Computing the derivatives of the mean and amplitude of physiological variables with respect to the parameters of a mathematical model

A. Pironet, P. C. Dauby, J. A. Revie,
J. G. Chase, T. Desaive

iSMIT– Baden-Baden – September 6th 2013

Lumped-parameter models

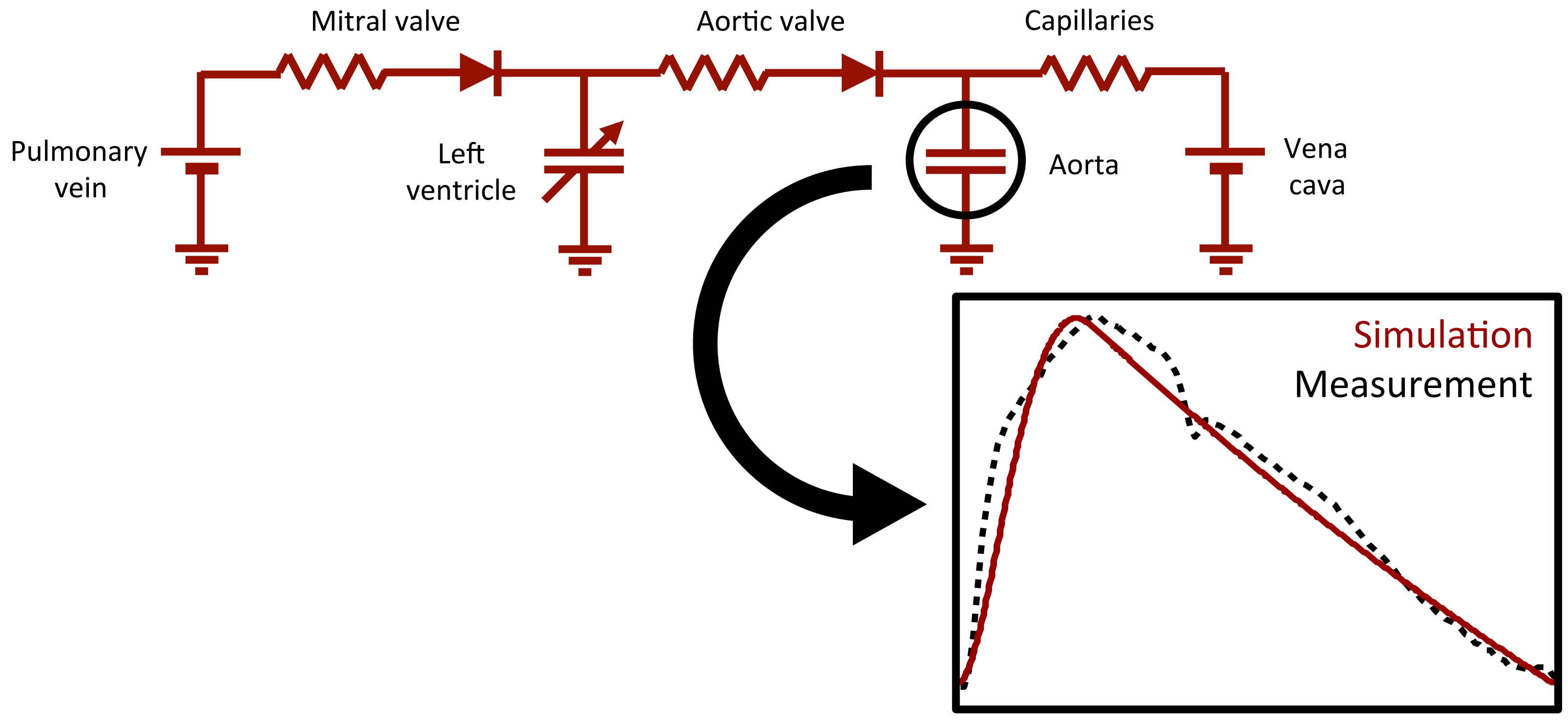
- In medicine, only the mean and amplitude of physiological variables are usually available (*e.g*. aortic pressure).

Lumped-parameter models

- The models have to serve as
  - diagnosis,
  - monitoring and
  - simulation tools.
- Consequently, they have to
  - require few computation time
  - be simple.
- We rely on *lumped-parameter* models.

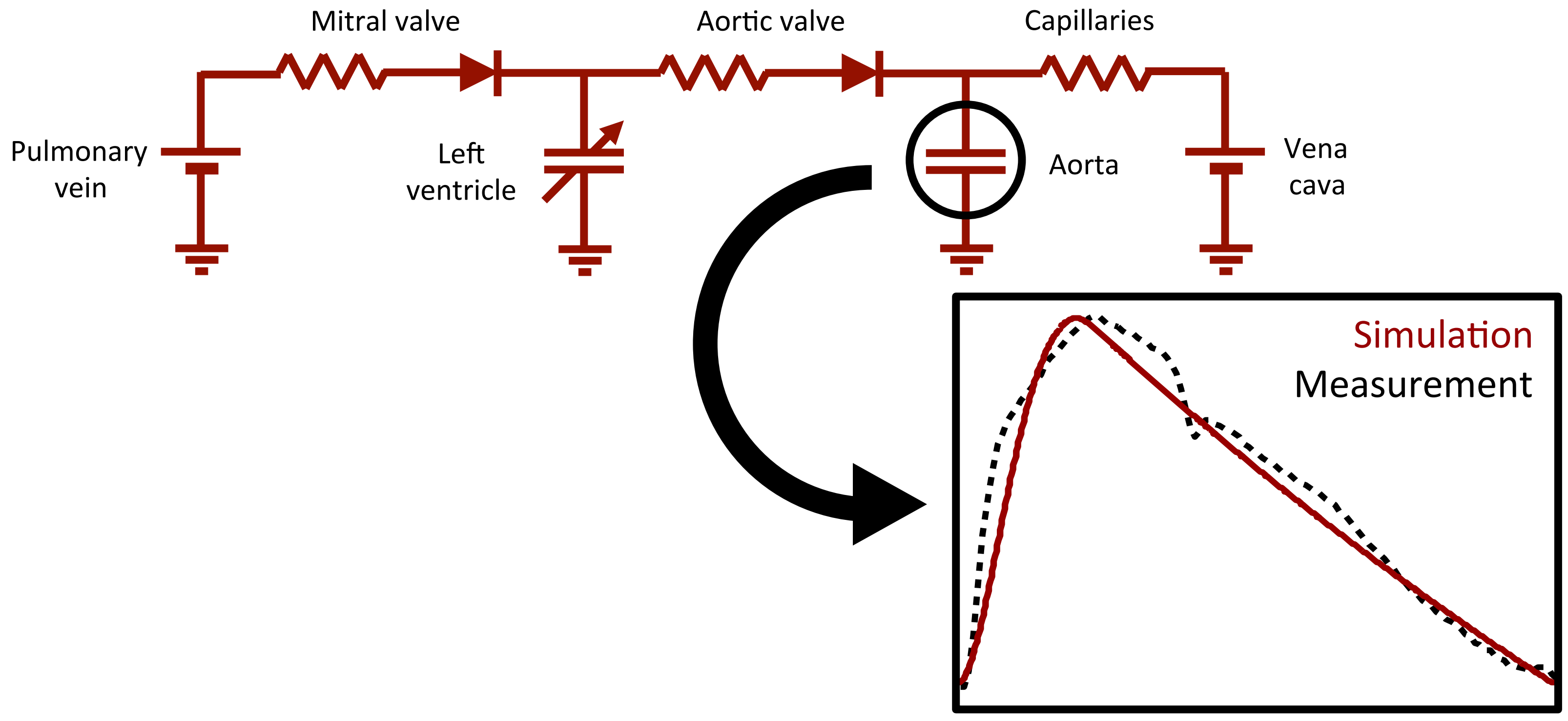
Lumped-parameter models

- Lumped-parameter models cannot represent all the various features of physiological waveforms.



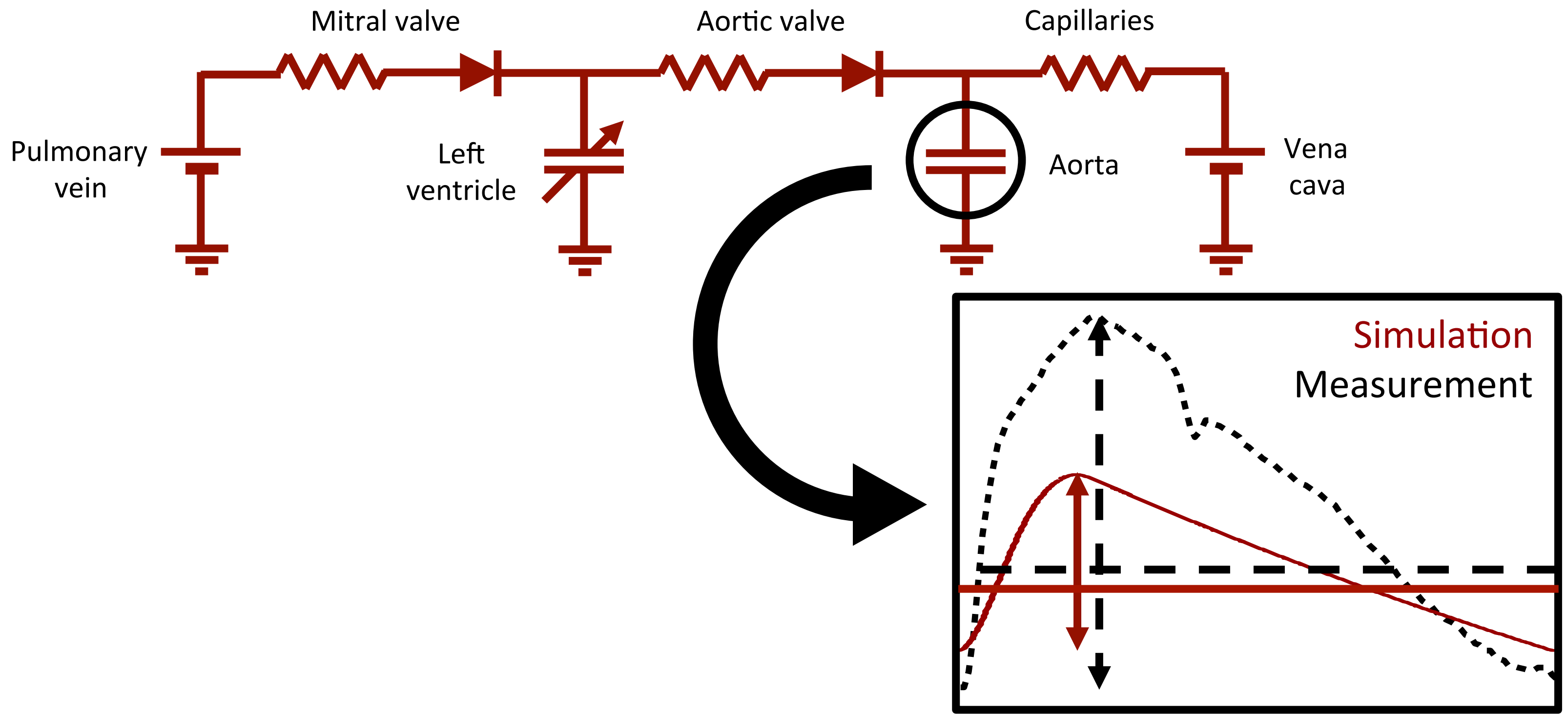
Lumped-parameter models

- We would like the model to correctly reproduce the measured mean and amplitude of the physiological waveform.



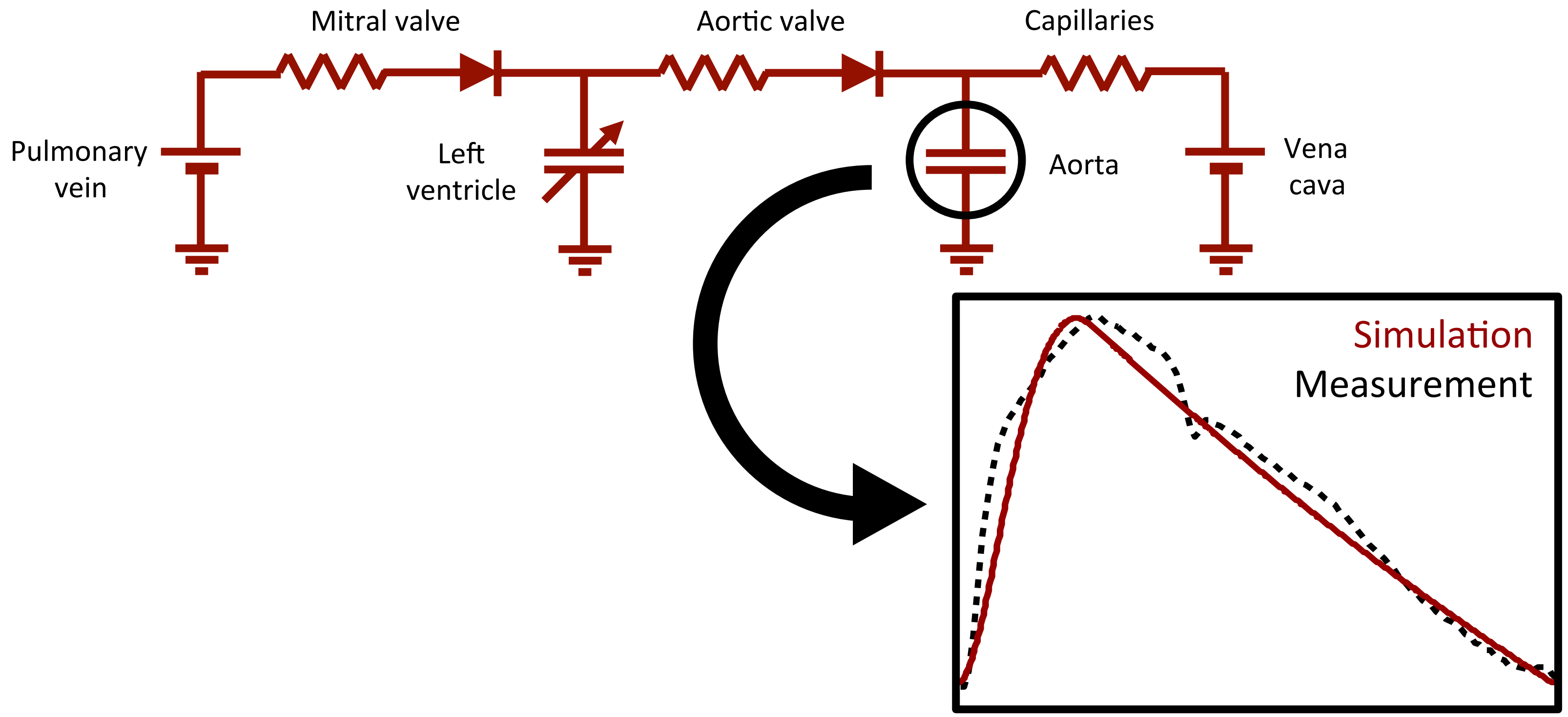
Parameter identification

- To do so, a *parameter identification* step is necessary, which aims to find the best values for all model parameters p_k.



Parameter identification

- To do so, a *parameter identification* step is necessary, which aims to find the best values for all model parameters p_k.



Parameter identification

- To adjust some parameter p_k, one must know how the means $\bar{y}_i$ and amplitudes Δy_i of simulated variables $y_i(t)$ will change if p_k is increased (or decreased).
- In mathematical terms, one would like to compute:

$$\frac{\partial \bar{y}_i}{\partial p_k} \text{ and } \frac{\partial \Delta y_i}{\partial p_k}$$

Lumped-parameter models

- To ID the model parameters p_k, we rather rely on the mean $\bar{y}_i$ and amplitude Δy_i of physiological variables $y_i(t)$ than on their whole timecourse.
- Thus, we would like to compute

$$\frac{\partial \bar{y}_i}{\partial p_k} \text{ and } \frac{\partial \Delta y_i}{\partial p_k}$$

to know if the parameter value p_k has to be increased or decreased.

Lumped-parameter models

"Brute force" approach: finite difference approximation

- **One-sided**: $$\frac{\partial \bar{y}_i}{\partial p_k} \approx \frac{\bar{y}_i(p_k + \varepsilon) - \bar{y}_i(p_k)}{\varepsilon}$$
  (1 more model simulation per derivative)

- **Central**: $$\frac{\partial \bar{y}_i}{\partial p_k} \approx \frac{\bar{y}_i(p_k + \varepsilon) - \bar{y}_i(p_k - \varepsilon)}{2\varepsilon}$$
  (2 more model simulations per derivative)

Lumped-parameter models

New approach:

Compute the partial derivatives

$$\frac{\partial y_i(t)}{\partial p_k}$$

→

Fourier analysis to get

$$\frac{\partial \bar{y}_i}{\partial p_k} \text{ and } \frac{\partial \Delta y_i}{\partial p_k}$$

Step 1: partial derivatives $\partial y_i / \partial p_k$

Different methods (Carmichael *et al.*, 1997):

- Solve the variational equations
  (1 more equation per derivative)
- Adjoint model
  (1 adjoint model simulation)
- Automatic differentiation
- Green's function
- …

Step 2: Fourier analysis

- To get $\partial\bar{y}_i/\partial p_k$, we take the mean of the partial derivative over one signal period

$$\frac{\partial\bar{y}_i}{\partial p_k} = \frac{\partial}{\partial p_k}\left(\frac{1}{T}\int_0^T y_i(t)\ dt\right)$$

$$= \frac{1}{T}\int_0^T \frac{\partial y_i(t)}{\partial p_k}\ dt$$

$$= \overline{\frac{\partial y_i}{\partial p_k}}$$

Step 2: Fourier analysis

- To get $\partial \Delta y_i / \partial p_k$, we use the 1st order Fourier approximation of $y_i(t)$:

$$y_i(t) \approx \frac{1}{T}\hat{y}_{i,0} + \frac{2}{T}\hat{y}_{i,1} e^{j\frac{2\pi}{T}t}$$

with

$$\hat{y}_{i,0} = \int_0^T y_i(t)\ dt$$

$$\hat{y}_{i,1} = \int_0^T y_i(t) e^{-j\frac{2\pi}{T}t}\ dt$$

Step 2: Fourier analysis

- Hence, the amplitude of $y_i(t)$ can be approximated by:

$$\Delta y_i \approx \frac{2}{T}|\hat{y}_{i,1}|$$

and its derivative w.r.t. p_k:

$$\frac{2}{T}\frac{\partial}{\partial p_k}(|\hat{y}_{i,1}|) = \frac{2}{T}\frac{\partial}{\partial p_k}\left(\sqrt{\Re(\hat{y}_{i,1})^2 + \Im(\hat{y}_{i,1})^2}\right)$$

Step 2: Fourier analysis

- After some computation:

$$\frac{\partial \Delta y_i}{\partial p_k} \approx \frac{2}{T|\hat{y}_{i,1}|}\left[\Re(\hat{y}_{i,1})\Re\left(\left\langle \frac{\partial y_i}{\partial p_k} \right\rangle_1\right) + \Im(\hat{y}_{i,1})\Im\left(\left\langle \frac{\partial y_i}{\partial p_k} \right\rangle_1\right)\right]$$

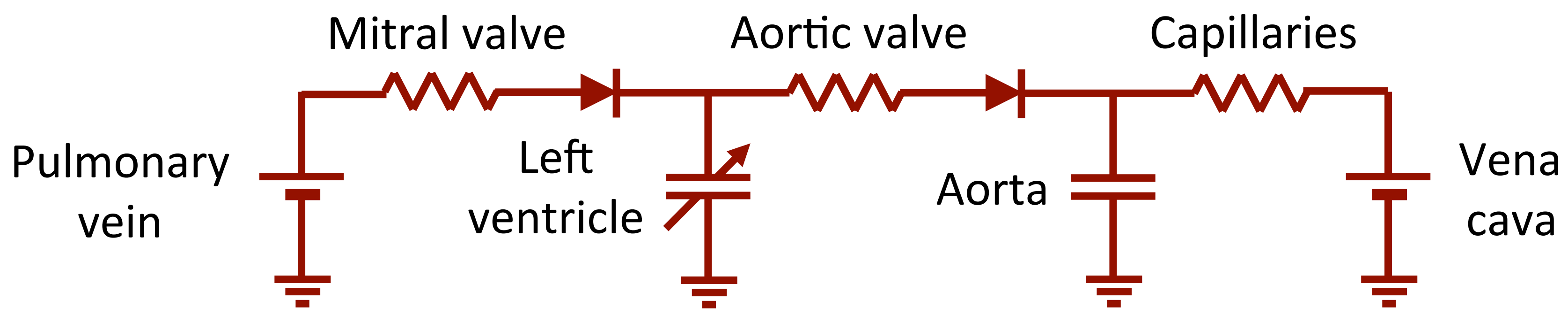
where $\langle \partial y_i / \partial p_k \rangle_1$ is the 1st order Fourier coefficient of $\partial y_i(t)/\partial p_k$.

Results

- At least as fast as the brute-force method (depending on the method used to get $\partial y_i(t)/\partial p_k$).
- Exact computation of $\partial \bar{y}_i/\partial p_k$.
- Approximation of $\partial \Delta y_i/\partial p_k$
(gives the sign, which is needed for parameter identification).

Results

Test on a 2-chamber CVS model:



7 parameters:

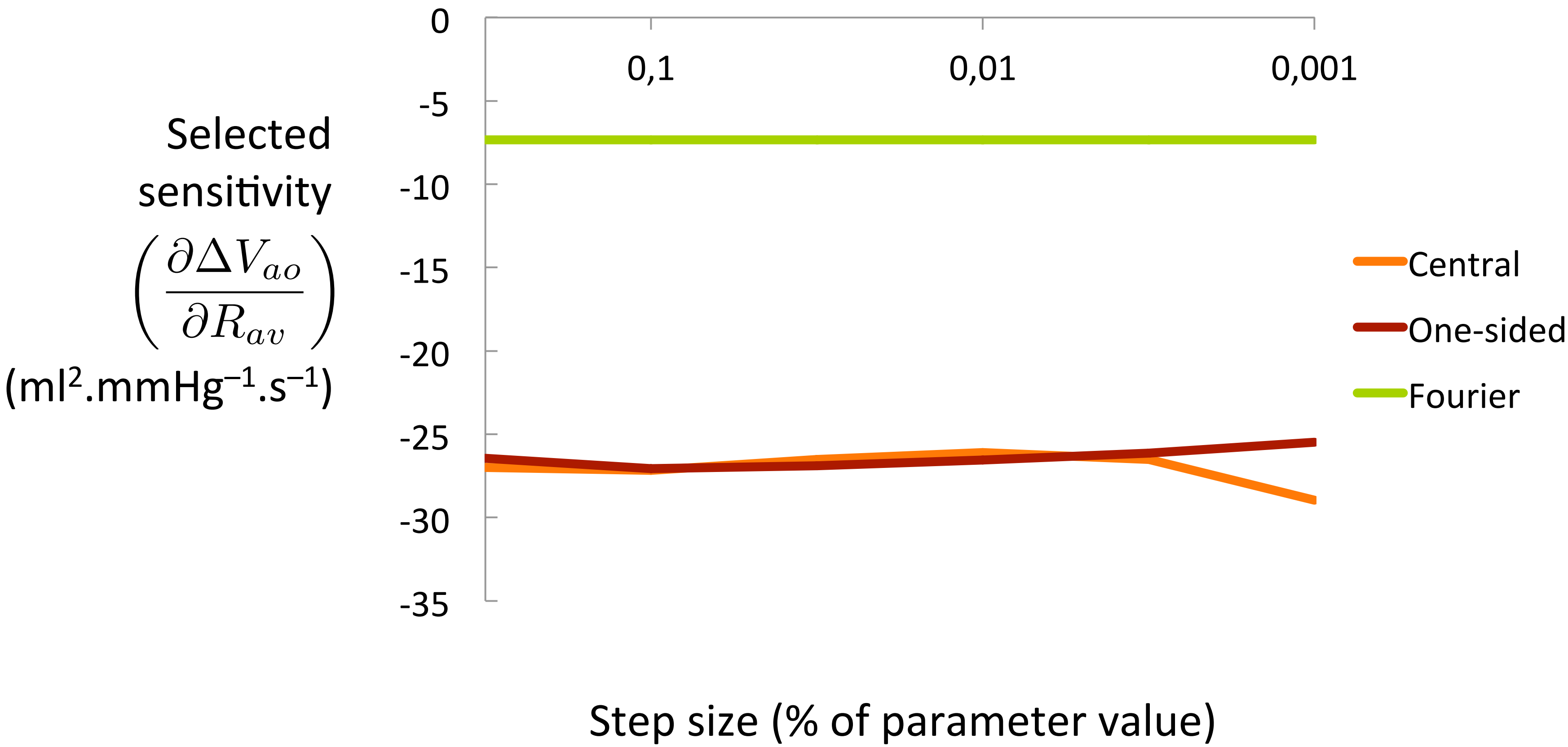
- 2 venous pressures
- 3 resistances
- 2 compliances

2 state variables:

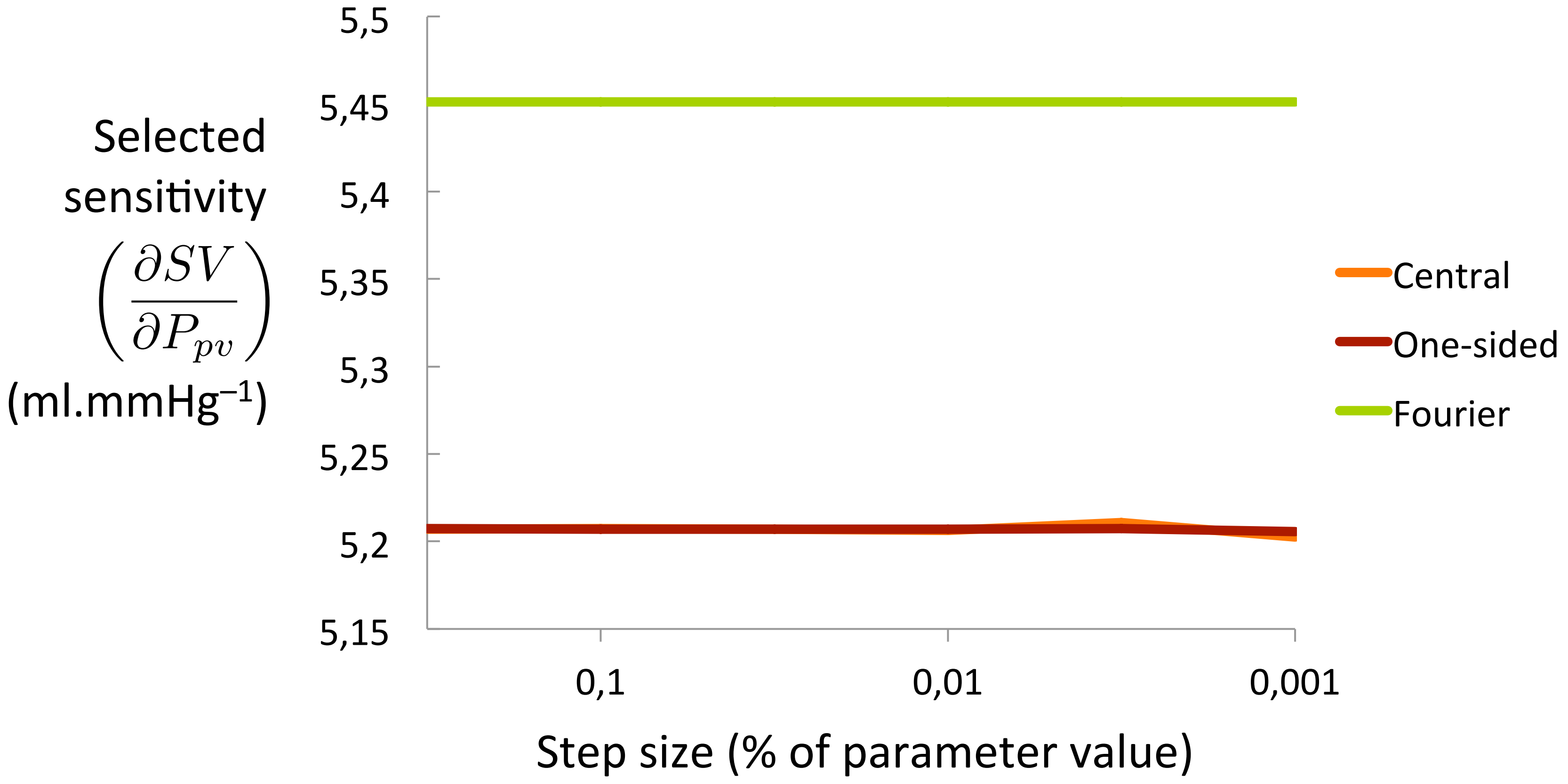
- LV volume
- Aortic volume

Results: mean

Results: amplitude (worst)



Results: amplitude (best)



Conclusion

- Faster than the “brute force” method.
- Exact value for the derivative of the mean.
- Gives only the sign for the derivative of the amplitude.
- Uses:
  - to fasten parameter identification process
  - to perform a sensitivity analysis
  - to select an appropriate step size.

Thanks for your attention!

Université de Liège

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND