Impedance boundary conditions for general transient hemodynamics and other things

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Overview

Long term goal: non-invasive continuous measurement of cerebral blood flow (CBF)

- “cheap" measurements: Transcranial Doppler to measure blood flow velocity (BFV)
- patient database and analysis thereof
- computational hemodynamics

Challenges

In increasing order of “stochasticity"

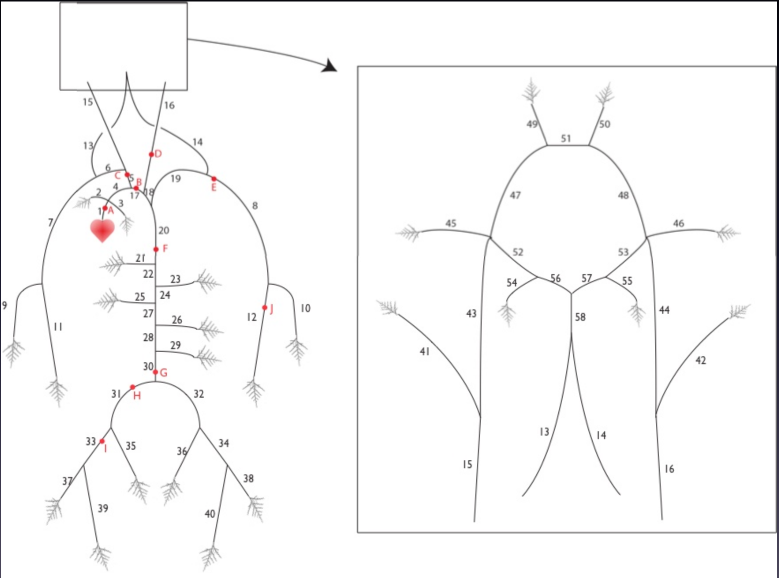
- closures for hemodynamics models:
  how to model what isn’t in the computational domain (BCs)
- uncertainties in models, geometries and parameters
- uncertainties in data:
  lack of gold standard method, patient biases

We need error bars to our predictions

This talk

- impedance boundary conditions (outflow)
- machine learning for CBF data (inflow)

Example: systemic arterial tree



Outflow BCs are fundamental

- inflow vessels: few and "easy" to measure $\Leftarrow$ DATA
- outflow vessels: many and hard to measure $\Leftarrow$ MODEL
- vasculature is reactive (autoregulation)

Arterial flow model: single vessel

approach

- not interested in flow details but in vascular networks "throughput"
- one-d is often (but not always!) good enough
  - computational justification (Grinberg et al., ABE, (2011))
  - derived BCs are general: can be adapted to multi-d

Arterial flow model: single vessel

material assumptions

- incompressible Navier-Stokes
- flow is axisymmetric without swirls
- equations are averaged on cross-sections
- vessels are elastic

Arterial flow model: single vessel

equations (Barnard et al., Biophys. J., 1966)

$$\partial_t A + \partial_x Q = 0$$

$$\partial_t Q + \frac{\gamma + 2}{\gamma + 1} \partial_x \left(\frac{Q^2}{A} \right) + \frac{A}{\rho} \partial_x P = -2\pi(\gamma + 2) \frac{\mu}{\rho} \frac{Q}{A}$$

where

- $A = A(x, t)$ surface area
- $Q = Q(x, t)$ flowrate
- $P = P(A) = P_0 + \frac{4Eh}{3r_0} \left(1 - \sqrt{\frac{A_0}{A}} \right)$ pressure
- μ, ρ viscosity and density
- γ flow profile ($\gamma = 2 \Leftrightarrow$ Poiseuille)

Arterial flow model: single vessel

Above equations are a system of hyperbolic balance laws

At operating regime

- solutions are smooth (no shock!)
- Jacobian has one positive and one negative eigenvalue

We need

- one inflow condition (measured velocity)
- one outflow condition

At junctions

- conservation of mass
- continuity of pressure

Outflow BCs must

- mimic the part of the vasculature that is not modeled (downstream from computational domain)
- not create numerical artifacts
- be cheap to run
- be simple to implement
- require a minimum of calibration

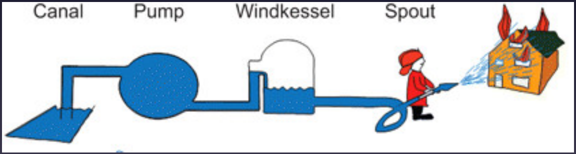
Outflow BCs: the classics

- Dirichlet (or Neumann) BC
- impose a relationship between P and Q
  - resistance:

$$P = R\,Q$$

  - RCR Windkessel:

$$P + R_2\,C\,\partial_t P = (R_1 + R_2)Q + R_1\,R_2\,C\,\partial_t Q$$



R. Saouti et al., Euro. Respir. Rev., 2010

Outflow BCs: the classics

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  - RCR Windkessel:

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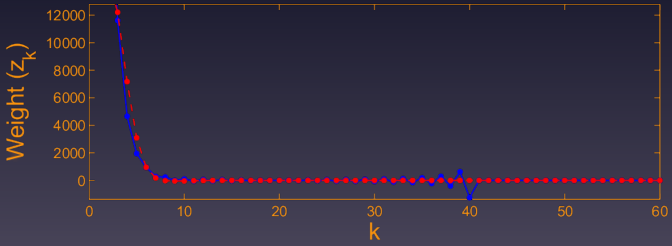
Issues

- limited physiological basis
- determination of parameter values

Impedance bc

- takes the form of a convolution
- z_j's: impedance weights

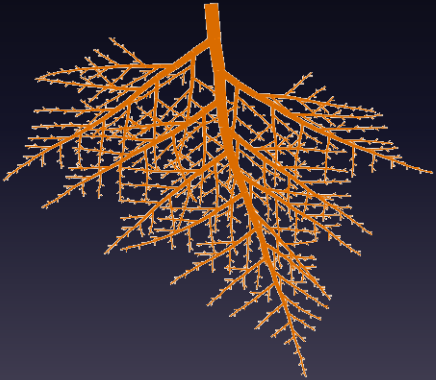
$$P_n = \sum_{j=0}^{n} z_j Q_{n-j} + P_{term}$$



Structured tree BC

Proposed by M.G. Taylor (1966), developed by M. Olufsen (1999)

- assumes simplified fractal geometry of downstream vascular tree
- linearizes flow equations
- uses Fourier and junction conditions to define tree impedance



New impedance BC

- Fourier $\rightarrow$ Laplace:
  allows general flows (instead of just periodic ones)
- fractal structure $\rightarrow$ effective tiered structure:
  greatly reduces need for calibration
- can be used in lieu of calibration for other BCs
- better termination criterion

Tree geometry

Governed by four rules

rule 0: there are only bifurcations

rule 1: $r_{d_1} = \alpha\, r_p$, $r_{d_2} = \beta\, r_p$

rule 2: $\ell = \lambda\, r$

rule 3: terminate vessel if $r < r_{min}$

where r is radius, ℓ is length and p and d_i are parent/daughters

Potential issue

- scaling parameters are not constant (more later)

Linearization (in A about A_0)

$$C\,\partial_t P + \partial_x Q = 0$$

$$\partial_t Q + \frac{A_0}{\rho}\,\partial_x P = -2\pi(\gamma + 2)\,\frac{\mu}{\rho}\,\frac{Q}{A_0}$$

where $C = dA/dP$ is the vessel compliance.

We Laplace transform and solve exactly

$$\hat{Q}(0,s) = s d_s C \hat{P}(\ell,s)\sinh\left(\frac{\ell}{d_s}\right) + \hat{Q}(\ell,s)\cosh\left(\frac{\ell}{d_s}\right)$$

$$\hat{P}(0,s) = \hat{P}(\ell,s)\cosh\left(\frac{\ell}{d_s}\right) + \frac{1}{s d_s C}\hat{Q}(\ell,s)\sinh\left(\frac{\ell}{d_s}\right)$$

Vessel impedance

Defined through its Laplace transform

$$\hat{Z}(x,s) = \frac{\hat{P}(x,s)}{\hat{Q}(x,s)}$$

and thus

$$\hat{Z}(0,s) = \frac{\hat{Z}(\ell,s) + \frac{1}{s d_s C} \tanh L/d_s}{s d_s C\, \hat{Z}(\ell,s) \tanh L/d_s + 1}$$

- links the impedance at beginning and end of the vessel
- for imaginary s, i.e., $s = i\omega$, $\omega \in \mathbb{R}$, $\hat{Z}$ is the "old" impedance

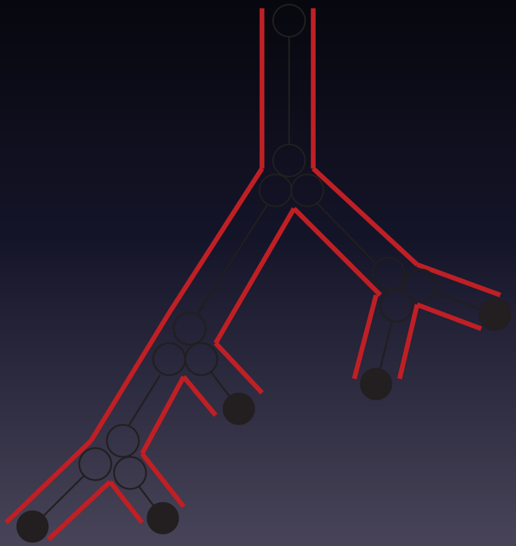
Tree impedance

can be defined recursively using junction conditions

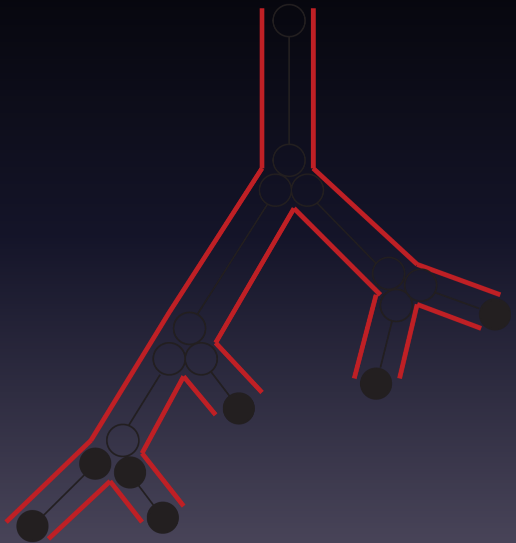
- conservation of mass: $Q_p(\ell, t) = Q_{d_1}(0, t) + Q_{d_2}(0, t)$
- continuity of pressure: $P_p(\ell, t) = P_{d_1}(0, t) = P_{d_2}(0, t)$

$$\Rightarrow \frac{1}{\hat{Z}_{pa}(\ell, s)} = \frac{1}{\hat{Z}_{d1}(0, s)} + \frac{1}{\hat{Z}_{d2}(0, s)}$$

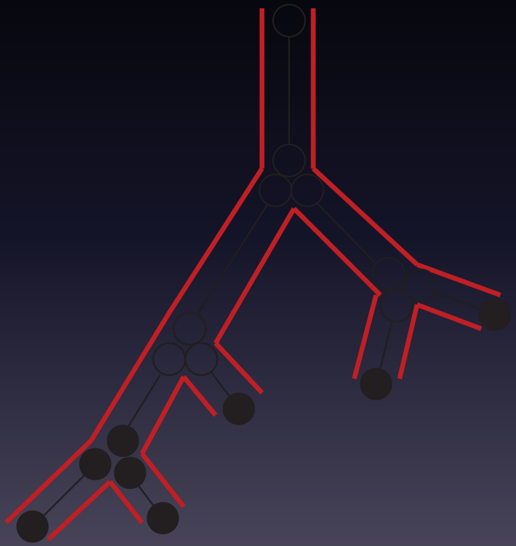
First set $\hat{Z}(s) = \hat{Z}_{term}$ at terminals



Use Single Vessel Solution



Use Junction Relation



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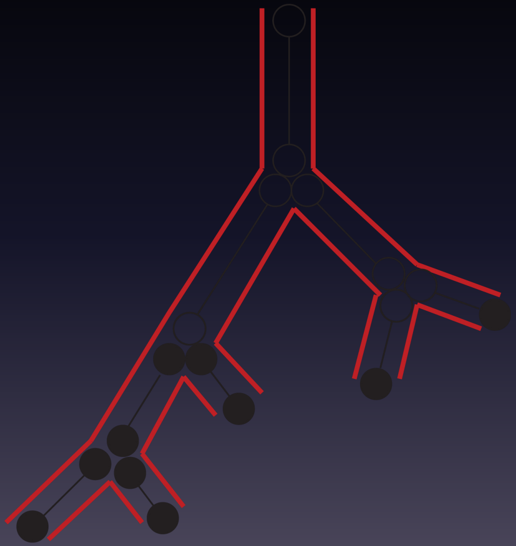

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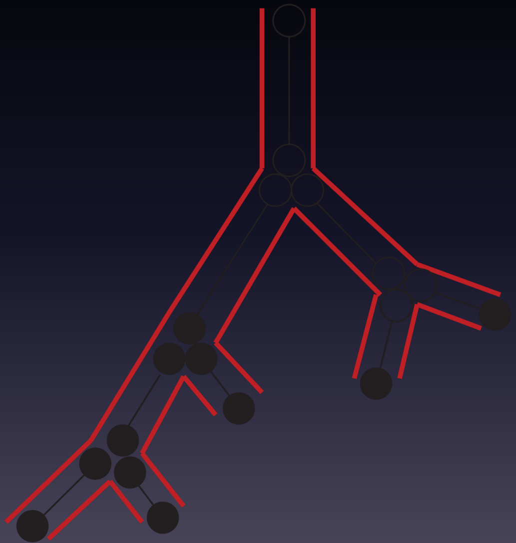

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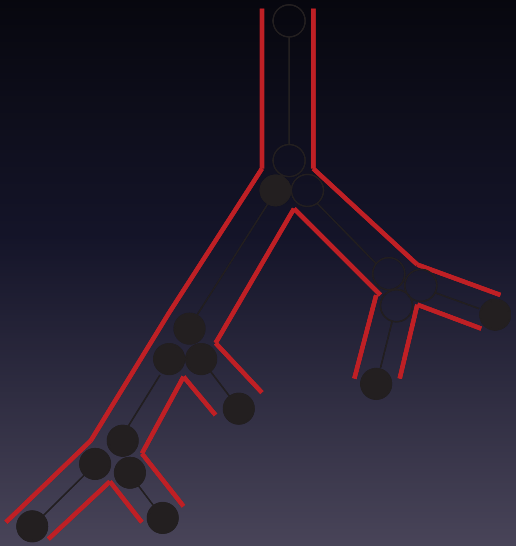

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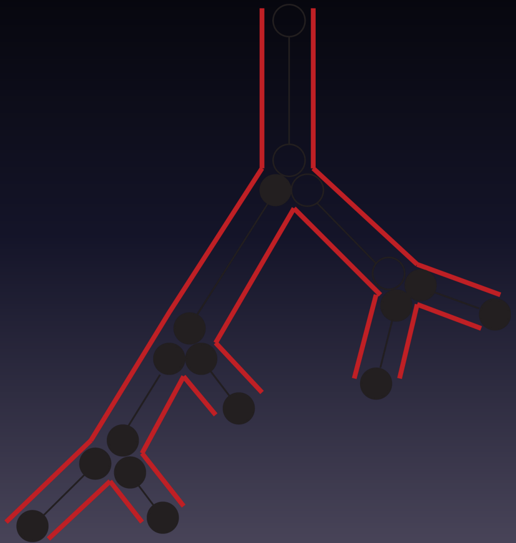

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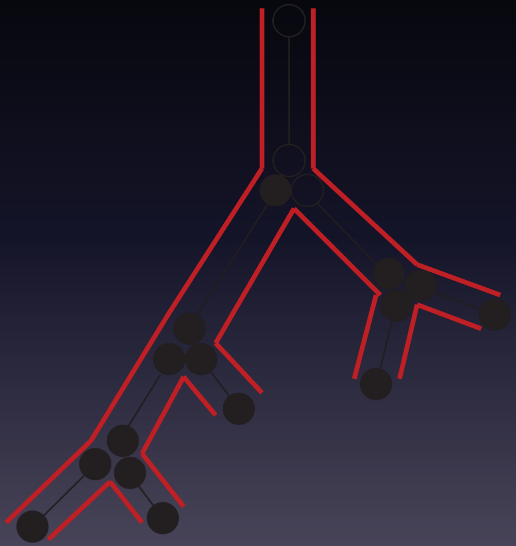

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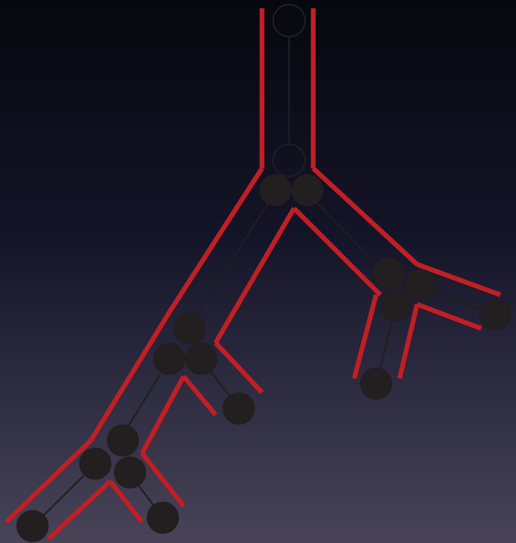

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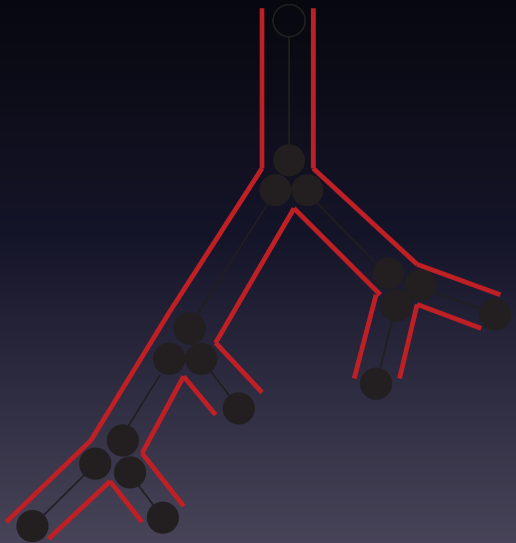

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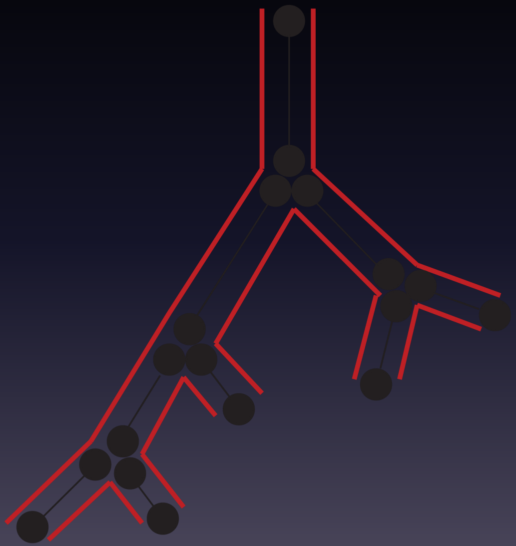


Algorithm to compute impedance

procedure IMPEDANCE
Input: r - radius of vessel
Output: ZPA_0

if $r < r_{min}$ **then**
$ZPA\_L = Z_{term}$
else
$ZD1 = \text{IMPEDANCE}(\alpha \cdot r)$
$ZD2 = \text{IMPEDANCE}(\beta \cdot r)$
$ZPA\_L = ZD1 \cdot ZD2/(ZD1 + ZD2)$
end if
$ZPA\_0 = singleVesselImp(ZPA\_L)$
end procedure

Implementation: intro

- we have just computed $\hat{Z}(s)$
- convolution $\Rightarrow P(t) = \int_0^t Z(\tau)\, Q(t-\tau)\, d\tau$

Problem: we need $Z = \mathcal{L}^{-1}(\hat{Z})$ and

$\mathcal{L}^{-1}$ is an ill-posed numerical nightmare

Implementation: trick

convolution quadrature (Lubich, 1988)
allows the calculation of (an approximation to) P

$$P(t) = \int_0^t Z(\tau) Q(t-\tau) d\tau \approx \sum_{j=0}^{n} z_{n-j} Q(j\Delta t)$$

without having to compute Z

Implementation: CQ details

- Mellin's inversion formula $Z(\tau) = \frac{1}{2\pi i} \int_{\nu - i\infty}^{\nu + i\infty} \hat{Z}(\lambda) e^{\lambda\tau} \, d\lambda$
- Theorem If $\hat{Z}_{term}$ has nonnegative real part, then $\hat{Z}(s)$ is analytic for all $\Re s \geq 0$ except at $s = 0$, where it has a removable singularity
- $P(t) = \frac{1}{2\pi i} \int_{\nu - i\infty}^{\nu + i\infty} \hat{Z}(\lambda) \, y(\lambda; t) \, d\lambda, \qquad y(\lambda; t) = \int_0^t e^{\lambda t} Q(t - \tau) \, d\tau$
- y as solution to ODE
- discretize ODE through multistep method
- re-express integral and efficient quadratures for Cauchy integrals...

Implementation

procedure IMPEDANCEWEIGHTS

Input:

t_f = final simulation time
Δt = time step size
N = number of time steps ($N = t_f/\Delta t$)
ϵ = accuracy of computation of $\hat{Z}$

Output:

impedance weights z_n, $n = 0, ..., N$

$M = 2N$
$r = \epsilon^{1/2N}$
for $m = 0 : M - 1$ **do**
$\zeta = re^{i2\pi m/M}$
$\Xi = \frac{1}{2}\zeta^2 - 2\zeta + \frac{3}{2}$
$Z^{(m)} = \hat{Z}\left(\Xi/\Delta t\right)$
end for
for $n = 0 : N$ **do**
$z_n = \frac{r^{-n}}{M}\sum_{m=0}^{M-1} Z^{(m)} e^{-i2\pi mn/M}$
end for
end procedure

Implementation: cost

- impedance weights computed for each outflow prior to simulation
- requires $2N$ evaluations of $\hat{Z}$
- one eval. of $\hat{Z}$ = $\mathcal{O}((\#\text{generations})^2)$ operations (a few thousand)
- in short: it is cheap

Computational example

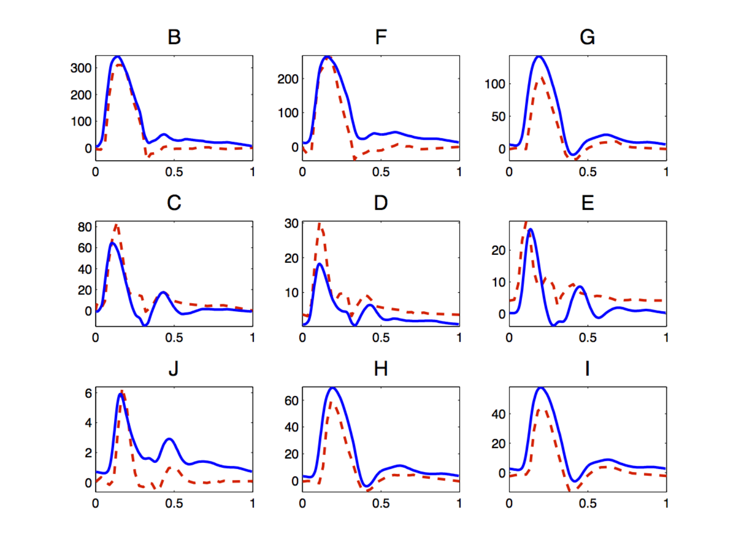
- consider specific network (Circle of Willis, "full body")
- use 1D nonlinear model

$$\partial_t A + \partial_x Q = 0$$

$$\partial_t Q + \frac{\gamma + 2}{\gamma + 1} \partial_x \left(\frac{Q^2}{A} \right) + \frac{A}{\rho} \partial_x P = -2\pi(\gamma + 2) \frac{\mu}{\rho} \frac{Q}{A}$$

- pseudospectral Chebyshev collocation in space
- 2nd order Backward Difference Formula in time
- inflow bc velocity measurements from V. Novak, BIDMC, Harvard
- outflow bc impedance

Look Ma' No calibration!



Some implementation details

- r_{min} taken as 30μm
- $Z_{term} = 0$ is a terrible idea
  Can be corrected through

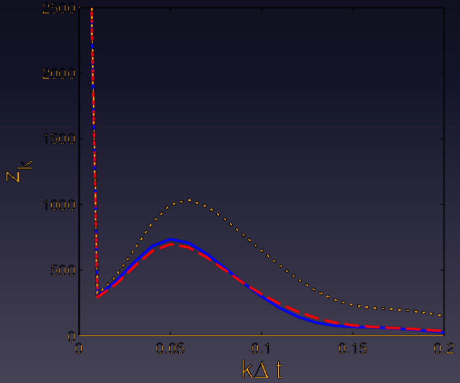
$$P_n = \sum_{j=0}^{n} z_j Q_{n-j} + P_{term}$$

with $P_{term} \approx 45$ mmHg

Towards autoregulation

What happens to the impedance under radii change?

- multiply tree vessel radii by C_{AR}
- observe $z_k(C_{AR}) \approx z_k(1)\, e^{M_{AR} k \Delta t}$, $k = 0, \dots, N$



Towards autoregulation (2)

- match has been checked over wide range of parameters
- “memory" of structured tree $\approx$ .25 sec
- time scale of autoregulation responses $\approx$ 5-20 sec
- $\Rightarrow$ auto-regulation induced microvascular changes

$$\tilde{z}_k(M_{AR}(t)) = z_k e^{M_{AR}(t) k \Delta t}, \qquad k = 0, \ldots, N.$$

- scalar (!) M_{AR} is obtained from specific autoregulation model

Towards autoregulation (3)

- variation of tree resistance away from baseline value $R_{eq} = (P_{eq} - P_{term})/Q_{eq}$
- auxiliary equation

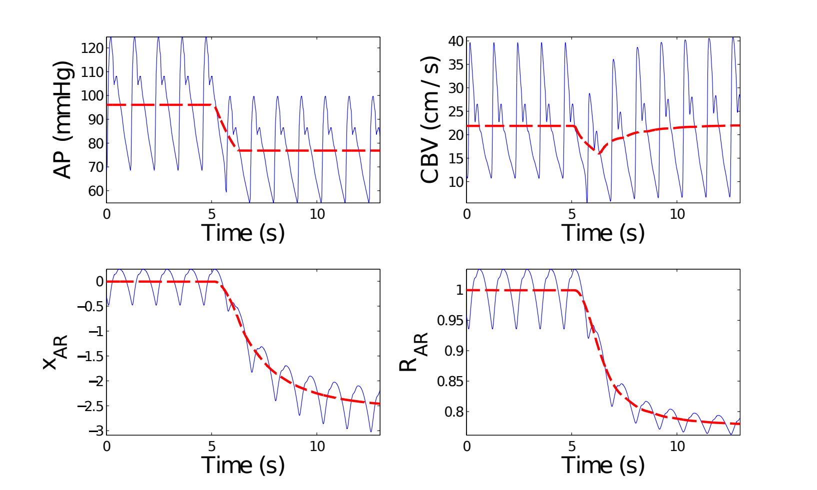
$$\frac{dx_{AR}}{dt} = G_{AR}\left(\frac{Q(t) - Q_{eq}}{Q_{eq}}\right)$$

- R_{AR} obtained from x_{AR} by imposing limits (sigmoid)
- M_{AR} obtained from

$$\sum_{k=0}^{N} \tilde{z}_k(M_{AR}) = R_{AR} \sum_{k=0}^{N} z_k$$

Towards autoregulation (4)

- impose $P(t) = P_{baseline}(t)f(t)$ at aorta
- 20% drop in MAP
- immediate flow decrease followed by return to baseline



Database from BIDMC

	total		male		female	
participants	167		86		81	
age	66.5±8		65.6±9		67.3±8.	
group	**hyper**	**%**	**no hyper**	**%**	**total**	**%**
control	14	8.4	48	28.7	62	37.1
stroke	26	15.6	16	9.6	42	25.1
DM	36	21.6	27	16.2	63	37.7

Database from BIDMC (2)

For each patient: MCA data

- BFV post-processed from Trans Cranial Doppler (TCD)
- CBF from CASL MRI

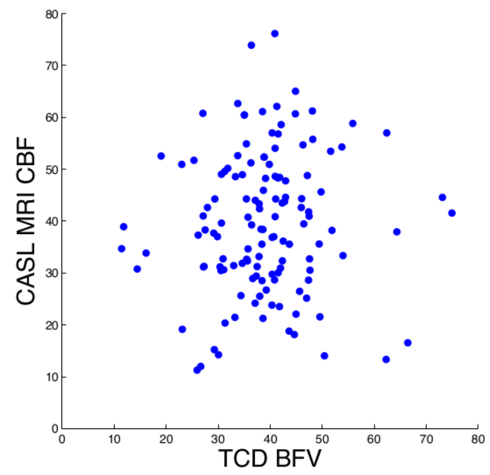
HCT, CO_2	from lab
age, height, weight	from lab
head size (front to back and side to side)	from lab
gender, diabetes (y/n), hypertension (y/n)	from lab

radius R	from images
insonation angle θ	from images

M territory mass from “maps" and post processing

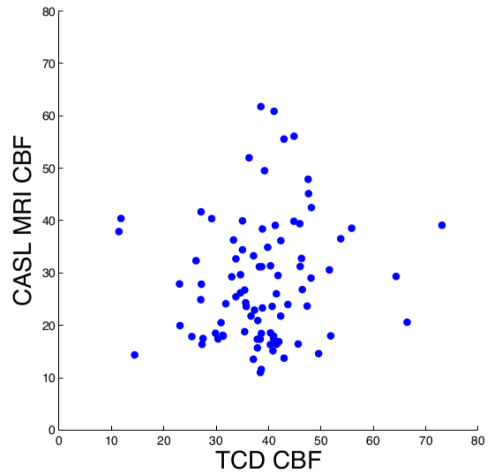
TCD vs MRI

Direct comparison between TCD-BFV and MRI-CBF



TCD vs MRI (2)

Direct estimate: $CBF_{TCD} = \frac{\pi R^2}{M} \frac{v}{2\cos\theta}$

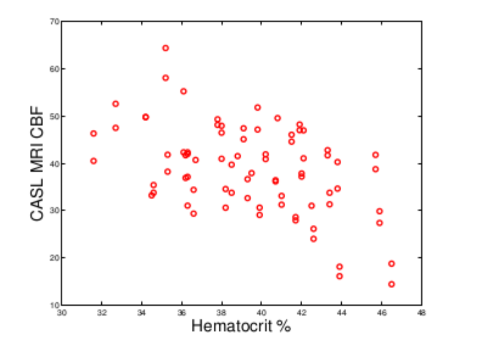


Sources of uncertainties, TCD

- insonation angle
- velocity profile
- vessel radius
- territory mass

Sources of uncertainties, CASL MRI

CASL MRI CBF is correlated with HCT% ($r = -.49$, $p = 7.5 \times 10^{-6}$)



Predicting CBF?

- y : response variable CASL MRI CBF
- $\mathbf{x}$: predictor variables, TCD BFV, age, height,...

Prediction: $y = f(\mathbf{x})$ based on

- partitioning the data and applying local models
  - regression trees
  - random forests

Trees and forests

- y_i, $i = 1, \ldots, N$ (N observations)
- $\mathbf{x}_i = (x_{i,1}, \ldots, x_{i,p})$, $i = 1, \ldots, N$, $p = 14$
- parameter space: partitioned in K regions Ω_k, $k = 1, \ldots, K$
- response function approximated by

$$y \approx f(\mathbf{x}) = \sum_{k=1}^{K} c_k \, \chi_k(\mathbf{x})$$

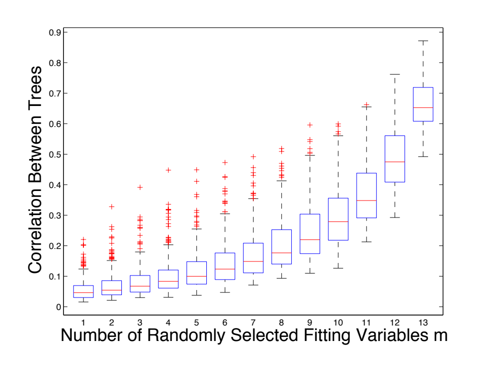
  χ_k = indicator function of Ω_k; c_k = simple local model
- for instance $c_k = 1/|I_k| \sum_{j=1}^{|I_k|} y_j$, $I_k = \{j; x_j \in \Omega_k\}$
- ideally, MSE $\frac{1}{N} \sum_{i=1}^{N} (y_i - f(x_i))^2$ is minimized over all partitions Ω_k, $k = 1, \ldots, K$
- computational feasibility $\Rightarrow$ Ω_k's taken as “rectangular" and minimization replaced by recursive partitioning

Trees and forests (2)

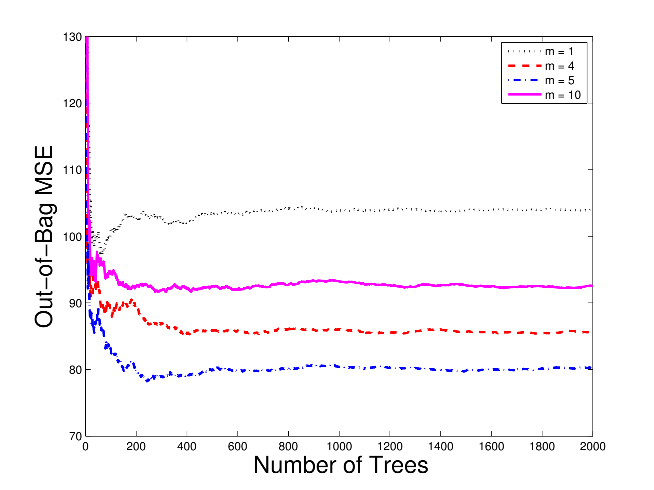
Trees as above can be unstable. Improvements:

- consider an ensemble of trees (bootstrapping)
- consider fixed number of predictive variables for splitting

$\Rightarrow$ decreases tree correlation and estimate variance

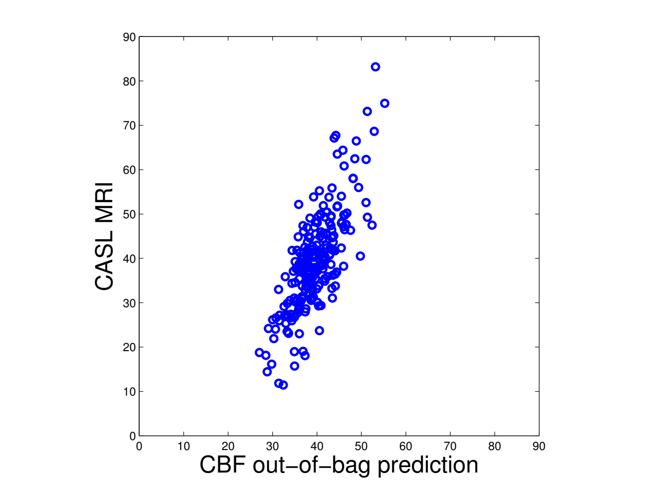


Trees and forests (3)

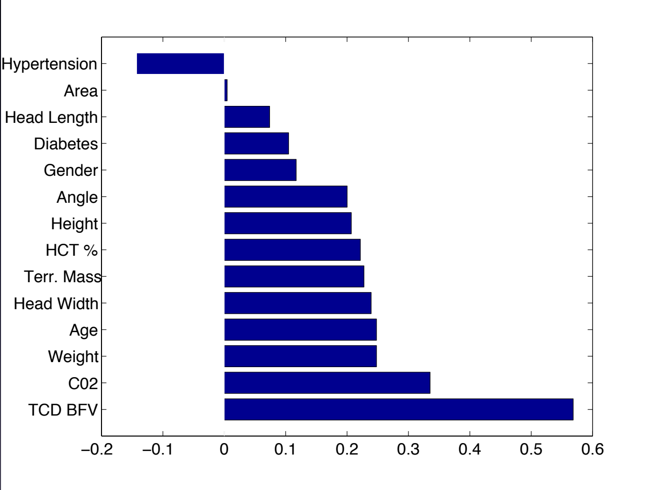


$m = 5 < p = 14$ wins

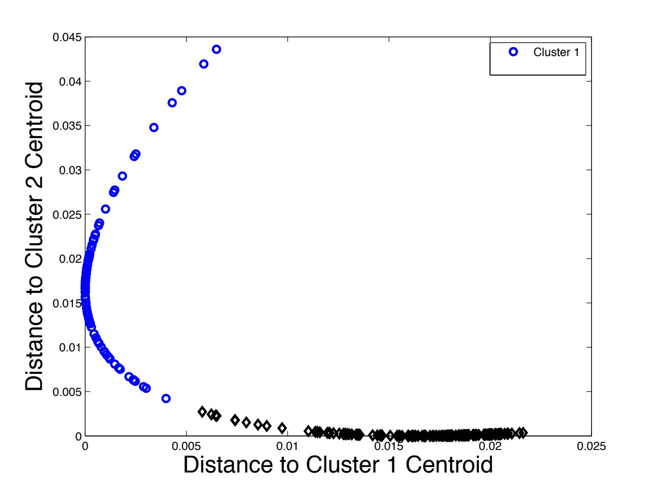
Some results: correlation



Some results: variable importance



Some results: clustering



Future work

- organ specific BCs
- analysis of role played by calibration
- efficient uncertainty representation in comp. hemodynamics
- local regression methods for patient clustering

references

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