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Institute for *in silico* Medicine

Use of a GP emulator and 1D model to characterize cardiovascular pathologies and guide treatment

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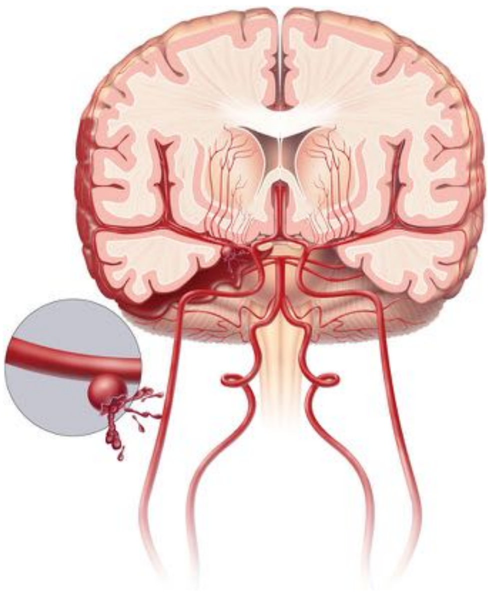
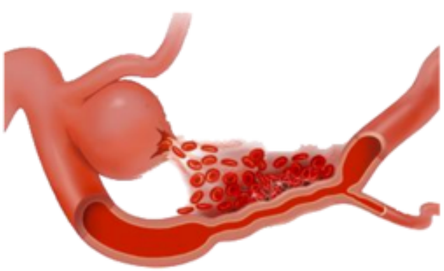
Cerebral vasospasm



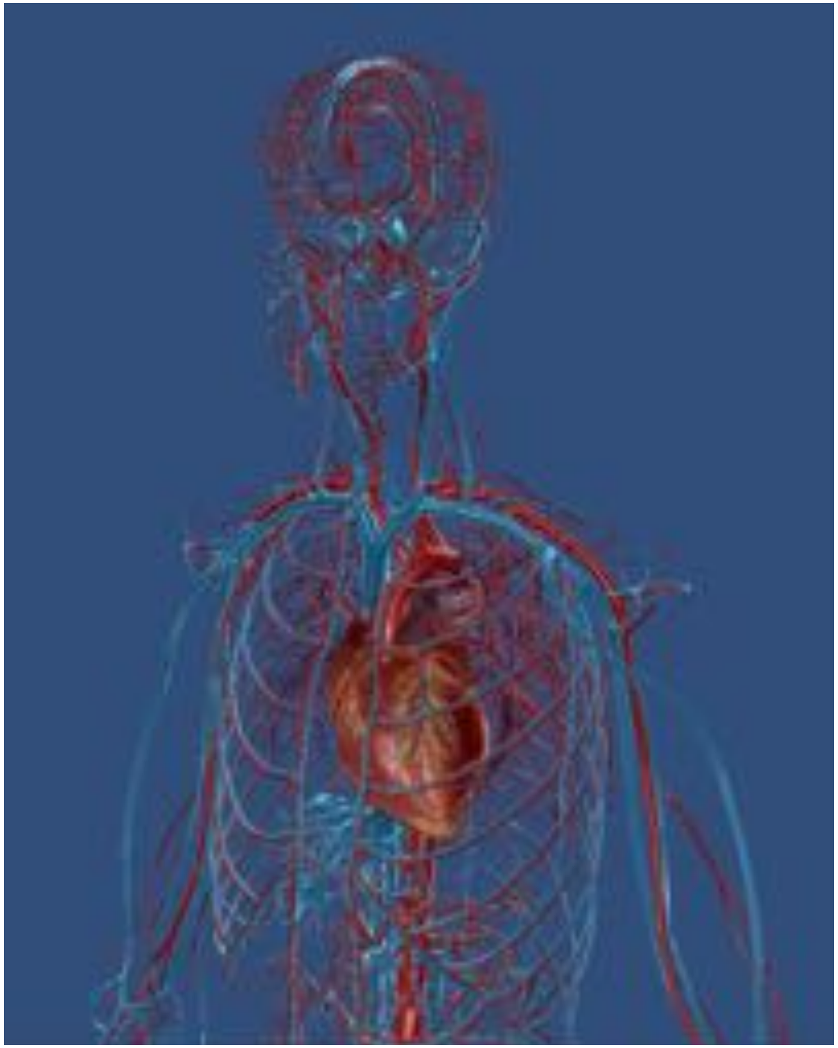
www.strokecenter.org



- Progressive and prolonged narrowing of arteries after stroke/SAH
- CVS major cause of cerebral ischemia (death of brain tissue cells)
- Economic costs and hospital stay higher than stroke-only patients ($120M/year in US, 2006)
- Trans-cranial Doppler (TCD) used for to detect increase in **blood velocity** at locations affected by CVS
- TCD has low sensitivity when CVS affects peripheral vessels

Source: Stroke data –NHS England

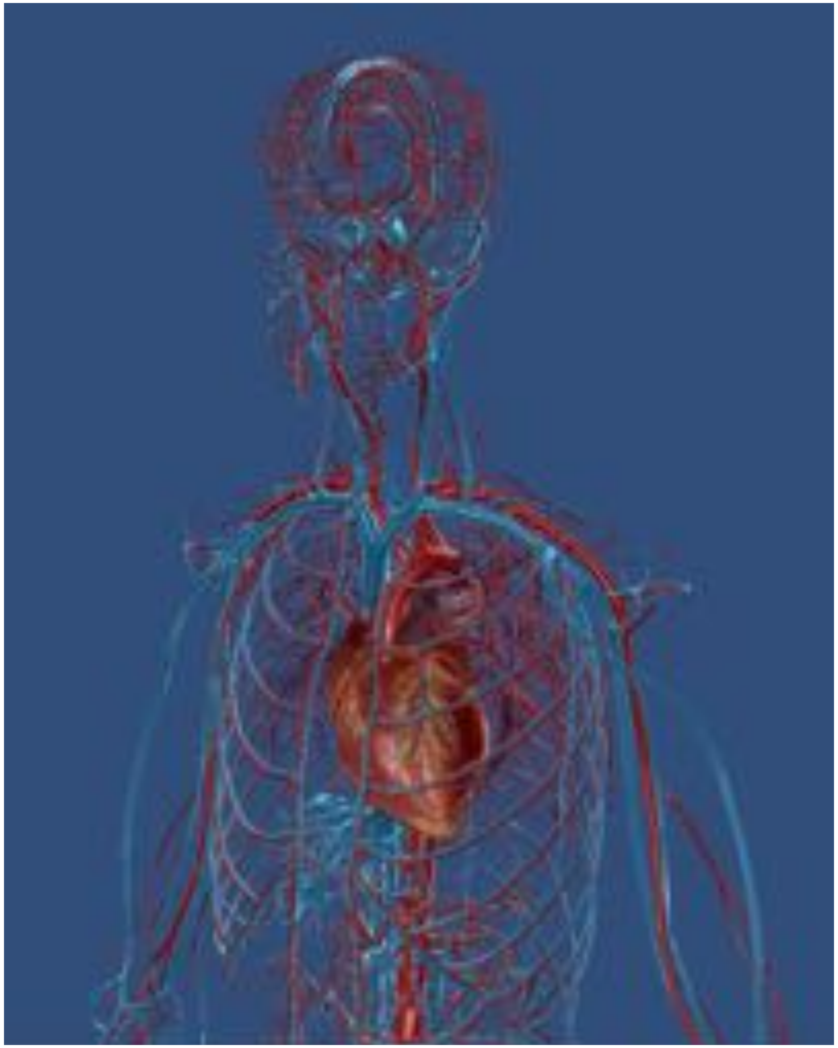
Pulse waves in the cardiovascular system



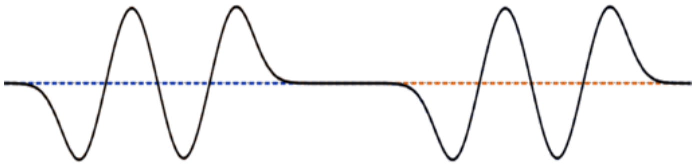
- Pressure waves originate from intermittent contraction of the heart
- Waves propagate through the elastic vessels of the CV system
- Waves reflect at points of discontinuity (e.g. bifurcations, bends, tapering, change in compliance)

O. Alexandrov, https://commons.wikimedia.org/w/index.php?curid=3148138

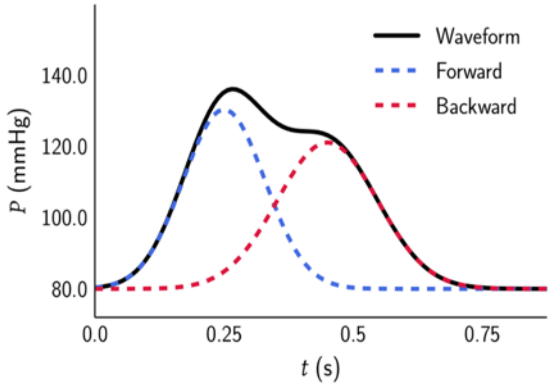
Pulse waves in the cardiovascular system



- This has an effect on the waveforms
- Waveforms carry rich diagnostic information about the system through which they propagate

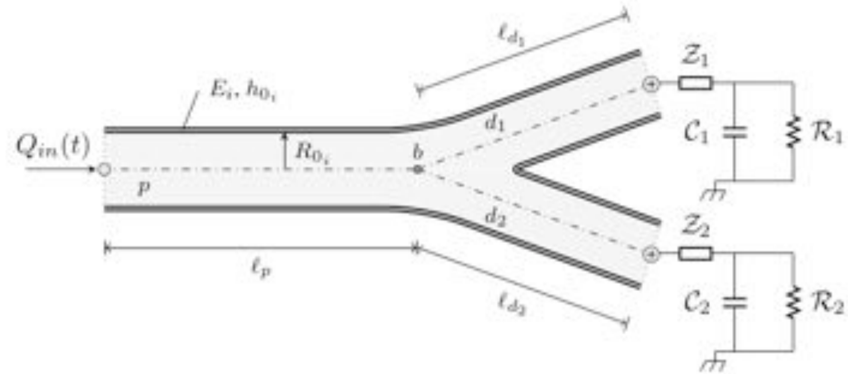


Tom Walsh http://www.ophysics.com/



1D cardiovascular model (OpenBF)

- Whole-circulation model based on reduced 1D form of N-S equations for incompressible flows in tapered elastic tubes
- Linear-elastic constitutive equation relating transmural pressure to cross-sectional area
- Governing equations discretized using Finite Volume Method

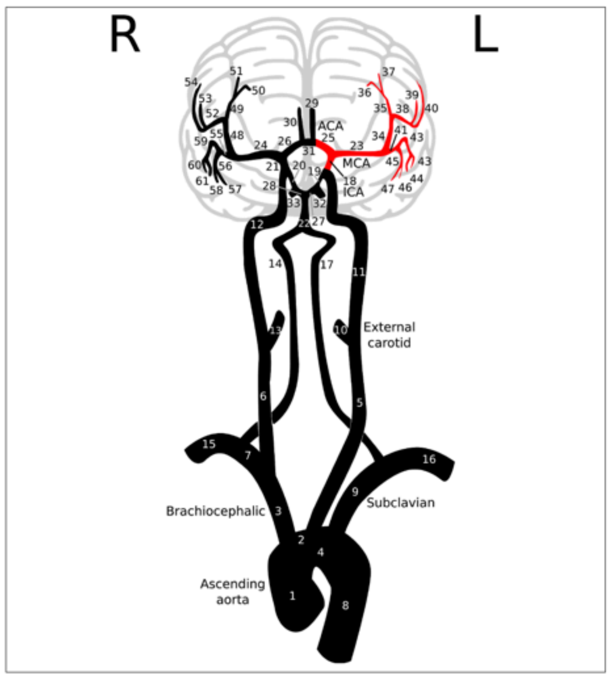


$$
\begin{cases}
\dfrac{\partial A}{\partial t} + \dfrac{\partial (Au)}{\partial x} = 0, \\[2ex]
\dfrac{\partial (Au)}{\partial t} + \dfrac{\partial (Au^2)}{\partial x} + \dfrac{A}{\rho}\dfrac{\partial P}{\partial x} = -8\pi \dfrac{\mu}{\rho} u, \\[2ex]
P = P_{ext} + \beta \left[\left(\dfrac{A}{A_0} \right)^{1/2} - 1 \right], \quad \beta = \sqrt{\dfrac{\pi}{A_0}} \dfrac{E h_0}{1 - \sigma^2},
\end{cases}
$$

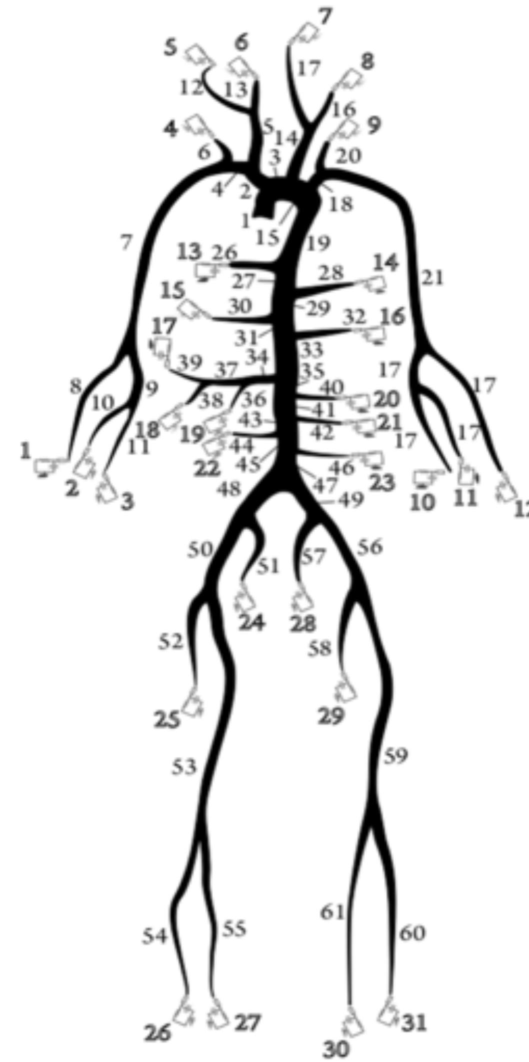
Melis *et al* *Int J Numer Meth Biomed Engng*. 2017

1D cardiovascular model (OpenBF)

- 77 arteries, including cerebral network
- Subject-generic mechanical properties from literature



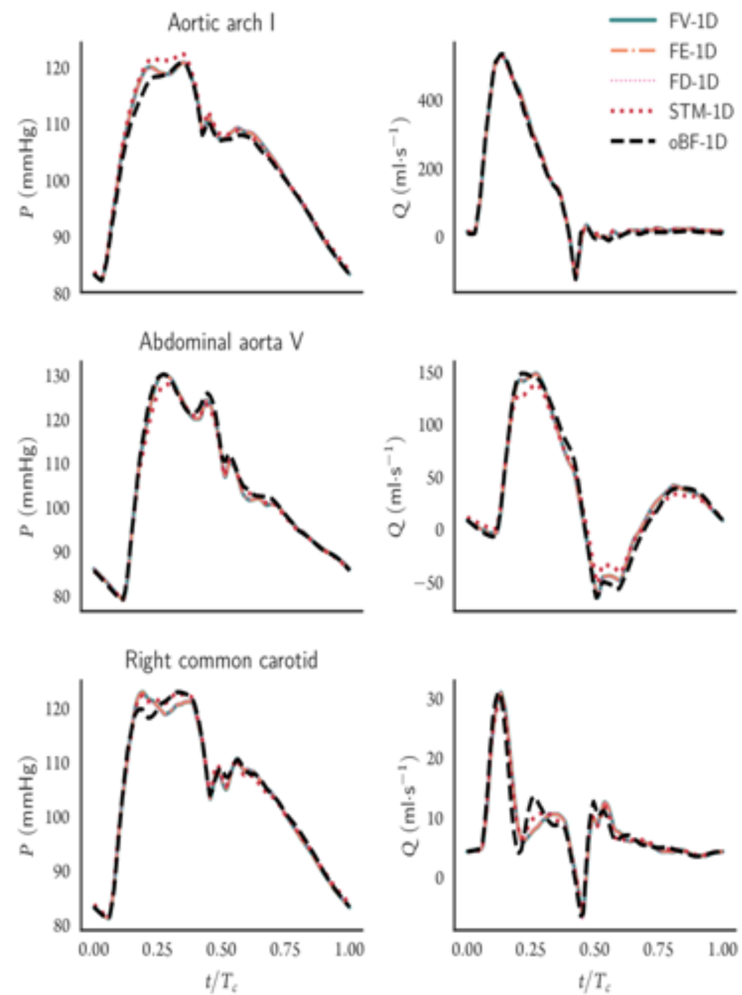
Post-MCA vasculature model, network based on Tanriover *et al* (2003).



Melis *et al* *Int J Numer Meth Biomed Engng*. 2017

1D cardiovascular model (OpenBF)

- 77 arteries, including cerebral network
- Subject-generic mechanical properties from literature
- Verified, and validated through quantitative comparison with other established models and experimental data



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1D cardiovascular model (OpenBF)

- Model and documentation available via GitHub
  https://insigneo.github.io/openBF/

openBF
installation,
tutorial,
and docs

openBF documentation

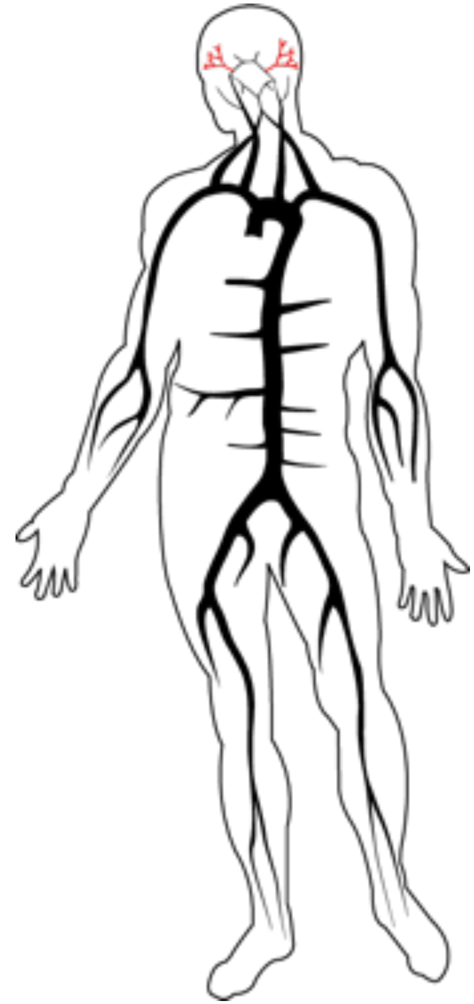
- Installation
- Tutorial
- Docs - API Index

Installation

openBF has been developed and tested on Ubuntu 14.04 and written with julia 0.3.2. To install julia please refer to its official page.

Additional packages required by openBF are listed here. To install additional packages, start a julia interactive session by typing `julia` in a terminal window, and use the command `Pkg.add("package name")` to install. For further informations see julia documentation.

openBF uses signal processing functions from `scipy.signal` library. This library requires Python 2.7.3. To install Python and SciPy please refer to their linked websites.



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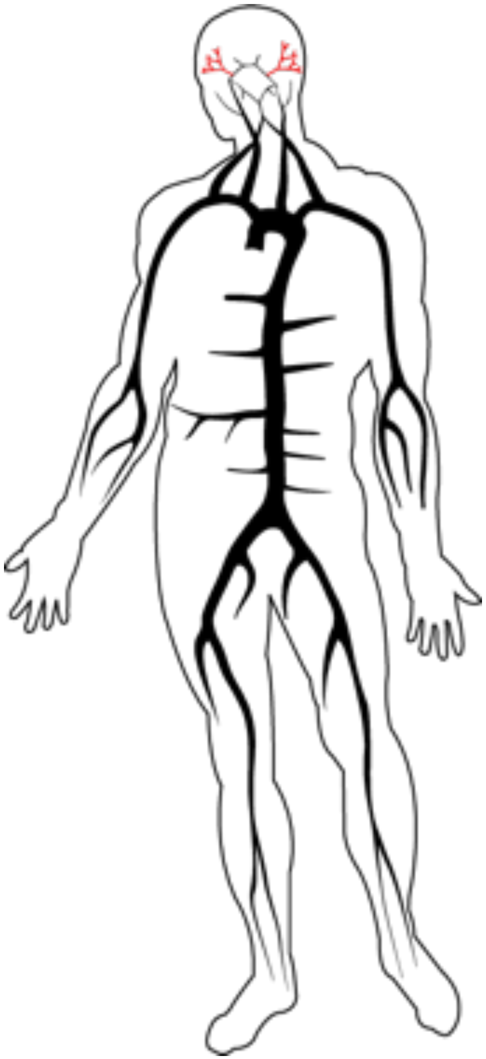
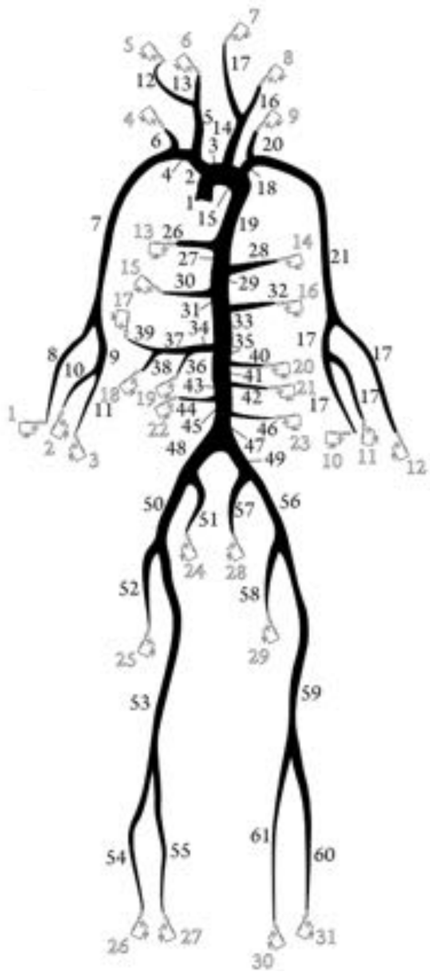
1D model approach





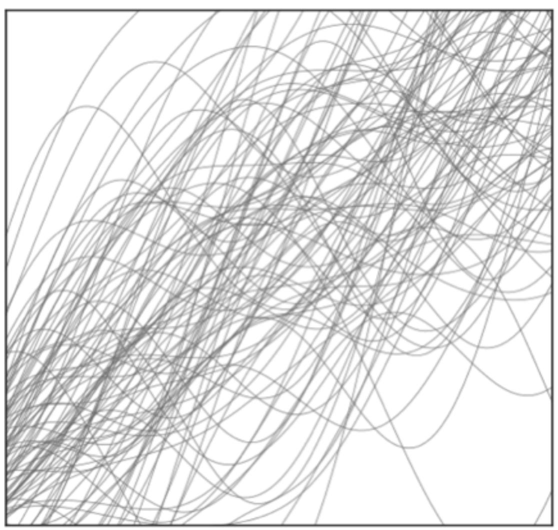
- ***Problem:*** 1D model parameters set for a typical individual
- Different parameterization will also have influence on waveforms
- Robustness of potential biomarkers under a range of model parameterizations
- → **Uncertainty analysis:** computationally demanding (Complete Monte Carlo analysis est. 600 hrs)

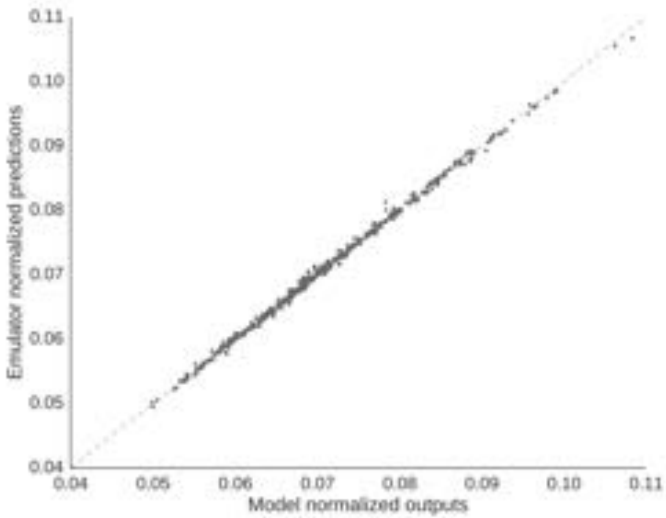
Gaussian process statistical emulators

- From a few runs of the model a GP emulator can reproduce the model behaviour

- The emulator can be used to perform uncertainty analyses with high accuracy and reducing computational time by 95%

- An uncertainty analysis will identify waveform features that are strongly correlated with vessel narrowing





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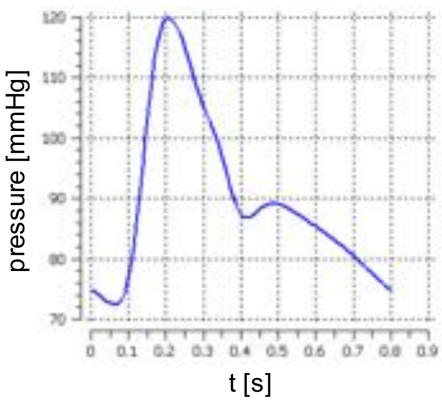
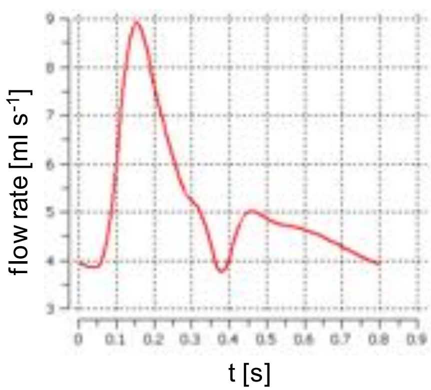
Sobol's uncertainty analysis

pressure waveform



flowrate waveform



	$\mathbf{T}_i$					$\mathbf{H}_i$				
	R_0	E	ℓ	R_p	C_p	R_0	E	ℓ	R_p	C_p
$\min(P)$	1	1	1	99	0	0	1	1	3	0
$\min(\partial_t P)$	90	7	6	0	2	5	3	5	0	1
$\min(\partial_{tt} P)$	94	6	4	0	0	4	3	3	0	0
$\min(Q)$	71	22	36	7	6	66	24	23	5	2
$\min(\partial_t Q)$	88	5	12	0	4	10	1	6	0	1
$\min(\partial_{tt} Q)$	73	7	25	1	5	8	4	9	0	0
$\min(u)$	97	0	2	0	0	1	1	1	0	0
$\min(\partial_t u)$	89	1	6	0	6	4	2	5	0	1
$\min(\partial_{tt} u)$	93	1	5	0	1	1	2	3	0	0
$\mathrm{mean}(P)$	3	0	1	98	0	0	0	0	3	0
$\mathrm{mean}(\partial_t P)$	50	33	46	9	5	32	23	33	1	3
$\mathrm{mean}(\partial_{tt} P)$	31	50	41	32	0	31	49	45	3	0
$\mathrm{mean}(Q)$	81	9	17	14	4	60	36	52	14	2
$\mathrm{mean}(\partial_t Q)$	59	54	54	0	1	46	43	43	1	0
$\mathrm{mean}(\partial_{tt} Q)$	65	35	65	0	1	54	27	46	1	1
$\mathrm{mean}(u)$	97	0	2	0	0	1	1	1	0	0
$\mathrm{mean}(\partial_t u)$	92	4	13	2	0	8	2	11	0	0
$\mathrm{mean}(\partial_{tt} u)$	88	16	35	0	2	29	10	28	0	2
$\max(P)$	18	1	2	81	0	1	1	1	3	0
$\max(\partial_t P)$	93	7	4	0	1	3	3	4	0	0
$\max(\partial_{tt} P)$	93	6	4	0	1	3	3	4	0	0
$\max(Q)$	92	3	16	4	1	41	5	24	4	1
$\max(\partial_t Q)$	86	2	17	3	2	28	1	15	2	1
$\max(\partial_{tt} Q)$	83	8	13	0	6	9	4	7	0	0
$\max(u)$	97	0	2	0	0	1	1	1	0	0
$\max(\partial_t u)$	97	1	2	0	0	1	1	1	0	0
$\max(\partial_{tt} u)$	88	3	8	0	5	3	3	4	0	0

CV biomarker	$\mathbf{T}_{R_0}$	$\mathbf{H}_{R_0}$
$\mathrm{mean}(u)$	97.43	0.82
$\max(u)$	97.28	0.84
$\min(u)$	97.23	0.93
$\max(\partial_t u)$	96.83	0.90
$\min(\partial_{tt} P)$	93.76	3.62
$\max(\partial_{tt} P)$	93.05	3.35
$\min(\partial_{tt} u)$	92.98	1.16
$\max(\partial_t P)$	92.52	3.48

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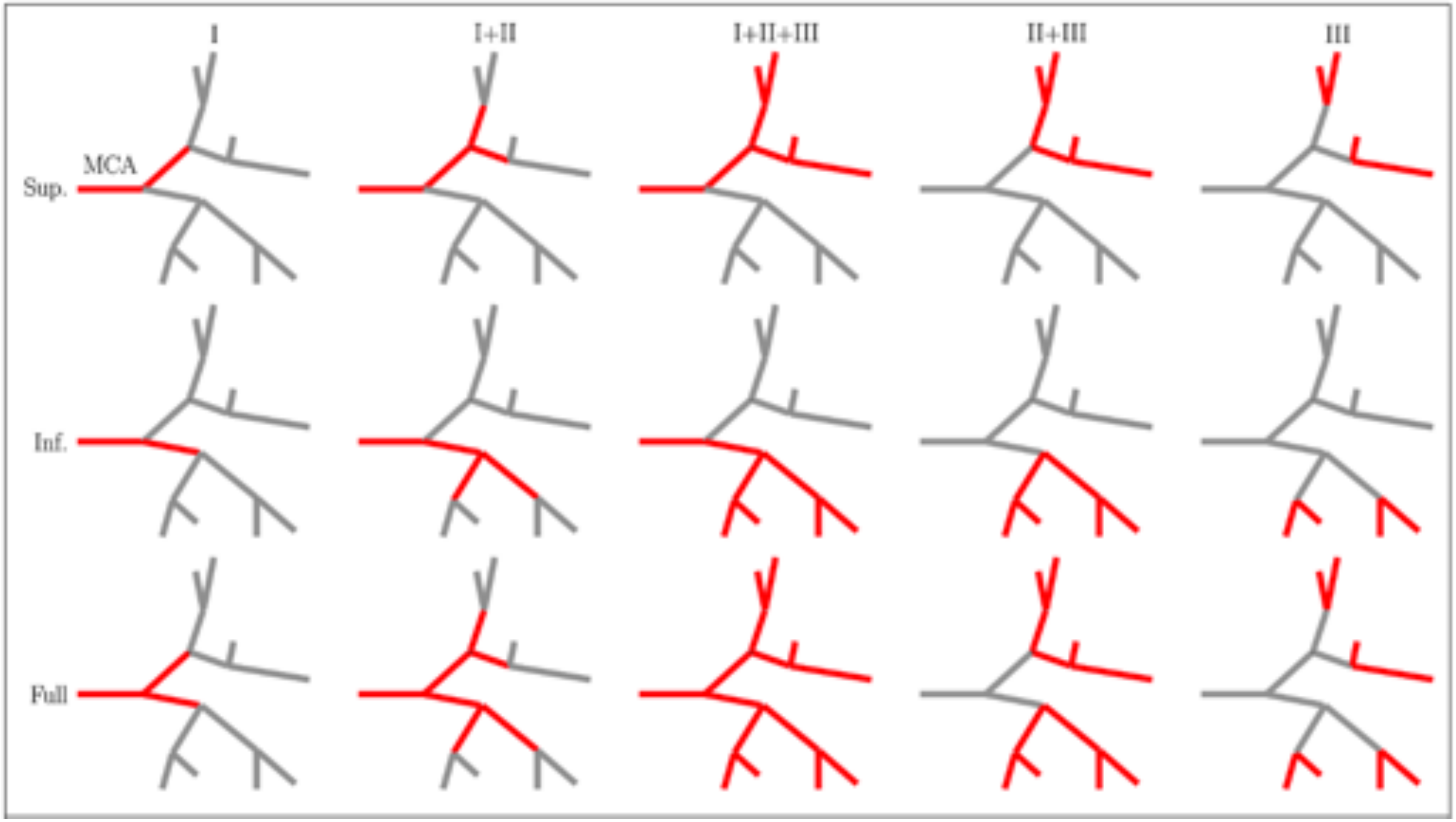
Vasospasm characterization



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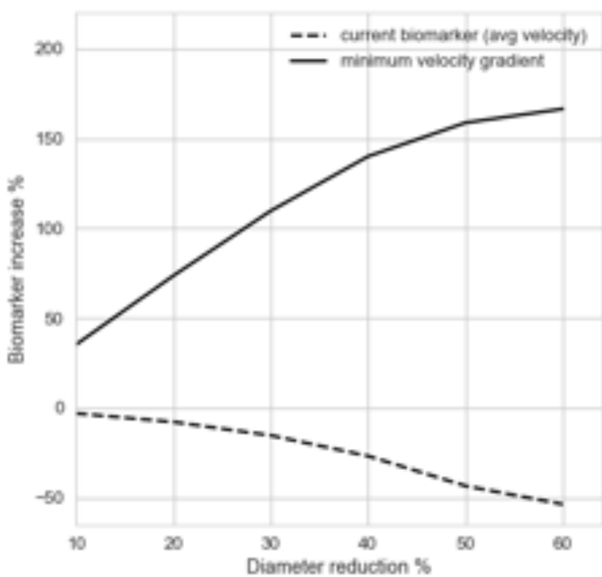

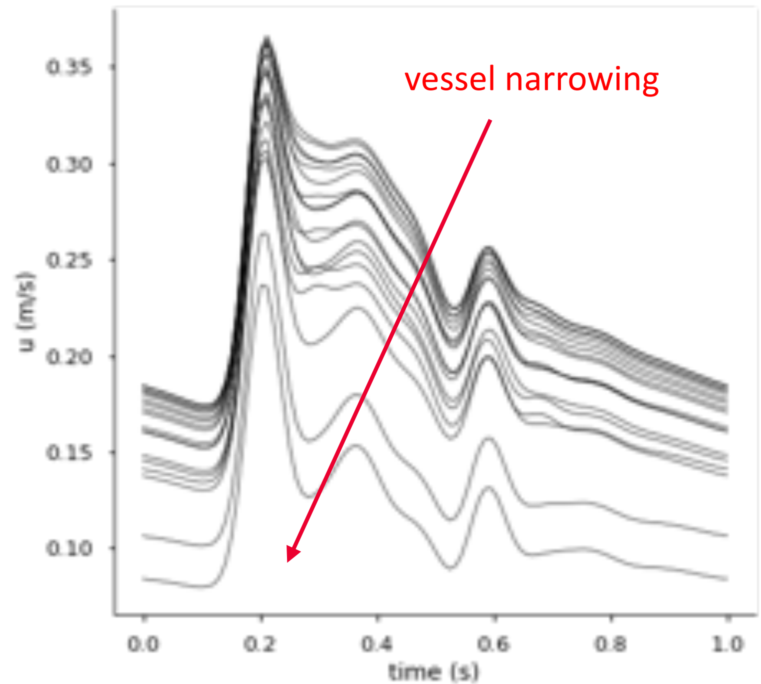

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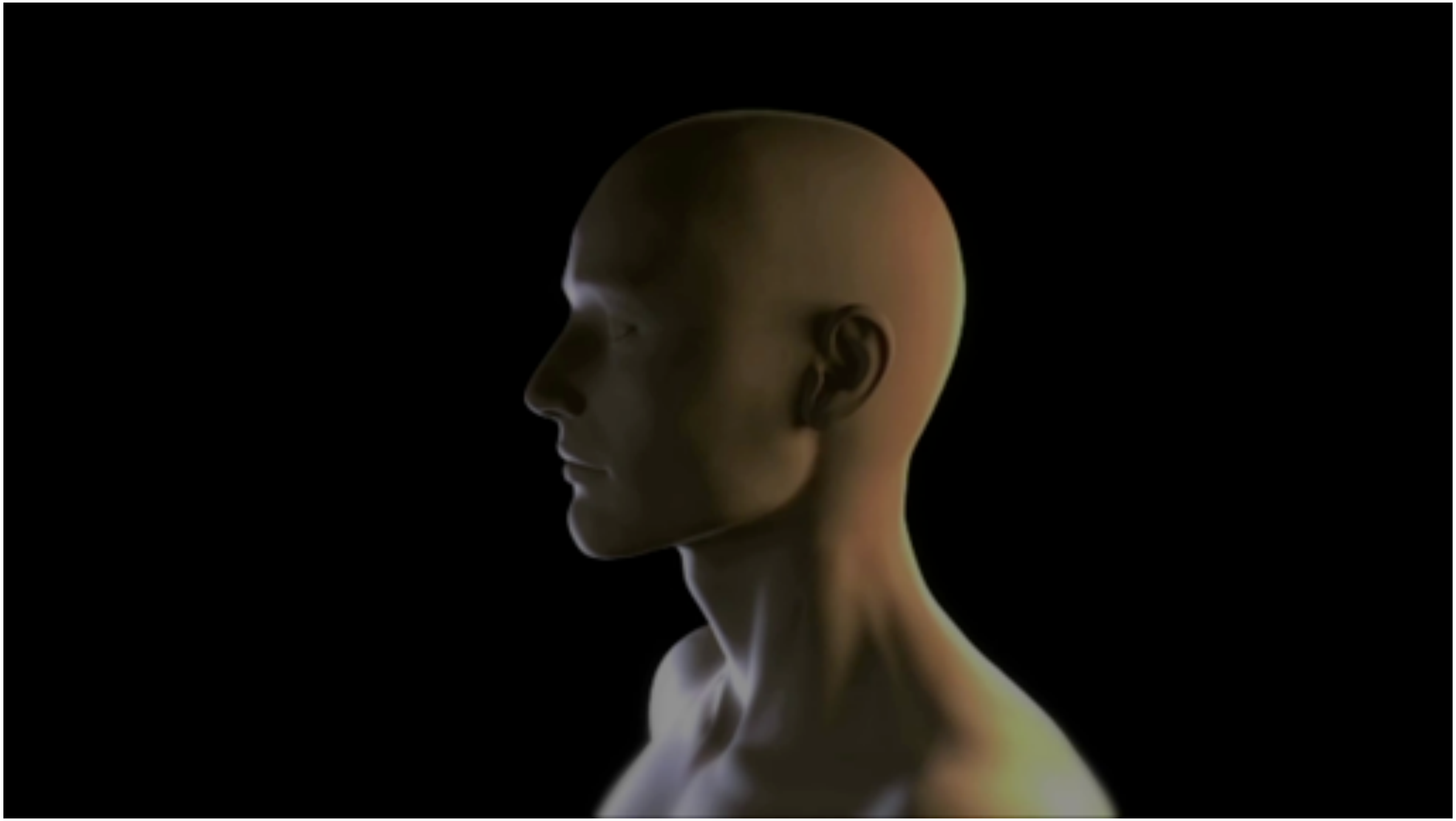
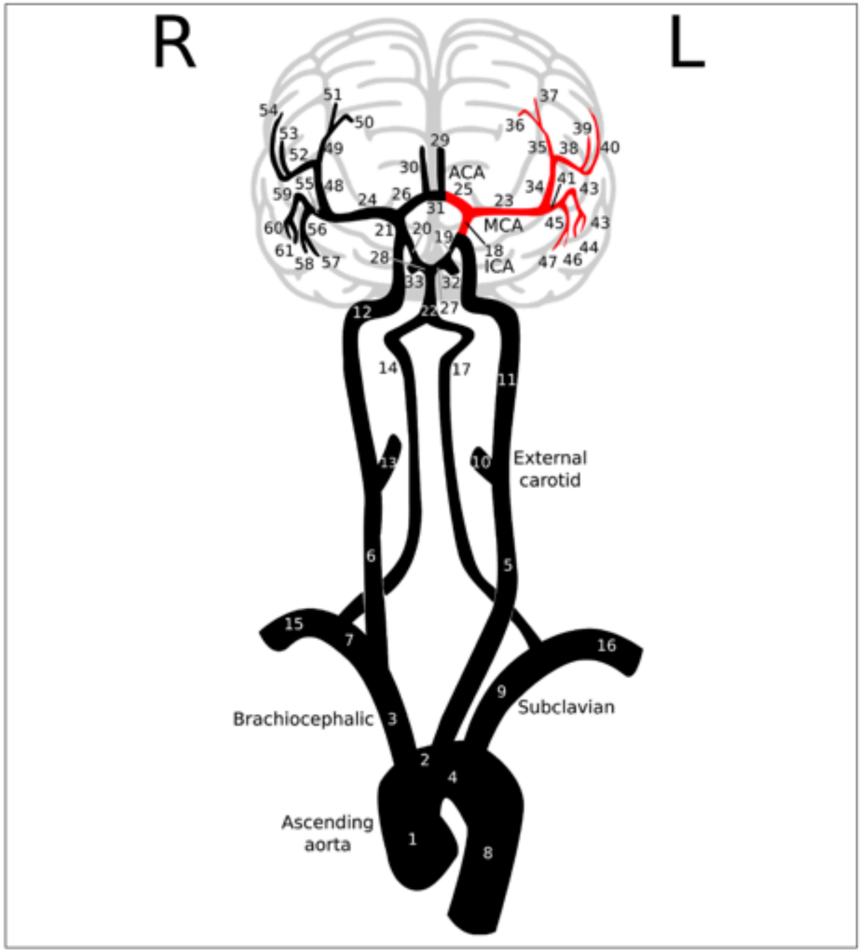
OpenBF developments
Treatment of ischemic stroke

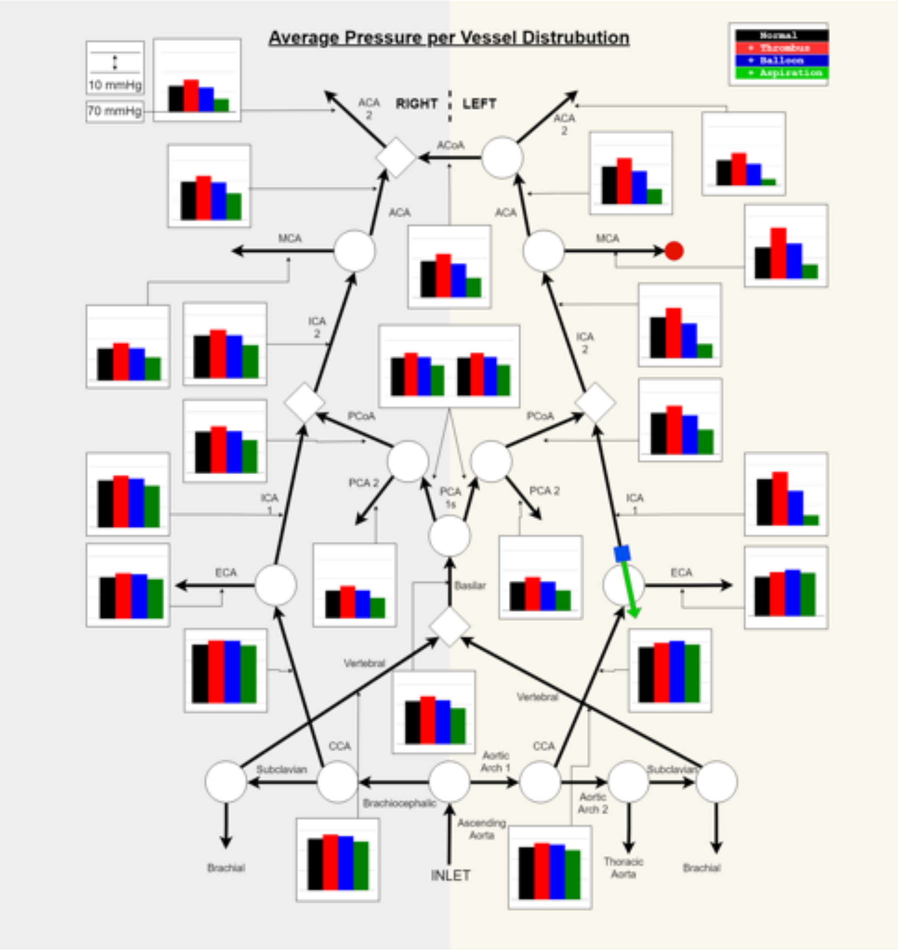


Source: Covidien – Solitaire revascularization device product animation

OpenBF developments

Treatment of ischemic stroke – OpenBF simulations





Acknowledgements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Thank You!

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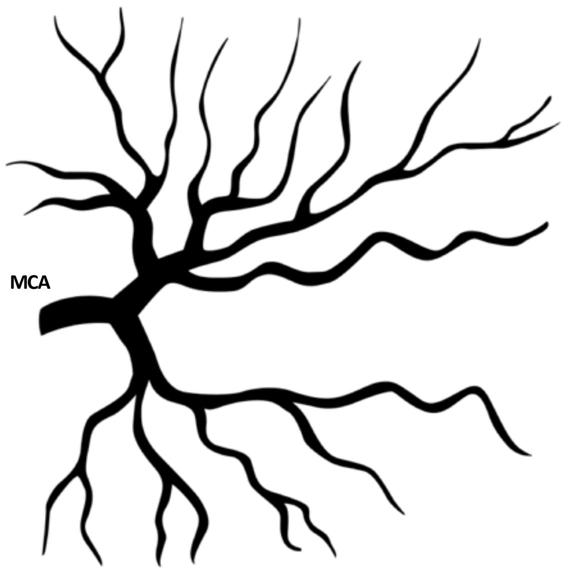
Anatomy based 1D model



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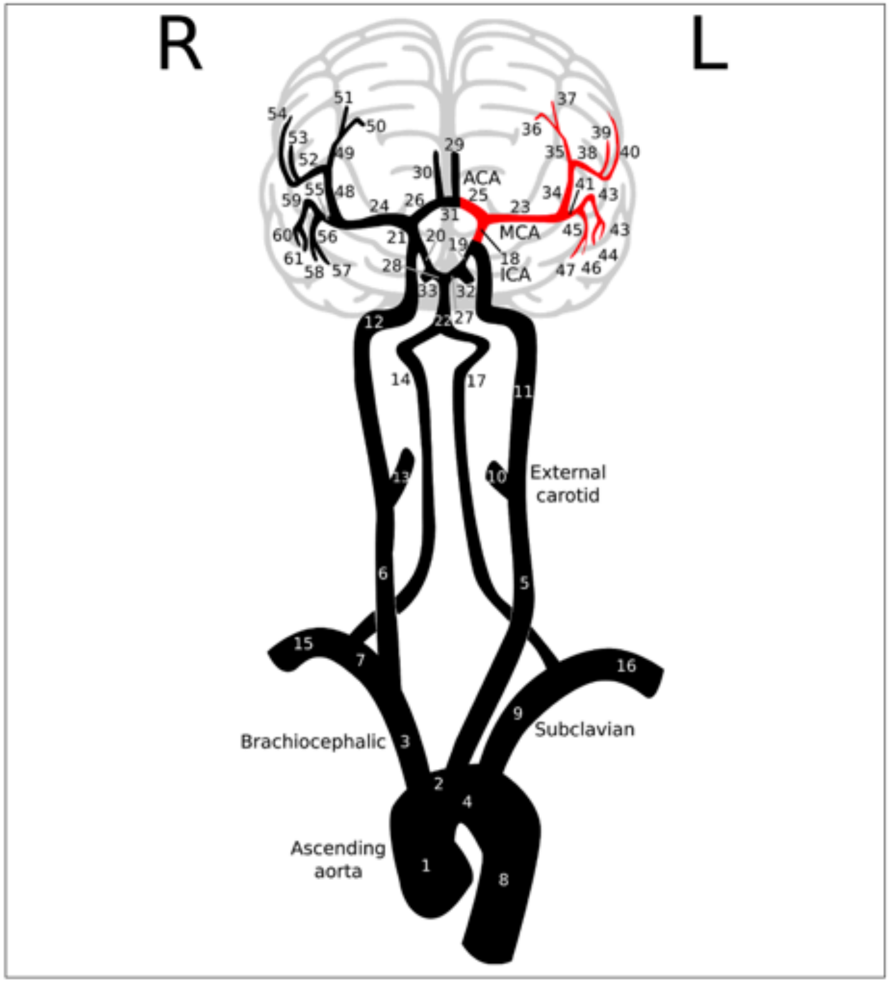
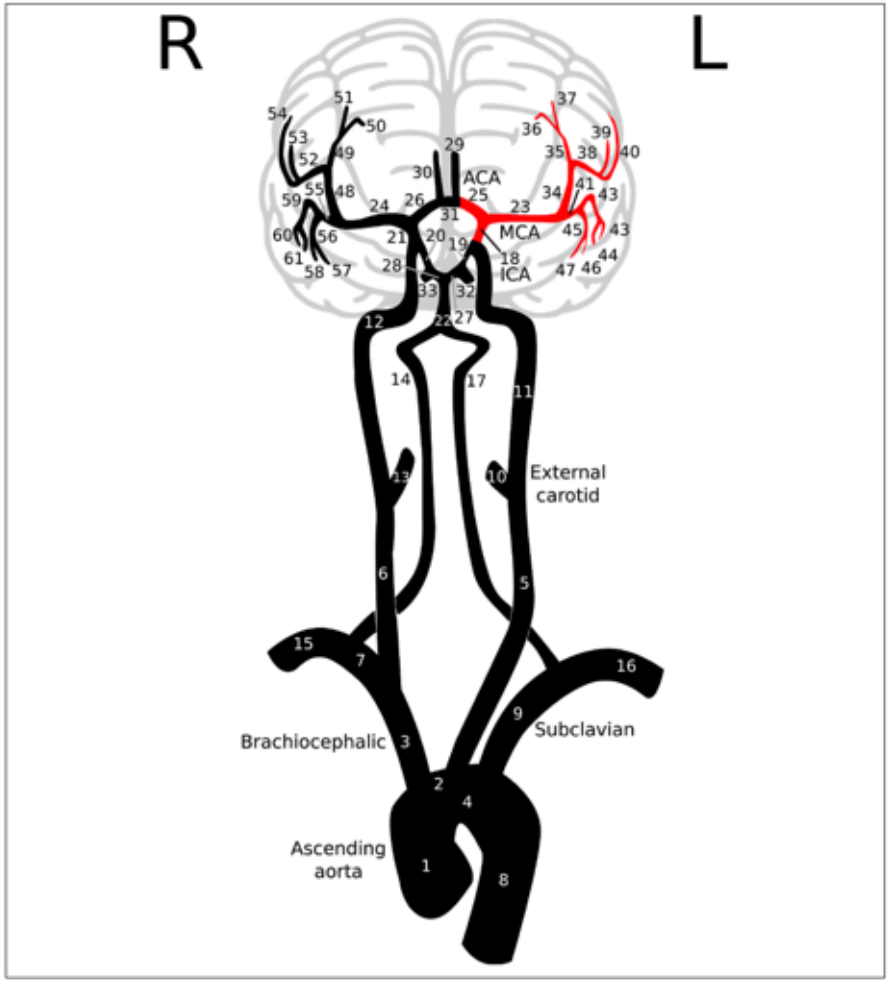
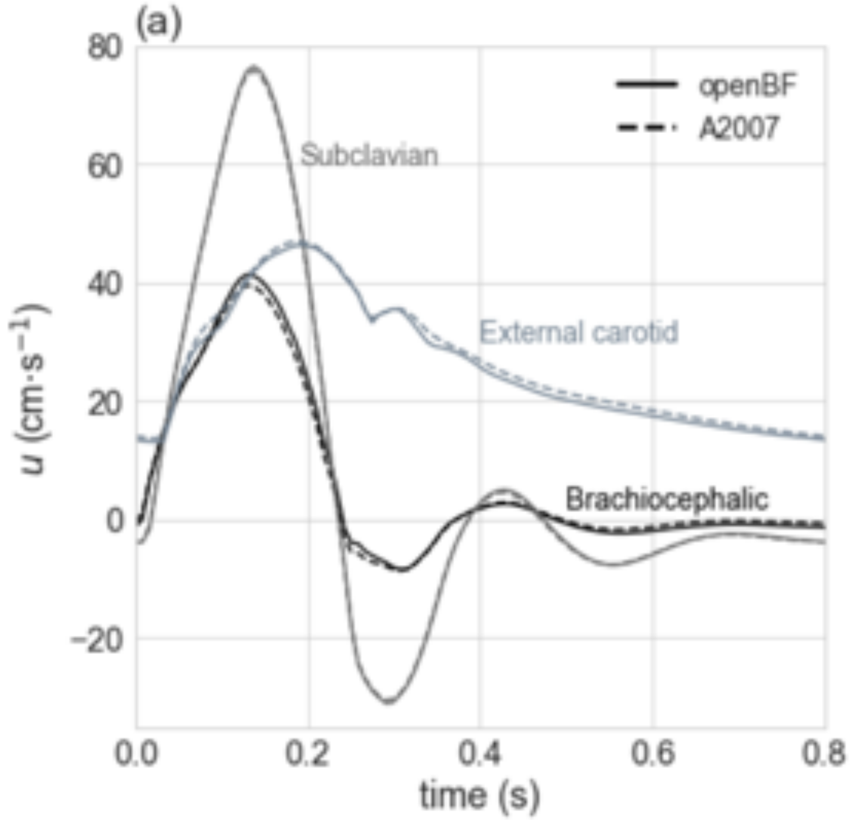


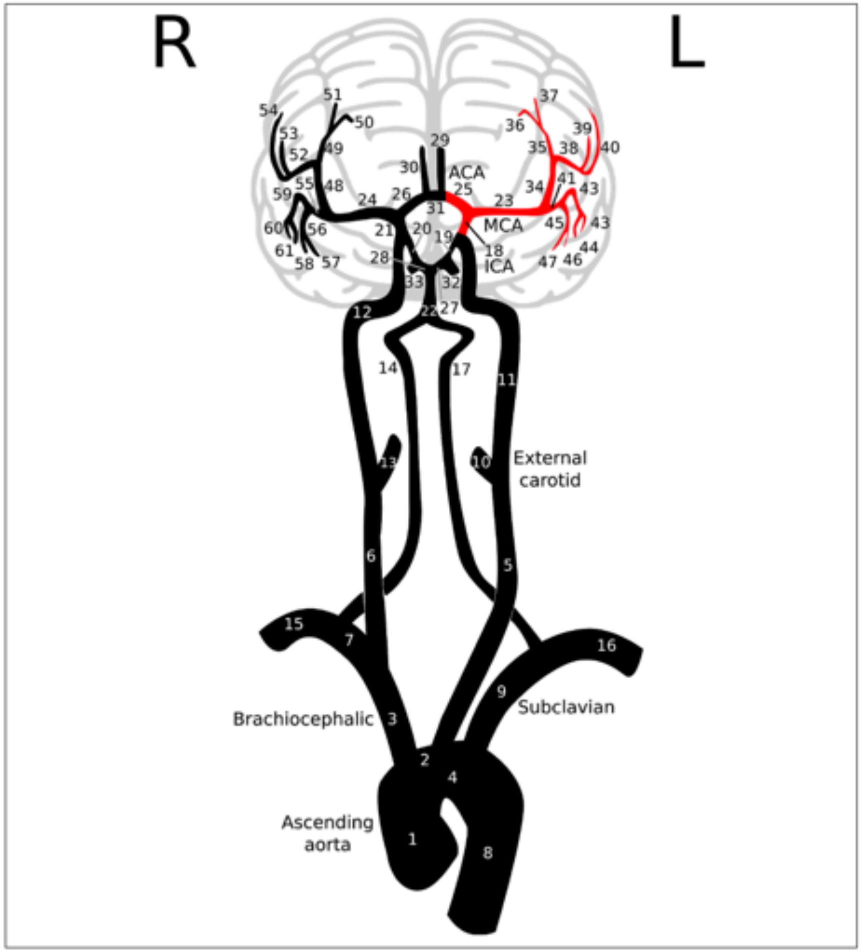
Validation of extended model

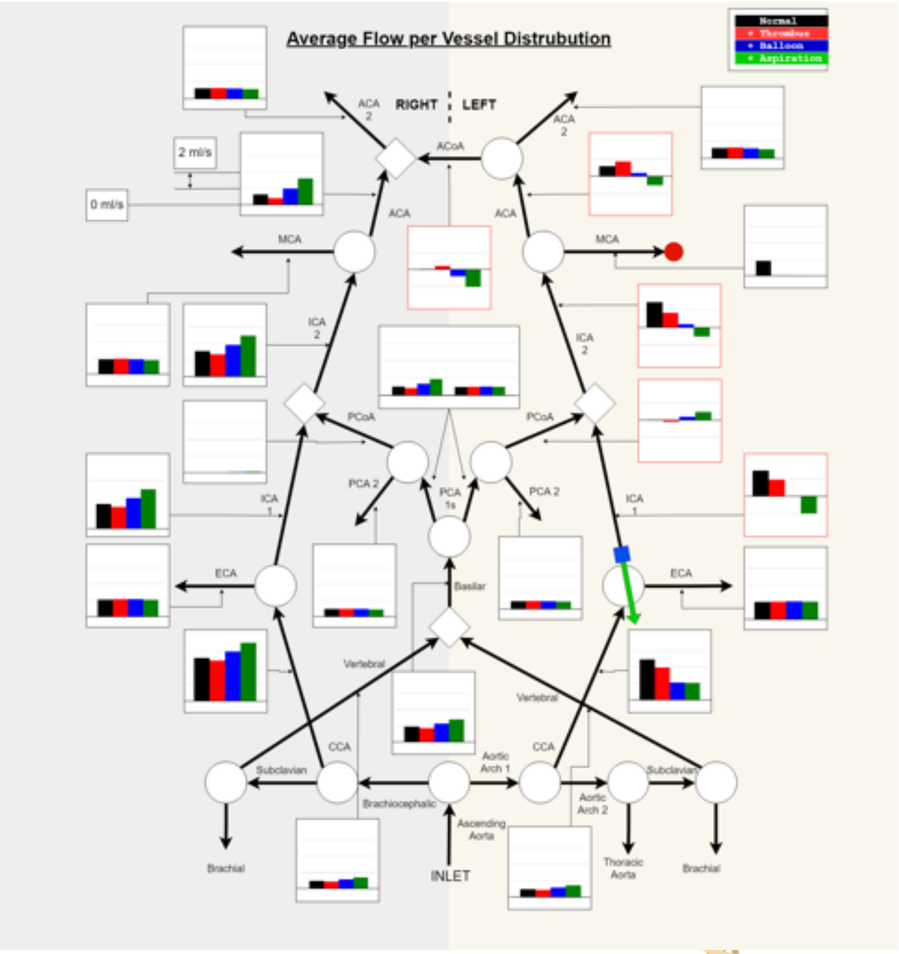




OpenBF developments

Treatment of ischemic stroke – OpenBF simulations





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