15th International Symposium on Computer Methods in Biomechanics and Biomedical Engineering
and
3rd Conference on Imaging and Visualization
CMBBE 2018
P. R. Fernandes and J. M. Tavares (Editors)

Plenary Lecture

MODELLING AND MEASURING CELL-MATRIX MECHANICAL INTERACTIONS

Hans Van Oosterwyck[(1)], Tommy Heck[(1)], Alicia Izquierdo-Alvarez[(1)], Alvaro Jorge-Peñas[(1)], Christian Steuwe[(2)], Marie-Mo Vaeyens[(3)], Diego A. Vargas[(1)]

[(1)]**Biomechanics Section, Department of Mechanical Engineering, KU Leuven, Belgium**
hans.vanoosterwyck@kuleuven.be, tommy.heck@kuleuven.be, alicia.izquierdo@kuleuven.be, alvaro.jorgepenas@kuleuven.be, diego.vargas@kuleuven.be

[(2)]**Center for Surface Chemistry and Catalysis, KU Leuven, Belgium**
christian.steuwe@kuleuven.be

[(3)]**Biomechanics Section, Department of Mechanical Engineering, KU Leuven, Bahrain**
mariemo.vaeyens@kuleuven.be

Keywords: angiogenesis, cell mechanics, particle-based models

Summary: Cells mechanically interact with their extracellular matrix by adhering and applying force to it. These cellular forces play an important role in the dynamics of cell adhesion and migration as part of single cell or multicellular, collective behaviour and more in general can modulate cell signaling in a process called mechanotransduction. We have worked on microscopy-based methods of quantifying these cellular forces during single endothelial cell migration and vascular invasion. In vitro models compatible with live cell fluorescence microscopy imaging were established and time lapses of cell and matrix movements were recorded. The extracellular matrix was mimicked by the use of deformable natural and synthetic hydrogels. Cell-induced hydrogel deformations were calculated by registering positional information, coming either from hydrogel-embedded fluorescent beads or hydrogel fibers that were imaged label-free.

2D endothelial cell migration assays on polyacrylamide gels suggested that cell traction magnitude was affected by gel stiffness and adhesion proteins (collagen versus fibronectin), while force polarity was only affected by adhesion proteins and not by stiffness. When analyzing traction exertion at a subcellular scale, adhesion proteins were found to affect the distribution and dynamics of traction focal areas. These results are further analysed by computational models of single cell mechanics that deal with the discrete, spatially non-uniform nature of focal adhesion turnover, protrusion and stress fiber formation.

3D vascular invasion assays demonstrated complex, spatially non-uniform hydrogel deformation patterns around angiogenic sprouts into collagen. Highest deformations were found at the base and the tip of the sprouts and suggested that sprouts were mechanically interacting with the hydrogel as a force dipole along the sprout principal direction. Computational models of sprout-hydrogel mechanics and dynamics are created in order to further quantify force patterns. The models are based on smoothed particle hydrodynamics (SPH), resulting in a discretization of hydrogel viscoelasticity and degradation, cell cortex viscoelasticity and contractility, protrusion and adhesion dynamics. By model fitting the measured deformation fields, the model is able to estimate the location and magnitude of cellular tractions. Simulation results also suggest that the observed long-range deformations require strain stiffening of the collagen hydrogels.

Acknowledgements: FP7/2007-2013)/ERC n° 308223