Upscaling Nonlinear Reactions in Tissues: Closure via Machine Learning

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Taghizadeh, Ehsan, Helen M. Byrne, and Brian D. Wood. "Explicit physics-informed neural networks for nonlinear closure: The case of transport in tissues." Journal of Computational Physics 449 (2022): 110781.

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Background on MLPs

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Textbook Chapter

- Many options!
- Here is one by me: Google “brian d wood researchgate”
- On Researchgate:
  Textbook: *Introduction to Advanced Engineering Mathematics and Analysis*
  “Chapter 10: Primer on feedforward neural networks: An analytical approach”

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Overview of ANNs

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The Multilayer Perceptron Network for Regression

- Multilayer perceptrons (MLPs) are a kind of ANN for high-dimensional representation of a regression functional
- The functional itself consists of an nested network of weighted nonlinear compositions

$$f(x_1, x_2, \ldots x_N) = \underbrace{\sigma_M \circ \sigma_{M-1} \circ \sigma_{M-1} \circ}_{nonlinear} \ldots \underbrace{\ell_1(x_1, x_2, \ldots, x_N)}_{linear}$$

- The depth of the compositional structure is frequently termed the number of *layers* in the network
- A *sum* of such compositions are interpreted as a *neural network*.

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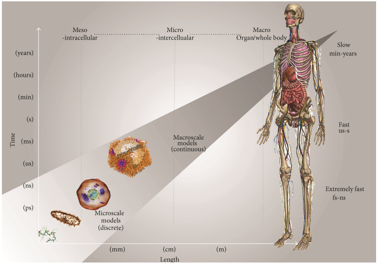
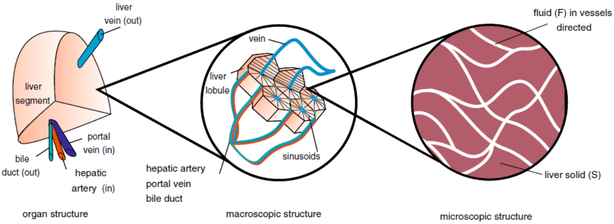
Upscaling Tissue Transport





Macro (liver, lobes and segments), meso (lobule) and microstructure (microcirculation in sinusoids) of the liver

Representative Volume (RV) and Averaging

$$\mathcal{V}(\mathbf{x}) = \mathcal{V}_\beta(\mathbf{x}) \cup \mathcal{A}_{\beta\sigma}(\mathbf{x}) \cup \mathcal{V}_\sigma(\mathbf{x})$$

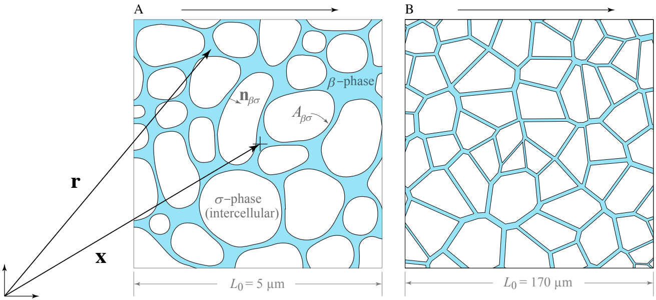


Figure: Cell-scale images of (left) brain cortex and (right) liver lobule tissues. Note that $\boldsymbol{x}$ points to the center of the averaging volume $\mathcal{V}$; $\boldsymbol{r}$ points to any location within the volume.

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Results from Averaging Step

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One-Equation Macroscale Model and Simplifications

- The time scale for mass transfer across cell wall is small compared to the macroscale characteristic time for mass transport
- The intercellular phase can be treated as being *quasi-steady* compared to the extracelluar transport
- Diffusion is independent of reaction
- Both $\mathbf{D}^*$ and $\langle R \rangle$ *depend on the structure of the deviation field,* $\tilde{c}_\beta$ (details not shown) and the volume fraction ε_β

$$\boxed{\frac{\partial \langle c_\beta \rangle^\beta}{\partial t} = -\langle \mathbf{v}_\beta \rangle^\beta \cdot \nabla \langle c_\beta \rangle^\beta + \nabla \cdot \left(\mathbf{D}^* \cdot \nabla \langle c_\beta \rangle^\beta \right) + \varepsilon_\beta^{-1} \langle R \rangle}$$

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Dispersion Tensor

The Dispersion Tensor and Effectiveness Factors

For nearly isotropic particles, the dispersion tensor can be estimated *numerically* by solving

$$\mathbf{D}^* = D_{eff}\mathbf{I} - \langle \tilde{\boldsymbol{v}}_\beta \otimes \boldsymbol{b}_\beta \rangle^\beta$$

$\Rightarrow$ Only 1 parameter (Pe). *ML not needed.*

Correction or Effectiveness Factor

$$\langle R \rangle = -\eta \left(\varepsilon_\sigma k_m \frac{\langle c_\beta \rangle^\beta}{\langle c_\beta \rangle^\beta + K} \right), \qquad \text{where,} \quad \eta = \frac{\langle R \rangle}{R_0}$$

$\Rightarrow \eta$ *depends on many parameters (defined in coming slides)– ML needed.*

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Physics-driven Feature Engineering

Feature Engineering

- MLPs are a *supervised* method of ML
- The term *supervised* indicates only that the set of independent variables on which the target (η) depends are treated as being *known*
- *Feature engineering* is the process by which we search for / identify the appropriate set of independent variables
- In our case, these come exclusively from the
  - physical
  - mathematical

  structure of the problem

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Physics-driven Feature Engineering

Nondimensionalized Balance Equations

$$\frac{\partial C_\beta}{\partial \tau} = -Pe\frac{\mathbf{v}_\beta}{U}\nabla \cdot C_\beta + \nabla^2 C_\beta$$

$$I.C.1 \qquad C_\beta(\mathbf{Z},0) = I_\beta(\mathbf{Z})$$

$$B.C.\ 1 \qquad -\mathbf{n}_{\beta\sigma}\cdot\nabla C_\beta = -\mathbf{n}_{\beta\sigma}\cdot(D_r\nabla C_\sigma), \text{ at cell surface}$$

$$B.C.\ 2 \qquad C_\beta = C_\sigma, \text{ at cell surface}$$

$$\frac{\partial C_\sigma}{\partial \tau} = D_r\nabla^2 C_\sigma - \varphi^2\frac{C_\sigma}{C_\sigma + 1}$$

$$I.C.2 \qquad C_\sigma(\mathbf{Z},0) = I_\sigma(\mathbf{Z})$$

Features based on underlying physics

$$D_r = \frac{\mathscr{D}_\sigma}{\mathscr{D}_\beta} \qquad Pe = \frac{Ur_0}{\mathscr{D}_\beta} \qquad \varphi^2 = \frac{k_m r_0^2}{K\mathscr{D}_\beta}$$

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Identified Features

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Full Feature Set– Six in Total

- Parametric Features

$$Pe$$

$$D_r$$

$$\phi^2$$

$$\epsilon_\beta$$

- Macroscale Source Term Features

$$\langle c_\beta \rangle^\beta$$

$$\nabla \langle c_\beta \rangle^\beta$$

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Generation of the Example Ensemble

Table: Data amalgamated from literature sources

Parameter	Brain	Liver (hepatocyte spheroids)
$\mathscr{D}_\beta$ $(\frac{m^2}{s})$	$6 \times 10^{-10} - 20 \times 10^{-10}$	$6 \times 10^{-10} - 20 \times 10^{-10}$
$\mathscr{D}_\sigma / \mathscr{D}_\beta$	$0.1 - 1.0$	$0.1 - 1.0$
c_{max} $(\frac{mol}{m^3})$	$0 - 1.8$	$1 \times 10^{-3} - 1.0$
ε_β	$0.23 - 0.49$	$0.02 - 0.41$
k_m $(\frac{mol}{m^3 \cdot s^{-1}})$	$0.01 - 1667$	$5 \times 10^{-6} - 0.45$
K $\frac{mol}{m^3}$	$0.003 - 528$	$5 \times 10^{-4} - 0.14$
Pe	$0.01 - 8.0$	$0.01 - 117$
r_0 (m)	0.46×10^{-6}	11.7×10^{-6}
φ^2 $(-)$	$0 - 100$	$0 - 77$
κ (m^2)	$2 \times 10^{-14} - 2 \times 10^{-8}$	$1 \times 10^{-10} - 7.5 \times 10^{-8}$

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Geometry

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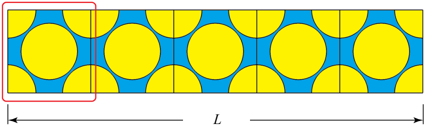
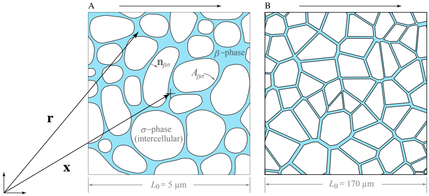
- Abstract but representative geometry
- Used for training MLP



- Two examples of complex geometry from literature
- Used for testing trained MLP fidelity



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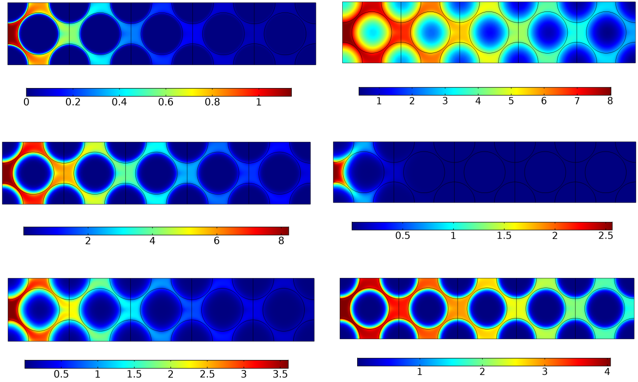
Training Data Examples

- Several examples from the ensemble of possible *feature vectors* $\boldsymbol{X} = (Pe, D_r, \varphi^2, \varepsilon_\beta, \langle c_\beta \rangle^\beta, \nabla \langle c_\beta \rangle^\beta)$
- For each value of $\boldsymbol{X}$, a corresponding value of η can be computed



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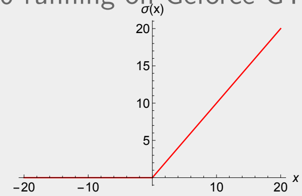
The Multilayer Perceptron Network

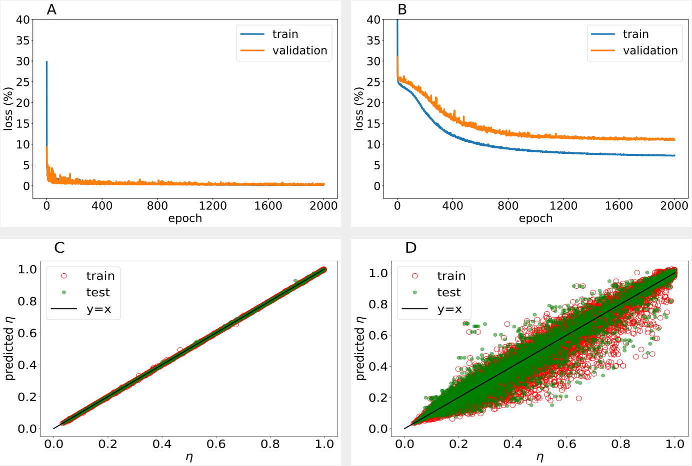
MLP

- Rectified linear unit (ReLU) basis function
- L_1 loss function
- 4 hidden layers– 512, 256, 64 and 16 neurons
- Adam gradient-based optimization scheme (modified gradient decent)
- 74% as training, 6% as validation,and 20% as test data
- Tensorflow 2.3.0 running on Geforce GTX 1080 Ti GPU array



Training and Prediction Results

With Macroscale Source Features (left) and Without (right)



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Validating the Learned Model

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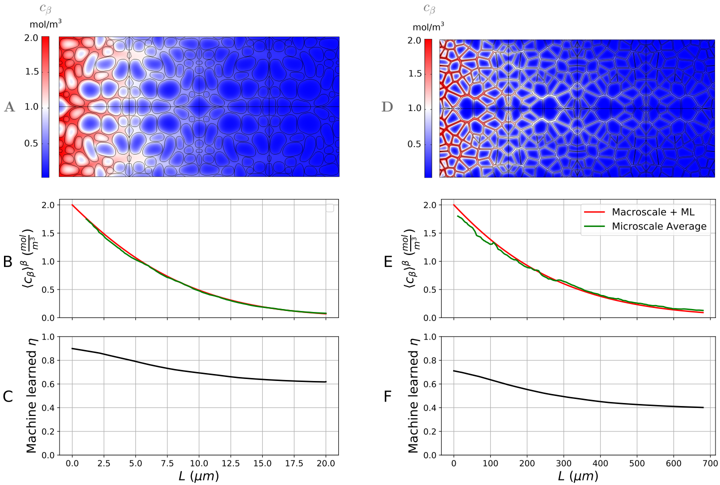

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Summary and Conclusions

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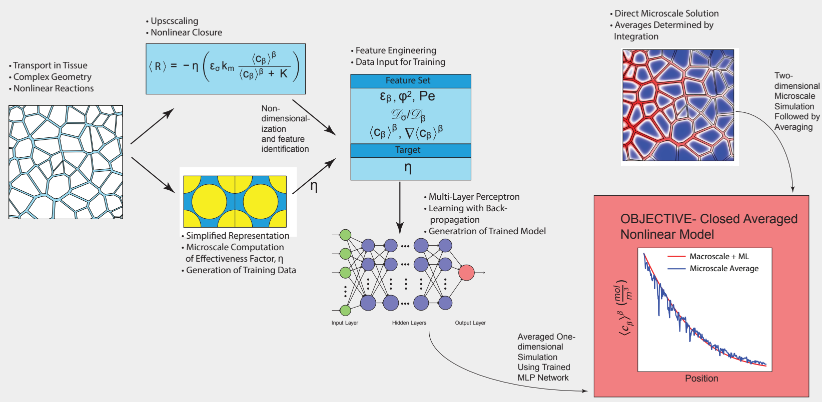
Summary of Workflow



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Summary and Conclusions

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Questions?