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Effective Binding Affinities of Mucin-like Polymers, A Computational Study EMIKO ZUMBRO, KATHARINA RIBBECK, ALFREDO ALEXANDER-KATZ, Massachusetts Institute of Technology — Mucins are proteoglycan polymers found in mucus that play a key role in preventing infection, but their capabilities have yet to be mimicked by synthetic materials. Mucins have a dense bottlebrush structure that may display many low-affinity binding sites to interact with proteins such as lectins. Polyvalent binding site displays enhance the binding strength for low-affinity monovalent interactions but it is unknown how polyvalent system shape, size, and binding site density affect these interactions. Since the parameter space of polyvalent inhibitors is large and difficult to sample experimentally, we built a simulation to predict structural effects on binding affinities of polyvalent motifs. To evaluate the relative K_D's of polyvalent and monovalent inhibitors, we use a Brownian dynamics bead-spring model coupled with a reactive polymer-pathogen binding model. It bridges length and timescales and can sample large polymer systems that bind proteins at the sub-nanometer lengthscale. We are using competitive inhibition assays to validate the simulation and measure the enhanced inhibitory effect that polyvalency gives over free binding sites. This simulation gives design principles to optimize the structure and effectiveness of polyvalent inhibitors.

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