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A compartmental model to investigate intracranial pulsatility

Bachelor's thesis defense

Degree on Biomedical Engineering

Leganés, 12th July 2023

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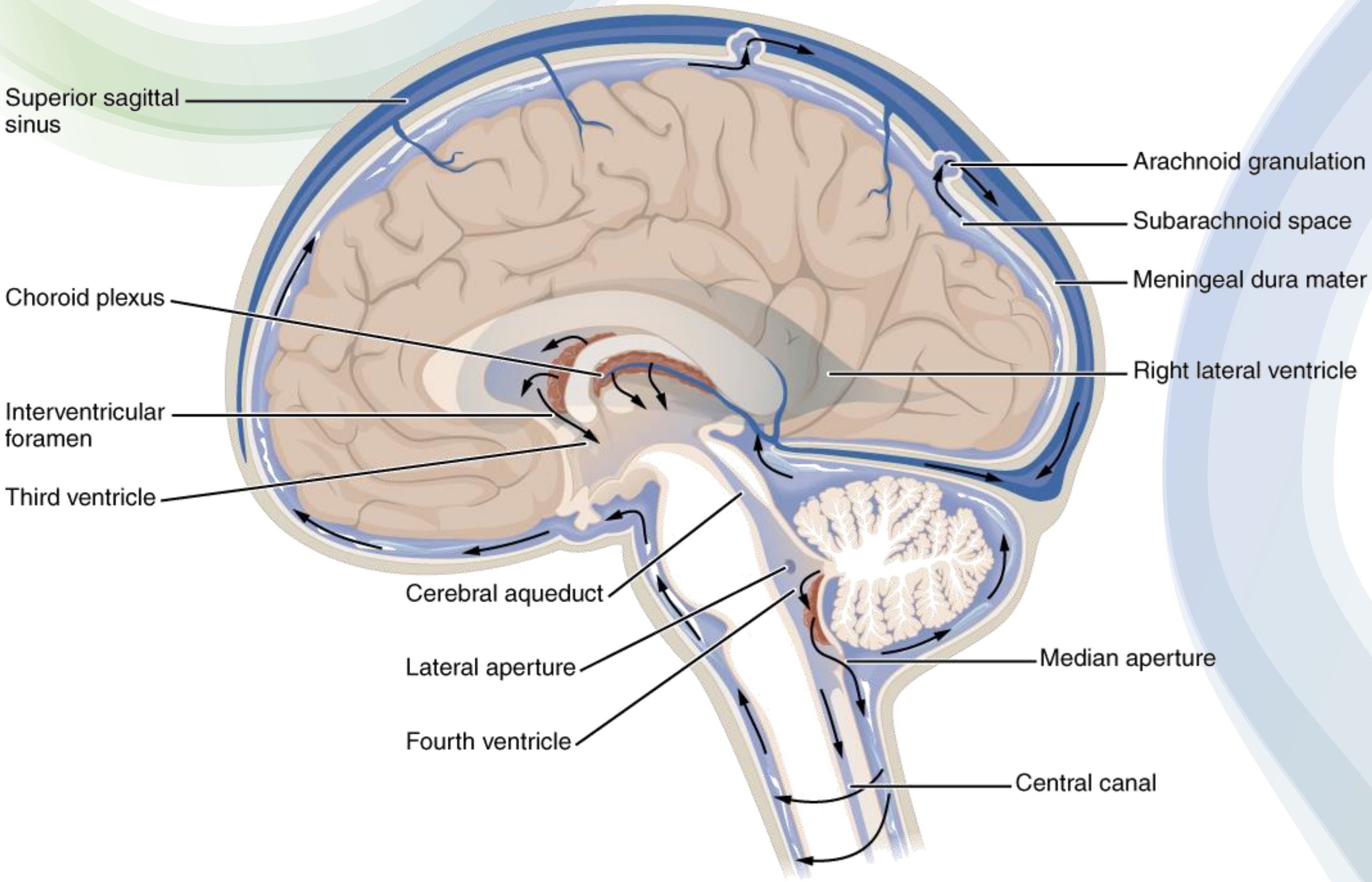
INTRODUCTION

Biological background



FUNCTIONS

- Nourishment
- Clearance
- Cushioning
- Pressure

MOTIONS

- Bulk flow
- Pulsatility

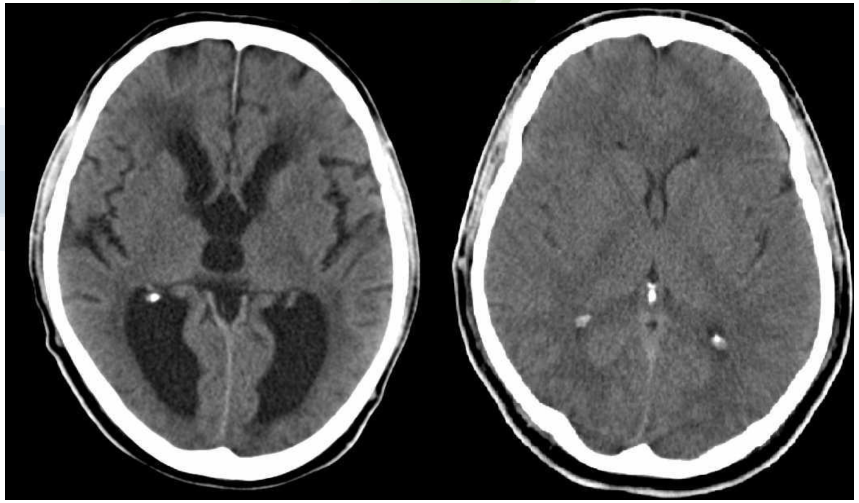
PATHOLOGICAL CONDITIONS

Fibrosis, brain/spinal tumor, Chiari malformation

Hydrocephalus, syringomyelia, cerebral edema

INTRODUCTION

Motivation



CSF DISORDERS

Life-threatening
Delicate surgeries
Not definitive
Constant monitorization

Change focus from **treatment** to early **detection**

Comprehend CSF dynamics

METHODOLOGIES

Pathology indicators
Computational fluid dynamics
Compartmental modeling

INTRODUCTION

State of the art

MATHEMATICAL MODELING

COMPUTATIONAL FLUID DYNAMICS

- Detailed geometry
- High-resolution 3D imaging
- Computationally expensive
- Spatial and temporal resolution

- 2022 Causemann *et al.*

COMPARTMENTAL MODELING

- Conceptual spaces
- Regular 2D imaging
- Computationally efficient
- No spatial resolution

- Monro–Kellie doctrine 1783
- Sorek *et al.* 1989
- Linninger *et al.* 2009

ALTERNATIVES Phase-contrast MRI, transcranial Doppler ultrasound, lumbar puncture, intracranial pressure monitoring

INTRODUCTION

Objectives

Tool to obtain fundamental knowledge

LITERATURE REVIEW

FLOW OBTENTION

MODEL DESIGN

MODEL VALIDATION

Simplicity
Computational efficiency

1 INTRODUCTION

Biological background
Motivation
State of the art
Objectives

2 METHODOLOGY AND RESULTS

Data acquisition and processing
Model construction
Model study

3 DISCUSSION AND CONCLUSION

Evaluation of results
Limitations and future outlook
Final review

Data acquisition and processing

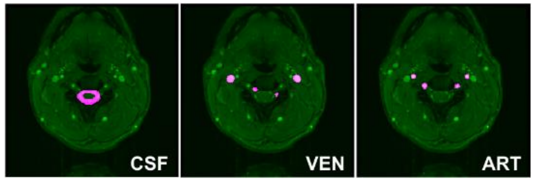
METHODOLOGY AND RESULTS

Data acquisition and processing

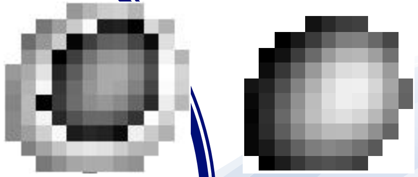
METADATA EXTRACTION

DICOM
Digital Imaging and Communications in Medicine

ROI SELECTION



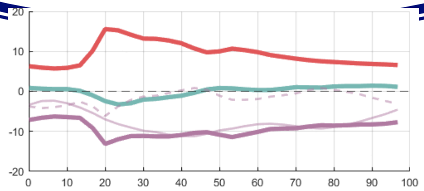
ALIASING REMOVAL



FLOW COMPUTATION

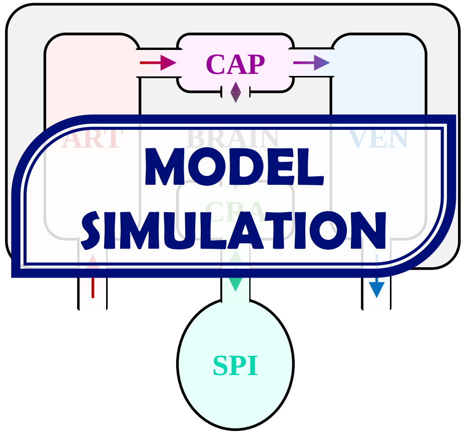
$$Q = \iint_{ROI} U dS$$

RESULTS DISPLAY



FOURIER COEFFICIENTS

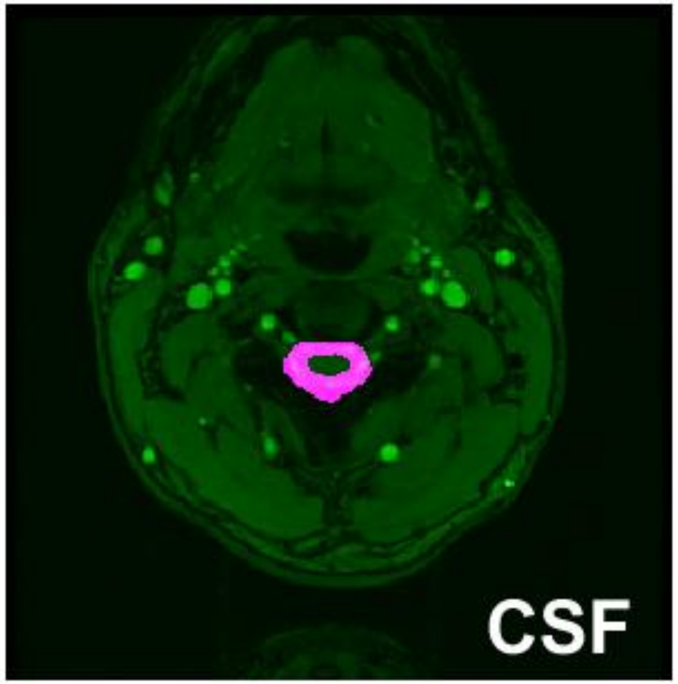
$$x(t) = \sum_{n=0}^{N} X_n e^{in\omega t}$$

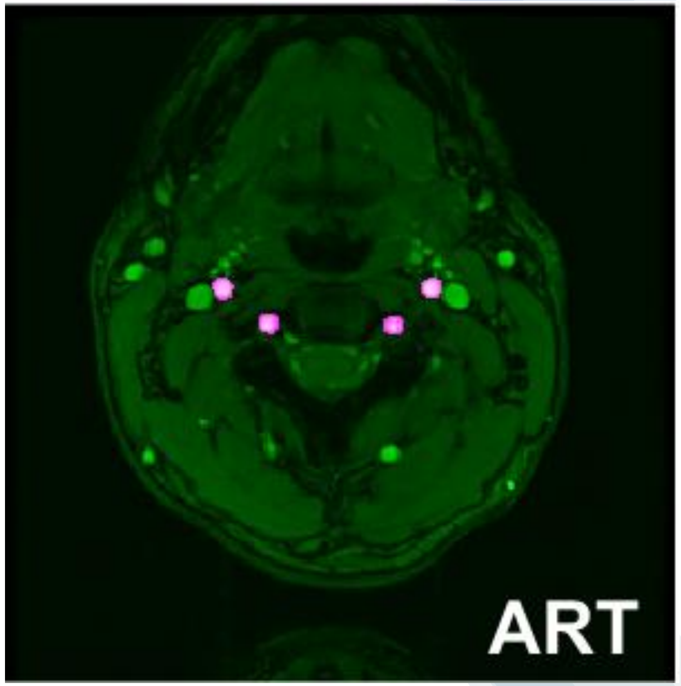


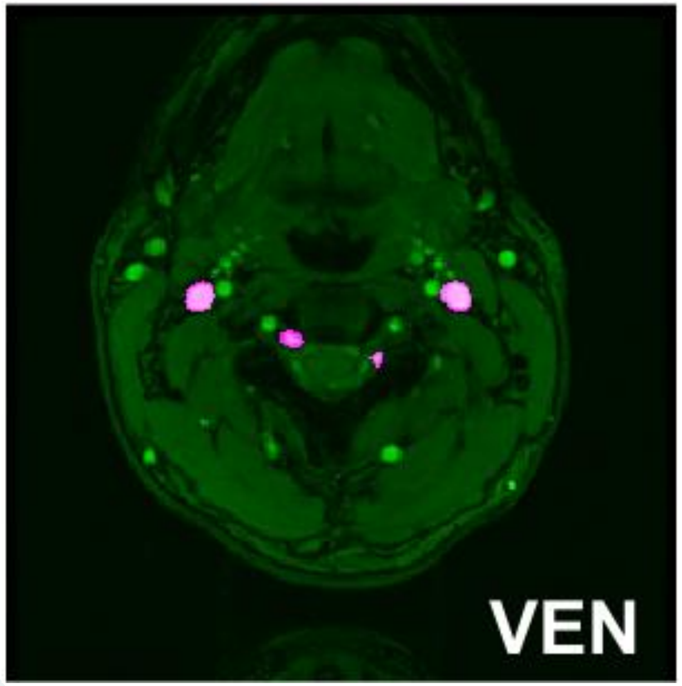
METHODOLOGY AND RESULTS

Data acquisition and processing

ROI SELECTION



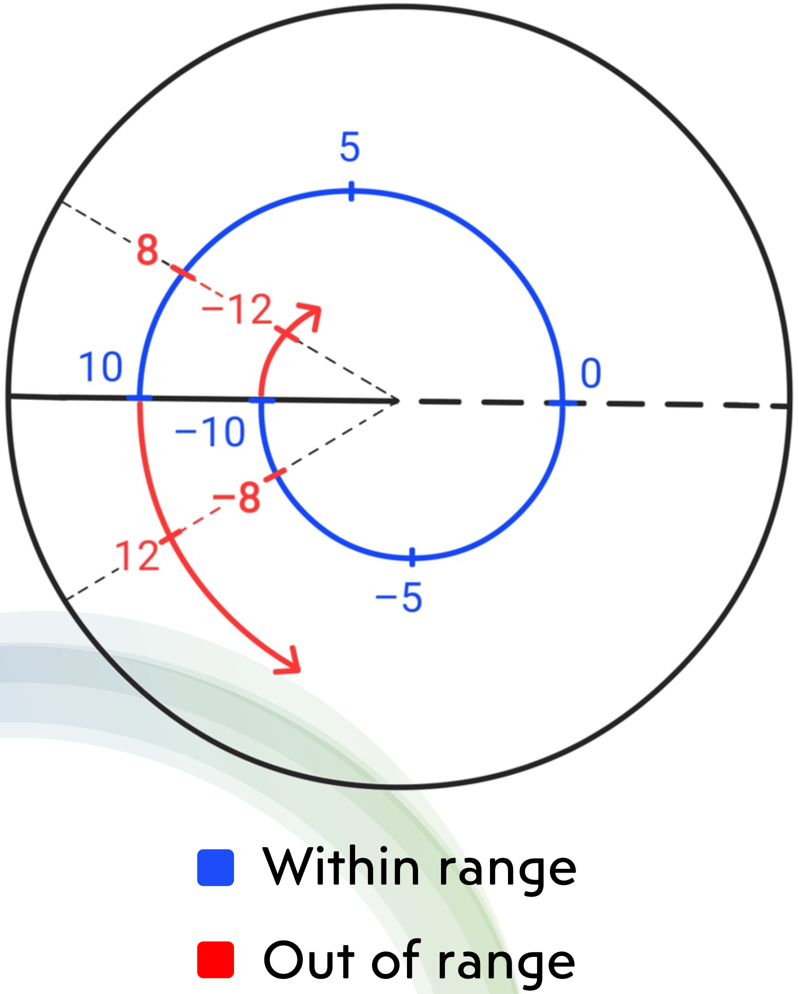


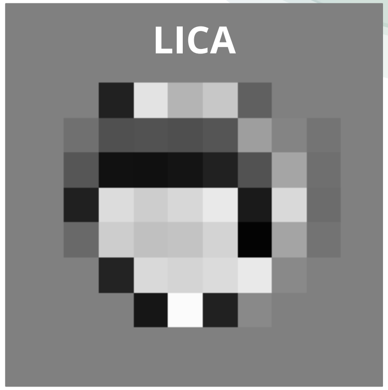


METHODOLOGY AND RESULTS

Data acquisition and processing

ALIASING REMOVAL





METHODOLOGY AND RESULTS

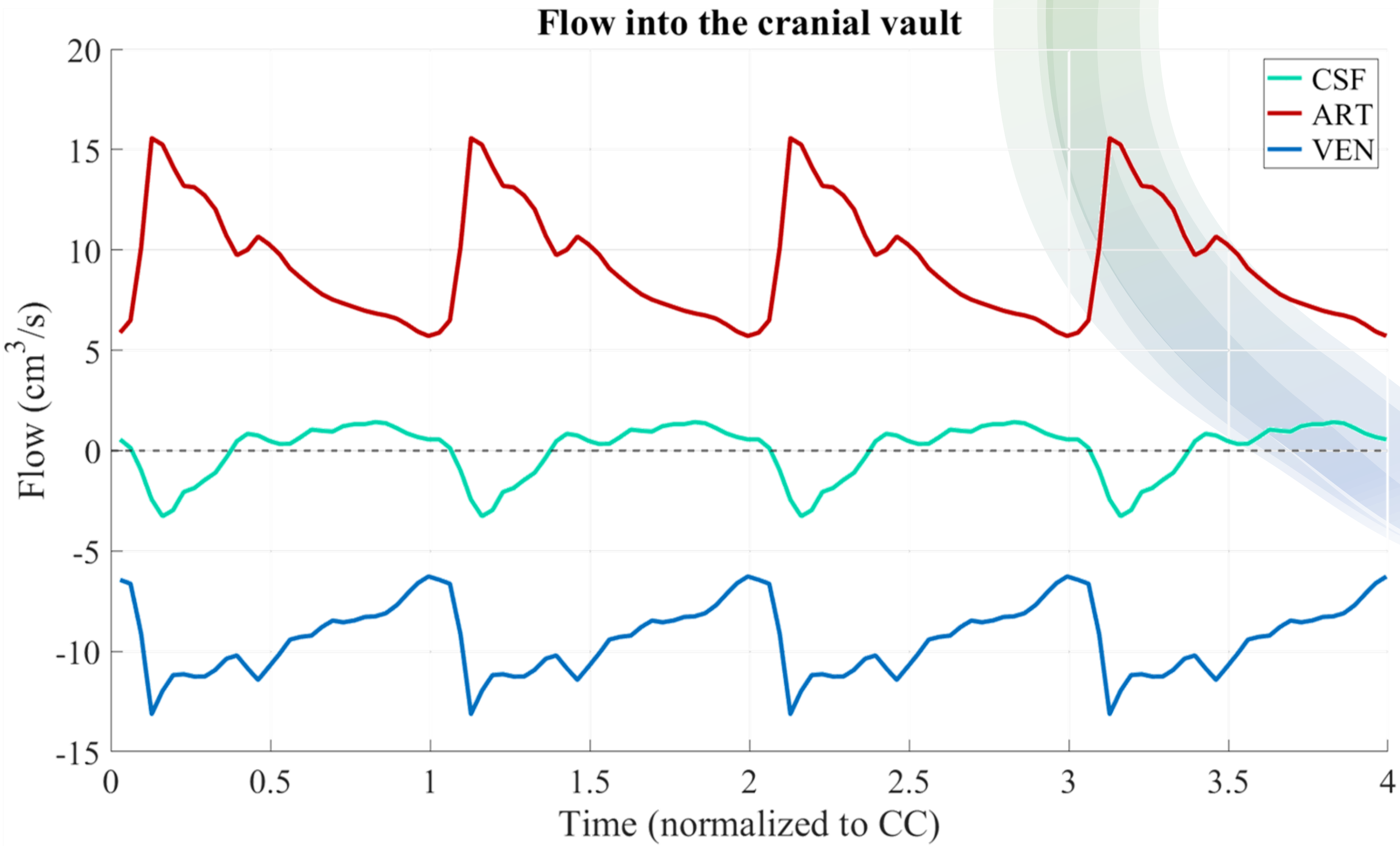
Data acquisition and processing

FLOW COMPUTATION

$$Q = \iint_{ROI} U \mathrm{d}S$$

$$Q_{art} > 0$$
$$Q_{ven} < 0$$
$$\langle Q_{blood} \rangle = 9.36 \text{ cm}^3$$

$$\langle Q_{csf} \rangle = 0.377 \text{ cm}^3$$



METHODOLOGY AND RESULTS

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Data acquisition and processing

FOURIER COEFFICIENTS

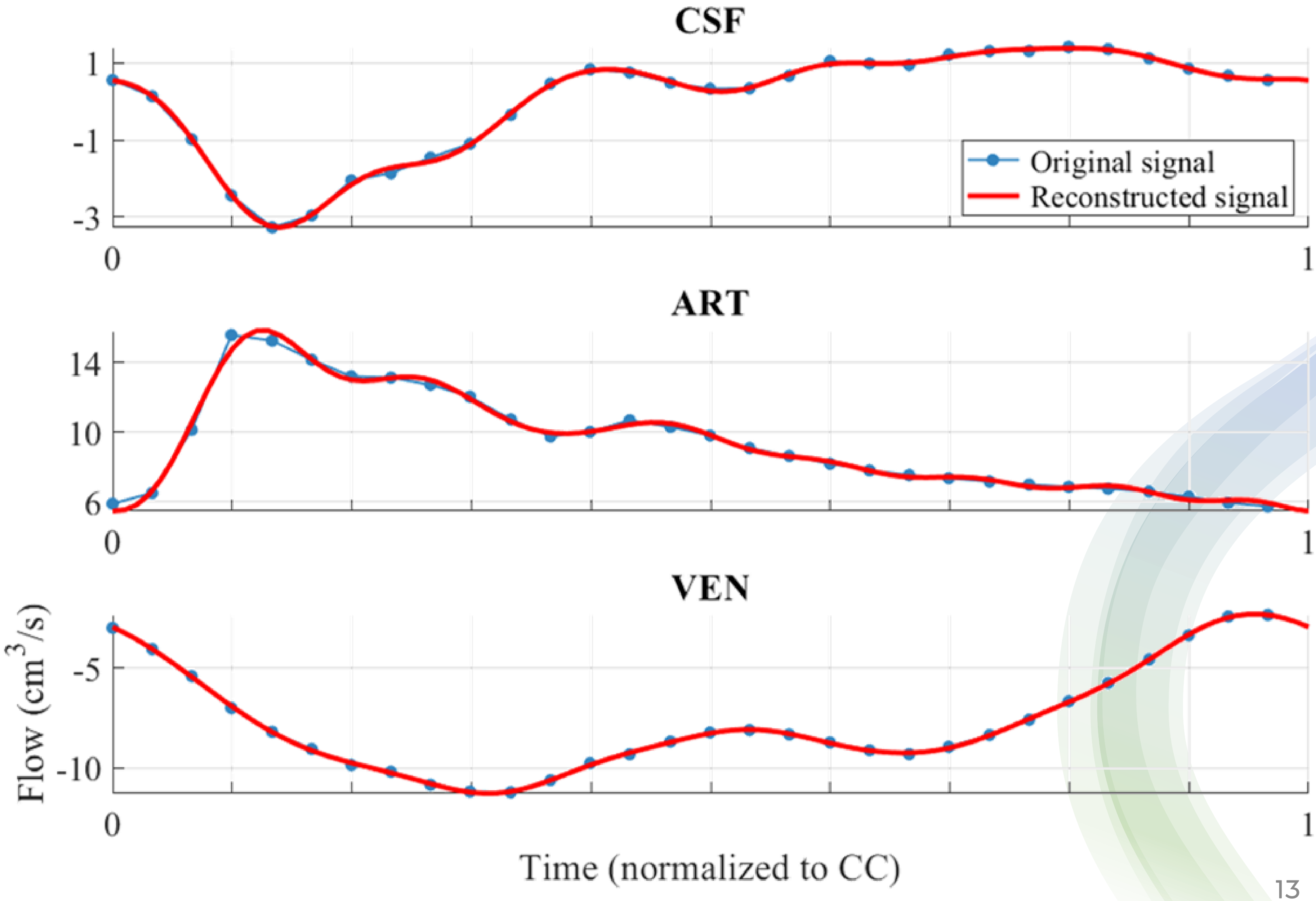
$$x(t) = \sum_{n=0}^{N} X_n e^{in\omega t}$$

$$X_n = a_n + b_n i$$

Easy temporal reconstruction

Linearity

Coherence



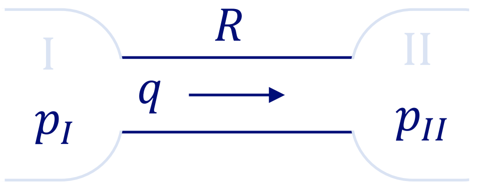
Model construction

METHODOLOGY AND RESULTS

Model construction

EQUATIONS

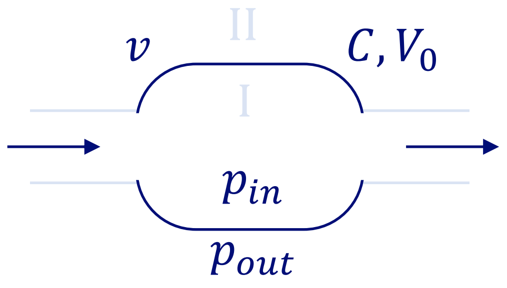
Pressure drop

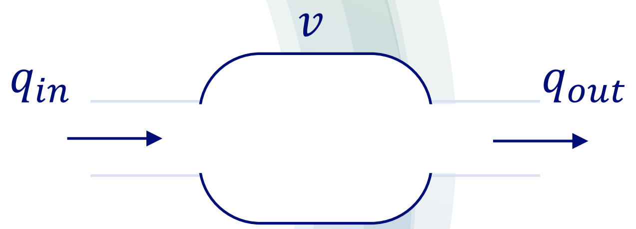


$$\Delta p(t) = p_I(t) - p_{II}(t) = Rq(t)$$

Compartment distensibility

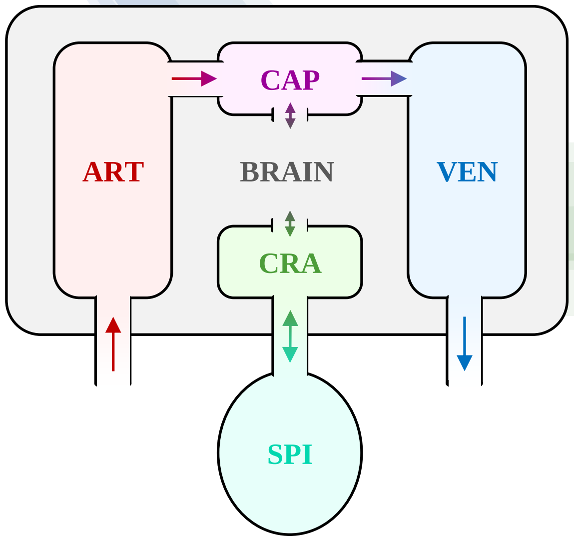
$$p_{in}(t) - p_{out}(t) = \frac{v(t) - V_0}{C}$$

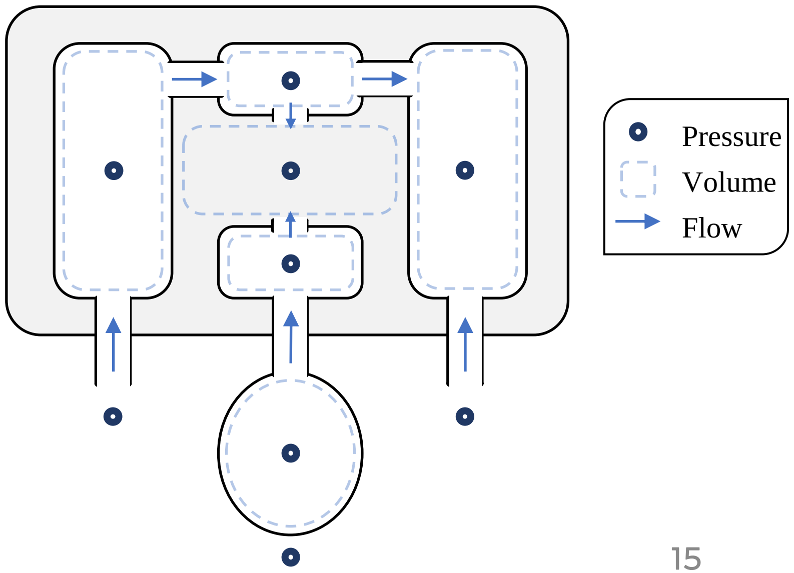




Flow continuity

$$\frac{\mathrm{d}v(t)}{\mathrm{d}t} = q_{in}(t) - q_{out}(t)$$





METHODOLOGY AND RESULTS

Model construction

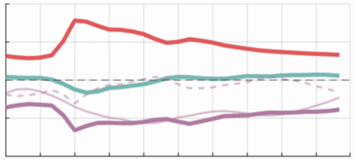
INPUT & OUTPUT

Pressure drop	Compartment distension	Flow continuity
① $p_{car} - p_{art} = R_{art}\, q_{art}$	⑤ $p_{art} - p_{bra} = \frac{v_{art} - V_{o,art}}{C_{art}}$	⑩ $\frac{dv_{art}}{dt} = q_{art} - q_{cap}$
② $p_{art} - p_{ven} = R_{cap}\, q_{cap}$	⑥ $p_{ven} - p_{bra} = \frac{v_{ven} - V_{o,ven}}{C_{ven}}$	⑪ $\frac{dv_{ven}}{dt} = q_{ven} + q_{cap}$
③ $P_{jug} - p_{ven} = R_{ven}\, q_{ven}$	⑦ $p_{cra} - p_{bra} = \frac{v_{cra} - V_{o,cra}}{C_{cra}}$	⑫ $\frac{dv_{cra}}{dt} = q_{sas}$
④ $p_{spi} - p_{cra} = R_{sas}\, q_{sas}$	⑧ $p_{spi} - P_{out} = \frac{v_{spi} - V_{o,spi}}{C_{spi}}$	⑬ $\frac{dv_{spi}}{dt} = -q_{sas}$

Monro– Kellie doctrine

⑨ $v_{art} + v_{ven} + v_{cra} = V_{tot}$

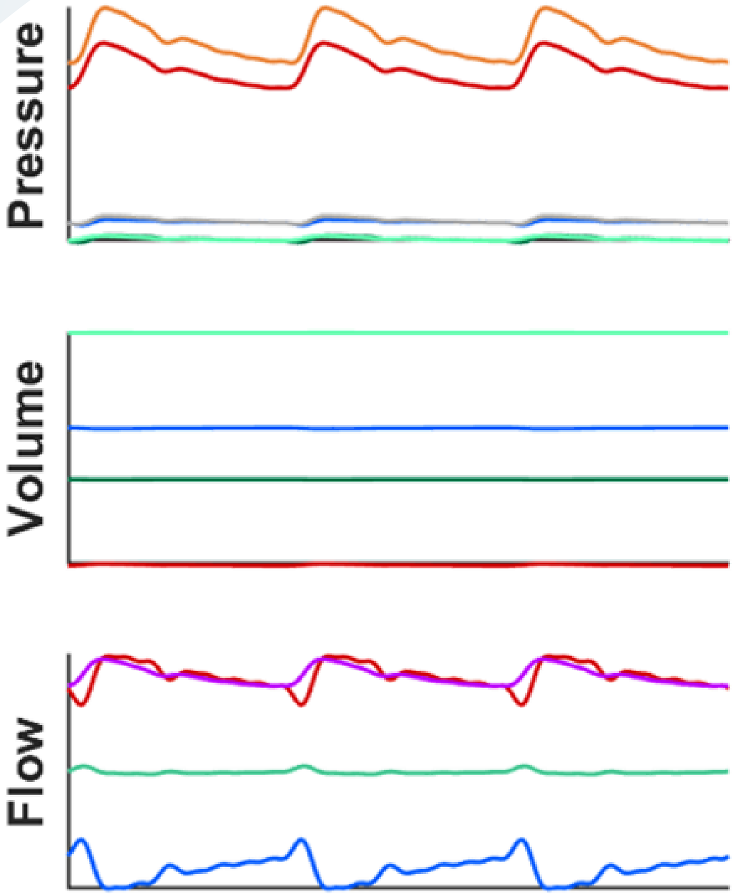
(2.5)



INPUT

$q_{art}(t)$ extracted from MRI

OUTPUT



METHODOLOGY AND RESULTS

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Model construction

IMPLEMENTATION

$$p_I(t) - p_{II}(t) = Rq(t) \xRightarrow{x(t)=\sum_{n=0}^{N} X_n e^{in\omega t}} \sum_n P_n^I e^{in\omega t} - \sum_n P_n^{II} e^{in\omega t} = R \sum_n Q_n e^{in\omega t} \xRightarrow{\text{separating modes}}$$

$$\Rightarrow \begin{cases} P_0^I e^0 - P_0^{II} e^0 = RQ_0 e^0 \\ P_1^I e^{i\omega t} - P_1^{II} e^{i\omega t} = RQ_1 e^{i\omega t} \\ \vdots \\ P_8^I e^{8i\omega t} - P_8^{II} e^{8i\omega t} = RQ_8 e^{8i\omega t} \end{cases} \xrightarrow{\text{exponentials cancel out}} \begin{cases} P_0^I - P_0^{II} = RQ_0 \\ P_1^I - P_1^{II} = RQ_1 \\ \vdots \\ P_8^I - P_8^{II} = RQ_8 \end{cases} \Rightarrow \boxed{P_n^I - P_n^{II} = RQ_n}$$

Fourier coefficients

$$p_{in}(t) - p_{out}(t) = \frac{v(t) - V_0}{C} \longrightarrow \boxed{P_n^{in} - P_n^{out} = \frac{V_n - V_0}{C}}$$

$$\frac{dv(t)}{dt} = q_{in}(t) - q_{out}(t) \longrightarrow \boxed{in\omega V_n = Q_n^{in} - Q_n^{out}}$$

Code implementation

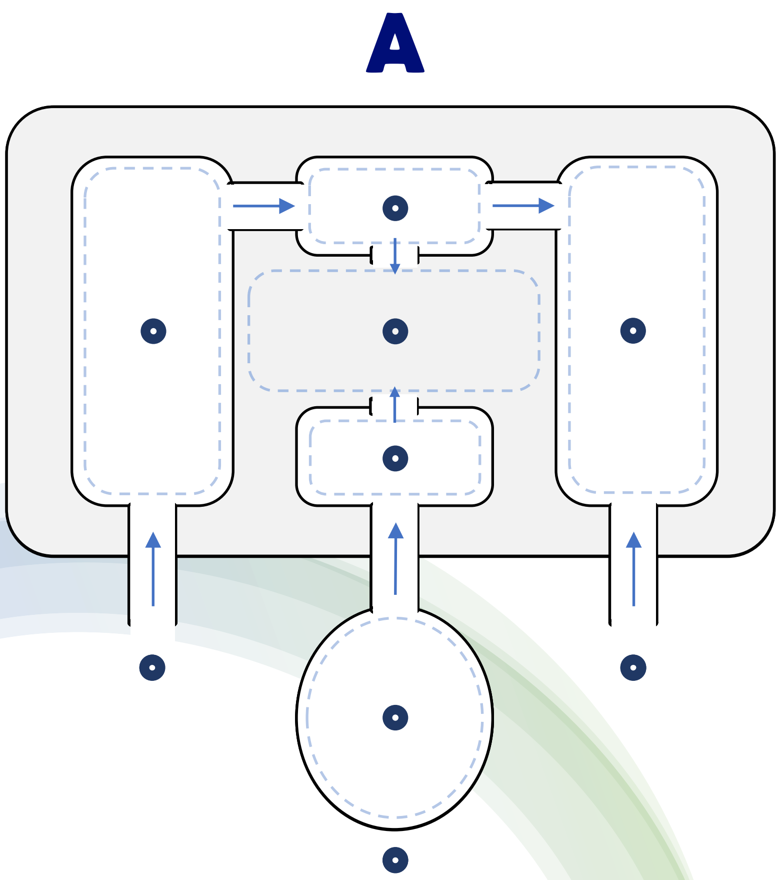
```
% Solving the unknowns of the model
for n = 0:N-1 % 0 to 8
    inw = 1i*n*w;

    A = [... % coefficients of the system
        1 -1  0  0 0 0 0 0 0 0 -R.art 0    0     0   ;...
        0  1 -1  0 0 0 0 0 0 0    0 -R.cap 0     0   ;...
        0  0 -1  0 0 0 0 0 0 0    0     0 -R.ven 0   ;...
        0  0  0 -1 1 0 0 0 0 0    0     0    0 -R.sas;...

        0 C.art 0    0    0 -C.art -1  0  0  0 0 0 0 0;...
        0    0 C.ven 0    0 -C.ven  0 -1  0  0 0 0 0 0;...
        0    0    0 C.cra 0 -C.cra  0  0 -1  0 0 0 0 0;...
        0    0    0    0 C.spi  0   0  0  0 -1 0 0 0 0;...
        0    0    0    0    0   0   1  1  1  1 0 0 0 0;... %MK const.

        0 0 0 0 0 0 inw 0 0 0 -1  1  0  0;...
        0 0 0 0 0 0 0 inw 0 0  0 -1  0  0;...
        0 0 0 0 0 0 0 0 inw 0  0  0 -1  0;...
        0 0 0 0 0 0 0 0  0 inw 0  0  0  1;...
        inputA];

    B = [zeros(1,13) inputB]'; % independent terms of the system

    % Constants only affect the mode zero (n=0)
    if n==0
        B = [ 0 0 -Pjug 0 ...
            -Vo.art -Vo.ven -Vo.cra C.spi*Pout-Vo.spi Vtot ...
            0 0 0 0 inputB]';end

    Xn = A\B; % unknowns of the system, Xn = [Pn Vn Qn]
end
```

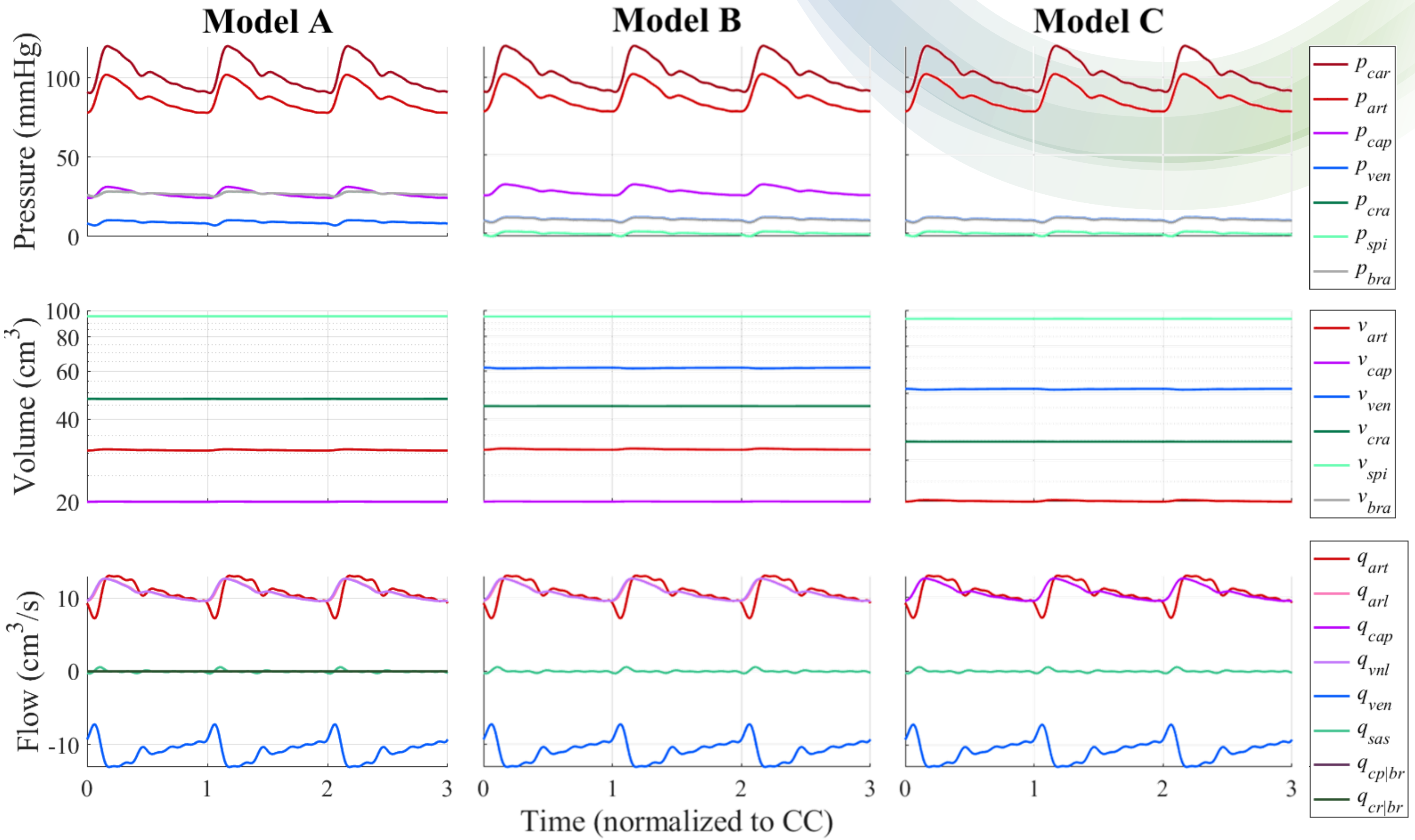
Model study

METHODOLOGY AND RESULTS

Model study

MODEL COMPARISON





METHODOLOGY AND RESULTS

Model study

COEFFICIENT TUNING

Initial values from literature

Adaptation to subject

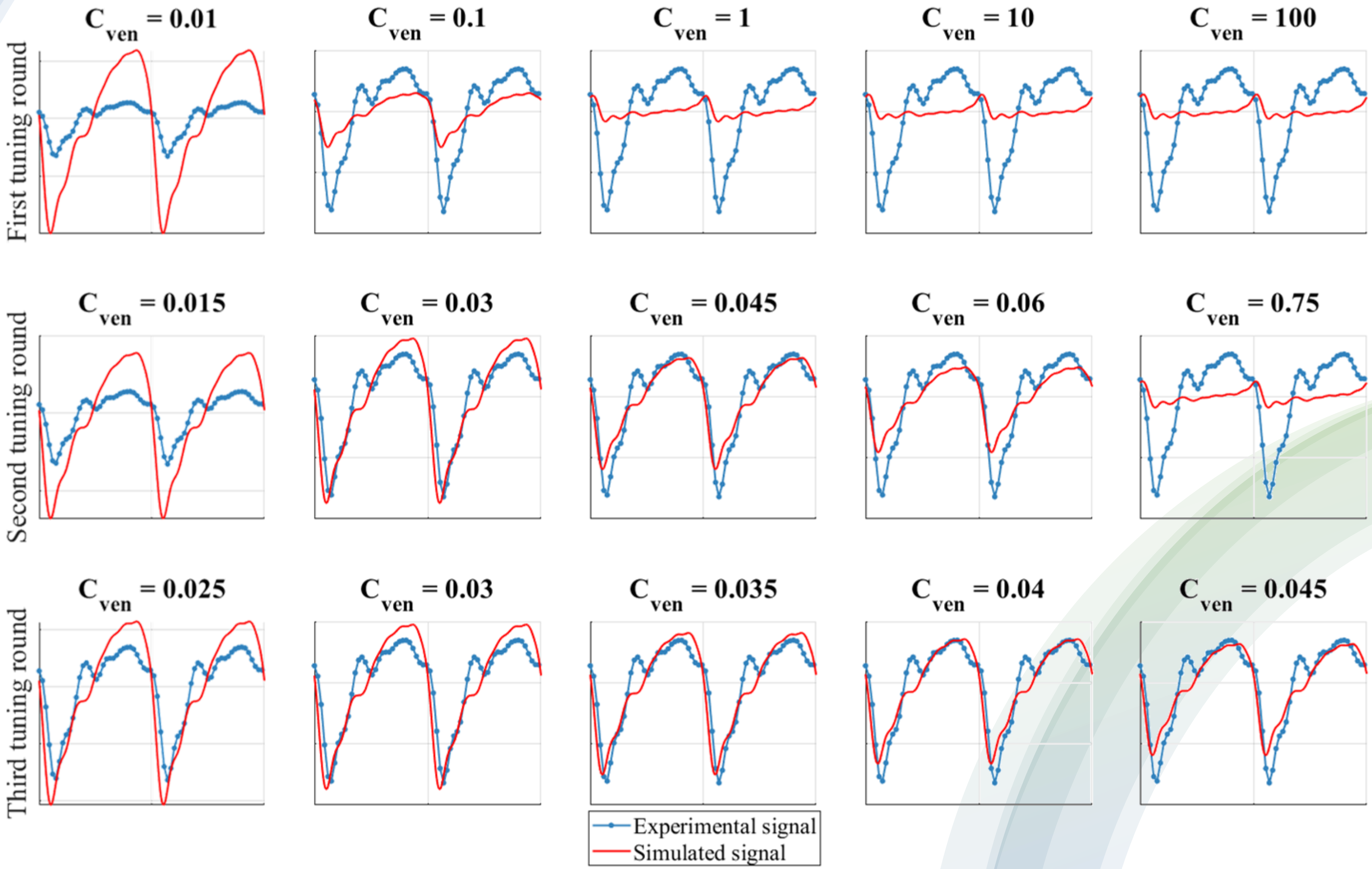
Visual assessment + SAD

Not relevant: V_o

Slightly relevant: R

Very relevant: C

Most relevant: R_{sas}, C_{cra} and C_{spi}



1

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DISCUSSION AND CONCLUSION

Evaluation of results
Limitations and future outlook
Final review

DISCUSSION AND CONCLUSION

Evaluation of results

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Velocity aliasing removal
Fourier coefficient representation

IMAGE PROCESSING AND FLOW EXTRACTION

- ✓ Successful algorithms
- ✓ Accurate flow dynamics measurements

MODEL OUTCOMES

- ✓ Model design: simplicity works
- ✓ Consistent resistance and compliance values

DISCUSSION AND CONCLUSION

Limitations and future outlook

CLINICAL VALIDATION

Patient medical images
Strict regulation

RESPIRATION EFFECT

Relevant?
Breathing component

ROI SELECTION

Manual selection

- time-consuming
- expertise
- inaccurate

Frequency-based automation

- user-friendly
- fast
- accurate

COEFFICIENT TUNING

Manual tuning

- time-consuming
- non-efficient
- limited

Optimization algorithm

- similarity cost function
- Fourier domain
- fast
- genetic, particle swarm

DISCUSSION AND CONCLUSION

Final review

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- PROMISING RESULTS FOR INVESTIGATION OF CSF PULSATILITY
- SIMULATIONS ADJUSTED TO EXPERIMENTAL MEASUREMENTS
- SATISFACTORY PERFORMANCE OF IMAGE PROCESSING SCRIPT
- ROOM FOR FURTHER ENHANCEMENTS IN METHODOLOGY
- IMPLEMENTATION ON PATHOLOGICAL SUBJECTS

Josué Pérez Sabater

Supervisor: Wilfried Romain Stefan Coenen

A compartmental model to investigate intracranial pulsatility

Thank you for your attention!

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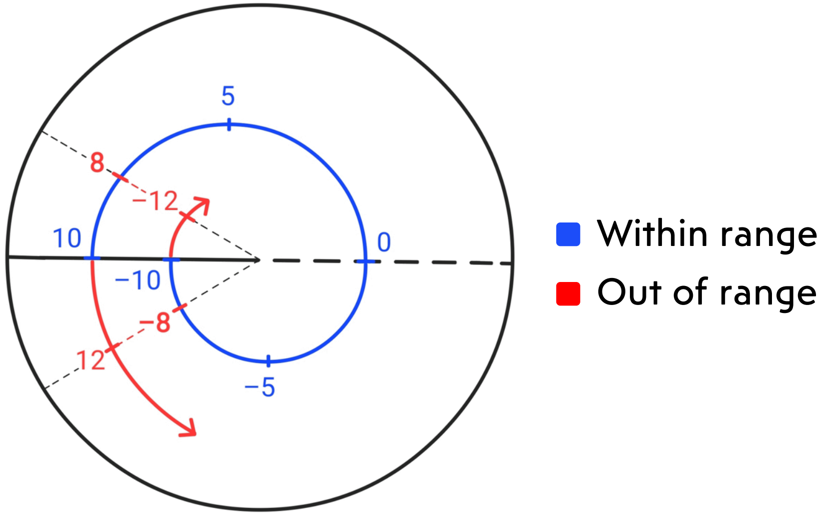
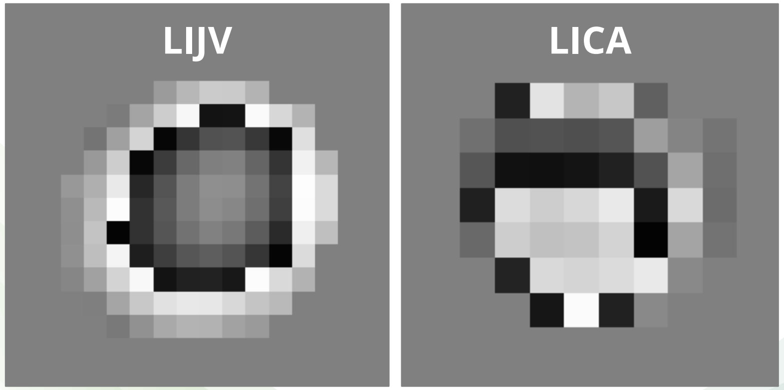
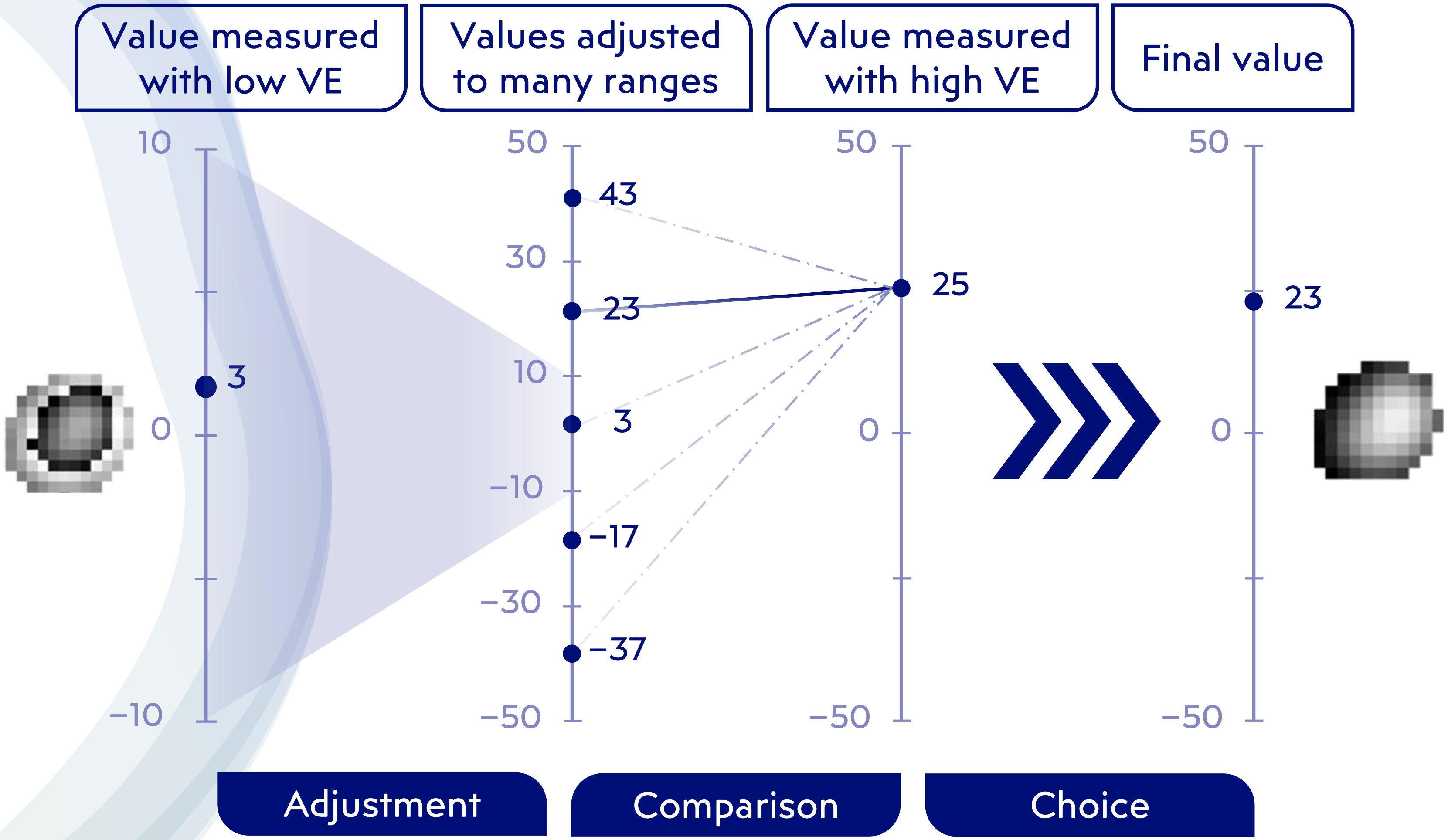
ANNEX

ALIASING REMOVAL







ANNEX

- Nomenclature of anatomical structures
- Initial and tuned values of constant parameters

Abbreviation	Anatomical description	Type
ART	Arterial vascular tree inside the cranium.	Compartment
CAP	Capillary bed inside the cranium.	Compartment/Passage
VEN	Venous vascular tree inside the cranium.	Compartment
CRA	Cranial subarachnoid space.	Compartment
SPI	Spinal subarachnoid space (out of the cranium).	Compartment
BRA	Brain tissue, assumed to occupy all space within the cranium that is not a blood- or CSF-filled compartment.	Compartment
ARL	Arterioles connecting arteries to capillaries.	Passage
VNL	Venules connecting capillaries to veins.	Passage
SAS	Subarachnoid space passage connecting cranial and spinal SAS.	Passage
CP|BR	Passage from capillaries to brain tissue.	Passage
CR|BR	Passage from cranial SAS to brain tissue.	Passage
CAR	Carotid artery, right before entering the cranium.	Reference
JUG	Jugular vein, right after exiting the cranium.	Reference
OUT	Space surrounding the spinal cord, out of the model boundaries.	Reference

	Parameter	Initial value	Final value	Source
Volume at rest (cm^3)	$V_{o,art}$	30–46	30	Linninger
	$V_{o,cap}$	20	—	Linninger
	$V_{o,ven}$	60	60	(Estimated)
	$V_{o,cra}$	45–50	47.5	Linninger
	$V_{o,spi}$	90–100	95	Linninger
	$V_{o,bra}$	1400	—	Linninger
Compliance (cm^3/mmHg)	C_{art}	0.0147	0.025	Linninger
	C_{cap}	6.06×10^{-3}	—	Linninger
	C_{ven}	0.0293–0.16	0.040	Linninger
	C_{cra}	0.0792–6.33	0.725	Linninger
	C_{spi}	0.0127	0.0220	Linninger
	C_{bra}	18.7–187	40	Linninger
Resistance (mmHg s/cm^3)	R_{art}	1.40	1.40	Zhang
	R_{arl}	5.60	56	Sorek
	R_{vnl}	1.68	1000	Sorek
	R_{ven}	0.558	0.4	Sorek
	R_{sas}	0.045–0.06	3.75	Støverud
	$R_{cp\|br}$	8×10^5	—	Sorek
	$R_{cr\|br}$	800.3	—	Sorek
Pressure (mmHg)	p_{jug}	3	3	Linninger
	p_{out}	10	10	(Estimated)

ANNEX

- Equations and code to perform model simulation

$$
\left\{
\begin{array}{lll}
\text{Pressure drop} & \text{Compartment distension} & \text{Flow continuity} \\
\text{①}\ p_{car} - p_{art} = R_{art}\, q_{art} & \text{⑤}\ p_{art} - p_{bra} = \dfrac{v_{art} - V_{o,art}}{C_{art}} & \text{⑩}\ \dfrac{\mathrm{d}v_{art}}{\mathrm{d}t} = q_{art} - q_{cap} \\
\text{②}\ p_{art} - p_{ven} = R_{cap}\, q_{cap} & \text{⑥}\ p_{ven} - p_{bra} = \dfrac{v_{ven} - V_{o,ven}}{C_{ven}} & \text{⑪}\ \dfrac{\mathrm{d}v_{ven}}{\mathrm{d}t} = q_{ven} + q_{cap} \\
\text{③}\ P_{jug} - p_{ven} = R_{ven}\, q_{ven} & \text{⑦}\ p_{cra} - p_{bra} = \dfrac{v_{cra} - V_{o,cra}}{C_{cra}} & \text{⑫}\ \dfrac{\mathrm{d}v_{cra}}{\mathrm{d}t} = q_{sas} \\
\text{④}\ p_{spi} - p_{cra} = R_{sas}\, q_{sas} & \text{⑧}\ p_{spi} - P_{out} = \dfrac{v_{spi} - V_{o,spi}}{C_{spi}} & \text{⑬}\ \dfrac{\mathrm{d}v_{spi}}{\mathrm{d}t} = -q_{sas} \\
 & \text{Monro– Kellie doctrine} & \\
 & \text{⑨}\ v_{art} + v_{ven} + v_{cra} + v_{spi} = V_{tot} &
\end{array}
\right.
$$

```
% Solving the unknowns of the model
for n = 0:N-1 % 0 to 8
    inw = 1i*n*w;

    A = [... % coefficients of the system
        1 -1  0  0 0 0 0 0 0 0 -R.art 0    0     0  ;...
        0  1 -1  0 0 0 0 0 0 0    0 -R.cap 0     0  ;...
        0  0 -1  0 0 0 0 0 0 0    0     0 -R.ven 0  ;...
        0  0  0 -1 1 0 0 0 0 0    0     0    0 -R.sas;...

        0 C.art 0   0   0 -C.art -1  0  0  0 0 0 0 0;...
        0   0 C.ven 0   0 -C.ven  0 -1  0  0 0 0 0 0;...
        0   0   0 C.cra 0 -C.cra  0  0 -1  0 0 0 0 0;...
        0   0   0   0 C.spi  0    0  0  0 -1 0 0 0 0;...
        0   0   0   0   0    0    1  1  1  1 0 0 0 0;... %MK doct.

        0 0 0 0 0 0 inw 0   0   0 -1  1  0  0;...
        0 0 0 0 0 0  0 inw  0   0  0 -1 -1  0;...
        0 0 0 0 0 0  0  0 inw   0  0  0  0 -1;...
        0 0 0 0 0 0  0  0   0 inw  0  0  0  1;...
        inputA];

    B = [zeros(1,13) inputB]'; % independent terms of the system

    % Constants only affect the mode zero (n=0)
    if n==0
        B = [ 0 0 -Pjug 0 ...
            -Vo.art -Vo.ven -Vo.cra C.spi*Pout-Vo.spi Vtot ...
            0 0 0 0 inputB]';end

    Xn = A\B; % unknowns of the system, Xn = [Pn Vn Qn]
end
```