Toward Artificial Tissues That Are Both Soft and Firm

Biological tissues often have a unique combination of "softness" and "firmness": they are soft because they easily deform at small mechanical loads, but firm because they are much stiffer when larger forces are applied. Synthetically reproducing this behavior would enable significant advances in biomaterials for improved artificial tissues, wearable electronics, and implanted devices. Conventional polymer networks composed of flexible linear chains have difficulty pairing softness and firmness, because the fully extended length of a typical polymer chain can easily be $10^1$–$10^3$ times larger than its equilibrium dimensions.

In this issue of ACS Central Science, Keith et al. have overcome this challenge by using linear–bottlebrush–linear polymer architectures, achieving mechanical signatures that are characteristic of many biological tissues.1

The key to the success of these materials is the unique design of their polymeric building blocks, composed of poly(dimethylsiloxane) (PDMS) bottlebrushes attached to linear poly(methyl methacrylate) (PMMA) polymers on both ends (Figure 1). In this central bottlebrush, a smaller linear polymer called a side chain is attached to every monomer that forms the backbone. These side chains sterically crowd the backbone, causing bottlebrushes to be much more rigid than linear polymers. It is perhaps not a coincidence that similar architectures and characteristics are present in the molecules found in biomaterials such as connective tissues. For example, cartilage contains proteoglycans composed of densely grafted polysaccharide chains extending from a central protein, and collagen forms relatively stiff architectures through triple helix folding of the underlying polypeptides. In bottlebrushes, the side chains also dilute the backbones such that polymer entanglements are less important, providing the desired softness. The PDMS bottlebrushes also provide firmness because their rigid backbones are already prestretched compared to a coiled linear polymer. Additional firmness stems from the separation of the linear PMMA end-blocks from the thermodynamically incompatible PDMS bottlebrushes, thus stretching the bottlebrushes even further. This work is an excellent demonstration of the inherent versatility in polymer science.

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and tunability of the resulting material properties when one utilizes different monomers, branching, blockiness, etc., in molecular design.

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This study builds upon considerable work in the community exploring the fundamental physics and exciting applications of bottlebrush polymers. Research on this architecture has drastically accelerated in the past decade, enabled in part by advances in synthetic techniques such as ring-opening metathesis and controlled radical polymerization strategies. A wide range of advantageous properties arise as a direct result of the unique bottlebrush architecture. In solution, bottlebrushes are attractive for drug delivery applications because their large size enables easy incorporation of multiple functional agents. In bulk materials, rheological studies have directly shown that the effects of chain entanglement are much less significant for bottlebrushes \( (M_e \sim 10^3 \text{ kg/mol}) \) compared to linear polymers \( (M_e \sim 1 \text{ kg/mol}) \). As a result, bottlebrush block copolymers readily self-assemble into classical microphase separated morphologies, while linear counterparts of similar size typically become kinetically trapped into poorly ordered nanostructures. Due to their backbone stiffness and inherently larger size, the length scales attainable by self-assembled bottlebrushes can approach visible wavelengths and interact with visible light, producing structural color. The resulting photonic materials are highly tunable and enable access to a variety of colors with relative ease in synthesis and processing. Finally, reduced chain entanglements are directly useful for mechanical properties in bottlebrush-based elastomers. The softness characteristics in the present study have previously been demonstrated in the seminal work also by Sheiko and Dobrynin, in collaboration with other theory and synthesis groups. This was the first demonstration of extremely low elastic moduli without the use of solvent, in materials coined "supersoft elastomers".

The unique molecular design based on prestretching polymer chains to achieve these mechanical signatures is reminiscent of other ideas for attaining favorable properties in polymer networks. In particular, double-network hydrogels and elastomers achieve superior mechanical toughness over simpler materials, by incorporating a rigid, prestretched polymer network that is mixed with another soft and stretchable polymer network. When cracks form in the first brittle network, propagation is suppressed by the second network. This concept was further expanded by Ducrot et al. by swelling the first network in the presence of monomer that forms a second and then a third polymer network, etc. Stress–strain curves in those materials display extremely high extensibility similar to the present study. This work’s linear–brush–linear elastomer design has also been previously explored in other work by Sheiko and Dobrynin. They had proposed a constitutive model that characterizes this key strain-stiffening behavior using a parameter \( \beta \), which is defined as the ratio of a polymer’s equilibrium dimensions to its size when fully stretched. While a larger \( \beta \) implies more strain-stiffening, and thus better mechanical mimicry to biological tissues, the materials from previous studies were limited to \( \beta < 0.7 \). This work has further explored the molecular parameter space, particularly the bottlebrush side chain length, now attaining \( \beta > 0.9 \). These new materials can now successfully mimic extremely soft but firm tissues, such as adipose and fetal membranes.

The success of this work opens several lines of further investigation. While the study provides compelling evidence for the prestretched rigid bottlebrush mechanism through X-ray scattering and theoretical analysis, further confirmation through alternative characterization techniques would enable more rational design of these materials. To our surprise, basic questions such as directly measuring the rigidity of bottlebrushes in bulk materials have not been experimentally explored in the literature. Prestretching polymers for strain-stiffening also raises questions about mechanical failure. Indeed, a classical hydrogel (e.g., polyacrylamide) is often cross-linked heterogeneously, containing regions where chains are inherently prestretched. This prestretching does not result in strain-stiffening, likely because these regions serve as weaker areas that initiate crack formation before stiffening can occur. A systematic study of mechanical failure in the present materials would provide interesting comparisons and mechanistic insights. Finally, this work opens significant possibilities in synthetic biomaterials for applications where faithful reproduction of mechanical behavior is of paramount importance. However, design of fully artificial tissues requires not only mechanical mimicry as this study has remarkably achieved, but also biochemical mimicry through incorporating water-soluble monomers, growth factors, and other bioactive agents.

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