Discrete modelling of focal adhesions building phenomenon during filopodium retraction.

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ABSTRACT

In order to advance in the comprehension of cell migration processes it is crucial to understand the mechanical cues that regulate the interaction between the extracellular matrix (ECM) and the cytoskeleton (CSK). These interactions are performed through molecular clutches known as focal adhesions or focal contacts and serve as anchoring points for the cell to migrate over them.

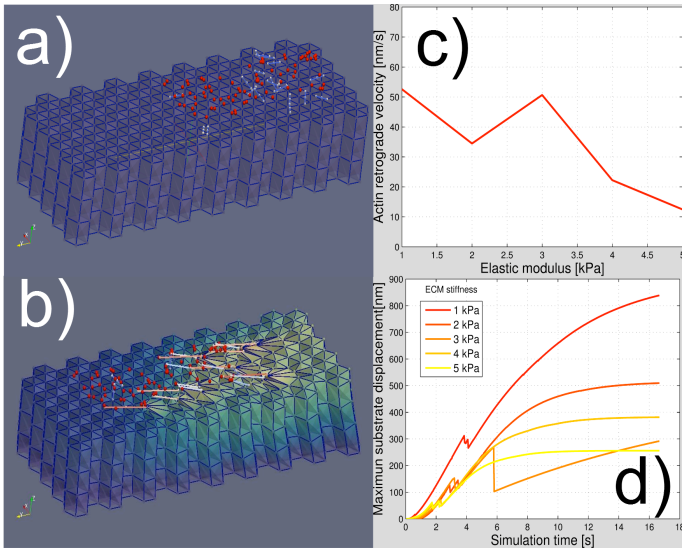

Figure 1. a,b) Model representation at 0s and 10s, respectively. Actin: red. Talin: purple. We can observe how adhesions are built along time; talin stretches under the force and transmits it to the substrate causing its deformation. c) Average actin speed depending on substrate stiffness. d) Evolution of substrate deformation along time for different substrate stiffness.

We propose a 3D discrete stochastic model that simulates an experimental assay of a cell migrating over a flat substrate. The aim of these experiments is to analyse the influence of different ECM substrate stiffness on filopodium actin retrograde velocity and substrate deformation.
The model is an extension of a previous 2D discrete approach[1]. It reproduces the focal adhesion building process during actin retrograded flow in filopodia protrusion. It is based on Brownian dynamics and it considers different proteins involved such as myosin, actin, talin or substrate ligands. Protein binding/unbinding, talin unfolding and clutch reinforcement are also simulated in the model.
The predictive potential of the model is tested through some experimental assays which complement previous studies[2]. Besides, we perform a sensitivity analysis for different conditions in order obtain a deeper insight of the phenomenon.

REFERENCES

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[2] Elosegui-Artola A, Bazellières E, Allen MD, et al. Rigidity sensing and adaptation through regulation of integrin types. Nat. Mater. 2014;13(6):631–7.