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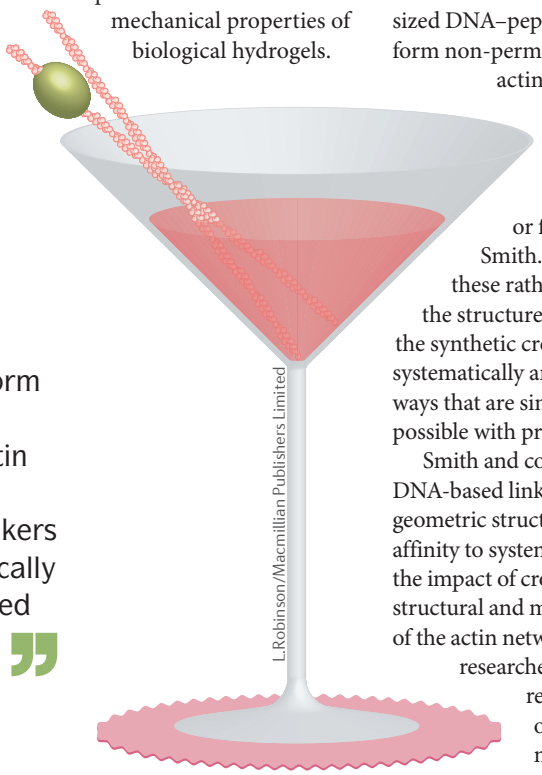
DNA NANOTECHNOLOGY

Crosslinked, not stirred

The actin cytoskeleton provides cells with the ability to dynamically change their mechanical properties. This behaviour is facilitated through protein-based linkers, which form transient crosslinks between actin filaments, making actin networks highly adaptive and mechanically flexible.

Now, Smith and colleagues, writing in *Advanced Materials*, have used a combination of DNA strands and short peptides to construct synthetic mimics of these protein linkers to recreate the broad parameter space of the actin cytoskeleton in vitro. Thereby, the researchers could engineer the mechanical signatures of natural actin networks and provide a DNA-based modular platform to tune the mechanical properties of biological hydrogels.



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Many synthetic polymer systems are based on permanent chemical crosslinks, which confine the mechanical degrees of freedom of the material to one network type. By contrast, natural biopolymers, such as the actin cytoskeleton, exhibit the coexistence of different structural phases, that is, parallel and perpendicular fibres, established through the transient crosslinking with proteins varying in binding strength, flexibility and structure. This crosslinking variability is of crucial importance for their dynamic mechanical behaviour.

Smith and colleagues recreated this structural polymorphism through the use of purely synthetic DNA-based crosslinkers. "We synthesized DNA–peptide constructs that form non-permanent links between actin filaments. These synthetic crosslinkers are analogous to cellular proteins, such as alpha-actinin or fascin," explains Smith. "But in contrast to these rather complex proteins, the structure and properties of the synthetic crosslinkers can be systematically and easily modified in ways that are simply not practical or possible with proteins."

Smith and co-workers use these DNA-based linkers to decouple the geometric structure from the binding affinity to systematically investigate the impact of crosslinking on the structural and mechanical properties of the actin network. Thereby, the researchers could synthetically recreate the formation of fibre bundles and networks by varying the binding strength of the linkers and the linker–actin filament ratio. This modulation of morphology also allows for the elasticity of the material to be regulated.

The relationship between linkers, network formation and mechanical properties provides the basis of the DNA-based modular platform constructed by the researchers to rationally design the structure and thus, the mechanical and rheological properties of the biopolymer network. Moreover, the use of DNA-based linkers adds another layer of regulation to the platform. "By using DNA, we also have the ability to add a regulatory mechanism to turn the linkers on or off," says Smith. "We can use a DNA-targeting enzyme, but there is also the possibility to do this with aptamers, strand displacement or even RNA transcription circuits."

The team are now exploring their toolbox for the precise engineering of biocompatible hydrogels for 3D cell culture, in which the mechanical properties of the material have a crucial impact on cell behaviour. Furthermore, the influence of actin crosslinking on cell behaviour may be studied by introducing these synthetic crosslinkers into living cells. "We want to use longer or shorter crosslinkers and design branched structures to be able to link more than two actin filaments together. This would allow us to better explore the fundamental physics of how these materials behave," concludes Smith.

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