

STIFFNESS VERSUS PRESTRESS RELATIONSHIP AT SUBCELLULAR LENGTH SCALE: INSIGHT INTO CYTOSKELETAL CONTRIBUTIONS TO CELL MECHANICAL PROPERTIES

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The ability of cells to regulate their vital functions, including mechanotransduction, migration, spreading and invasion, demands that cells can easily adjust their rigidity both globally, at the whole cell level, and locally, at the subcellular level [1]. It has been observed that on average cell stiffness increases approximately linearly with increasing cytoskeletal contractile stress (prestress) [2-4]. Those observations have been often interpreted in terms of the cellular tensegrity model [2]. Ingber postulated that cells can use this tensegrity mechanism locally in order to regulate their functions globally [1]. If so, then the linear relationship between stiffness and prestress must extend to subcellular variations. However, experimental evidence to support this claim is lacking. One reason is that generating detailed maps of intracellular prestress and stiffness distributions with subcellular resolution at the same time is a technically difficult task. Therefore, past attempts to map subcellular prestress and stiffness distributions had to rely on some *a priori* assumptions regarding the nature of those distributions.

In this study we used biomechanical imaging to generate spatial maps of subcellular shear modulus and prestress distributions [5]. This technique is based on the ability to measure traction forces that arise at the cell-substrate interface, while simultaneously observing cell deformation, combined with capability to solve an elastic inverse problem to find cell shear modulus and prestress distributions. We demonstrated the application of this technique by carrying out detailed mapping of the shear modulus and cytoskeletal prestress distributions of living 3T3 fibroblasts, making no *a priori* assumptions regarding those distributions or the correlation between them. From these distributions, we obtained relationships between local

shear modulus and prestress for individual cells.

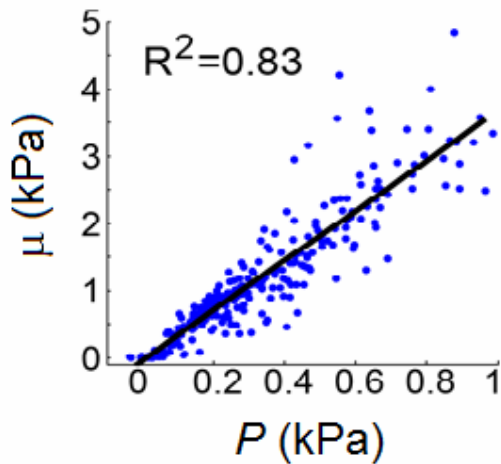


Figure 1. A typical subcellular shear modulus (μ) vs. prestress (P) relationship obtained from biomechanical imaging of a 3T3 fibroblast cell.

We found that the shear modulus vs. prestress relationships at the subcellular level exhibited a positive linear correlation (Fig. 1), consistent with the behavior previously observed on the whole cell level. We used a microstructural model [6] to analyze the experimental data. Based on this analysis we concluded that a) microtubules may play an important role in the intracellular force balance and b) that they may have important contribution to the cellular shear modulus. Taken together, these findings suggest that the cytoskeleton of fibroblast cells may be viewed as a prestress-supported structure, consistent with the cellular tensegrity model.

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