

Bottom-up Engineering of Nanoscale Devices to Program Biological Systems

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Biologically evolved soft materials are often used as inspiration in the design and development of new materials; however, the molecular toolbox provided by biological systems has been evolutionarily optimized to carry out the necessary functions of cells. The resulting inability to systematically modify basic properties such as biopolymer rigidity in experimentally available model systems hinders a meticulous examination of parameter space. We circumvent these limitations using model systems and components assembled from programmable nanomaterials such as DNA and peptides.

Micrometer-long nanotubes with tunable diameters and rigidity can be constructed from small sets of DNA strands. By systematically varying the sequences of the DNA strands of these synthetic, semiflexible filaments in low-density entangled networks, we for the first time experimentally determine the dependence of bulk stiffness on the previously inaccessible parameter of persistence length. Curiously, we found a linear dependence, which stands in contrast to the sublinear behavior predicted by long-accepted theory. Introducing crosslinks into the entangled system through DNA hybridization interactions significantly stiffened the network. These provide multiple mechanisms by which the mechanics of bio-matrices can be precisely programmed using purely synthetic nanoscale components, and open routes to controlling emergent behaviors such as strain hardening or signal responsiveness.

We take a similar approach to program the properties of natural biological materials such as actin networks or living cells. Synthetic constructs for crosslinking actin filaments are fabricated from DNA strands which have been conjugated to different actin-binding peptides. These were shown to modulate bulk network elasticity in accordance with binding strength, concentration and size of the crosslinking construct. Introduction of these synthetic constructs into living cells hinders their motility, indicating a temporary and controllable "jamming" of the internal actin network. These protein-sized components can be easily modified to vary parameters like length, valency or binding strength, and offer the unique possibility to control cellular behaviors such as the epithelial to mesenchymal transition while bypassing the genetic machinery.

[1] Glaser, Schnauß et al., 2016, in review

[2] Yin, Peng, et al. "Programming DNA tube circumferences." *Science* 321.5890 (2008): 824-826.

[3] Schiffels, Daniel, et al. "Nanoscale structure and microscale stiffness of DNA nanotubes." *ACS nano* 7.8 (2013): 6700-6710.

[4] Schuldt et al., 2016, submitted

[5] Lorenz, Schnauß et al., 2016, in preparation