Simulating Organogenesis in COMSOL: Deforming and Interacting Domains

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COMSOL CONFERENCE EUROPE 2012

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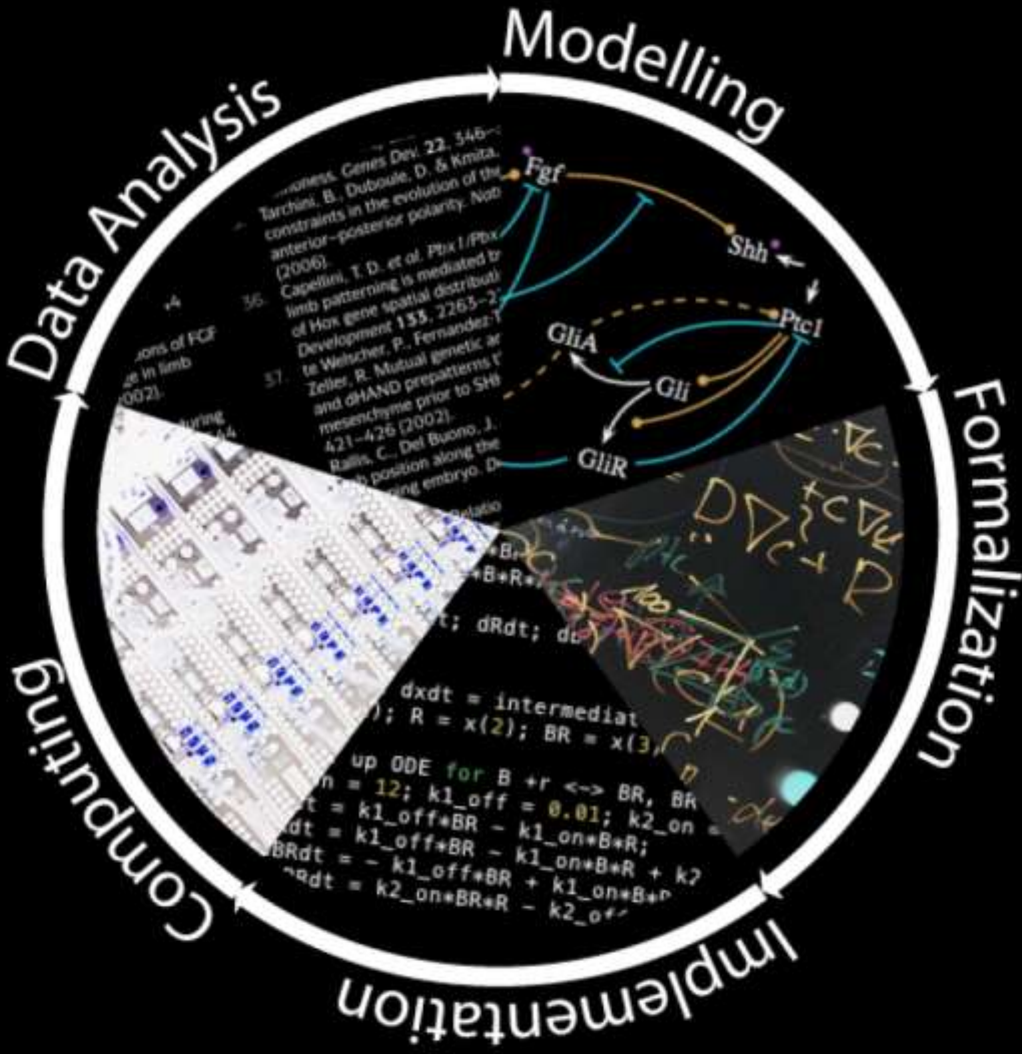
Work Flow


Modelling
Formalization
Implementation
Computing
Data Analysis

Building a Mathematical Model: overview

We use systems of reaction-diffusion (RD) equations

$$\dot{X} + \nabla(u \cdot X) = D_{\mathrm{X}} \Delta X + R_{\mathrm{X}}(X, Y, ...)$$
$$\dot{Y} + \nabla(u \cdot Y) = D_{\mathrm{Y}} \Delta Y + R_{\mathrm{Y}}(X, Y, ...)$$

...

Speed *u* might be given or might be a function of variables

We solve RD equations on 1D, 2D and 3D deforming and static domains

We have from 3 to 20 variables

The size of the problem is usually from 10 000 to 500 0oo DOF

Building a Mathematical Model: typical reactions

- Reaction diffusion equation based

$$\dot{X} = D\Delta X + R_X$$

- Simplest reaction is decay

$$R_X = -\delta X$$

- Often we have complex dynamics

$$R_L = -k_{on} \cdot L \cdot R$$

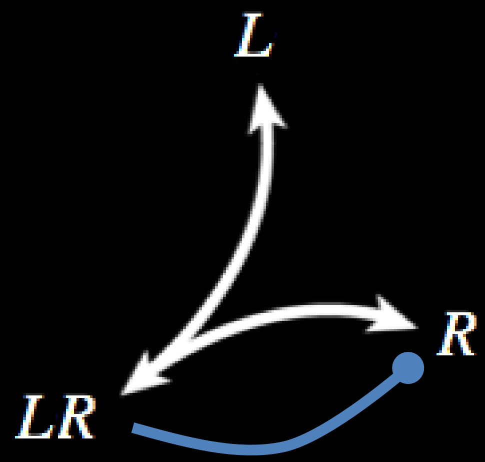
$$R_R = -k_{on} \cdot L \cdot R$$

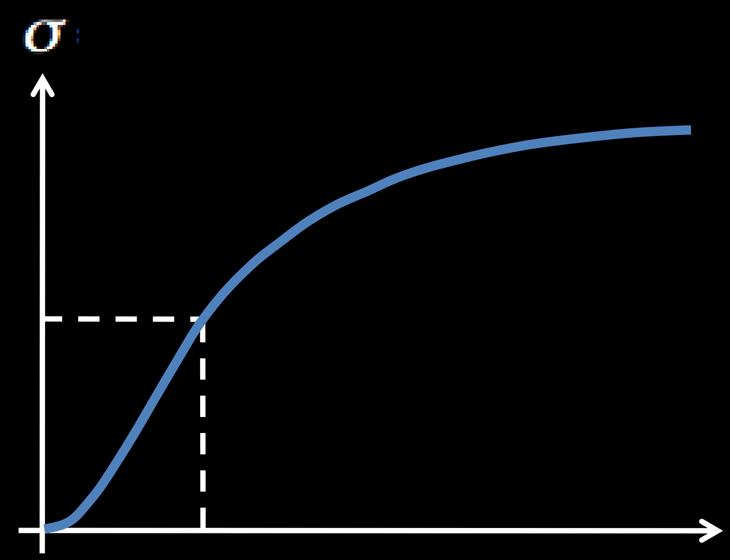
$$R_{LR} = k_{on} \cdot L \cdot R$$

- Or activation and inhibition respectively

$$\sigma = \frac{X^n}{X^n + K^n}$$

$$\bar{\sigma} = \frac{K^n}{K^n + X^n}$$





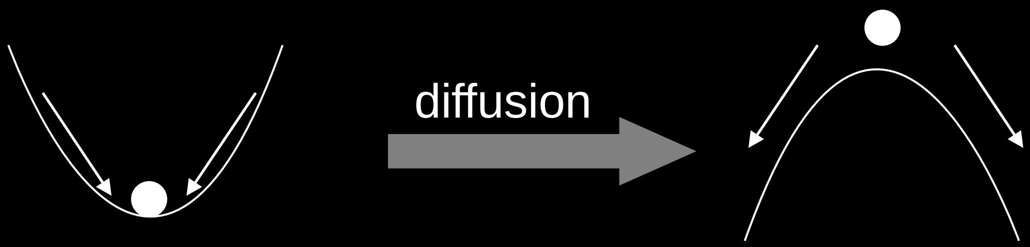
Optimizing COMSOL models on a constant domain

- 36 h using Sledgehammer method (smaller relative error, limited timesteps & Jacobian update at each iteration)
- ➢ Not acceptable for finding parameters and testing ideas efficiently
- 9 h removing discontinuities in production terms and initial conditions and relaxing solver settings
- < 3 h using cubic Lagrange elements (instead of quadratic) on a coarser grid
- 30 minutes using manual scaling for the error estimation, allowing for quadratic elements on coarser grids
- 5 minutes segregating the delicate complex formations from the rest

German *et al* Proc COMSOL Conf 2011

Turing Models

spatial patterns result from the diffusion-driven instability



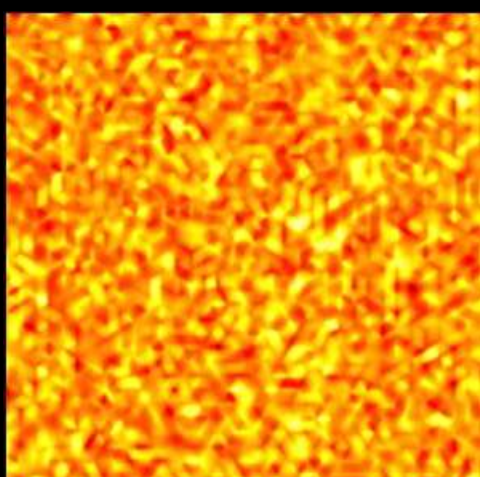
$$\dot{U} = \Delta U + \gamma(a - U + U^2 V)$$
$$\dot{V} = D\Delta V + \gamma(b - U^2 V)$$

$$\left(\frac{\partial f_{\mathrm{i}}}{\partial x_{\mathrm{j}}}\right)_{\mathrm{SS}}$$

no positive eigenvalues

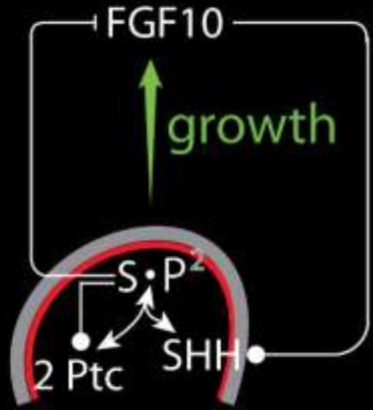
$$\left(\frac{\partial f_{\mathrm{i}}}{\partial x_{\mathrm{j}}} - k^2 D\right)_{\mathrm{SS}}$$

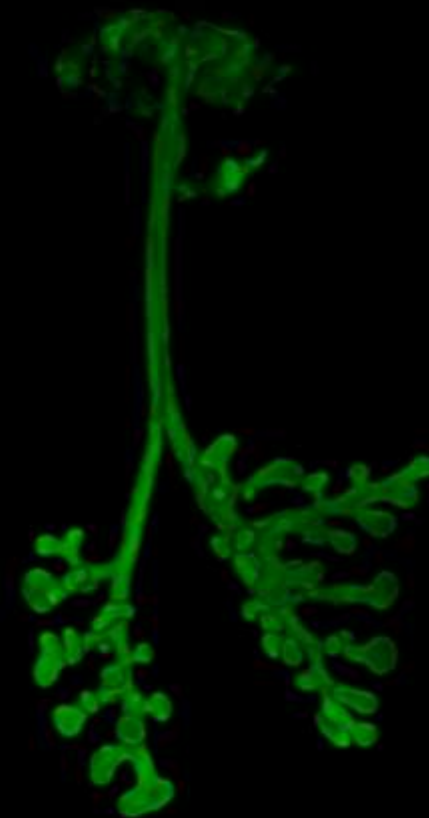
at least one positive eigenvalue



Kondo *et al.* Science 2010
Maini *et al.* Science 2006
Sick *et al.* Science 2006
Turing Phil Transact Royal Soc 1952

Branch Mode Selection during Early Lung Development





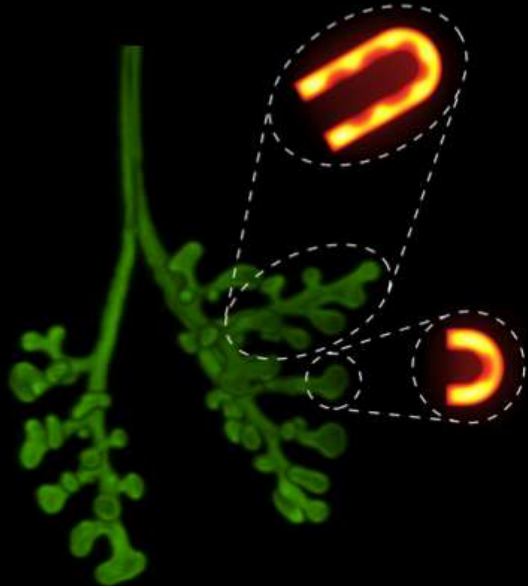
$$\dot{F} = \Delta F + \rho_{\mathrm{F}} \frac{1}{(P^2 S)^n + 1} - \delta_{\mathrm{F}} F$$

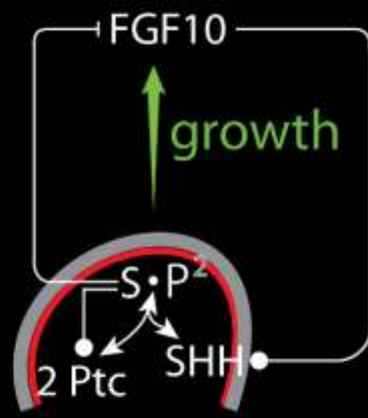
$$\dot{P} = D_{\mathrm{P}} \Delta P + \rho_{\mathrm{P}} - \delta_{\mathrm{P}} P + (\nu - 2\delta_{\mathrm{C}}) P^2 S$$

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

Menshykau *et al*, (2012) *PLoS Comp Biol*

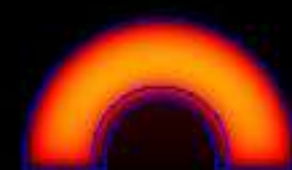
Lung Branching Point Selection





SLOW GROWTH

BIFURCATION

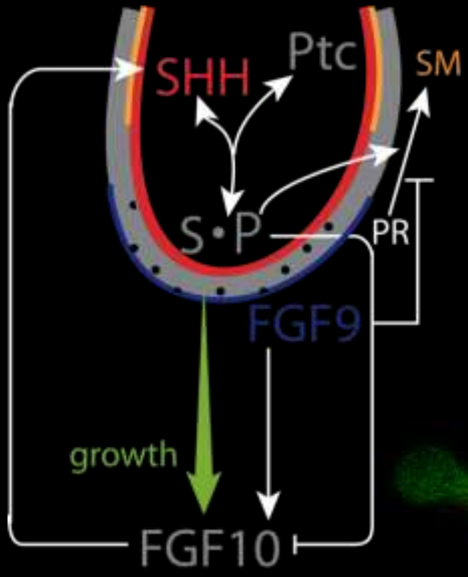


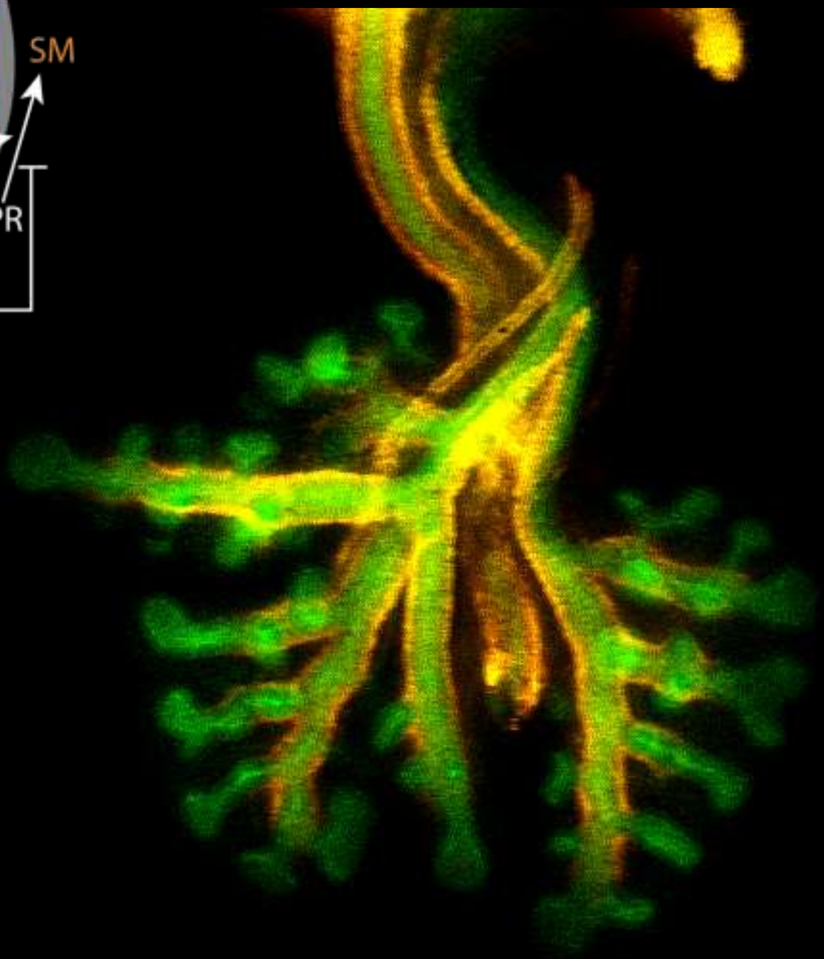
FAST GROWTH

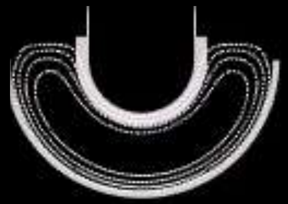
LATERAL
BRANCHING

Menshykau et al *PLoS Comp Biol* 2012

Smooth Muscle (SM) and Vein Formation







min SM max

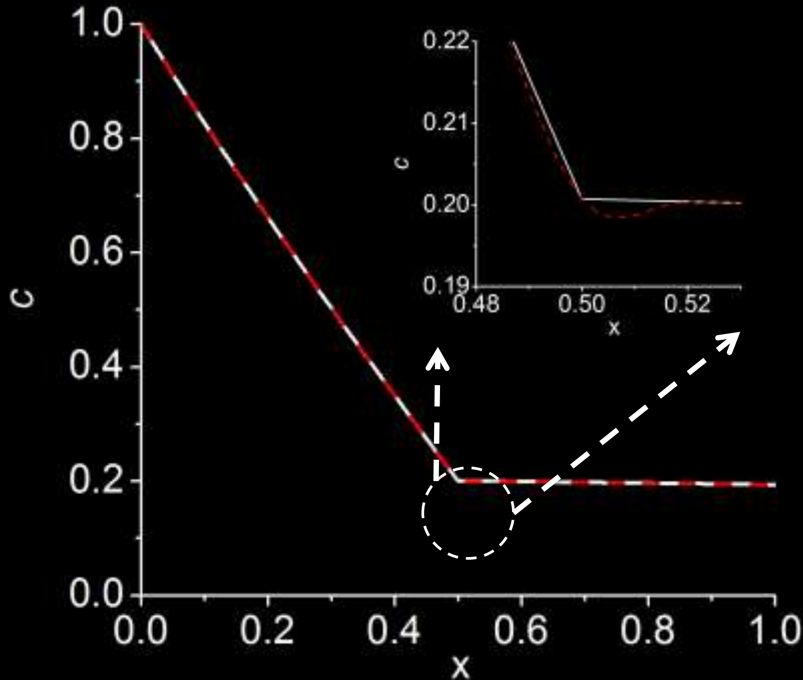
Celliere *et al OpenBiol* 2012

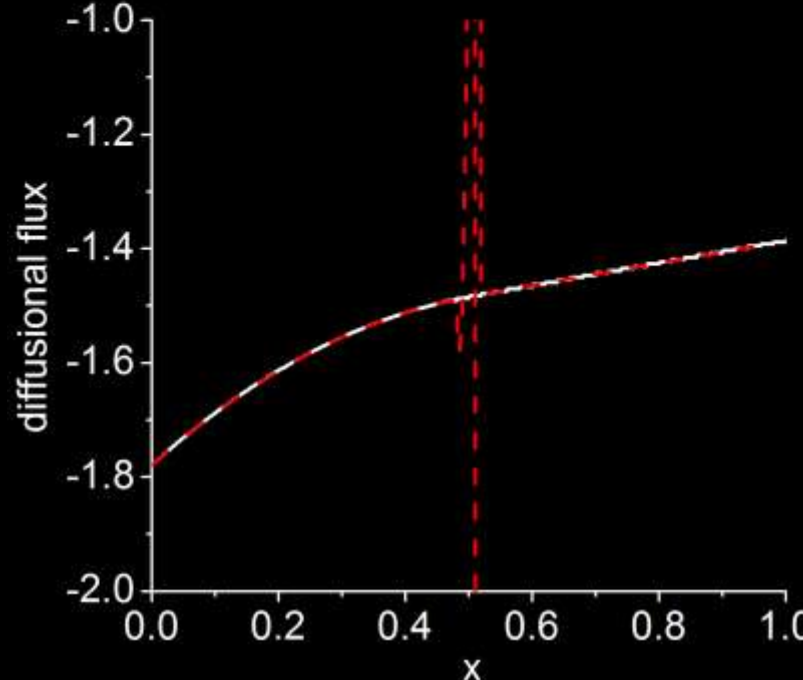
Reaction-Diffusion on a Static Composite Domain

Global PDE: $\dot{L} = D_\mathrm{i}\Delta L - \sigma L$

Coupled Local PDEs:

$$\dot{L}_1 = D_1\Delta L_1 - \sigma L_1$$
$$\dot{L}_2 = D_2\Delta L_2 - \sigma L_1$$
$$L_1 = L_2$$

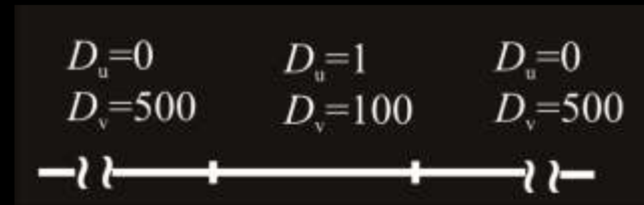


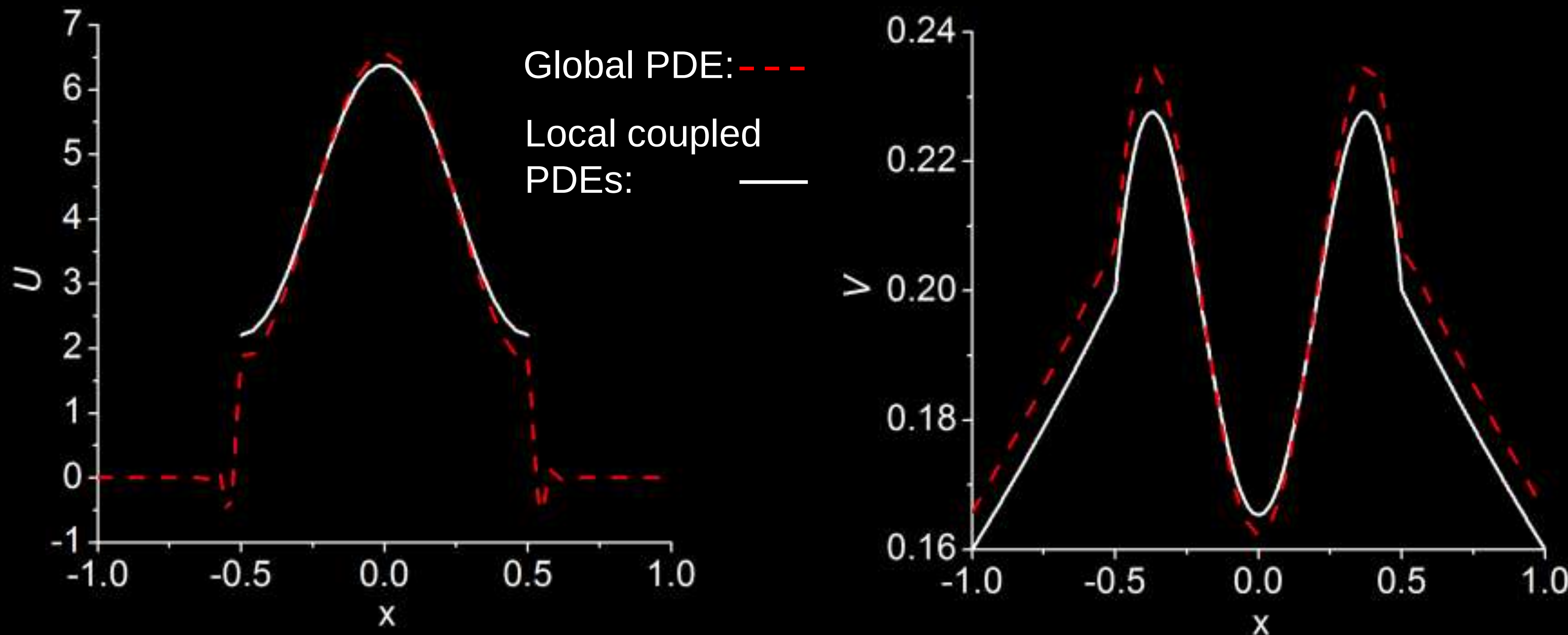


Menshykau & Iber *Proc COMSOL Conf* 2012

Reaction-Diffusion on a Static Composite Domain

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





Advantages of the local definition of PDEs:

- provides accurate solution of the problem;
- problem has less DOF;

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Reaction-Diffusion on a Deforming Composite Domain

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

dx=nx f(*U*,*V*)
dy=ny f(*U*,*V*)

We use ***General Extrusion Coupling Operators*** to ensure synchronous deformation of a composite domain.

U *V*

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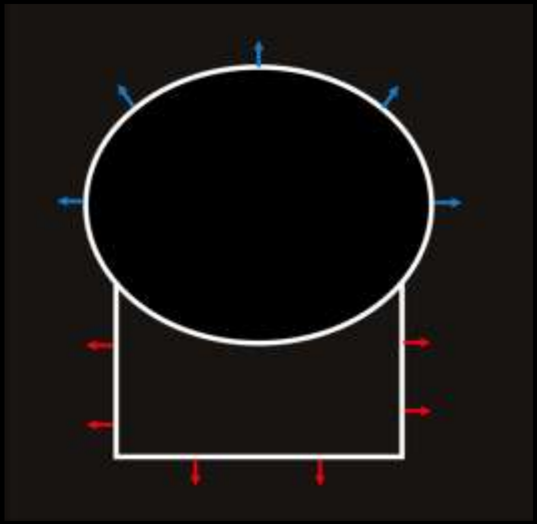
Explicitly Defined Deformation of a Composite Domain

We use ***assembly*** of the subdomains together with ***Continuity*** node in the ***Coefficient form PDE*** interface to ensure accurate accurate solution



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FNSNF Swiss National Science Foundation

ETH Eidgenössische Technische Hochschule Zürich Swiss Federal Institute of Technology Zurich

SIB Swiss Institute of Bioinformatics

SystemsX.ch The Swiss Initiative in Systems Biology