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Mobility and Conformational Dynamics of large DNA diffusing through Cytoskeletal Networks¹ KATHRYN REGAN, SHEA RICKETTS, DE-VYNN WULSTEIN, RYAN MCGORTY, RAE M. ROBERTSON-ANDERSON, University of San Diego — The high concentrations of proteins crowding cells greatly influence intracellular DNA dynamics. These crowders, ranging from small mobile proteins to large cytoskeletal filaments such as semiflexible actin and rigid microtubules, can hinder diffusion and induce conformational changes in DNA. The rigidity, mobility, and concentration of crowders all play a role in DNA transport, yet previous studies have mainly focused on the effect of small mobile crowders on transport. At the same time the rigid cytoskeleton has been identified as a key factor suppressing viral transfection and gene delivery. Here, we use fluorescence microscopy and custom single-molecule conformational tracking algorithms to measure center-of-mass transport and time-varying conformational sizes and shapes of single 115 kbp DNA molecules diffusing in networks of actin filaments and microtubules. We determine the dependence of protein concentration $(6 - 23 \ \mu M)$ and rigidity (actin vs microtubules) on DNA dynamics. Corresponding measurements with monomeric actin and tubulin identify the roles that network rigidity versus excluded volume play in transport. Initial results show that crowding by microtubules induces anomalous transport and larger, slower conformational fluctuations of DNA.

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