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Cross-correlated TIRF/AFM reveals asymmetry in self-assembled Myosin filaments - a Dyck paths model of asymmetry and implications for Motility ANDRE BROWN, ALINA HATEGAN, DANIEL SAFER, YALE GOLDMAN, DENNIS DISCHER, University of Pennsylvania — Myosin-II's rod-like tail drives filament assembly with a head arrangement that should generate equal and opposite contractile forces on actin – if one assumes that the filament is a symmetric bipole. Self-assembled myosin filaments are shown here to be asymmetric in physiological buffer based on cross-correlated images from both atomic force microscopy (AFM) and total internal reflection fluorescence (TIRF). Quantitative cross-correlation of these orthogonal methods produces structural information unavailable to either method alone in showing that fluorescence intensity along the filament length is proportional to height. This implies that myosin heads form a shell around the filament axis, consistent with F-actin binding. A motor density of ∼50-100 heads/micron is further estimated but with an average of 32% more motors on one half of any given filament compared to the other, regardless of length. A purely entropic pyramidal lattice model is developed and mapped onto a Dyck path problem that qualitatively captures this lack of length dependence and the distribution of filament asymmetries. Such strongly asymmetric bipoles are likely to produce an imbalanced contractile force in cells and in actin-myosin gels, and thereby contribute to motility as well as cytoskeletal tension.

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