

PRF#: 56823-DNI7. Resolving the Impact of Mesoscopic Heterogeneities on the Transport Properties of Microgels. Chaitanya K. Ullal, Rensselaer Polytechnic Institute.

I. Research Progress: Efforts in the second year of this New Investigator project have focused on further diversifying the functional crosslinkers that can be incorporated into PNIPAM microgel networks.

Modification of α -carbon substituent in click functional crosslinker

In the previous year, we developed a novel functional crosslinker, *N,N'*-(2-aminopropane-1,3-diyl)-*bis*-(2-methylacrylamide). The primary amine handle allowed for the quantitative derivatization with NHS modified fluorophores and the selective tagging of crosslinks. Since the nature of the substituent in α -substituted acrylamides is known to affect their free-radical polymerization kinetics and in turn the incidence of spatial heterogeneities, we replaced the methyl substituent with hydrogen (Fig. 1a). This was done through a change of the acylating agent to acryloyl chloride, while keeping the synthetic route identical.

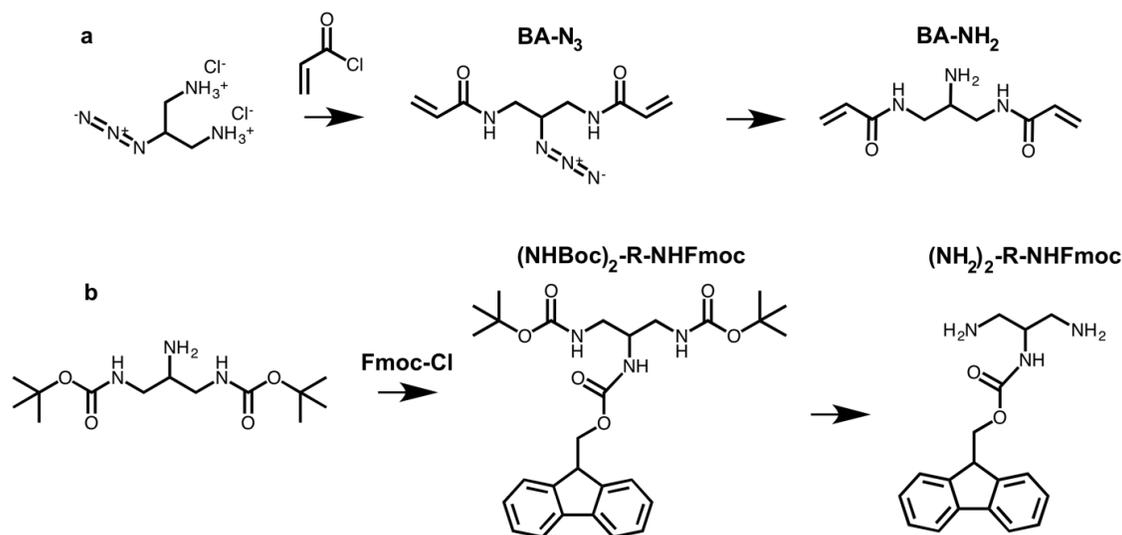


Figure 1. Synthetic schemes for the preparation of BA-NH₂ via (a) the established and (b) a novel route.

Interestingly, this approach consistently resulted in low yields (<10%) for both BA-N₃ and BA-NH₂. With the aim of maximizing the yield we developed a new protocol involving the orthogonal protection of amine groups (Fig. 1b). Specifically, the Boc-protected amine DAP-Boc-NH₂ was treated with Fmoc-Cl in sodium bicarbonate/dioxane yielding the intermediate (BocNH)₂-R-NHFmoc after workup with DCM/H₂O. Deprotection of the Boc groups in ethyl acetate/6M HCl yielded diamine (NH₂)₂-R-NH-Fmoc as a hydrochloric salt which was easily isolated and purified with trituration in ethyl acetate/diethyl ether. The major advantage is that the (NH₂)₂-R-NHFmoc linker can be easily prepared in gram scale and bypasses the use of the 2-azidopropane-1,3-diaminium chloride which cannot be isolated in quantities higher than 1 gram (C/N<1). Also, the presence of the bulky Fmoc group is expected to facilitate purification with silica gel chromatography after the subsequent acylation step and finally afford the free amine with a simple and rapid deprotection step with piperidine/DMF. Additionally, the study of the kinetics between acrylamide and methacrylamide derivatives has a broader impact since contradicting results was identified in the literature.

Probing the transport properties of heterogeneous microgels with fluorogenic click reactions

The diffusion profiles of solutes is a means by which we can study the impact of the mesoscale heterogeneities on the transport properties of gels. Although an existing body of work deals with the diffusivity of small molecules from microgel matrices, the impact of embedded nanoclusters that we have recently revealed remains unexplored (see impact section on impact). We conceived a pathway that utilizes the fluorogenic 1,3-dipolar cycloaddition of 3-azidocoumarin (CAz), as a model reaction for the study of small molecule transport within heterogeneous microgels. During our initial trials, we have successfully monitored the evolution of the fluorogenic click reaction qualitatively, both in solution (AM-Alk@CAz) and in post-functionalization of microgels in suspension (PNM-Alk@CAz) (Fig. 2).

The kinetics of the click reactions can be easily studied qualitatively with UV-Vis spectroscopy since the absorption signal can be correlated with the reaction extent. We anticipate that the preparation of BA-NH₂ with high yield will allow the synthesis of an alkyne-functional crosslinker variant (BA-Alk). The fluorogenic click kinetics of alkyne-tagged crosslinking points inside the highly crosslinked clusters is expected to elucidate the diffusivity of CAz inside these regions and allow the comparative study with alkyne backbone-tagged microgels. We also verified that the incorporation of the MA-Alk monomer is compatible with the presence of the commonly used *N*-(3-aminopropyl)methacrylamide (APMA) monomer, resulting in doubly-functional particles with orthogonal reactivity. We have sequentially performed post-polymerization click and NHS active ester conjugation reactions yielding microgels with tunable emission in respect to temperature. This class of materials is particularly promising for colorimetric sensing applications.

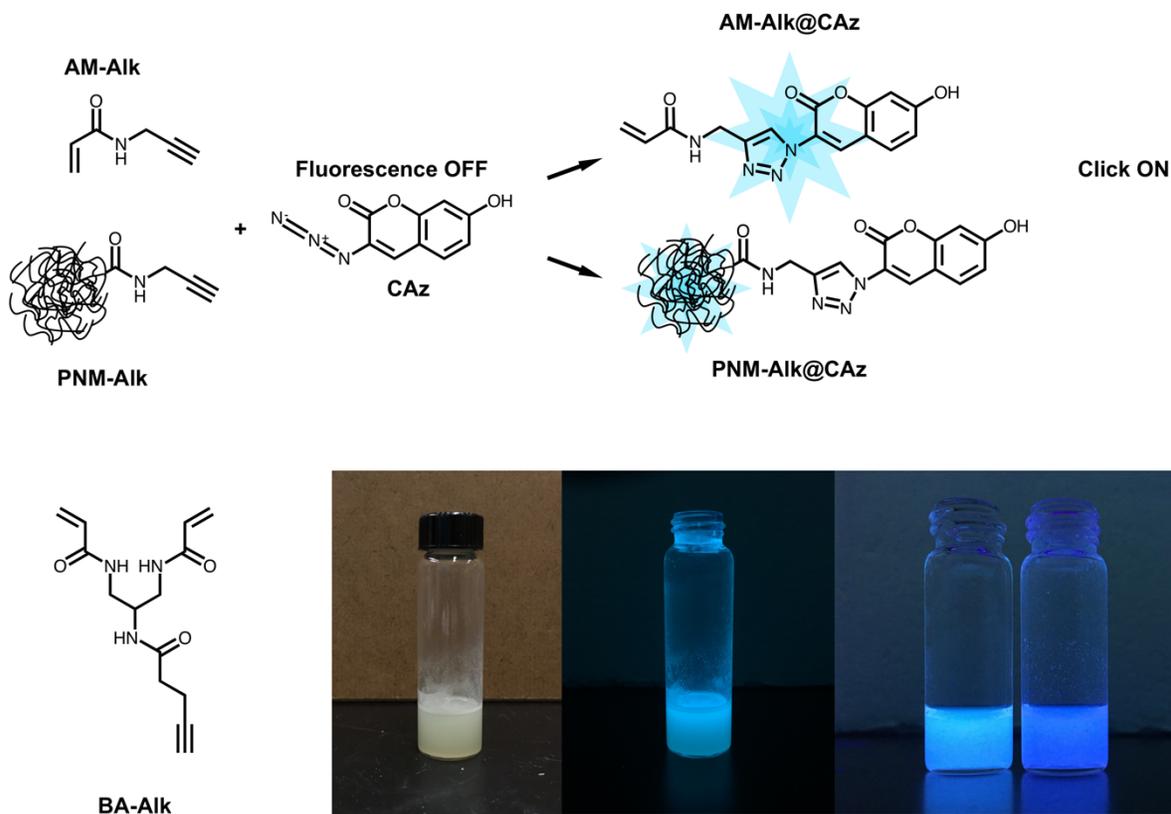


Figure 2. Summary of fluorogenic click reactions, proposed compounds and prepared materials.

II. Impact of PRF DNI funding on PI and students' careers.

Funding, Publications, and Conferences. This PRF DNI has nucleated a new and important research direction in the PI's group. Specifically, the functional crosslinker developed in this project was reported along with separate results from an associated NSF funded project in a high impact interdisciplinary materials journal (Karanastasis, A.A.; Zhang, Y.; Kenath, G.S.; Lessard, M.D.; Bewersdorf, J.; and Ullal, C.K., 3D mapping of nanoscale crosslink heterogeneities in microgels, *Materials Horizons*, 2018, Advance Article, DOI: 10.1039/C8MH00644J). The results from this project were presented at the ACS 2018 Fall Meeting in Boston, the 2018 Gordon Research Conference on Polymer Physics, as well as at invited talks at the University of Connecticut's Polymer Program, the University of Iowa's Physics Department and Bard College's Chemistry Department.

Students

In the second year of this project, the funding has continued to support a post-doc with significant interests in this area of research. The strong progress on this project has resulted in the post-doc presenting results at an ACS Meeting and first authorship of a peer reviewed article in a high impact journal.