From Spiral Nanostructures to Membrane Fusion: Force-Directed Self-Assembly of Viral Peptides at Soft Interfaces

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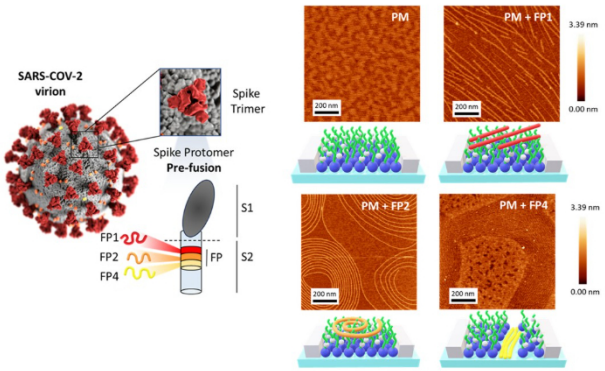
Understanding how molecular self-assembly at fluid interfaces translates into mechanical work is a central challenge in colloid and interface science. Here, we address this question using fusion peptides (FPs) derived from the SARS-CoV-2 Spike protein as model amphiphilic building blocks that spontaneously organize at lipid-decorated air–water interfaces, coupling supramolecular assembly with targeted membrane restructuring [1,2].
Three peptide sequences — FP1 (residues 816–837), FP2 (835–856), and FP4 (885–909) — were investigated at biomimetic plasma membrane monolayers comprising phospholipids, sphingomyelin, and cholesterol (~50 mol%). By modulating lateral packing through uniaxial compression in a Langmuir–Blodgett trough, we explored how interfacial confinement governs peptide oligomerization, lipid phase behavior, and mechanical response. Grazing-incidence X-ray diffraction and neutron reflectometry revealed that all three FPs displace cholesterol-rich nanodomains, suppressing raft-like order and increasing local membrane fluidity through competitive peptide–lipid packing [3].
Each peptide contributes a distinct mechanical function. FP1 forms rigid fibrils (persistence length ≈ 2.3 μm) that anchor into the acyl chain region. FP2 assembles into flexible spirals (persistence length ≈ 0.14 μm) storing ~25 k_BT of elastic energy per spiral — released upon compression as a loaded-spring mechanism reminiscent of ESCRT-III filament behavior [3]. FP4 transitions from surface-adsorbed to membrane-inserted β-sheet fibrils under high lateral packing, disrupting bilayer continuity. A tandem FP1–FP2 construct confirmed the cooperative nature of anchoring and curvature generation.
Atomic force microscopy, laser direct infrared spectroscopy, and interfacial shear rheology provided complementary morphological, structural, and viscoelastic characterization. The spiral nanostructures additionally served as templates for sub-10 nm metallic replicas over cm^2 areas, illustrating how mechanically active peptide assemblies can be repurposed for functional nanofabrication [4].
These results establish a framework in which simple peptide motifs at fluid interfaces capture, store, and release mechanical energy with spatial precision — offering design principles for responsive soft materials and adaptive colloidal systems.



Left: Schematic of the SARS-CoV-2 virion and the Spike protein in its prefusion conformation, highlighting the location of fusion peptides FP1 (red), FP2 (orange), and FP4 (yellow) within the S2 subunit. Right: AFM topographical micrographs and corresponding topographical profiles.

References:

[1] A. Maestro, *Curr. Opin. Colloid Interface Sci.* , 2019, 39, 232. [2] A. Santamaria, A. Maestro *et al.* ,*J. Am. Chem. Soc.* , 2022, 144, 2968. [3] N. Pawar, A. Alvarez-Fernandez, A. Maestro *et al.* , *Nat. Commun.* , 2026, 17, 915. [4] A. Alvarez-Fernandez, N. Pawar *et al.* , *Adv. Funct. Mater.* , 2024, 2411061.

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