Author's Accepted Manuscript

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PII: S1751-6161(17)30243-6
DOI: http://dx.doi.org/10.1016/j.jmbbm.2017.06.006
Reference: JMBBM2365

To appear in: *Journal of the Mechanical Behavior of Biomedical Materials*

Received date: 1 April 2017
Revised date: 27 May 2017
Accepted date: 5 June 2017

Cite this article as: Eóin Mcevoy, Vikram Deshpande and Patrick Mcgarry, Free Energy Analysis of Cell Spreading, *Journal of the Mechanical Behavior of Biomedical Materials,* http://dx.doi.org/10.1016/j.jmbbm.2017.06.006

Free Energy Analysis of Cell Spreading

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ABSTRACT
In this study we present a steady-state adaptation of the thermodynamically motivated stress fiber (SF) model of Vigliotti *et al*. (2015). We implement this steady-state formulation in a non-local finite element setting where we also consider global conservation of the total number of cytoskeletal proteins within the cell, global conservation of the number of binding integrins on the cell membrane, and adhesion limiting ligand density on the substrate surface. We present a number of simulations of cell spreading in which we consider a limited subset of the possible deformed spread-states assumed by the cell in order to examine the hypothesis that free energy minimization drives the process of cell spreading. Simulations suggest that cell spreading can be viewed as a competition between (i) decreasing cytoskeletal free energy due to strain induced assembly of cytoskeletal proteins into contractile SF, and (ii) increasing elastic free energy due to stretching of the mechanically passive components of the cell. The computed minimum free energy spread area is shown to be lower for a cell on a compliant substrate than on a rigid substrate. Furthermore, a low substrate ligand density is found to limit cell spreading. The predicted dependence of cell spread area on substrate stiffness and ligand density is in agreement with the experiments of Engler *et al.* (2003). We also simulate the experiments of Théry *et al*. (2006), whereby initially circular cells deform and adhere to "V-shaped" and "Y-shaped" ligand patches. Analysis of a number of different spread states reveals that deformed configurations with the lowest free energy exhibit a SF distribution that corresponds to experimental observations, i.e. a high concentration of highly aligned SFs occurs along free edges, with lower SF concentrations in the interior of the cell. In summary, the results of this study suggest that cell spreading is driven by free energy minimization based on a competition between decreasing cytoskeletal free energy and increasing passive elastic free energy.

Graphical abstract

Abbreviations

SF, Stress fiber; FA, Focal adhesion; RVE, Representative volume element

Keywords: Cell Spreading, Thermodynamically Consistent Active Model, Cytoskeletal Free Energy, Cell Adhesion, Finite Element

1. INTRODUCTION