Cell reorientation under cyclic stretching

A. Livne¹, E. Bouchbinder², B. Geiger¹* ¹ The Weizmann Institute of Science, Department of Molecular Cell Biology ² The Weizmann Institute of Science, Department of Chemical Physics * benny.geiger@weizmann.ac.il

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Abstract

Mechanical cues from the extracellular microenvironment play a central role in regulating the structure, function and fate of living cells. Nevertheless, the precise nature of the mechanisms and processes underlying this crucial cellular mechanosensitivity remains a fundamental open problem. Here we provide a novel framework for addressing cellular sensitivity and response to external forces by experimentally and theoretically studying one of its most striking manifestations – cell reorientation to a uniform angle in response to cyclic stretching of the underlying substrate. We first report on extensive new experiments of adherent cell reorientation under cyclic stretching and show that they cannot be quantitatively explained by existing models. We then propose a new theory which focuses on the cell's stored elastic energy, corresponding to a 2D anisotropic linear elastic material. The variation of this energy with the cell's orientation is shown to drive the dissipative reorientation process. Our theory is in excellent quantitative agreement with the complete temporal reorientation dynamics of individual cells, measured over a wide range of experimental conditions, thus elucidating a basic aspect of mechanosensitivity. It, moreover offers new venues for predicting and controlling cell behavior in response to mechanical cues from the microenvironment.