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A Kappa model for hepatic stellate cells activation by TGFB1

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The understanding of the dynamics of HSC activation and regulation by TGFb1 is essential to identify markers and therapeutic targets likely to promote the resolution of fibrosis at the expense of its progression. Here we develop a combined model to characterize the dynamics of HSC activation and identify the key regulations.

Introduction

Kappa

- Rule-based language for modeling systems of interacting agents
- Proxies are graphical structures, rules are graph rewrite
- Rules locally modified the state of a system

Tools

- Stochastic simulation toolbox
  a. sample trajectory according to their probability density
  b. rules or a representation of the state of the system as a site graph
  c. set of events that may be applied in the current state is randomized

Model

Conclusions

- Normalized HSC (MFB) are key regulators
- TGFB1 is necessary to induce HSC activation but chronic stimulation by TGFB1 doesn’t allow to reach a fibrotic state characterized by persistent high level of ECM

Perspectives

Because ECM deposition induced by activated HSC and MFB lead to an increase of stiffness, which may also constitute a trigger for HSC activation, the two challenges will be the integration of a new agent ECM to take into account this information.