Immunoglobulins

Structure and Function

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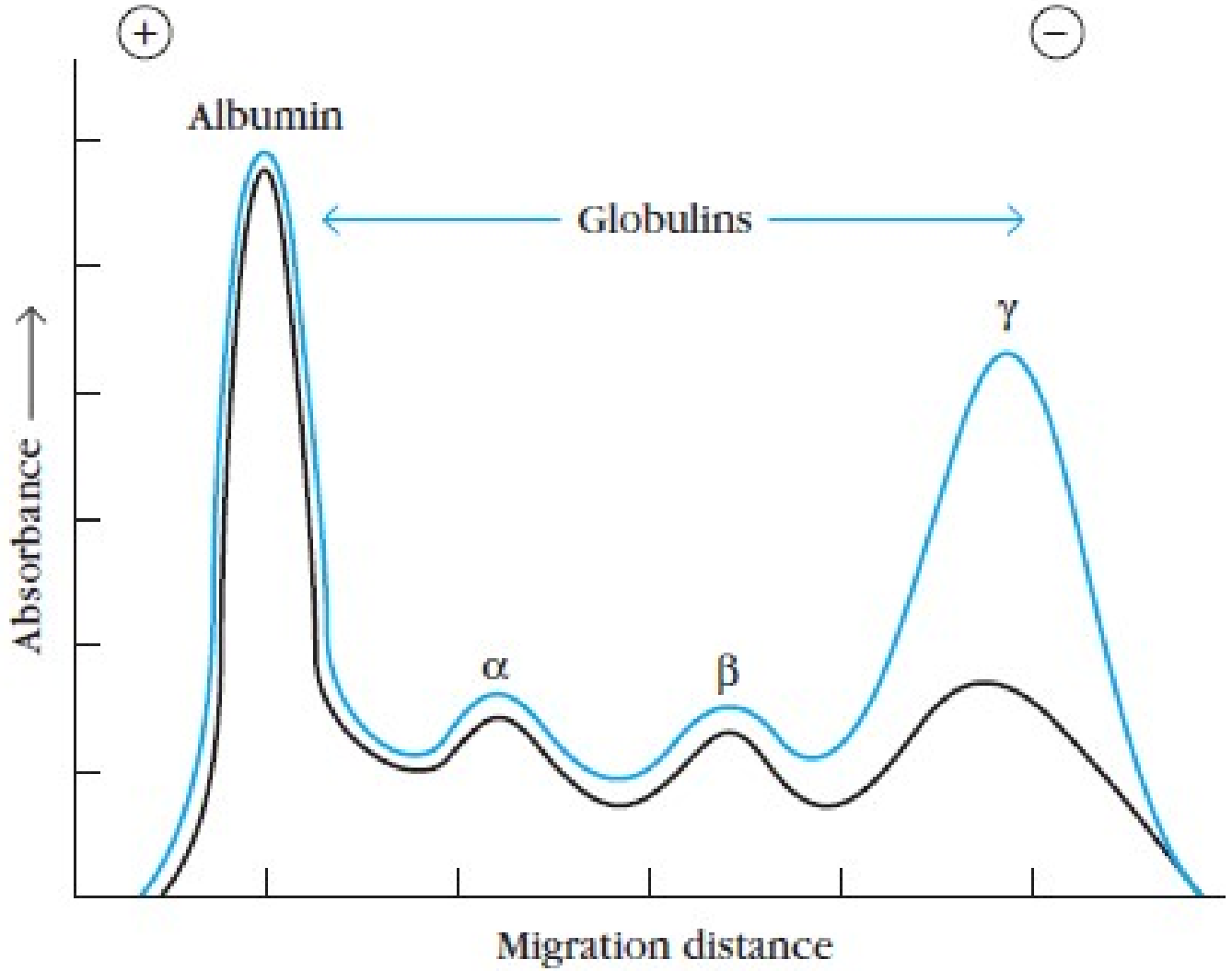
Introduction

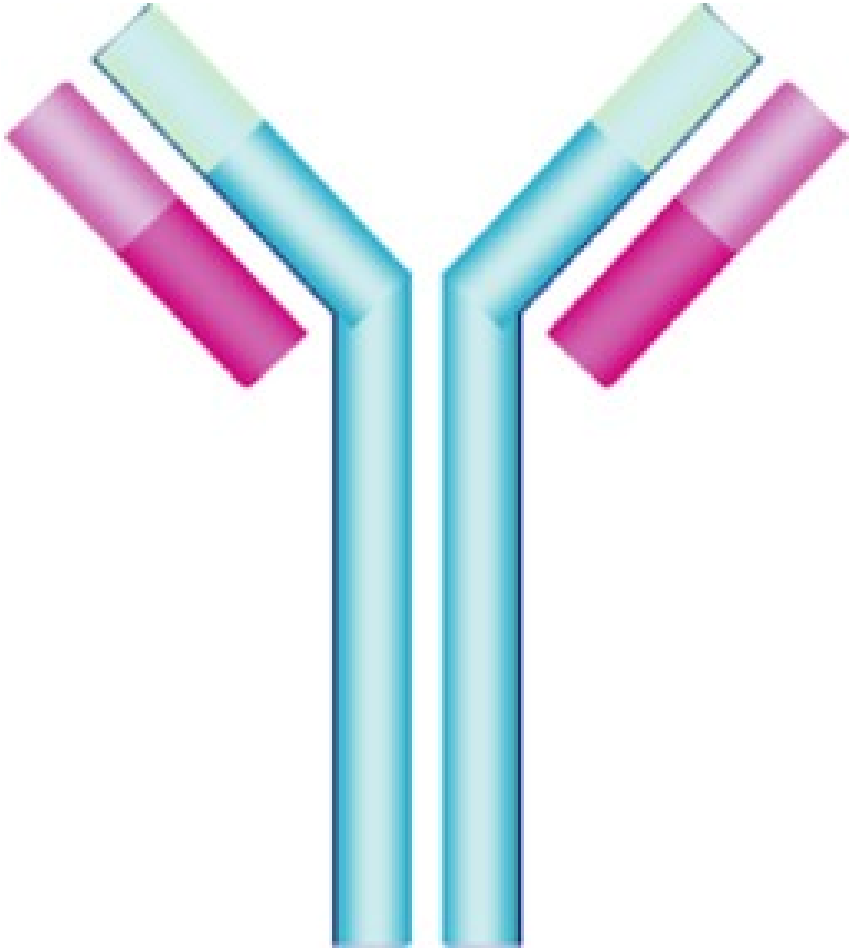
- Immunoglobulins (Igs) are glycoprotein molecules also called antibodies(Abs)
- Antigen binding proteins present on the B-cell membrane and secreted by plasma cells
- Membrane-bound antibody confers antigenic specificity on B cells
- Secreted antibodies circulate in the blood, where they serve as the effectors of humoral immunity, complement system

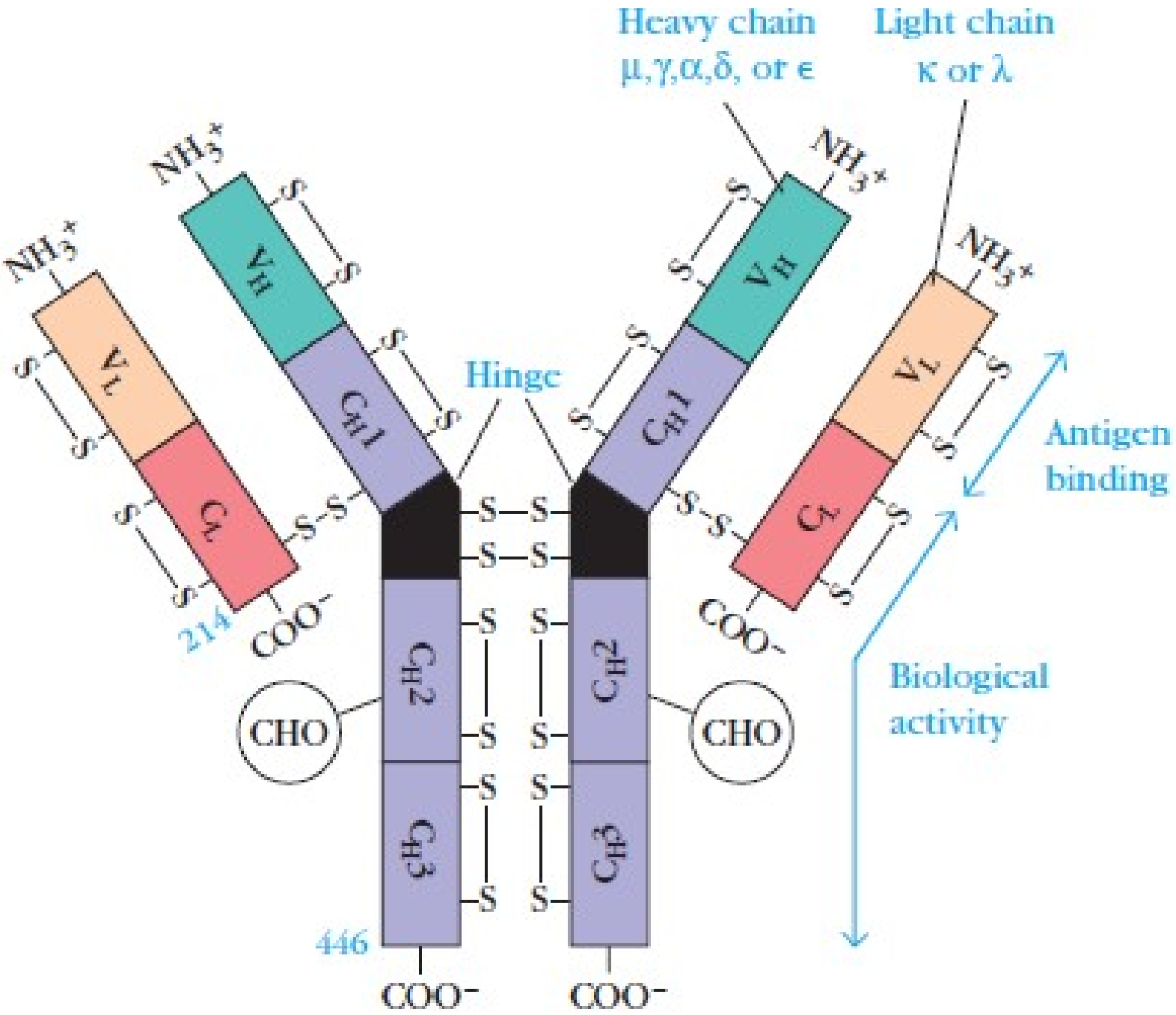
Discovery

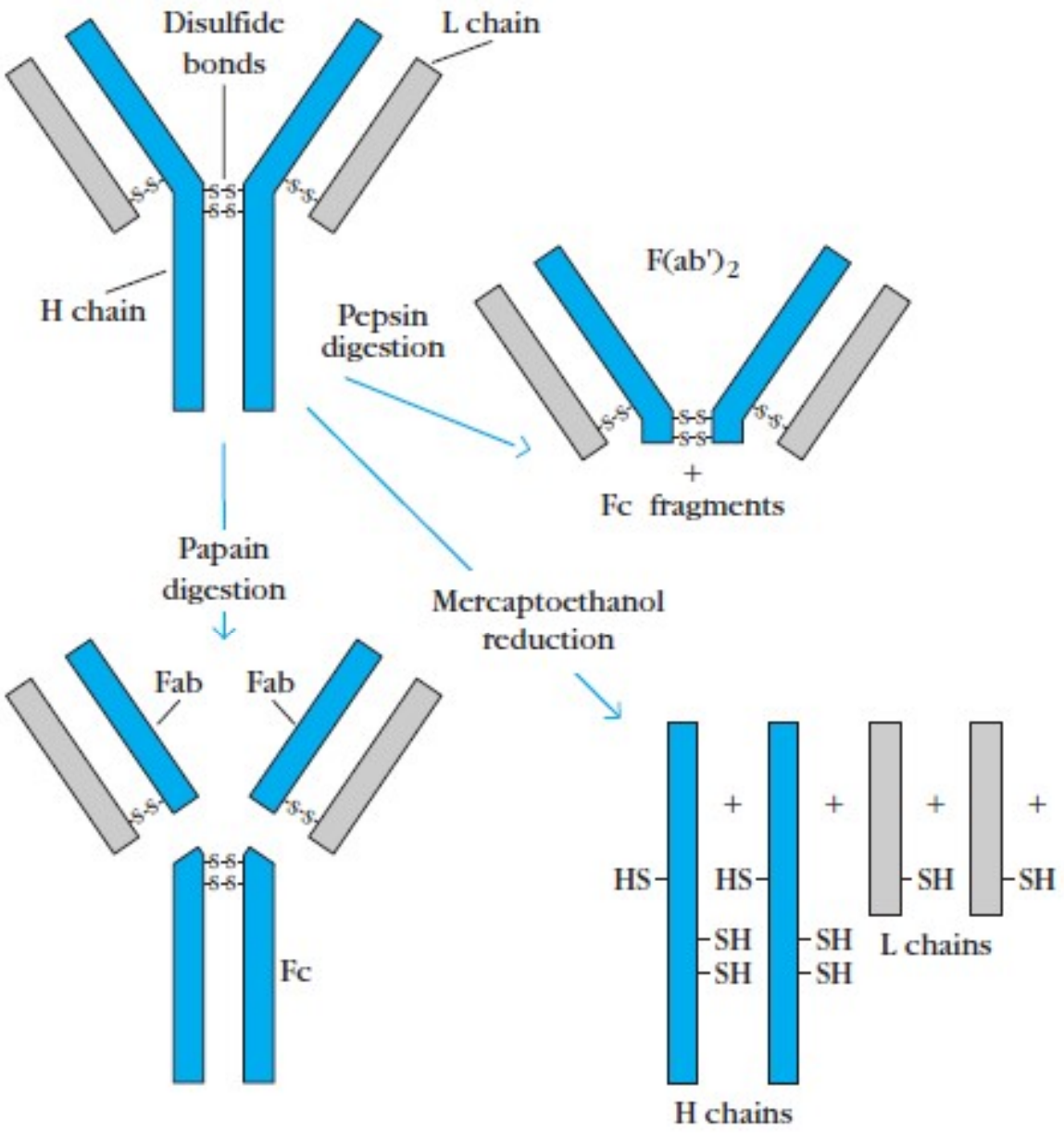


Structure of Ig

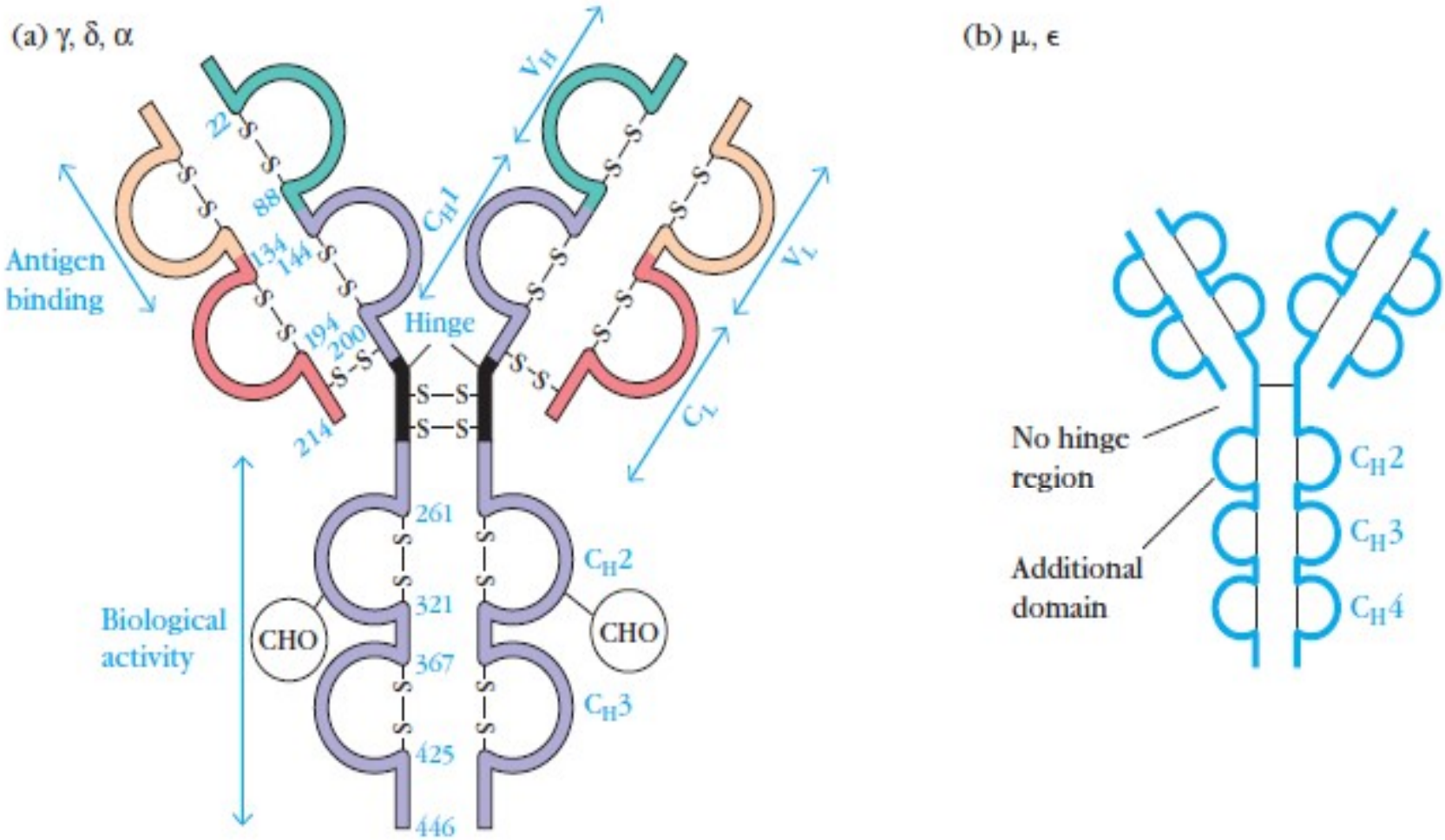
- 2x Heavy chain (light blue)
- 2x light chain (dark blue)
- Variable regions → antigen binding
- Constant regions




Heavy chain
μ,γ,α,δ, or ε
Light chain
κ or λ
NH3+
VH
CH1
VL
CL
Hinge
S–S
CH2
CH3
CHO
214
446
COO–
Antigen
binding
Biological
activity



Fragments of Ig



Folding of heavy chain and light chain

Functions of Immunoglobulin

- Effectors of humoral immunity
- Opsonization
- Activation of Complement system
- Kill cells through ADCC
- Transcytosis and passive immunity

Ig Heavy Chains and Light Chains

Heavy chain types:

- IgG - gamma (γ) heavy chains
- IgM - mu (μ) heavy chains
- IgA - alpha (α) heavy chains
- IgD - delta (δ) heavy chains
- IgE - epsilon (ε) heavy chains

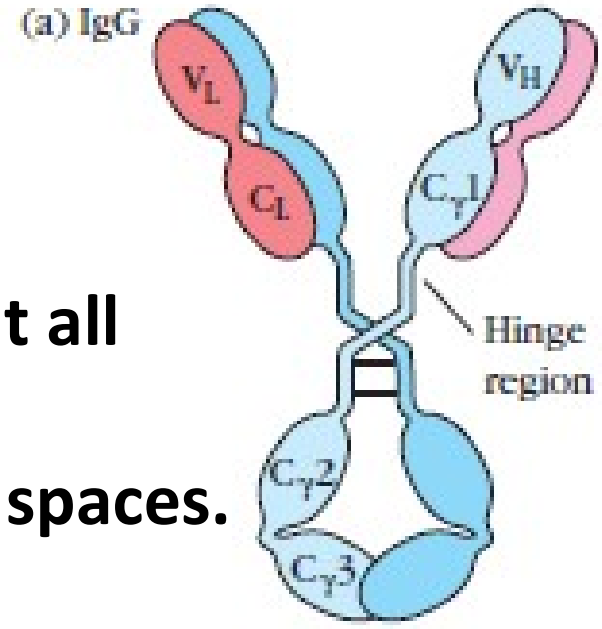
Light chain types:

- *kappa (κ)*
- *lambda (λ)*

Human Antibody Class

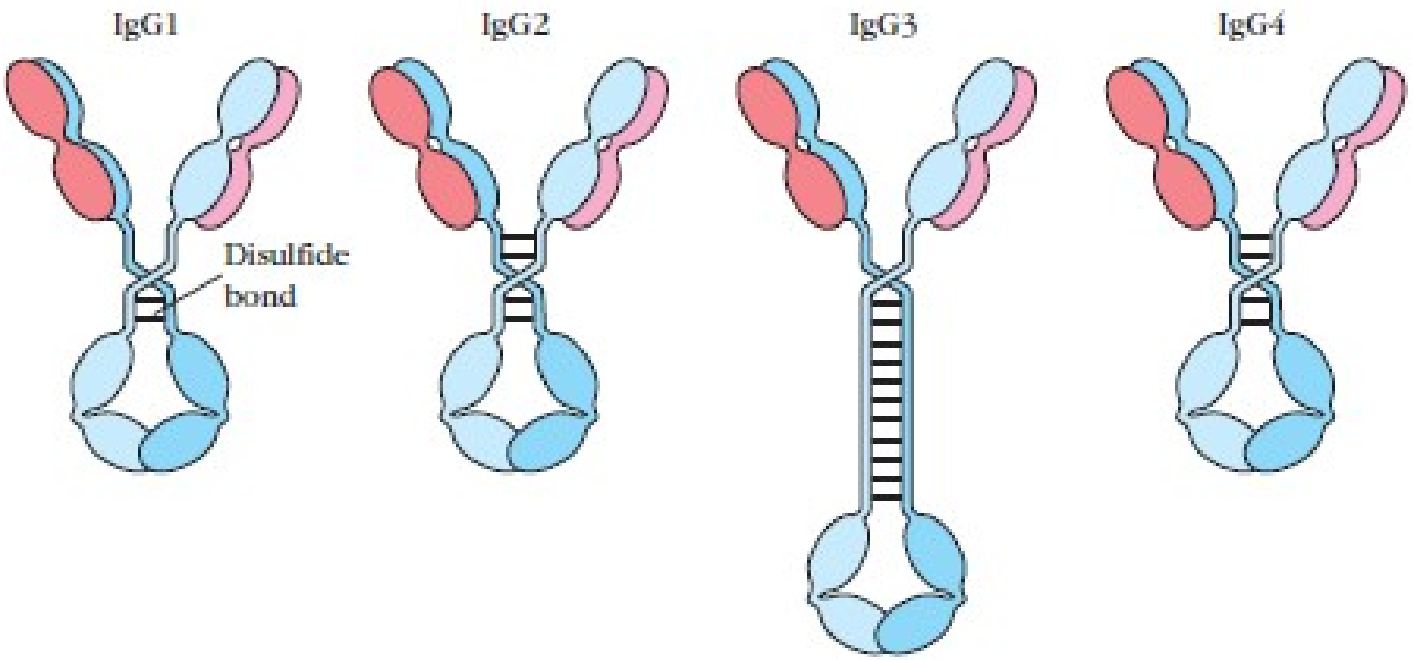
Class	IgG	IgM	IgA	IgD	IgE
Heavy Chain	γ - *Gamma*	μ - *Mu*	α – *Alpha*	δ - *Delta*	ε - *Epsilon*
Light Chain	*kappa* (κ) Or *lambda* (λ)				
No. of C domain in Heavy chain	3	4	3	3	4
Form	Monomer	Pentamer	Mono/di/tri	Monomer	Monomer
Valency for Ag Binding	2	5	2	2	2
Conc. range in normal serum	8-16mg/ml	.5-2mg/ml	1.4-4mg/ml	0-0.4mg/ml	17-450ng/ml
% of total Ig	80	6	13	1	0.002
Distribution	Abundant in internal body fluid	In Serum	Seromucus secretion milk, saliva, tear etc.	Present on lymphocyte of new born	Attach to mast cell

IgG



- Most versatile Ig and can carry out all functions of Ig molecules.
- Major Ig in serum &extravascular spaces.
- Major Ig in
- Only Ig that crosses the placenta.
- Fixes complement although not all subclasses do this well.
- It binds to cells and is a good poisoning substance that enhances phagocytosis

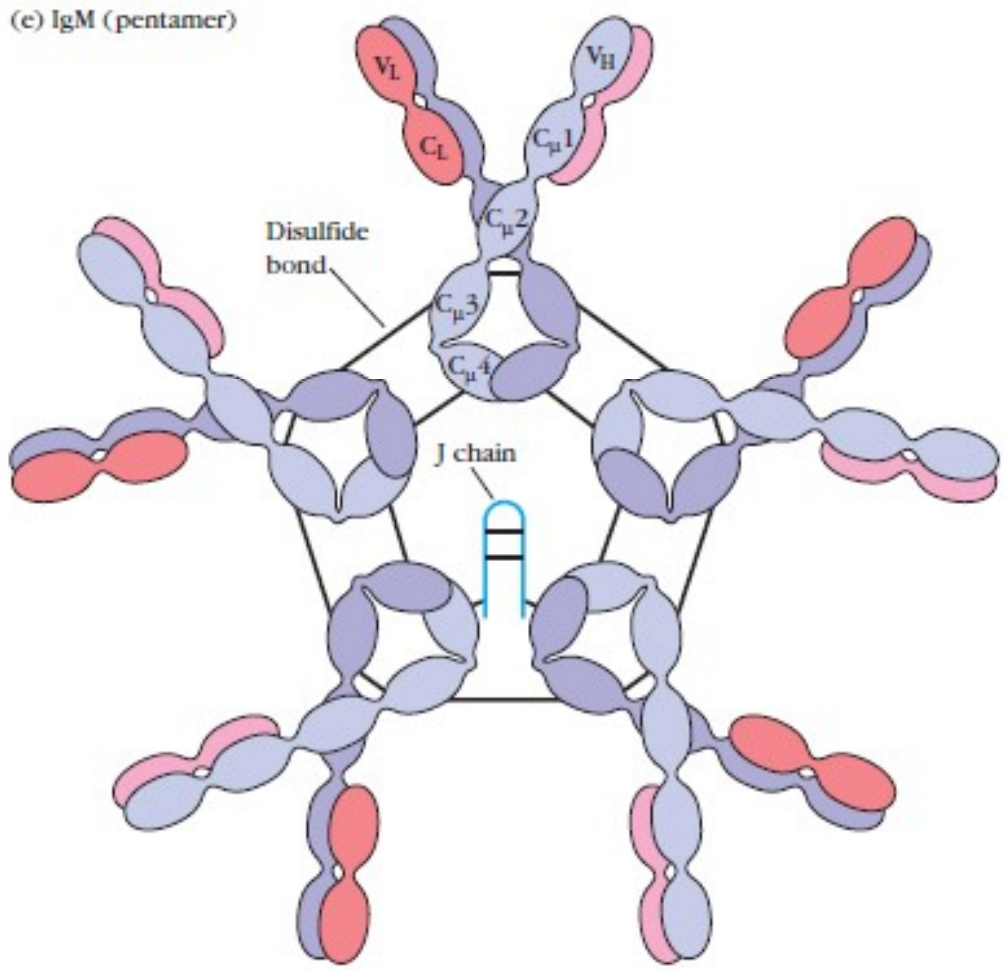
Sub Class of Ig



IgM

- First Ig to be made by fetus in most species and new B cells when stimulated by Ags.
- 3rd most abundant Ig in serum.
- Good complement fixing Ig leading to lyses of microorganisms
- Good agglutinating Ig, hence clumping microorganisms for eventual elimination from the body.
- Able to bind some cells via Fc receptors.
- B cells have surface IgMs , which exists as monomers and lacks J chain
- But have an extra 20 amino acid at the C-terminal that anchors it to the cell membrane.

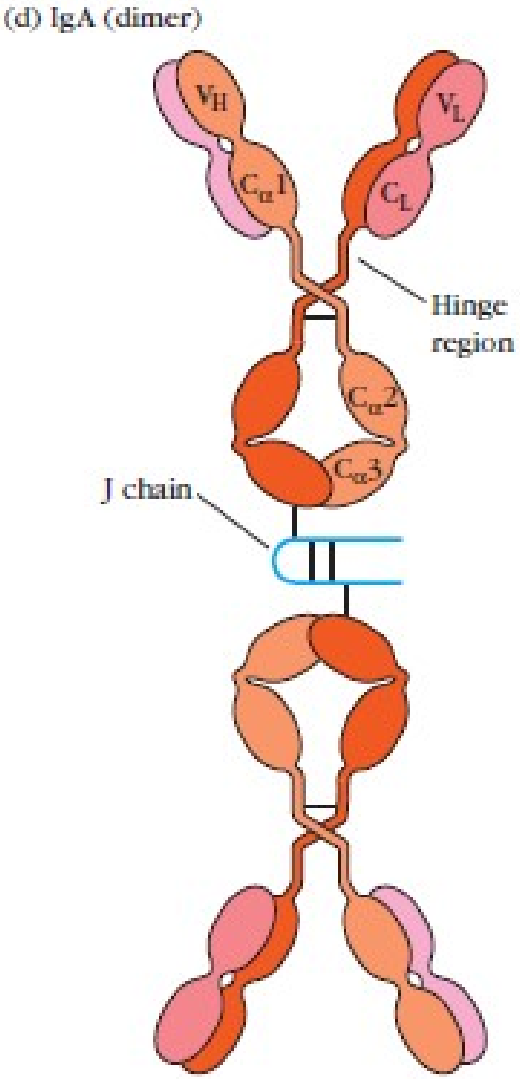
Ig M


(e) IgM (pentamer)
V_L
V_H
C_L
$C_\mu 1$
$C_\mu 2$
Disulfide bond
$C_\mu 3$
$C_\mu 4$
J chain

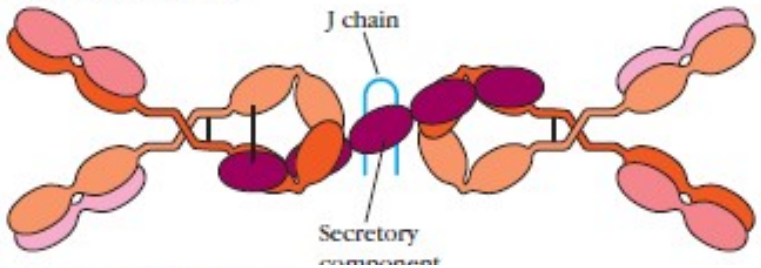
Ig A

- Serum IgA is monomeric, but
- IgA found in secretions is a dimer having a J chain.
- Secretory IgA also contains a protein called secretory piece or T- piece
- T- piece, made in epithelial cells and added to the IgA as it passes into secretions
- Helping the IgA to move across mucosa without degradation in secretions
- It is the second most abundant Ig in serum
- Major class of Ig in secretions- tears, saliva, colostrums, mucus and is important in mucosal immunity.
- It does not normally fix complement.

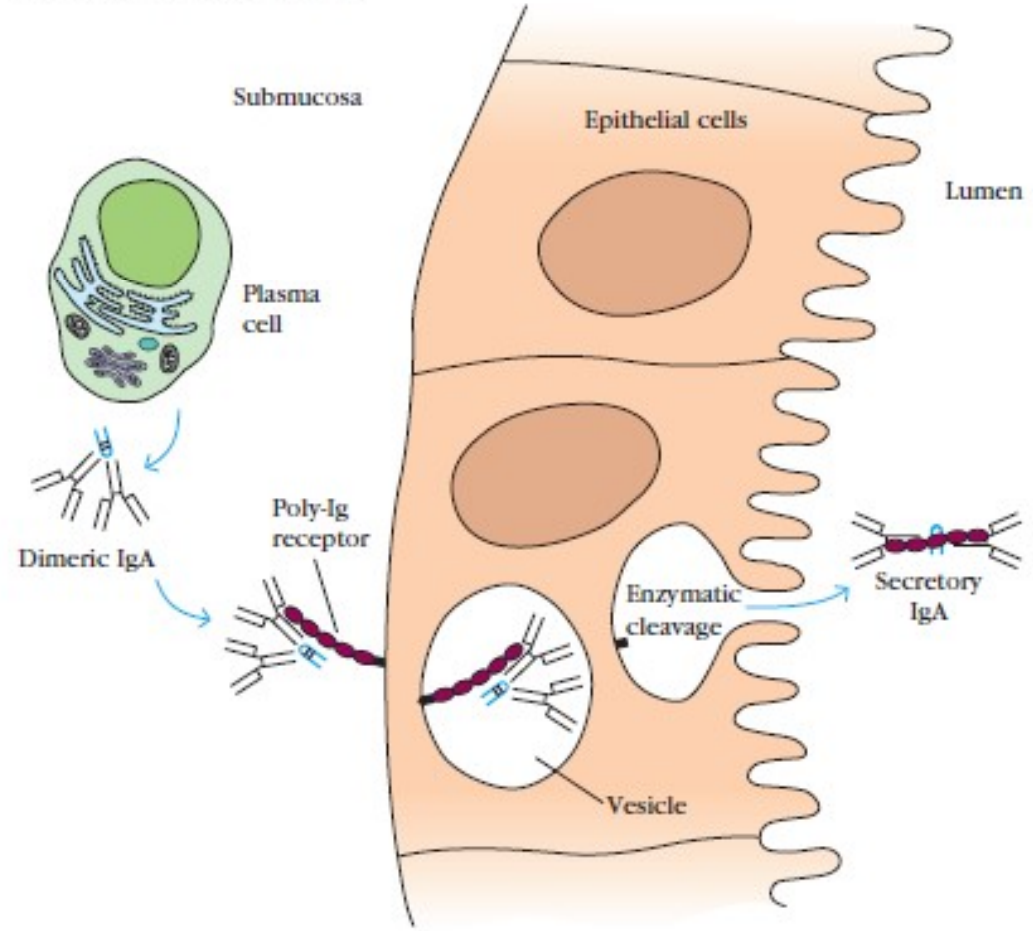
IgA


(d) IgA (dimer)
V_H
V_L
$C_\alpha 1$
C_L
Hinge region
$C_\alpha 2$
$C_\alpha 3$
J chain

(a) Structure of secretory IgA

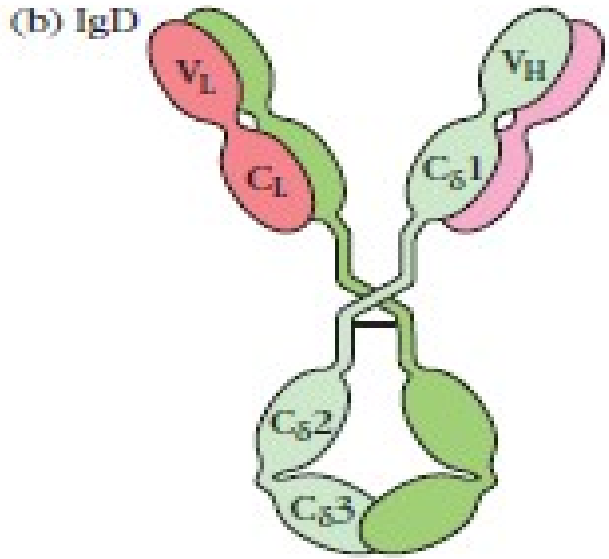


(b) Formation of secretory IgA

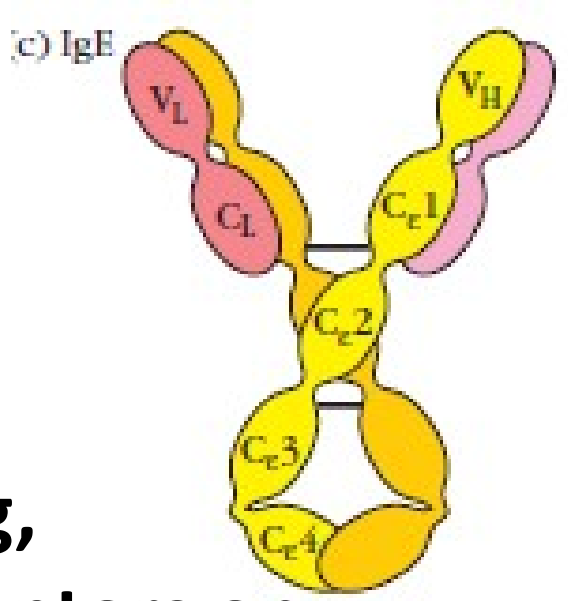


IgD

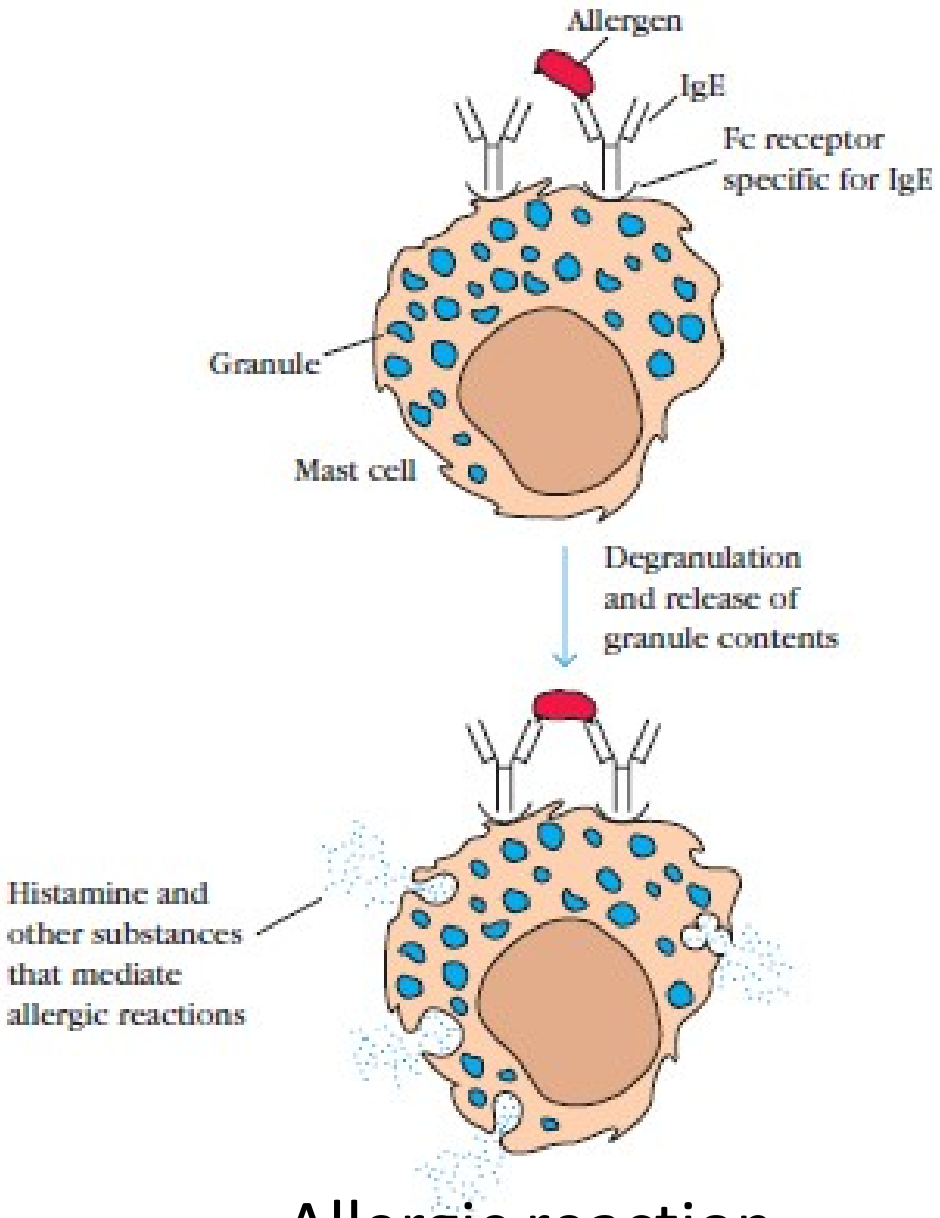
- It is found in low levels in serum and its role in serum is uncertain
- It is found primarily on B cells surface and serves as a receptor for Ag. It does not fix complement.



Ig E



- **It is the least common serum Ig, but it binds very tightly to Fc receptors on basophils and mast**
- **Cells even before interacting with Ags.**
- **It is involved in allergic reactions because it binds to basophils and mast cells.**
- **It plays a role in parasitic helminthic diseases. Serum levels rise in these diseases.**



Allergic reaction

Isotypes, allotypes, & idiotypes