# Nanogels as Macromolecular Precursors to Polymer Network Development and Modification

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Statement of Purpose: Nanogels are internally crosslinked polymeric nanoparticles with overall dimensions below 100 nm[1]. Significant control over the chemical and physical composition, colloidal stability, and capacity for surface modification has made nanogels a popular candidate for biomedical applications, notably in the controlled release of therapeutic agents[2][3]. More recent studies have focused on the integration of microgels and nanogels into composite polymer networks to investigate the effects of manipulating local network construction on bulk network properties[4][5]. We are interested in using nanogels as the primary network building block, particularly in water-based networks for biomedical applications. Densely functionalized nanogels allow for control over the content and distribution of chemical and physical properties in networks in a manner that is not directly available from conventional monomer polymerization. Studies of the structure-property relationship between nanogels and the resulting networks inform the design of materials including but not limited to hydrogels, adhesives, and coatings.
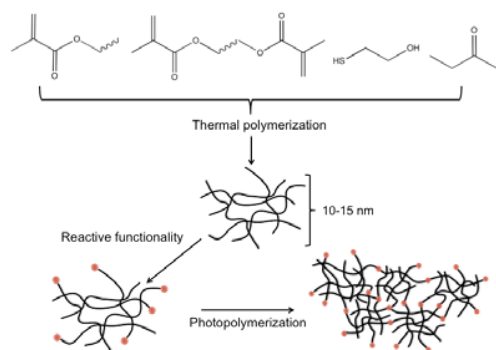
Methods: Nanogels were synthesized from a thermally initiated solution free radical copolymerization of polyethylene glycol methacrylate and urethane dimethacrylate (UDMA), tetraethylene glycol dimethacrylate (TEGDMA), or polyethylene glycol dimethacrylate (PEGDMA) with a thiol chain transfer agent and methyl ethyl ketone as solvent. Methacrylate, acrylate, or norbornene groups were introduced through the resulting hydroxyl groups on the nanogels. Molecular weight and hydrodynamic radius was determined using triple-detection gel permeation chromatography. Nanogel-based networks were formed from the photopolymerization of dispersions of nanogels between 25 and 75 wt% in solvent, typically in water. The chemical and mechanical properties of networks formed from or modified by nanogels were characterized using IR, NMR, and UV-Vis spectroscopy, confocal microscopy, parallel plate rheometry, dynamic mechanical analysis, and MTS testing sytems.

Results: Nanogels with molecular weights in the range of 50-150 kDa with diameters of 10-15 nm were produced from the stated method. NMR spectroscopy reveals a product composition that closely matches the comonomer ratios as well as successful incorporation of pendant reactive groups. Solutions of up to 75 wt% nanogel in water do not exhibit phase separation or settling, including dispersons of nanogels containing UDMA or TEGDMA which exhibit very low water solubility in monomer form. This allows for stable, transparent formulations ranging from highly fluid at low loading to putty or gel-like at high loading. Significant control over nanogel composition and content of both covalent and non-covalent crosslinking units allows for highly tunable mechanical properties and creates a platform for broad application ranging from soft, highly hydrated gels to high strength materials. Nanoclusters of thiol-containing CRGDS peptides were prepared via base-catalyzed Michael addition to acrylated nanogels. Composite hydrogels composed of peptide and non-peptide functionalized nanogels were prepared and were shown to promote cell adhesion, providing a basis for the exploration of cellular interaction with heterogeneously presented biomolecules in hydrogels. Adhesive formulations containing acid or nitrile groups to promote non-covalent bonding were incorporated into adhesive formulations to modulate interaction with the substrate, increase crosslinking density, and reduce water sorption into the interface. Water-based nanogel adhesives were shown to withstand shear forces in excess of 150 N on model glass surfaces, and examination of adhesion to polymer-based substrates of varying composition is in progress. Nanogel-based coatings were explored for thiol-ene networks that have been applied as shape memory polymers[6]. The ability to control the release of small molecules along with facile inclusion of reactive groups makes nanogels a potential platform for creating drug release coatings on implantable shape memory networks. In these networks, norbornene-functionalized nanogels were covalently linked to excess thiol functionality with simple dip coating followed by a rapid, highly orthogonal photoinduced reaction. Separate studies show extended release of model compounds over 4-6 weeks from nanogels in solution. Efforts to combine these results are underway.

Conclusions: Nanogels were synthesized from starting materials with diverse structure and polarity and enable the efficient formation of water-based networks with tunable chemical and physical properties. Enhanced control over material chemistry enables application into several areas of biomaterials research.

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