Miktoarm star copolymers as interfacial connectors for stackable amphiphilic gels

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Abstract

Using a combination of modeling and experiments, we show that miktoarm star macromolecules act as molecular/mechanical linkers in the fabrication of multilayer stackable gels, which are formed by sequential controlled radical polymerization of successive layers in incompatible solvents. Dissipative particle dynamics simulations indicate that miktoarm star copolymers localize at the interface between the incompatible solvents and act as molecular bridging agents between the respective gel layers. Miktoarm stars composed of poly(*n*-butyl acrylate)-co-poly((oligo(ethylene glycol) methacrylate) were synthesized by atom transfer radical polymerization (ATRP) and successfully used as an interfacial compatibilizer/linker in mechanically interconnected bilayer stacks comprised of a primary layer of cross-linked hydrophobic *n*-butyl methacrylate polymerized in toluene and of a secondary layer of cross-linked hydrophilic 2-(dimethylamino)ethyl methacrylate polymerized in water. Without the miktoarm stars, no connection between the two layers could be obtained.

Introduction

Polymer gels can be formed from a remarkably wide variety of monomers and, by tuning the degree of cross-linking within the network, can display a tremendously broad range of mechanical behavior. Due to this versatility of chemical and mechanical properties, gels play a vital role in a number of applications such as consumer goods, food additives,[1, 2] absorbents,[3-6] soft electronics[7-9] and soft-actuators.[10] They are also increasingly used for biomedical applications[11] as primary components in contact lenses, wound dressings,[12,

13] in tissue engineering[14-16] and drug delivery systems.[17] There remains, however, a significant challenge in assuring good mechanical connectivity between polymer networks with different mechanical or chemical characteristics, as needed in the formation of novel hybrid materials. Attempts by different groups to address this challenge[18, 19] have shown that conventional joining methods, such as gluing, are only of limited effectiveness in this regard. A particularly interesting approach to mechanically linking different pieces of hydrogels has been demonstrated recently by Leibler *et al*, who used silica nanoparticles as interfacial linking agents.[20] While this approach has been remarkably effective in facilitating tissue healing,[21] it may, however, be limited to specific types of gels and hydrogels.

Work presented herein extends our recent results, where we demonstrated that amphiphilic gels can be fabricated into mechanically robust, “stacked” gels by successive controlled/living polymerizations, such as Atom Transfer Radical Polymerization (ATRP).[22-24] In this prior work, the variant of ATRP based on the use of Initiators for Continuous Activator Regeneration (ICAR ATRP)[25] was successfully used to fabricate a bilayer stack comprised of poly(n-butyl methacrylate) (p-BMA) and poly(2-(dimethylamino)ethyl methacrylate) (p-DMAEMA) layers by carrying out the polymerizations in the single solvent (dimethylformamide, DMF). The successful mechanical linking between the layers was attributed to the use of a controlled/living polymerization process, which facilitated molecular continuity across the networks by reaction of either the living chains from the first network with the second monomer or of the new chains with the unreacted double bonds in the first network.

Interestingly, this approach failed to yield robustly connected stacks when the successive polymerizations were carried out in different, immiscible solvents (water/toluene). The limitation to single solvent systems could seriously diminish the applicability of our otherwise highly promising approach to the fabrication of stacked gels by ATRP, by limiting it to the pairs of monomers soluble in the same solvents. The present study was aimed at finding the solution to this problem.

We hypothesized that the failure to develop a molecularly connected stack by carrying successive polymerization in two immiscible solvents was caused by undesired partitioning of growing chain ends away from the water/toluene interface. Given this hypothesis, in the present study, we attempted to address this problem through the use of miktoarm star polymers (MSPs) as molecular compatibilizing/linking agents. The choice of MSPs for this purpose was inspired by past results, which demonstrated their ability to act as highly efficient multifunctional surfactants and compatibilizers.[26, 27]

To gain deeper insight into the microscopic processes occurring at the interface, we have developed a functional dynamic model of sequential polymerization of two different monomers at the water/toluene interface. Simulations carried out using this model confirmed that the use of miktoarm star linkers may indeed lead to the desired improvement of connectivity across the interface. This prediction was then verified experimentally by examining the effect of the introduction of poly(n-butyl acrylate)-co-poly((oligo(ethylene glycol)methacrylate) (pBA/pEGMA) miktoarm star copolymers in the preparation of crosslinked p-DMAEMA/pBMA stacks using the water/toluene system.

II. Methodology

A. Computational Model

Dissipative particle dynamics (DPD)[28-30] was used to model the dynamic behavior of this multi-component system. DPD is a mesoscopic, particle-based simulation method that captures the time evolution of a many-body system through numerical integration of Newton's equation of motion: $m d\mathbf{v}_i / dt = \mathbf{f}_i$. The beads in the system represent molecules (or clusters of molecules) rather than atoms, as typically used in molecular dynamics (MD) simulations. The effective force $\mathbf{f}_i(t)$ acting on bead i is the sum of three pairwise additive forces: $\mathbf{f}_{ij}(t) = \sum (\mathbf{F}_{ij}^C + \mathbf{F}_{ij}^D + \mathbf{F}_{ij}^R)$, where the sum runs over all beads j within a certain cutoff radius r_c . The three forces are the conservative force $\mathbf{F}_{ij}^C$, drag or dissipative force $\mathbf{F}_{ij}^D$, and random force $\mathbf{F}_{ij}^R$. We describe each pairwise force below.

The conservative force is a soft repulsive force, given by $\mathbf{F}_{ij}^C = a_{ij}(1 - r_{ij})\hat{\mathbf{r}}_{ij}$, where a_{ij} measures the maximum repulsion between beads i and j , $r_{ij} = |r_i - r_j| / r_c$ and $\hat{\mathbf{r}}_{ij} = \mathbf{r}_{ij} / |\mathbf{r}_{ij}|$. The soft-core repulsion permits a degree of overlap between neighboring beads and the use of larger time steps than those typically used in MD simulations, which commonly involve hard-core potentials (e.g., the Lennard-Jones potential).[29] The drag force is $\mathbf{F}_{ij}^D = -\gamma\omega_D(r_{ij})(\hat{\mathbf{r}}_{ij} \cdot \mathbf{v}_{ij})\hat{\mathbf{r}}_{ij}$, where γ is a simulation parameter related to viscosity arising from the interactions between beads (polymer-polymer, polymer-solvent, and solvent-solvent), ω_D is a weight function that goes to zero at r_c , and $\mathbf{v}_{ij} = \mathbf{v}_i - \mathbf{v}_j$. The random force is $\mathbf{F}_{ij}^R = \sigma\omega_R(r_{ij})\xi_{ij}\hat{\mathbf{r}}_{ij}$, where ξ_{ij} represents a zero-mean Gaussian random variable of unit variance and $\sigma^2 = 2\gamma k_B T$ relates the amplitude of the noise to the friction coefficient, as specified by the fluctuation-dissipation theorem.[28, 29] The value of $\gamma = 4.5$ was chosen to

ensure relatively rapid equilibration of the temperature of the system and the numerical stability of the simulations for the specified time-step.[29] In the latter expression, k_B is the Boltzmann constant, and T is the temperature of the system. The weight functions were chosen to take the following form: $\omega_D(r_{ij}) = \omega_R(r_{ij})^2 = (1 - r_{ij})^2$ for $r_{ij} < r_c$.[29] Each of these three pairwise forces conserves the momentum locally, and thus, DPD simulations reproduce correct hydrodynamic behavior even in systems containing only a few hundred particles.[28-30]

The time evolution of the system was captured by integrating the equation of motion via a modified velocity-Verlet algorithm.[31] In the simulation, r_c was taken as the characteristic length scale and $k_B T$ as the characteristic energy scale. We used the dimensionless value of $r_c = 1$ and room temperature was set as the reference temperature by specifying $k_B T_0 = 1$ where $T_0 = 298.15^\circ \text{K}$. The interaction parameter q_j was given in terms of $k_B T_0 / r_c$; the reduced temperature was then introduced as $T^* = T / T_0$, and the characteristic time scale was defined as $\tau = (m r_c^2 / k_B T_0)^{1/2}$. The remaining simulation parameters [29] were the time step $\Delta t = 0.02\tau$ and the total bead number density $\rho = 3$. The polymer chains were simulated as a bead-spring model with the harmonic bond potential given by $E_b = 1/2 K_b (r - r_0)^2$. Here, $K_b = 128$ is the elastic constant and $r_0 = 0.5$ is the equilibrium bond distance.

Our recently developed DPD approach for ATRP [32] was used to model the formation of a polymer gel. The reactive species in this system are initiators, monomers, and bifunctional cross-linkers; these species are all modeled as DPD beads. The bifunctional cross-linker encompassed two reactive cross-linking units and was modeled by one DPD bead with five different “states”, which indicated the extent to which it has reacted.[22, 32] The reaction kinetics for the ATRP were simulated by a set of elemental reactions and coupled to the dynamics of the system. Due to the characteristics of the ATRP living polymerization process, termination and chain transfer reactions were excluded from the simulation.[23, 32] Further details of the simulated ATRP reaction scheme as implemented within the DPD approach can be found in ref 23.

The polymerization process in our approach is similar to that previously modeled *via* coarse-grained MD and Monte Carlo simulations.[33-39] In each reaction step, a reactive bead was selected and for each reactive bead, another bead was chosen within the interaction radius r_i . This pair of beads can form a bond with a polymerization probability P_r , with each

successful reaction resulting in irreversible bond formation. In this simulation, the initiation probability $P_r^i = 5 \times 10^{-3}$, the monomer addition (propagation) probability $P_r^{p,M} = 5 \times 10^{-3}$, and the cross-linking probability $P_r^{p,X} = 2P_r^{p,M}$ were selected to maintain the first-order reaction kinetics. Regarding the cross-linking process of the pendant group, $P_r^{p,P} = 3P_r^{p,M}$ was chosen to account for the fact that a single bead models the bifunctional cross-linker.[34] The rate constants of the respective reactions can be adjusted by choosing different reaction probabilities[22, 23, 32] but the values should remain sufficiently small to ensure controlled polymerization growth in the kinetically controlled reaction regime.[39] The interaction radius was set to be $r_i = 0.7$ since smaller values of r_i resulted in delayed gelation and taking $r_i > 0.7$ led to considerable deviations from linear first-order kinetics.[32] The reactions were performed every ten-time steps.[36]

The size of the simulation box was set as $25 \times 25 \times (25N)$ (in the unit of the characteristic length scale r_c) [32], where N is the number of layers, i.e., the two-gel system encompassed two layers. Periodic boundary conditions were imposed in the lateral directions (x and y). Solid walls bounded the system in the transverse (z) directions. The top and bottom walls were modeled by repulsive beads (with height $h = 1$ and density $\rho_{wall} = 3$) that effectively repelled the gel and all the rest of the beads in the system.[40] Bounce-back boundary conditions were applied at the fluid-solid interfaces to prevent solvent and gel beads from penetrating into the walls, producing a no-slip boundary conditions with minimal interfacial density oscillations.[41]

The initial configuration of each new solution with the dissolved components (initiator, cross-linker, monomer, and solvent) was generated by randomly placing beads within a box of size $25 \times 25 \times 25$. The ratio of the initiator, cross-linker, and monomer concentrations in the solution was set as $[Ini]_0/[X]_0/[M]_0 = 1/5/75$ and the corresponding solvent concentration was $[S]_0 = 50\%$ i.e, the volume fraction of the solvent beads was 0.5. The total bead number density of the system was $\rho = 3$. These respective concentrations were chosen to match the common reactant ratio used in the experimental polymerization studies.[22] During the simulation, each solution was equilibrated for 5×10^4 simulation time steps before allowing the polymerization reaction to proceed; this procedure ensured that the diffusion between the current gel layer and the new solution was not influenced by the initial configuration of the solution.

The miktoarm star polymers, MSPs, were modeled with two different types of arms emanating symmetrically from a single core. Each MSP contained an equal number of A-type

and B-type arms, (A_nB_n) , and each arm had a fixed length ($l_m = 20$ beads). For the reference case, a MSP with eight arms (i.e., $n=4$) was considered; thus, each MSP contained $N_m = 1 + 2n \times l_m$ beads. The bond potential for the arms was the same as that for the polymer gel, with $E_b = 1/2 K_b (r - r_0)^2$, where $K_b = 128$ is the elastic constant and $r_0 = 0.5$ is the equilibrium bond distance.

The interaction parameter between any two beads that are compatible was set to $a_{ij} = 25$ (in units of $k_B T / r_c$)[29] and the interaction parameter between incompatible species were set to $a_{ij} = 60$ (see Table 1).

	Bottom Gel	Bottom Solvent	Top Gel	Top Solvent	Miktoarm A (Blue)	Miktoarm B (Red)
Bottom Gel	25	25	60	60	25	60
Bottom Solvent		25	60	60	25	60
Top Gel			25	25	60	25
Top Solvent				25	60	25
Miktoarm A (Blue)					25	60
Miktoarm B (Red)						25

Table 1: DPD interaction parameters between different components at $T_0=298.15$ K

B. Experimental Part

Materials: n-Butyl methacrylate (BMA, 99%, Aldrich), 2-(dimethylamino) ethyl methacrylate (DMAEMA, 98%, Aldrich) and poly(ethylene glycol) dimethacrylate (pEGDMA₇₅₀, average molecular weight 750, Aldrich) and butyl acrylate (BA) were passed through a small column of basic alumina to remove radical inhibitors prior to use. Poly(ethylene glycol) methacrylate (pEGMA₂₀₈₀, average molecular weight 2080, Aldrich) was purified by solubilizing it in dichloromethane and precipitating it in hexane. Copper(II)

bromide (99.999%, Aldrich), Ethyl α -bromoisobutyrate (EBiB, 98% Aldrich), azo-initiators 2,2'-azobis[2-(2-imidazolin-2-yl)-propane] dihydrochloride (VA-044, Wako) and 2,2'-azobis(4-methoxy-2,4-dimethylvaleronitrile) (V70, Wako), methacryloxyethylthiocarbamoylrhodamine B (rhodaminemethacrylate, Polysciences Inc.), fluorescein methacrylate (Sigma-Aldrich), divinylbenzene (DVB, 80%, Aldrich), purified water (Thermo scientific nanopure, 18.2 M Ω -cm) and N,N-dimethylformamide (DMF, ACS grade, Fisher Scientific) were used as received. Tris(pyridin-2-ylmethyl)amine (TPMA)[42-44] and poly(ethylene glycol) α -bromoisobutyrate (pEG_{2K}iBBr, average molecular weight 2000)[44] were prepared as previously reported in the literature. Corning slides 75x50 Corning Incorporated® were purchased from Aldrich. The slides were treated with Rain-X®, an anti-adhesive and water repellant to prevent gel adhesion to the glass. Seals were made by cutting to the right dimension McMaster-Carr extreme temperature silicone rubber® 1mm thick. Molds were made by sandwiching a silicone rubber seals between two glass plates. ARGET ATRP was used as polymerization technic for the synthesis of the miktoarm star polymer. ICAR ATRP was used as polymerization technic for the formation of the stacked gels.

i. Synthesis of the pBA/pEGMA miktoarm stars by ARGET ATRP:

Arm-first method was used to synthesize miktoarm stars containing hydrophobic poly(n-butyl acrylate (pBA) and hydrophilic poly(ethylene glycol) methacrylate (pEGMA₂₀₈₀, M_n = 2080) arms. ARGET ATRP was used as the polymerization technique since it allows one to reach high conversion with good control of the polymerization using a minimal amount of Cu^{II} catalyst.

General conditions for the synthesis of pBA macroinitiator (pBA-Br): The initial molar ratio of reagents were [BA]₀/[EBiB]₀/[Sn^{II}(EH)₂]₀/[CuBr₂]₀/[TPMA]₀ = 67/1/0.05/0.0033/0.05 ([BA]₀ = 0.2 M). CuBr₂ (7.8 mg, 50 ppm), TPMA (150.0 mg) and 50 mL anisole were added to a 200 mL Schlenk flask. The mixture was bubbled with nitrogen (N₂) for 30 min to remove O₂. BA was purified by passing through a basic alumina column to remove inhibitor and then bubbled with N₂ for 30 min. 50 mL BA was transferred to the reaction flask by syringe under protection of N₂. The initiator, EBiB (2.02 mL), was added to the flask. A mixture of Sn^{II}(EH)₂ (0.27 mL) and anisole (10 mL) was deoxygenated by bubbling N₂ for 5-10 min, and 1 mL of the mixture was added to the reaction flask under protection of N₂ to reduce part of the Cu^{II} catalyst complex and initiate the polymerization. The flask was sealed with a glass stopper and immersed in an oil bath set at 70 °C. At timed intervals, samples were withdrawn and diluted

with THF for GPC (with PMMA calibration) and with CDCl_3 for NMR analysis. The reaction was stopped after 3h and was quenched by adding an excess amount of oxygenated THF. The resulting polymers were purified by passing the solution through a neutral alumina column to remove the catalyst followed by rotary evaporation to remove the solvent and the residue was dried under vacuum at room temperature. Final product $M_n = 2700$.

Figure 1: GPC curves of PBA-Br. The molecular weights were determined by PMMA calibration.

General conditions for the synthesis of pBA/pEGMA miktoarm stars: The initial molar ratio of reagents were $[\text{DVB}]_0/[\text{pBA-Br}]_0/[\text{pEGMA}_{2080}]_0/[\text{Sn}^{\text{II}}(\text{EH})_2]_0/[\text{CuBr}_2]_0/[\text{TPMA}]_0 = 14/0.5/0.5/0.2/0.01/0.1$ ($[\text{pBA}]_0 = [\text{pEGMA}]_0 = 0.01 \text{ M}$)

A clean dry Schlenk flask was charged with CuBr_2 (2.3 mg, 0.01mmol) and tris(2-pyridylmethyl)amine (TPMA, 30.3 mg, 0.1mmol). A solution of pBA-Br (2.5g, 1.04mmol) and pEGMA₂₀₈₀ macromonomer (0.88g, 1.04 mmol) and DVB (2.08 mL, 14.58 mmol) in anisole (100 mL) was added and the mixture was bubbled with N_2 for 60 min. The reaction flask was sealed with a glass stopper and immersed in an oil bath thermostated at 110 °C. An aliquot (0.1 mL) of $\text{Sn}(\text{EH})_2$ (0.68 mL, 0.21mmol) in anisole (10 mL) previously degassed for 10 min is added to the reaction flask. The reaction was stopped after 25h and quenched by adding an excess amount of THF. The resulting polymers were purified by passing the solution through a neutral alumina column to remove the catalyst followed by rotary evaporation to remove the solvent. The residue was dried under vacuum at room temperature.

Figure 2: DMF GPC following of pBA/pEGMA miktoarm stars formation. The molecular weights were determined by PSt-DPE calibration. MW = 16800, dispersity:1.80.

The conversion of macromonomer to star was around 80%, according to THF GPC trace. The GPC trace of the prepared miktoarm star is shown in Figure 2.

ii. Synthesis of the first gel layer by ICAR-ATRP

BMA hydrophobic monomeric stock solution was prepared from BMA (1.06 g, 7.5 mmol), EBiB (196 mg, 0.1 mmol), pEGDMA₇₅₀ (375 mg, 0.5 mmol), and 1.46 g of toluene. To 1 ml of this stock solution a DMF solution (150 μ l) containing CuBr₂ (20 mM) and TPMA (160 mM) was added. The solution was bubbled under N₂ for 10 min and was then transferred in a vial containing the azo initiator V70 (8 mg, 0.026 mmol) previously degassed for 10 min. The reaction mixture was further degassed for 5 min and 0.3 mL of the mixture was injected into the mold and maintained at 45°C for 3h to form the first gel. The ratio of the different reactants were the following: $[BMA]:[EBiB]:[pEGDMA_{750}]:[CuBr_2]:[TPMA]:[V-70] = 75:1:5:0.1:0.8:0.9$; $VM:VS = 1:1$ in water. Conversion as measured by NMR on gel extract: 73%.

iii. Injection of a star solution at the interface

A degassed solution (0.1 mL) of the pBA/pEGMA₂₀₈₀ miktoarm stars in THF (100 mg/ml) was injected under nitrogen on top of the first gel layer.

iv. Polymerization of the second layer by ICAR-ATRP

DMAEMA hydrophilic monomeric stock solution in water was prepared from DMAEMA (1.178 g, 7.5 mmol), pEG₂kiBBR (200 mg, 0.1 mmol), pEGDMA₇₅₀ (375 mg, 0.5 mmol), and 1.75 g of distilled water. To 1 ml of this stock solution, a DMF solution (150 µl) containing CuBr₂ (20 mM) and TPMA (160 mM) were added. After 10 min of degassing under N₂, a water solution (17 µl) of azo initiator VA-044 (60mg/mL) was added. The reaction mixture was further degassed for 5 min and was injected into the mold and incubated at 45°C for 3h to give the staked gels. The ratio of the different reactants were the following: $[DMAEMA]:[pEG_{2kiBBR}]:[pEGDMA_{750}]:[CuBr_2]:[TPMA]:[VA-044] = 75:1:5:0.1:0.8:0.1$; $VM:VS=1:1$ in toluene. Conversion as measured by NMR on gel extract: 99%.

In order to visually differentiate the layers, an aqueous solution (50 µl of 10 mg/mL) of fluorescein methacrylate was copolymerized within the DMAEMA layers.

A similar procedure was used for the polymerization of multi-layer gels without incorporation of miktoarm stars at the interface (see figure 7) and with a variation of the order of polymerization (BMA first layer | DMAEMA second layer; DMAEMA first layer | BMA second layer). The obtained material was compared with the gel containing miktoarm stars at the interface.

III. Results and Discussion

A. Simulation Results

Figures 3 a-d show the structural evolution of the first gel layer (shown in white). The gel formation was initiated from a well-equilibrated solution of initiator, cross-linker, and monomer, using the respective ratio of these species: $[Ini]_0/[X]_0/[M]_0 = 1/5/75$. The solvent concentration was set at $[S]_0 = 50\%$. As these different species are mutually compatible, all the interaction parameters were set to $a_{ij} = 25$. The reaction probabilities used were the following: $P_r^i = 5 \times 10^{-3}$, $P_r^{p,M} = 5 \times 10^{-3}$, $P_r^{p,X} = 1 \times 10^{-2}$, and $P_r^{p,p} = 1.5 \times 10^{-2}$; these probabilities were chosen to capture the accurate ATRP polymerization in the simulation.[22, 32] The monomer conversions at the time steps shown in Figs. 3 a-d were (a) 3.5%, (b) 18%, (c) 76%, and (d) 95%, respectively. For clarity, the solvent beads are not shown in the figures.

Figure 3: (a-d) Time evolution of the first gel layer. Snapshots taken at the following time steps: (a) 1×10^4 , (b) 5×10^4 , (c) 3×10^5 , and (d) 1×10^6 ; monomer conversions at these time steps are (a) 3.5, (b) 18, (c) 76, and (d) 95% respectively. The white bead represents polymer strands, and pink beads are cross-linkers. The top and bottom wall beads are shown in brown color. (e-f) The polymerization kinetics in a solution with $[Ini]_0/[M]_0/[X]_0=1/5/75$ and $[S]_0=50\%$. Reaction probabilities are set as $P_r^i = 0.005$, and $P_r^{p,M} = 0.005$. (e) Monomer (black line) and cross-linker (red line) conversions and (f) $\ln([C]_0/[C])$ as a function of the simulation time steps; $[C]$ is the current concentration of unreacted moieties. Error bars arise from averaging over five independent runs.

By plotting the temporal evolution of the monomer (black line) and cross-linker (red line) conversion (Fig. 3e), the polymerization kinetics could be efficiently characterized. Namely, the dependence of $\ln([C]_0/[C])$ on time (Fig. 3f) revealed a linear first-order kinetics; where $[C]_0$ represented the initial concentration of the given moiety and $[C]$ represented the current concentration of the unreacted moiety. The saturation of the monomer and cross-linker conversion showed that the system was nearly fully polymerized ($\sim 95\%$) at late times. Hence, our DPD scheme accurately reproduced the first-order kinetics of ATRP polymerization.[23,

24, 45, 46] It is worth noting that the downward curvature in the concentration of cross-linker at late times indicated a decrease in the number of the active cross-linkers.

To simulate the growth of the second gel layer, a solution containing initiator, cross-linker, and monomer (in the ratio $[Ini]_0/[X]_0/[M]_0 = 1/5/75$) was introduced on top of the first gel layer, and the components underwent living copolymerization. In this case, the top and bottom solvents were incompatible, and both gels were also incompatible, i.e., the interaction parameters between the relevant beads were set to $a_{ij} = 60$ (see Table 1).

Figure 4: (a-d) Evolution snapshots of the second gel layer (yellow) on the top of first gel layer (white) at different time steps as indicated. Monomer conversions at these time steps are (a) 0, (b) 39, (c) 67, and (d) 95%. The pink and maroon beads represent the cross-linker in first and second gel layers respectively. (e) Conversions and $\ln([C]_0/[C])$ of monomer (solid lines) and cross-linker (dashed lines) on reaction times during polymerization with ratios $[Ini]_0/[X]_0/[M]_0 = 1/5/75$. (f) Number density profiles of the stacked two-layer gel. The inset shows the temporal variation of the number of contacts formed between gel layers. The error bars arise from averaging over five independent runs.

The snapshots in Figs. 4b-d show the structural evolution of the second gel (in yellow) at the following values of the monomer conversion: (b) 39%, (c) 67%, and (d) 95%. The red curves in Fig. 4e indicate monomer (solid lines) and cross-linker (dashed lines) conversion as a function of time. The saturation of these curves close to one revealed that the polymerization for the second gel layer was also nearly complete ($\sim 95\%$). The black curves in the figure presents the time dependence of $\ln([C]_0/[C])$, which clearly displays first-order kinetics for both monomer (solid lines) and cross-linker (dashed lines), as observed for the first gel layer.

Because the two gels and their mutual solvents were incompatible, we anticipated the formation of a sharp interface between the white and yellow layers. The density profile of the system along the transverse (z) direction in Fig. 4f confirmed this hypothesis. Moreover, the plot revealed a gap in the density profile around $z = 25$. This clarified that the active radicals from the first gel remained buried within the first layer due to the incompatibility with the upper solution. Therefore, they could not contribute to forming a strong interface. This lack of available exposed radicals strongly affected the bonding between the two layers, resulting in a poor connection between these layers. The inset presented in Fig. 4f shows the evolution of the number of contacts between the gel layers as a function of time. Focusing on a bead in a given gel, the plot was obtained by calculating the number of beads of the other gel lying within the interaction radius r_c of the given bead. We then average over all gel beads. In these simulations, we do not consider any active chain-ends in the bottom gel in order to focus on the interactions of the miktoarm stars at the interface.

The experimental studies on the comparable system are in agreement with this simulation since a weak interface between such gel layers was obtained, i.e., the fused gel layers were very poorly connected at the interface (see Fig. 7). The tension generated at the interface of the material could not be supported by the few covalent bonds that formed the links between the two layers.

As a route to potentially improving the connectivity of the two incompatible gel layers, miktoarm star copolymers were introduced in the system. First, 12 miktoarm star copolymers (A_nB_n ; $n=4$ and volume fraction $\phi_{MSP}=0.02$) were added at the top of the first gel layer (monomer conversion $\sim 95\%$), as shown in Fig. 5a.

Figure 5: (a) Initial configuration of MSPs at the top of first gel layer (see enlarged view in the inset). (b) Equilibrium configuration of MSP at the interface. (c-e) The time evolution of second gel layer in the presence of MSPs. Other simulation details are described in the text. (f) Number density profiles of the stacked two-layer gel without MSP (black line), with 12 MSPs (red line), and with 20 MSPs (green line). Inset reveals the effect of MSP at gel interface. Dashed lines show the number density profiles of MSPs. (g) Shows temporal variation of the number of contacts formed between gel layers and MSPs. The error bars arise from averaging over five independent runs.

The inset in Fig. 5a displays the components of each MSP where the blue chains (A-type bead) were set as compatible with the first gel layer (white gel) whereas the red chains (B-type bead) were set as compatible with the second gel layer. The remaining species ($[\text{Ini}]_0/[\text{X}]_0/[\text{M}]_0$ in the same ratio as for the first gel) needed to form the second gel layer were then added. After equilibrating this configuration for 5×10^4 simulation time steps (Fig. 5b; unreacted species are not shown), the system was allowed to undergo ATRP copolymerization. The temporal evolution of the second gel layer in the presence of MSPs is shown in Figs. 5c-e. The monomer conversions at the indicated time steps are (c) 38%, (d) 65%, and (e) 98%, respectively.

A comparison of the density profiles along the transverse (z) direction of the stacked gels in the presence of 12 MSPs (red line in Fig. 5f) and absence of MSPs (black line) reveals that MSPs reduce the density gap at the interface (see the enlargement in the inset). Thus, the affinity of the arms to the respective compatible gels promoted a bridging of the two layers. Increasing the number of MSPs to 20 ($\phi_{MSP}=0.034$) led to a greater concentration of copolymers at the interface and further improved the connectivity between the two layers, as shown by the green lines in Fig. 5f.

To further quantify the bridging capability of MSPs, the numbers of contacts formed between the miktostar arms and the respective compatible layers (for the temporal evolution shown in Figs. 5c-e) were calculated and are presented in Fig. 5g. For the calculation, the number of contacts between a MSP and the gel is defined as the number of gel beads within the interaction radius r_c of a MSP bead. This value was compared with the number of contacts formed between the gel layers in the absence of MSPs (black line) shown in Fig. 4f. Recall that the MSP solution was added on the top of the first gel layer (white), and the A-type arms were defined as having an affinity with the white layer. The system was then equilibrated for 5×10^4 simulation time steps before polymerization started in the top layer. During equilibration, A-type arms optimized their interaction with the bottom gel layer and therefore, the number of contacts formed between the A-type arms and the lower gel remains constant while polymerization was taking place (see the red line in Fig. 5g). The number of contacts between the B-type arms and growing yellow layer, however, increased with time (purple line) and overlapped with the red line. A significant increase in the number of contacts indicated a strong interface between the gels was obtained. The green and the blue lines revealed that there were negligible contacts between the arms and the respective incompatible layers, i.e., between the A-type arms and the yellow layer, and the B-type arms and the white layer.

Furthermore, Fig. 6a shows the number density profiles of the stacked two-layer gel in the presence of 12 MSPs (red line) with reactive ends. The comparison with the density profile of two-gel layer without MSPs (black line) reveals that MSPs reduce the density gap at the interface. The green line shows the density profile of MSPs. Figure 6b displays a comparison of the number of contacts formed between B-type arms and the top gel layer for two different MSP concentrations as a function of time. The red line marks the data for 12 MSPs (volume fraction $\phi_{MSP}=0.02$), and the green line marks the data for 20 MSPs (volume fraction $\phi_{MSP}=0.034$). The black line marks the number of contacts between gel layers in the absence

of MSPs. Our results illustrated that increasing the MSP concentration at the interface enhanced the number of contacts between the incompatible gel layers even further.

Finally, MSPs with reactive ends (shown in the inset of Fig. 6a) were used in the simulation to combine two incompatible gel layers. The reactive MSPs are added on top of the first gel. Based on their affinity to the different gels, the arms rearrange on either side of the interface. We then add initiators, cross-linker, and monomers in the ratios $[Ini]_0/[X]_0/[M]_0=1/5/75$. The growth of the second gel layer starts from the reactive ends of the MSPs, as well as from the initiators in the bulk. In this manner, we form two incompatible gel networks that are covalently linked to each other. In Fig. 6b, we calculate the number of contacts formed between the gel and 12 MSPs at the interface. As anticipated, the number of contacts formed between two gel layers is significantly greater for MSPs with reactive ends (blue line) than for MSPs that do not encompass these reactive ends (red line).

Figure 6: (a) Number density profiles of the stacked two-layer gel in the presence of 12 MSPs (red line) with reactive ends, and compared with the density profile of two gel layer without MSPs (black line). The green line shows the density profile of MSPs. The Inset reveals the MSP with initiator embedded red arms. (b) Comparison of the time evolution of the number of contacts between B-type arms and the top gel layer at different MSP concentrations.

B. Experimental Results

All double layer stackable hydrophilic–hydrophobic gels were prepared by ICAR ATRP. Each solution contained a monomer, a cross-linker, an ATRP initiator, an ATRP catalyst, a radical initiator (azo-compound) and a solvent. Similar to the above simulations, the initial molar ratios $[monomer]:[ATRP\ initiator]:[cross-linker]$ were equal to $[M]_0:[Ini]_0:[X]_0$

= [75]:[5]:[1]. In all cases the monomer and solvent volumes were equal, while the ratios of $[In]_0:[azo-initiator]_0$ were equal to [1]:[0.9] and [1]:[0.1] for the BMA and DMAEMA layers, respectively. The ATRP initiators were selected to be soluble in the respective solvents, i.e., EBiB for BMA ATRP solution in toluene and pEG_{2K}-iBBR for DMAEMA solution in water. The ATRP catalyst was a complex CuBr₂/TPMA. The same cross-linker was used in both cases (pEG₇₅₀DMA). The thermally activated azo-radical-initiators for the reduction of CuBr₂ were soluble in the respective solvents (VA-044 for aqueous solution and V-70 for toluene). For both systems, these conditions resulted in gelation in less than three hours and yielded gels with mechanical properties suitable for overall handling.[22] The synthesis of the stackable gels was carried out in a successive manner in a vertical mold.

The first series of experiments was comprised of two sets. In the first set, the first layer was obtained by copolymerization of BMA solution in toluene (BMA/toluene). The second layer was then obtained by the copolymerization of DMAEMA solution in water (DMAEMA/water) on the top of the first gel layer. In the second set, the sequence of polymerization was reversed. For both sets, the resulting materials consisted of two disconnected gel layers, indicating an inefficient interfacial connectivity (Fig. 7 and Fig. 8, top left and right).

The purpose of the second series of experiments was to establish if the application of miktoarm star polymers between two layers could improve their connectivity. As before, two sets of experiments with different polymerization sequences were performed, but the solution containing pBA/pEGMA miktoarm stars was added on top of the first synthesized gel layer before injection of the second polymerization mixture.

Under these conditions, the polymerization of BMA in toluene followed by polymerization of DMAEMA in water yielded a well-connected double layer stacked gel (Fig. 7 and Fig. 8, bottom left). However, when the order of polymerizations was reversed, the resulting stacked gels were still poorly connected (Fig. 7 and Fig. 8, bottom right).

Figure 7: Representation of the different polymerization systems.

Figure 8: Images of the gels after the sequential polymerization of the two layers. The toluene contained in the DMA layer partially evaporated, resulting in visible shrinking of the transparent layers.

The strength of the bonding between two gels depends on the sequence of layer polymerizations. This behavior can be explained by the different solubility of the monomers/polymers in the respective solvents. Indeed, the DMAEMA monomer (which was polymerized in water) is also soluble in toluene, and thus, it could diffuse across the interface from water to toluene, facilitating additional interconnectivity between the gels linked by miktoarm stars. In contrast, the BMA monomer polymerized in the toluene solution as the second layer is insoluble in water. Thus, it could not diffuse efficiently to the aqueous phase, preventing the additional interconnectivity. Note that this experimental behavior was only

partially predicted by simulation as the bottom and the top gel were treated as incompatible. Hence, the order of the polymerization did not matter in the simulation.

3. Conclusions

DPD simulations revealed that the fabrication of bilayer gels stacks by successive ATRP polymerization carried out in immiscible solvents could yield weak interfaces, as evident from the calculations of the number of contacts and of the number density profiles across the interface. Furthermore, the simulations predicted that the connectivity across the interface could be substantially improved through the use of bridging interfacial surfactants such as miktoarm star copolymers.

This prediction was tested in a set of experiments demonstrating that the introduction of pBA/pEGMA miktoarm star copolymers at the interface might indeed lead to the improvement of inter-layer connectivity when stacked gels are prepared by sequential ATRP polymerizations in immiscible solvents. Interestingly, the bridging of two incompatible gel layers with miktoarm stars was effective only when the first layer was comprised of pBMA polymerized in toluene, and it failed when it was comprised of pDMAEMA polymerized in water. This asymmetric behavior can be attributed to the fact that DMAEMA monomer is soluble in both solvents, while BMA is soluble only in toluene.

It should be noted that the experimental synthetic approach differed from simulation predictions in the second case. This could be explained by the fact that the scale of the simulation is limited to the nanoscale and might not reflect all the phenomena taking place at the interface on larger length scales.

The findings of this study point to the possibility of extending the ATRP-based methodology to the fabrication of “stacked gels” across incompatible solvent interfaces through the use of compatibilizers/linkers comprised of multifunctional miktoarm stars. The main implication of the obtained results is that they demonstrate the possibility of preparing robustly connected multilayer gels of dissimilar polymers with well-defined diverse architectures and functionalities afforded by controlled radical polymerizations. It appears that some limitations in using miktoarm linkers to connect dissimilar gels that were still revealed by this study (the dependence of the success of bridging on the order of polymerizations) can be addressed by carrying out the polymerizations in the favorable order. Further studies including the exploration of different compositions may lead to more general ways to eliminate these limitations.

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