Win, lose or tie: a computational model of the competition at the cell-ECM interface

Zeynep Karagöz[1], Thomas Geuens[1], Vanessa LaPointe[1], Martijn van Griensven[1], Aurélie Carlier[1]

z.karagoz@maastrichtuniversity.nl

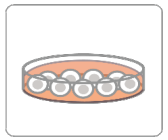
[1] Department of Cell Biology- Inspired Tissue Engineering, MERLN Institute, Maastricht University, the Netherlands

BACKGROUND: Biophysical cues provided by the extracellular matrix (ECM) are translated into biochemical signals by transmembrane integrin molecules. Previous studies suggest that fine-tuning the ECM composition and mechanical properties can improve organoid development.

METHODS

- Define ordinary differential equation model to represent biochemical reactions between integrins and extracellular ligands.
- Reaction rate parameters derived from literature, ECM ligand concentrations derived from proteomics analysis of kidney organoid ECM.
- Local perturbations and sensitivity analysis to define important parameters.

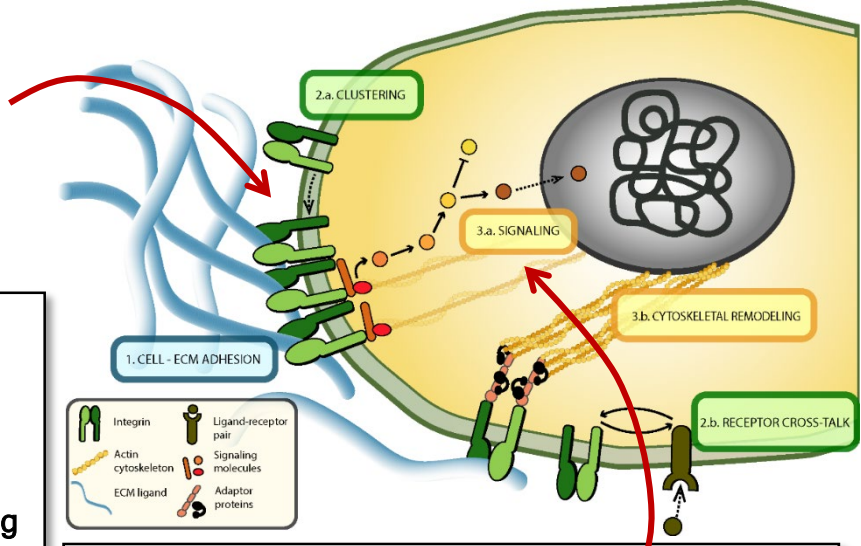
1-



Experimental observations:

- Kidney organoid development is disrupted after 18 days in cell culture
- Major changes in the composition of ECM

Need to understand how integrin signaling is affected by these changes to fine-tune the cell culture environment.



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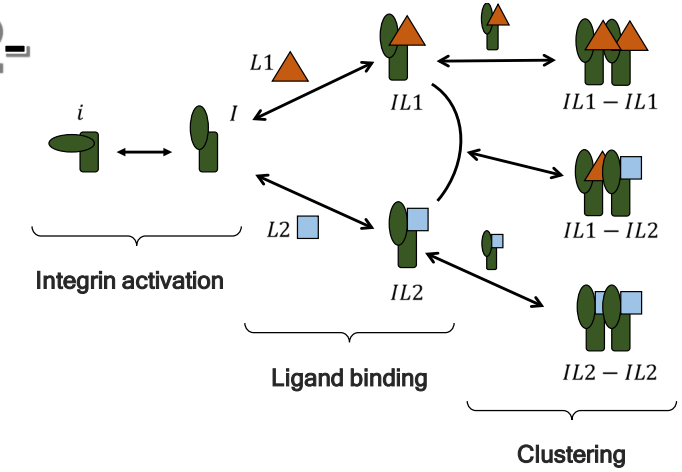

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- Changes in initial concentration of ligands affect the timing of binding
- Competition between ligands is driven by the difference in their binding rates.

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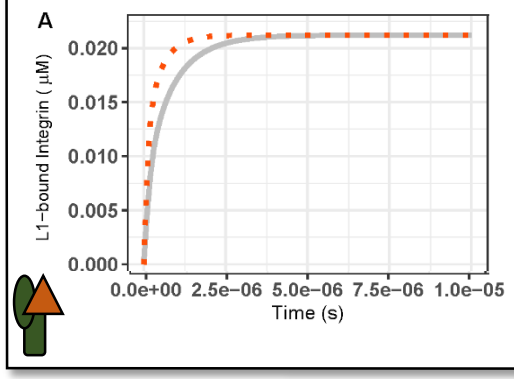
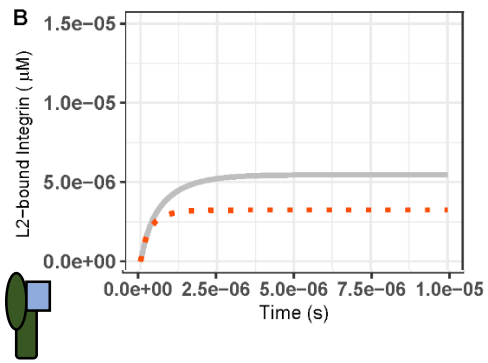
Up next:

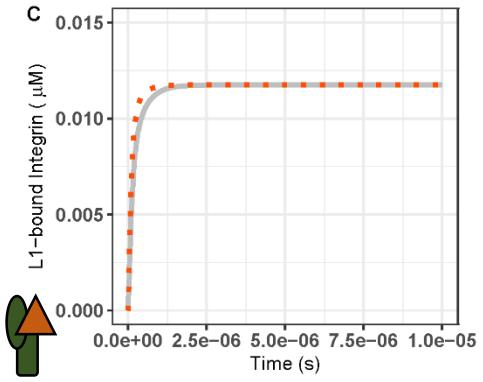
- Include cellular signaling to the model & obtain cellular behavior estimations (e.g. proliferation, differentiation, motility)

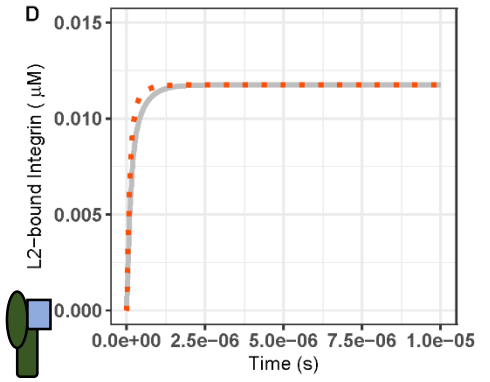
When ligands have different binding rates





When ligands have equal binding rates





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