From Physical Constraints to Biological Insights: DNA Confinement and Protein Interactions

Fundamental Physics: DNA Under Spatial Constraints

A fundamental challenge in biophysics is understanding how spatial constraints alter DNA behavior. My research systematically investigates this question by applying soft matter physics principles to biological macromolecules.

My work encompasses both single-end and double-end grafted DNA systems under spatial constraints. In a collaborative work published in *Physical Review Letters* [1], I contributed to understanding the dynamics of single-end grafted DNA under mechanically induced confinement by bio-adhesive spreading vesicles. This study revealed DNA internal friction and topological complexity, providing crucial insights into the fundamental physics.

Building on this foundation, my primary contribution, published in *European Physical Journal Special Topics* [2], investigated double-end grafted DNA systems where giant unilamellar vesicles adhere to DNA carpets. This work established controlled bio-interface confinement systems and demonstrated how spatial constraints modulate DNA accessibility and conformational dynamics.

The most technically challenging aspect of my research involved investigating true strong confinement physics, where DNA is compressed within bio-adhesion channels. These systems create geometric constraints of approximately 10 nm height and 7 nm width, operating in the regime where DNA persistence length (50 nm) significantly exceeds the confinement dimensions. This regime suppresses DNA fluctuations and enforces extended polymer configurations, which is distinct from weak confinement. While conventional nanofluidic fabrication techniques can achieve weak confinement near the persistence length, they require complex microfabrication processes. To extend these physical insights to biologically relevant systems, RecA polymerization offers a biomimetic approach to modulate DNA stiffness, thereby bridging the gap between pure physical studies and biologically relevant systems.

Biological Applications: Protein-DNA Interaction Studies

RecA, an essential recombinase in bacterial DNA repair, polymerizes on DNA to form nucleoprotein filaments, which have a persistence length of nearly 950 nm. By employing RecA, this approach enables persistence-length-scale confinement studies using more accessible microfluidic channels. This approach naturally redirected my research toward biologically relevant protein-DNA interactions, which address fundamental questions in living systems.

My current research investigates RecA-mediated homologous recombination by FRET and CoSMoS. A key discovery (a manuscript preparation) [3] demonstrates that RNA substitution significantly affects RecA-mediated strand exchange reactions. This work shows that RecA discriminates between DNA and RNA at multiple stages of strand exchange through distinct mechanisms.

Through collaboration on a study of eukaryotic recombinases and their accessory proteins, published in *Nature Communications* [4], I gained valuable insights into multi-protein regulation mechanisms in eukaryotic systems.

Integrated Expertise and Research Vision

My systematic progression from physical constraint studies to biological mechanism analysis has developed unique cross-disciplinary expertise. These experiences have equipped me with distinctive capabilities spanning single-molecule microscopy, microfluidic control, and quantitative protein-DNA analysis.

This integrated expertise enables systematic investigation of protein-DNA competition under physiologically relevant constraints. By combining physical understanding with biological insights, this approach opens new paradigms for gene regulation studies with therapeutic implications.

References

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[2] Yuting Sun, Carlos M Marques, and André P Schröder. Adhesion of giant unilamellar vesicles on double-end grafted DNA carpets. *European Physical Journal Special Topics*, 223:1755–1769, 2014. doi: 10.1140/epjst/e2014-02224-9.

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