The primary sequence of *B. mori* silk heavy chain resembles that of an amphiphilic block co-polymer, with hydrophobic blocks alternating with hydrophilic ones (Ha et al. 2005; Yucel et al. 2014) (Fig. 1c). This block co-polymer is flanked by hydrophilic C- and N-termini composed of completely non-repeating amino acid residues. Specifically, the heavy chain has 12 long hydrophobic, "crystallisable" blocks that are interspaced by 11 nearly identical, less repetitive and more hydrophilic "amorphous" blocks that have an anionic character; the result is an overall silk isoelectric point of approximately 4 (Fig. 1b). The crystallisable blocks are made up of GX repeats and account for 94% of the silk heavy chain sequence (Zhou et al. 2001) (Fig. 1c). The hexa-amino acid sequence, GAGAGS, is the main component of the typical silk β-sheet crystal and is interspersed with small, irregular GAAS tetrapeptides and 60 residues containing GY (GY~GY) sequences (Ha et al. 2005). These GAGAGS/GY~GY crystalline building blocks are usually composed of glycine (G), alanine (A), serine (S), and tyrosine (Y), while valine (V), threonine (T), isoleucine (I) and phenylalanine (F) are not major residue types but sometimes appear in GAGAGS/GY~GY blocks (Ha et al. 2005).

One silk heavy chain has 12 intramolecular antiparallel β-strands and 11 amorphous regions. The amorphous regions typically consist of 31 amino acid with sequence irregularity (GT~GT), but always contain proline residues that can act as major factors for changing the backbone direction (Fig. 1b). The crystalline and amorphous blocks in the silk heavy chain contribute significantly to the fibre's physical properties (Ha et al. 2005). In particular, sequence motifs, such as poly alanine-glycine (polyAG) and polyalanine (polyA) (β sheet–forming), GXX (31-helix), GXG (stiffness), and GPGXX (β spiral), are key components, and their relative positioning and arrangement are intimately tied to the overall material properties (Omenetto and Kaplan 2010).

Manipulation of the crystal form and content allow fine-tuning of the physical properties of silk and subsequently affect its performance as a drug delivery system (Yucel et al. 2014). In aqueous solutions, the crystallisable domains of silk form β-strands and 3-stranded β-sheets, which are stabilised through hydrogen bonding; the increasing interaction of the hydrophobic blocks drives β-sheet formation through lateral and facial packing (Ha et al. 2005; Yucel et al. 2014). The hydrophobic, crystallisable blocks are interspaced by hydrophilic blocks and capped by N- and C-terminal sequences; this block copolymer arrangement drives the formation of 100–200 nm sized spherical micellar structures that contain a hydrophobic core of crystalline/amorphous domains, and a hydrophilic shell of the terminal domains (Jin and Kaplan 2003) (Fig. 1c). These micelles remain loosely assembled, and the assembly process is reversible (Lu et al. 2012).

Under aqueous conditions that mimic the *B. mori* silk gland microenvironment, these nanometre-sized micelles assemble into larger microscale globules (0.8–15 μm) and gel-like states, while maintaining solubility (Werner and Meinel 2015). However, a number of external triggers, such as stretching, shearing, electromagnetic fields, solution concentration, pH and ionic strength cause irreversible physical intermicellar and inter globular crosslinking (Werner and Meinel 2015). The resulting silk networks have an increased β-sheet content and are formed though the self-assembly process detailed above, thereby eliminating the need for use of any harsh chemicals or crosslinkers. The self-assembly of silk into these globular micelles is