

- a. PRF# 57757-ND3  
 b. Project Title: **Mapping Mechanically Activated Pathways of Metal Coordination Complexes**  
 c. Principal Investigator: **Prof. Katherine J. Franz, Department of Chemistry, Duke University**  
 d. Co-PI name: **Prof. Stephen L. Craig, Department of Chemistry, Duke University**

## Objective

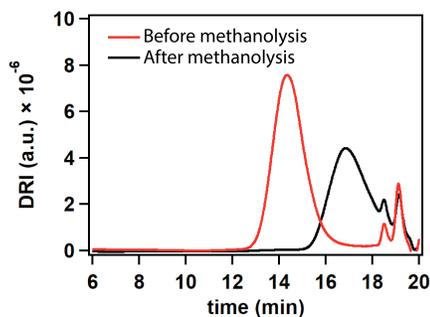
The objective of the proposal, which has not changed, is to address the question: What forces are required to induce physical or chemical changes to transition metal complexes embedded within polymers as mechanophores? This question probes the hypothesis that mechanical force can distort the coordination environment about a metal center in ways that access unique structural, electronic, and reactivity profiles that are otherwise unattainable. We proposed two Specific Aims: **1)** design and synthesize novel metallomechanophore constructs containing polydentate ligands intimately connected within polymer chains, and **2)** use single molecule force spectroscopy to measure force-extension curves for these new metallopolymers as a method to quantitate the forces necessary to release length stored in polydentate metal-ligand coordination complexes. In the first year of the grant we have made significant progress on Aim 1 and are poised to accomplish Aim 2 in the second year.

## Progress of research

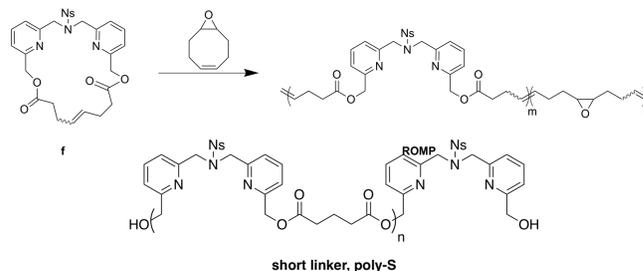
In order to quantify the effects of force on metallomechanophores, it is necessary to have a polymer system that incorporates metal chelating units directly in the main chain of the polymer so the metal center experiences the full effect of the transduced force, is compatible with single molecule force spectroscopy (SMFS), and contains multiple mechanophore units per polymer chain. We have successfully optimized two polymerization techniques for the synthesis of chelating polymers that fulfill these requirements: RCM/ROMP (ring closing metathesis/ring-opening metathesis polymerization) and polycondensation (**Figure 1**). We used dipyriddyamine as the chelating unit because it can be modified easily with polymer handles, can be derivatized to span multiple coordination numbers, and is known to complex a variety of metals.

To successfully synthesize a copolymer by ED-ROMP, the dpa ligand was first functionalized with terminal alkenes then made into a macrocyclic monomer by RCM, which was then co-polymerized with epoxyCOD to form a ROMP polymer (Figure 1, top). These steps required significant optimization to find conditions to prevent deactivation of the Ru Grubbs-type catalysts by the metal-chelating dpa units. After testing a variety of additives, solvents, temperatures and ratios, we now have reliable methods that enable synthesis of ROMP polymers embedded with 10% ligand and with molecular weights up to 60 kDa, suitable for SMFS.

Because of the nature of the AFM experiments, it is necessary the ligand be randomly dispersed throughout the entire backbone of the polymer. The rate of polymerization for epoxyCOD is much faster than for the ligand macrocycle, so if the copolymerization has living characteristics, the resulting copolymer would have diblock character. Conversely, if the copolymerization was entropically driven and reached a thermodynamic equilibrium, the distribution of the comonomers would be random along the polymer chain. A method developed by the Craig group that involves methanolysis of the main chain ester linkages was used to validate that our ROMP polymers indeed have random character (Figure 2).



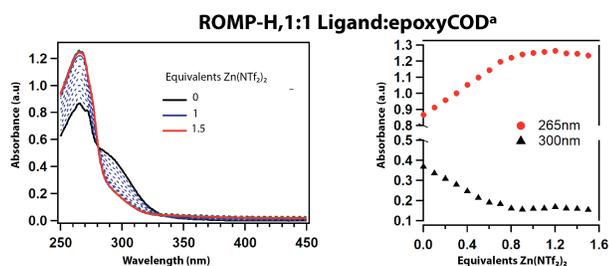
**Figure 2:** Differential refractive index (dRI) trace before (red) and after (black) hydrolysis. ROMP polymer had 12% ligand-incorporation and an  $M_n = 42$  kDa. Oligomers after methanolysis had  $M_n = 3.3$  kDa; comparison of found vs. oligomers calculated for diblock copolymers indicate random character for this polymer.



**Figure 1. (top)** ROMP polymers with 10% dpa units and molecular weights up to 60 kDa have been prepared and are suitable for force spectroscopy. **(bottom)** Polymerization by polycondensation resulted in polymers ~50% incorporation of ligand to comonomer, which can either be a short (**poly-S**, shown) or long linker.

The first targeted metallopolymer was a Zn(II) complex, as it is a non-redox active metal that can accommodate multiple geometries and coordination numbers, and is diamagnetic, which facilitates characterization. Complex formation was successful using  $Zn(NTf_2)_2$  as the Zn(II) source.  $Zn(NTf_2)_2$  has excellent solubility in MeCN with limited solubility in DCM, a solvent in which the polymer has good solubility. Addition of  $Zn(NTf_2)_2$  in MeCN to a ROMP polymer solution in DCM results in complex formation almost instantaneously, confirmed by  $^1H$  NMR (not shown). The binding ratio of ROMP polymers with  $Zn^{2+}$  was determined by titration monitored by UV-visible spectroscopy. The results for multiple ROMP polymers were similar. As seen in Figure 3 for one example, the peak at 265 nm increased with the addition of Zn, and plateaued at 1 equivalent. Excess Zn did not induce additional spectral changes. These results indicate that ROMP polymers with different amounts of incorporated ligand form a 1:1 ligand to Zn complex.

Like ED-ROMP, polycondensation allows for main-chain ligand incorporation, high loadings of the ligand, and metal addition at the final step; however, unlike ED-ROMP, polycondensation does not require a metal catalyst,



**Figure 3.** UV-vis spectra resulting from titration of Zn(NTf<sub>2</sub>)<sub>2</sub> to polymer. **Left:** Addition of 4  $\mu$ L aliquots of 4.75 mM Zn(NTf<sub>2</sub>)<sub>2</sub> to 75  $\mu$ M polymer in DCM. Molarity of both polymers were determined using the MW sum of the monomer unit based off of the % ligand incorporation determined by <sup>1</sup>H-NMR. **Right:** Absorbances at 265 nm and 310 nm plotted against equivalents of Zn, indicating a 1:1 ligand:Zn complex.

Preliminary SMFS experiments were conducted on a ROMP Zn metallopolymer. Cantilevers typically used for these SMFS experiments are non-coated silicon tips because they allow for the highest detachment forces (>1 nN), and have a spring constant around 20 pN/nm; however, because of the nature of metal-ligand bonds, such high detachment forces are not necessary. SMFS experiments on the polymers were run using a gold-coated cantilever with a smaller spring constant (~6 pN/nm) that provides better resolution of small force regimes (<200 pN). In a preliminary experiment, the metallopolymer was deposited onto the stage by evaporation of a dilute polymer solution in a mixture of 15% MeCN in DCM. Approach/withdraw cycles at 200 nm/s resulted in a force curve that appeared to have a plateau around 20 pN (Figure 4). This plateau is putatively the release of stored length from metal-ligand bond dissociation. The apo-polymer was subjected to a similar treatment, and no obvious plateau is apparent (Figure 4, right side).

While these preliminary data show exciting potential for quantifying force-induced metal-ligand bond dissociation, the force at which this potential plateau occurs is very low, and is at the limit of detection of the instrument. Furthermore, the extension of the pull was short, which also results in a short plateau length, making fitting the curves difficult. These challenges are symptoms of poor tip adhesion. Better adhesion of the metallopolymer to the tip may provide longer force-extension curves that could alleviate this challenge. Since these experiments utilize a gold-coated cantilever, incorporation of a sulfur-containing comonomer may improve tip adhesion compared to the epoxide-containing comonomer and provide longer force-extension curves. The Craig lab has previously reported a sulfur-containing macrocycle for ED-ROMP by first synthesizing a bis-alkene compound by the esterification of 3,3'-thiodipropionic acid.

In summary, we have made several key accomplishments in the preparation and characterization of novel metallopolymers. Our next steps are focused on optimizing these systems for single molecule force measurements.

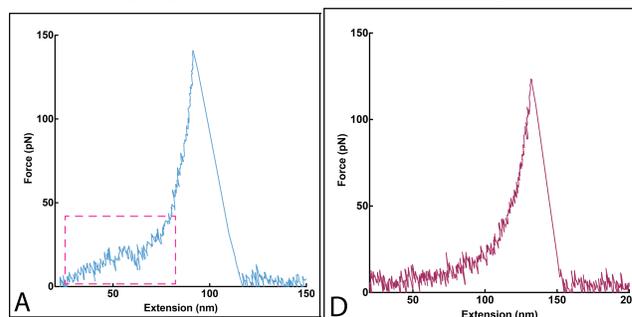
### Impact on career

This grant has established a strong collaboration between the PI and co-PI labs. It has been the impetus for biweekly joint group meetings that enrich the intellectual landscape for both labs. For the PI, this project has enabled be to branch into a new area of science that is exciting and extremely stimulating.

### Impact on students

The biggest impact to date has been to students. The graduate student who initiated the project was able to complete her PhD dissertation and is currently looking for industry jobs, notably in petrochemical and related fields. An undergraduate also contributed significantly to this project received Graduate with Distinction for his honors thesis. He is currently a first-year graduate student in Chemistry at Stanford University. We were able to hire a joint post-doc who bridges both Franz and Craig labs, and another graduate student in the Craig lab, while not funded directly from this grant, has benefited significantly by the collaborative intellectual landscape around metallomechanochemistry that has been catalyzed by this grant.

which could be advantageous for polymerizing chelating ligands. We have successfully synthesized polycondensation polymers containing the dpa ligand with comonomers of different lengths (Figure 1, bottom). Formation of the Zn metallopolymer with POLY-S and POLY-L polymers proceeded smoothly and was verified by <sup>1</sup>H NMR and UV-Vis to form 1:1 ligand:Zn complexes, similar to the ROMP polymers above. One advantage of polycondensation compared to the ED-ROMP strategy is the lack of a metal catalyst. The major drawback of this method is the resulting polymers are small, and high molecular weight polymers (>100 kDa) are desired for SMFS experiments. Continued work towards optimizing chain-extension reactions could allow for the synthesis of high molecular weight polymers suitable for SMFS experiments.



**Figure 4.** Representative force-extension curves for ROMP polymers. The Zn metallopolymer is on the left, and the metal-free polymer is on the right. A plateau around 20 pN for the Zn sample may be indicative of stored length release from metal-ligand bond dissociation. No obvious plateau is observed in the metal-free sample.