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Exploring the Dynamics of Red Blood Cell Flickering with Holographic Optical Tweezers

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About the Study

The Translational Biophysics research team, based in Complutense University and the Institute for Biomedical Research of the Hospital 12 de Octubre in Madrid, Spain, has initiated on an innovative exploration of Red Blood Cell (RBC) dynamics, particularly focusing on the fascinating phenomenon of RBC flickering. Our ground-breaking work represents a fusion of advanced scientific inquiry and cutting-edge technology, utilizing life imaging microscopy, Holographic Optical Tweezers (HOTs) and cell biophysics to address biomechanical aspects of RBC dynamics [1].

Our investigation focuses on understanding RBC flickering, characterized by the rapid shape fluctuations of the RBC membrane. These subtle active movements of the living RBCs, usually observed as softening interactions at the equatorial cell rim [2], have long fascinated researchers due to their close connection with the metabolic activity and their potential importance in RBC physiology, both in health and disease. Recently, the flickering phenomenon has captured the interest of biophysicists linking cell physiology and thermodynamics to metabolic efficiency [3]. The unique biophysical properties of RBCs, including flexibility, deformability, and mechanobiological adaptability in circulation, enable them to navigate through the bloodstream, including narrow microcapillaries, without being damaged.

Holographic optical tweezers or HOTs, the technological centerpiece of our current study [1], offer a significant advancement in optical manipulation of living cells. Unlike traditional optical tweezers, which rely on single focused beams to handle microscopic objects, HOTs provide unparalleled spatial precision and flexibility of micromanipulation. By utilizing programmable holograms generated by spatial light modulators, HOTs can apply finely tuned optical forces to individual cells, allowing for precise micromanipulation under minimal invasiveness. A key advantage of HOTs is their ability to create three-dimensional holographic traps, enabling the manipulation of multiple objects simultaneously, regardless of their position relative to the microscope's focal plane. This capability is particularly valuable in the study of cellular biomechanics and the possible manipulation of intracellular structures, where the complex three-dimensional architecture of cells requires precise control over distributed forces. Furthermore, HOTs offer biocompatibility and minimal phototoxicity, especially when operating in the near-infrared spectral range. This ensures that cellular integrity is preserved during cell manipulation, which is essential when studying delicate mechanobiological structures like the flickering configurations of RBCs. The development of a custom-designed algorithm for real-time manipulation of the RBC membrane contour further highlights the sophistication and adaptability of the presented approach. This computational tool not only enables precise control over cellular dynamics but also opens opportunities for further exploration and refinement of HOT-based techniques in cellular biomechanics.

In this paper, we report on the holographic optical tweezers developed to create a space-extended force field that covers the equatorial membrane contour of individual RBCs. We observed different flickering patterns in freely suspended RBCs, which is attributed to specific membrane regions known as "kickers". By using holographic optical forces, we were able to selectively stop these active kickers with minimal disruption.

Beyond its implications for basic research, this study holds promise for a wide range of applications in diagnostics, therapeutics, and tissue engineering. Insights gained from manipulating RBC flickering activity could lead to the development of innovative diagnostic tools for hematological disorders and other diseases characterized by changes in cellular mechanics. By looking ahead, the research lays the foundation for transformative advancements in cellular engineering and biophysics. The integration of HOTs with computational modelling and advanced imaging techniques is poised to unlock new frontiers in our understanding of cellular mechanics and pave the way for the development of next-generation biomedical technologies.

In conclusion, the study of RBC dynamics using HOTs represents a significant advancement in the field of cellular biomechanics. By utilizing innovative technologies and integrated approaches, new insights into the complexities of cellular dynamics can be unvailed. This could pave the way for the development of innovative solutions to some of the most pressing challenges in human health and disease.

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