

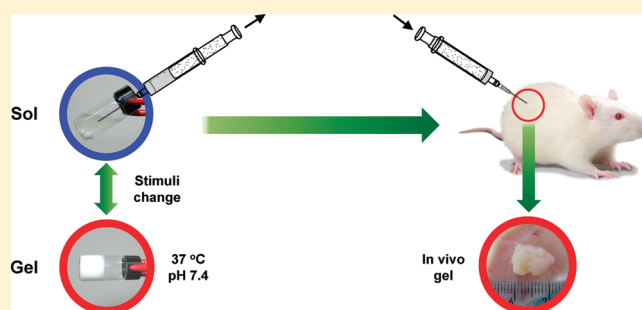
# Injectable Block Copolymer Hydrogels: Achievements and Future Challenges for Biomedical Applications

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**ABSTRACT:** In the past two decades, physical polymeric hydrogels have been extensively explored for biomedical applications, such as drug delivery and tissue engineering. These hydrogels exhibit a sol–gel phase transition in response to external stimuli, such as pH, temperature, glucose, electric field, magnetic field, ionic strength, or their combination. Hydrogel precursors can be mixed with bioactive molecules or cells and then simply injected into the body at specific sites. Substantial progress has been made in the development of novel hydrogels and applications. In this Perspective, we report recent progress in physically cross-linked hydrogels responding to pH and/or temperature and their pharmaceutical and tissue engineering applications. The outlook for the future, including remaining challenges of injectable hydrogels, is also discussed.



## 1. INTRODUCTION

Hydrogels are three-dimensional hydrophilic polymeric networks that can absorb a large amount of water or biological fluids and maintain their semisolid morphology.<sup>1–3</sup> Injectable polymeric hydrogels are very attractive materials for biomedical applications, especially drug delivery and tissue engineering.<sup>1–11</sup> Such injectable hydrogel systems are of particular interest because of the advantages they offer: (i) they require no surgical or implantation procedures; (ii) their precursor solutions can be easily mixed with bioactive molecules such as drugs, proteins, DNA, or cells prior to gelation or injection; (iii) the formed gels become drug carriers for localized delivery or act as scaffolds for tissue regeneration.

Injectable hydrogels can be classified into two basic types depending on cross-linking method: chemical or physical. Chemically cross-linked hydrogels can be generated via enzymes,<sup>12–14</sup> Schiff base,<sup>15–17</sup> Michael-addition reactions,<sup>18–22</sup> and photopolymerization,<sup>23–25</sup> and they usually exhibit a noticeable volume change. Although chemically cross-linked hydrogels possess strong mechanical properties, the requirement of enzymes, cross-linking agents, photoinitiators and/or organic solvents, which may damage cells as well as denature incorporated bioactive molecules, may limit their applications. In contrast, physically cross-linked hydrogels, formed via self-assembly of amphiphilic block/graft copolymers in response to external stimuli, such as pH and/or temperature, offers a mild method for preparing hydrogels. Moreover, such preparations exhibit a sol–gel transition without a significant volume change.

Polymers employed to prepare injectable hydrogels should meet several critical criteria:

- The viscosity of the polymer solutions must be low enough to facilitate injection as well as encapsulation of bioactive molecules or cells at room temperature.
- Following injection, the gels should form quickly to prevent dissolution of polymers and/or incorporated molecules.
- The gels should be biodegradable. Biodegradability is necessary for transport of therapeutic agents, nutrients, waste, and growth factors; migration of cells; and formation of new tissues.
- Polymers and their degradation products must be biocompatible or evoke a minimal inflammatory response by host tissues.
- Gels must form a suitable substrate for cells. Interaction of polymers with cells is important for cell migration, differentiation and proliferation, which collectively promote connections between hydrogels and host tissues at specific implant sites.
- Gels must exhibit application-appropriate physical and mechanical properties. For example, hard gels are desirable for bone regenerative whereas soft gels are suitable for soft-tissue applications.

This Perspective will focus on recent developments in injectable physical hydrogels and their pharmaceutical and tissue-regeneration applications. The outlook for injectable hydrogels, including future challenges, is also discussed.

**Received:** June 3, 2011

**Revised:** July 25, 2011

**Published:** August 04, 2011

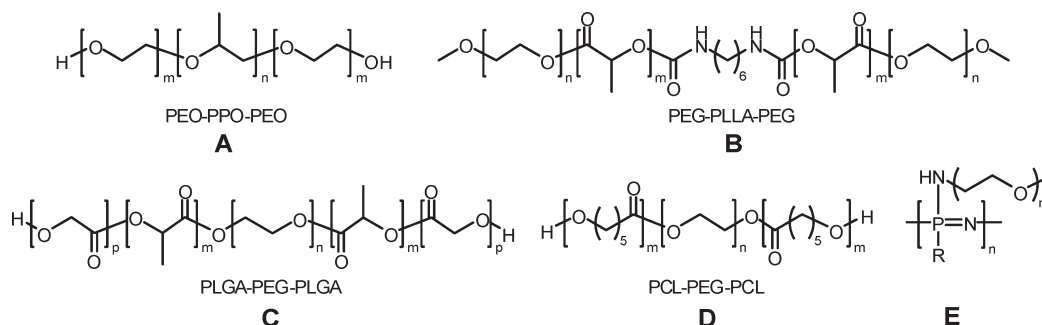


Figure 1. Chemical structures of several typical temperature-sensitive copolymers.

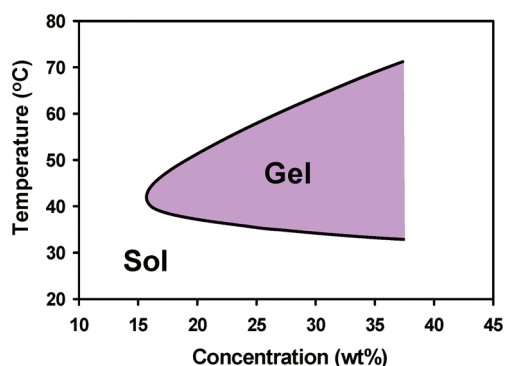


Figure 2. Phase diagram of PEG-PLGA-PEG triblock copolymer aqueous solutions.

## 2. INJECTABLE TEMPERATURE-SENSITIVE HYDROGELS

Temperature is among the easiest parameters to experimentally manipulate; thus, not surprisingly, temperature-sensitive hydrogels have been widely studied for both *in vitro* and *in vivo* applications. These hydrogels exist as a solution at low temperatures and undergo a sol-gel phase transition at higher temperatures.<sup>2–5</sup> Amphiphilic copolymers consisting of hydrophilic poly(ethylene glycol) (PEG or PEO) and hydrophobic poly(propylene oxide) (PPO) or aliphatic polyesters, such as poly(glycolide) (PGA), poly(lactide) (PLA), poly( $\epsilon$ -caprolactone) (PCL) and others, have been widely studied as temperature-sensitive hydrogels for drug delivery and tissue engineering.

PEO-PPO-PEO (Figure 1A), known as Pluronic (BASF) or Poloxamer (ICI), can self-assemble in water to form micelles, and micellar association upon heating of the polymer solution results in a sol-to-gel phase transition.<sup>26–30</sup> The gel-to-sol phase transition at elevated temperatures is caused by partial dehydration of the PEO blocks, leading to a reduction in micellar interactions.<sup>30–32</sup> The sol state of Pluronic in aqueous media at room temperature facilitates incorporation of bioactive molecules, and the gel state at physiological temperature allows the hydrogels to serve as a drug-delivery depot. However, the weak mechanical strength, low molecular weight, nonbiodegradability, short residence time, and high permeability may limit the applicability of Pluronic hydrogels.<sup>3,6</sup> Several efforts have been made to improve the biodegradability and/or mechanical strength of Pluronic hydrogels for applications in drug delivery and tissue engineering.<sup>33–36</sup> For example, the thermosensitive hydrogel, PoligoGel (Samyang Corp., Korea),

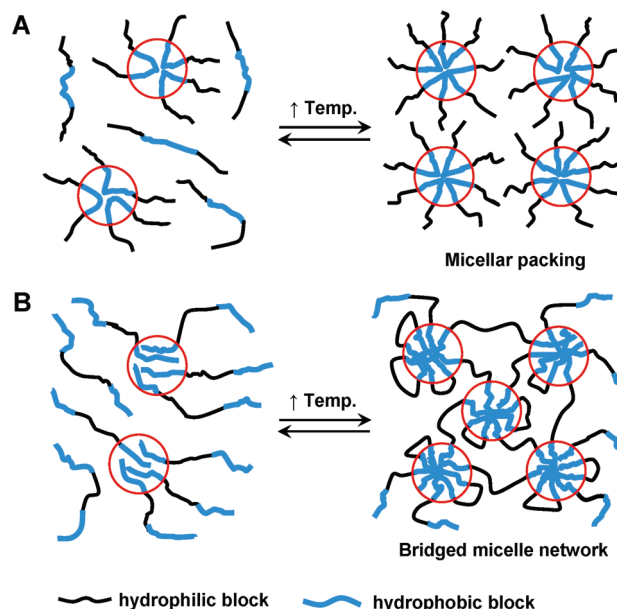


Figure 3. Schematic diagram for the sol-gel transition mechanisms of ABA-type (A) and BAB-type (B) triblock copolymer in aqueous solution with increasing temperature (A is PEG and B is a hydrophobic block such as PLGA, PCL, and PCLA).

a multiblock copolymer of PEO-PPO-PEO, has been used for delivery of bone marrow-derived rat mesenchymal stem cells (rMSCs).<sup>37</sup>

A triblock copolymer, PEG-poly(L-lactide)-PEG (PEG-PLLA-PEG) (Figure 1B), has been reported as an alternative to PEO-PPO-PEO.<sup>38</sup> This copolymer solution in water shows a gel-to-sol phase transition upon heating that can be controlled by changing the biodegradable PLLA block length, hydrophobic/hydrophilic ratios, and the stereoregularity of the hydrophobic block.<sup>39–41</sup> However, because this system gels at low temperatures, bioactive molecules or cells must be encapsulated at high temperatures (sol state) conditions that may damage labile molecules and/or injure cells. In addition, the injection of copolymer solutions at high temperatures may be uncomfortable for patients. Subsequent efforts led to the development of the triblock copolymer PEG-poly(D,L-lactide-co-glycolide)-PEG (PEG-PLGA-PEG), which offers a mild method for incorporating bioactive molecules or cells. Aqueous solutions of PEG-PLGA-PEG flow freely at room temperature but change to a gel (sol-to-gel phase transition) at

body temperature (Figure 2).<sup>42,43</sup> The sol-to-gel phase transition of PEG–PLGA–PEG is induced by the close packing of micelles, as shown in Figure 3A.<sup>42–46</sup> Drug incorporation and release studies have shown that hydrogels formed from PEG–PLGA–PEG release a hydrophilic drug (ketoprofen) by simple diffusion, whereas diffusion followed by degradation was proposed as the mechanism for release of a hydrophobic drug (spironolactone).<sup>47</sup>

Aqueous solutions of PLGA–PEG–PLGA (Figure 1C) exhibit a reversible sol-to-gel phase transition with increasing temperature.<sup>48–50</sup> The proposed gelation mechanism for PLGA–PEG–PLGA solutions is formation of bridged micelles at low temperatures and the association of bridged micelles at higher temperatures caused by the increase in hydrophobicity of the PLGA (Figure 3B). Regel, a commercial PLGA–PEG–PLGA product, has been extensively examined both in vitro and in vivo for its potential to support the sustained release of paclitaxel (PTX).<sup>50</sup> Regel has also been investigated for the incorporation/release properties of other bioactive molecules, including insulin, (glycosylated) granulocyte colony-stimulating factor (G-CSF), porcine growth hormone (pGH), recombinant hepatitis B surface antigen (rHBsAg), and the incretin hormone glucagon-like peptide-1 (GLP-1).<sup>51–53</sup> PLGA–PEG–PLGA hydrogels were shown to degrade in 6–8 weeks in vitro at body temperature. Moreover, by grafting PLGA to PEG or PEG to PLGA, the persistence time of the hydrogels could be modulated over a range from 1 week to 2 months. Importantly, PLGA-g-PEG hydrogels encapsulating chondrocytes were shown to improve articular cartilage defects.<sup>50,54–56</sup>

Diblock polymers containing PCL, a hydrophobic, biodegradable and biocompatible polymer, have also been studied as drug-delivery hydrogel scaffolds. Aqueous solutions of MPEG–PCL diblock polymers gel upon heating.<sup>57–59</sup> MPEG–PCL hydrogels incorporating bovine serum albumin (BSA) have been shown to support the sustained release of BSA for up to 1 month, both in vitro and in vivo.<sup>60</sup> MPEG–PCL hydrogels are also suitable for use as biocompatible drug carriers and scaffolds for the delivery of doxorubicin (DOX) and PTX to inhibit the growth of tumors in mice,<sup>61,62</sup> and for bone and muscle tissue regeneration.<sup>63,64</sup> Subsequently, a series of PCL–PEG–PCL (Figure 1D) and PEG–PCL–PEG triblock copolymers were introduced, and their aqueous solutions were shown to undergo a sol-to-gel phase transition with an increase in temperature.<sup>65,66</sup> PCL–PEG–PCL hydrogels possess stronger gel strength ( $G' \approx 10,000$  Pa) than that of PEG–PCL–PEG hydrogels ( $G' \approx 100$  Pa) because of differences in the structural topologies of the two copolymers. These hydrogels have been investigated for the delivery of a hydrophilic drug (VB12), hydrophobic drugs (honokiol and lidocaine), and protein (BSA).<sup>67–69</sup>

Gelation of thermosensitive hydrogels is strongly influenced by the end groups of the copolymers. PLGA–PEG–PLGA triblock copolymers with different terminal groups (hydroxyl, acetyl, propionate, or butanoyl) exhibit significant differences in gelation windows.<sup>70,71</sup> Star-shaped PEG(–PLLA)<sub>8</sub> end-capped with cholesterol in aqueous solutions exhibits temperature-induced gelation, and the formed gel has been used as a substrate for cell growth.<sup>72</sup> Recently, a hydrogel of poly( $\epsilon$ -CL-co-LA)–PEG–poly( $\epsilon$ -CL-co-LA) (PCLA–PEG–PCLA) modified with Lys-Arg-Gly-Asp-Lys-Lys (KRGDKK) was shown to release DOX in a more sustained manner than did the parent triblock copolymer.<sup>73</sup> Moreover, functionalization with Arg-Gly-Asp (RGD) enhanced the cell-adhesion properties of PCLA–PEG–PCLA.<sup>74</sup> PEG-containing

triblock polymers with poly( $\delta$ -valerolactone) (PVL–PEG–PVL) have also been examined. These PVL–PEG–PVL copolymers, conjugated with vascular endothelial growth factor (VEGF), were used to fabricate an injectable hydrogel scaffold for stabilizing myocardial infarct and inducing angiogenesis.<sup>75</sup>

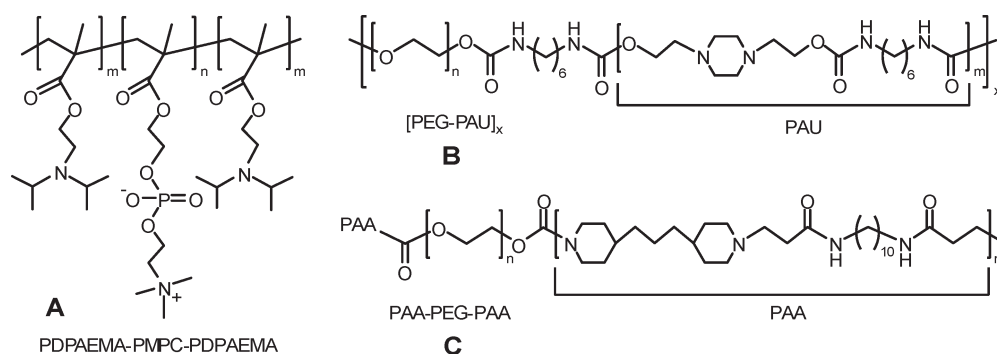
Degradation products of PEG/polyesters are acidic molecules that may damage drugs or promote inflammatory responses by host tissue. Recently developed polypeptide-based hydrogels, which have zwitterionic amino acid degradation products, have the potential to overcome this limitation.<sup>76</sup> Polyalanine–poloxamer–polyalanine block copolymer hydrogels have been shown to enhance the proliferation and protein expression by encapsulated chondrocytes.<sup>77</sup> Polyphosphazene (Figure 1E) is also a promising material because its degradation product is phosphate. Polyphosphazene hydrogels have shown sustained release of DOX and PTX.<sup>78–81</sup> Poly(organophosphazene) modified with RGD has been used as an injectable scaffold for delivery of rabbit MSCs to enhance ectopic bone formation.<sup>82</sup> Protamine-modified polyphosphazene hydrogels have been shown to release human growth hormone (hGH) over 7 days in vitro. In vivo studies in cynomolgus monkeys showed that a single injection of a hGH/polyphosphazene solution induced increases in plasma hGH and insulin like growth factor-1 (IGF-1) levels that were sustained for up to 3 days and 13 days, respectively.<sup>83</sup> Poly-L-arginine-modified polyphosphazene hydrogels were also shown to release hGH for up to 3 days.<sup>84</sup> A recent study showed that an acid-labile, acetal-linkage multiblock polymer containing poloxamer and di(ethylene glycol) divinyl ether released poloxamer, diethylene glycol, and acetaldehyde during its degradation. The hydrogel exhibited enhanced gene delivery (pDNA) to the myocardium and skeletal muscle cells.<sup>85</sup> Moreover, such hydrogels loaded with expression plasmids for VEGF greatly enhanced angiogenesis in a rat myocardial infarction model.<sup>86</sup>

Several other block copolymers in aqueous solutions can also form a gel, suggesting potential applications in drug delivery and tissue engineering. These copolymers include those based on poly[(R)-3-hydroxybutyrate] (PHB),<sup>87,88</sup> poly(ethylene/butylene) (PEB),<sup>89,90</sup> poly(propylene fumarate) (PPF),<sup>91</sup> poly(trimethylene carbonate) (PTMC),<sup>92</sup> and polyorthoester,<sup>93</sup> among others.

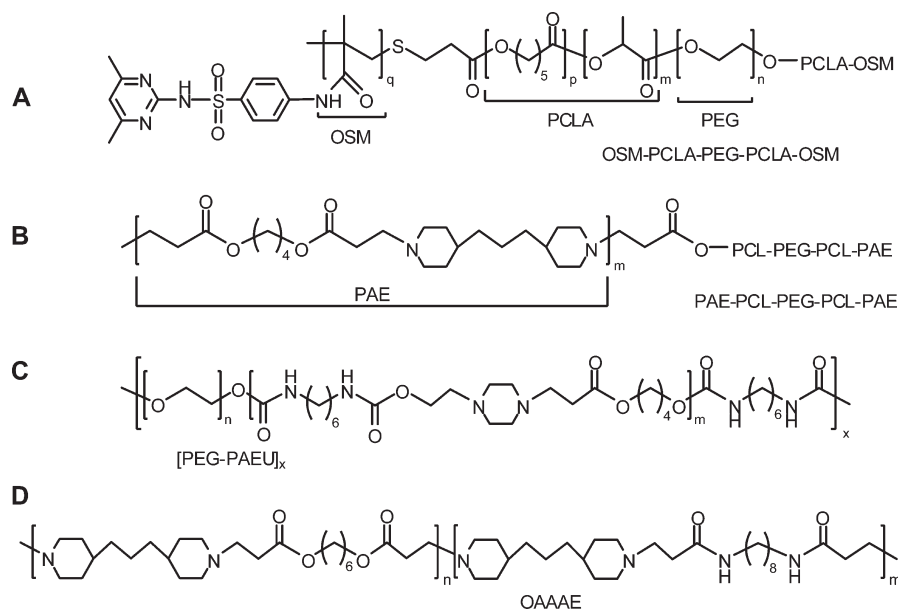
### 3. INJECTABLE PH- AND TEMPERATURE-SENSITIVE HYDROGELS

“Intelligent” polymers capable of responding to multiple stimuli, especially pH and temperature, have drawn considerable research interest because of their advantages in terms of chemical structure and ability to form an ionic complex with therapeutic agents. This dual response can prevent gelation within the injection needle. These polymers can be classified into two categories: nonbiodegradable and biodegradable.

Nonbiodegradable hydrogels are of interest for therapeutics delivery, where bioactive agents, especially proteins, are protected from denaturation.<sup>90</sup> A solution of copolymer consisting of poly[2-(diisopropylamino) ethyl methacrylate] (PDPAEMA) and poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC) (PDPAEMA–PMPC–PDPAEMA) (Figure 4A) shows a reversible sol-to-gel transition with an increase in pH from 2 to 9,<sup>94</sup> and the resulting gel is capable of sustained release of a hydrophobic drug (dipyridamole) under physiological conditions. An aqueous solution of the pentablock copolymer, PDEAEMA–F127–PDEAEMA,



**Figure 4.** Chemical structures of several nonbiodegradable injectable pH- and temperature-sensitive copolymers.



**Figure 5.** Chemical structures of several biodegradable, injectable pH- and temperature-sensitive copolymers.

containing Pluronic F127 with poly(2-(diethylamino)ethyl methacrylate) (PDEAEMA) at the ends, undergoes a sol–gel transition as a function of temperature in the pH range 7.7–8.3. PDEAEMA–F127–PDEAEMA hydrogels thus formed have been shown to release Nile blue chloride and lysozyme with zero-order kinetics under physiological conditions.<sup>95,96</sup> Hydrogels formed from poly(*N*-isopropylacrylamide-*co*-propylacrylic acid) (p(NIPAAm-*co*-PAA) copolymers are capable of maintaining the bioactivity of basic fibroblast growth factor (bFGF) for 40 h and provide sustained release of VEGF over a period of 3 weeks.<sup>97</sup> Poly(NIPAAm-*co*-PAA-*co*-butyl acrylate) (p(NIPAAm-*co*-PAA-*co*-BA) hydrogels have also been shown to release bFGF in a sustained manner, leading to improved angiogenesis in the ischemic myocardium of experimental animals.<sup>98</sup> Aqueous solutions of Pluronic F127 end-capped by amine groups exhibit a closed-loop, sol–gel–sol transition as a function of temperature and pH.<sup>99</sup>

Recently, our group reported pH- and temperature-sensitive hydrogel copolymers composed of PEG and poly(amino urethane) (PAU) (Figure 4B).<sup>100,101</sup> We found that these copolymer hydrogels released chlorambucil, an anticancer drug, for 2 weeks in vitro. Studies conducted at the same time on the

bioadhesive poly(amido amine)–PEG–poly(amido amine) (PAA–PEG–PAA) (Figure 4C) showed that the PAA blocks were hydrophilic at acidic pH, but became hydrophobic at physiological pH.<sup>102,103</sup> At pH ≥ 7.0, copolymer solutions transitioned to a strong gel in response to increases in temperature due to hydrophobic interactions and hydrogen bonding between the PAA blocks.

Biodegradation of biomaterials is indispensable for the diffusion of therapeutic agents and/or formation of new tissues. It also eliminates the need for surgery to remove the material introduced into the body. The first example of biodegradable, pH- and temperature-sensitive polymers was based on the anionic oligomer sulfamethazine (OSM). Copolymer solutions of OSM-modified PCL–PEG–PCL or poly(ε-CL-*co*-GA)–PEG–poly(ε-CL-*co*-GA) (PLGA–PEG–PLGA) exhibit a reversible sol-to-gel phase transition with increasing temperature at pH 7.4 (Figure 6B).<sup>104–110</sup> When loaded with PTX, these hydrogels showed antitumor efficacy for up to 2 weeks after one injection into tumor-bearing mice.<sup>107</sup> Injection of OSM–PCL–PEG–PCL–OSM hydrogels incorporating human MSCs and recombinant human bone morphogenetic protein-2 (rhBMP-2) resulted in high levels of alkaline phosphatase up to 7 weeks after injection in mice.<sup>109</sup>



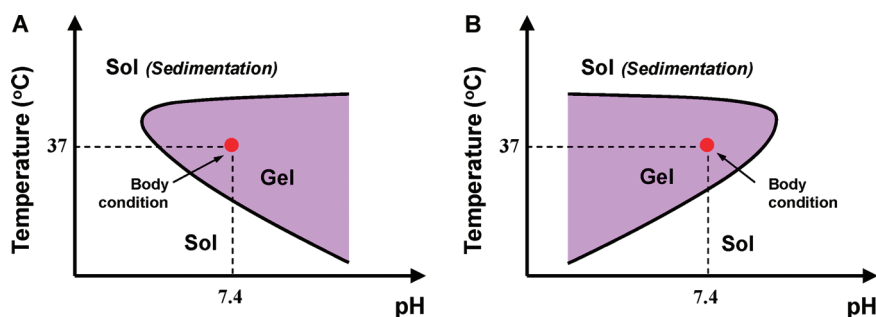


Figure 6. Phase diagrams of typical cationic copolymer (A) and anionic copolymer (B) aqueous solution.

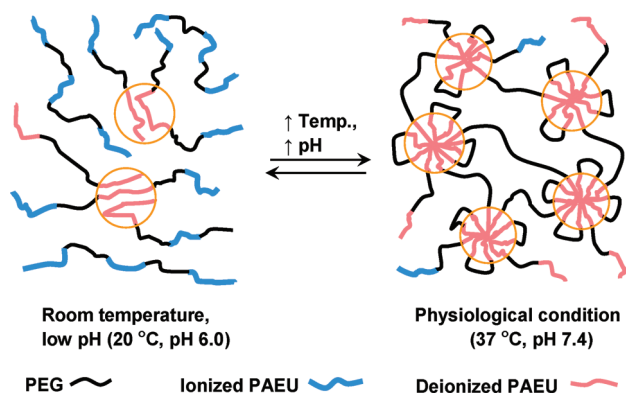


Figure 7. Schematic diagram for the sol-gel transition mechanism of multiblock  $[\text{PEG-PAEU}]_x$  copolymer hydrogels.

Poly( $\beta$ -amino ester) (PAE), which is noncytotoxic and forms a good complex with negatively charged proteins or pDNA at physiological pH, was introduced as a cationic, biodegradable polymer.<sup>111–114</sup> Aqueous solutions of PAE-PCL-PEG-PCL-PAE (Figure 5B) undergo a sol-to-gel transition as a function of both pH and temperature (Figure 6A).<sup>114–117</sup> The degradation rates of these gels can be tuned by replacing the hydrophobic PCL blocks with the less hydrophobic PCLA. Graft copolymer of (PAE-*g*-PCL)-PEG-(PAE-*g*-PCL) exhibited a different gelation window than the linear PAE-PCL-PEG-PCL-PAE copolymers.<sup>118</sup> With a single injection of insulin-loaded PAE-PCL-PEG-PCL-PAE hydrogels into Sprague-Dawley (SD) rats, the insulin concentration in serum was maintained at a high level for 2 weeks without an initial burst, whereas insulin-loaded PCL-PEG-PCL hydrogels showed a remarkable initial burst with complete insulin release within 1 day.<sup>114</sup> The sustained release of insulin from PAE-based hydrogels was attributable to the formation of an ionic complex between insulin and degradable PAE segments.<sup>114</sup> In addition, aqueous solutions of PAE-PEG-PAE or PEG(-PAE)<sub>4</sub> undergo a sol-to-gel and gel-to-sol phase transition with increasing pH and temperature, respectively.<sup>119,120</sup> These two polymers do not contain hydrophobic blocks, and are thus easily dissolved in water at a relatively low pH.

Combining the nondegradable PAU (Figure 4B) with the biodegradable triblock copolymer PCL-PEG-PCL yielded the biodegradable, pH- and temperature-sensitive multiblock copolymer,  $[\text{PCL-PEG-PCL-PAU}]_x$ .<sup>121</sup> PTX-loaded  $[\text{PCL-PEG-PCL-PAU}]_x$  hydrogels exhibited sustained in vitro release of PTX over 1 month. However, polymers containing PCL-PEG-PCL are difficult to dissolve in water. Efforts to prepare a biodegradable

PAU-based polymer without hydrophobic blocks led to the recent development of poly( $\beta$ -amino ester urethane)-based copolymers (PAEU) (Figure 5C).<sup>122–125</sup> The  $[\text{PEG-PAEU}]_x$  multiblock copolymers and PAEU-PEG-PAEU triblock copolymers easily dissolve in water at low pH, and exhibits a sol-to-gel phase transition with a changing of pH and temperature to physiological conditions, a transition that is attributable to hydrophobic interactions and hydrogen bonds between the deionized PAEU segments (Figure 7). The degradation rate of PAEU-based hydrogels could be controlled by varying the structure of the PAEU segments. PAEU-based hydrogels were found to be noncytotoxic, and released DOX for more than 5 weeks in vitro.<sup>124</sup> The in vitro and in vivo release of hGH from PAEU-PEG-PAEU hydrogel were more than 5 and 3 days, respectively.<sup>125</sup>

pH- and temperature-sensitive block copolymers possess complicated structures and their preparation requires several steps. In contrast, low molecular weight gelators, such as oligo( $\beta$ -amino ester urethane) (OAEU) and oligo(amido amine)s (OAAs), have simple structures and can be prepared via a simple one-step synthesis.<sup>126,127</sup> The gelation and mechanical properties of OAA gelators can be controlled by varying the structure of the gelator. Subsequently, a biodegradable oligo(amido amine amino ester) (OAAAE) hydrogel (Figure 5D) was reported to release insulin for up to 1 week in vitro.<sup>128</sup> With a single injection of the insulin-loaded OAAAE hydrogel into SD rats, serum insulin concentrations were maintained for 4 days without an initial burst.

#### 4. OUTLOOK AND FUTURE CHALLENGES OF INJECTABLE HYDROGELS

As highlighted in this perspective, significant progress has been achieved in the past 2 decades in the field of injectable hydrogels for delivery of therapeutic agents and tissue regeneration. Studies have been conducted to address a number of potential issues, including needle clogging, acidic degradation products, complicated copolymer structure, degradation rates, and burst release, among others. However, several challenges need to be pointed out for further development of physically injectable cross-linked hydrogels. First, the initial burst release of therapeutic agents, especially DNA, protein, and low molecular weight and hydrophilic drugs, is of concern. Although pH- and temperature-sensitive hydrogels have the potential to reduce the burst-release effect, hydrogels that have sufficient affinity for therapeutic molecules should be put in mind. Second, degradation rate is important for controlling drug delivery and tissue formation. For example, faster degradation results in a high local concentration of released drugs as well as degradation

products, which may evoke a host inflammatory response whereas a low local concentration of drugs is released when degradation time of hydrogels is too long. Degradation rate of hydrogels needs considering for specific applications and can be controlled by varying the composition, crystallinity, and topology of the polymers. Third, the cytotoxicity of hydrogels containing cytotoxic moieties, such as poly(amido amine) and among others, may also cause inflammation at the injection site. The structures of copolymers consisting of cytotoxic moieties should be well-defined so as to minimize inflammation. Fourth, pH- and temperature-sensitive pentablock or multiblock copolymers possess complicated structures that may make it difficult to obtain approval from the Food and Drug Administration. Thus, the development of polymers with simple, well-defined structures remains an ongoing challenge. Fifth, research on physical hydrogels has been skewed toward drug-delivery applications; the potential development of such hydrogels for tissue-regeneration applications should also be given comparable consideration. Properties of hydrogels that foster cell adhesion are crucial for cell migration, proliferation and differentiation. Also, sustained delivery of ionic growth factors capable of interacting with ionic hydrogels is desirable for tissue regeneration. In summary, a more complete understanding of polymer properties, such as degradation rates, nature of degradation products, gel modulus, and ability to bind therapeutics or cells should ultimately allow for the design of hydrogels that produce the desired outcomes.

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Cong Truc Huynh was born in Tien Giang Province (Viet Nam) in 1980. He obtained his B.S.E. degree in 2003 and M.S.E. degree in 2006 from Ho Chi Minh City University of Technology (Viet Nam), majoring in Chemical Engineering and Polymer Material Technology, respectively. He received his Ph.D. degree, working on the field of polymeric hydrogels for drug delivery system, in August 2011 from Sungkyunkwan University (South Korea) under the supervision of Prof. Doo Sung Lee. He is

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Minh Khanh Nguyen was born in 1980 in Ho Chi Minh city (Viet Nam). He earned his B.S.E. (2003) in Chemical Engineering at Ho Chi Minh City University of Technology (Viet Nam) and received his Ph.D. (2010) from Sungkyunkwan University (South Korea) under the guidance of professor Doo Sung Lee. He is currently working as a postdoctoral researcher at Case Western Reserve University (Cleveland, OH). His main research is focused on the development of biodegradable injectable polymeric hydrogels for controlled drug delivery and tissue engineering.



Doo Sung Lee received his B.S. degrees in Chemical Engineering from the Seoul National University in 1978 and his M.S. and Ph.D. in Chemical Engineering from the Korea Advanced Institute of Science and Technology (KAIST) in 1984. Doo Sung Lee is currently a Professor in Department of Polymer Science and Engineering at the Sungkyunkwan University. He has served as a Dean of College of Engineering at Sungkyunkwan University. He was elected as a member of the Korean Academy of Engineering in 2007. He is now a director of the Theranostic Macromolecules Research Center funded by the NRF of Korea. His research group studies on the development of functionalized and biodegradable injectable hydrogels and micelles for controlled drug and protein delivery and molecular imaging.

## ■ ACKNOWLEDGMENT

This work was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) grant funded by the Korean Government (MEST) (2010-0027955).

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