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ANTIBODY

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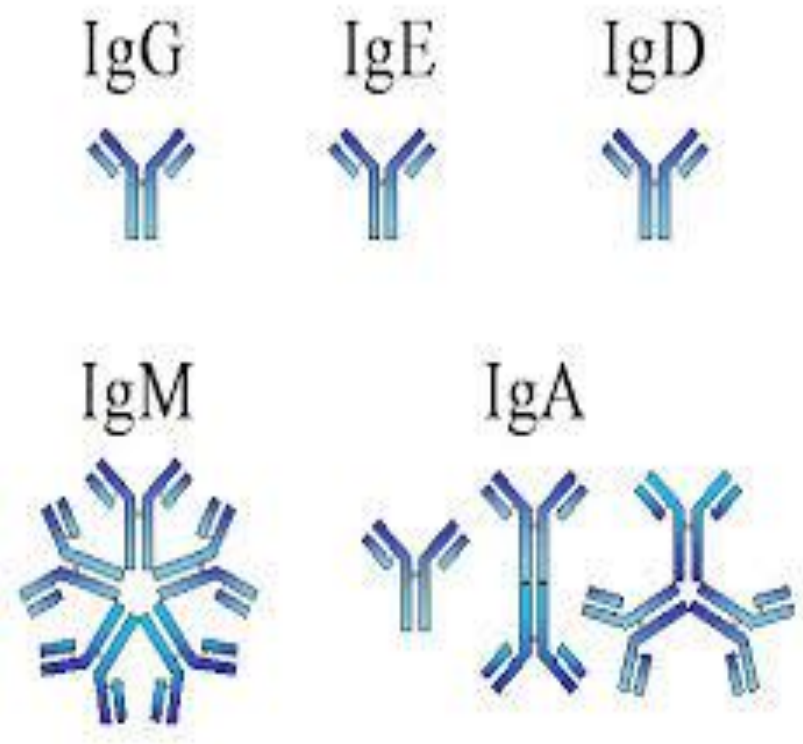
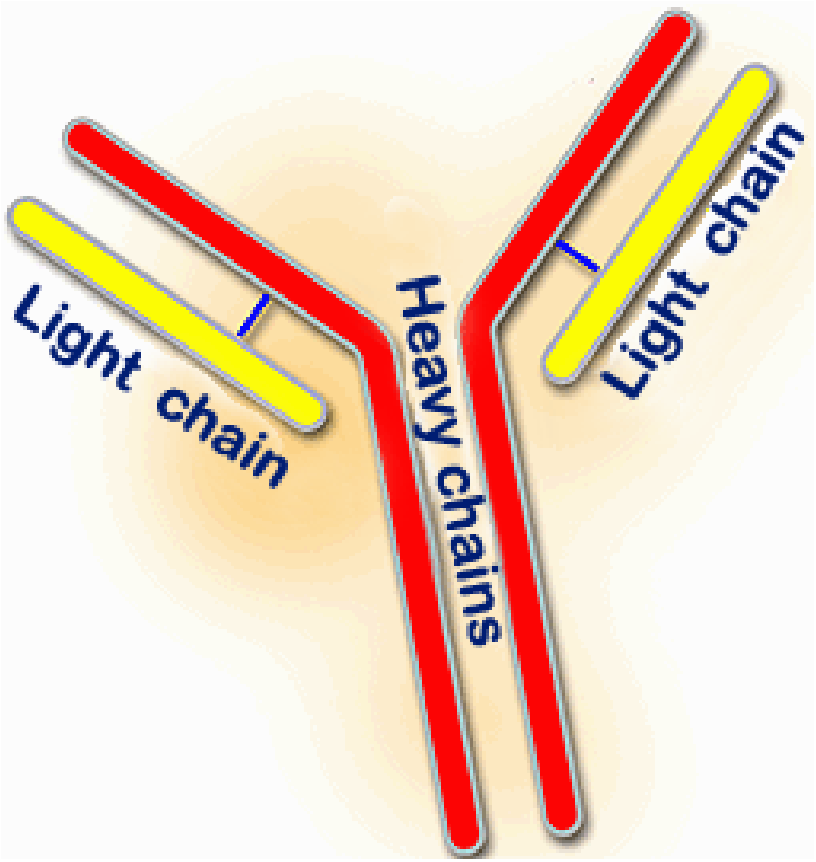
IMMUNOGLOBULINS

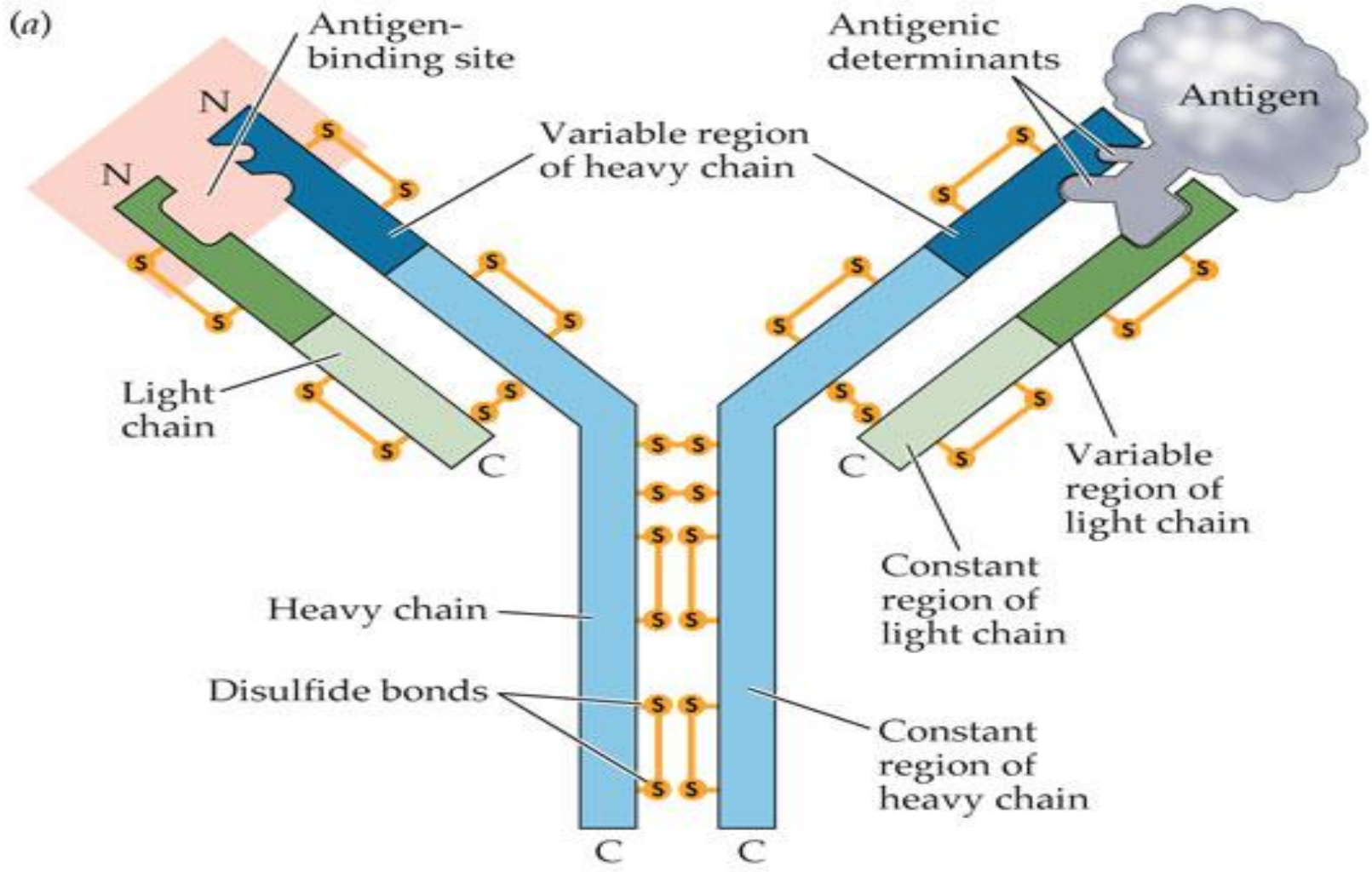
- are glycoproteins found in the serum portion of the blood
- Composed of 82% - 96% polypeptide and 2% - 14% carbohydrate
- Humoral branch of the immune response
- Primary role is antigen recognition and in biological activities related to immune response and complement activation
- Has five major classes (IgG, IgM, IgA, IgD, IgE)

TETRAPEPTIDE STRUCTURE

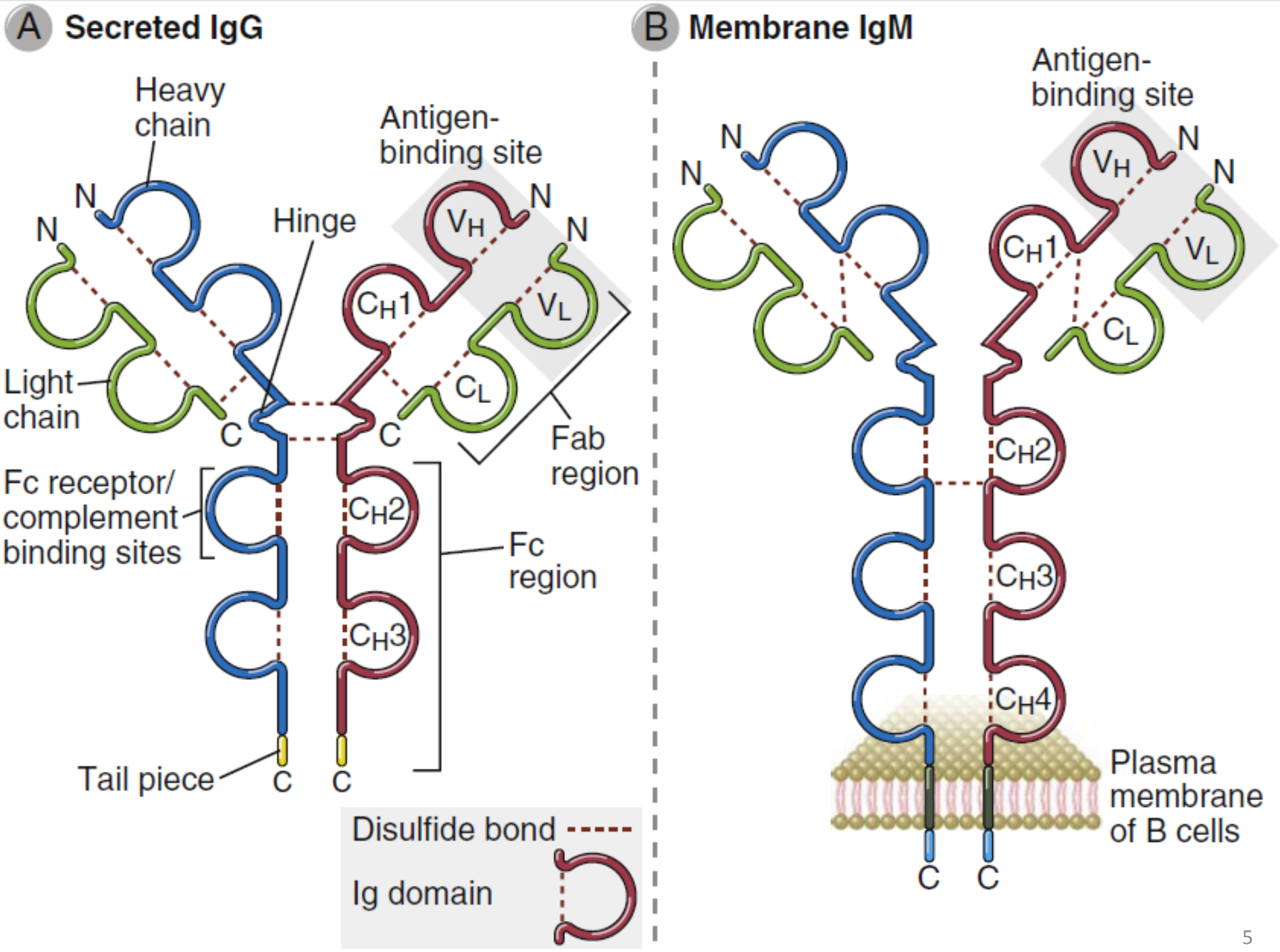




Structural configuration of Antibody



LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 18.10 Structure of Immunoglobulins (Part 1)


A Secreted IgG
Heavy chain
N
N
Hinge
Antigen-binding site
N
VH
N
CH1
VL
Light chain
CL
C
C
Fab region
Fc receptor/ complement binding sites
CH2
Fc region
CH3
Tail piece
C
C
Disulfide bond
Ig domain
B Membrane IgM
Antigen-binding site
N
N
N
VH
N
N
CH1
VL
CL
CH2
CH3
CH4
Plasma membrane of B cells
C
C

Different classes of Antibodies

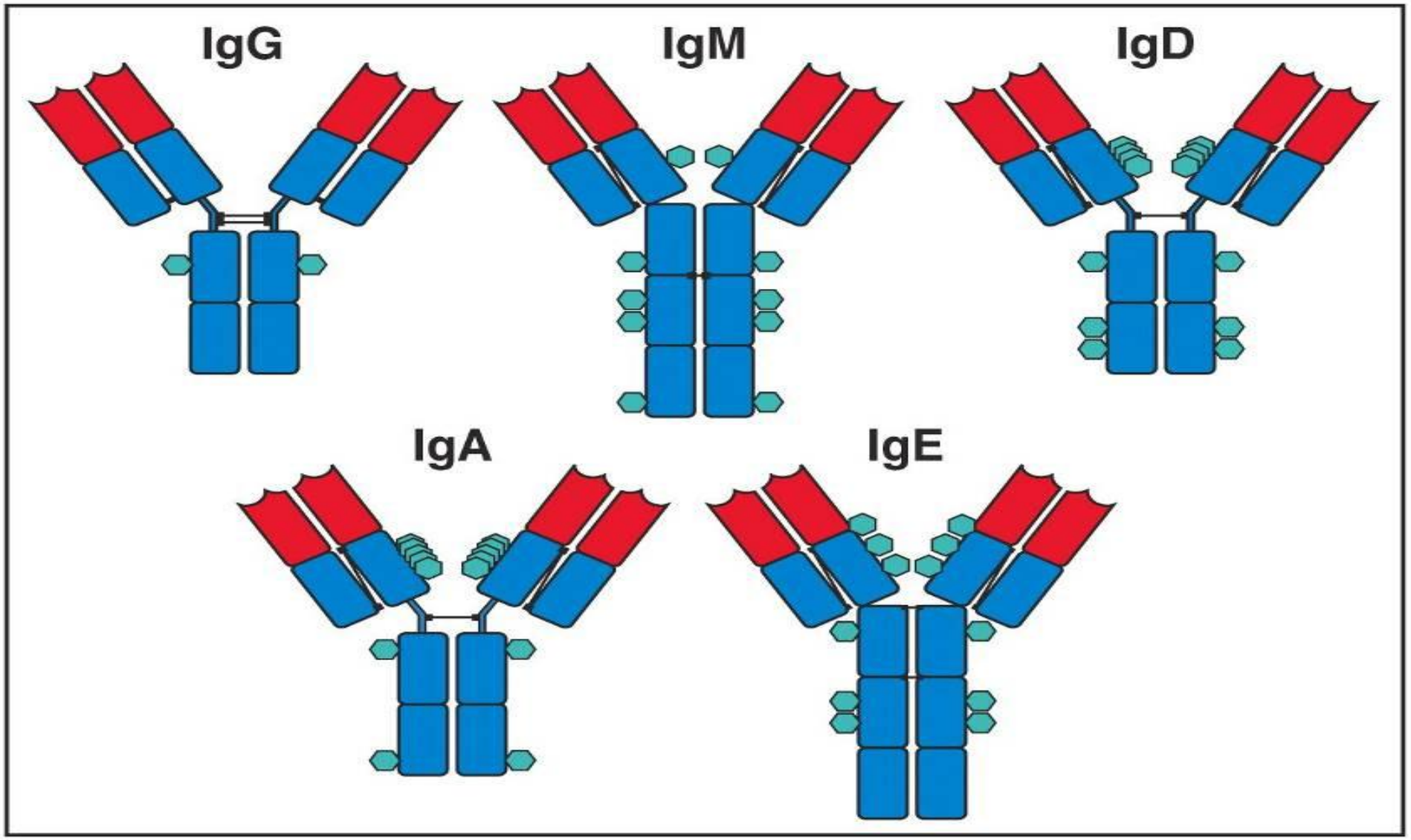
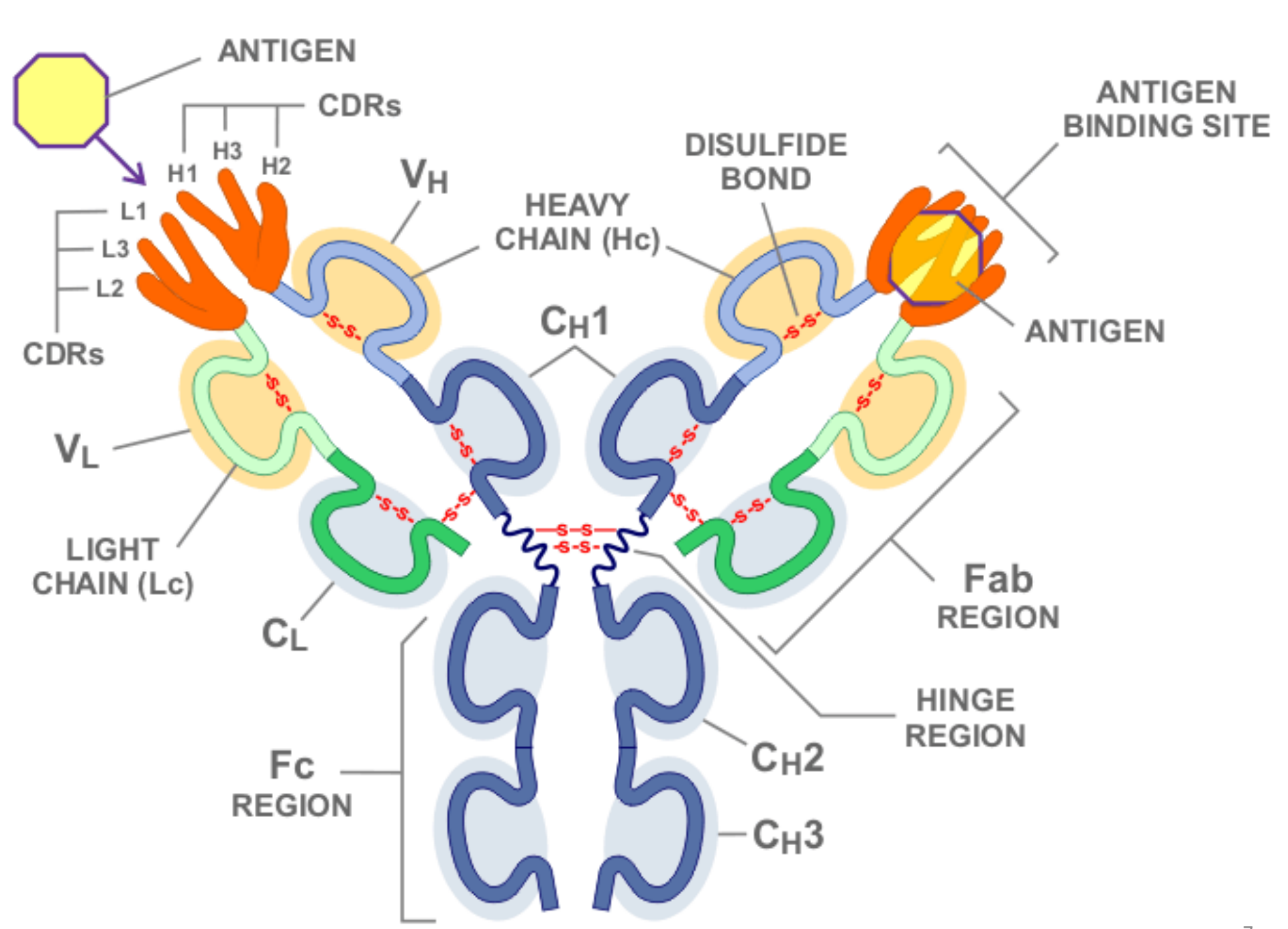


Figure 2.4 The Immune System, 2/e (© Garland Science 2005)


ANTIGEN
CDRs
H1
H3
H2
L1
L3
L2
CDRs
V_H
HEAVY CHAIN (Hc)
DISULFIDE BOND
ANTIGEN BINDING SITE
ANTIGEN
C_H1
V_L
LIGHT CHAIN (Lc)
C_L
Fab REGION
HINGE REGION
Fc REGION
C_H2
C_H3

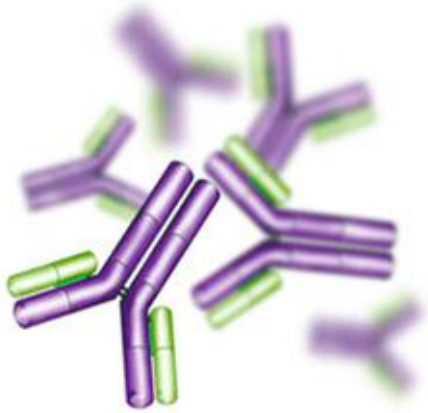
NATURE OF LIGHT CHAINS

- Bence-Jones Proteins
  - Kappa (Є)
  - Lambda (λ)
  - Constant region
    - is the C-terminal end and contains similar amino acids for each class of antibody.
  - Variable region
    - includes 110-130 amino acids of the light and heavy chains, and is responsible for binding to antigen. This part of the antibody shows variations in amino acids when the specificity of the antibody for antigen is changed.

Heavy chain sequencing

- Variable domain – first 110 amino acids at the amino-terminal domain
- The remaining amino acid can be divided up into three or more constant regions with very similar sequences, C_H1, C_H2, C_H3.

- 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



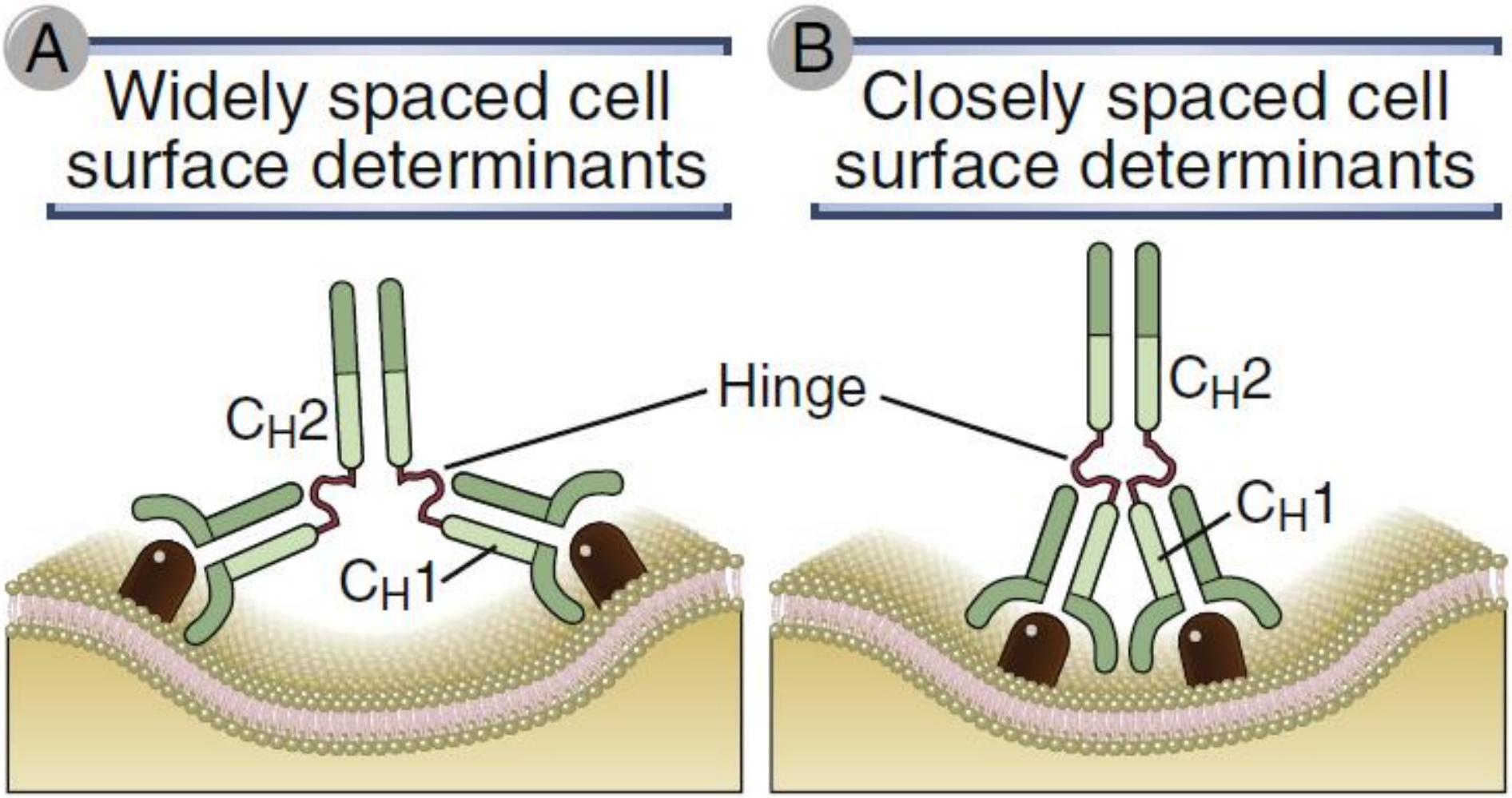
HINGE REGION

- flexible amino acid stretch in the central part of the heavy chains of the IgG and IgA immunoglobulin classes, which links these 2 chains by disulfide bonds

  ✓High content of proline and hydrophobic residues

  ✓Flexibility assists initiation of the complement cascade

- rich in cysteine and proline amino acids, extremely variable in amino acid sequence,
- no resemblance to any other immunoglobulin region
- Gamma, delta and alpha chains have hinge region
- Mu and epsilon chains do not have hinge region


A
Widely spaced cell surface determinants
B
Closely spaced cell surface determinants
C_H2
Hinge
C_H1
C_H2
C_H1

CARBOHYDRATE FUNCTIONS

- All types of immunoglobulins contain a carbohydrate portion located between C_H2 domains of the two H chains
  - They function as:
    1. Increases the solubility of the immunoglobulin
    2. Provides protection against degradation
    3. enhances functional activity of the F_C domains

TYPES OF IMMUNOGLOBULIN

- IgG
  - Structure:
    - ✓ *All IgG's are monomers. The subclasses differ in the number of disulfide bonds and length of the hinge region.*
  - Properties
    - ✓ *most versatile immunoglobulin because it is capable of carrying out all of the functions of immunoglobulin molecules.*

a) IgG is the major Ig in serum - 75% of serum Ig is IgG

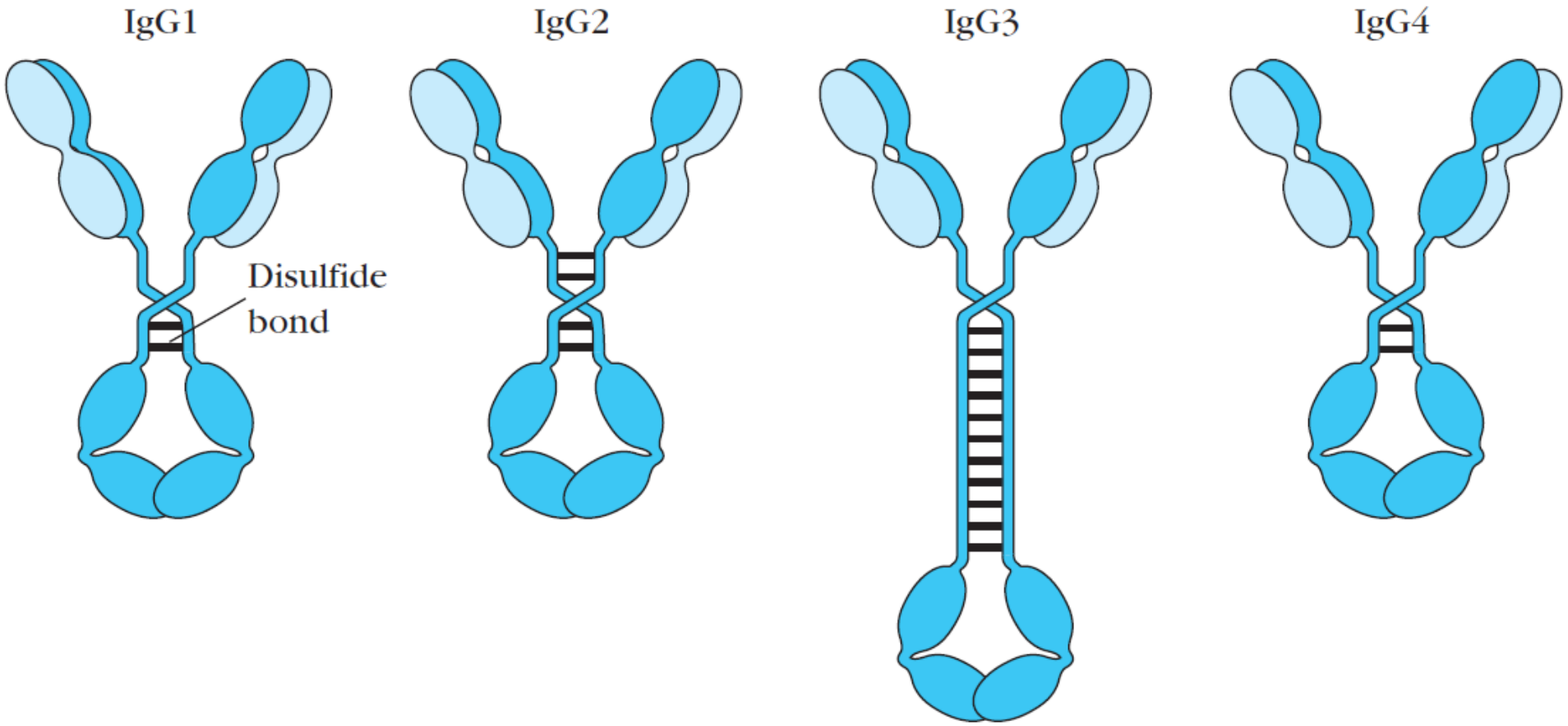
SUBCLASSES

a) IgG1 - Gamma 1 heavy chains
- *67%*

b) IgG2 - Gamma 2 heavy chains
- *22%*

c) IgG3 - Gamma 3 heavy chains
- *7%*
- ***Largest hinge region***

d) IgG4 - Gamma 4 heavy chains
- *4%*


IgG1
IgG2
IgG3
IgG4
Disulfide
bond

TYPES OF IMMUNOGLOBULIN

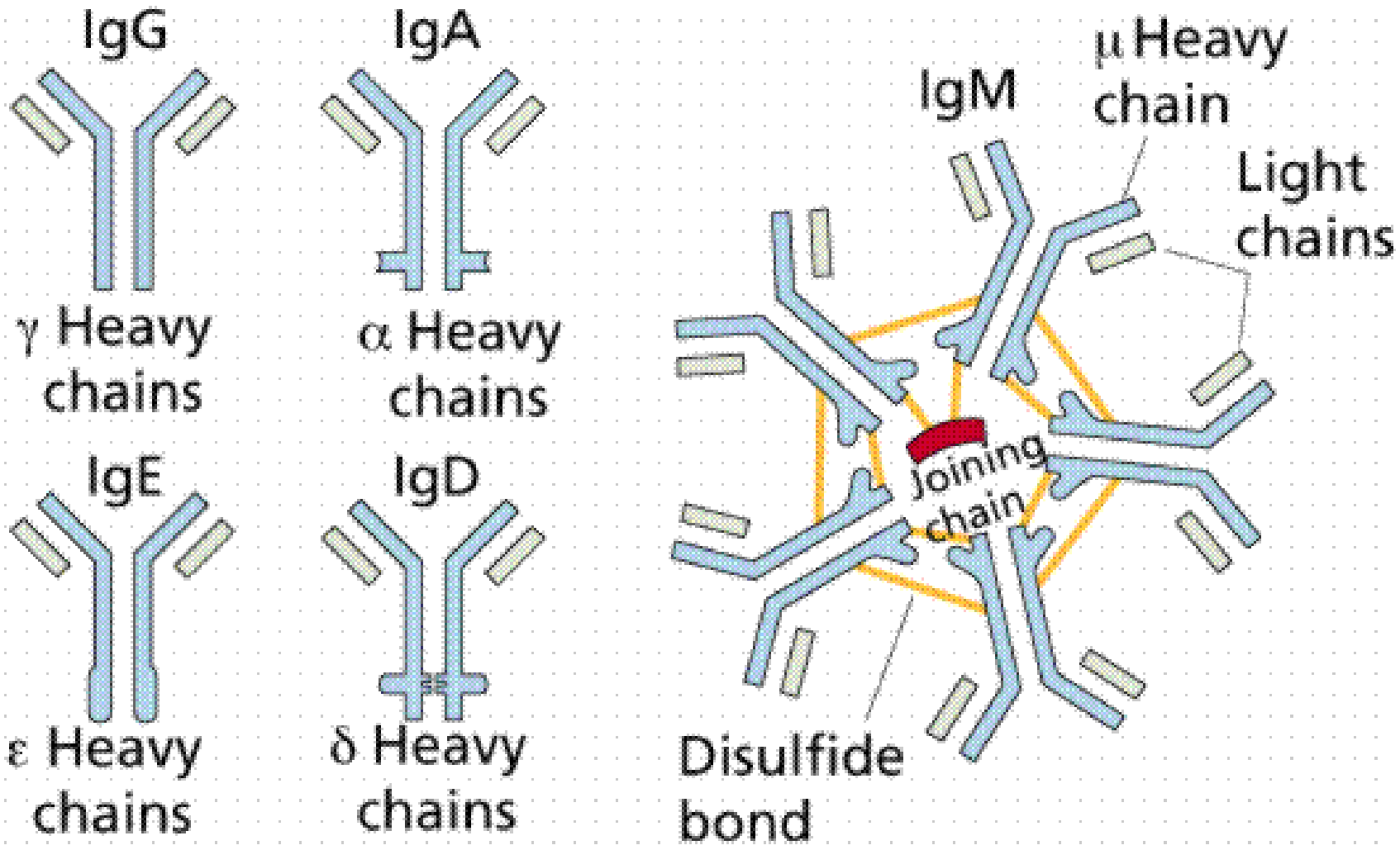
b) Placental transfer - IgG is the only class of Ig that crosses the placenta. Not all subclasses cross equally well; IgG2 does not cross well.

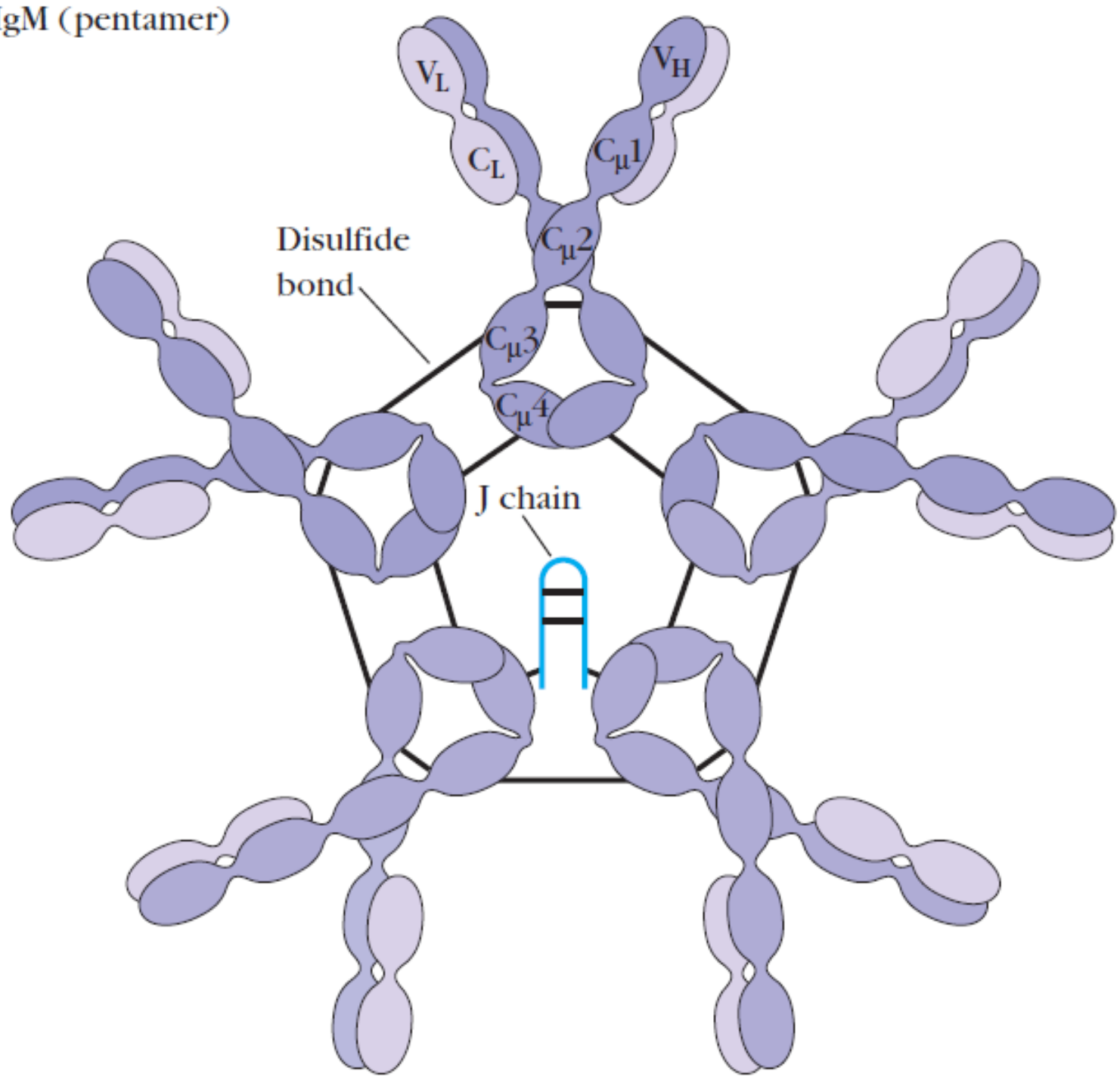
c) Fixes complement - Not all subclasses fix equally well; IgG4 does not fix complement

d) The term opsonin is used to describe substances that enhance phagocytosis. IgG is a good opsonin.

TYPES OF IMMUNOGLOBULIN

- IgM
  - Structure:
    - ✓ IgM normally exists as a pentamer but it can also exist as a monomer.
    - ✓ IgM has an extra domain on the mu chain (C_{H4}) and it has another protein covalently bound via a S-S bond called the Joining chain or J chain. This chain functions in polymerization of the molecule into a pentamer.
    - ✓ macroglobulin


IgG
γ Heavy chains
IgA
α Heavy chains
IgE
ε Heavy chains
IgD
δ Heavy chains
IgM
μ Heavy chain
Light chains
Joining chain
Disulfide bond

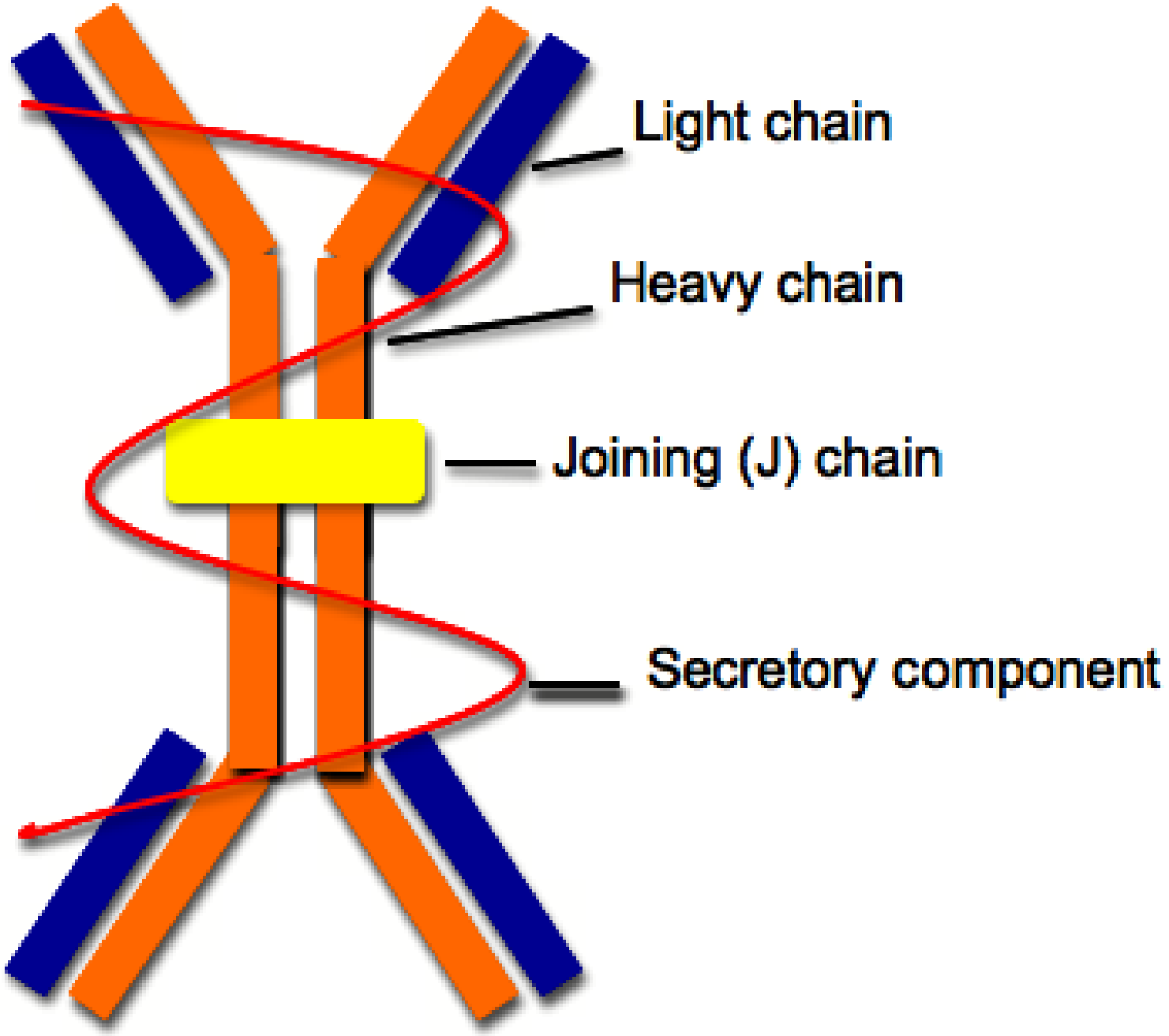

IgM (pentamer)
V_L
V_H
C_L
$C_\mu 1$
Disulfide bond
$C_\mu 2$
$C_\mu 3$
$C_\mu 4$
J chain

TYPES OF IMMUNOGLOBULIN

- Properties:
  - ✓ a) IgM is the third most common serum Ig.
  - ✓ b) IgM is the first Ig to be made by the fetus and the first Ig to be made by a virgin B cells when it is stimulated by antigen.
  - ✓ c) As a consequence of its pentameric structure, IgM is a good complement fixing Ig.
  - ✓ d) IgM is also a good agglutinating Ig .

TYPES OF IMMUNOGLOBULIN

- IgA
  - Structure:
    - ✓ Dimer
    - ✓ When IgA is found in secretions is also has another protein associated with it called the secretory piece
    - ✓ The secretory piece helps IgA to be transported across mucosa and also protects it from degradation in the secretions.


Light chain
Heavy chain
Joining (J) chain
Secretory component

TYPES OF IMMUNOGLOBULIN

- Properties:

  a) IgA is the 2nd most common serum Ig.

  b) IgA is the major class of Ig in secretions - tears, saliva, colostrum, mucus. Since it is found in secretions secretory IgA is important in local (mucosal) immunity.

  c) Normally IgA does not fix complement, unless aggregated.

TYPES OF IMMUNOGLOBULIN

➢ **IgD**

- Structure:

✓ Monomer

✓ Percentage serum antibodies: 0.2%

✓ Half-life in serum: 3 days

✓ Complement Fixation: No

✓ Placental Transfer: No

✓ Known Functions: In serum function is unknown. On B cell surface, initiate immune response.

TYPES OF IMMUNOGLOBULIN

➢ **IgE**

- Structure:

✓Monomer

✓Percentage serum antibodies: 0.002%

✓Half-life in serum: 2 days

✓Complement Fixation: No

✓Placental Transfer: No

✓Known Functions: Allergic reactions. Possibly lysis of worms.

TABLE 3-2 Chain composition of the five immunoglobulin classes

Class*	Heavy chain	Number of C_H Ig domains	Subclasses	Light chain	J chain	Molecular formula
IgG	γ	3	γ1, γ2, γ3, γ4 (human) γ1, γ2a, γ2b, γ3 (mouse)	κ or λ	None	$\gamma_2\kappa_2$ $\gamma_2\lambda_2$
IgM	μ	4	None	κ or λ	Yes	$(\mu_2\kappa_2)_n$ $(\mu_2\lambda_2)_n$ n = 1 or 5
IgA	α	3	α1, α2	κ or λ	Yes	$(\alpha_2\kappa_2)_n$ $(\alpha_2\lambda_2)_n$ n = 1, 2, 3, or 4
IgE	ε	4	None	κ or λ	None	$\epsilon_2\kappa_2$ $\epsilon_2\kappa_2$
IgD	δ	3	None	κ or λ	None	$\delta_2\kappa_2$ $\delta_2\lambda_2$

*See Figure 3-22 for general structures of the five antibody classes.


“IF YOU REALLY WANT TO DO SOMETHING, YOU WILL FIND A WAY. IF YOU DON'T, YOU'LL FIND AN EXCUSE.”
JIM ROHN
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