Friedrich-Alexander-Universität
Naturwissenschaftliche Fakultät

Department
MATHEMATIK

Micro-macro models for reactive transport in elastically deformable biological tissue

Jonas Knoch, Markus Gahn, Nicolas Neuß, Maria Neuss-Radu

Motivation

Describe reactive transport of nutrients, drugs, respiratory gases or waste products through deformable tissues such as lung tissue, heart tissue or vessel walls.

- Cellular structure leads to **multi-scale character** of biological tissue
- Diseases like Cancer, Covid-19 or Sepsis lead to **impairment of cellular reaction networks** (e.g. energy metabolism)
- *Lung-on-a-chip*: a microdevice illustrates effect of **cyclic stretching** on transport processes in deforming bio-engineered lung tissue

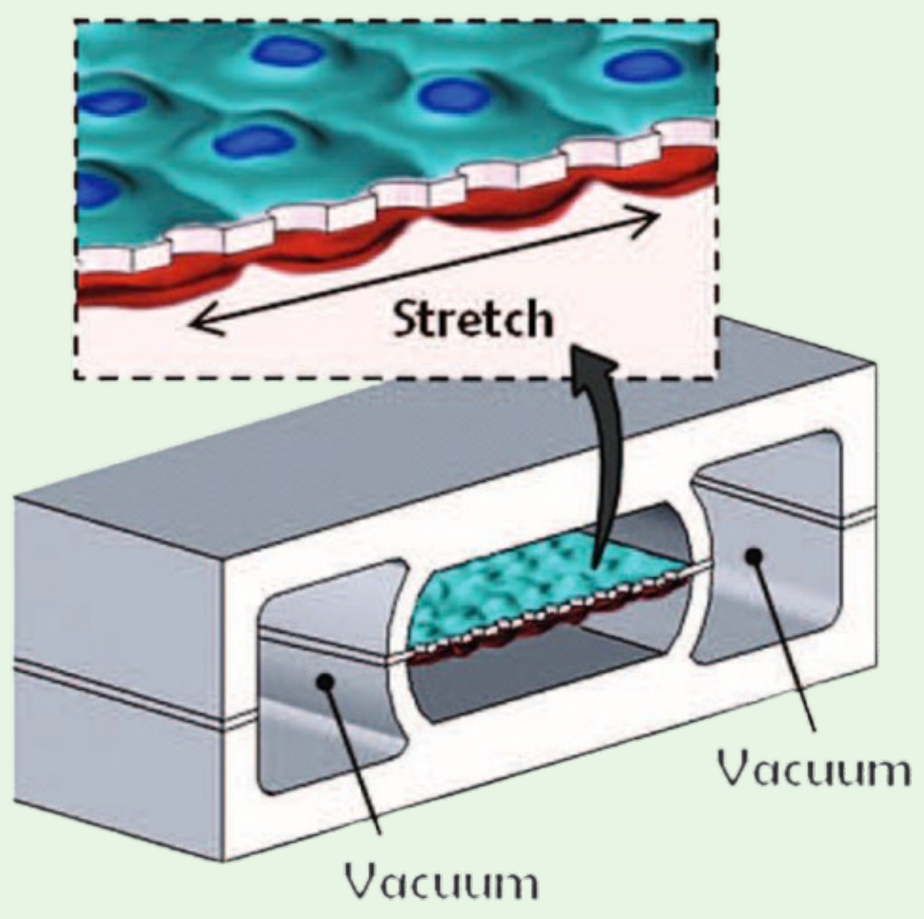


Figure: *Lung-On-A-Chip*, [1].

Multi-Scale Modeling

- System of **linear elasticity** and **reactive transport** in mixed ***Eulerian*/*Lagrangian* framework** on the periodic microscopic domain:

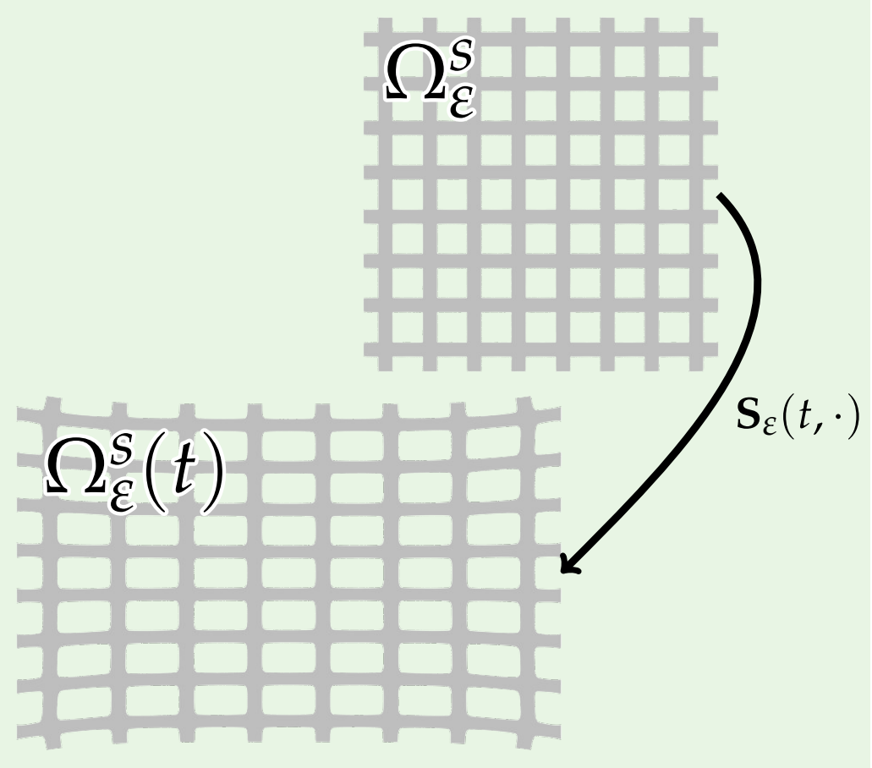
$$\begin{aligned} \varepsilon^2\partial_{tt}\mathbf{u}_\varepsilon - \nabla\cdot(\mathbf{A}\mathbf{e}(\mathbf{u}_\varepsilon)) &= \mathbf{f}_e && \text{in } (0,T)\times\Omega_\varepsilon^{\mathsf{s}},\\ \partial_t\widehat{c}_\varepsilon + \widehat{\nabla}\cdot\left(\widehat{\mathbf{v}}_\varepsilon\widehat{c}_\varepsilon - \widehat{\mathbf{D}}^m\widehat{\nabla}\widehat{c}_\varepsilon\right) &= f_d^m(\widehat{\mathbf{c}}_\varepsilon) && \text{in } \cup_{t\in(0,T)}\{t\}\times\Omega_\varepsilon^{\mathsf{s}}(t), \end{aligned}$$

  with unknown deformation $\mathbf{S}_\varepsilon$:

$$\mathbf{S}_\varepsilon(t,x) := x + \mathbf{u}_\varepsilon(t,x),$$

  and current deformed domain $\Omega_\varepsilon^{\mathsf{s}}(t)$:

$$\Omega_\varepsilon^{\mathsf{s}}(t) := \{\widehat{x}\in\mathbb{R}^n \mid \widehat{x} = \mathbf{S}_\varepsilon(t,x),\ x\in\Omega_\varepsilon^{\mathsf{s}}\}.$$



- **Pull-back** of the transport problem using the deformation $\mathbf{S}_\varepsilon$ to obtain a microscopic model in **unified *Lagrangian* framework** with

$$c_\varepsilon(t,x) := \widehat{c}_\varepsilon(t,\mathbf{S}_\varepsilon(t,x)).$$

- **Upscale** transformed problem using the method of **two-scale asymptotic expansions** to obtain an **effective micro-macro model** in the homogeneous domain Ω:

$$\begin{aligned} -\nabla\cdot(\mathbf{A}^*\mathbf{e}(\mathbf{u}_0)) &= |Y^s|\mathbf{f}_e && \text{in } (0,T)\times\Omega,\\ \partial_t(J^*c_0) - \nabla\cdot(\mathbf{D}^*\nabla c_0) &= J^*f_d(c_0) && \text{in } (0,T)\times\Omega. \end{aligned}$$

- The system is nonlinearly coupled via **effective coefficients** $\mathbf{A}^*$, J^* and $\mathbf{D}^*$, which are obtained by means of auxiliary **cell problems** on the fixed reference cell Y^s, e.g.

$$\begin{aligned} -\nabla_y\cdot[\mathbf{D}_0(t,x,y)(\mathbf{e}_i+\nabla_y\eta_i(t,x,y))] &= 0 && \text{in } (0,T)\times\Omega\times Y^s,\\ -\mathbf{D}_0(t,x,y)(\mathbf{e}_i+\nabla_y\eta_i(t,x,y))\cdot\mathbf{n}_\Gamma &= 0 && \text{on } (0,T)\times\Omega\times\Gamma, \end{aligned}$$

$$\eta_i \text{ is } Y^s\text{-periodic in } y,\quad \int_{Y^s}\eta_i \mathrm{d}y = 0,$$

  for $i = 1, \dots, n$.

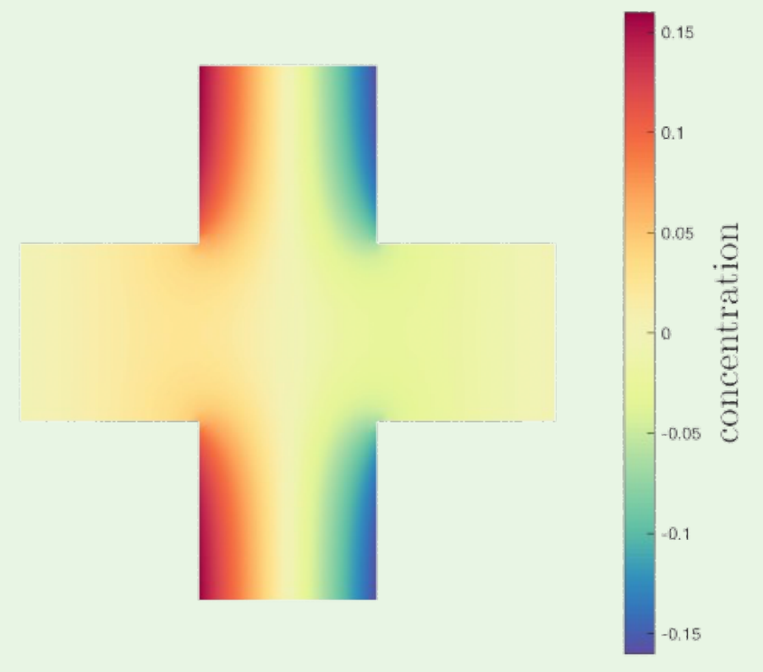


Figure: $\eta_1(0,0,\cdot)$

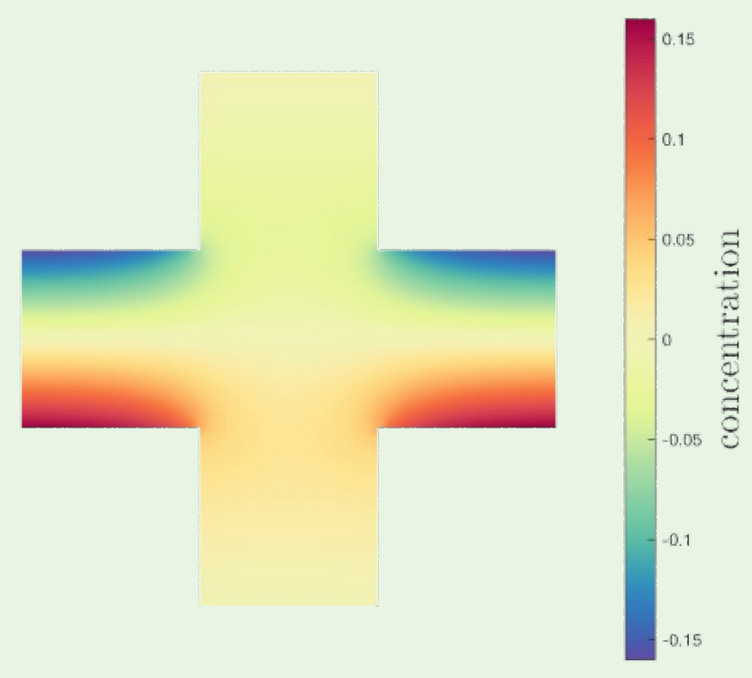
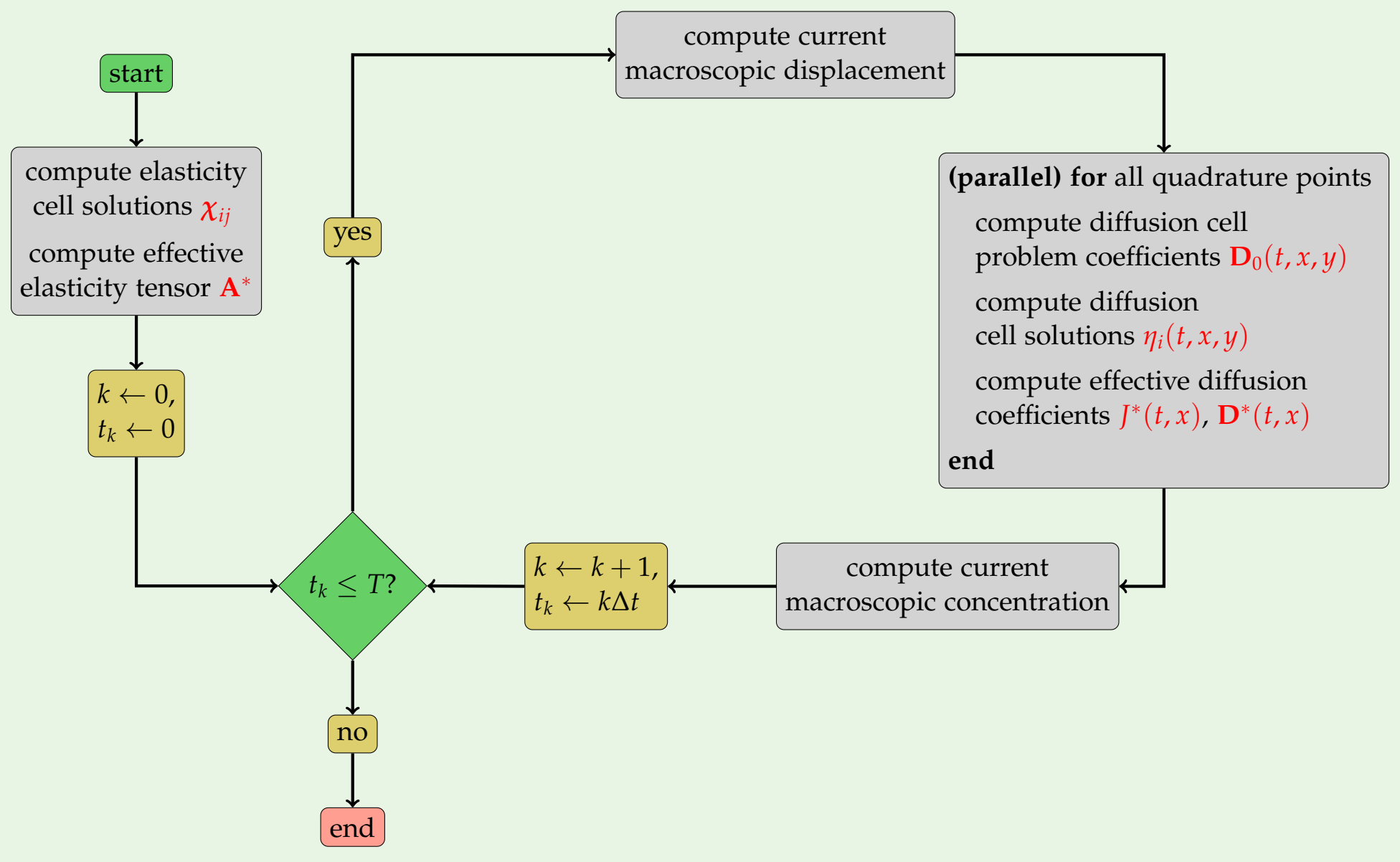


Figure: $\eta_2(0,0,\cdot)$

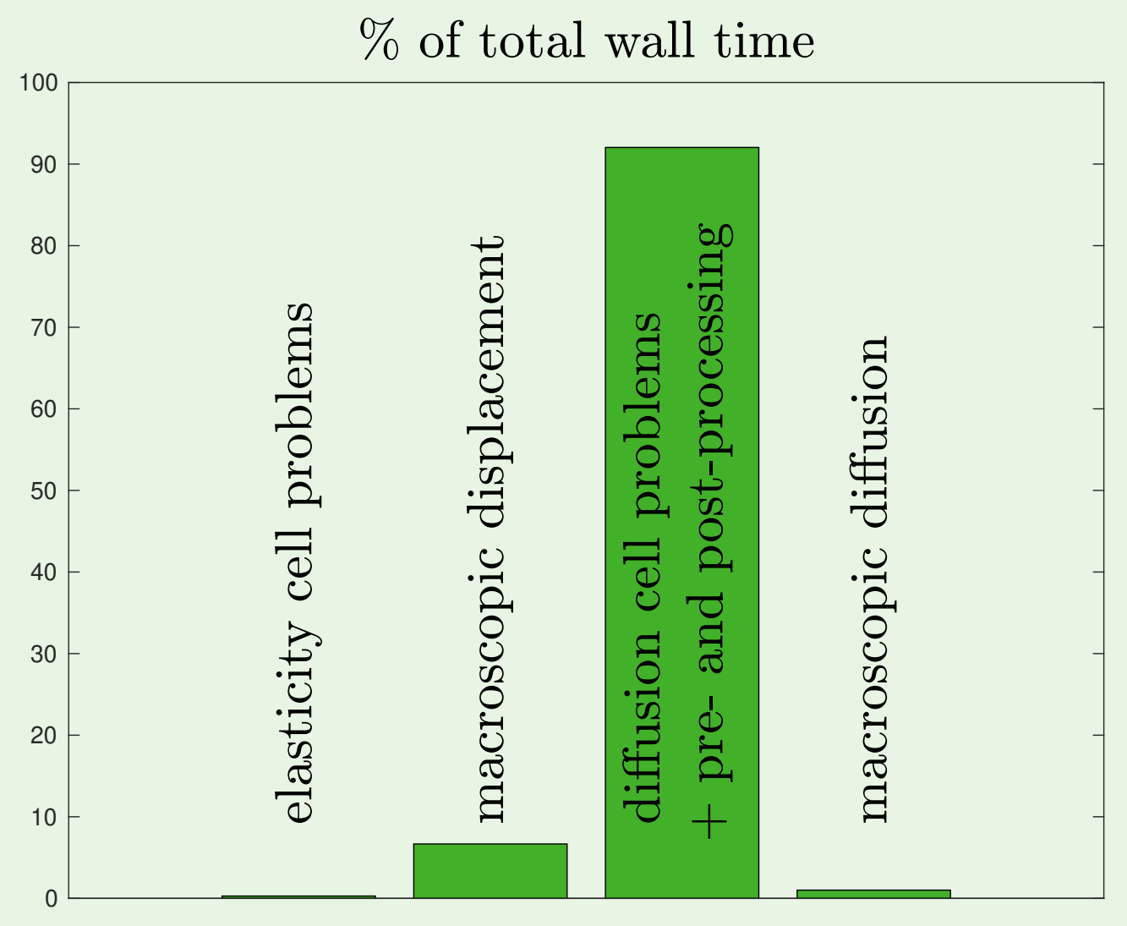
An Efficient Computational Framework



Challenge: large number of diffusion cell problems (see bar graph)

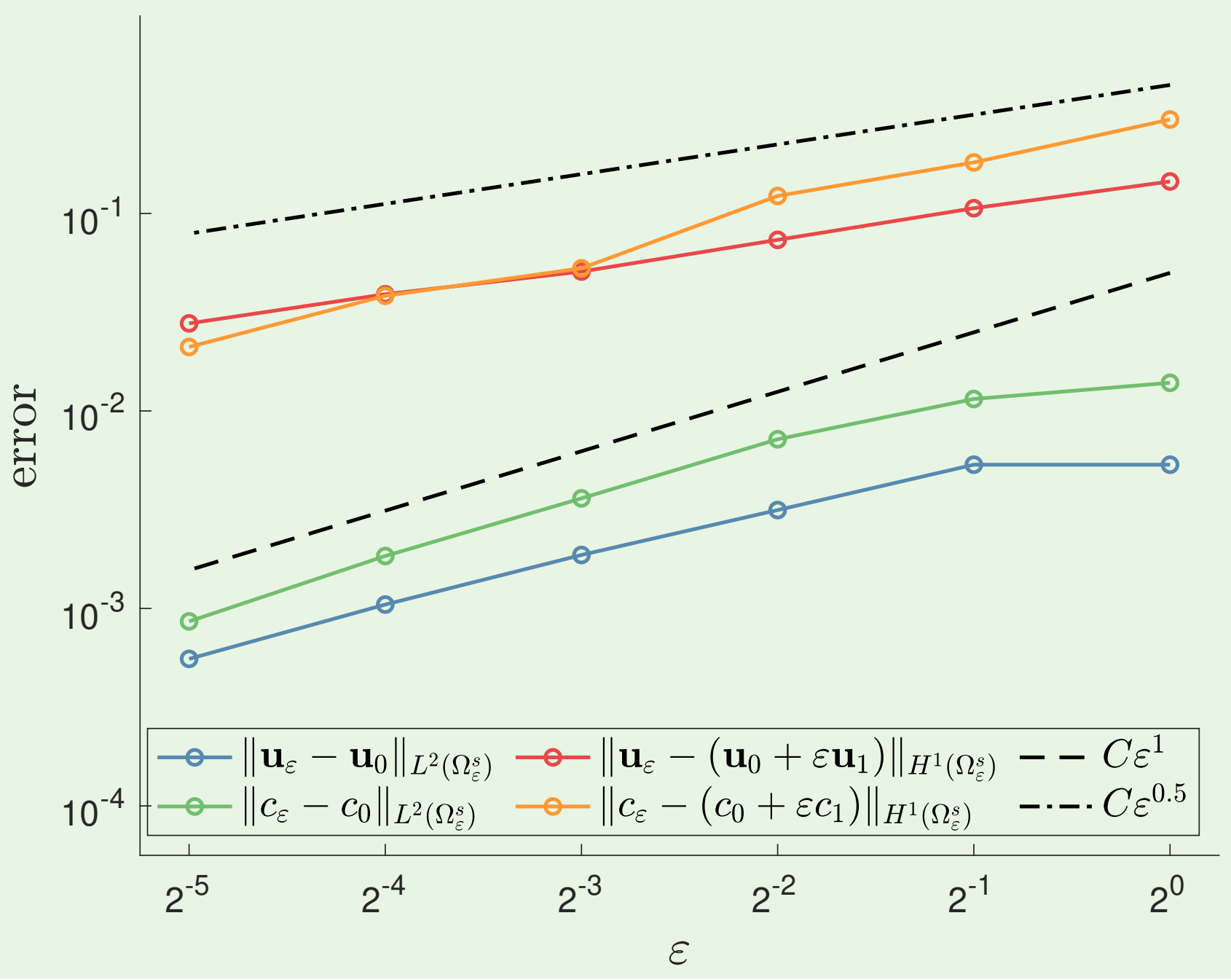
→ Use **feed-forward neural network** to compute effective coefficients **700 times faster**

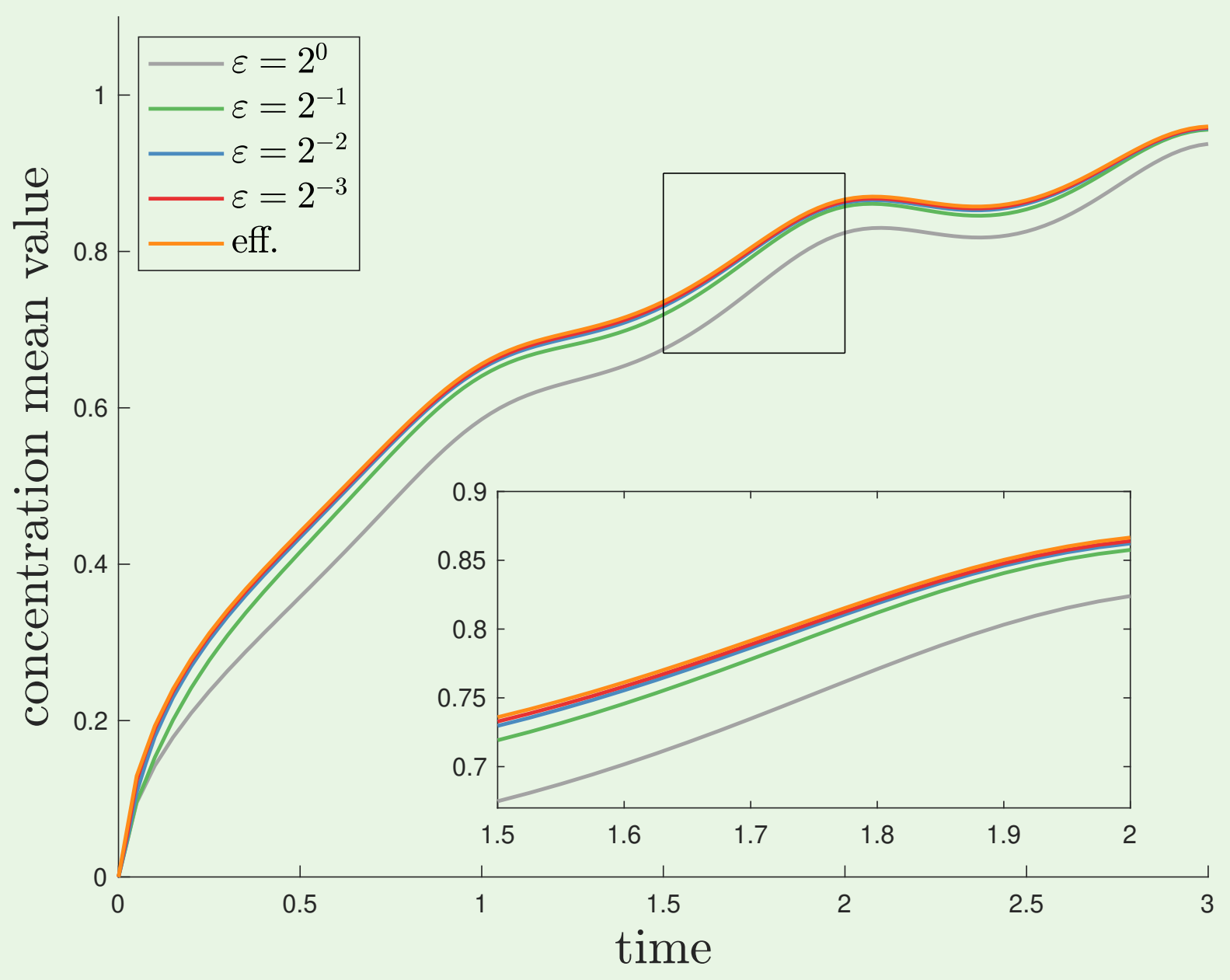
- software library: *deal.II*
- spatial discretization: *Lagrangian* FE
- temporal discretization: *Crank-Nicolson* method



Numerical Justification of the Effective Model

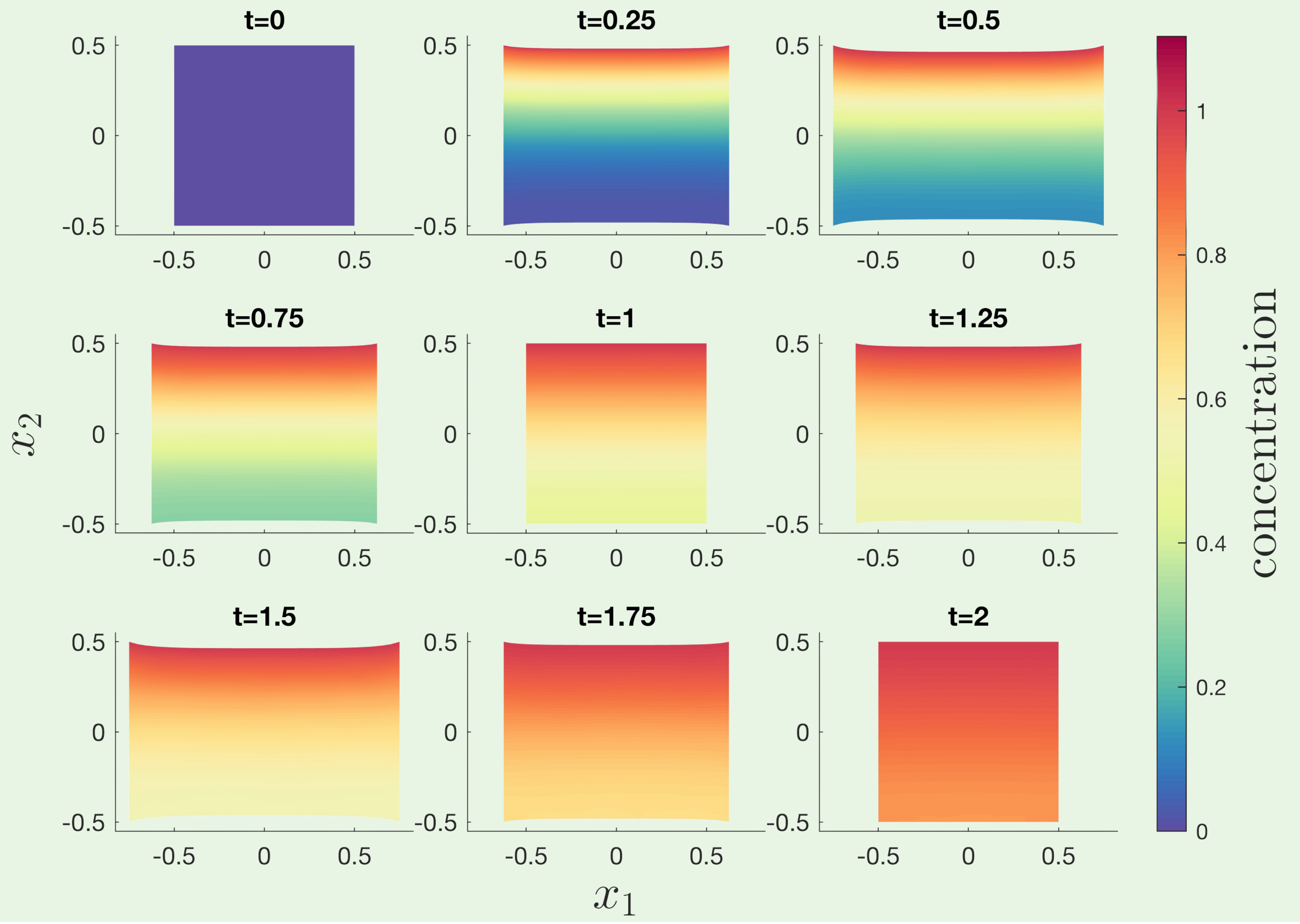
Is the effective micro-macro model a **good approximation** of the microscopic model?





Simulation Results

Time-evolution of concentration while domain is under cyclic elastic deformation, mimicking e.g. the **breathing movement**:



References

[1] Huh, D., et al. Reconstituting organ-level lung functions on a chip. *Science*, 2010.

[2] Knoch, J., et al. Multi-scale modeling and simulation of transport processes in an elastically deformable perforated medium. *Transport in Porous Media*, 2023.

[3] Knoch, J. Investigation of micro-macro models for reactive transport in elastically deformable perforated media, *Doctoral Thesis*, 2024.

jonas.knoch@fau.de