Harnessing the Mechanical Bond for Biomedicine

Abstract

The mechanical bond offers a distinctive way to control molecular structure, dynamics and function beyond the limits of conventional covalent design. Although mechanical bonds have been widely studied in supramolecular chemistry, their potential in biomedicine remains largely unexplored. Integration with biomolecular systems is still challenging, and the consequences of mechanical bonding and motion in biological settings remain unclear. In this presentation, we describe our efforts to explore this potential through three interconnected directions. First, we developed mechanically interlocked peptide rotaxanes as a new class of peptide architectures, showing that the mechanical bond can be introduced into bioactive peptide systems to expand their accessible chemical space. We then examined peptide catenanes, in which topological constraint reshapes peptide behaviour more profoundly. These interlocked peptide architectures display altered properties relevant to biomedical applications, highlighting catenation as a powerful strategy for modulating peptide function. Finally, we translated programmable molecular motion into supramolecular drug delivery by developing programmable release systems based on controlled molecular dethreading, in which release profiles can be tuned through component engineering. Taken together, these studies show that the mechanical bond can serve not only as a structural feature, but also as a functional design element for biomolecular engineering. It allows molecular properties and behaviour to be tuned in ways that are difficult to achieve using classical molecular design alone. More broadly, our work highlights the mechanical bond as a versatile platform for the development of functional supramolecular systems for biomedicine.

References [1] A. Li†, H. Zhang†, N. B. Nazri, M. Wan, and C. Tian*. JACS Au 2025, 5, 4845. [2] S. Sheng†, Y. Li†, R. R. Y. Lee, Y. Gao, H. Han, Z. Wan, C. Owh, C.-A. M. Y. Chua, Z. Y. Chong, N. W. H. Ng, W. Tang, and C. Tian*. Nat. Commun. 2025, 16, 9390. [3] M. Wan, P. Yuan, H. Zhang, Y. Han, N. C. Y. Wong, H. K. E. Ng, Q. Chen, C. J. Y. Wang, L. R. R. Turqueza, N. W. H. Ng, B. B. R. Kee, H. N. Duong, and C. Tian. ChemRxiv 2026, DOI: 10.26434/chemrxiv.10001583/v2.