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Photopolymerizable Nanogels as Macromolecular Precursors to Covalently Crosslinked Water-Based Networks

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Abstract

We present a strategy for directly and efficiently polymerizing aqueous dispersions of reactive nanogels into covalently crosslinked polymer networks with properties that are determined by the initial chemical and physical nanogel structure. This technique can extend the range of achievable properties and architectures for networks formed in solution, particularly in water where monomer selection for direct polymerization and the final network properties are quite limited. Nanogels were initially obtained from a solution polymerization of a hydrophilic monomethacrylate and either a hydrophilic PEG-based dimethacrylate or a more hydrophobic urethane dimethacrylate, which produced globular particles with diameters of 10–15 nm with remarkably low polydispersity in some cases. Networks derived from a single type of nanogel or a blend of nanogels with different chemistries when dispersed in water gelled within minutes when exposed to low intensity UV light. Modifying the nanogel structure changes both covalent and non-covalent secondary interactions in the crosslinked networks and reveals critical design criteria for the development of networks from highly internally branched, nanoscale prepolymer precursors.

Introduction

Nanogels are internally crosslinked polymeric nanoparticles with dimensions that can range from less than ten to a few hundred nanometers¹. Their characteristic network structure, tunable size and chemical content, and capacity for both surface and internal modification have led to significant investigation into the bioengineering related applications of nanogels². The most common reports involve the controlled delivery of small molecule therapeutics, DNA, RNA and proteins, though other biomedical fields such as imaging and sensing also benefit highly from the use of nanogels^{3, 4}. Preparation of nanogels from a variety of both natural and synthetic precursors has led to a large library of structures with features including controllable degradation, RAFT and ATRP functionality, thermal and pH-

Supporting Information

Supporting Information Available: DLS of EHEMA-PEG550DMA nanogels, GPC analysis of nanogel formation as a function of time, ¹H NMR spectrum of EHEMA-UDMA nanogels, real time conversion via FTIR of networks formed from EHEMA-TTEGDMA nanogels, frequency sweeps of 50 wt% nanogel dispersions, and glass transition behavior of UDMA, TTEGDMA, PEG550DMA, and PEG750DMA homopolymers.

responsive behavior, functional inorganic metal components, and click chemistry moieties for preparing surface decorated particles^{2,4-6}. Emulsion polymerization, precipitation polymerization, solution polymerization, single-chain collapse, microfluidics, and lithographic techniques have all been demonstrated as effective methods of forming nanogels^{4, 7-13}, which further highlights the extensive research into these materials.

While a large number of biomedical applications involve nanogels as freely dispersed particles, more recent studies have applied nanogels (and their microscale analogue microgels) as functional fillers or additives in the preparation of composite polymer networks¹⁴. Examples include reducing polymerization-induced shrinkage stress in dental resins¹⁵, forming reinforced double-network hydrogels^{16,17}, developing thermally responsive composite materials^{18,19}, and controlled release in cell-laden hydrogels^{20,21}. In these systems the nanogel (or microgel) component content typically reaches as high as 40% by weight. Hierarchical materials have been synthesized by linking nanogels with a multifunctional monomer, which leads to discrete nanostructures based on the assembly of multiple covalently tethered nanogels at low concentrations and macrogels at higher concentrations of nanogel and monomer^{22,23}. Nanogel-based macrogels have also been formed without small monomers via non-covalent self-assembly through hydrophobic interactions to form nanostructured hydrogels²⁴. This approach represents a unique platform for controlling polymer network structure over multiple length scales, from molecular interactions between monomers, to nano-scale interactions between nanogels, to long-range interactions in the gel, but has received little exploration in the literature.

We are interested in applying nanogels as a primary or even the sole network component in covalently crosslinked polymer networks given the wide range of available nanogel structures and the potential ability to construct macroscopic networks from pre-designed nanoscale precursors. In this study we aim to develop a strategy for synthesizing nanogels with varying chemical content and then polymerizing them directly into covalently crosslinked, monolithic networks in a controlled manner. Our approach for forming nanogels uses a solution free radical copolymerization of a monomethacrylate and a dimethacrylate monomer with a thiol-based chain transfer agent in a mutually compatible solvent of intermediate polarity. Appropriate solvent and chain transfer agent content reduces the kinetic chain length and favors intramolecular cyclization and crosslinking, which prevents macrogelation even at high conversion of monomers²⁵. In comparison to emulsion or precipitation polymerizations, this method allows for the combination of monomers with varying hydrophilic or hydrophobic character and remains a homogeneous solution throughout the polymerization process. The solvent choice and concentration along with monomer selection provides a means to alter swelling potential of the nanogel particles. The incorporation of methacrylate groups through an alcohol-isocyanate reaction is a facile and well-controlled way of introducing polymerizable groups after nanogel formation. Nanogels produced by this method can then be dispersed in an inert solvent or a reactive secondary monomer along with a photoinitiator and rapidly cured in the presence of ultraviolet light. UV curing is of broad interest in the synthesis of crosslinked polymers²⁶, and was chosen here to investigate the direct and potentially rapid crosslinking of nanogels into macroscopic networks in mild conditions with temporal control over initiation. We are particularly interested in water-based networks since the highly polar aqueous environment severely

limits choices of starting monomers. Typical precursors to water-soluble materials include natural biopolymers, poly(ethylene glycol) macromers, charged species, and certain monovinyl monomers such as hydroxyethyl (meth)acrylate and (meth)acrylamides^{27–29}. Networks formed from these conventional water-compatible monomers can have a restricted range of obtainable network structures, particularly regarding limited crosslink densities, and polymeric mechanical properties unless more complicated synthetic routes are used. We hypothesize that manipulating nanogel chemistry and architecture offers an opportunity for nanoscale control over bulk network properties with straightforward reaction mechanisms and may allow access to properties not directly obtainable from conventional monomer polymerization.

Experimental

Materials

All monomers, reagents, and solvents were obtained from Sigma-Aldrich unless noted otherwise. Polyethylene glycol methacrylate (referred to here as ethoxylated hydroxyethyl methacrylate, EHEMA, to distinguish it as the monomethacrylate component) ($M_n=526$), urethane dimethacrylate (UDMA, Esstech), polyethylene glycol dimethacrylate (PEGDMA, $M_n=550$ or 750), tetraethylene glycol dimethacrylate (TTEGDMA), 2-mercaptoethanol (ME), dibutyltin dilaurate, hydroquinone, methyl ethyl ketone (MEK), methanol, hexane, 2-isocyanatoethyl methacrylate (IEM, TCI America) and Irgacure 2959 (Ciba) were used without further purification. Azobisisobutyronitrile (AIBN) was recrystallized from methanol.

Nanogel Synthesis

Nanogels were prepared using a thermally initiated solution free radical polymerization. EHEMA was combined with UDMA, TTEGDMA, PEG550DMA, or PEG750DMA in a 7:3 molar ratio of monomethacrylate:dimethacrylate in MEK at 6x volume excess over monomers. 2-Mercaptoethanol was added at 15 mol% relative to the total monomer content along with AIBN at 1 wt% relative to total monomer mass. EHEMA-TTEGDMA was also prepared with 5x or 8x MEK to examine the effect of monomer concentration on nanogel properties and are indicated accordingly. The final monomer mass fraction was 15%, 13%, or 10% for 5x, 6x, or 8x MEK respectively. Similarly, chain transfer agent concentration was 0.083 M, 0.069 M, or 0.052 M depending on the respective solvent concentration used. The monomer solution was purged with nitrogen for 30 min while stirring, transferred to a 75 °C oil bath with a reflux column and magnetically stirred for 4–6 h. The methacrylate conversion was determined from the mid-IR analysis of the vinyl peak at 1640 cm^{-1} . Following polymerization, the reaction solution was transferred to an ice bath and air was briefly bubbled through the solution to quench the reaction. IEM was added at 15 mol% relative to monomer along with a catalytic amount of dibutyltin dilaurate. The reaction was allowed to proceed overnight at room temperature, after which the complete conversion of isocyanate functionality was confirmed from the disappearance of the mid-IR peak at 2270 cm^{-1} . The nanogel product was precipitated into a 10x volume of hexanes, redispersed in methanol, and dialyzed against an 8,000 molecular weight cutoff membrane in methanol for 3 days. After this time, a trace amount of hydroquinone was added to prevent inadvertent

polymerization and the solvent was removed under reduced pressure to yield highly viscous liquid-like products. Typical yield was 50–70% resulting from a total initial monomer mass of approximately 10 g. The final nanogel products are referred to as EHEMA-UDMA, EHEMA-TTEGDMA (formed in 6x MEK unless otherwise noted), EHEMA-PEG550DMA, or EHEMA-PEG750DMA.

Nanogel Characterization

The molecular weight and hydrodynamic radius for EHEMA-UDMA, EHEMA-TTEGDMA, and EHEMA-PEG750DMA nanogels were determined using triple-detection gel permeation chromatography (Viscotek) with I-Series column sets (7.8 mm × 30 cm) and linear poly(methyl methacrylate) as an internal standard. Number and weight average molecular weight, hydrodynamic radius, and intrinsic viscosity were collected using in-line refractive index detector, right/low-angle light scattering detector, and capillary viscometer respectively. Sample injections were 100 μ L and were eluted at 1 mL/min and 35 °C with THF as solvent. All samples were passed through a 0.45 μ m filter prior to injection. Hydrodynamic radius of EHEMA-PEG550DMA nanogels was determined in water using dynamic light scattering (Wyatt Technology) at 20 °C. A sample concentration of 0.2 mg/mL was used and the sample was passed through a 0.45 μ m filter prior to analysis. The ratio of EHEMA to UDMA in the isolated nanogel was determined using peak integrals from ^1H NMR spectroscopy (Bruker) (400 MHz, CDCl_3 , EHEMA: δ 3.55–3.80 ppm (m, $-\text{CH}_2\text{CH}_2\text{O}-$), UDMA: δ 4.20–4.40 ppm (m, $-\text{OCH}_2\text{CH}_2\text{O}-$)).

General Formation of Nanogel-Based Networks

Methacrylated nanogels were dispersed in water at 50 wt% with 1.0 wt% Irgacure 2959 (relative to prepolymer mass), loaded into a silicon rubber mold, sealed between glass slides, and exposed to 365 nm light for 10 min at 10 mW/cm² using a mercury arc lamp (Acticure, Exfo). This nanogel loading level is well beyond the percolation threshold and effectively produces a continuous overlapping solvent-swollen nanogel morphology as has previously been demonstrated by dynamic mechanical analysis for nanogels polymerized in a reactive monomer matrix¹⁵.

Swelling Capacity

Solutions of 50 wt% nanogel in water were polymerized into discs 5.0 mm in diameter and 0.5 mm thick, washed with DI water and held under vacuum at 60 °C for 48 h to remove water. Desiccated samples were weighed and then placed in fresh DI water. The mass was recorded after 48 h and the equilibrium swelling ratio was determined using the formula $(W_s - W_i)/W_i$ where W_s is swollen mass and W_i is initial mass.

Rheology

The viscosity of nanogel solutions was determined using a fixed-strain parallel plate rheometer (Ares, TA). Solutions of varying weight fraction of nanogel in water were prepared and sheared between 1–2000/s on 20 mm steel plates with a 0.2 mm gap. The viscosity was taken from the portion of the plot that did not exhibit shear-rate dependence. Real-time photorheology was conducted on 20 mm quartz plates with a custom mirror

fixture to direct UV light perpendicular to the plates. The reaction mixtures were exposed to 365 nm UV light at 10 mW/cm² using a mercury arc lamp and quartz light guide while a 10% strain at 10 rad/s was applied. Shear modulus G' of water-equilibrated photocured gels was determined using a strain sweep from 0.1–10% strain at 10 rad/s. Frequency sweeps of nanogels dispersed in water at 50 wt% were conducted from 10–500 rad/s at 10% strain.

Dynamic Mechanical Analysis

Rectangular gels with approximate dimensions of 15 mm × 2 mm × 1 mm were prepared as described above. Samples were subjected to a cyclic tensile strain of 0.01% at 1 Hz while a temperature ramp was applied at 3.0 °C/min using DMA (Q800 DMA, TA). Temperature ranges were selected to accurately capture the full range of glass transition and storage modulus. The glass transition temperature was determined from the maximum value of the tan delta curve and the rubbery modulus E was determined from the plateau of the storage modulus at $T = T_g + 40$ °C.

Electron Microscopy

Fracture surfaces of photocured samples were imaged using a field emission scanning electron microscope (JSM-7401F FESEM, JEOL). These nanogel-based gels were swollen for 48 h, quickly frozen in liquid nitrogen, fractured with a razor blade and lyophilized for 48 h. Samples were mounted on aluminum stubs with carbon tape and sputter coated with approximately 3 nm of gold. Images were acquired using an accelerating voltage of 4.0–10 kV.

Results and Discussion

Nanogels were formed using a solution free radical polymerization in a moderately polar solvent using a hydrophilic monomethacrylate (EHMA) combined with either a hydrophobic (UDMA), moderately polar (TTEGDMA), or hydrophilic (PEGDMA) crosslinker and 15 mol% mercaptoethanol as a chain transfer agent. These monomer structures and the general synthesis scheme are depicted in Figure 1. EHMA-TTEGDMA nanogels were formed in 5, 6, or 8x solvent volumes as indicated to examine the effects of more or less dilute reaction conditions on nanogel formation. Triple-detection GPC is a useful method for the simultaneous determination of molecular weight, hydrodynamic radius, and structural conformation for the isolated nanogel products³⁰. The number average molecular weight, average hydrodynamic radius (R_h), polydispersity index (PDI), and Mark-Houwink alpha parameter (MH- α) for each nanogel sample are listed in Table 1. The EHMA-PEG550DMA nanogel was analysed via DLS only due to extended tailing in the GPC trace that prevented accurate analysis despite extended dialysis (Figure S1). Solution free radical polymerization produced particles with molecular weight in the 30–150 kDa range and radius <10 nm while avoiding macrogelation. The MH- α values are significantly reduced compared to typical values for a linear polymer and correspond well to previous reports on the GPC analysis of nanogels and hyperbranched polymers^{25,31,32}.

Interestingly, the PDI for certain formulations was very low, a result that was unexpected for a polymerization method that typically produces polymers with PDI of 2–4 or above⁹.

populations. Further studies will be needed to fully demonstrate the origin of the low polydispersity.

^1H NMR analysis was conducted on EHEMA-UDMA to compare the ratio of functional groups in the nanogel to the monomer feed (Figure S3). UDMA contains two symmetric ethyl chain segments per monomer for a total of 8 protons while EHEMA contains an average of 10 ethylene glycol repeat units per monomer for a total of 40 protons. In a 7:3 monomer ratio the predicted EHEMA:UDMA peak integral ratio is 11.7:1. NMR indicates a 10.5:1 ratio, indicating that the product composition was in reasonable agreement with the mono- and dimethacrylate monomer feed ratio in the reported conditions. The polymerizable methacrylate protons are also observable at $\delta=5.6$ and 6.1. Similar analysis was not possible for the other nanogels due to a lack of distinguishable protons between the respective PEG-based monomers.

The viscosity of aqueous dispersions of EHEMA-TTEGDMA nanogels of varying M_n and R_h was determined using parallel-plate shear rheology (Figure 3). For all nanogels, the viscosity scales linearly up to 10 wt% and approximately follows the Krieger-Dougherty model for non-interacting hard spheres (eqn. 1)

$$\eta_r = \left(1 - \frac{\Phi}{\Phi_m}\right)^{-[\eta]\Phi_m} \quad (1)$$

where Φ is mass fraction, Φ_m is the dense packing limit of monodisperse hard spheres (≈ 0.64) and $[\eta]$ is the intrinsic viscosity of hard spheres which has been shown to be 2.5^{33} . The model closely matches the nanogel viscosity between 1 and 10 wt% when the particles are in the dilute regime below the percolation threshold. Beyond 10 wt% the nanogel viscosity abruptly scales exponentially due to long-range interactions that indicate the onset of percolation. Polymerizing nanogel solutions greater than ≈ 15 wt% results in solid, well-formed macroscopic gels while attempts to gel solutions below this concentration resulted in inconsistently crosslinked materials or no gelation at all. The unpolymerized nanogel viscosity values at higher loading are significantly higher than model predictions, which do not account for particle interpenetration and physical entanglements that occur in crosslinked particles. The larger EHEMA-TTEGDMA 5x and 6x MEK samples both scale similarly and have higher viscosity than EHEMA-TTEGDMA (8x MEK). This observation is a deviation from hard-sphere rheology where viscosity increases with decreasing particle size due to cube-square scaling of volume and surface area. Since smaller nanogels imbibe proportionally less water than larger nanogels, there is more water remaining as a dispersive matrix that causes the decrease in viscosity with size at a given loading level. A shift in the crossover of the linear and exponential fits toward higher values of Φ for the 8x MEK nanogels can also be observed and attributed to the smaller particle size. The viscosity of nanogels with varying chemical composition and similar size was determined at 50 wt% loading in water. EHEMA-UDMA nanogels exhibit the highest viscosity due to shear flow becoming dominated by the breaking and reforming of interparticle hydrogen bonds between the urethane groups that persist even in the aqueous environment. An exponential

increase in viscosity with crosslinker molecular weight was observed when changing the crosslinker from TTEGDMA (4 EG repeats) to PEG550DMA (9 EG repeats) to PEG750DMA (13 EG repeats). We hypothesize that this is due to the longer crosslinker permitting a greater degree of nanogel interpenetration above the percolation threshold, which is facilitated by greater water uptake and enhanced chain mobility in the more hydrophilic nanogels.

The real-time modulus development of the nanogel-based networks under UV irradiation was monitored using photorheology (Figure 4). Prior to UV exposure, all nanogel dispersions exhibited viscous behavior and did not exhibit physical gelation. This was confirmed using a frequency sweep of 50 wt% nanogel dispersions, which verified that the loss modulus (G'') dominated over the storage modulus (G') and no G'/G'' crossover occurred (Figure S5). Dispersions of EHEMA-TTEGDMA (6x) nanogels in water with varying nanogel concentrations and 1.0 wt% photoinitiator were exposed to UV light to observe real-time gelation and modulus development. At the percolation threshold (approximately 10 wt%), an extended induction time was observed followed by gradual gel formation. When the nanogel concentration was increased to 25 wt%, gelation occurred significantly more rapidly, and the modulus plateaued after 15 min of irradiation. Further increasing the concentration to 50 wt% resulted in gelation within minutes and a gel with shear modulus > 100 kPa was achieved. At 75 wt% the increase in modulus was modest compared to increases from lower concentrations, indicating that very high nanogel weight fractions are not required to produce highly crosslinked networks.

The morphology of the nanogel-based networks formed at different weight fractions of nanogel was evaluated using SEM (Figure 5). Networks formed at 25 wt% EHEMA-TTEGDMA nanogel in water, which is just above the percolation threshold, have a continuous network structure with some evidence of porosity. At 50 wt% the network structure is dense and nonporous, which is consistent with the viscosity measurements at that loading level that indicate an overlapping, confluent array of nanogels prior to polymerization.

The rubbery modulus and glass transition temperature (T_g) of covalently crosslinked networks formed from the direct photopolymerization of methacrylate-functionalized nanogels were determined to characterize the influence of nanogel size and chemical composition on final material properties (Figure 6). All nanogels were synthesized to between 80 and 90% final conversion and functionalized with equivalent mole fractions of IEM to ensure that the residual methacrylate group content was approximately equivalent among all materials prior to network formation. Real-time FTIR spectroscopy was used to monitor the methacrylate double bond conversion during the photopolymerization process in which nanogel and photoinitiator were dispersed in water and polymerized into a macroscopic crosslinked network. It was confirmed that after 10 min of UV irradiation, quantitative conversion of the appended methacrylate groups was achieved in a 50 wt% solution of EHEMA-TTEGDMA nanogel in water (Figure S4) through a combination of intra- and inter-particle reaction.

No significant change in the nanogel-based network T_g was observed between the three EHEMA-TTEGDMA nanogels, though the modulus decreases significantly for the network formed from the EHEMA-TTEGDMA 8x nanogel (Figure 6A). This nanogel was shown to be the least branched from the Mark-Houwink plot (Figure 2B) and accordingly produced the lowest overall network crosslink density. Since the modulus decreased in this case while the glass transition temperature remained constant, we hypothesize that the network chains are arranged in a manner that produces relatively fewer intermolecular crosslinks but does not affect the cooperative motion that occurs during the glassy-to-rubbery transition. The effect of changing the nanogel composition while maintaining similar size and molecular weight is shown in Figure 6B. Glass transition temperatures of the networks follow the trend of the bulk homopolymers formed from the crosslinker used in the nanogel preparation, that is $T_{g,UDMA} > T_{g,TTEGDMA} > T_{g,PEG550DMA} > T_{g,PEG750DMA}$ (Figure S6). The full width at half-maximum (FWHM) of the tan delta curves also increases as T_g increases due to the greater difference in relaxation temperatures between EHEMA and the increasingly hydrophobic crosslinkers (Table 2). EHEMA, PEG550DMA, and PEG750DMA monomers are all soluble in water above 40 wt%. TTEGDMA monomer was only fully soluble in water below 1 wt%, and UDMA monomer exhibits marginal solubility even at 0.1 wt%, which was reflected in the increasing network heterogeneity in these water-based networks. Compared to the observed glass transitions, a reverse trend in rubbery modulus is observed with the exception of EHEMA-PEG750DMA. UDMA, being a more hydrophobic monomer, will tend to a more collapsed configuration in water and participate primarily in intramolecular hydrogen bonding, which along with reduced interpenetration leads to a comparatively lower modulus material. EHEMA-TTEGDMA and EHEMA-PEG550DMA begin to interpenetrate significantly as demonstrated with the viscosity results, and this physical crosslinking that bolsters the non-covalent connections between particles is apparent in the increase in network modulus. Though EHEMA-PEG750DMA has the highest viscosity of the PEG-based nanogels, the modulus is significantly reduced compared to the other materials. The reason may be twofold: the relatively high value of the tan delta maximum indicates that the longer, more flexible PEG750DMA is mobile enough to outweigh interpenetration effects at high temperatures, and the lower intrinsic viscosity from the Mark-Houwink plot (Figure 2B) could indicate more primary cyclization compared to all other nanogels, which results in fewer elastically active crosslinks per nanogel in the polymerized network. This result is further supported by a calculation of crosslinking density ρ_x from rubbery modulus (Table 2) using eqn. 2 where ν is Poisson's ratio (estimated to be 0.5 assuming an incompressible material), E is rubbery modulus, R is the gas constant, and T is temperature where the rubbery modulus plateaus.

$$\rho_x = \frac{E}{2(1-\nu)RT} \quad (2)$$

Network formation from the copolymerization of nanogels with different composition was also possible. A 1:1 or 1:3 weight ratio of EHEMA-UDMA and EHEMA-PEG550DMA were combined and dispersed in water at a 50 wt% total concentration (Figure 7). In contrast to single component nanogel solutions, the blended solutions became hazy and the

polymerized gels were translucent, indicating a degree of both pre- and post-polymerization phase separation, though no macroscopic phase separation or settling was observed prior to polymerization. The tan delta curve for each network is significantly broadened and a slight shoulder on each curve can be observed. Adjusting the proportions of each nanogel component shifts the glass transition temperature between that of each pure component, that is the 1:1 blend has the main tan delta peak at the EHEMA-UDMA T_g while the 1:3 blend has the main peak at the EHEMA-PEG550DMA T_g . For both formulations, the rubbery modulus is similar to that of pure EHEMA-PEG550DMA despite the addition of the lower modulus EHEMA-UDMA component. This result suggests that blending nanogels containing hard and soft segments could be a straightforward pathway to generating networks with multiphase structure.

The previous analysis of mechanical properties was performed on dehydrated samples, so it is necessary to examine the properties of fully hydrated materials to better understand the effects of changing nanogel chemistry on final network structure in water-based polymerizations. Water equilibrated gels had swelling ratios and equilibrium water contents at the lower end for materials that are conventionally called hydrogels, which typically consist of 80–99% water (Table 3). However, these macrogel networks all take up significantly more water than that present at the time of initial network formation.

EHEMA-UDMA nanogels form networks that contain the least water, and nanogels formed with increasingly hydrophilic crosslinkers contain progressively more water with the exception of EHEMA-PEG550DMA, which contains a statistically similar amount of water as EHEMA-TTEGDMA. Swelling ratio and shear modulus are typically inversely related since higher water content indicates lower crosslinking density. However, the anomalous trend in rubbery modulus observed in the DMA testing occurs again for the water-swollen networks (Figure 8). While the material with the highest water content, EHEMA-PEG750DMA, has the lowest modulus, EHEMA-TTEGDMA and EHEMA-PEG550DMA both have higher moduli than EHEMA-UDMA, which has the lowest water content. This result is consistent with the prediction that physical entanglements persist in the swollen state and contribute significantly to crosslinking density in both dry and hydrated networks.

Fracture surfaces of water swollen nanogel-based networks were imaged using SEM as shown in Figure 9 to determine whether microscale morphological differences between swollen samples are observable due to interpenetration. Shear modulus and viscosity data indicate that EHEMA-UDMA and EHEMA-TTEGDMA based networks have relatively lower levels of interpenetration in the set of materials studied. The corresponding fracture surfaces are relatively featureless compared to EHEMA-PEG550DMA and EHEMA-PEG750DMA, which are highly interpenetrated networks and have highly textured fracture surfaces due to features that arise when significant quantities of non-covalent crosslinks are ruptured. Further magnification (Figure 9, bottom row) shows that the features in the EHEMA-PEG750DMA networks persist to the submicron scale but are not apparent to the same extent for the other nanogel-based networks, which are significantly less swollen. All networks exhibited a dense, continuous morphology and no discrete particles were able to be distinguished in any of these materials.

Conclusions

Nanogels with varying chemical and physical composition were synthesized in a surfactant-free solution free radical polymerization and functionalized with polymerizable methacrylate groups. This method produced particles with a diameter of 10–15 nm and in some cases a very low polydispersity index. Conventionally hydrophobic or hydrophilic dimethacrylate monomers were copolymerized with a hydrophilic monomethacrylate and the resulting nanogels formed transparent, homogeneous dispersions in water beyond 75 wt%. Changing the nanogel crosslinker significantly affects final network properties and can permit or restrict interpenetration in systems well above the percolation threshold. Networks formed in this manner have potential applications in hydrogel design, functional coatings, composite materials, and patterned networks in which specific manipulation of nanogel chemistry can provide a unique content and distribution of both chemical and physical properties within network structures with potential for relatively high crosslink densities from water compatible materials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

A: Monomers used in the nanogel synthesis. B: Schematic of the solution free radical polymerization to form nanogels with reactive methacrylate groups. C: Schematic for the synthesis of macroscopic crosslinked gels from the photopolymerization of aqueous nanogel dispersions.

Figure 2. Nanogel characterization from triple-detection GPC. A: differential weight fraction vs. molecular weight. B: intrinsic viscosity $[\eta]$ vs. molecular weight.

Figure 3.

Reduced viscosity (η_r) vs. weight fraction (Φ) of A: EHEMA-TTEGDMA 5x MEK (○), B: 6x MEK (□) and C: 8x MEK (△) in water along with the Krieger-Dougherty model (+). D: Absolute viscosity of nanogels with varying chemical composition at 50 wt% in water.

Figure 4. Real-time photorheology of various concentrations of EHEMA-TTEGDMA nanogel in water. All formulations contained 1.0 wt% I2959 and were irradiated at 10 mW/cm² with 365 nm light. Irradiation began at 30 s. For clarity only the storage modulus, G' , is plotted.

Figure 5.

SEM images of crosslinked EHEMA-TTEGDMA nanogel-based networks. Nanogels were dispersed in water at 25 wt% (top) and 50 wt% (bottom) with 1.0 wt% I2959 and irradiated for 10 min at 10 mW/cm². The resulting networks were swollen in water, freeze-fractured, and lyophilized prior to imaging.

Figure 6.

A: rubbery modulus and tan delta of networks formed from EHEMA-TTEGDMA 5x (▲), 6x (●), or 8x (■) nanogels. B: rubbery modulus and tan delta of networks formed from EHEMA-UDMA (▼), EHEMA-TTEGDMA (▲), EHEMA-PEG550DMA (■) or EHEMA-PEG750DMA (●).

Figure 7. Rubbery modulus and tan delta of networks formed from EHEMA-UDMA (▼), EHEMA-PEG550DMA (▲), 1:1 blend by weight of EHEMA-UDMA and EHEMA-PEG550DMA (■), and a 1:3 blend by weight of EHEMA-UDMA and EHEMA-PEG550DMA (●).

Figure 8. Shear modulus (G') vs. shear strain (τ) of water-equilibrated networks formed from nanogels of varying composition.

Figure 9. FESEM images of the fractures surfaces of A: EHEMA-UDMA, B: EHEMA-TTEGDMA, C: EHEMA-PEG550DMA, D: EHEMA-PEG750DMA at 500x magnification (top, scale bar = 10 μm) or 10,000x magnification (bottom, scale bar = 1 μm).

Table 1

Nanogel size, molecular weight, and Mark-Houwink alpha parameter obtained from triple-detection GPC.

Nanogel	M_n (g/mol)	Hydrodynamic Radius (nm)	Polydispersity Index	MH- α
EHEMA-TTEGDMA (5x MEK)	1.5×10^5	7.9	1.1	0.35
EHEMA-TTEGDMA (6x MEK)	1.1×10^5	7.2	1.5	0.44
EHEMA-TTEGDMA (8x MEK)	3.6×10^4	5.3	1.5	0.36
EHEMA-UDMA	8.0×10^4	6.8	1.2	0.55
EHEMA-PEG550DMA *	-	5.8 *	13% *	-
EHEMA-PEG750DMA	5.3×10^4	6.3	3.0	0.41

* Obtained from dynamic light scattering only. PDI is calculated as the coefficient of variation of the diameter distribution.

Table 2

Glass transition temperature (T_g), full width at half-maximum of the tan delta curve (FWHM), rubbery modulus, and crosslinking density of nanogel-based networks

Material	T_g (C)	FWHM (C)	Rubbery Modulus (MPa)	Crosslinking Density (mol/L)
EHEMA-UDMA	18 ± 0.8	46 ± 2.0	0.51 ± 0.09	0.06 ± 0.01
EHEMA-TTEGDMA	-0.39 ± 1.3	32 ± 1.4	0.74 ± 0.13	0.09 ± 0.02
EHEMA-PEG550DMA	-9.5 ± 1.9	24 ± 1.6	1.2 ± 0.15	0.14 ± 0.02
EHEMA-PEG750DMA	-22 ± 1.6	22 ± 0.09	0.26 ± 0.05	0.031 ± 0.006

Table 3

Swelling ratio and equilibrium water content of swollen networks formed from nanogels of varying composition.

Material	Swelling Ratio	Equilibrium Water Content (%)
EHEMA-UDMA	1.6 ± 0.07	61 ± 1.1
EHEMA-TTEGDMA	2.2 ± 0.09	68 ± 0.9
EHEMA-PEG550DMA	2.4 ± 0.12	70 ± 0.8
EHEMA-PEG750DMA	3.8 ± 0.26	79 ± 1.2