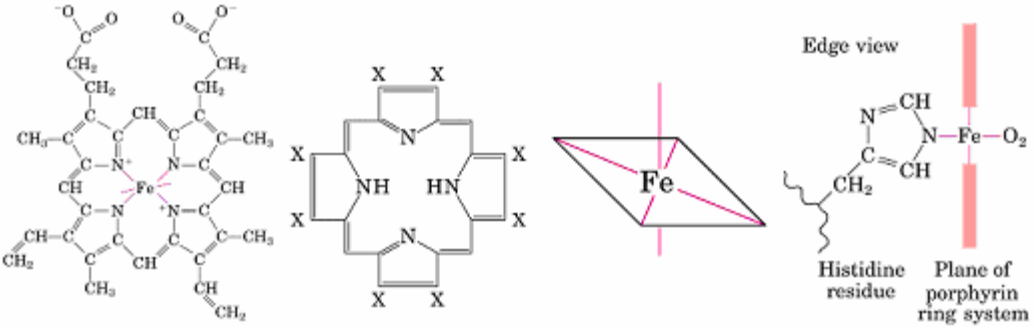
Protein Function

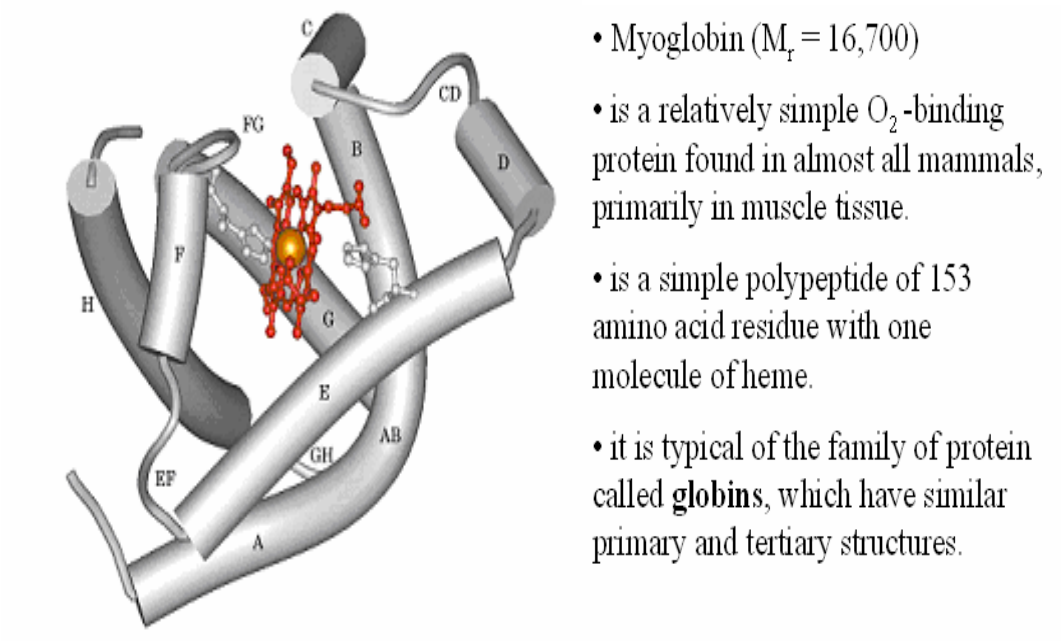
- A molecular bound reversibly by a protein is called a **ligand**.
- A ligand binds at a site on the protein called the **binding site**, which is complementary to the ligand in size, shape, charge and hydrophobic or hydrophilic character.
- The structural adaptation that occurs between protein and ligand is called **induced fit**

Haeme group.

- Oxygen reacts at one of the two 'open' coordination bonds of iron.
- When O2 binds – colour changes from dark purple to bright red
- Some molecules such as carbon dioxide (CO) and nitric oxide (NO) coordinate the heme iron with greater affinity than does O2

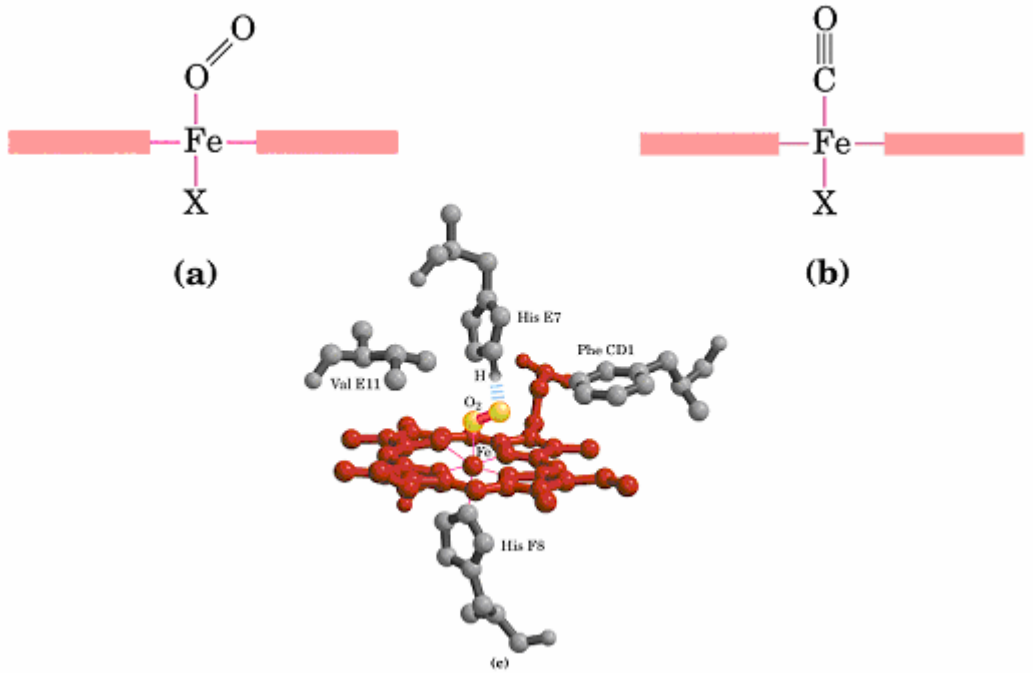


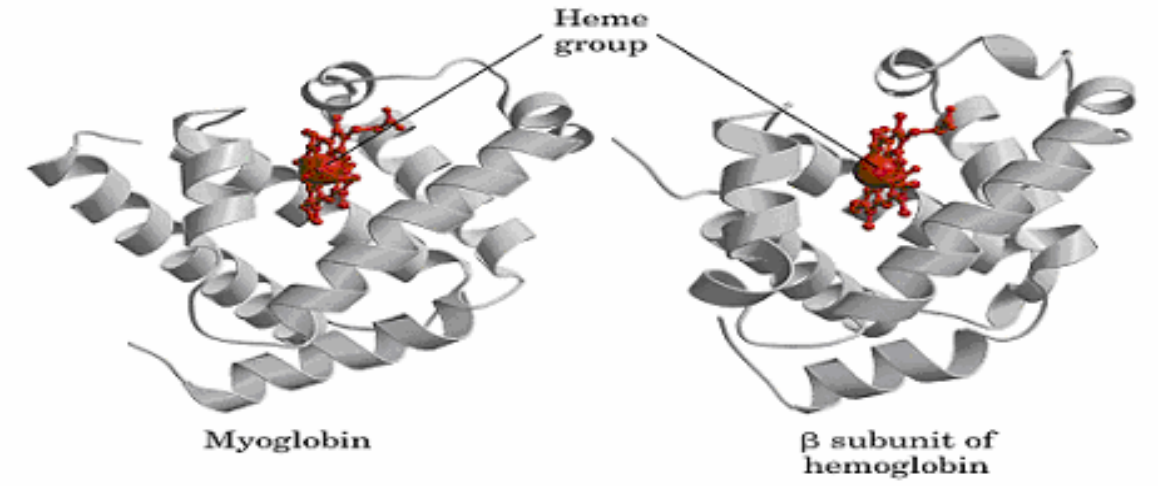
Structure of myoglobin



- Myoglobin (M_r = 16,700)
- is a relatively simple O_2-binding protein found in almost all mammals, primarily in muscle tissue.
- is a simple polypeptide of 153 amino acid residue with one molecule of heme.
- it is typical of the family of protein called **globins**, which have similar primary and tertiary structures.

Steric effects on the binding of ligands to the heme of myoglobin



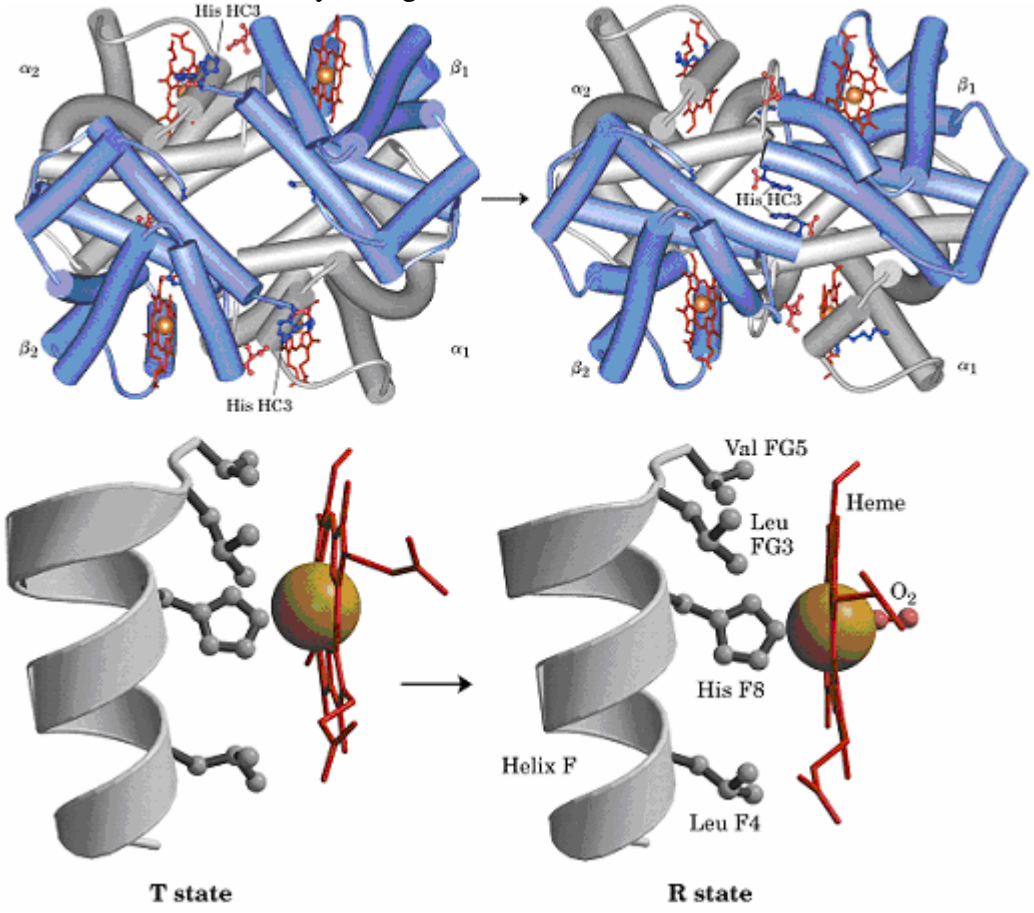


- Nearly all the oxygen carried by the whole blood in animals is bound and transported by hemoglobin in **erythrocytes** (red blood cells).
- Normal human erythrocytes are small (6 to 9 µm in diameter), biconcave disks. They are formed from precursor stem cells called **hemocytoblasts**.
- Erythrocytes are unable to replicate and survive only 120 days.
- Myoglobin is relatively insensitive to small changes in the conc. of dissolved oxygen and so functions well as an oxygen-storage protein. Hemoglobin with its multiple subunits, is better suited to oxygen transport.

The T and R transition

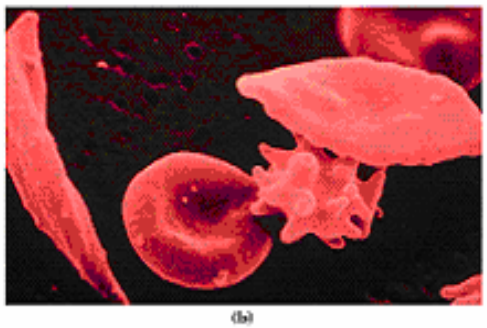
R state = relaxed
T state = tense

- Although oxygen binds to hemoglobin in either state, it has a significantly higher affinity for hemoglobin in the R state. Oxygen binding stabilises the R state.
- When oxygen is absent, the T state is more stable and is this the predominant conformation of deoxyhemoglobin.

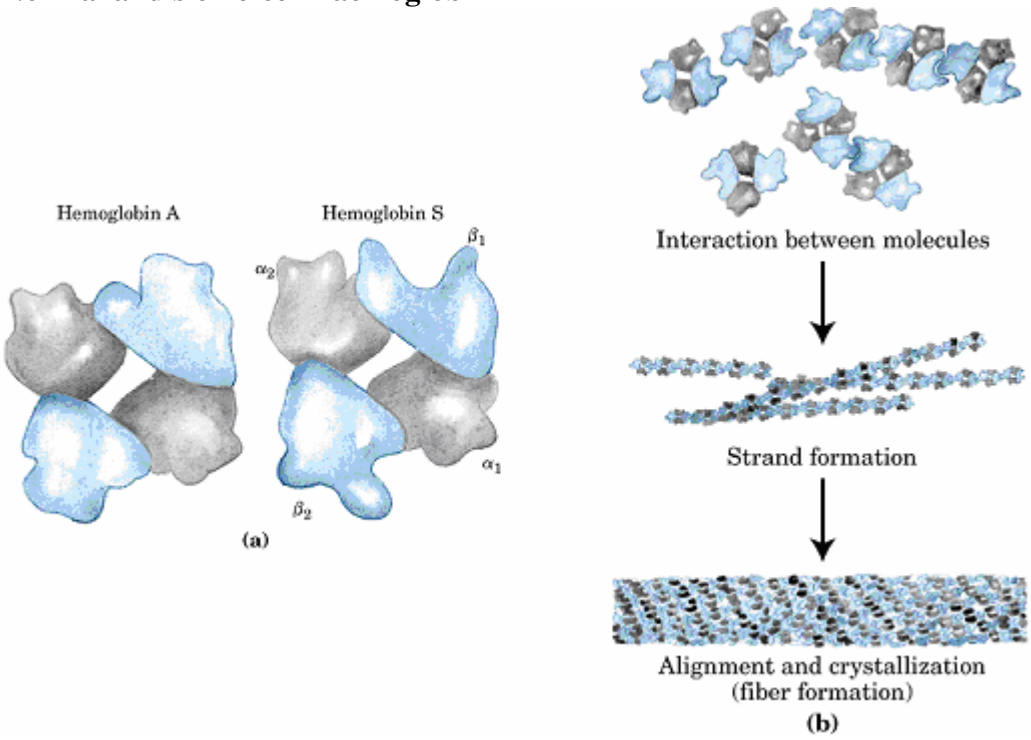


Normal red blood cell

Sickle-cell hemogoblin



Normal and sickle-cell haemoglobin



The immune system.

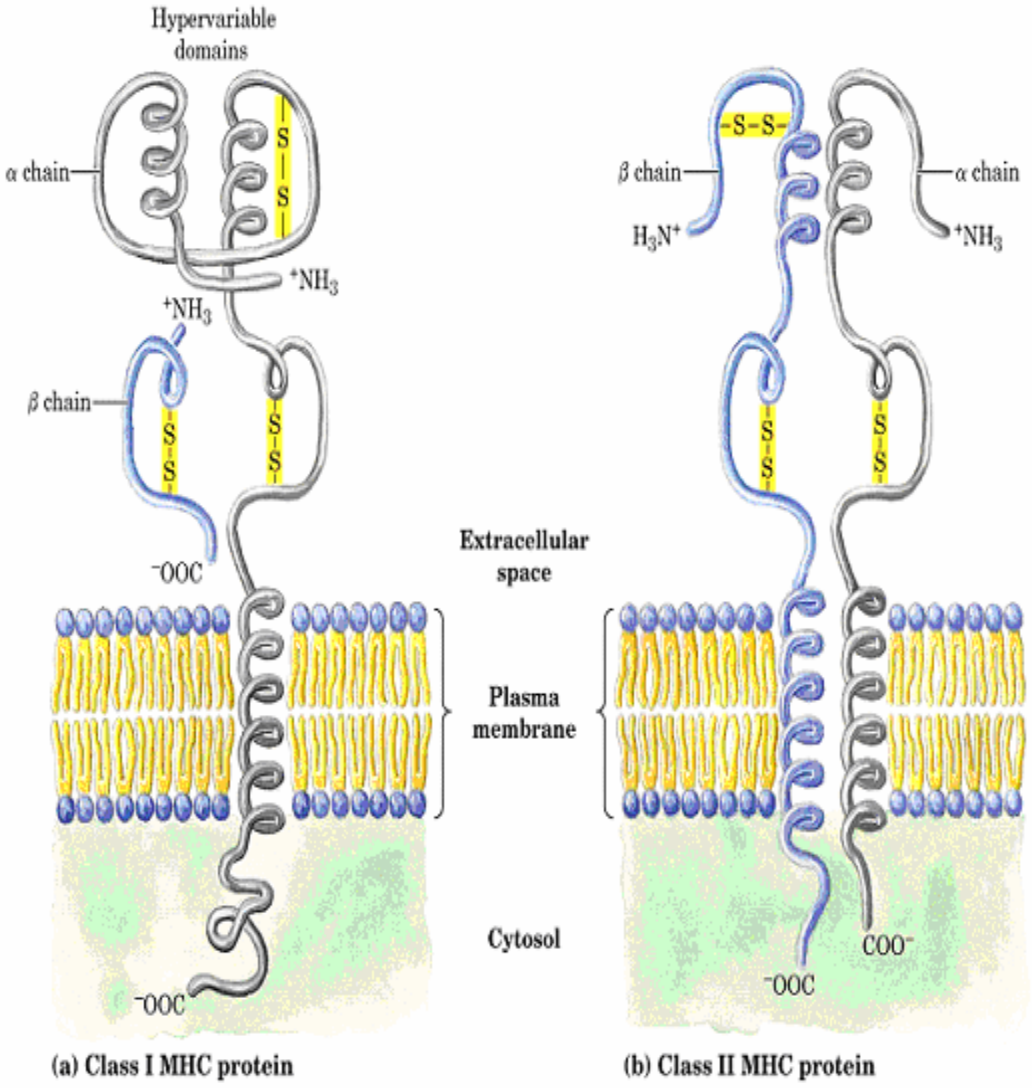
- Leukocytes (white blood cells), including macrophages and lymphocytes all arise from undifferentiated stem cells in the bone marrow.
- Immune response consists of two complementary systems

1. **Humoral immune system** - directed at bacterial infections and extracellular viruses, but can also respond to individual proteins introduced into the organism.
2. **Cellular immune system** – destroys host cells infected by viruses and also destroys some parasites and foreign tissue.

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.

MHC (**Major Histocompatibility complex**) proteins

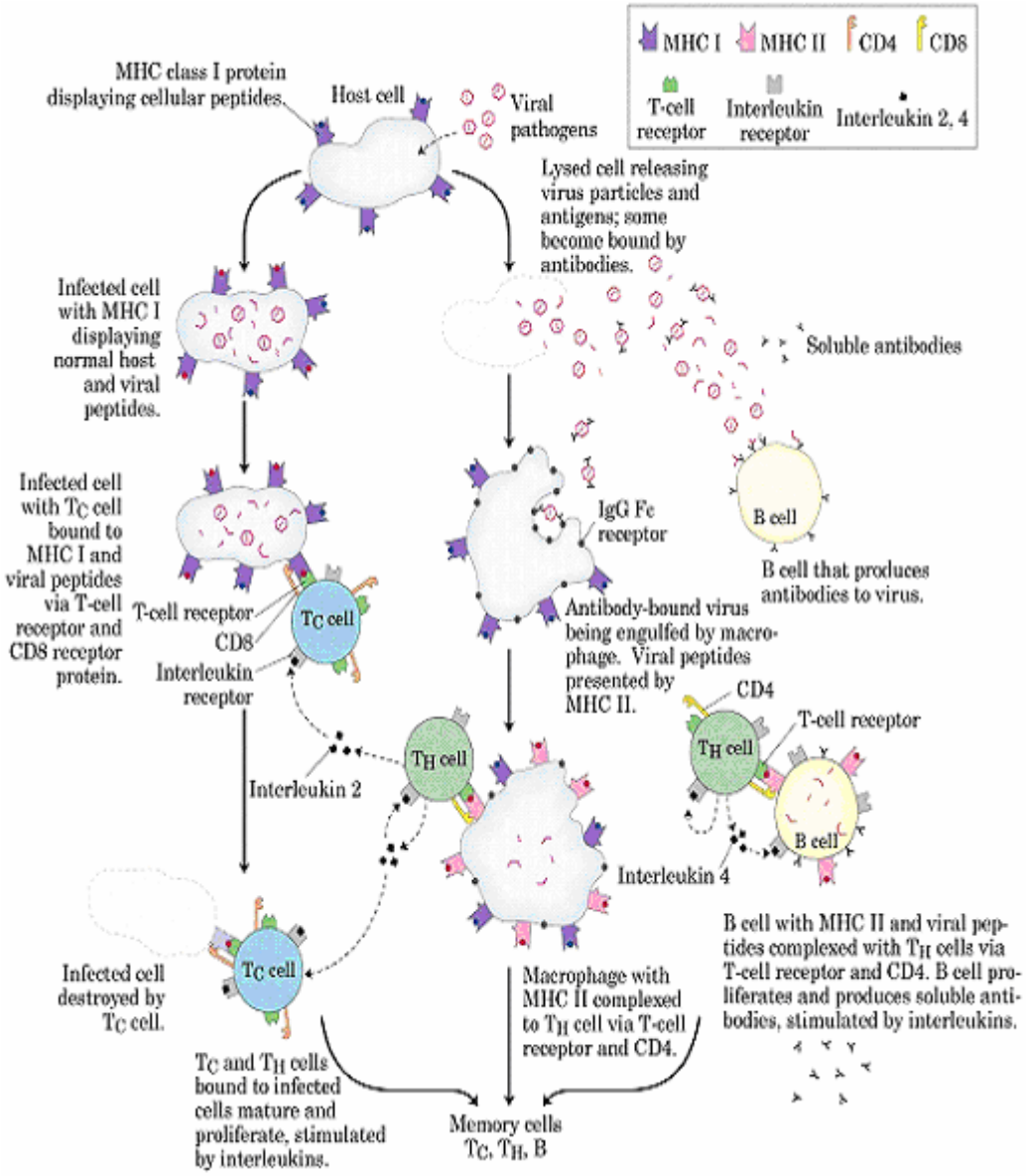


MHC Proteins

- There are two classes of MHC proteins which differ in their distribution among cell types and in the source of digested proteins

1. **Class I MHC** - are found on the surface of virtually all vertebrate cells. These complexes of peptides and class I MHC proteins are the recognition targets of the **T-cell** receptors of the **T_c cells** in the cellular immune system.

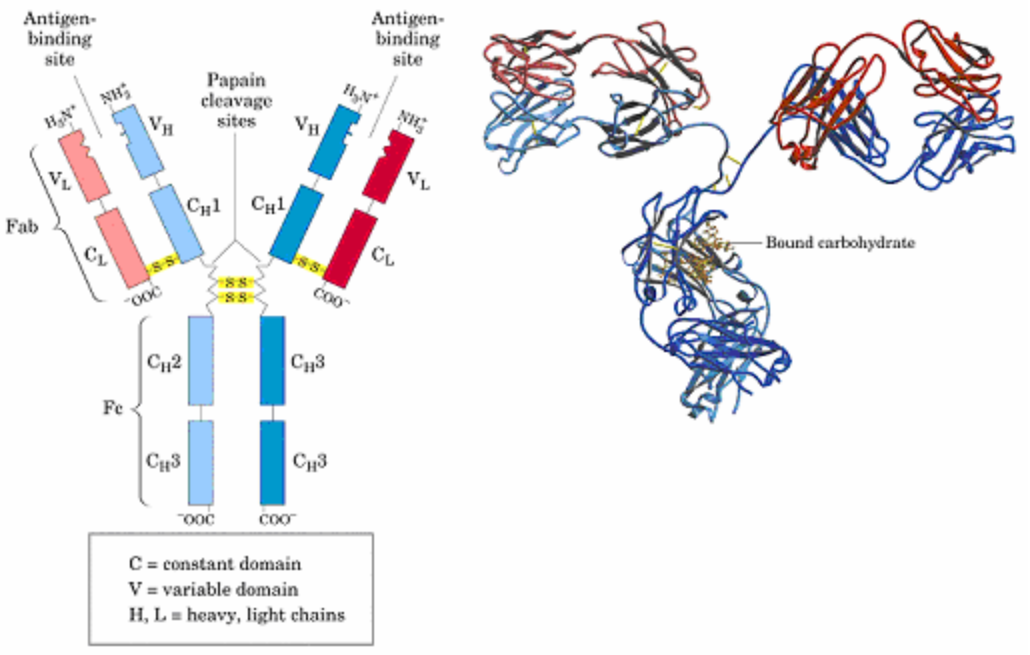
2. **Class II MHC** – occur on the surface of a few types of specialised cells that take up foreign antigen, including macrophages and B lymphocytes. Class II MHC are highly polymorphic, with many variants in the human population. Each human is capable of producing 12 variants, and thus it is unlikely that any two individuals have an identical set of variants.



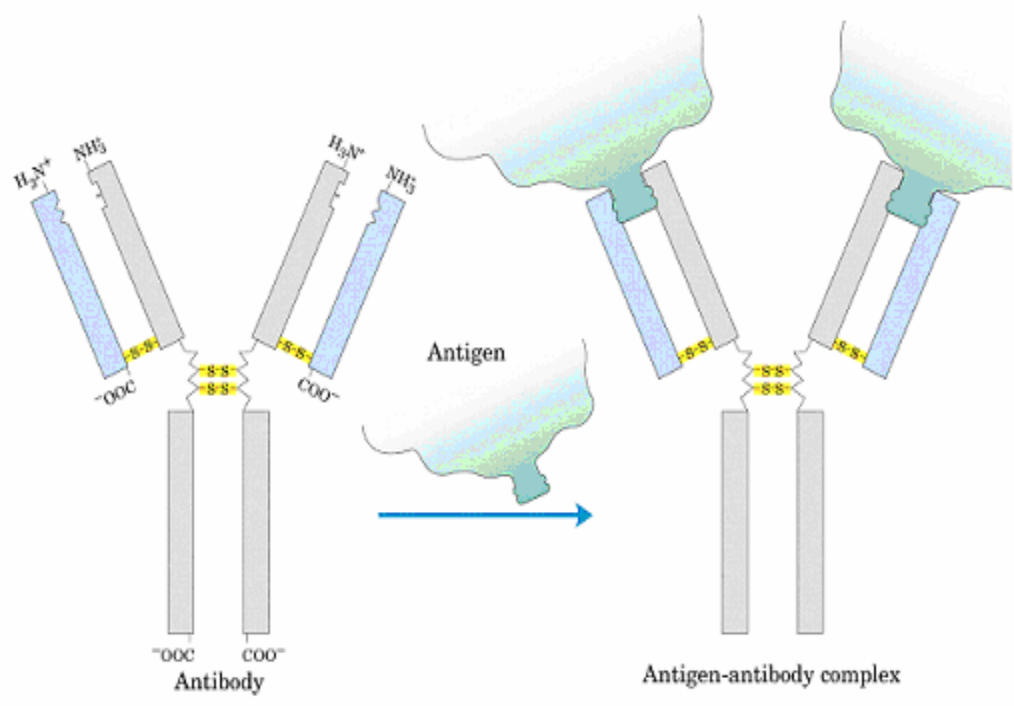
Structure of Immunoglobulin G (IgG)

- IgG has four polypeptide chairs: two large ones (**heavy chains**) and two **light chains**, linked by non-covalent and disulfide bonds

- When cleaved it produces a basal fragment, called **Fc** because it usually crystallises readily, and two branches, which are called **Fab**, the antigen-binding fragment.



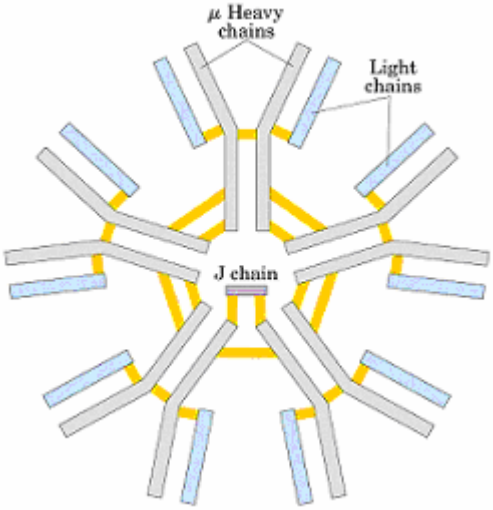
Binding of IgG to an antigen



The constant domains have a characteristic structure know as the immunoglobulin fold, a well-conserved motif in the all-β class

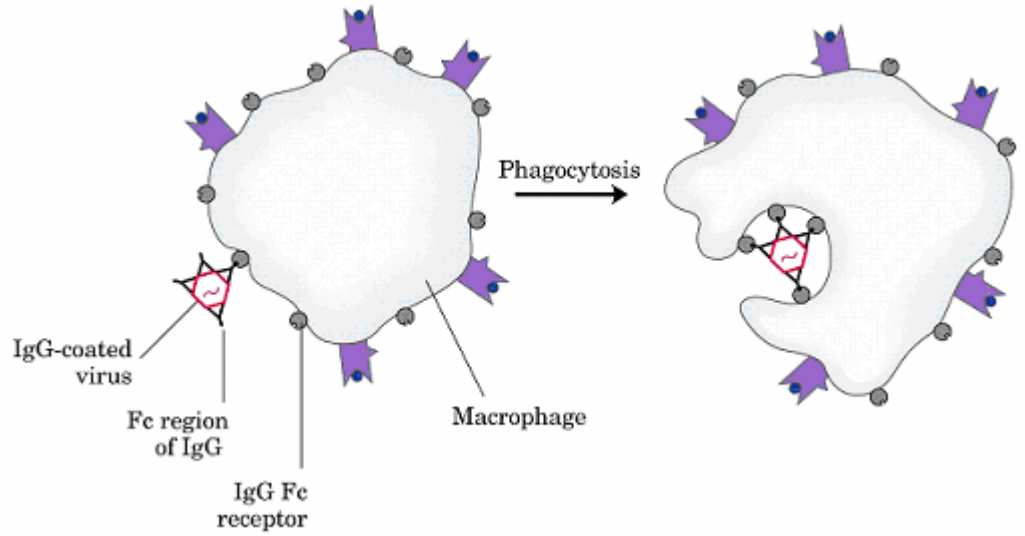
IgM pentamer of immunoglobulin units

IgG is only one of five classes of immunoglobulins. Each class has a characteristic type of heavy chain, denoted by **α, δ, ε, γ**, and **μ** for **IgA, IgD, IgE, IgG** and **IgM** respectively. Two types of light chain, **κ** and **λ** occur in all classes of immunoglobins.



The overall structures of IgG and IgE are similar to that of IgG. IgM occurs either in monomeric (membrane-boudn form) or a secreted form that is a cross-linked pentamer.
IgA, found principaly in secretions (saliva, tears and milk), can be a monomer, dimer or trimer.

Phagocytosis

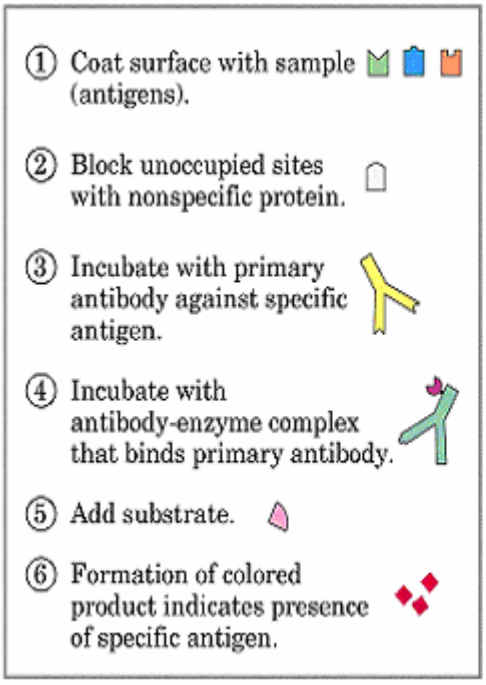


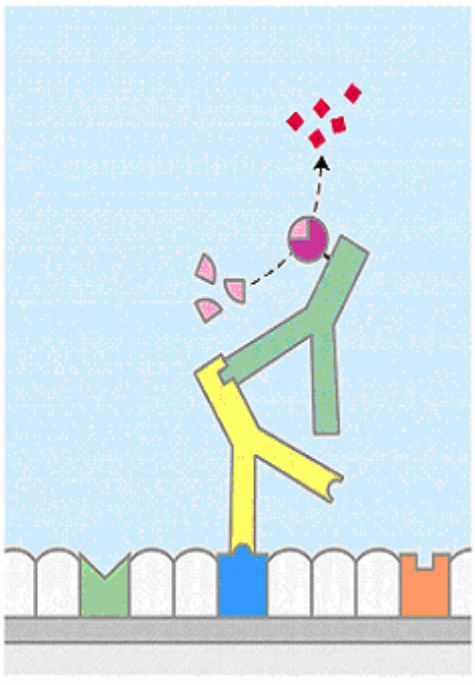
Two types of antibody preparations are in use:

1. **Polyclonal antibodies**, are those produced by many different D lymphocytes responding to one antigen, such as a protein injection into an animal.

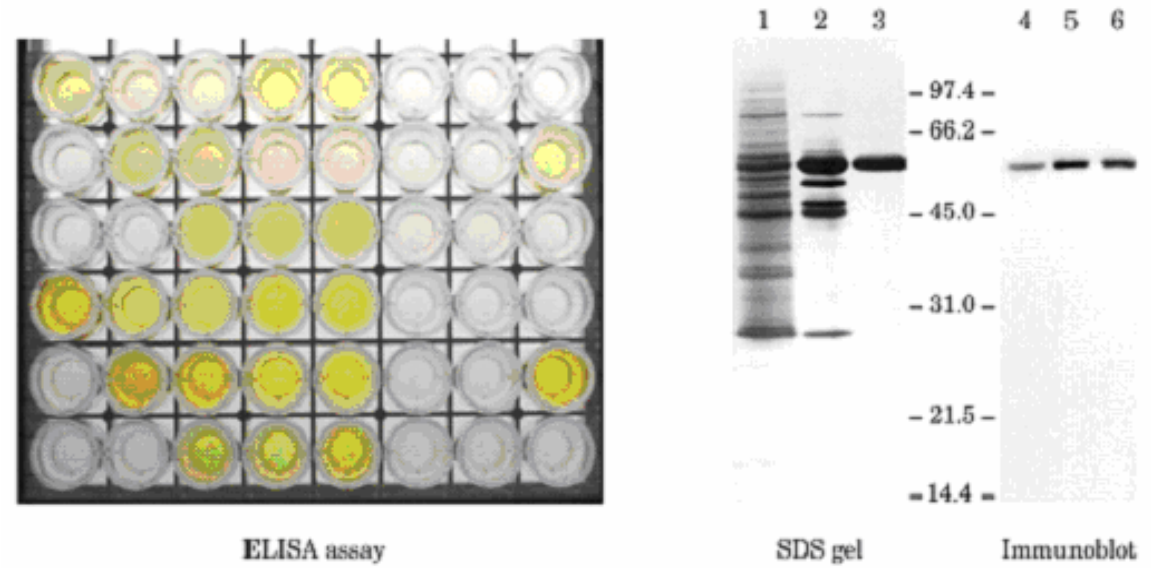
2. **Monoclonal antibodies**, are synthesised by a population of identical B cells (a clone) grown in cell culture. These antibodies are homogeneous, all recognising the same epitope.

Antibody techniques



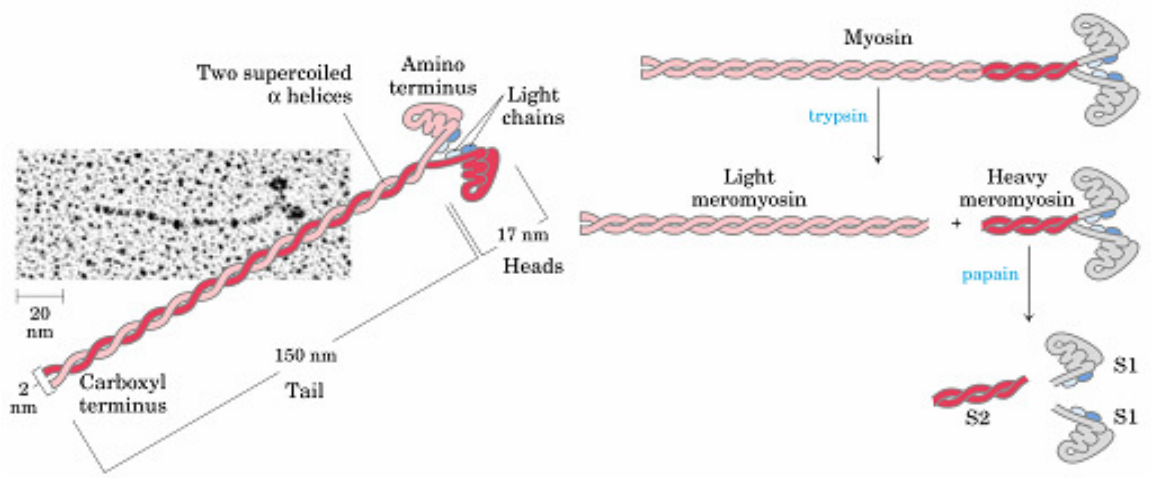


ELISA (enzyme-linked immunosorbent assay) and Immunoblot assays



Myosin

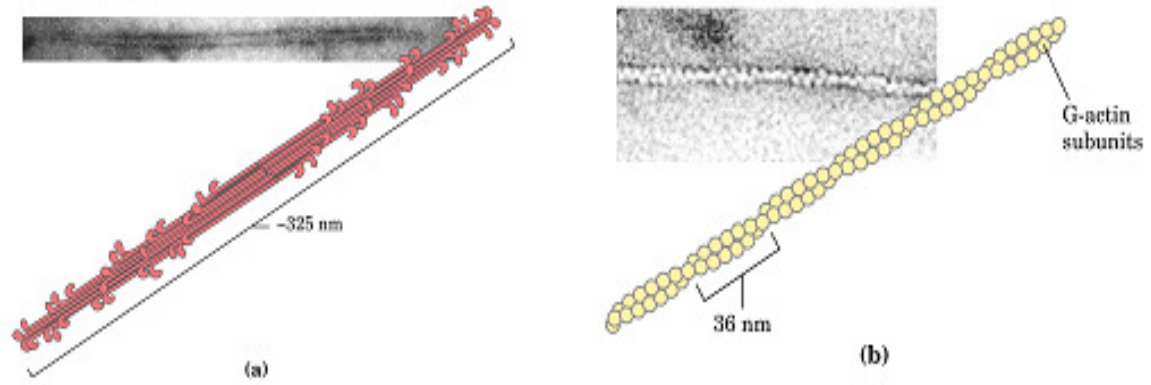
(Mr 540,000) has six subunits: two heavy chains (Mr 220,000) and four light chains (Mr 20,000). In muscle cells, molecules of myosin aggregate to form structures called **thick filaments**.



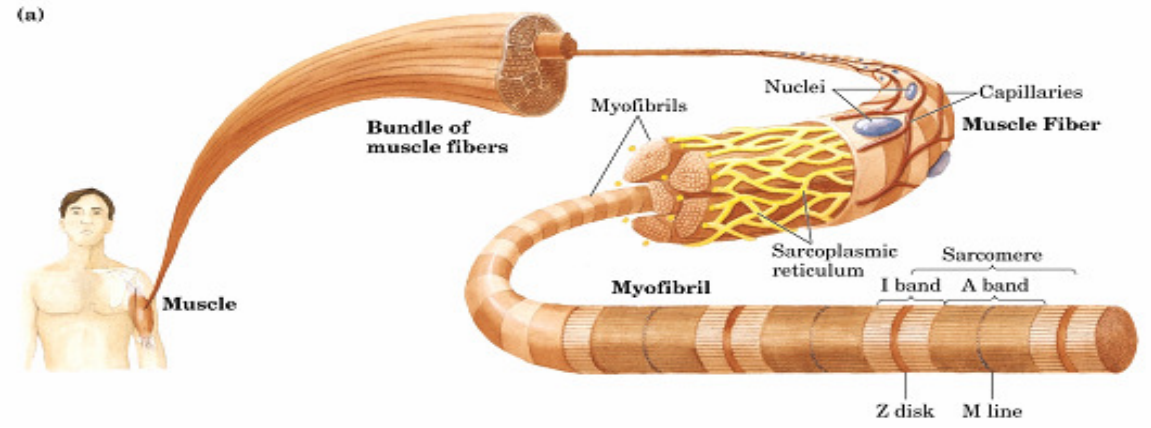
Major components of muscle

The second major muscle protein is actin.

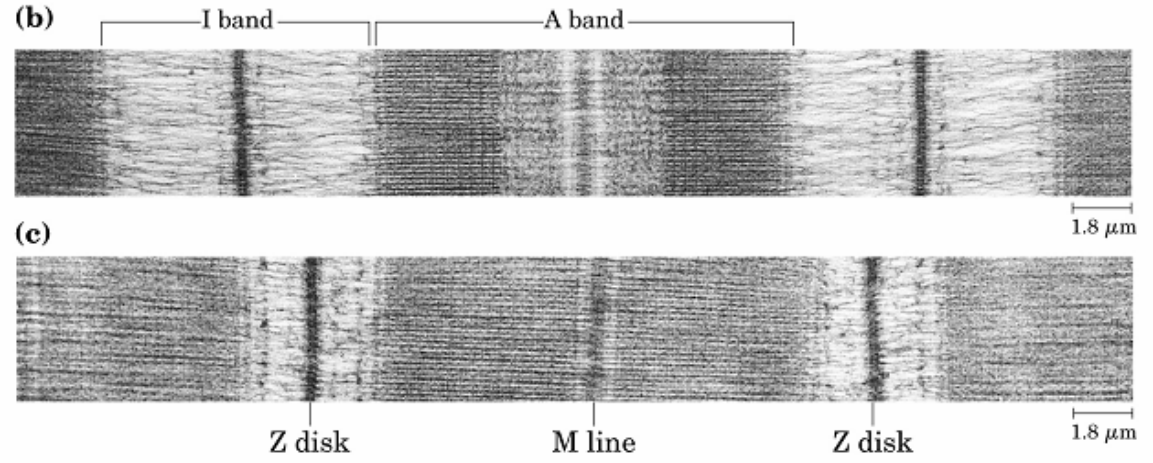
In muscle, molecules of monomeric actin, called **G-actin** (globular actin), associate to form a longer polymer called **F-actin** (Filamentous actin).
Thin filament consists of F-actin along with the proteins troponin and tropomyosin.
Myofilbrils consists of vast numbers of regularly arrayed thick and thin filaments complexed to other proteins



Structure of skeletal muscle

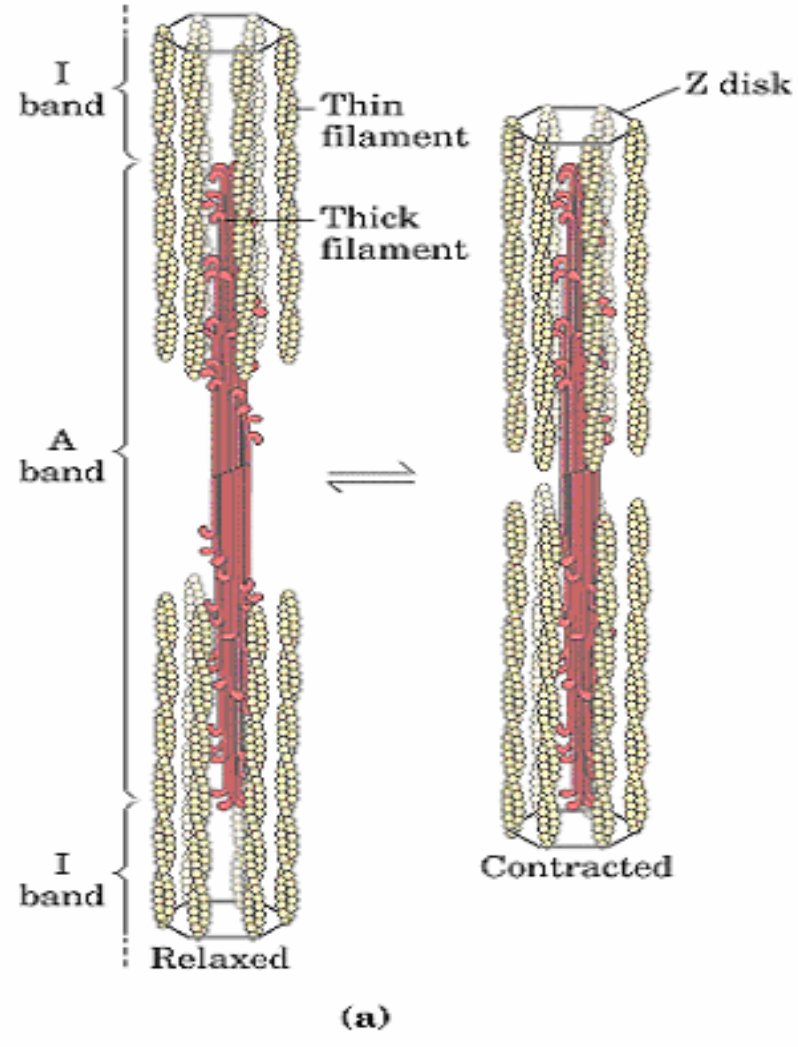


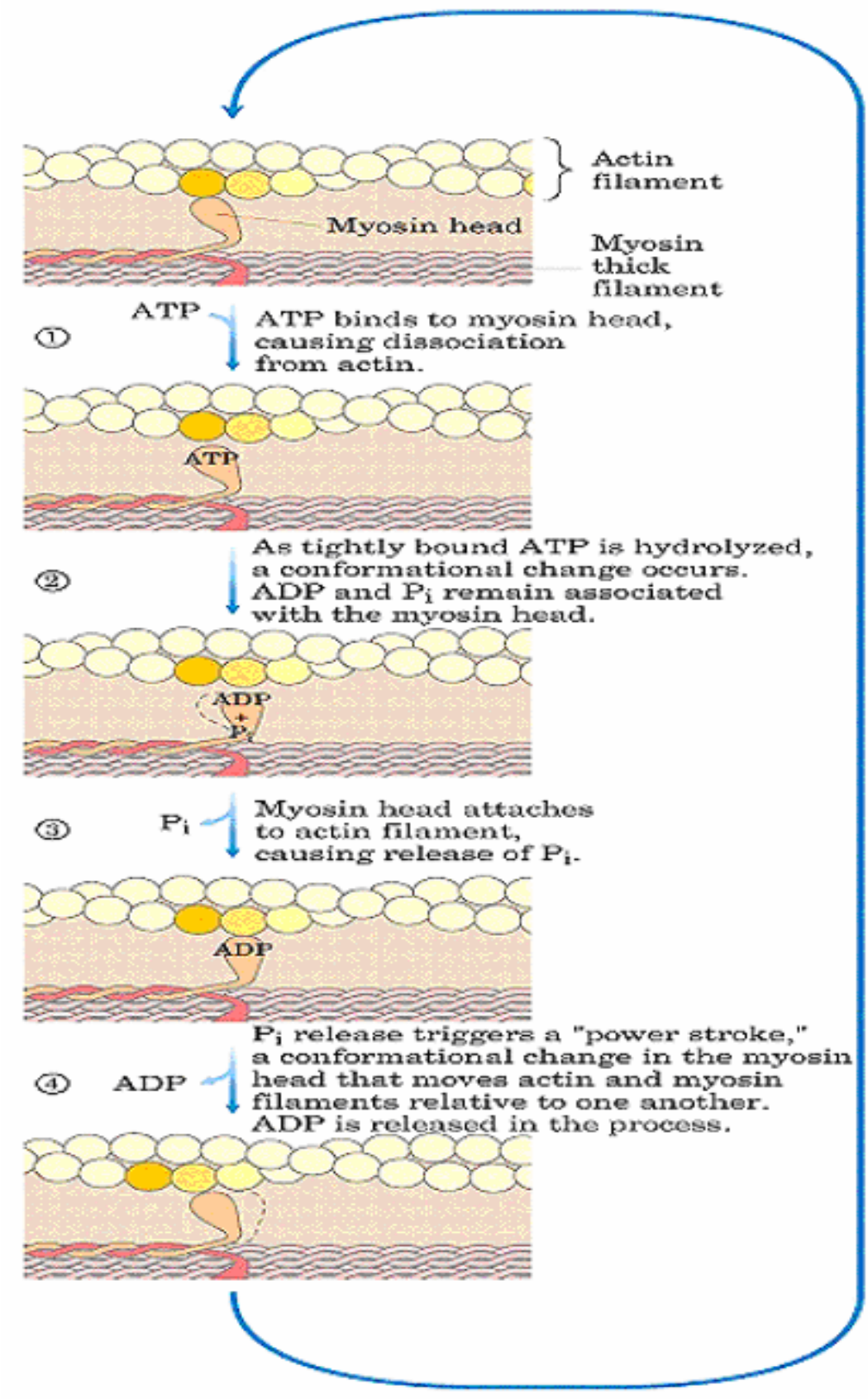
Relaxed



Contracted

Muscle contraction




Actin filament
Myosin head
Myosin thick filament
ATP
① ATP binds to myosin head, causing dissociation from actin.
ATP
② As tightly bound ATP is hydrolyzed, a conformational change occurs. ADP and P_i remain associated with the myosin head.
ADP + P_i
③ P_i Myosin head attaches to actin filament, causing release of P_i.
ADP
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.