹


MHC I
MHC II
CD4
CD8
T-cell receptor
Interleukin receptor
Interleukin 2, 4
MHC class I protein displaying cellular peptides.
Host cell
Viral pathogens
Lysed cell releasing virus particles and antigens; some become bound by antibodies.
Infected cell with MHC I displaying normal host and viral peptides.
Soluble antibodies
B cell
B cell that produces antibodies to virus.
IgG Fc receptor
Infected cell with T_C cell bound to MHC I and viral peptides via T-cell receptor and CD8 receptor protein.
T-cell receptor
CD8
Interleukin receptor
T_C cell
Antibody-bound virus being engulfed by macrophage. Viral peptides presented by MHC II.
CD4
T-cell receptor
T_H cell
B cell
Interleukin 2
Interleukin 4
B cell with MHC II and viral peptides complexed with T_H cells via T-cell receptor and CD4. B cell proliferates and produces soluble antibodies, stimulated by interleukins.
Infected cell destroyed by T_C cell.
Macrophage with MHC II complexed to T_H cell via T-cell receptor and CD4.
T_C and T_H cells bound to infected cells mature and proliferate, stimulated by interleukins.
Memory cells T_C, T_H, B

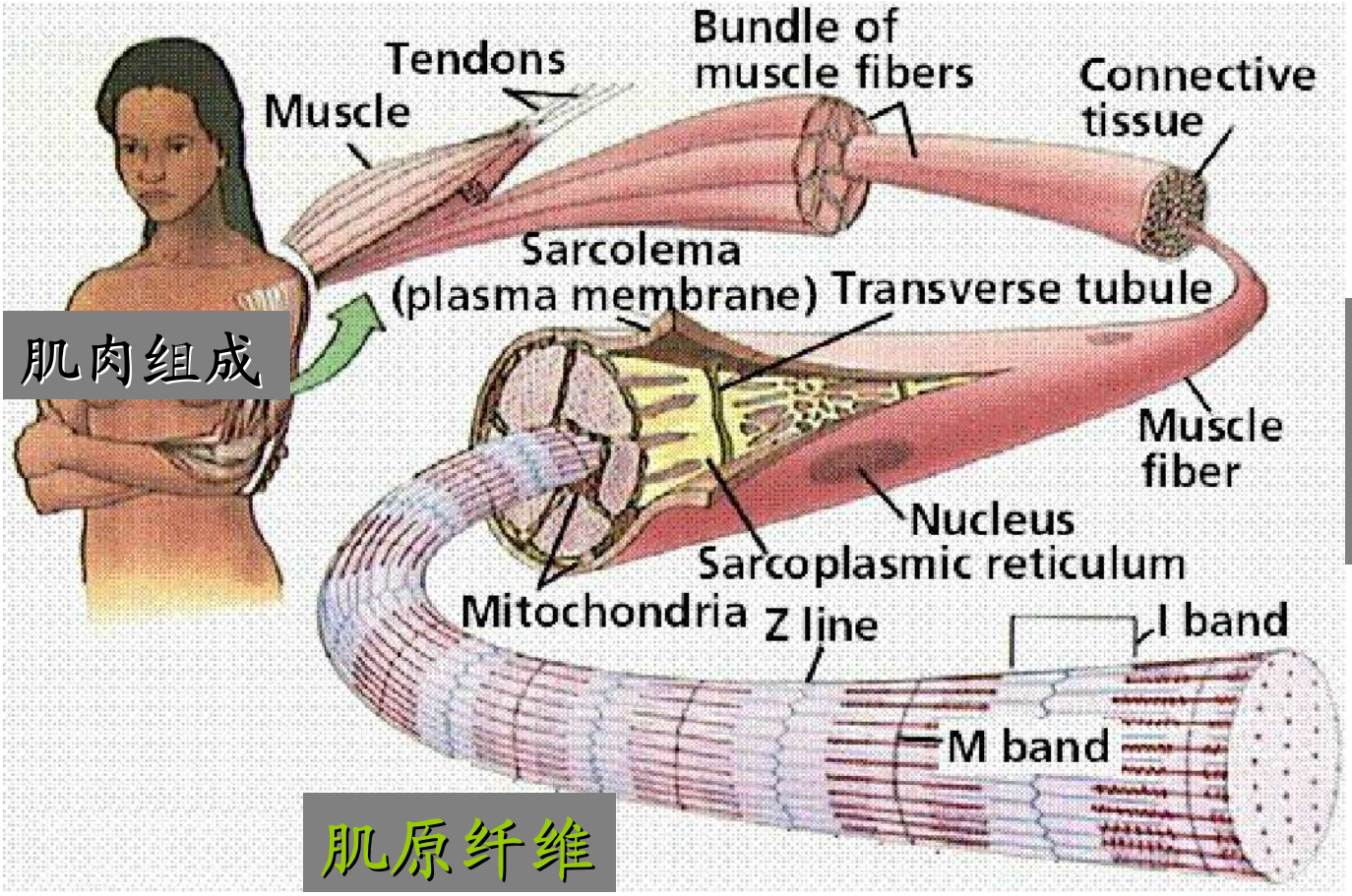
六、肌球蛋白和肌动蛋白

参与需能的收缩活动



肌肉

肌纤维束

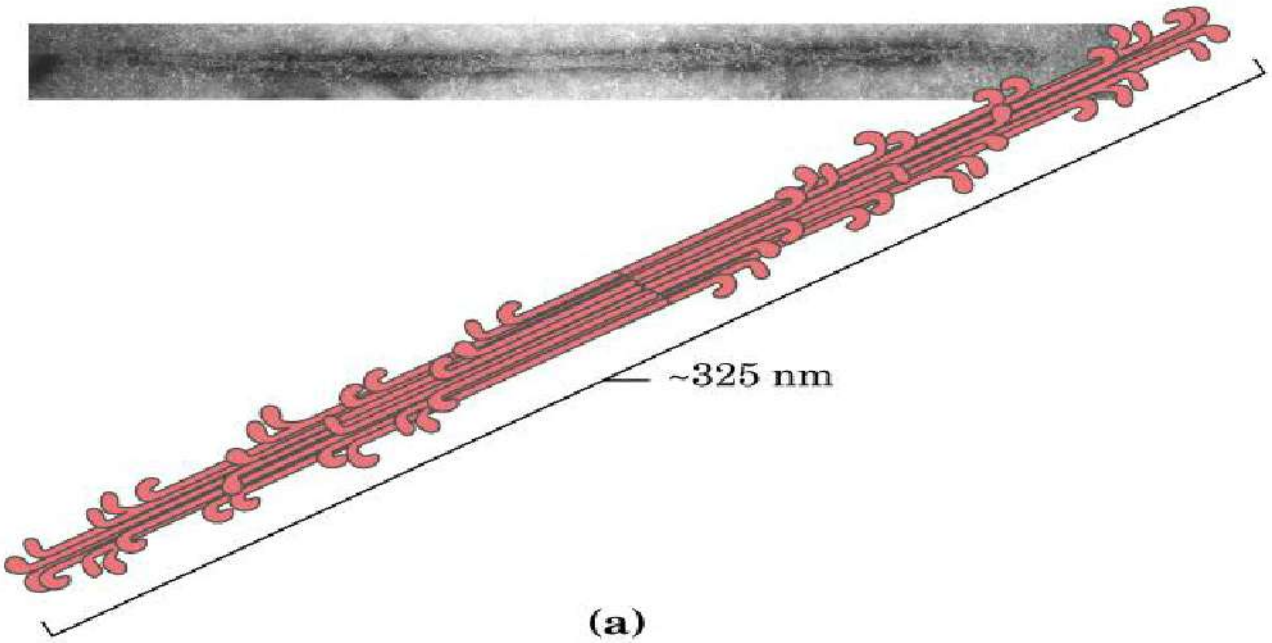


肌肉组成

肌纤维

肌原纤维

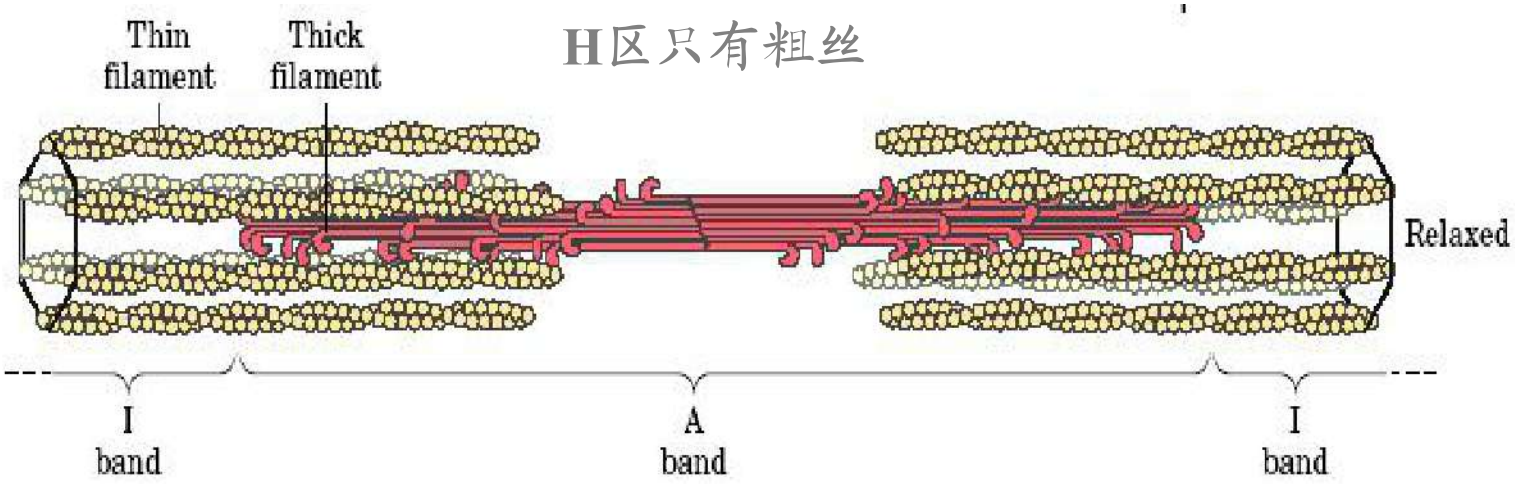
肌原纤维：明带和暗带

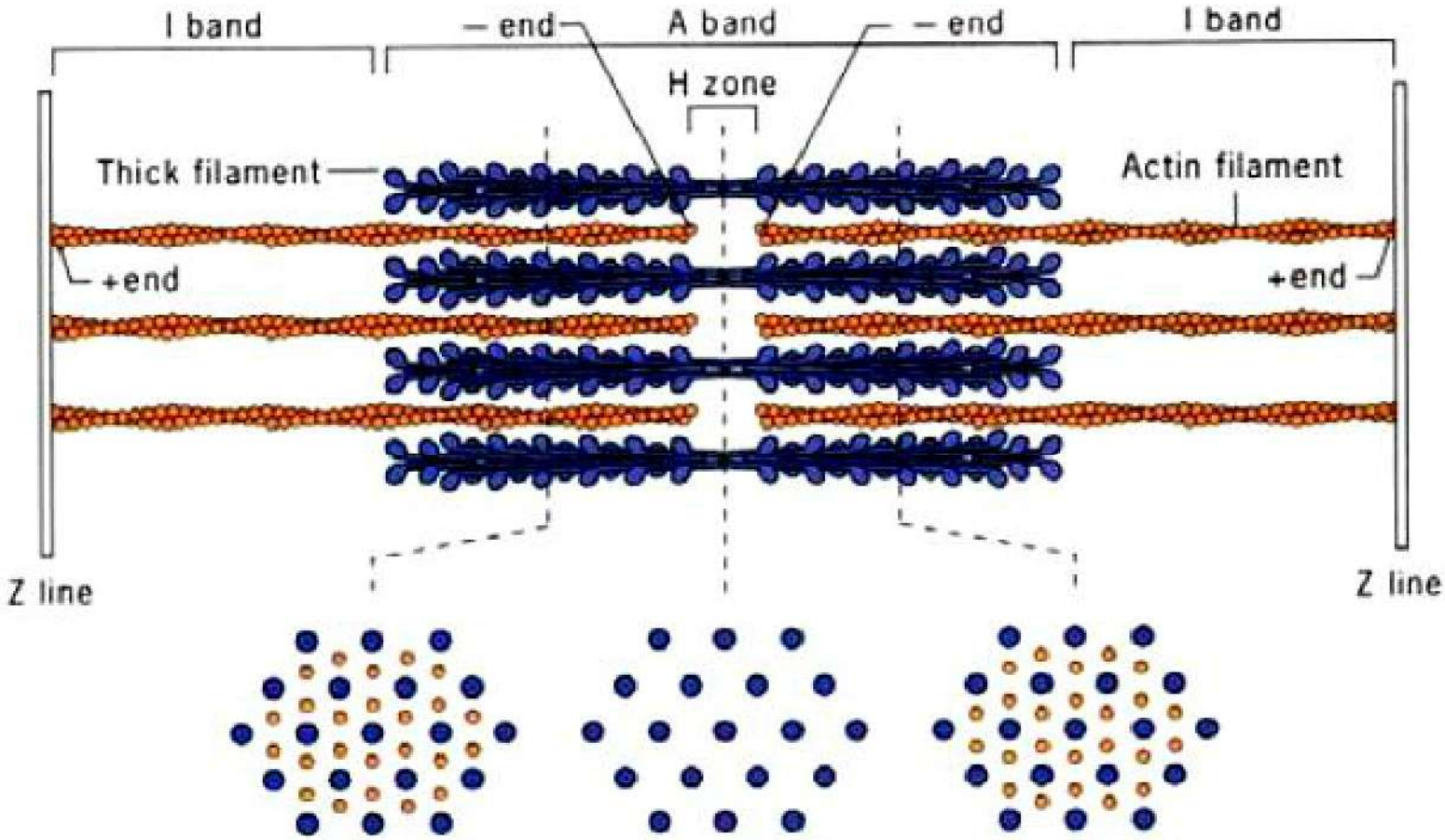


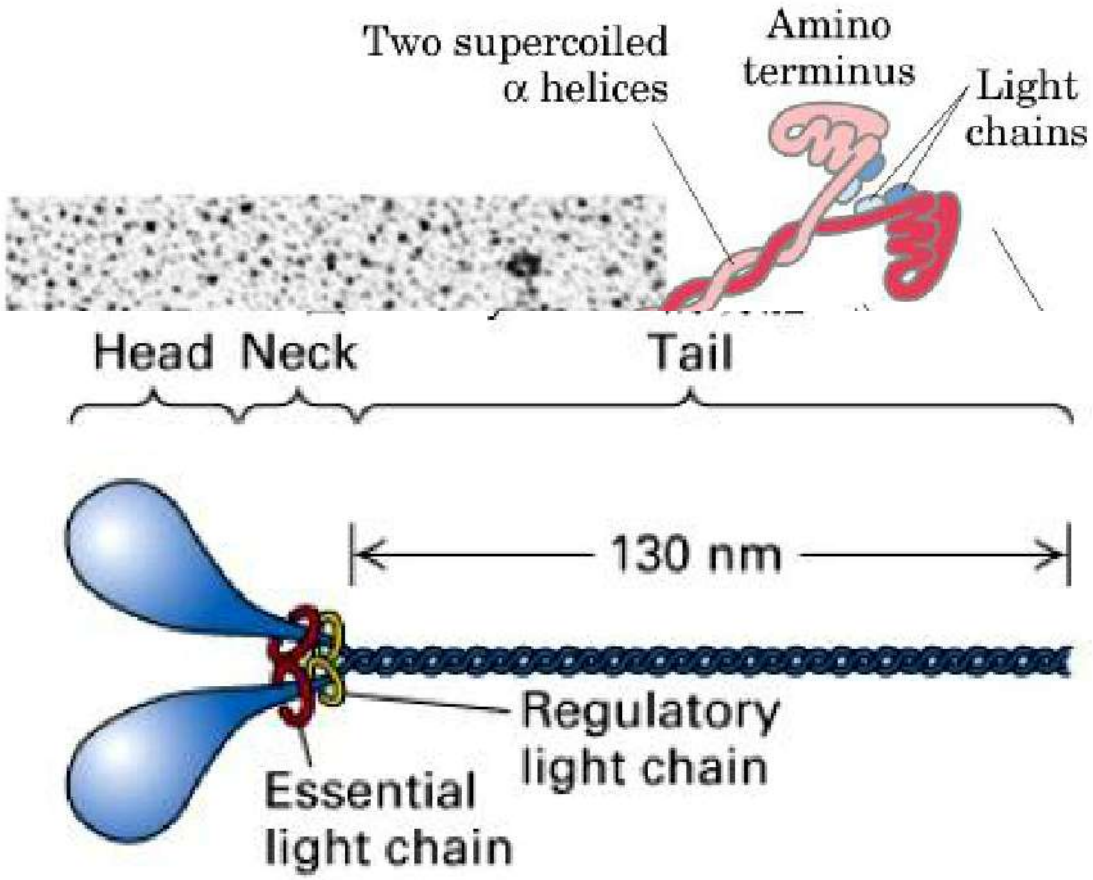
(a)

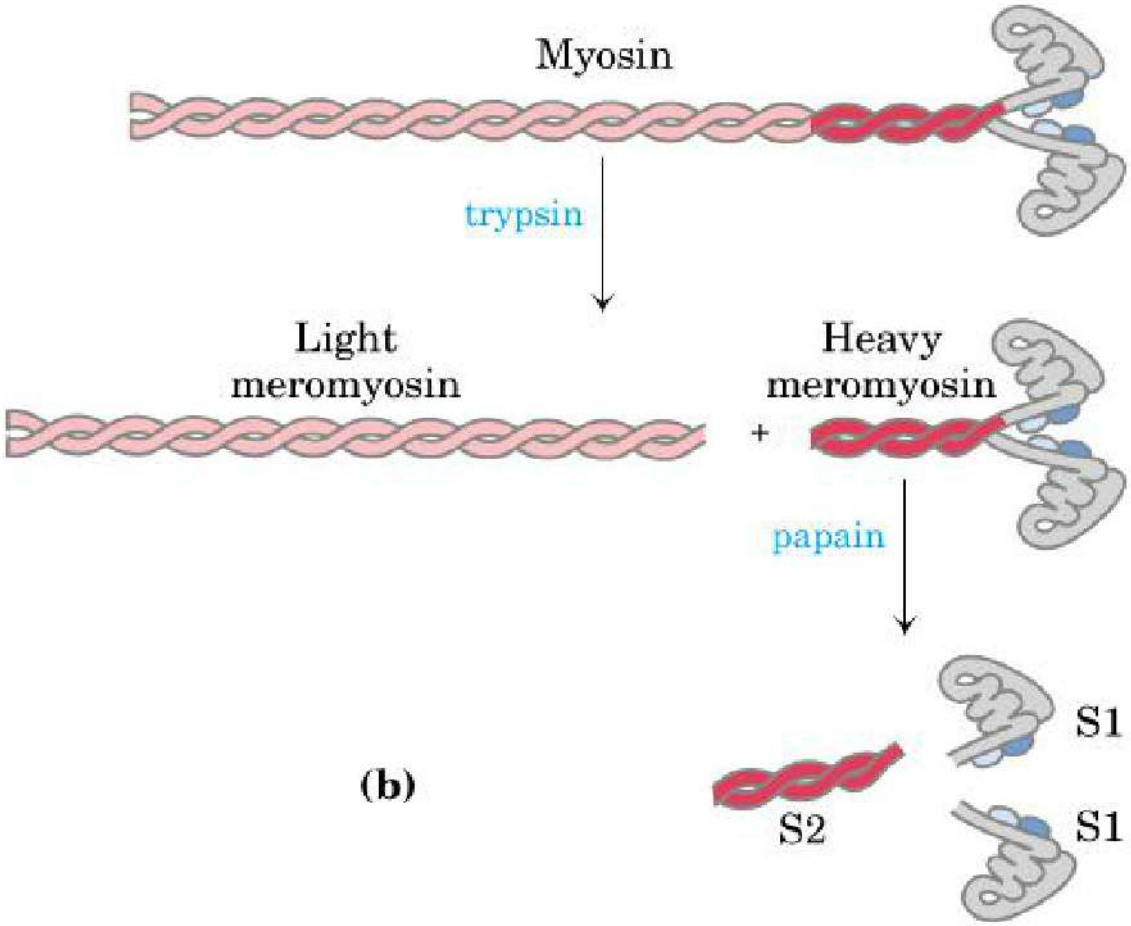
肌原纤维由纵向排列的肌丝组成：

- 粗丝（thick filament）
  ——只分布于暗/A带
  肌球蛋白
- 细丝（thick filament）
  ——I带只有细丝
  肌动蛋白




I band
– end
A band
– end
I band
H zone
Thick filament
Actin filament
+end
+end
Z line
Z line


Two supercoiled
α helices
Amino
terminus
Light
chains
Head
Neck
Tail
130 nm
Regulatory
light chain
Essential
light chain

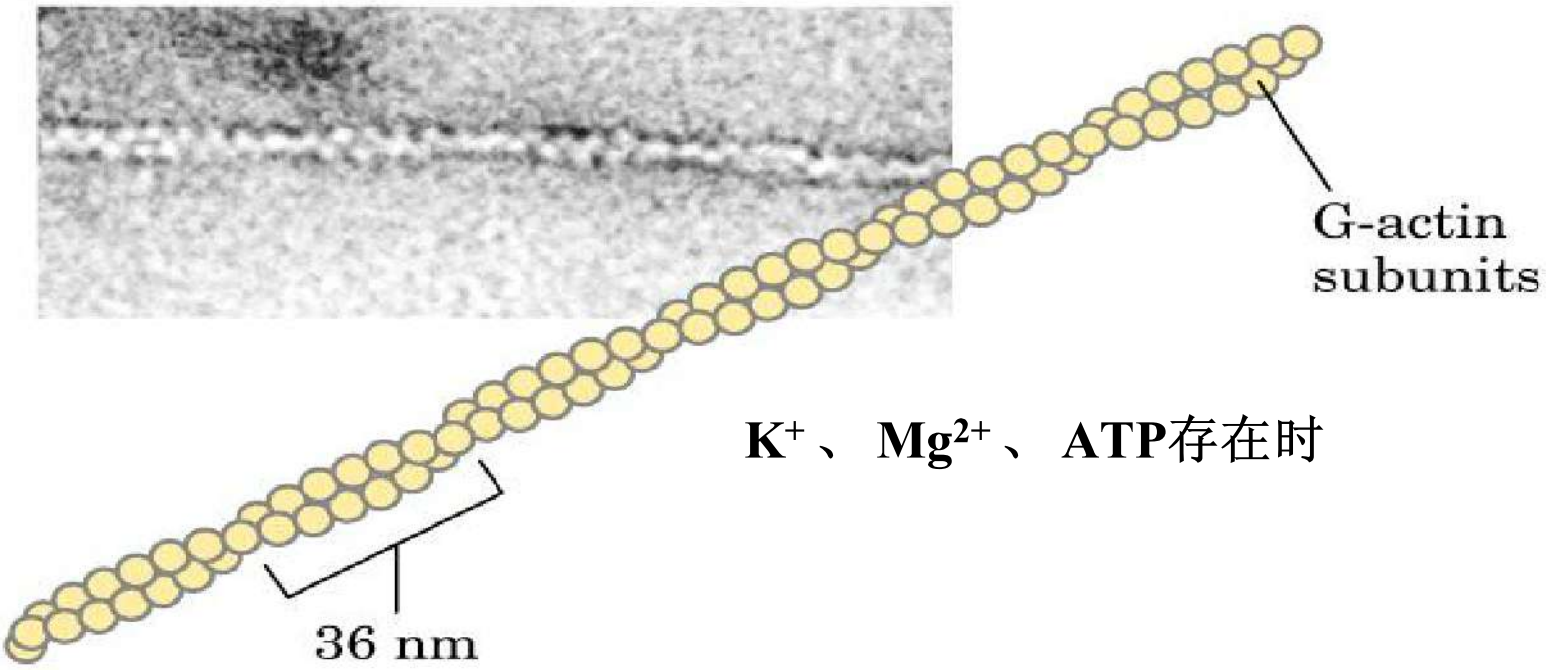

Myosin
trypsin
Light
meromyosin
Heavy
meromyosin
+
papain
S1
S2
S1

(b)

肌动蛋白的两种形式:

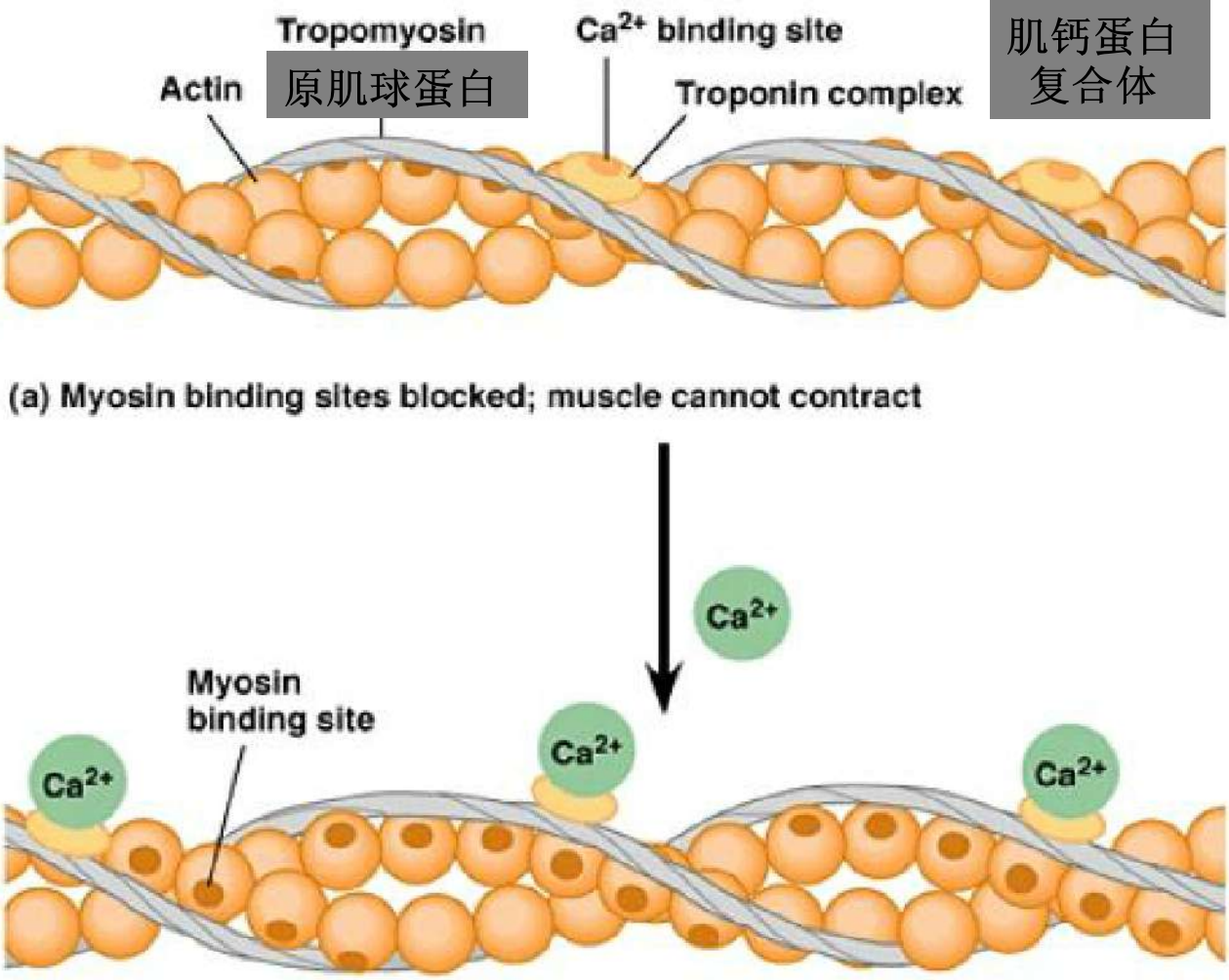
球状 ∽ (G — actin) 单体形式

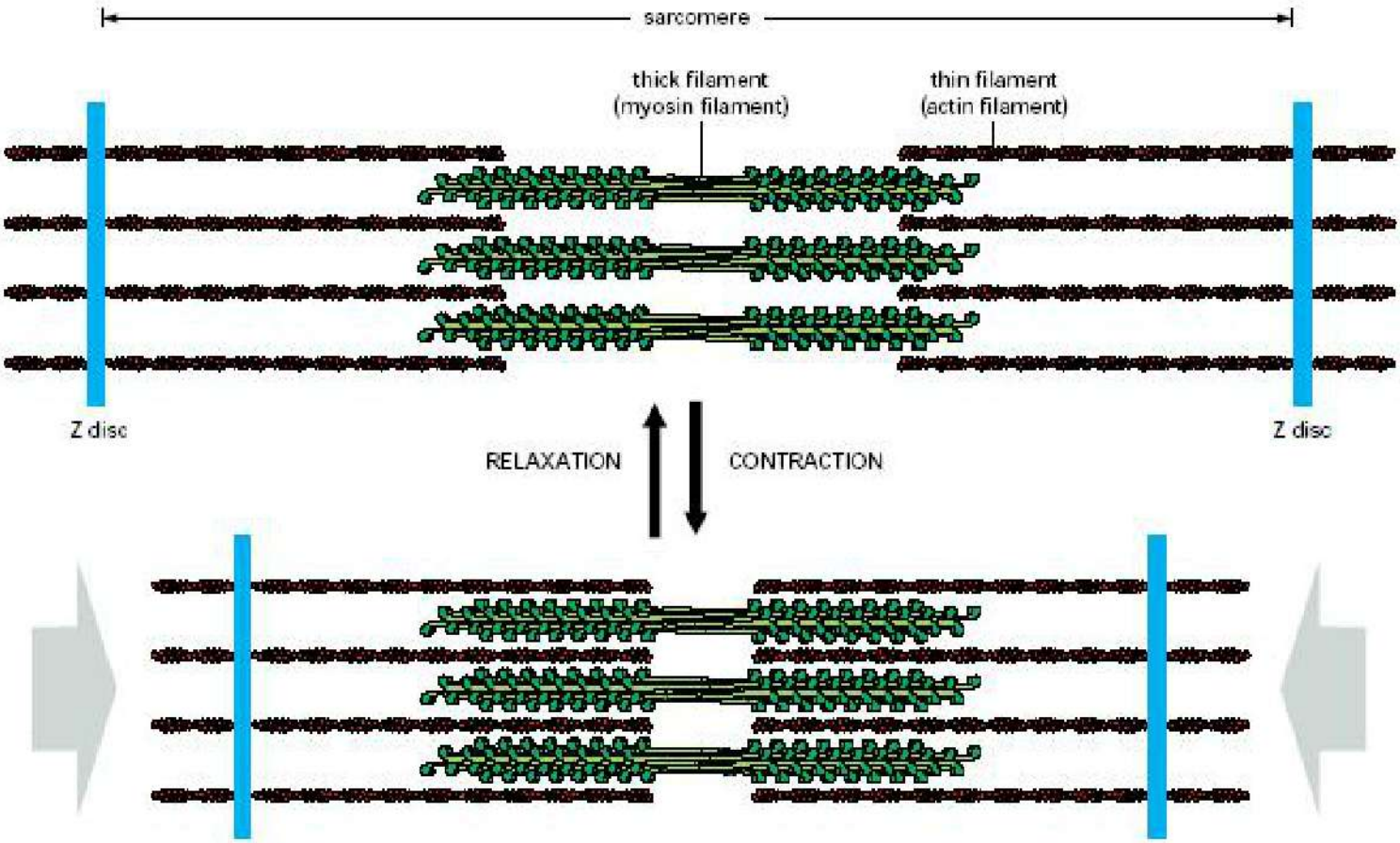
纤维状 ∽(F — actin) 聚合形式

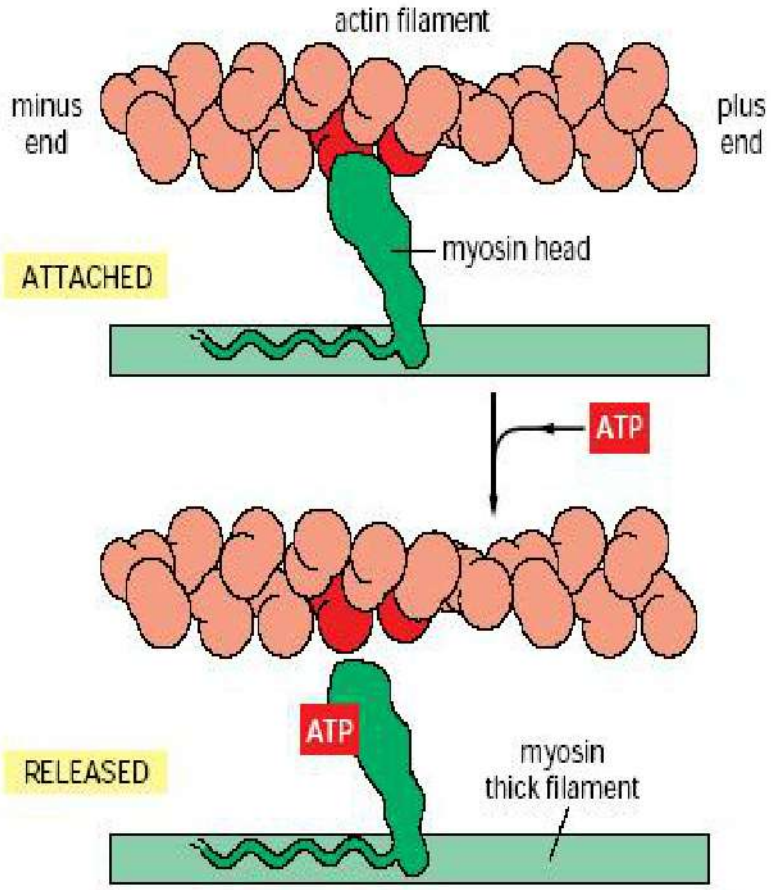


K^+、Mg^{2+}、ATP存在时

(b)

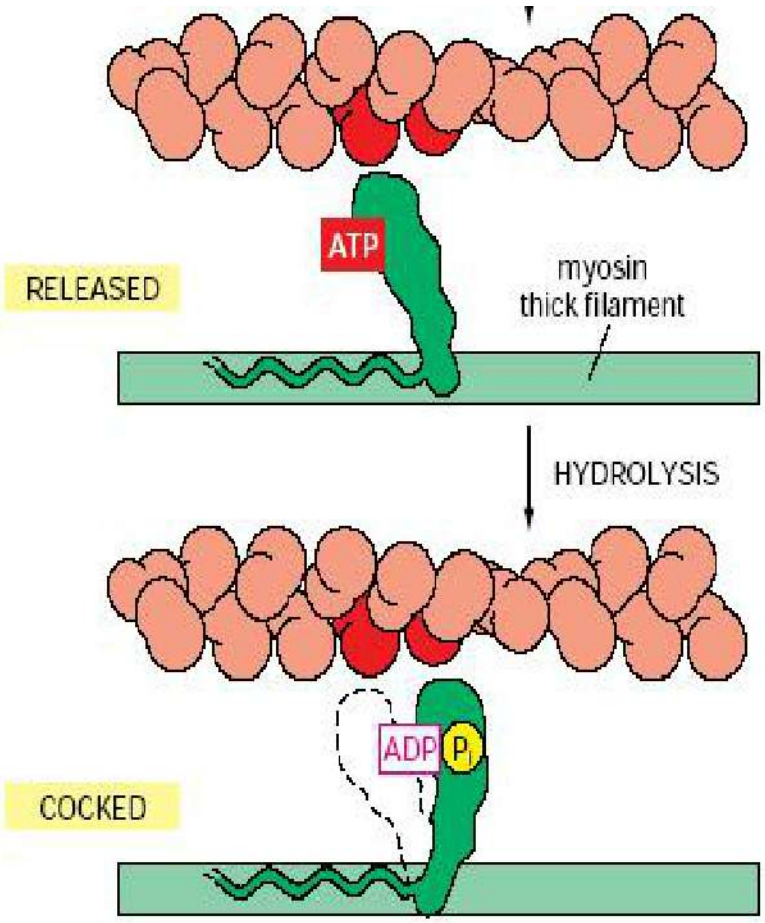



sarcomere
thick filament
(myosin filament)
thin filament
(actin filament)
Z disc
Z disc
RELAXATION
CONTRACTION



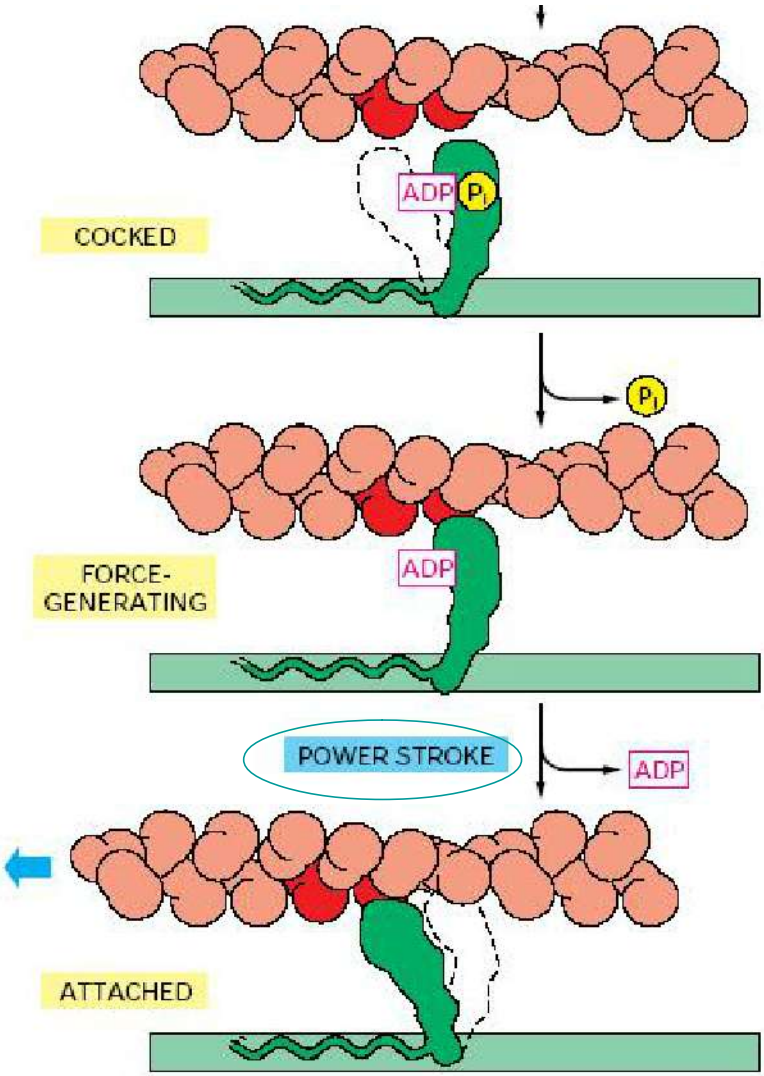
ATTACHED—At the start of the cycle shown in this figure, a myosin head lacking a bound nucleotide is locked tightly onto an actin filament in a *rigor* configuration (so named because it is responsible for *rigor mortis*, the rigidity of death). In an actively contracting muscle this state is very short-lived, being rapidly terminated by the binding of a molecule of ATP.

RELEASED—A molecule of ATP binds to the large cleft on the "back" of the head (that is, on the side farthest from the actin filament) and immediately causes a slight change in the conformation of the domains that make up the actin-binding site. This reduces the affinity of the head for actin and allows it to move along the filament. (The space drawn here between the head and actin emphasizes this change, although in reality the head probably remains very close to the actin.)



RELEASED—A molecule of ATP binds to the large cleft on the "back" of the head (that is, on the side farthest from the actin filament) and immediately causes a slight change in the conformation of the domains that make up the actin-binding site. This reduces the affinity of the head for actin and allows it to move along the filament. (The space drawn here between the head and actin emphasizes this change, although in reality the head probably remains very close to the actin.)

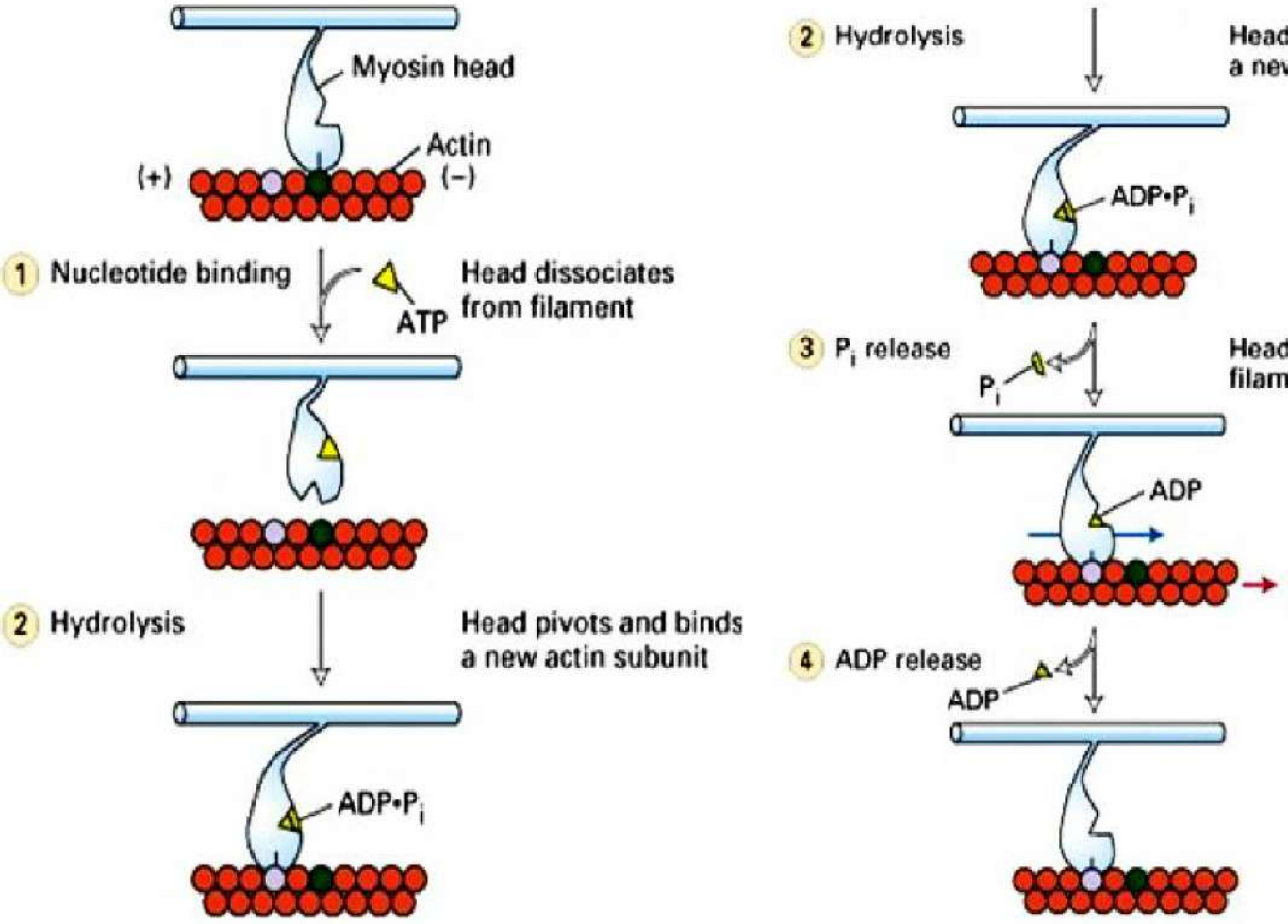
COCKED—The cleft closes like a clam shell around the ATP molecule, triggering a large shape change that causes the head to be displaced along the filament by a distance of about 5 nm. Hydrolysis of ATP occurs, but the ADP and P_i produced remain tightly bound to the protein.

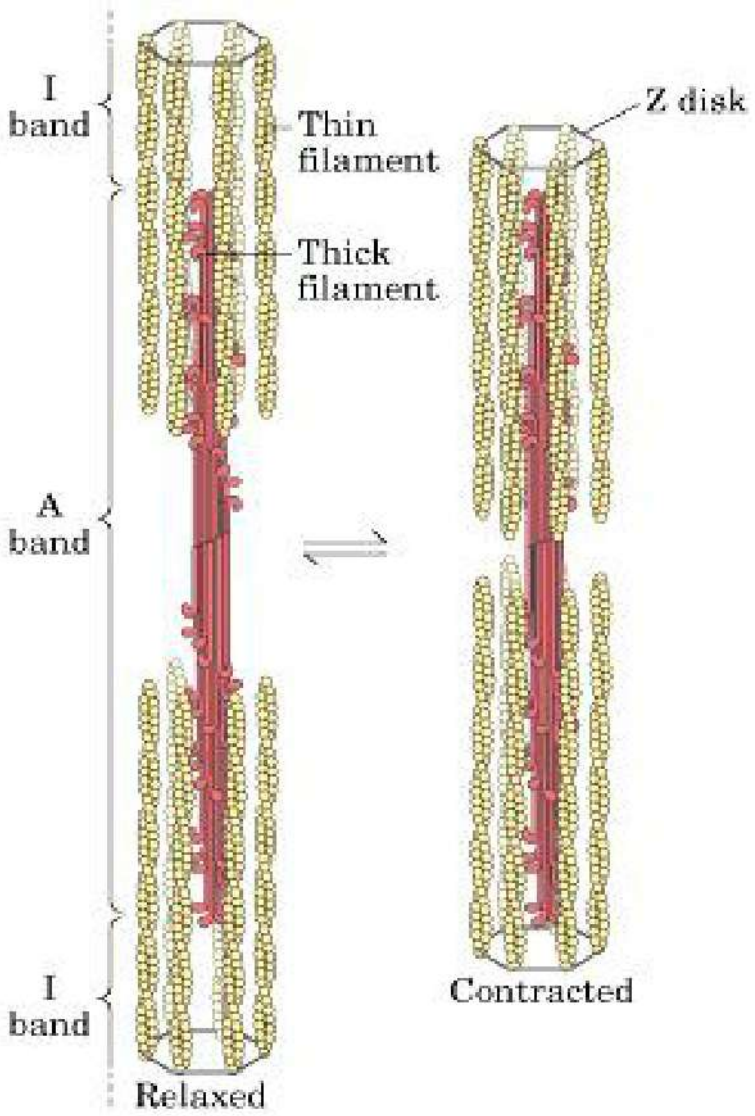


COCKED—The cleft closes like a clam shell around the ATP molecule, triggering a large shape change that causes the head to be displaced along the filament by a distance of about 5 nm. Hydrolysis of ATP occurs, but the ADP and P_i produced remain tightly bound to the protein.

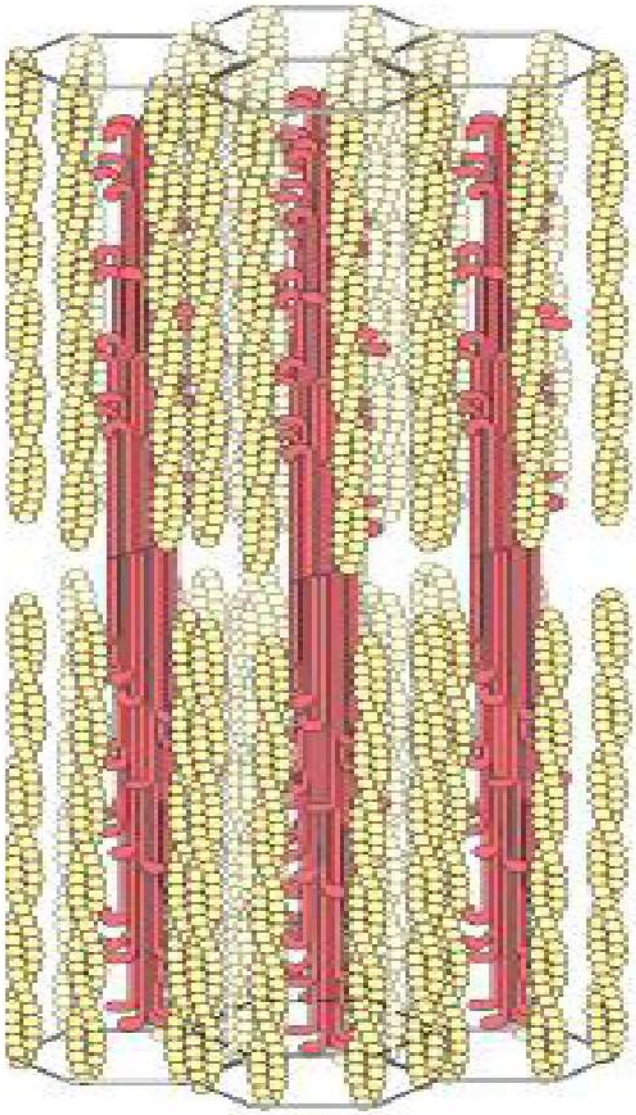
FORCE-GENERATING—The weak binding of the myosin head to a new site on the actin filament causes release of the inorganic phosphate produced by ATP hydrolysis, concomitantly with the tight binding of the head to actin. This release triggers the power stroke—the force-generating change in shape during which the head regains its original conformation. In the course of the power stroke, the head loses its bound ADP, thereby returning to the start of a new cycle.

ATTACHED—At the end of the cycle, the myosin head is again locked tightly to the actin filament in a rigor configuration. Note that the head has moved to a new position on the actin filament.

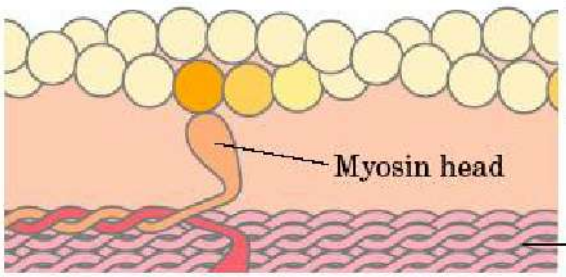

Myosin head
Actin
(+)
(–)
1 Nucleotide binding
ATP
Head dissociates from filament
2 Hydrolysis
Head pivots and binds a new actin subunit
ADP•Pi
2 Hydrolysis
Head pivots and binds a new actin subunit
ADP•Pi
3 Pi release
Pi
Head pivots and move filament (power stroke
ADP
4 ADP release
ADP


I band
Thin filament
Thick filament
A band
I band
Relaxed
Z disk
Contracted

(a)

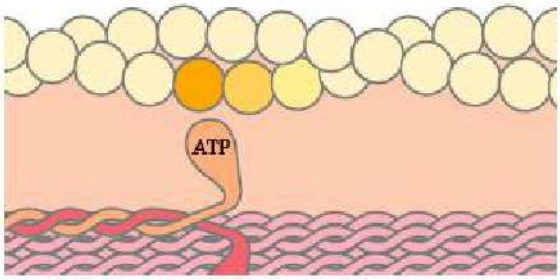


(b)

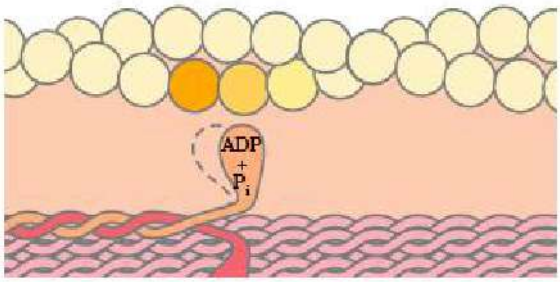


① ATP

ATP binds to myosin head, causing dissociation from actin.

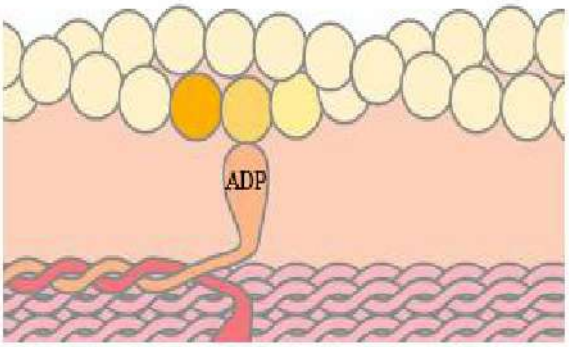


② As tightly bound ATP is hydrolyzed, a conformational change occurs. ADP and P_i remain associated with the myosin head.



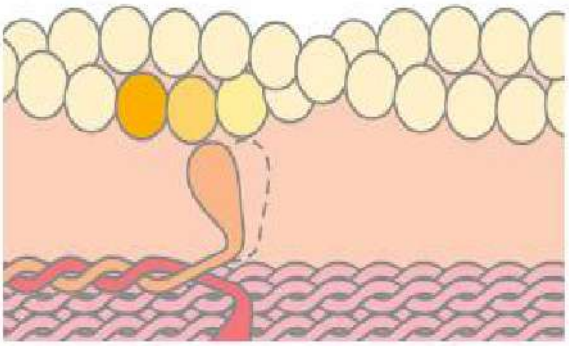
③ P_i

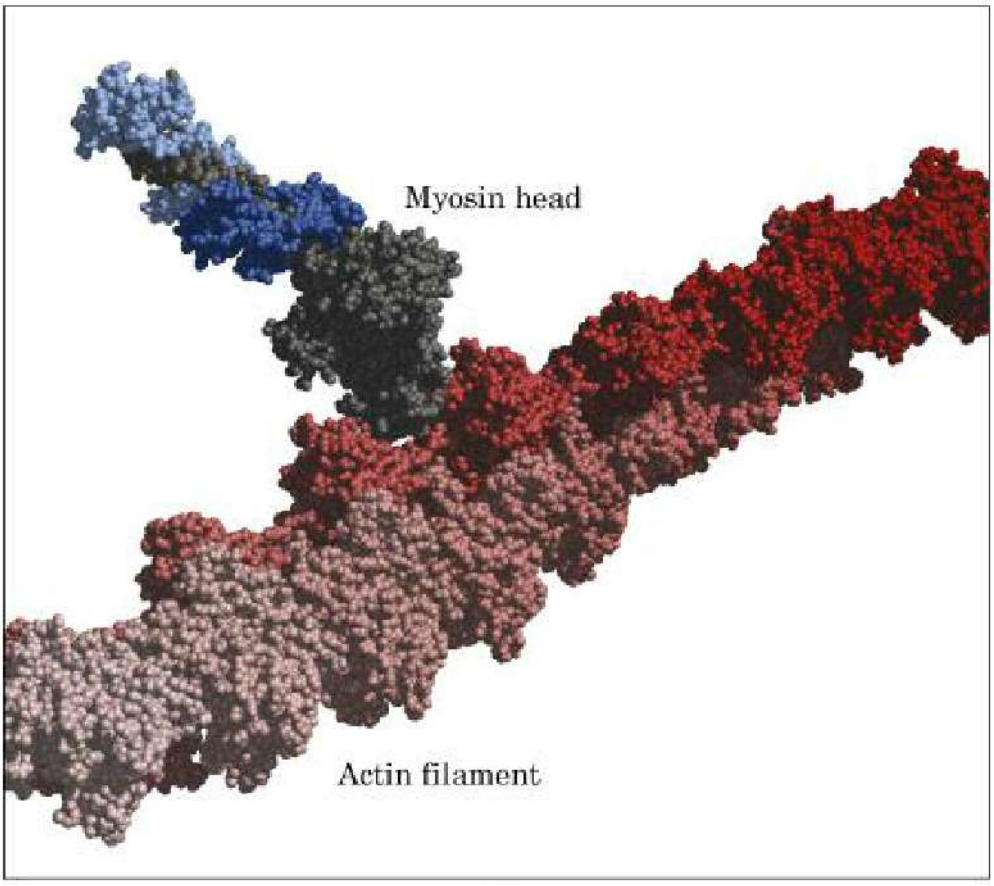
Myosin head attaches to actin filament, causing release of P_i.



④ ADP

P_i release triggers a "power stroke," a conformational change in the myosin head that moves actin and myosin filaments relative to one another. ADP is released in the process.





(c)

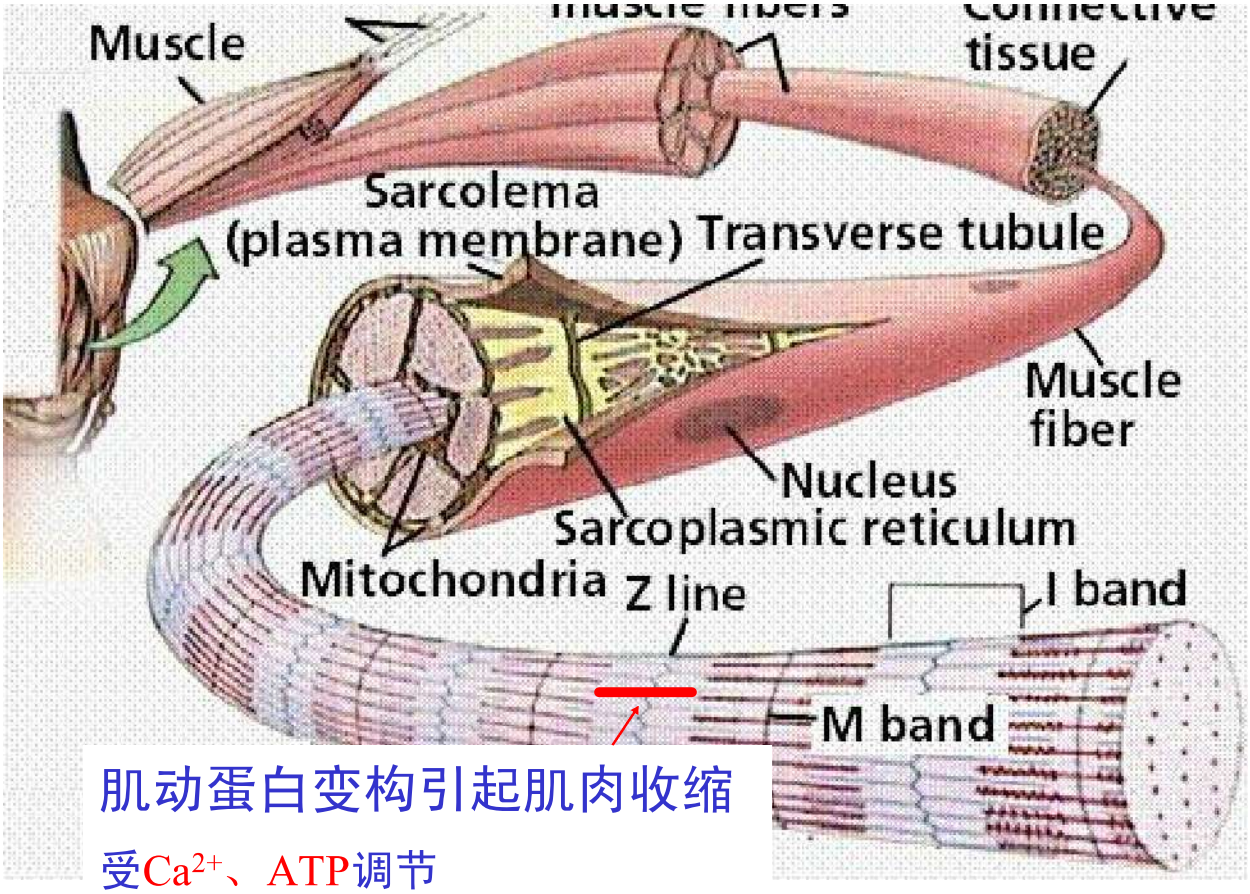
七、蛋白质结构和功能的进化

1. 蛋白质的功能是由空间构象决定的

2. 蛋白质空间构象由关键部位AA顺序决定

3. 关键部位AA的变化会引起功能改变

目前对具体结构与功能的对应规律研究尚刚刚起步



肌动蛋白变构引起肌肉收缩

受Ca^{2+}、ATP调节

前几章小节

1. 蛋白质的组成（元素组成、化学组成）及蛋白质含量的测定，蛋白质的分类
2. 二十种氨基酸的结构、分类及名称（三字缩写符、单字缩写符）
3. 氨基酸的重要理化性质：两性解离、光谱特性、化学反应（茚三酮显色、与2,4-二硝基氟苯（DNFB）反应、与异硫氰酸苯酯（PITC）的反应）
4. 蛋白质的性质：大分子性质、蛋白质分子量的测定（离心法、凝胶过滤法、SDS-聚丙烯酰胺凝胶电泳法）、两性解离（等电点、电泳、离子交换）、胶体性质、蛋白质沉淀（可逆沉淀、不可逆沉淀）、蛋白质变性、紫外吸收及颜色反应
5. 蛋白质的一级结构：肽、肽键、活性多肽及一级结构的测定
6. 蛋白质的空间结构：二级结构单元（α-螺旋、β-折叠、β-转角、自由回转）、三级与四级结构（超二级结构、结构域、亚基）及结构与功能的关系