SIMULATION OF STRESS FIBRES AND FOCAL ADHESION FORMATION OF CELLS ON GROOVED SUBSTRATES

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In this study we apply a coupled bio-mechano-chemical model for the analysis of the response of a cell layered on a grooved substrate. A model predicting the time evolution of stress fibres is coupled with a signal generation model [1, 2, 3, 4]. The model consists of two submodels: a model for the stress fibres growth and evolution, and a model for signal generation. The stress fibres model includes their formation in the presence of Ca^{2+} ions released from the endoplasmic reticulum, and their dissociation in the presence of the negative strain rates caused by contraction of the cytoskeleton. The signal generation model combines the release of inositol 1,4,5-triphosphate (IP₃) upon perturbation of integrins equilibrium, and the aperture of Ca^{2+} channels when IP₃ interacts with its receptor on the endoplasmic reticulum. The two biochemical models are coupled enforcing mechanical equilibrium between the forces generated by the stress fibres and the reaction of the focal adhesions, linking the extra cellular matrix to the substrate. The model provides means to interpret the dynamics of the interaction between the cell and the grooves, and can justify, many cell behaviours. It predicts the clustering of focal adhesions in the presence of grooves or asperity of the substrate, and relates them to the deformation of the integrins-ligands bond [5]. Also we show that the predicted orientation of the stress fibres, as a function of the grooves width is in good agreement with experimental observations described in the literature [6].

REFERENCES

 Deshpande, V.S. and McMeeking, R.M. and Evans, A.G. A bio-chemo-mechanical model for cell contractility. *PNAS*, Vol. 103, 17065, 2006.

- [2] Deshpande, V.S. and McMeeking, R.M. and Evans, A.G. A model for the contractility of the cytoskeleton including the effects of stress-fibre formation and dissociation. *PRSA*, Vol. 463, 787–815, 2007.
- [3] Deshpande, V.S. and Mrksich, M. and McMeeking, R.M. and Evans, A.G. A biomechanical model for coupling cell contractility with focal adhesion formation. *JMPS*, Vol. 56, 1484–1510, 2008.
- [4] Pathak, A. and Deshpande, V.S. and McMeeking, R.M. and Evans, A.G. The simulation of stress fibre and focal adhesion development in cells on patterned substrates. JRSI. Vol. 5, 507–524, 2008.
- [5] Hamilton, D.W. and Wong, K.S. and Brunette, D.M. Microfabricated discontinuousedge surface topographies influence osteoblast adhesion, migration, cytoskeletal organization, and proliferation and enhance matrix and mineral deposition in vitro. *Calc. Tiss. Int.*. Vol <u>78</u>, 314-325, 2006.
- [6] Lamers, E. and Frank Walboomers, X. and others. The influence of nanoscale grooved substrates on osteoblast behavior and extracellular matrix deposition. *Biomaterials*. Vol. **31**, 3307–3316, 2010.