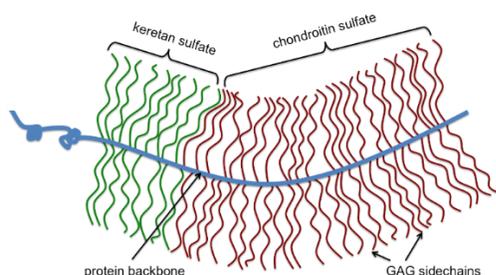


## Designing polymer brush-modified nanoparticles for improving lubricity in water.

The gradual wear of articular surfaces and the depletion of natural lubricants in our joints is expected to affect greater than 50% of the aging population leading to osteoarthritis and other autoimmune diseases such as rheumatoid arthritis.<sup>1</sup> Within healthy joints, a complex synergy of multiple lubrication and wear prevention processes involving the structural and chemical components of cartilage and synovial fluid lead to low friction coefficients and high wear resistance. Articular lubrication involves charged glycoproteins, such as aggrecan and lubricin, which are expressed at the cartilage surface. These glycoproteins exhibit a unique macromolecular bottlebrush architecture consisting of a flexible backbone with densely grafted side-chains.<sup>2</sup> If the backbone length is longer than the side-chains, a bottlebrush polymer typically adopts a cylindrical shape with the side-chains protruding outward from the backbone as shown in **Fig. 1**. Hydration of this unique architecture gives rise to the remarkable biolubrication properties of these joints. Mimicking articular lubrication via the design of new materials, therefore, continues to serve as one of many grand challenges in biomaterials science and engineering. To date, synthetic lubricants have not duplicated the ultra-low friction coefficients found in the human hip or knee, particularly under the extreme pressures found between the sliding bone and cartilage surfaces.<sup>1,3</sup>



**Fig. 1** 2-D representation of the structure of aggrecan, an example of a bottlebrush polymer consisting of a protein backbone and glycosaminoglycan side-chains.

nanoparticles employed as the core in these investigations were high modulus inorganic silica nanoparticles. The *objective of this proposal* is to elucidate how the lubrication properties of charged spherical nanoparticles are influenced by key design parameters – including grafting density, charge density, molecular weight, and modulus of the nanoparticle core. We postulate that the lubrication properties of brush modified nanoparticles can be tuned in a modular fashion using the knowledge gained from successful completion of this project. To test our hypothesis, we propose the following *specific aims* –

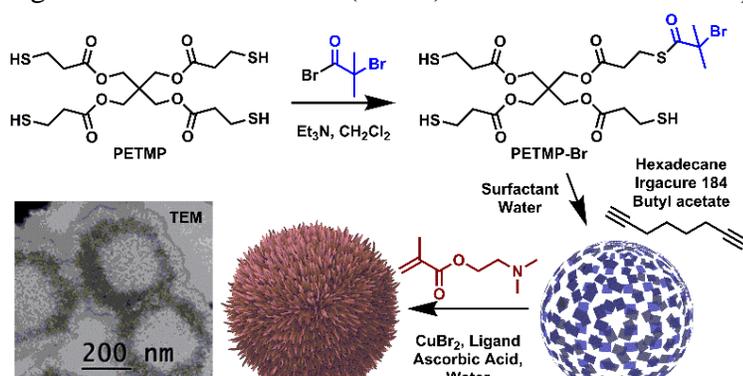
- 1) To use thiol-ene photopolymerization in miniemulsion to fabricate polymer nanoparticle cores with a broad range of mechanical properties. Modulus will be tuned via judicious choice of multifunctional thiol and alkene monomers, with higher modulus nanoparticles available using multifunctional alkynes. Surface initiators will be incorporated in the nanoparticle using a modified thiol monomer in the photopolymerization.
- 2) To modify the surface of the polymer nanoparticles with polyelectrolyte brushes using surface-initiated polymerization (SIP). Grafting density will be tuned by controlling stoichiometry of the functional thiol in the photopolymerization and charge density will be

Recent literature suggests that synthetic polyelectrolyte brushes grafted from surfaces offer a viable route to mimic the lubrication properties of articular joints.<sup>4</sup> Additionally, polyelectrolyte brushes grafted from the surface of nanoparticles (i.e. core-shell morphologies) have been explored to mimic the spherical and complex architecture found in natural glycoproteins – an approach that may provide a path to injectable therapeutics to alleviate pain associated with joint damage.<sup>5</sup> Nanoparticles have been postulated to reduce friction between sliding surfaces via a “rolling” mechanism. However, the variable space describing the grafted brush (i.e. grafting density, charge density, molecular weight, etc.) was narrow, and the only

tuned using monomer feed in the SIP process.

- 3) To evaluate the lubricity of the brush modified nanoparticles as a function of design parameters.

In pursuit of *specific aim 1 and 2*, we have developed a one pot approach for the synthesis of brush modified polymer nanoparticles. The primary formation of the nanoparticle core was achieved using thiol-alkyne photopolymerization under miniemulsion conditions. A miniemulsion is a kinetically-trapped, thermodynamically unstable emulsion produced by high-energy homogenization. It yields stable and narrowly distributed droplets with a size ranging from 50 to 500 nm.<sup>6</sup> Thiol-alkyne miniemulsions were prepared by adding an organic phase containing monomers [1,7-octadiyne, pentaerythritol mecaptopropionate (PETMP)], photoinitiator, hydrophobe (hexadecane), inhibitor, and butyl acetate (solvent) to an aqueous phase consisting of water and surfactant.<sup>7</sup> To enable the sequential surface-initiated polymerization by atom transfer radical polymerization (ATRP), one of the thiols of PETMP was first reacted with bromoisobutyl bromide to yield PETMP-Br – multifunctional thiol containing one ATRP initiator per molecule as the primary product. We exploited the step-growth radical mechanism of thiol-alkyne photopolymerization to fabricate functional nanoparticles that express bromoisobutyl groups at the particle surface. Exposure of the thiol-alkyne miniemulsions to ultraviolet light resulted in high monomer conversion (>99%). In future work under *specific aim 1*, we will tune the crosslink



**Fig. 2** Synthetic route to develop brush-modified polymer nanoparticles using a one-pot approach.

density of the thiol-ene network, via choice of monomer functionality, to tailor the modulus of the nanoparticle. With bromoisobutyl-functionalized nanoparticles in the reaction pot, the next step involved surface-initiated ATRP to grow polymer brushes from the particle surface. Copper-catalyzed ATRP was performed in the aqueous continuous phase of the miniemulsion with vitamin C (ascorbic acid) as a mild reducing agent. Since the ATRP initiator is bound to the nanoparticle surface, polymerization only occurs from the particle surface yielding a core-shell morphology. Importantly, the ATRP approach can be conducted in the presence of oxygen eliminating the need for stringent reactions conditions and enables the controlled growth of polymers from the surface such that each nanoparticle expresses a similar overall size and shell thickness. Our preliminary results were obtained using dimethylaminoethyl methacrylate (DMAEMA) as the monomer. The tertiary amine side chain of DMAEMA provides a reactive handle for quaternization with an alkyl halide to yield a charged polymer brush. The core-shell morphology of the brush modified nanoparticle was characterized using transmission electron microscopy, as shown in **Fig. 2**. We postulate that increasing the amount of bromoisobutyl groups on the surface via the PETMP:PETMP-Br ratio used in the miniemulsion formulation will provide a facile route to tailor the brush grafting density (i.e. lower Br-groups on the surface will yield a lower grafting density). It is expected, based on previous work, that higher grafting density will yield enhanced lubricity and lower friction coefficients. Similarly, ATRP polymerization time will be employed to control the brush molecular weight, and ultimately, the brush thickness. Charge density along the polymer

chain will be tuned using copolymerization, where monomer feed ratios of charged and uncharged monomers will dictate the copolymer composition. The morphology of the brush modified nanoparticles will be evaluated by transmission electron microscopy to quantify particle size and brush thickness. Matching the viscosity of synthetic mimics to that of natural synovial fluid within articular joints is important, thus the viscosity of the nanoparticles in aqueous suspension will be investigated at various concentrations using rheometry. Finally, to address *specific aim 3*, we will investigate the lubrication properties of the brush modified nanoparticles in an aqueous suspension using an oscillating reciprocating friction and wear tester.

To date, I have had an active role in every aspect of this ongoing project. I have acquired synthetic skills ranging from small molecule organic transformations to polymerizations, and skills for advanced characterization of nanoparticle systems. My results from this project will be among the first platforms to utilize a combination of miniemulsion polymerization and aqueous ATRP for the development of brush modified nanoparticles aimed at reducing lubricity. The anticipated outcomes of this research project include the following:

- 1) Development of a simple one-pot synthetic approach to brush-modified polymer nanoparticles with tunable brush and nanoparticle properties.
- 2) Elucidation of the role polymer nanoparticle modulus plays in the lubrication performance of aqueous suspensions
- 3) Understand how polymer brush parameters (grafting density, thickness, charge density) reduce the friction coefficient under a range of contact pressures

The results of this project will be submitted for peer-reviewed publication and further disseminated to the scientific community through presentations at local and regional meetings, including the Mississippi Academy of Sciences, the Waterborne Symposium, and regional American Chemical Society meetings.

In summary, brush modified nanoparticles are of great interest as an approach to synthetic lubrication particularly considering nature uses these unique macromolecular structures as lubricants in a variety of biological systems – most prominently as components of articular cartilage in mammalian joints. As biological mimics, understanding the mechanical and interfacial properties of these model systems holds great potential in the design and development of advanced lubrication systems and may further our understanding of the mechanisms and processes leading to debilitating articular conditions such as osteo- and rheumatoid arthritis.

## References

1. Klein, J., *Science* **2009**, 323, 47-48.
2. Sheiko, S.; Sumerlin, B.; Matyjaszewski, K., *Prog. Polym. Sci.* **2008**, 33, 759-785.
3. Seror, J.; Merkher, Y.; Kampf, N.; Collinson, L.; Day, A. J.; Maroudas, A.; Klein, J., *Biomacromolecules* **2012**, 13, 3823-3832.
4. Raviv, U.; Giasson, S.; Kampf, N.; Gohy, J. F.; Jerome, R.; Klein, J., *Nature* **2003**, 425, 163-165.
5. Liu, G.; Cai, M.; Zhou, F.; Liu, W., *J. Phys. Chem. B* **2014**, 118, 4920-4931.
6. Crespy, D.; Landfester, K., *Beilstein J. Org. Chem.* **2010**, 6, 1132-1148.
7. Amato, D. N.; Amato, D. V.; Narayanan, J.; Donovan, B. R.; Douglas, J. R.; Walley, S. E.; Flynt, A. S.; Patton, D. L., *Chem. Commun.* **2015**, 51, 10910-10913.