Motor-clutch model for substrate stiffness sensing and cell migration

Benjamin L. Bangasser[1], Steven R. Rosenfeld[2], David J. Odde[1]*
[1]University of Minnesota, Department of Biomedical Engineering, 312 Church Street SE, Minneapolis, MN 55455 USA, oddex002@umn.edu
[1]Cleveland Clinic, Brain Tumor and Neuro-Oncology Center, 9500 Euclid Avenue, Cleveland, OH 44195 USA
* Corresponding Author

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Abstract

Cells sense the mechanical stiffness of their environment to control cell shape, differentiation, survival, proliferation, and migration. How cells sense the mechanical properties of their environment to make these vital decisions is not clear. We recently showed that a simple "motor-clutch" model exhibits stiffness sensitivity (Chan and Odde, Science, 2008). In particular, the F-actin retrograde flow rate and traction force exhibit a biphasic response to substrate Young's modulus, an effect that we tested using embryonic chick forebrain neurons. We now further explore the behavior of the motor-clutch model, and assess which model parameters control the stiffness at which sensing is optimal. Our exploration of parameter space reveals that no single parameter in the motor-clutch model can strongly control the set-point for optimal stiffness sensing. Rather, parameters need to be changed coordinately to effectively change the set-point. In particular, coordinate increases of both motor and clutch numbers effectively increases the set-point stiffness (Bangasser *et al*., Biophysical J., 2013). Using a Master Equation approach, we also developed an analytical description of the model, and obtained a dimensionless number that defines the optimal substrate stiffness (Bangasser and Odde, Cell. Molec. Bioeng. 2013). Our recent experimental studies with glioma cells are consistent with predictions of the motor-clutch model. We speculate that the motor-clutch model may be useful for *in silico* identification of combination drug targets for brain cancers, and is generally applicable to animal cell adhesion and migration in 1D, 2D, and 3D environments.