Modeling Stretch-Induced Release of Molecules in the Actin Cytoskeleton

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***Short Abstract* — Recent literature provides strong evidence for a causative link between mechanical stretch affecting the cytoskeleton and the release of signaling molecules [1]. Understanding the link between the mechanical input, the corresponding morphological changes in the actin cytoskeleton, and the final signaling molecule release is a poorly understood yet very significant problem in the field of mechanotransduction. Here, we present a coarse-grained actin network model that simulates architectural changes in the network in response to external mechanical stimulus to understand the interplay between actin network mechanics and resulting biochemical signaling.**

***Keywords* — coarse-grained modeling, mechanotransduction, biomechanics, actin, signaling**

I. Materials and Methods

Simulation setup: We develop a coarse-grained actin network model and examine the intrinsic angle geometry changes under mechanical stimulation. We have previously examined actin network mechanics with a derivative of this model [2]. The network is created with a circular solution space that is considered fixed to an underlying substrate at uniformly placed perimeter nodes representing focal adhesions. Filaments are formed by crosslinking opposite focal adhesions on the periphery (Fig. A). Intersections formed by crosslinking represent molecular linking of actin with affiliated attached molecules (e.g. filamin A and FilGAP) at each of the four angles created by that intersection. Stretch is simulated by moving the upper nodes while holding the bottom nodes stationary and balancing forces on the remaining nodes (Fig. B).

II. Results and Discussion

As stretch is applied to the network, the intersecting angle distribution transitions from a more peaked to a flatter distribution while still being centered at 90° (Fig. C). We also examined the difference in the stretched angle relative to the non-stretched angle ("delta angle"), and observe a shift in distribution as additional stretch is applied. At 1% stretch, the delta angles are small with almost no angle changes greater than 5 degrees, but at higher levels of stretch, the observed delta angle distribution is almost uniform (Fig. D). These histograms reflect similar results to simulations performed by Ehrlicher *et al.* on their experiments even though their simulations had different overall morphologies and boundary conditions [1].

These results are being incorporated into molecular release models that represent a potentially versatile platform for examining the biophysical interactions that link mechanical stimulus at the cellular level to response at the protein level and may underlie strain-induced signaling mediated by the cytoskeleton.

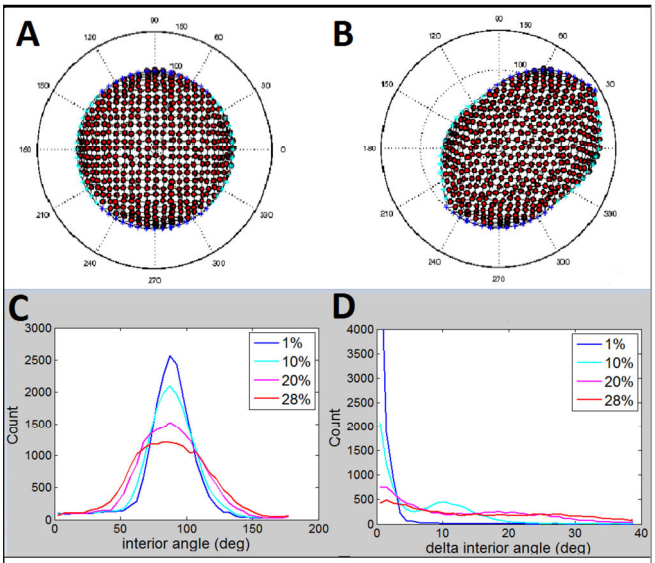

Figure: Model of Actin Network Deformation and Angle Change (**A**) Unstretched network. (**B**) 28% stretched network. **(C)** Histogram of interior intersection angles. **(D)** Histogram of the change in interior intersection angles relative to the unstretched state.

Acknowledgements: This work was supported by NIH grants #1R01AI076318, #1R01CA140214 , and T32 training grant T32 EB009403 as part of the HHMI-NIBIB Interfaces Initiative.

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