CELL SPREADING ON FIBROUS MATRIX PREDICTED BY HYBRID CELLULAR POTTS MODEL WITH DYNAMIC ADHESIONS

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Focal adhesion dynamics

The interaction between cells and the microenvironment plays an important role in health and disease. A key component of the microenvironment is the extracellular matrix (ECM), which consists of many small and large proteins that give mechanical support to cells and offers a medium for cell-cell communication [1]. Relative to the cell the ECM consists of fibers of size comparable to the cell. They can be mechanically connected to each other by crosslinkers. Cells adhere to and sense the ECM via mechanosensitive contact points called focal adhesions (FAs). FAs are large protein complexes, which dynamically assemble and disassemble under the influence of mechanical tension [2].

Recently, our group has developed a hybrid Cellular Potts and Molecular Dynamics Model that describes the mechanics of ECM fibers in detail (presented elsewhere in this conference). [2] Here, we extend this model by introducing mechanosensitive FAs between cells and ECM. The FAs are modelled individually (following [4]); they attach to individual fibers and assemble and disassemble dynamically based on the tension between them and the cell. This ensures that focal adhesions can mature on stiffer substrates where they endure a larger tension than compared with a soft substrate on which they quickly disassemble. Making the cell-ECM interaction explicit in this way extends the scope of possible study with this model. It makes it possible to study the interplay between network architecture and cell behavior by changing the average connectedness of the network. Here, we consider the effect of the network connectedness on the spreading behavior of a single cell. Furthermore, we find that the cell can reorient and restructure parts of its local environment.

Fiber recruitment and cell spreading

Activating the hybrid CPM with dynamic adhesions enables massive restructuring and reorientation of the ECM. On stiffer parts of the ECM, the cell deforms the ECM slightly and can use it as an anchor for further migration. On soft ECMs, however, the contractile forces of the cell deform the ECM completely. This can be seen in Fig 1, where fibers are fully pulled towards the cell.

Apart of reorienting and restructuring of the matrix we recognize the known effect of cell spreading on stiff matrices in our model. [5] We see that cell spreading increases by increasing the average number of crosslinkers per fiber. This statistic is used as a proxy for ECM stiffness.

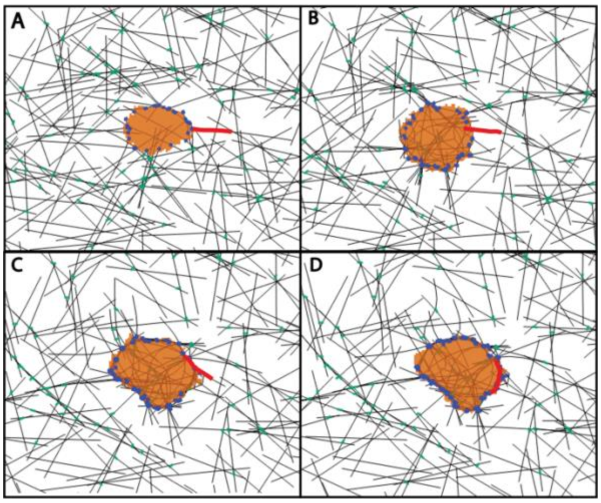

Figure 1: Recruitment of fibers by a simulated cell. From A-D a highlighted fiber is pulled inwards and place along the cells border.

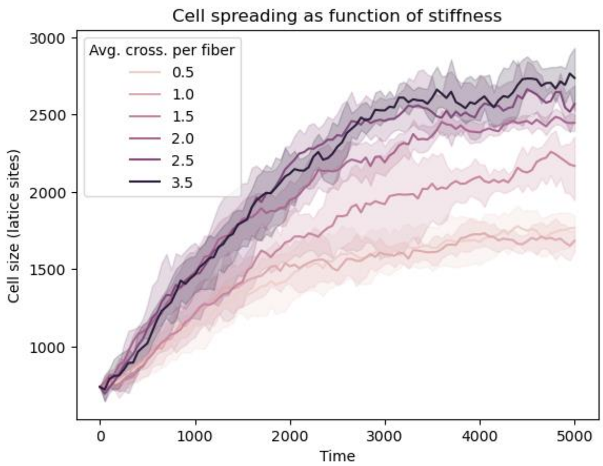

Figure 2: Increasing the number of crosslinker increases the overall cell area. This only occurs after the network is properly connected (after the average number of crosslinker per fiber is greater than 1.0).

References

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