Simulating Organogenesis in COMSOL

Parameter Optimization for PDE-based models

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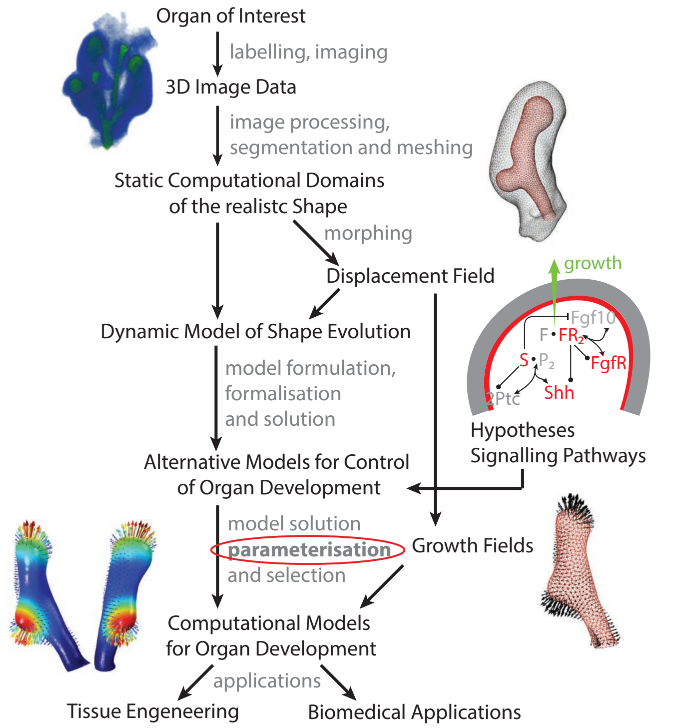
1 What are we doing?

Organogenesis is a process by which tissues develop and arrange into a complex organ. We are developing mechanistic models for a range of developmental processes with a view to integrate available knowledge and to understand mechanisms controlling morphogenesis. We have previously discussed how to build and solve data-based models for organogenesis in COMSOL.[1,2] Here we focus on the parametrisation of image-based[3,4] models for branching morphogensis.[5]

2 The Image-Based Modelling Approach



3 A Test Case - Simple Turing Type Model

We have previously proposed that a Turing type model based on receptor-ligand interactions governs lung and kidney branching morphogenesis.[3,6,7] The simplest form of such model is given by eq 1:

$$\dot{R} = \Delta R + (a - R + R^2 L)$$
$$\dot{L} = D\Delta R + (b - R^2 L) \quad (1)$$

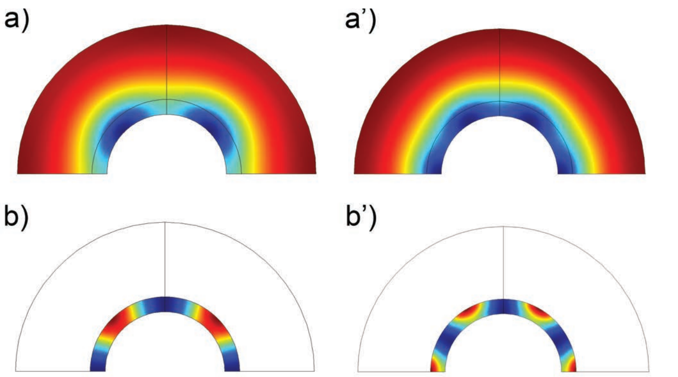


Figure 1. A steady state solution of a Turing type model on a two layer domain. Steady state distribution of a) the variable L and b) the variable R. D=100, a=0.3, b=0.5. Panels with and without apostrophe where calculated for γ=300 and γ=500 accordingly.

4 How Can We Recover Correct Parameter Values?

To test the optimization procedure we choose to optimize parameter values to reproduce the distribution of R^2L along the epithelium-mesenchyme border. We constructed the following cost function (eq 2):

$$\Delta = \sqrt{\int_L (R_0^2 L_0 - R^2 L)^2 dl} \quad (2)$$

We sampled a hundred points in a log uniform distribtuion: log(a): -2..0, log(b): 1.4..0.6 and log(γ): 1.4..3.4. Next we used these points as initial values for optimization solvers SNOPT and Coordinate Search. Figure 2 shows that both optimization solvers can recover the correct values of parameters only from a confined region of the parameter space.

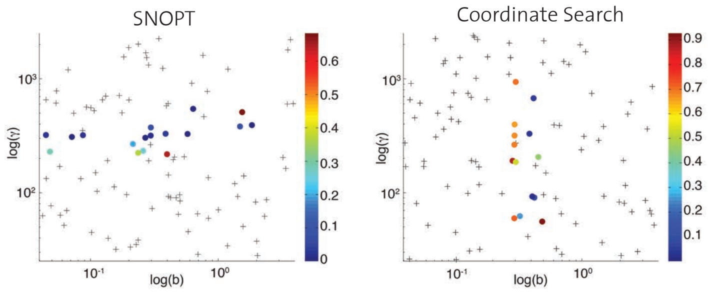


Figure 3. Convergence of the Optimization Solvers. Projection of the parameter space on b-γ plane. Points and crosses depict initial values for the optimization solver which lead to the convergence and failure of the solver, accordingly. Color code shows value of the objective function at the end of the optimization.

The tested optimization solvers cannot corectly recover parameter values of the test model. To overcome this problem we used the following approch: a) sample parameter space from log uniform distribution; b) calculate cost function and choose points with the minimal value; c) use chosen points as a starting condition for the optimization solver.

5 Applications: Kidney Brnaching Morphogensis

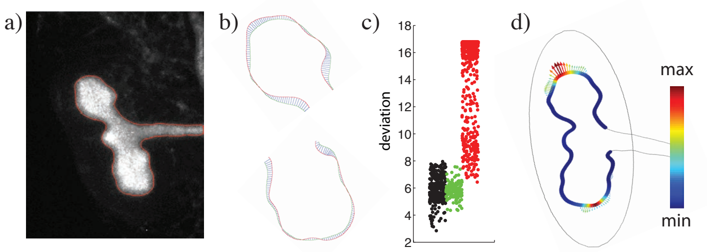


Figure 4. a) A snapshot from the time lapse movie; red line indicates the extracted border of the kidney epithelium; b) enlarged parts of the kidney explant and the calculated displacement field (blue), green and red lines show kidney shape in the earlier and later frames, accordingly; c) deviation (eq 2) for the points in the Turing space (black), intermedidate (green), and out of the Turing space (red); d) distribution of R^2L on the epithelium-mesenchyme border shown by the color code, arrows indicate the experimental growth field.

The proposed model correctly recapitulates experimentally defined growth areas. We conclude that a receptor-ligand based Turing mechanism governs kidney branching morphogensis.

5 References

(1) Germann P, Tanaka S, Menshykau D, Iber D *Proc COMSOL Conf* 2011.
(2) Menshykau D, Iber D *Proc COMSOL Conf* 2012.
(3) Adivarahan S, Menshykau D, Michos O and Iber D. *CMSB* 2013.
(4) Iber D, Tanaka S, Fried P, Germann Ph, Menshykau D *Meth Mol Biol 2013*.
(5) Menshykau D & Iber D *Open Biol 2013*.
(6) Menshykau D, Kraemer C. & Iber D *PLoS Comp Biol* 2012.
(7) Menshykau D & Iber D *Phys Biol* 2013

Excerpt from the Proceedings of the 2013 COMSOL Conference in Rotterdam