Simulating Organogenesis in COMSOL:
Parameter Optimization for PDE-based models

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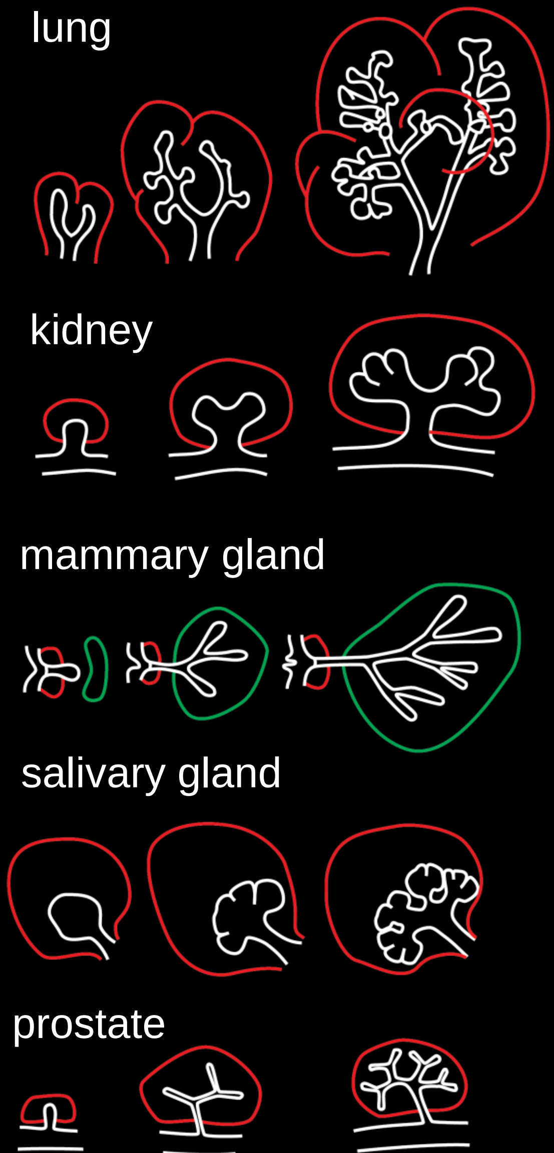
COMSOL
CONFERENCE
ROTTERDAM2013

Simulating Organogenesis in COMSOL

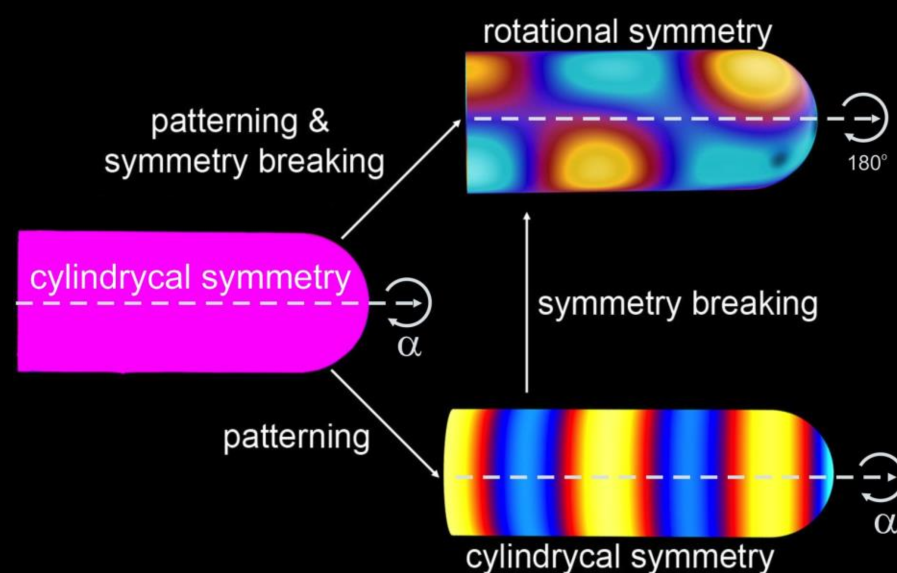
- Germann *et all 2011* Simulating Organogenesis in COMSOL
- Menshykau & Iber *2012* Simulation Organogenesis in COMSOL: Deforming and Interacting Domains
- Vollmer *et all 2013* Simulation Organogenesis in COMSOL: Cell-based Signaling Models
- Menshykau et all 2013 Simulating Organogenesis in COMSOL: Parameter Optimization for PDE-based models

Branching Morphogenesis



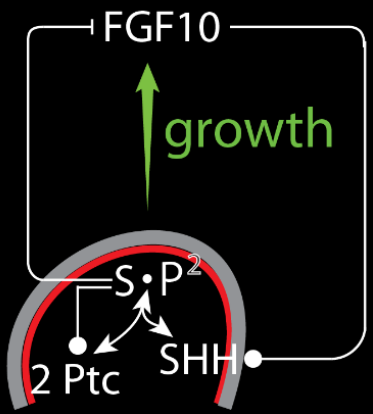
Thanks to Philipp Germann for the artwork!

Metzger *et al. Nature* 2008
Affolter *et al. Nature Reviews* Mol Cell Biology 2009

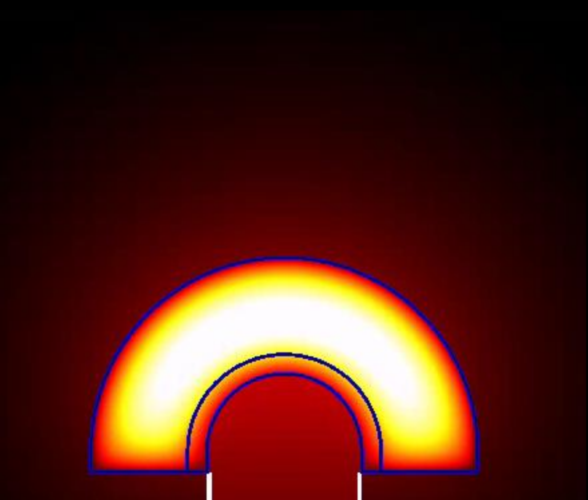


Iber & Menshykau *Biol Open* 2013

Lung Branching Point Selection

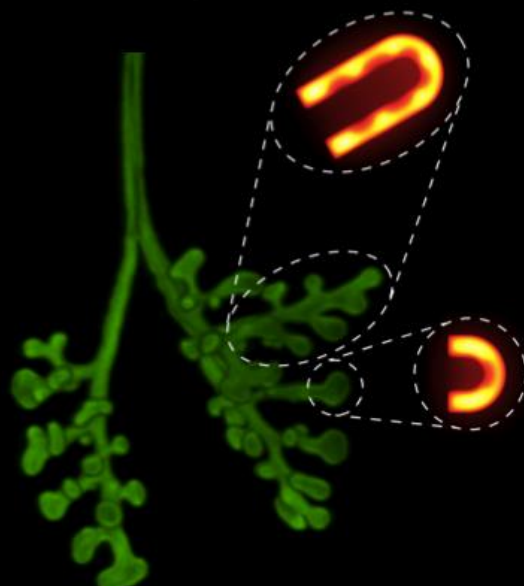


$$\dot{S} = D_{\mathrm{S}}\Delta S + \rho_{\mathrm{S}}\frac{F^n}{F^n+1} - \delta_{\mathrm{S}}S - \delta_{\mathrm{C}}P^2S$$
$$\dot{P} = D_{\mathrm{P}}\Delta P + \rho_{\mathrm{P}} - \delta_{\mathrm{P}}P + (\nu - 2\delta_{\mathrm{C}})P^2S$$
$$\dot{F} = \Delta F + \rho_{\mathrm{F}}\frac{1}{(P^2S)^n+1} - \delta_{\mathrm{F}}F$$

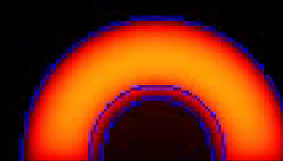


BIFURCATION

(video)



min FGF10 max

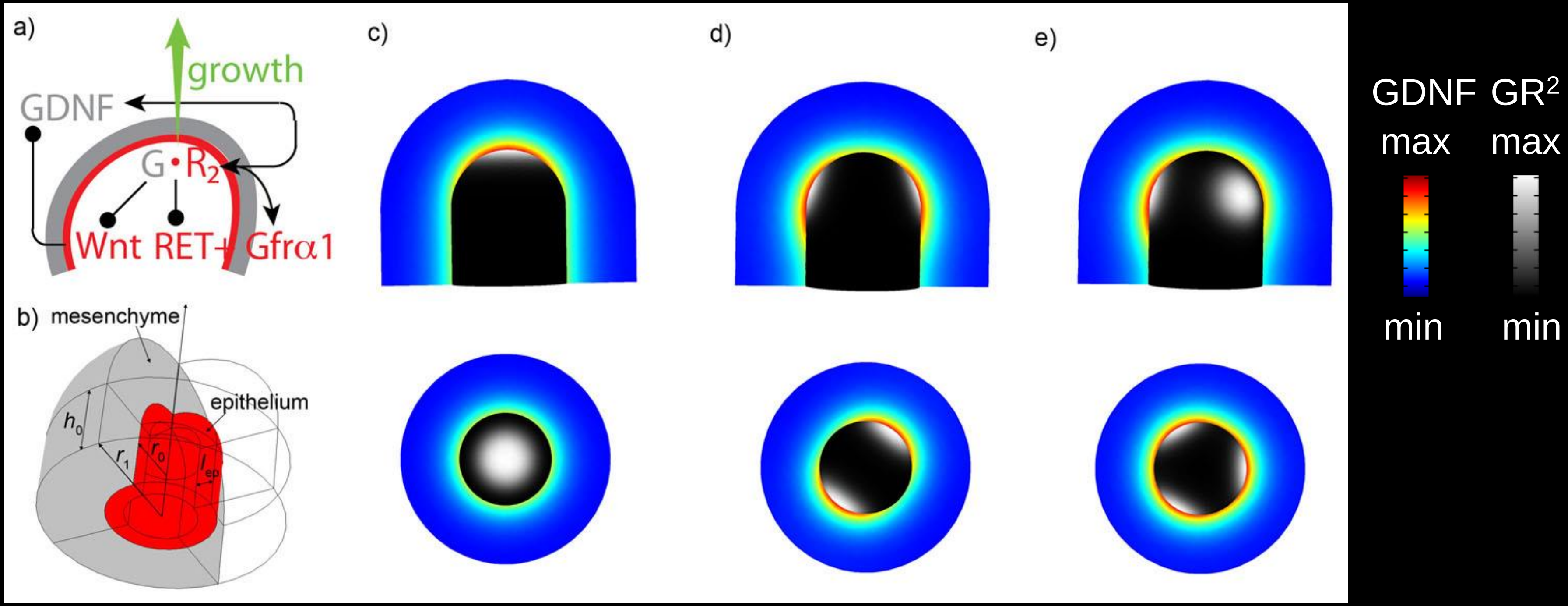


LATERAL BRANCHING

(video)

Menshykau *et al PLoS Comp Biol* 2012

Branching Point Selection During Kidney Branching



$$\dot{G} = \Delta G + \rho_{G0} + \rho_{G}\frac{W^2}{W^2+1} - \delta_{G}G - \delta_{C}R^2G$$

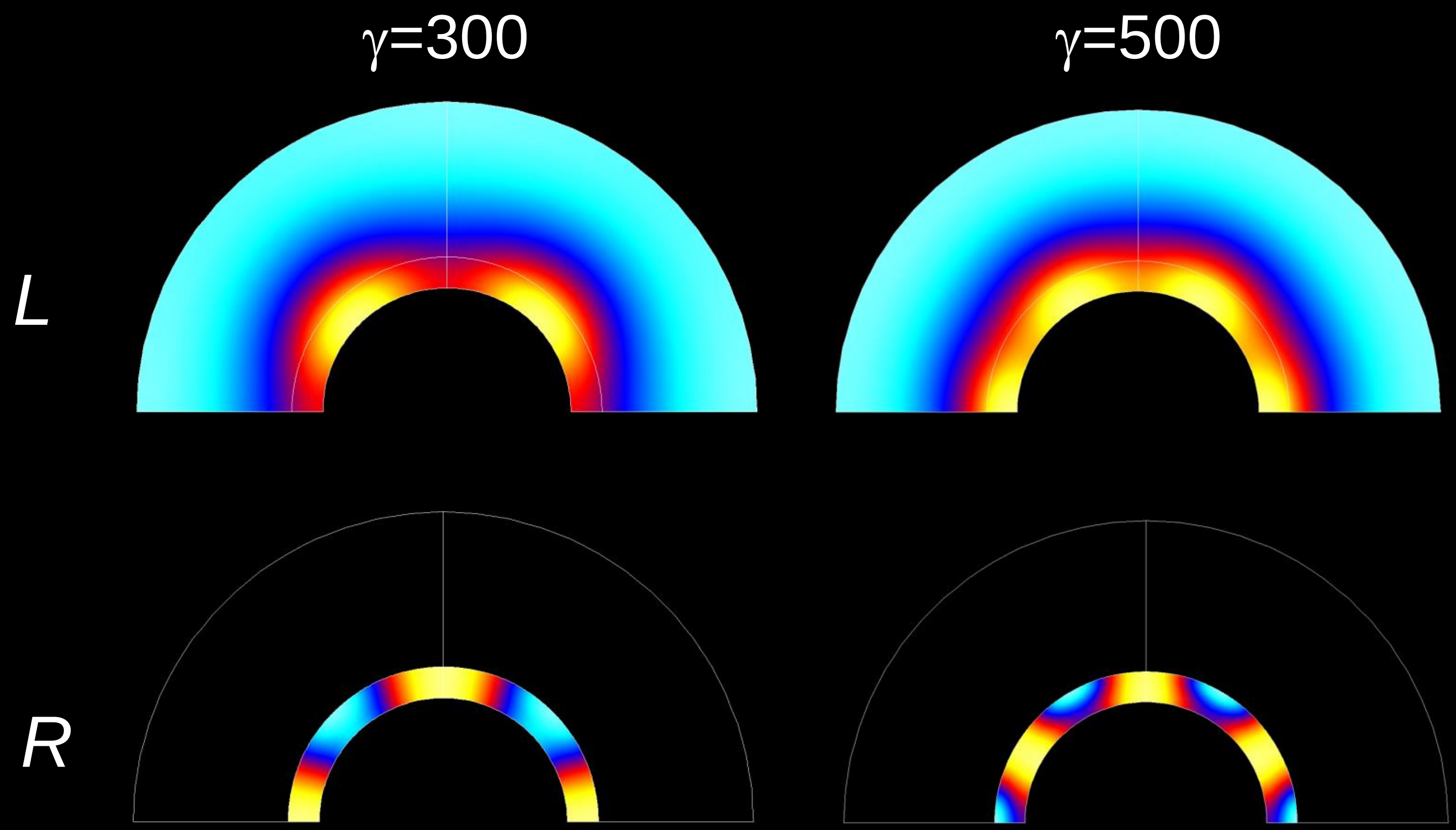
$$\dot{R} = D_{R}\Delta R + \rho_{R} + (\nu - 2\delta_{C})R^2G - \delta_{R}R$$

$$\dot{W} = D_{W}\Delta W + \rho_{W0} + \rho_{W}\frac{R^2G}{R^2G+1} - \delta_{W}W$$

Menshykau&Iber *Phys Biol 2013*

A Test Case – Simple Turing Type Model

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



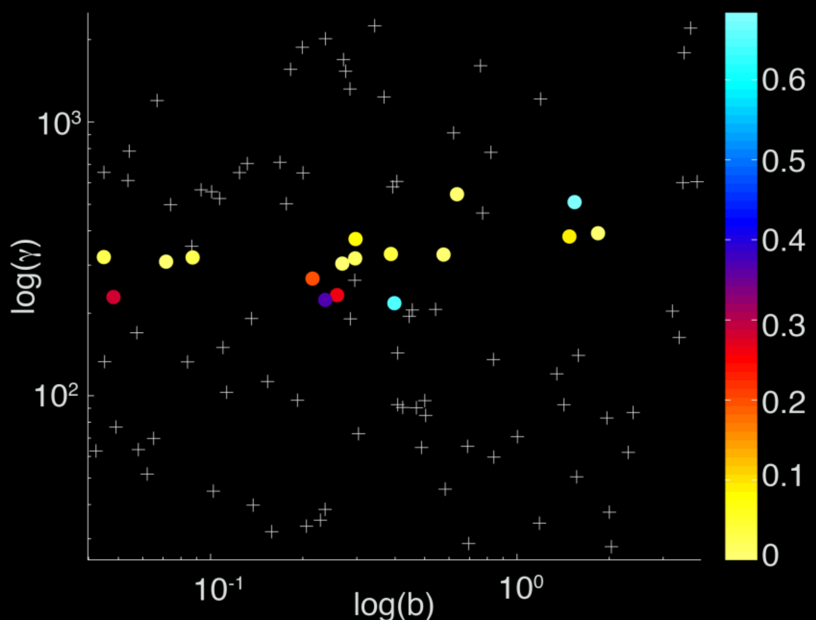
Menshykau et all *Proc Comsol Conf* 2013

How to Recover Correct Parameter Values?

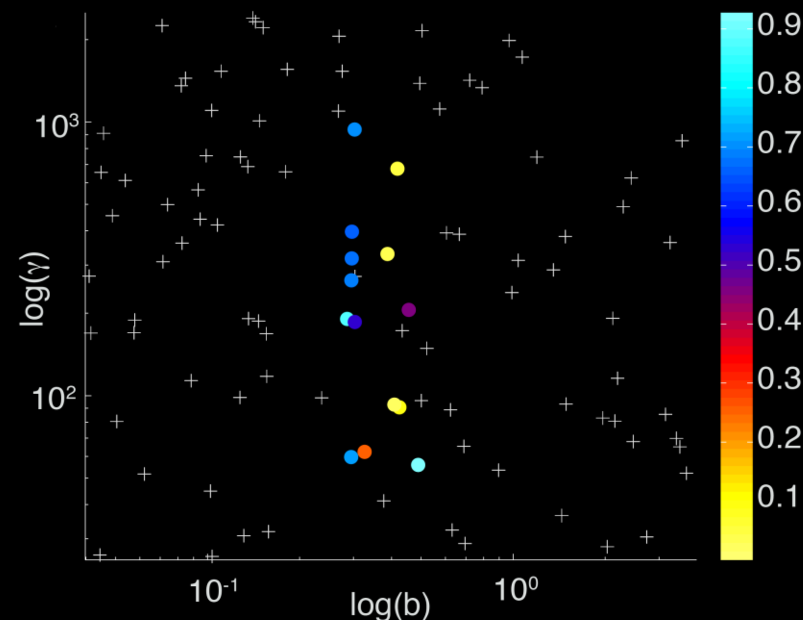
Cost function $\Delta = \sqrt{\int_L (R_0^2 L_0 - R^2 L)^2 dl}$

Via Matlab Live Link we sampled 100 points in a log uniform distribution. Next we used these points as initial values for optimization solvers

SNOPT



Coordinate Search

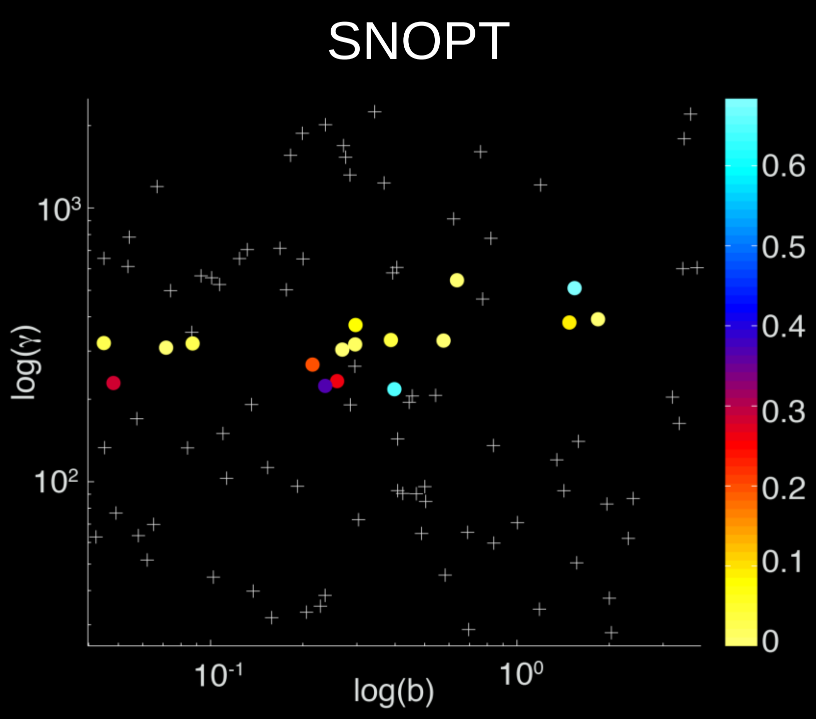


Menshykau et all *Proc Comsol Conf* 2013

How to Recover Correct Parameter Values?

Optimization strategy:

- sample parameter space from log uniform distribution;
- calculate cost function and choose points with the minimal value;
- use chosen points as a starting condition for the optimization solver.



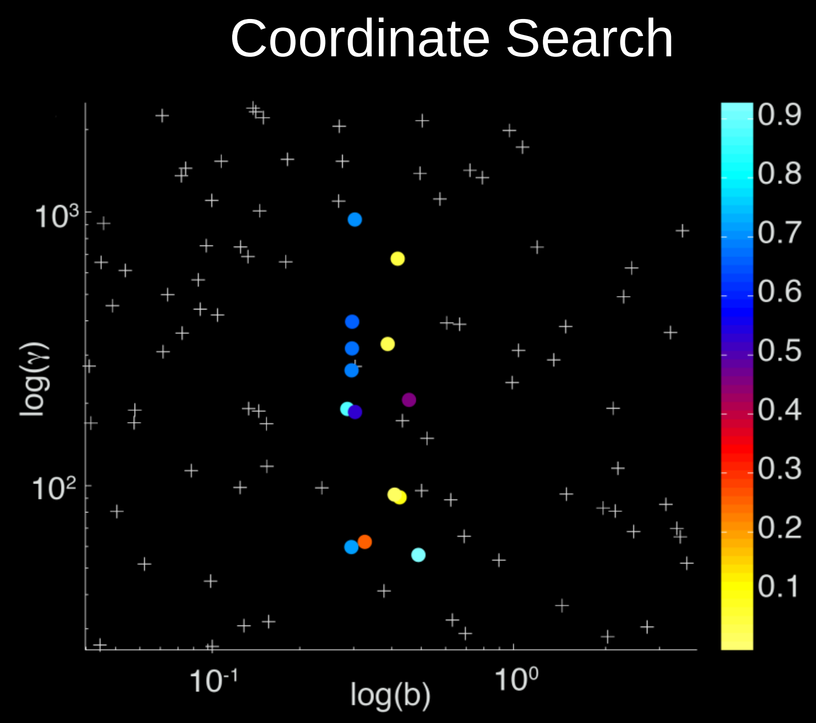


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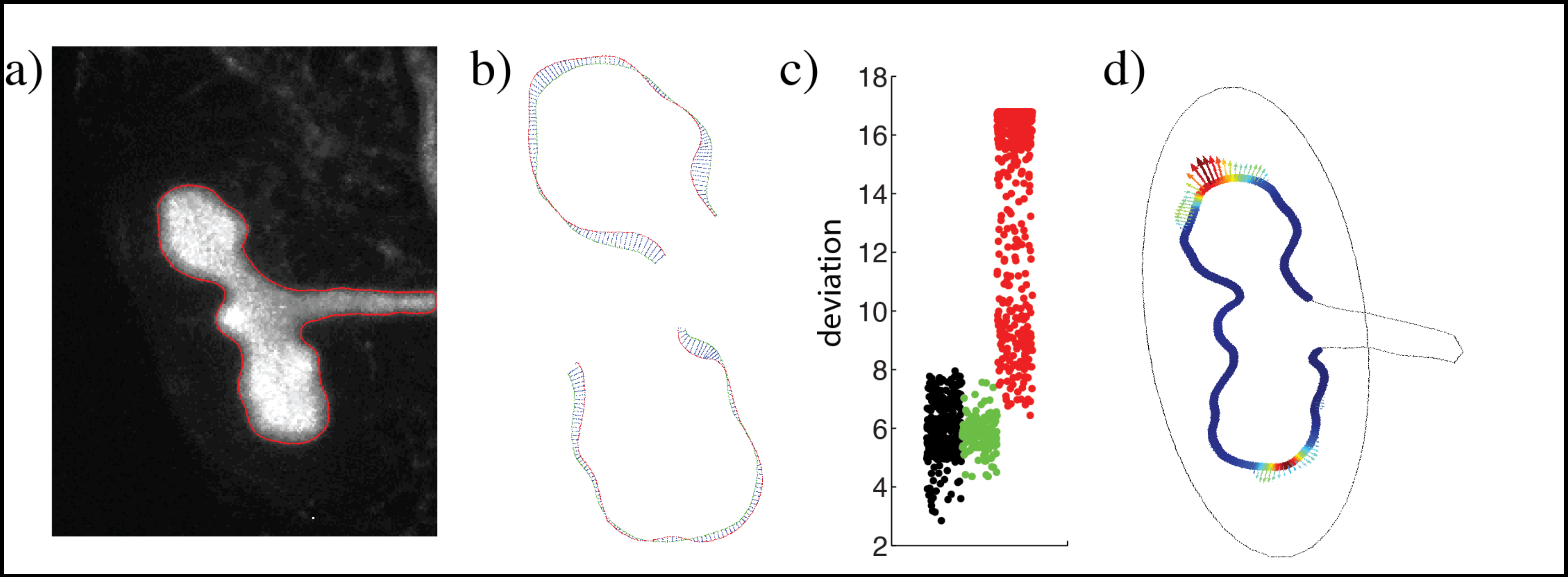
Image Based Modeling of Kidney Branching Morphogenesis



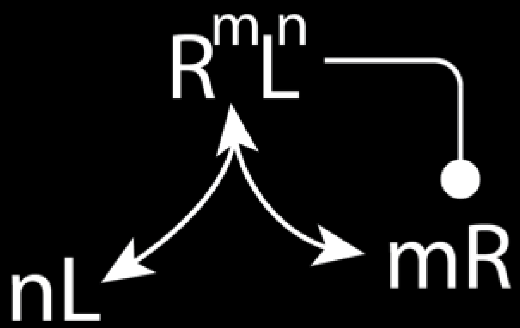
a) A snapshot from the time lapse movie; red line indicates the extracted border of the kidney epithelium; b) enlarged parts of the kidney explant and the calculated displacement field (blue), green and red lines show kidney shape in the earlier and later frames, accordingly; c) deviation (eq 2) for 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..

Menshykau et all *Proc Comsol Conf* 2013 Adivarahan et all CSMB 2013

Summary

Biology:

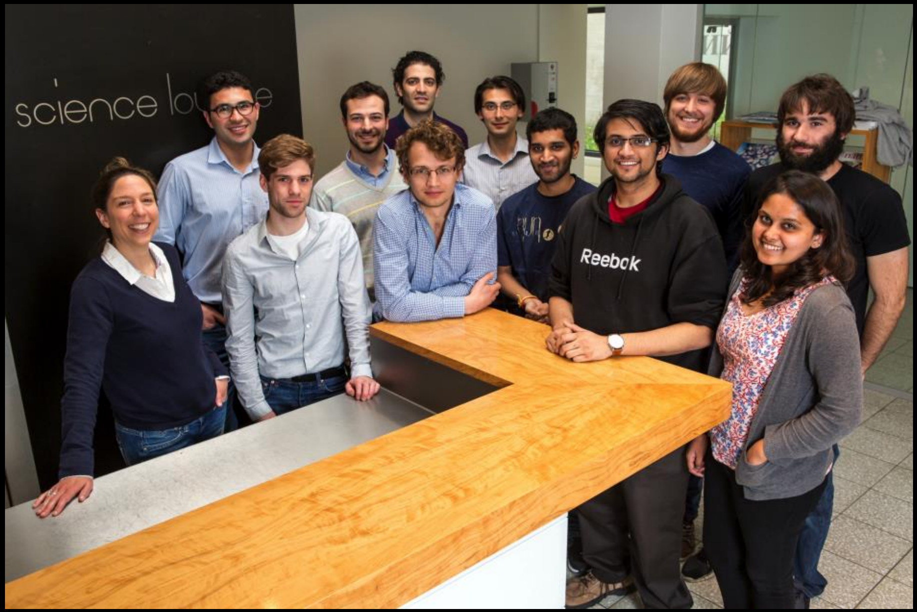
- the receptor-ligand interactions control domain patterning and branching via the Turing mechanism;



Methods

- image-based modeling approach is a powerful method to study mechanisms for organ development;
- the combination of random sampling with local optimization solvers is simple, yet efficient way to estimate parameter values and test alternative models;

THANKS!!



<u>Collaborators</u>

- Zeller group (U Basel)
- P. Blanc (Auvergne U)
- V. Sapin (Auvergne U)
- O. Michos (Sanger Institute)

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Swiss Federal Institute of Technology Zurich

SystemsX.ch
The Swiss Initiative in Systems Biology

SIB
Swiss Institute of Bioinformatics