Perfusion modeling
- The link between reservoir simulation and medical compartment modeling

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Concepts

Perfusion

Related to capillary flow. "Amount of arterial blood feeding a tissue volume pr. time unit."

Flow relative to volume or volume flux. [ml/s/ml]. Important concept in medicine.

(Notation: $P$)

Figure: A. Lundervold 2016
## Concepts

### Dynamic MR imaging
- Vascular properties of tissue is studied:
  - By injecting a contrast agent to the blood stream
  - Prior to dynamic MR imaging (4D),
  - And simple mathematical modelling

### Compartment modelling
- Within a volume $\Omega_i$ we expect various tissue types, and the blood can occupy different *compartments*.
- The distribution of blood between the compartments over time gives information on the vascular properties of the tissue.
- 1C model: Reveals information about volume fraction occupied by blood (porosity/CBV) and flow in/out of the region.
- State of the art medical compartment modelling does not take into account spatial information. (Structure of flow field in space etc.)
Traditional models

- Simplest example: One-compartment model
  - Used in i.e. CBF estimates (brain)
  - More advanced models with several compartments exists and have a wide range of useful applications (but will not be discussed here).

**Fundamental assumptions**

- One inlet, one outlet
- Incompressible fluid
- The transit time through the region $\Omega_i$ can be described with some probability distribution
- Known Arterial Input Function (AIF), $c_a(t)$
Traditional models

\[ C(t) = \text{concentration in tissue} \quad c(t) = \text{concentration in blood} \]

\[ C'(t) = P(c_a(t) - c_v(t)) \]

\[ C(t) = (I * c_a)(t), \quad I(t) = Pe^{-t/T} \]

\[ T = P/\phi \text{ is the mean transit time} \]
Traditional models

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Traditional models

Is the concept generic enough to be applied to voxels in an image? (Addressed by i.e. Malyssev and Lundervold in the early 2000)

- The image resolution is still too coarse to directly detect the flow through the pore networks
- We no longer are in control of the AIF
On real data

- **Perfusion CT (University Hospital of Nijmegen)**

  Toshiba Aquilion ONE scanner, pixel-size $0.43\,mm \times 0.43\,mm$, slice thickness $0.5\,mm$, contrast agent $50\,mL$ Xentix 300, total scan-time $114\,s$, time resolution ranging from $2.1\,s$ in the early- to $30\,s$ in the late phase of CA uptake.

![Arterial input function](image1)

![One slice of the voxel-wise CBF reconstruction](image2)

![Mean $C(t)$ curve for the whole volume of interest and reconstruction](image3)

- **Average voxel-wise CBF:** $64.357\,ml/min/100\,ml$
- **Averaging all time curves before computing CBF for entire brain:** $24.791\,ml/min/100\,ml$
Volume fluxes will depend on the spatial organisation of the sub-volumes (As addressed in the 90’s by Henkelman and others)

The volumes are feeding each other

No problem if we only have one region or if the sub-volumes are spread out across (not along) the flow.

\[ F_0 = \frac{F_0}{2V} \]

\[ V \]

\[ P_1 = \frac{F_0}{2V} \]

\[ V \]

\[ P_2 = \frac{F_0}{V} = 2P_1 \]

\[ \Delta V \]

\[ \Delta F_0 \]
When resolution increases

- The resolution of modern MR machines approach the point where capillaries are visible
- In most organs, the geometry is highly complex

Figure 6. Scanning electron micrograph revealing vasculature within the area corresponding to the maximum acoustically evoked intrinsic signal. The arteries (A) and veena (V) can be clearly distinguished. 1, 2, 3: three types of arterial collateral vessels (two seen) host an element of smooth muscle bundle (asterisk symbol) on arteriole vessels. Bar = 100 μm.

http://gauss.unh.edu/jel/images/brain_capillary.jpg
When resolution increases

- Perfusion is a scalar (ml/s/ml)
- It may be interoperated as a vector (flow/ml).

Problem #2

- Volume fluxes will depend on the shape of the volumes
- The flow is oriented, but the volume fluxes are not $\implies$ the perfusion will be orientation dependent.
When resolution increases

- Is it possible to estimate vectorial information from an image sequence?

**Optical Flow**

- "Apparent velocity vector field corresponding to the observed motion of patterns in successive image sequences"

- Classical field within image processing

- Also applied within PIV (particle image velocimetry) to quantify physical flows of fluids

Heitz et al. 2010
4D-image registration

- Ongoing project: Use image registration for the sake of estimating deformations, not aligning images.

Recent publication in By Hodneland et al.: Physical Models for Simulation and Reconstruction of Human Tissue Deformation Fields, in Dynamic MRI, *IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING*
Fluid transport in porous medium

Porous media

- Some fraction of the tissue is occupied by blood (porous medium)
- Flow driven by pressure differences
- Low velocity of fluid flow $\Rightarrow$ Possible to apply Darcy’s law
- Homogeneous material (no anatomical assumptions)
- Stationary flow

Source (AIF)

Homogeneous tissue
(Porous medium)

Sink
Simple spatial model

Capillary blood flow

Conservation of fluid mass: \( \nabla \cdot q = Q \) \( Q(x) = 0 \), except at source and sink

Darcy’s law:
\[
q = -\frac{k}{\mu} \nabla p. \quad k = \text{permeability}, \ \mu = \text{viscosity}
\]

Transport of contrast agent

Continuity equation:
\[
\phi \frac{\partial c}{\partial t} + \nabla \cdot (cq) = c_a Q_{so} + cQ_{si}
\]
\( x \in \Omega, \ t > 0, \)

Pressure field \( p(x) \)  
Flow field  
Average concentrations
Relation between ODEs and PDE

\[ \phi \frac{\partial c}{\partial t} + \nabla \cdot (cq) = c_a Q_{so} + cQ_{si} \]

- Solution of continuity equation using *method of characteristics*:
  - ODEs solved along streamlines
  - Give rise to the same equations as the 1-compartment model
Combine the notion of compartment with a porous media flow model
Multi-Continuum approach

2D+1 - Compartment modelling

- Blood is perfused due to pressure gradients
- Adding an artificial dimension accounting for the compartments
- Three layer model allowing for porous transport within the capillary system
- Perfusion is still a discretisation dependent scalar
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2D+1 - Compartment modelling

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Inverse modelling

- Fit the image data to the model with perfusion as parameter.
- Traditional models are often evaluated by first simulating data using the same simple model.

<table>
<thead>
<tr>
<th>Block size</th>
<th>(1,1)</th>
<th>(5,5)</th>
<th>(10,10)</th>
<th>Entire domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfusion from porous media model</td>
<td>![Image 1]</td>
<td>![Image 2]</td>
<td>![Image 3]</td>
<td>![Image 4]</td>
</tr>
<tr>
<td>Traditional deconvolution (bSVD)</td>
<td>![Image 5]</td>
<td>![Image 6]</td>
<td>![Image 7]</td>
<td>![Image 8]</td>
</tr>
<tr>
<td>Rel. error</td>
<td>93%</td>
<td>67%</td>
<td>44%</td>
<td>4%</td>
</tr>
</tbody>
</table>
Solution attempts

- Some works over the last 20 years have addressed the problems, but there are few attempts to solve them.

**Blind Deconvolution, (Taxt, Grüner, et al.)**

- In the solution of the traditional model: Approximate both the impulse response $I(t)$ and the AIF $C_a$ for each voxel.
- Highly underdetermined problem
- Solvable using information theoretical principles and a suitable set of constraints.
- Even more difficult to solve robustly than the regular deconvolution.
Solution attempts

- Nævdal, Sævereid, Lorentzen (IRIS)
  

- Porous media (dual porosity/dual permeability) forward model

- Ensemble Kalman filter parameter estimation

Figure 4: Estimated perfusion - CBF in units [mL/min/100mL].
Conclusions

- Using pours media flow we have illustrated a phenomena causing the traditional 1C models to overestimate perfusion.
- The error appears to be increasing with increasing number of voxels (finer resolution)
  - And will vary according to the relationship between the discretization and the anatomy.
- We don’t have tools capable of handling the increasing image resolution
  - In terms of discretisation
  - In terms of inverse modelling
- Images of increasing resolution and quality may challenge the traditional concept of perfusion
Thank You

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