exploited when generating silk nanoparticles (Werner and Meinel 2015); for example, the addition of an aqueous silk solution to a miscible organic solvent (e.g., acetone) results in nanoprecipitation and formation of nanoparticles (Seib et al. 2013) that are characterised by high crystallinity in the densely packed core (reviewed in (Zhao et al. 2015)).

The silk heavy chain shows crystalline polymorphism with three predominant forms, namely silk I, II and III (Marsh et al. 1955; Valluzzi et al. 1999; Asakura et al. 2013). Silk I is the metastable silk form present in silk solutions (Asakura et al. 2013); it is characterised by intra- and intermolecular bonding repeats of type II and a β-turn structure that result in a more compact silk conformation than seen with silk II (Asakura et al. 2013). Silk II represents the antiparallel β-sheets of crystallised silk that are found in spun silk fibres (Marsh et al. 1955; Asakura et al. 2013); silk III forms a 3-fold extended helix at a water-air interface (Valluzzi et al. 1999). Silk-based drug delivery devices are typically made up of a mixture of β-sheets, β-turns, helices and random coils, although the extent of each can be fined tuned, and this is known to influence drug release (Seib and Kaplan 2013; Yucel et al. 2014).

Spider silks

To date, *B. mori* silk cocoons are the most commonly used silk source for the development of drug delivery systems because *B. mori* silk can be readily mass-produced using sericultures (Seib and Kaplan 2013). In contrast, spiders cannot be farmed; therefore, spider silks are typically obtained by expression using a heterologous host via genetic engineering (Chung et al. 2012). Dragline spider silk is the most commonly studied spider silk because this silk is used to build the frames and radii of orb webs, as well as serving as the spider's safety line (Vollrath and Porter 2009; Porter et al. 2013). This silk is thus endowed with an exceptionally high tensile strength and elasticity to serve its function. Dragline silk is composed of two major proteins: the major ampullate spidroin 1 and 2 (MaSp1 and MaSp2) in silk from the Gold Orb weaver spider (*Nephila clavipes*) and *Araneus diadematus* fibroin 3 and 4 (ADF-3 and -4) in silk from the common European garden spider (Scheibel 2004). The small peptide motifs of spider silks can be grouped into four major categories: (i) crystalline β-sheet rich poly(A)/poly(GA) motifs (ii) helix forming GGX repeats, (iii) an elastic β-turn-like proline-rich region, composed of multiple GPGXX motifs (where P is proline and X is mostly glutamine) and (iv) a spacer region with currently unknown functions (Tokareva et al. 2014).

Across all araneid, the dragline spider silks have a very high molecular weight (reviewed in (Scheibel 2004)). For example, MaSP 1 and 2 silk proteins possess similar motifs and are approximately 3,500 amino acids long, resulting in a protein with a molecular mass of 250–350 kDa (Sponner et al. 2005; Ayoub et al. 2007). As is the case with *B. mori* silk, spider silks contain long repetitive sequences that are rich in glycine and alanine and are flanked at the C and N termini by non-repeating amino acid sequences approximately 100 amino acids in length (Ayoub et al. 2007); these non-repeating sequences are thought to orchestrate the self-assembly process during spinning (Jin and Kaplan 2003; Exler et al. 2007; Askarieh et al. 2010; Hagn et al. 2010). Analogous to the situation with *B. mori* silk, the polyalanine residues