Interactive Epithelium

Documentation for version 1.0.0

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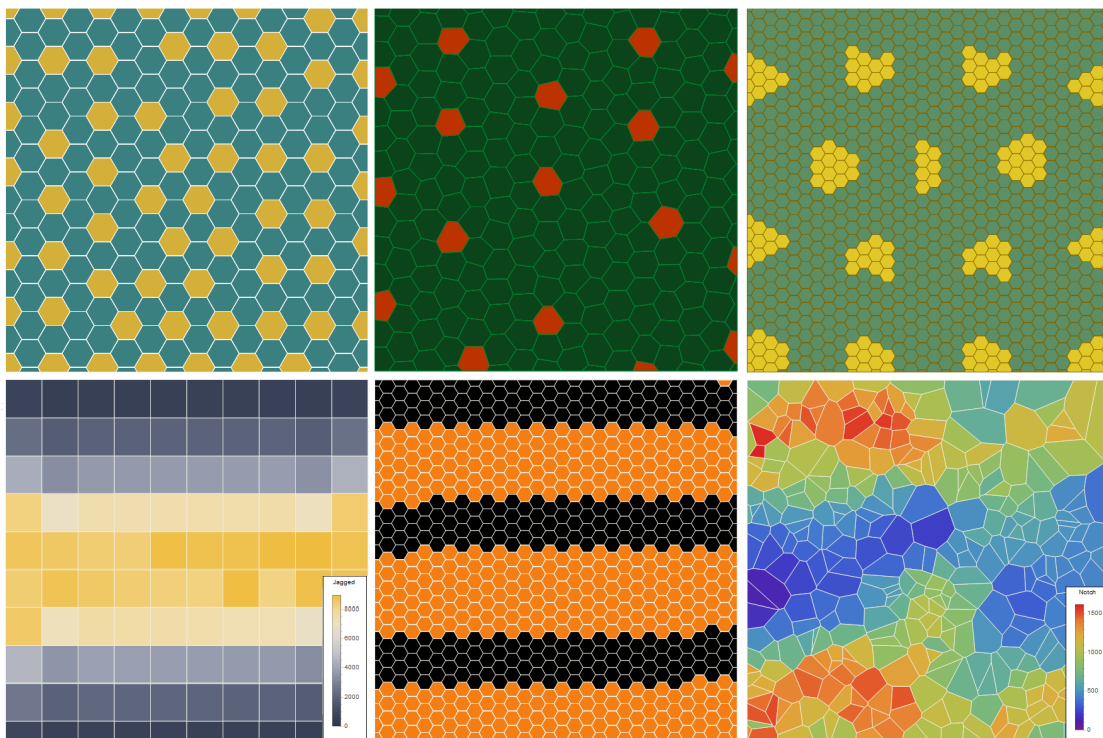University of Cambridge
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Figure 1: Examples of patterns in *Interactive Epithelium*.

1 Introduction

We introduce a new *Mathematica*-based software that enables modelling and simulations of hybrid intercellular signalling and mechanical properties of two-dimensional epithelial tissues. The code combines different mathematical models and simulation techniques to accurately reproduce the dynamics of these tissues in a variety of contexts. This approach allows for a more comprehensive understanding of the complex interactions between cells and the signalling pathways that drive tissue differentiation. Overall, the development of this software represents a significant advance in the field of tissue modelling and simulation, and it has the potential to greatly facilitate the study of epithelial tissue behaviour, for *Mathematica*-driven researchers.

Interactive Epithelium (IEp, version 1.0.0) aims to provide a practical tool for testing parameter robustness while simulating the dynamics of different signalling pathways in an epithelium. Among other features, the current version includes lateral inhibition, long-range signalling and stretching/compressing dynamics, with several parameters available for custom simulations. The main available models are the ϵ-Collier and Sprinzak models of juxtacrine signalling. This document provides a brief description of the interactive widgets available in IEp, together with the models of cell dynamics included in the current version. IEp was written in *Wolfram Mathematica* 13.0.1, so it is recommended that the same version is used.

Section 2 provides a brief description of the interactive widgets available in IEp. This section also contains some of the more technical information regarding the widgets, as well as some general remarks and known issues. Section 3 discusses the main widgets in detail. Finally, Section 4 references the main models in IEp.

To run IEp, open the notebook 'iEpithelium v1.0.0.nb' with *Mathematica*. Evaluate the cell group CODE first (Right Shift+Enter), and the remaining cells will be evaluated. Then, evaluate INTERACTIVEEPITHELIUM[] and the user interface will appear. Alternatively, reply 'Yes' to the message that pops up when first opening the notebook, to automatically evaluate the cells. See Section 5 for details on code availability. This code is far from perfect, containing some flaws discussed in Section 2.4.

2 User interface

IEp consists of two panels: an interactive panel with several widgets and an output panel that displays the simulation results (Figure 2). Default settings mainly show an animation of simulation, which can be tweaked in Options.
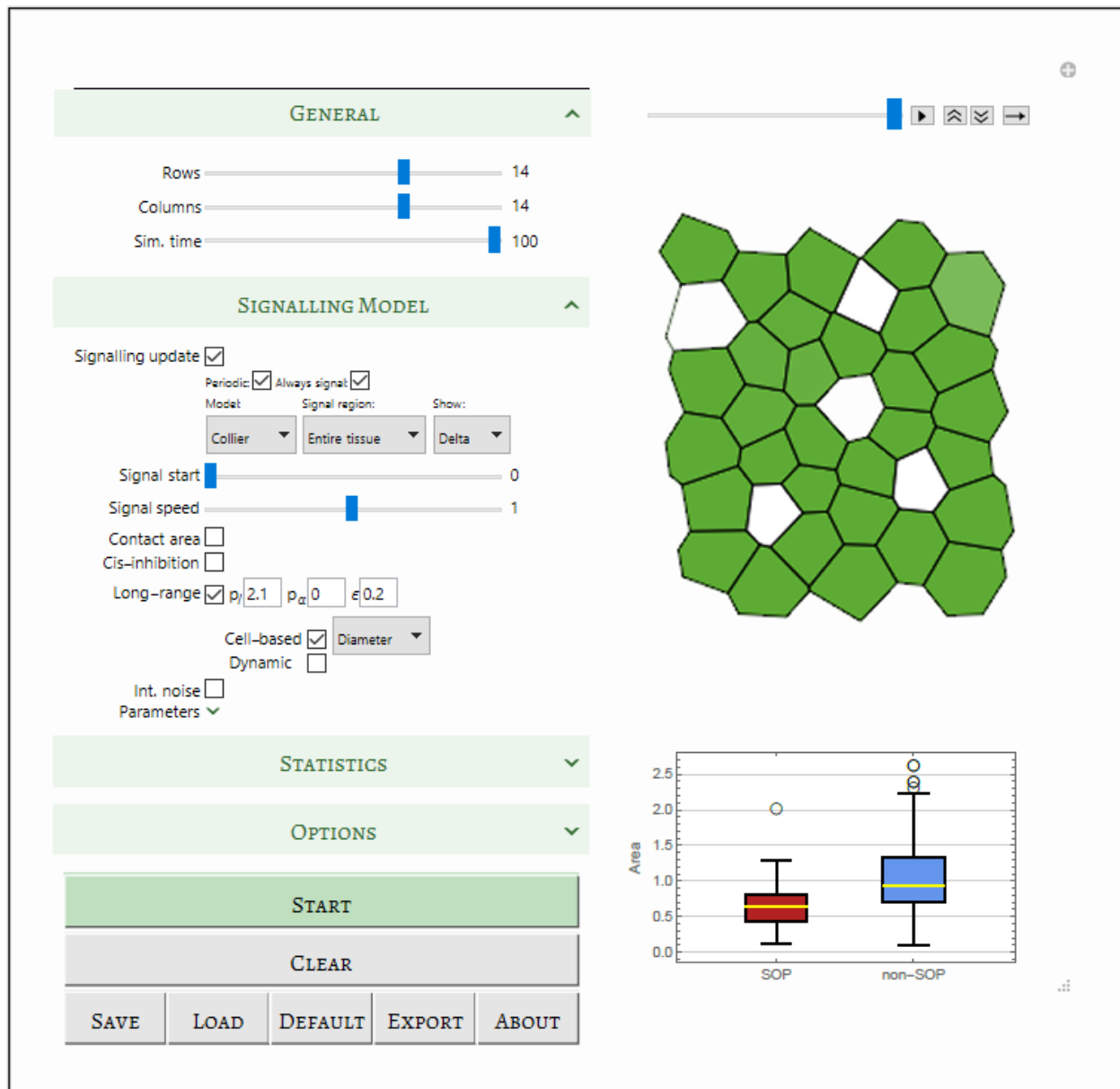

Figure 2: *Interactive Epithelium* user interface.
Two panels present interacting widgets in different sections and main buttons (left), and simulation outputs (right). Written in *Mathematica 13.0.1*.

2.1 Sections

The interactive panel is divided into multiple collapsing sections that help set up the modelling of the epithelium. Detailed on the widgets and parameters of each section can be found in Section 3. These sections are:

- GENERAL : Main lattice and simulation properties, including tissue dimensions and simulation time.

- SIGNALLING MODEL : Options for signalling models, including signalling region, marker details and model parameters. Noise and long-range signalling (ϵ-weighted model) are controlled in this section.

- STATISTICS : Analytical tools for statistics of SOP cells number, spacing, Delta activity, among others. Multiple simulations can be easily set up here, under different parameter ranges.

- OPTIONS : Detailed styling of tissues and customisation of exported files.

- SAVED MODELS : Contains all the saved models in the current session, allowing for a download of the save file in text form (see Section 2.3 on how to use this feature). This section emerges once a model is saved.
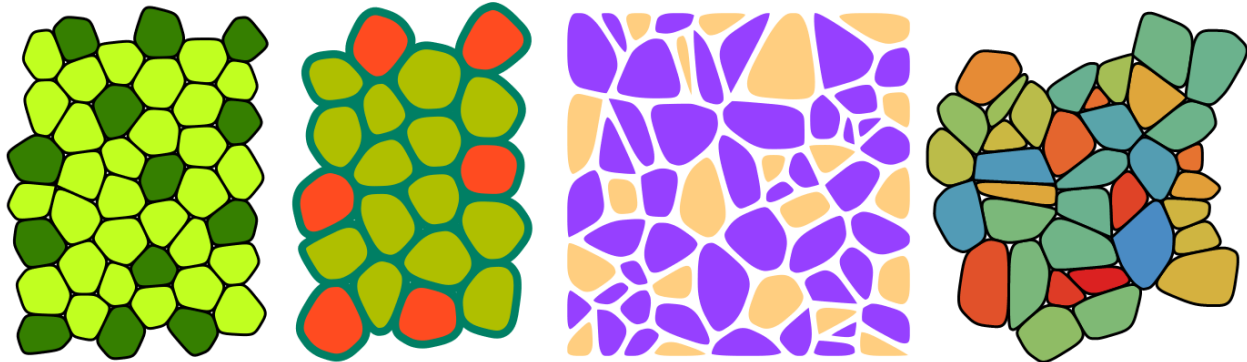

Figure 3: Styling in *Interactive Epithelium*.

2.2 Main buttons

Just below the different sections in the interactive panel, the main buttons used for simulation and model management are found. These include:

- Start : Performs the simulation given the parameters set in the multiple sections. This button is replaced by a Stop button when the simulation is ongoing.

- Clear : Clears the output window.

- Save : Saves the current parameter configuration.

- Load : Loads a set of parameters.

- Default : Resets the parameter values to their original values.

- Export : Exports the simulation results into `\Exports`, in image, video, and PDF formats.

- About : About section, detailing some of the elements in IEp, as well as various remarks and known issues.

2.3 Saving and loading

In the current version, the program is able to save the current set of parameters in list form (delimited by {}), in a text file under `\Models`. In order to load a specific model (or set of parameters), files must also be a list of parameters in a text file format similar to the file produced by Save.

2.4 Remarks, known issues and planned features

In the current version, the following might be taken into consideration for a smoother experience:

- Mouse over parameters will give you information on these;

- Press 'Save' to save current parameter configuration;

- Maximise window for better formatting.

Some known issues and planned features for IEp include:

- 'Stop' button fails early in simulation of large tissues;

- Exporting videos and images freezes the notebook, but it stops after a while;

- Occasional error messages of unknown source (try Quiet mode) ;

- Implementation of a vertex model;

- Implementation of signal periodic boundary conditions (if vertex model is periodic);

- Control over vertex model speed;

- Inclusion of iteratively defined tissues (from previous simulations).

3   Widgets and parameters

In this section, we present some of the main widgets and parameters available in IEp, as shown in Table 1. In addition to the modelling widgets, an editor for custom lattice generation was also implemented in IEp, accounting for a watershed-based image processing algorithm.

Section/Widget	Description	Type
GENERAL		
Rows	Number of rows in lattice	Integer
Columns	Number of columns in lattice	Integer
Sim. Time	Total simulation time	Integer
Signalling Model		
Horizontal/vert. factor	Stretch/compression factors in both axes	Real
Periodic	If checked, signalling is periodic (lattice is forced to be a torus)	Boolean
Always signal	If checked, signalling is constant (throughout the entire simulation)	Boolean
Model	Sets the type of signalling model (Collier or Sprinzak)	Popup menu
Signal region	Sets the region for signalling (whole tissue or double-stripe)	Popup menu
Show	Sets the marker (Notch or Delta)	Popup menu
Signal start/end	Sets the beginning and end of signalling simulation	Integer
Contact area	If checked, area contact is taken into account regarding juxtacrine signalling	Boolean
Cis-inhibition	Allows for cis-inhibition effects in the model	Boolean
Long-range	Allows for long-range signalling (in the theoretical form of protrusions). Length, noise and overall protrusion dynamics are editable here	Boolean/Reals
Signal parameters	Parameters of the signalling model	Reals
Statistics		
Plots	Plots regarding different statistics are computed (number, spacing, signal levels, among others)	Booleans
Random/Seed	Sets the random seed of the session (if fixed, all stochastic effects remain the same on different simulations)	Boolean/Integer
Tissues	Sets the number of tissues of repeating simulations	Integer
Multiple tests	Allows for a set up of multiple simulations with different ranging parameters	Boolean/Reals
Options		
Animation	If unchecked, only the last frame will be shown	Boolean
Tissue styling	Options for tissue styling, including colours and roundness of cell edges	Reals
Saved models		
Down arrow	Downloads the model into a text file containing the list of parameters	Buttons
Buttons	Deletion and simulation of saved models	Buttons

Table 1: Widgets and parameters of *Interactive Epithelium* 1.0.0.

4 Models and figure reproduction

IEp provides several models which can be tested via a variety of interactive widgets regarding epithelium size and cell shape. Furthermore, many parameters may be changed in order to understand parameter robustness and their role on patterning and cell differentiation. The model of Notch-Delta signalling is based on the original Collier model [1] and is inspired by the models presented in [2, 3]. Research on the patterning mechanics of different body parts of the fruit fly *Drosophila melanogaster* is part of the motivation behind the development of IEp [4, 5, 6]. A full explanation of the features of this code will be presented in the detailed documentation of IEp, on a future publication.

5 Code availability statement

The source code of IEp is available on a repository hosted on GitHub:
https://github.com/fberkemeier/Notch-Delta-Coupling-Dynamics.git.
Previous versions are available upon request. For any comments/suggestions, as well as copyright issues, please contact me at fp409@cam.ac.uk.

References

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