hydrolysis (Williams et al. 2009). The Xu group demonstrated reversible enzymatic formation of supramolecular hydrogels, proving enzymatic reactions can modulate the balance of hydrophobicity and hydrophilicity of small peptide molecules (Yang et al. 2006). Cleavage of a hydrophilic phosphate group from NapFFGEY-P(O)$(OH)_2$ in the presence of a phosphatase enzyme results in the formation of the more hydrophobic hydrogelator NapFFGEY. Addition of a kinase to the NapFFGEY hydrogel in the presence of adenosine triphosphate (ATP) converts the terminal tyrosine (Y) to tyrosine phosphate resulting in the restoration of NapFFGEY-P(O)$(OH)_2$ and the soluble phase. The level of control provided by this kinase/phosphatase switch demonstrates how simple it is to regulate the formation of supramolecular hydrogels by enzymatic approaches and is of great promise in the development of biomaterials for localized drug delivery and tissue engineering. Enzyme instructed reversible self-assembly and gelation is advantageous as it allows the hydrogels to respond to the presences of specific enzymes within specific tissues or diseases. Cancer (Saha et al. 2001), Alzheimer's (Yuan and Yankner 2000), diabetes (Hutton and Eisenbarth 2003), and multiple sclerosis (Auch et al. 2004) are associated with the abnormal kinase and/or phosphatase activity and are therefore viable biological targets for future therapies. The Xu group demonstrated the therapeutic potential of this approach by conjugating the antineoplastic drug paclitaxel to NapFFKY-P(O)$(OH)_2$ via a succinic acid linker (Gao et al. 2009). Alkaline phosphate transformed this precursor into the hydrogelating variant whilst providing localized antitumour activity and cytocompatibility. Intracellular hydrogel formation may also be exploited to direct cell death in cancerous cells. Xu also synthesized an ester-containing NapFF peptide precursor that only self-assembles intracellularly in response to endogenous esterase enzymes (Yang et al. 2007). HeLa cells, an immortalized cell line of cervical cancer, were demonstrated to possess increased intracellular esterase levels relative to NIH3T3 standard fibroblast cells. The intracellular formation of a nanofibrous hydrogel induces stresses on the HeLa cell preventing biochemical transport and triggering cell death.

Enzymes may also be utilized to mediate degradation of hydrogel networks for drug delivery and tissue remodelling. The Hartgerink group proved the matrix metalloproteinase protease (MMP) family, specifically MMP-2, was able to recognize and cleave the GTAGLIGQ amino acid sequence between glycine (G) and leucine (L) in a mixture of peptide amphiphiles (Jun et al. 2005). This resulted in cell-mediated proteolytic degradation of the hydrogel network, allowing cell migration through the hydrogel matrix and remodelling of the matrix with natural extracellular matrix. They hypothesized this would be of benefit for dental use with encapsulation of dental pulp cells feasible within the hydrogel matrix and inclusion of aspartic acid in the peptide primary sequence promoting calcium binding.

Shear-Responsive Hydrogels

Hydrogels can vary in their response to an applied shear force. Shear-thinning hydrogels demonstrate a reduced viscosity in response to the application of shear stress. Shear thickening express an opposing increased viscosity in response to shear and are exemplified by ceramic systems such as hydroxyapatite, utilized commonly as bone constructs (Cyster et al. 2005). In biomolecular peptide hydrogels shear-thinning