Title: Furan-Maleimide Mechanophores: Competitive Activation Experiments and Mechanically Triggered Drug Delivery Applications

Abstract:

Mechanical force is a unique external stimulus enabling the control of specific chemical reactions in stress-sensitive molecules called mechanophores. In turn, mechanophores are used to design innovative stimuli-responsive polymeric materials that address a variety of challenges. Research in polymer mechanochemistry aims to both deepen the knowledge of structure–activity relationships and the principles that govern mechanochemical transformations, and to develop functional applications uniquely enabled by mechanochemical reactions. First, we probe the relative mechanochemical reactivity of furan–maleimide (FM) and anthracene–maleimide (AM) Diels–Alder adducts through competitive activation experiments. Ultrasound-induced mechanochemical activation of bis-adduct mechanophores revealed pronouced selectivity for reaction of the FM adduct compared to the AM adduct. Second, we leverage a special furan–maleimide mechanophore comprising a masked 2-furylcarbinol derivative to develop a novel platform for mechanically triggered drug delivery using biocompatible focused ultrasound. We show that air-filled protein nanostructures called gas vesicles function as acousto-mechanical transducers, effectively coupling biocompatible focused ultrasound with the mechanochemical activation of mechanophores under physiological conditions to achieve the remote controlled release of small molecule chemotherapeutic payloads. These results demonstrate the translational potential of polymer mechanochemistry and set the stage for future therapeutic and bioimaging applications.