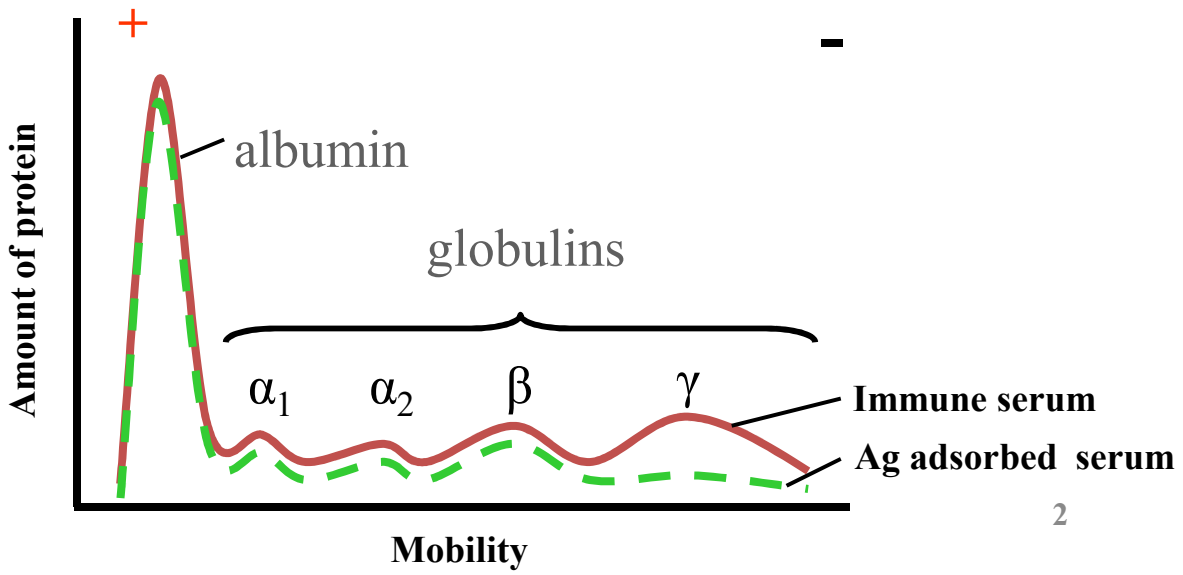
Immunoglobulins: Structure and Function

Immunoglobulins:

- Definition: Glycoprotein molecules that are produced by plasma cells in response to an immunogen and which function as antibodies

Association of Ab activity with gamma globulins was determined through experiments involving electrophoresis .



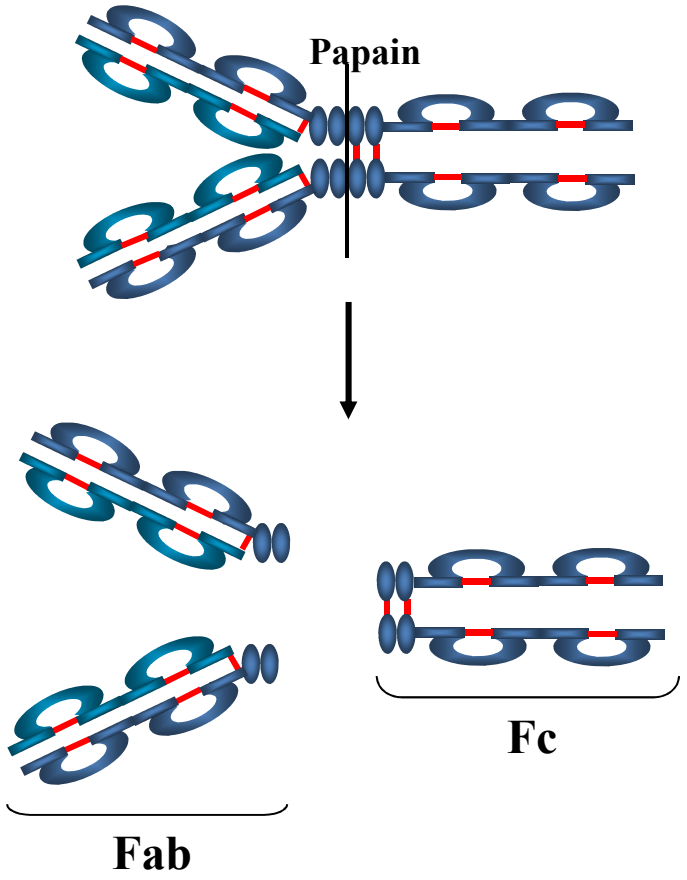
General Functions of Immunoglobulins

- Ag binding
  - Can result in protection
- Effector functions (Usually require Ag binding)
  - Fixation of complement
  - Neutralization
  - Opsonization

Immunoglobulin Fragments:

Porters Expt: Using the enzyme papain/gel filtration chromatography yielded 3 fragments

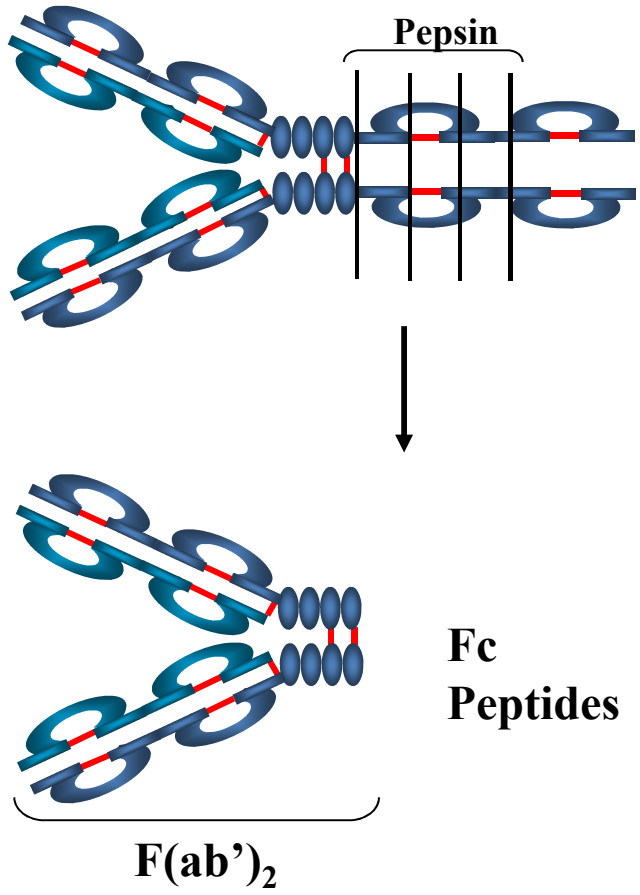
- 2 Fab fragments
  - Ag binding
  - Valence = 1
  - MW of 50,000 each
- 1 Fc fragment
  - cannot bind Ag
  - crystallizable fragment
  - Effector functions



Immunoglobulin Fragments:

Nisonoffs expt using pepsin

- 1 $F(ab')_2$
  - – Divalent
  - Fc fragments

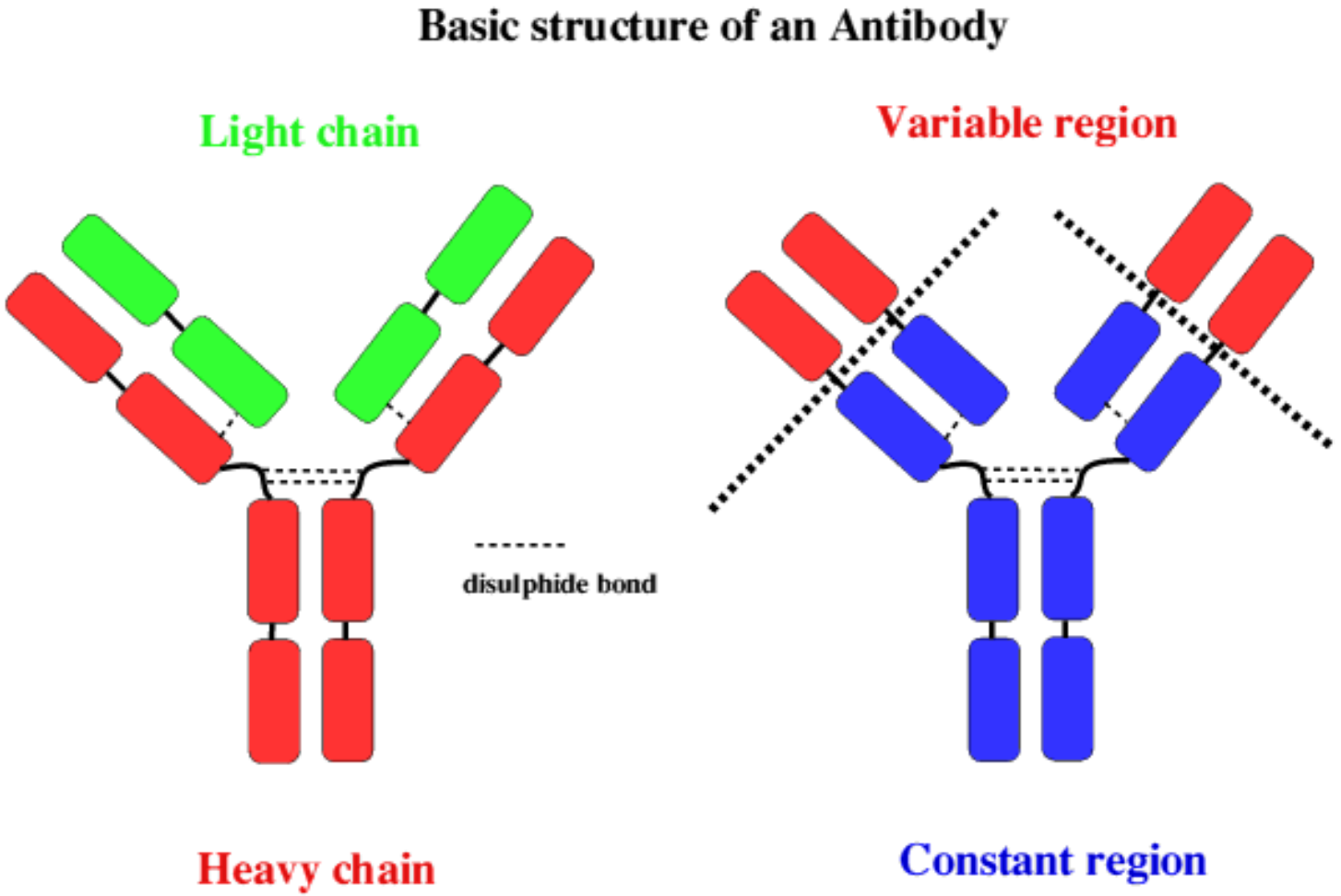


Basic Immunoglobulin Structure

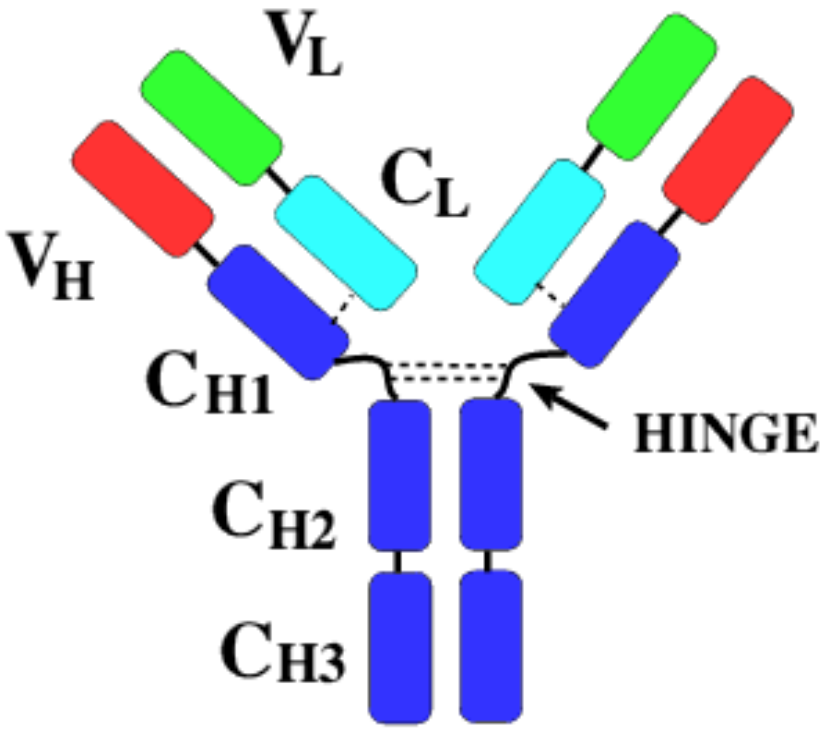
- Immunoglobulins – heterogeneous
  - 2 identical Light chains
  - 2 identical heavy chains
    - Fab has both H and L chains

- Multiple myeloma – large clone of cells producing one type of Ig. (cancerous Ab producing Plasma cells)
- Myeloma proteins – homogeneous
  - Bence Jones proteins are L chain dimers

Immunoglobulin Structure



ANTIBODY DOMAIN STRUCTURE

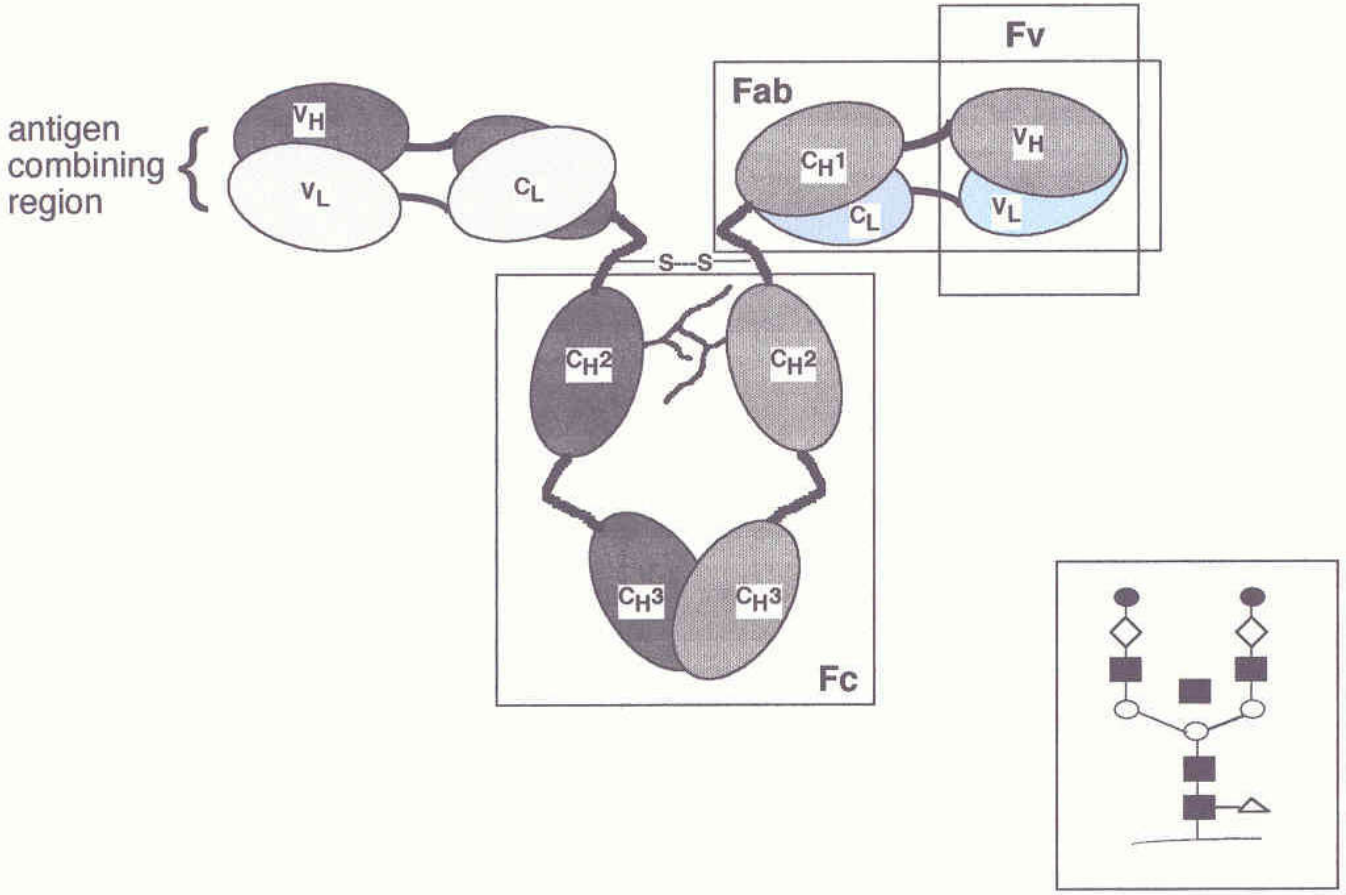


Immunoglobulin domains

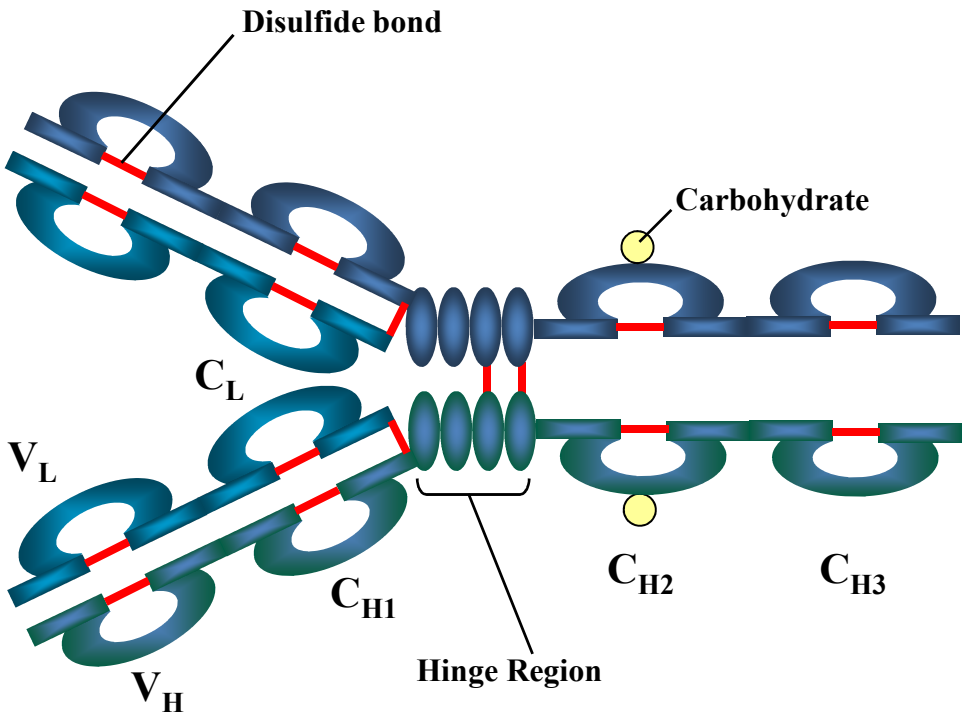
- Each chain has about 110 amino acids
- intrachain disulfide bonds
- Discrete compactly folded region

- 4 (or 5) in heavy chain, 2 in light chain.
- Both heavy and light chains have
- 1 variable domain at the N-terminus

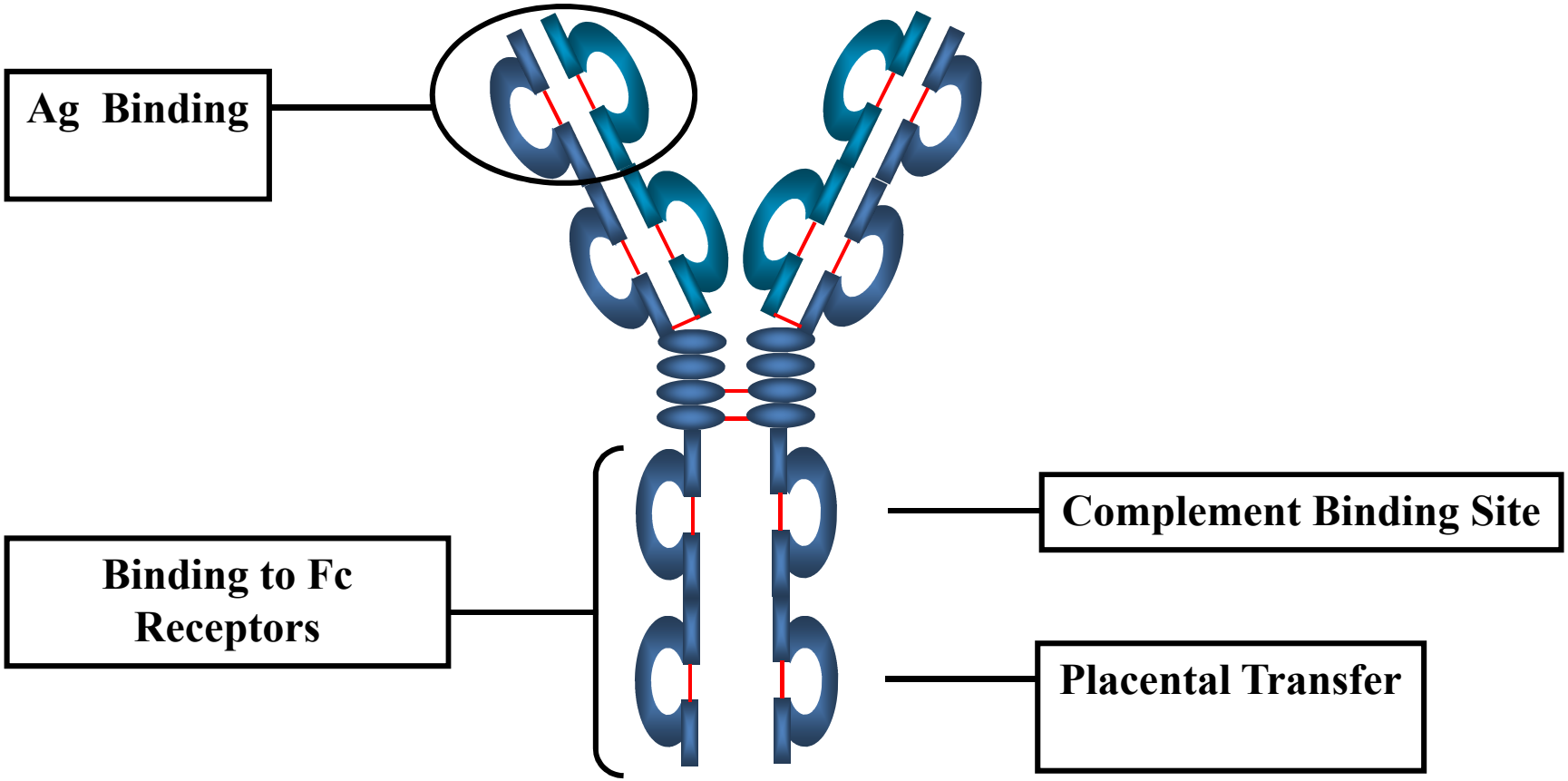
- Chains held together by
- disulfide bonds
- noncovalent interactions


antigen
combining
region
V_H
V_L
C_L
Fab
Fv
C_{H1}
V_H
C_L
V_L
S---S
C_{H2}
C_{H2}
C_{H3}
C_{H3}
Fc

- Heavy & Light Chains
- Disulfide bonds
  Inter-chain
  Intra-chain
- Variable & Constant Regions
  V_L & C_L
  V_H & C_H
- Hinge Region
- Domains
  - V_L & C_L
  - V_H & C_{H1} - C_{H3} (or C_{H4})
- Oligosaccharides



Immunoglobulin Fragments: Structure/Function Relationships



Human Immunoglobulin Classes

- 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

Human Immunoglobulin Subclasses

- IgG Subclasses
  - IgG1 - Gamma 1 (γ1) heavy chains
  - IgG2 - Gamma 2 (γ2) heavy chains
  - IgG3 - Gamma 3 (γ3) heavy chains
  - IgG4 - Gamma 4 (γ4) heavy chains
- IgA subclasses
  - IgA1 - Alpha 1 (α1) heavy chains
  - IgA2 - Alpha 2 (α2) heavy chains

Human Immunoglobulin Light Chain Types

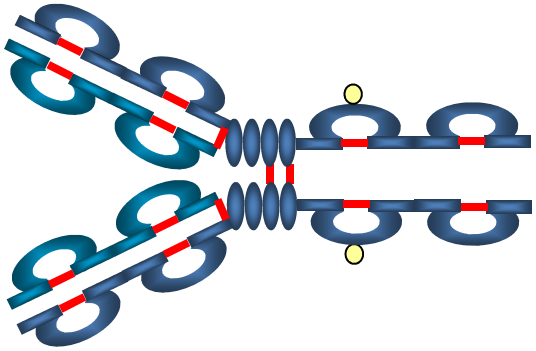
- Kappa (κ)
- Lambda (λ)

Human Immunoglobulin Light Chain Subtypes

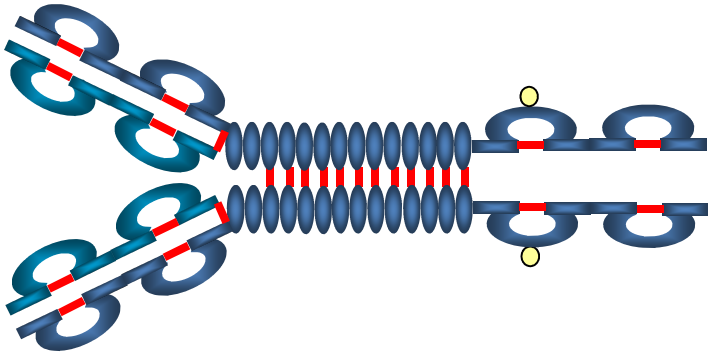
- Lambda light chains
  - Lambda 1 (λ1)
  - Lambda 2 (λ2)
  - Lambda 3 (λ3)
  - Lambda 4 (λ4)

IgG

- Structure
  - Monomer (7S)



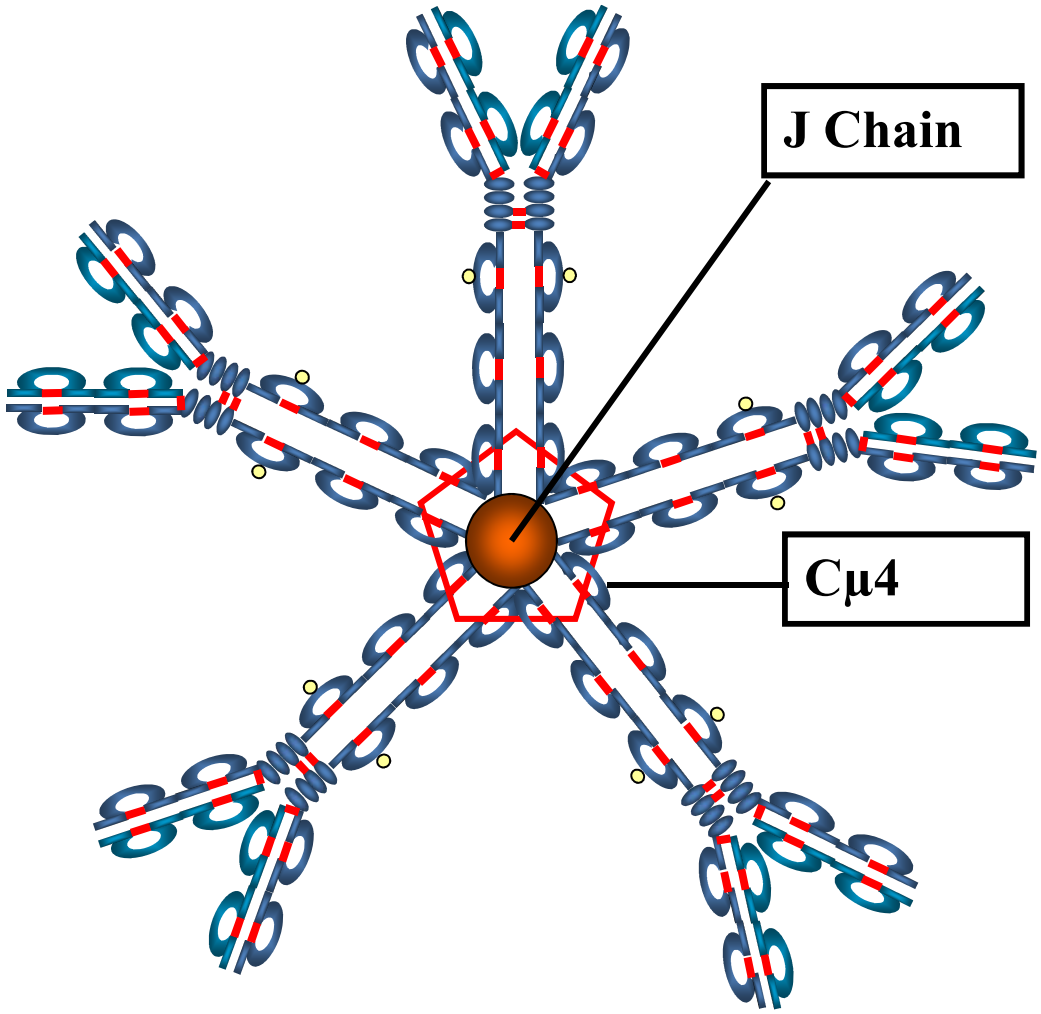
IgG1, IgG2 and IgG4



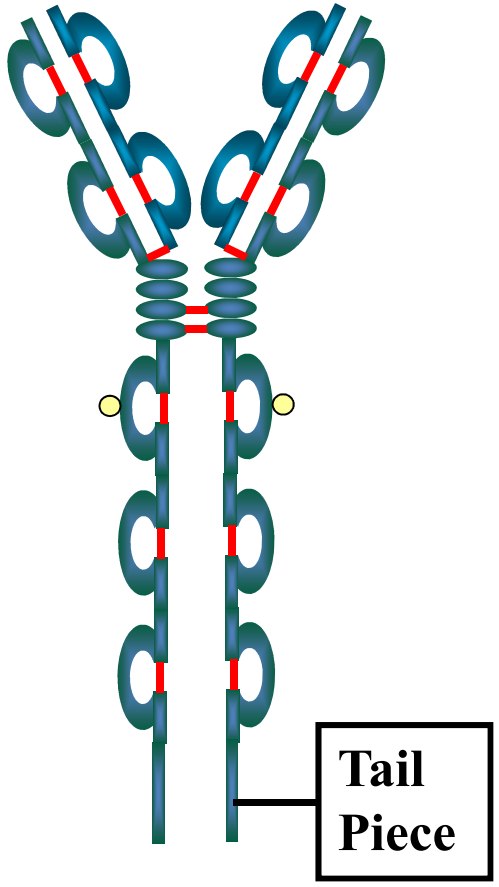
IgG3

IgM

- Structure
  - Pentamer (19S)
  - Extra domain (C_{H4})
  - J chain

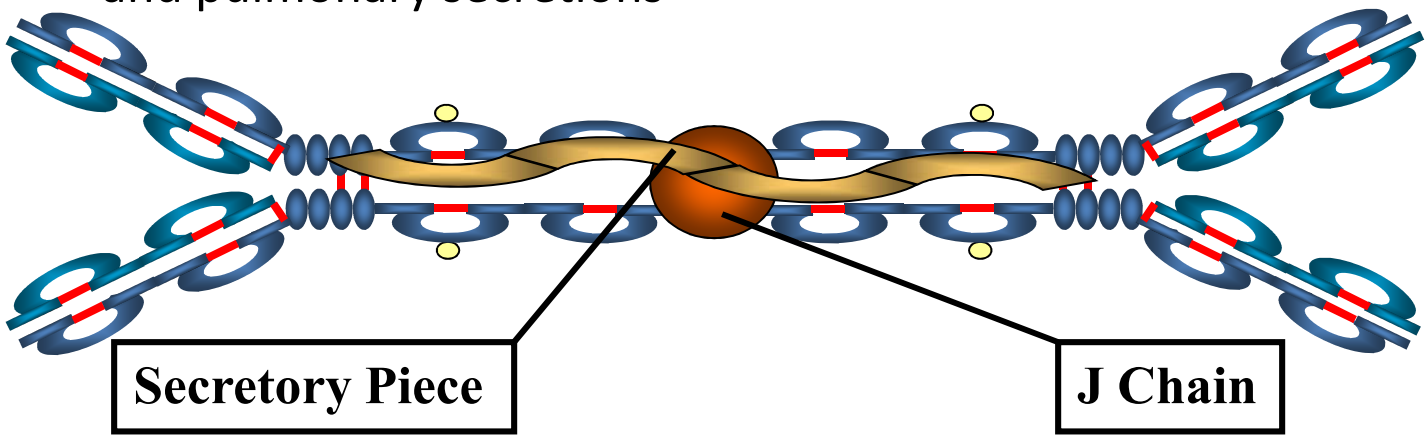


IgM



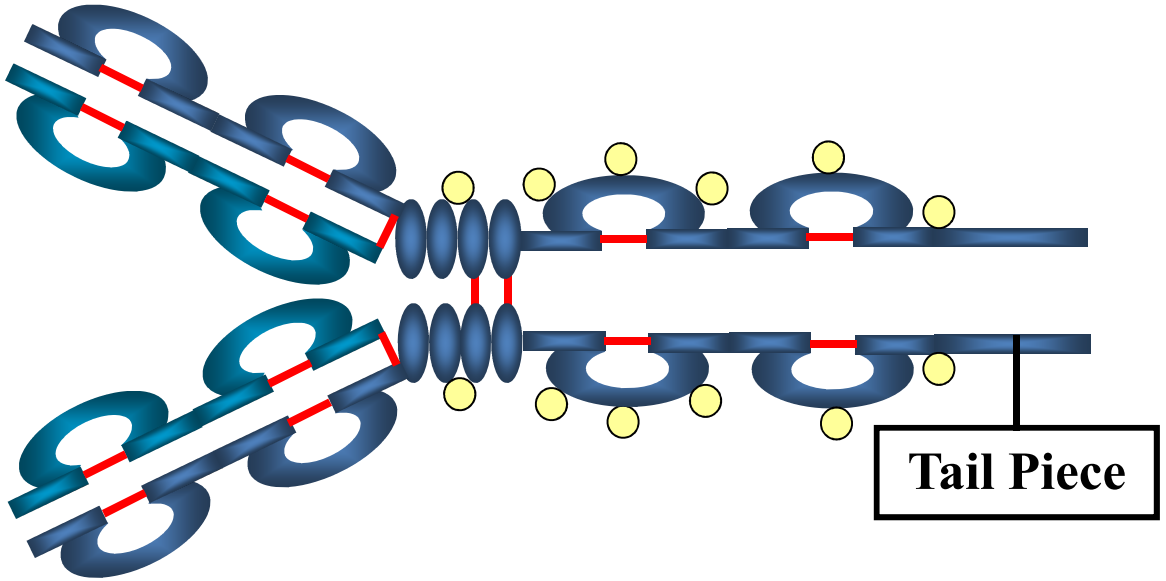
IgA

- Structure
  - Serum - monomer
  - Secretions (sIgA)
    - Dimer (11S)
    - J chain
    - Secretory component- Major secretory Ig (Mucosal or Local Immunity)Tears, saliva, gastric and pulmonary secretions



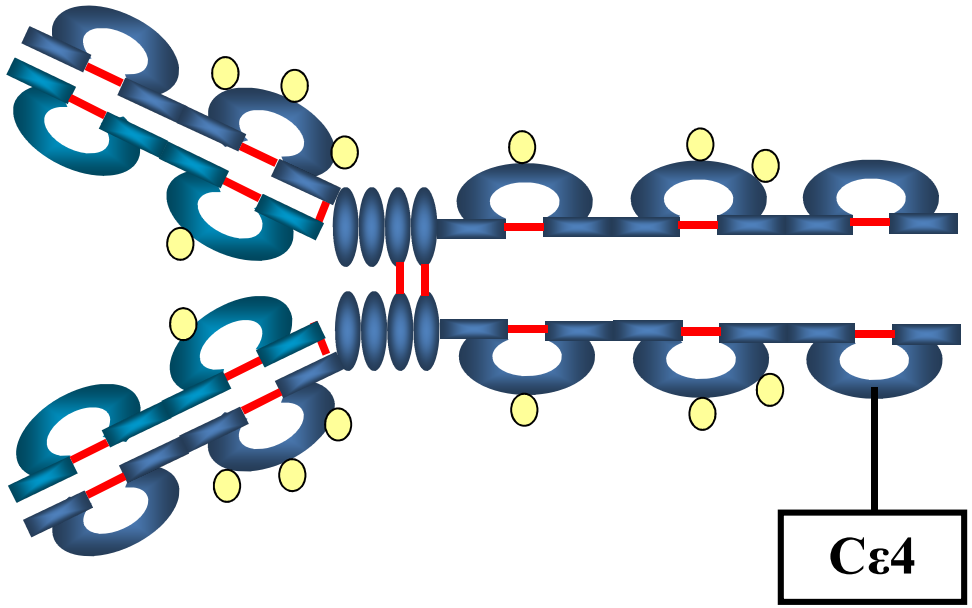
IgD

- Structure
  - Monomer
  - Tail piece



IgE

- Structure
  - Monomer
  - Extra domain (C_{H4})



IgE

- Structure
- Properties
  - Least common serum Ig
    - Binds to basophils and mast cells (Does not require Ag binding)
  - Allergic reactions
  - Parasitic infections (Helminths)
    - Binds to Fc receptor on eosinophils
  - Does not fix complement

Immunoglobulin subclasses differ in structure and function

	IgM	IgG1	IgG2	IgG3	IgG4	IgA1,2	IgE	IgD
form	pentamer	mono	mono	mono	mono	dimer	mono	mono
serum level (mg/ml)	1.5	9	3	1	0.5	3.5	0.00005	0.03
Complement activation	+++	+++	+	+++	-	-	-	-
Placental transfer	-	+	+	+	+	-	-	-
macrophage (Fc receptor) binding	-	+	-	+	-	-	-	-
present in external secretions	mucus etc	milk	milk	milk	milk	mucus etc	-	-