polymers to obtain thermogelation close to body temperature. Modification of gelatin is easily achieved at amino acid end points. Yang and Kao conjugated poly(ethylene glycol)-poly(D, L-lactide) with gelatin and developed a rapidly forming gel at 37°C (Yang and Kao 2006).

Alginate is a naturally occurring anionic polysaccharide composed of 1,4-linked β-D-mannuronte (M) and 1,4-linked α-L-guluronate (G) (Fig. 2d) in various compositions. Generally, in the presence of divalent cations such as ca^{2+}, alginate forms hydrogels. Thermosensitive alginates were prepared by conjugating alginate with other thermosensitive polymers such as poly(N-isopropylacrylamide) (PNIPAAm) and were explored for drug delivery and tissue engineering applications. Tan et al. developed thermosensitive aminated alginate-g-PNIPAAm by coupling carboxylic end capped PNIPAAm through amide bond linkages. The copolymer developed exhibited sol-to-gel transition with LCST around 35°C (Tan et al. 2012). Figure 4 represents the gelation mechanism of the hydrogel at physiological temperature which mainly involves dehydration of the PNIPAAm block. As a result of increased temperature, water molecules bound to the isopropyl side of PNIPAAm is released, which enhances inter- and intra-molecular hydrophobic interactions between isopropyl groups forming a gel structure.

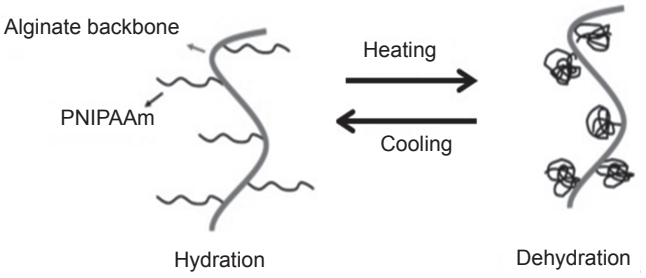

Fig. 4. Schematic representation of the gelation mechanism of alginate-g-PNIPAAm thermosensitive hydrogels (Adopted from (Sun and Tan 2013)).

Thermosensitive hydrogels based on synthetic polymers

Even though naturally derived thermosensitive hydrogels have excellent biocompatibility and biodegradability, the polypeptides or sugar rings have limited space for further modifications to fit various requirements for biomedical applications. To overcome this limitation, synthetic polymers have been used, as they offer capability of chemical modification.

N-isopropylacrylamide based systems

Thermosensitive hydrogels based on poly(N-isopropylacrylamide) (PNIPAAm) (Fig. 5a) are the most extensively investigated systems. PNIPPAm exhibits LCST, which is around 32°C in aqueous solutions. At temperatures above LCST the solution becomes cloudy and transforms into a gel due to hydrophobic interactions and coil-