

Polymer mechanochemistry enables the control of drugs, proteins and nucleic acids by ultrasound

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Polymer mechanochemistry refers to the control of chemical transformations by rearranging or cleaving specific bonds at precisely defined sites within polymer chains upon applying mechanical forces such as tension and compression or indirectly by ultrasound.[1] The force-sensitive moieties responsible for this process are known as mechanophores.[2] While polymer mechanochemistry employing functional mechanophores has found widespread applications in the field of material science ranging from damage detection,[3] stress sensing,[4] to self-regulating materials,[5] its exploration and utilization in the biomedical context is still in an early stage.

Here, we introduce 20 kHz ultrasound and high-intensity focused ultrasound (HIFU) as a mechanical stimulus to drive the activation of disulfide mechanophores residing in hyperbranched star polymers and cross-linked microgels. Through the application of force, thiols are formed that undergo further reactions like addition to Diels-Alder products or thiol-disulfide exchange to release different drugs carrying furan or hydroxy groups, respectively.[6]

Besides colloids from synthetic scaffolds, ultrasound-sensitive nucleic acid microgels will be presented. They are prepared by enzymatic processes involving rolling circle transcription or amplification. The sequences are designed in such a way that they encode multiple binding sites for small bioactives or proteins. Upon sonication with low intensity focused ultrasound or even imaging ultrasound, molecular cargoes are released by cleavage of non-covalent interactions. In this way, drugs, bioactives or proteins are released and can unfold their functions. In this way, drug action and cellular activities are controlled spatiotemporally *in vitro* and *in vivo*. [7,8] Ultimately, we are aiming to establish ultrasound in combination with mechano-sensitive soft colloids and microbubbles as a tool in precision nanomedicine and sonogenetics.[9]

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