give high tensile strength to the silk fibre. These hydrophobic polyalanine blocks are typically made up of six to nine alanines and several polyalanine chains are required to form the crystalline β-sheet stacks. The glycine-rich motifs, such as GGX or GPGXX, adopt flexible helical structures and act as molecular springs interspersed among the crystalline regions to provide elasticity to the silk thread (Chung et al. 2012; Tokareva et al. 2014).

Unlike *B. mori,* which can be raised as sericultures, spiders are more challenging to raise for silk production and are rarely used as a primary silk source. The large size of naturally occurring spider silks and the highly repetitive nature of these proteins also pose challenges during expression in heterologous hosts, in part due to the limits of the glycyl-tRNA pools in the expression host (Seib and Kaplan 2013). This has recently been overcome by the use of metabolically engineered *E. coli*, where recombinantly expressed silk matched the protein made by spiders with respect to its molecular weight and mechanical properties (Xia et al. 2010). However, most studies that have explored spider silks for drug delivery applications have used the ADF-4 and MaSp1 sequences to generate spider silk-inspired biopolymers that are tens of kDa in size. For example, eADF4-(C16) consists of 16 repeats of module C (GSSAAAAAAAASGPGGYG PENQGPSGPGGYGPGGP), which mimics the repetitive core sequence of ADF4 of the European garden spider and yields a biopolymer 48 kDa in size. This eADF4-(C16) biopolymer has been explored for various drug delivery applications, including silk nanoparticle (Lammel et al. 2011) and hydrogels (Schacht et al. 2015) for drug delivery. Recombinant silks have been the foundation for a number of spin out companies, including eADF4-(C16) which is central to AMSilk's commercial portfolio which now includes silk-based fibres, coatings and cosmetics.

In addition to ADF4, the *Nephila clavipes* MaSp1 silk consensus repeat SGRGGLGGQGAGAAAAAGGAGQGGYGGLGSQGT has been widely studied for the generation of silk (nano)particles, fibres, hydrogels and hybrid materials for both tissue engineering applications and drug delivery (Tokareva et al. 2014). The isolation of spider silk from the expression host will not be reviewed here (see excellent reviews; for example (Scheibel 2004; Chung et al. 2012; Ebrahimi et al. 2015)). However, the extraction procedure used to isolate silk from cocoons has a significant impact on the final biopolymer properties, so this will be briefly reviewed.

Reverse Engineering Silk Cocoons

Silkworm fibres consist of two types of proteins: silk fibroin (commonly referred to as silk) and sericins. Sericin is used by the worm during the spinning process to "glue" silk fibres together. Sericins are commonly removed when processing *B. mori* cocoons, as they are thought to induce an inflammatory response, especially in combination with silk (reviewed in (Altman et al. 2003)). Typical strategies for sericin removal include boiling (i.e., degumming) the cocoons in an aqueous alkaline solution (e.g., sodium carbonate) (Rockwood et al. 2011). While most studies report degumming times ranging from 20 to 60 minutes, a short 5 minute degumming process is usually sufficient to remove the sericin and minimise degradation of the silk. Silk is degraded into smaller fragments during prolonged boiling, which particularly affects the silk light chain, the disulphide bond between the light and heavy chain, and the amorphous