Summary:
- Immunoglobulin light and heavy chains contain variable and constant domains.
- The structural diversity of immunoglobulin antigen-binding sites arises from genetic recombination and somatic hypermutation of genes corresponding to the light and heavy chain variable region domains.
- Further diversity of κ and λ light chain constant domains arises from isotypic and allotypic variation.
- FLCs are secreted by plasma cells.
- sFLCs have a half-life of a few hours due to rapid renal clearance.
- Serum IgG has a prolonged and variable half-life due to FcRn recycling.

Antibody (immunoglobulin) molecules are composed of two identical heavy chains and two identical light chains. Heavy chains are each paired with a single light chain via a disulphide bridge and non-covalent interactions to form a heavy-light chain pair (or half-molecule). Two heavy-light chain pairs are linked by disulphide bonds in the so-called ‘hinge region’ to form a Y-shaped structure that is arranged symmetrically about a two-fold axis (Figure 3.1).

Immunoglobulin heavy and light chains each have constant and variable regions. A pair of heavy and light chain variable regions together forms the antigen-binding site. The variable regions exhibit enormous structural diversity, particularly of antigen-binding contacts, allowing the recognition of a huge variety of antigens.

Antibody heavy and light chains are composed of homologous structural units known as ‘immunoglobulin domains’. Each domain is approximately 110 amino acids long and is constructed from a series of antiparallel \( \beta \)-strands connected to form two \( \beta \)-pleated sheets. The sheets are covalently linked by an intrachain disulphide bridge and each domain adopts a roughly barrel-shaped structure characteristic of an immunoglobulin fold. 

![Figure 3.1. An immunoglobulin molecule](image)

![Figure 3.2. A FLC molecule showing the constant domains](image)

![Figure 3.3. Different forms of secreted antibody](image)
The light chain tertiary structure consists of two immunoglobulin domains joined by a loop to form a single variable region and single constant region (Figure 3.2). In humans, light chains are encoded by two different gene loci, resulting in the serologically distinguishable light chain types, \( \kappa \) and \( \lambda \). Immunoglobulin molecules are assembled in plasma cells with exclusively \( \kappa \) or \( \lambda \) light chain types, never both.

Similar to light chains, the heavy chain contains one variable domain corresponding to a single variable region. By contrast, the number of heavy chain constant domains (comprising the constant region) varies between immunoglobulin classes, of which there are five: IgG, IgA, IgM, IgD and IgE. Human IgG and IgA can be further divided into closely related subclasses IgG1, 2, 3 and 4, IgA1 and 2. These classes and subclasses are encoded by separate heavy chain constant genes (\( \gamma \)1-4, \( \alpha \)1-2, \( \mu \), \( \delta \) and \( \epsilon \), respectively). The constant regions of the heavy chain mediate most of the biological functions of antibodies by interacting with other effector molecules and immune cells. The majority of secreted antibodies are monomeric, although several immunoglobulin subtypes form oligomers, such as IgA and IgM (Figure 3.3).

In B-cells, the heavy chains, \( \kappa \) light chains and \( \lambda \) light chains are each encoded by independent chromosomal loci containing multiple copies of analogous gene segments. The gene segments within each locus are rearranged stochastically by somatic recombination and RNA processing mechanisms, ultimately resulting in the expression of functional immunoglobulin proteins. The light chain variable domain is constructed from variable (V) and joining (J) gene segments, whilst the constant domain is encoded by a separate constant (C) gene segment (Figure 3.4). The heavy chain variable domain is constructed from three gene segments: V, D (diversity) and J.

### Figures

**Figure 3.1.** An immunoglobulin molecule showing light and heavy chain constant and variable region domains.
V: light chain variable domain; C: light chain constant domain; V: heavy chain variable domain; C\(_1\) - C\(_3\): heavy chain constant domains 1 - 3.

**View source:**
- 3.1. Immunoglobulin structure

**Figure 3.2.** A FLC molecule showing the constant region (left) and variable region (right).

Each colour represents a β-pleated sheet.

**View source:**
- 3.1. Immunoglobulin structure

**Figure 3.4.** Construction of a light chain.
3.1. Immunoglobulin structure

Figure 3.6. Idiotypic, isotypic and allotypic variation of light chains.

References
