Synthesizing a library of sialic acid-functionalized polypeptides to investigate polyvalent interactions for influenza inhibition

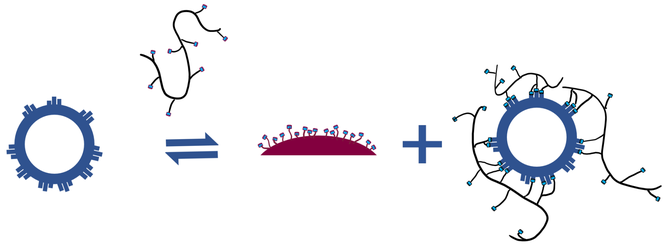
Zhen Shi, Rachel H. Bianculli, Jonathan D. Mase, Michael D. Schulz
Department of Chemistry
Virginia Tech, Blacksburg, VA 24061

Introduction

Influenza is a family of viruses that has caused two pandemics in the human history and is still infecting people each year.[1, 2]

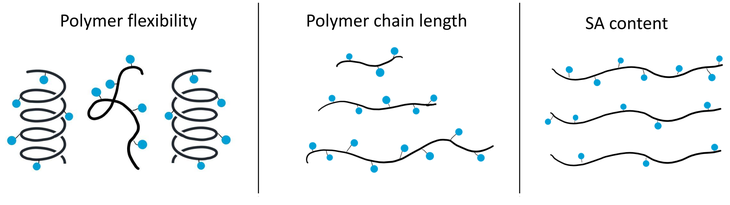
The influenza infection starts with polyvalent interactions– hemagglutinins (HAs) on the virus surface binding to sialic acids (SAs) on the cell surface to achieve viral attachment and entry.[3]

In here, we are trying to mimic this natural polyvalent interactions with synthetic polymers (polypeptides) and achieve viral inhibition by using our SA-containing polymers to bind to the viruses therefore inhibiting cell-virus interactions.



Research Question

Overall, we are curious about how polymer structural variations affect viral inhibition. Specifically, we are looking at structure parameters including polymer flexibility, polymer chain length, and SA content.

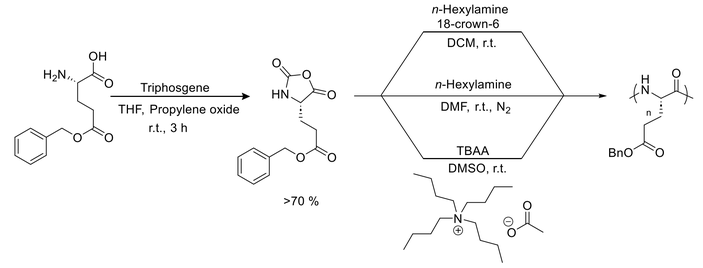


Progress

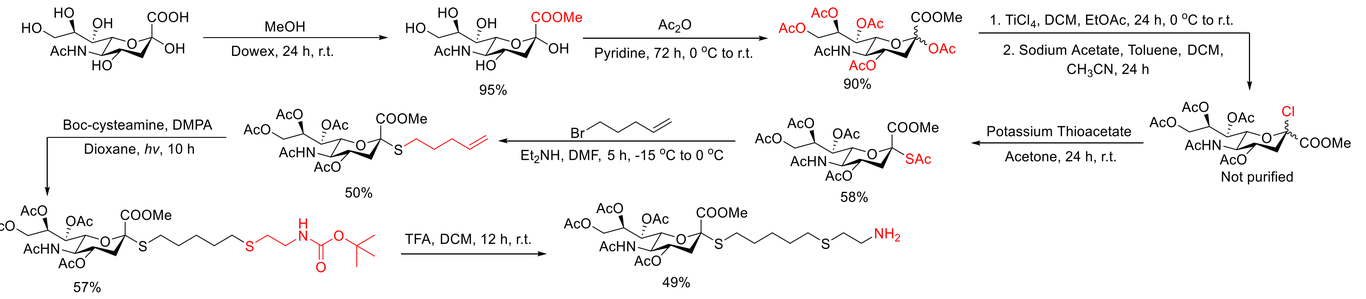
Research Goal

1. Synthesizing polypeptides (starting with benzyl glutamates – both the L isomers and D isomers) to achieve various chain length and chain conformation.
2. Modifying sialic acids.
3. Conjugate sialic acids onto polypeptide backbones.
4. Quantify viral inhibition *via* hemagglutination inhibition (HAI) assay.

Polypeptide Backbone Synthesis (L-isomer)

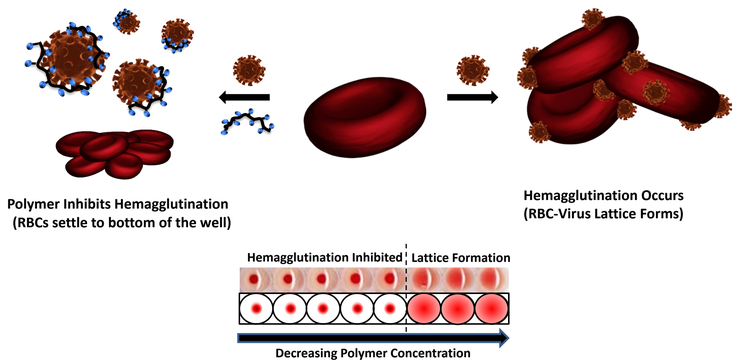


SA modification



Future work

- After successful synthesis and characterization of polypeptide backbones with L isomers, D isomers will be polymerized/ copolymerized to generate polymers with different conformations.
- The resulting polymers be deprotected yielding polyglutamic acids (PGAs) which can later participate in glycoconjugations.
- Sialic acids will be firstly deprotected and coupled to the PGAs *via* amidation.
- After generating a library of SA-conjugated polypeptides, our materials will be evaluated through HAI assays (depicted in the right graph). The antiviral inhibition of our materials with varying parameters will instruct us on how to better design a glycopolymer with structural properties maximizing its antiviral efficacy.



Acknowledgement

This work was supported by GlycoMIP, a National Science Foundation Materials Innovation Platform funded through Cooperative Agreement DMR-1933525.

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2. Bianculli, R. H.; Mase, J. D.; Schulz, M. D. Antiviral Polymers: Past Approaches and Future Possibilities. *Macromolecules* **2020**, 53 (21), 9158–9186
3. Mammen, M.; Choi, S. K.; Whitesides, G. M. Polyvalent Interactions in Biological Systems: Implications for Design and Use of Multivalent Ligands and Inhibitors. *Angew. Chemie - Int. Ed.* **1998**, *37* (20), 2754–2794.