silk and hyaluronan. In the 21st century scientists have endeavoured to define and replicate nature's biological structures via a bottom-up approach whereby biomolecule monomers of the natural building blocks of life (lipids, peptides, nucleic acids and carbohydrates) are uniquely tailored to meet clinical and mechanical needs. These so-called biomolecular hydrogels possess numerous advantages over synthetic polymers including: increased chemical versatility, tunable biodegradability, reduced immunogenicity, tailored gelation in response to stimuli and enhanced biocompatibility. Biomolecules demonstrate inherent inter and intramolecular interactions which are commonly found in monomers capable of hydrogel formation. For example, long chain hydrocarbon chains of lipids generate van der Waals forces and hydrophobic interactions. Carbohydrates consist of multiple hydroxyl moieties (–OH) capable of hydrogen bonding. Nucleobases (cytosine, guanine, adenine, thymine and uracil) demonstrate specific hydrogen bonds and pi-pi (π-π) electrostatic interactions. Protein and peptide molecules have the advantage of being easily functionalized due to an available array of chemical groups granted by the presence of a variety of R-groups. High specific intermolecular interactions (hydrogen bonds, ionic, electrostatic, hydrophobic, dipole-dipole, van der Waals) can be developed by modifying the primary sequence, alleviating the need for toxic chemical cross-linkers such as glutaraldehyde, phenol and formaldehyde. Non-native chemistries and functional groups are easily incorporated into the primary structure at the sequence level, as are synthetic monomers (forming polymeric hybrid), enabling biomolecular hydrogels to be tailored to specific functional requirements. This is an important attribute that widens their scope of applications in the medical field (McCloskey et al. 2014).

There has been significant interest in developing hydrogels with tunable properties and the ability to respond to changes in environmental stimuli. Introducing stimuli sensitivity to hydrogelators broadens their range of applications as biomaterials. The human body presents a diverse environment for physical, biological and chemical stimuli allowing hydrogel properties to be controlled in response to external conditions at different sites throughout the body. A variety of stimuli have been harnessed for biomedical applications including: pH, ionic strength, oxidation/reduction, temperature, enzymes, light, shear stress, magnetism, and electricity, with resultant physicochemical changes in the hydrogel network and supramolecular structure enabling tailored delivery of drugs, increased/decreased gel strength and optimal mechanical behaviour. Responsive hydrogels are highly desirable as evidenced by a rapid expansion of research into these technologies. Self-assembling peptides are particularly promising molecules in the creation of hydrogels that form in response to specific environmental conditions. The following chapter will explore each of these stimuli in greater detail, focusing on the unique potential of biomolecular, mainly peptide-based, hydrogel platforms and their development as "smart", environmentally-responsive materials with diverse applications particular within the fields of drug delivery, 3D cell culture, tissue repair and regenerative medicine.

pH-Responsive Hydrogels

The human body displays a vast diversity of pH ranges which serve as a popular method for the hydrogel targeted delivery of drugs. Disease has also been implicated in