Our own group pioneered the development of an ultrashort cationic peptide nanomaterials which demonstrates potent activity against resistant biofilm forms of medical device related pathogens including: staphylococci, *Escherichia coli* and *Pseudomonas aeruginosa* (Laverty et al. 2014). This group of peptides utilize a carboxylic acid terminated naphthalene-diphenylalanine (NapFF) backbone to provide pH-responsive hydrogel formation whilst the addition of two units of cationic charge (lysine, ornithine) allows the molecule to selectively target negatively charged bacterial membranes. NapFFKK proved particularly promising as an anti-biofilm hydrogel with potential future use as a biomaterial in wound-healing or as an infection-responsive hydrogel coating in medical implants such as intravascular catheters and hip replacements. A nanofibrous architecture is derived from β-sheet stacking of NapFF motifs. Highly aromatic naphthalene allows intermolecular π-π electrostatic interactions between delocalized π-electrons. Amide groups present as part of the peptide linkage allow formation of hydrogen bonds between peptide molecules but also with water. The overall hydrophobic-hydrophilic balance of the molecule will determines whether the peptide precipitates (too hydrophobic), dissolves (too hydrophilic) or forms a hydrogel (optimum balance) in solution. The presence of a terminal carboxylic acid moiety is also critical to driving the self-assembly process and supramolecular hydrogel formation. Basic pH, above the p*K*a of the carboxylic acid, results in removal of a proton (H^+) from the hydroxyl group of the carboxylic acid creating a carboxylate anion (COO^-) allowing full dissolution of the peptide in aqueous solution. Gradual acidification of this solution, using for example dilute hydrochloric acid or utilizing the hydrolysis of glucono-δ-lactone to gluconic acid in aqueous solution, to physiological pH (in the case of our NapFFKK peptide) or acidic pH (NapFF), results in the formation of a homogenous hydrogel at concentrations of ~0.5% w/v and above. The pH responsiveness of the NapFF motifs may have important applications as hydrogels in cancer therapeutics and infection. Some infections, for example those related to the presence of intravascular catheters, are associated with decreased local pH due to a combination of host inflammation, phagocytosis and microbial anaerobic fermentation owing to low oxygen tension. Local pH can be reduced to as low as pH 5.5 (Radovic-Moreno et al. 2012). This may serve as a stimulus to trigger self-assembly of a protective hydrogel surface when it is most required (infection development) extending the antimicrobial profile beyond the approximate one to two week protection granted by current medical device strategies (McCloskey et al. 2014).

Ionic Strength-Responsive Hydrogels

Ionic strength relates closely to pH in that they dictate formation and properties of hydrogels due to fundamental differences in molecular charge. At physiological pH (7.4) and low ionic strength, the MAX1 peptide does not gelate as it forms a random coil conformation even at concentrations as high as 4% w/v in water (Ozbas et al. 2004). An increase in ionic strength, corresponding to 150 mM buffered saline (NaCl) and cell culture media, promotes self-assembly and hydrogelation at 2% w/v due to β-hairpin formation. Increased ionic strength results in dampening of positive charged lysine residues in the MAX1 backbone allowing hydrogelation to proceed.