SIMCor

In-Silico testing and validation
of Cardiovascular IMplantable devices

Virtual cohort generation and validation

The SIMCor methodology

9 July 2023

Wouter Huberts
Eindhoven University of Technology

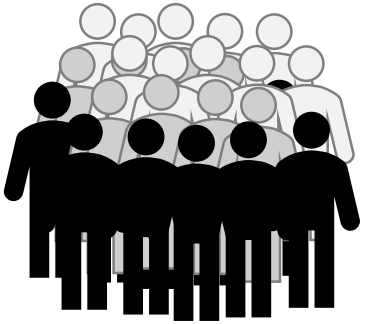
SIMCor

Aim and objectives

SIMCor

Overall aim

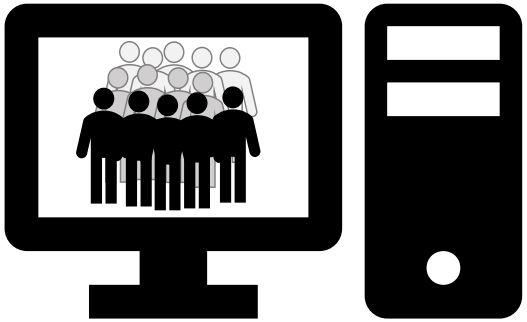
Real patient cohorts



Aortic valve stenosis (TAVI)
Heart failure (PAPS)

=

Virtual patient cohorts

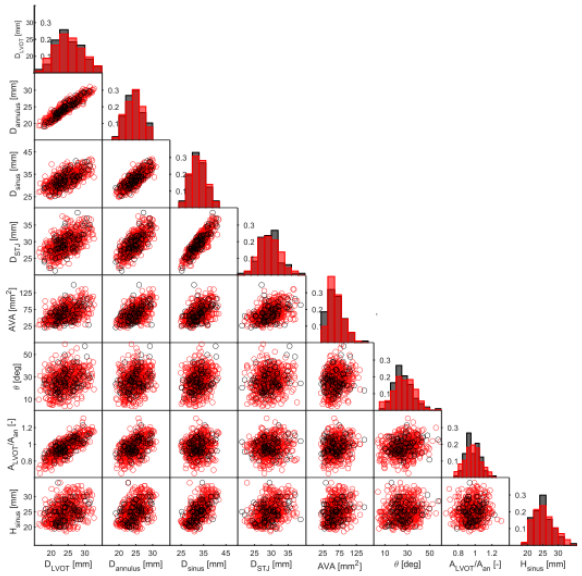


Aortic valve stenosis (TAVI)
Heart failure (PAPS)

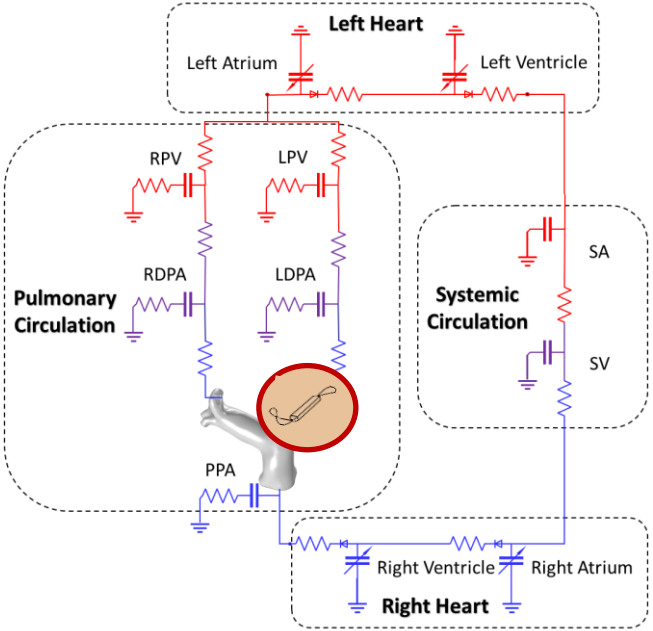
*In a sense that **relevant** statistical/physiological/geometrical **features** regarding medical device performance are **similar***

Overall aim

Population statistics



Individuals



Overall aim

SIMCor: A physiology-based, data-augmented, model serves as basis of our virtual cohort generator

Methodology

SIMCor

Methodology

input parameters

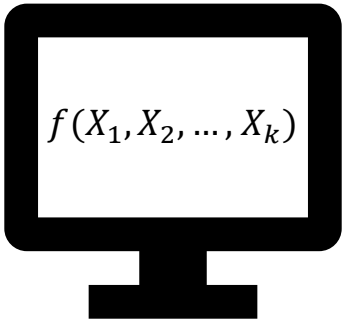
geometry

mechanical properties

boundary conditions

demography

numerical model



possible virtual patient

physiological outputs

relevant metrics

Each model realization *represents* ***a candidate*** *for inclusion into our virtual patient cohort*

Methodology

variation **of parameters**

geometry

mechanical properties

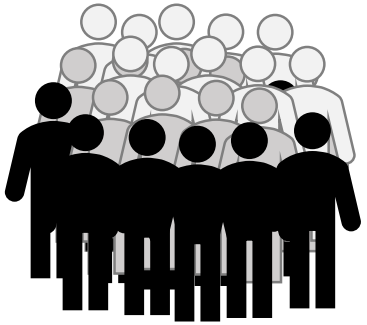
boundary conditions

demography

numerical model

$f(X_1, X_2, \ldots, X_k)$

possible virtual patients

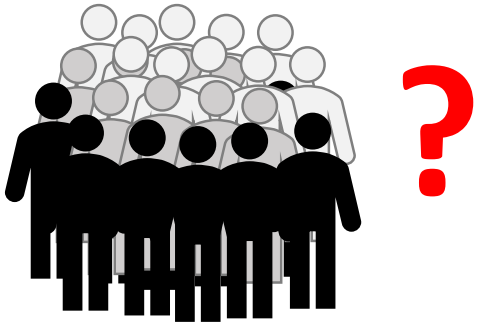


?

Each model realization *represents* ***a candidate*** *for inclusion into our virtual patient cohort*

Methodology

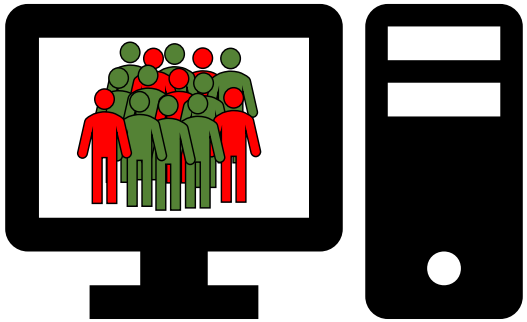
possible virtual patients



filtering

physiological?

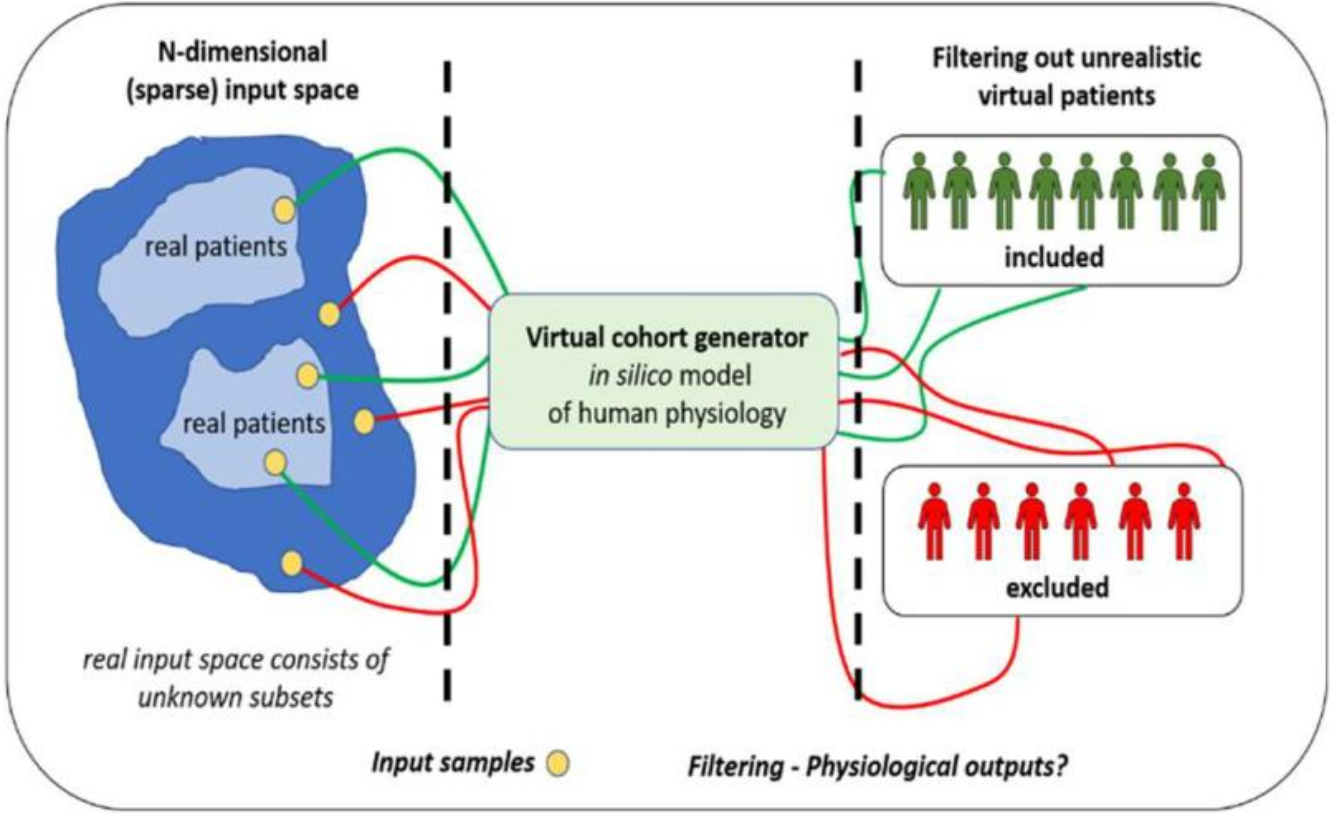
virtual patient cohorts



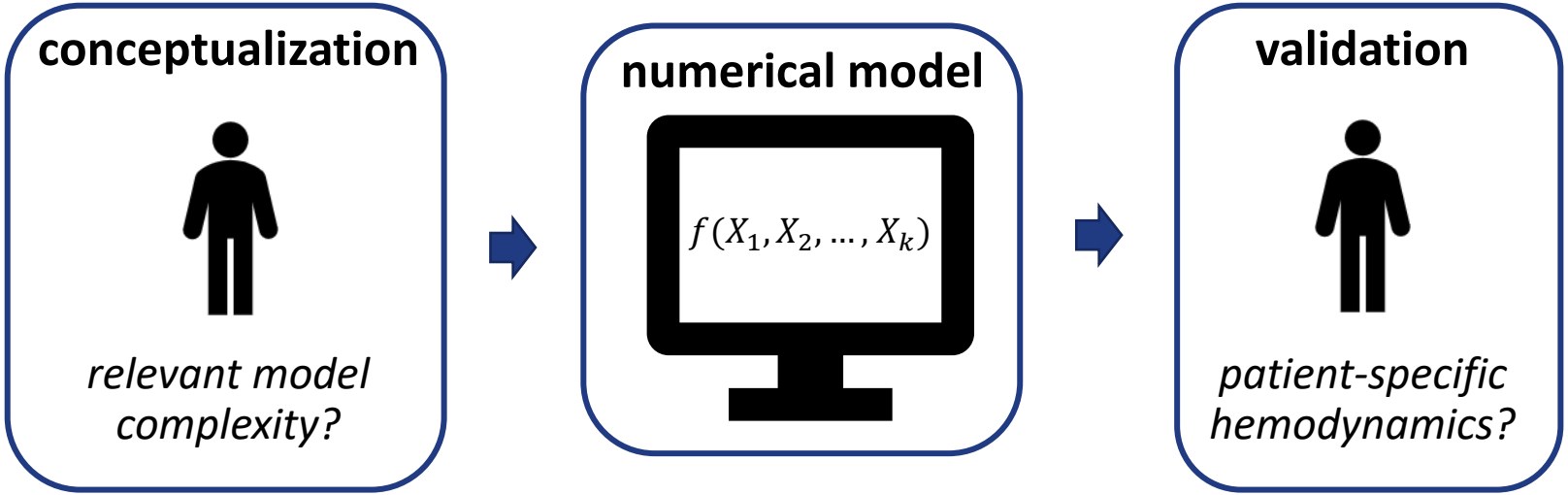
Non-physiological *model realizations* ***are rejected*** *as candidate for inclusion into our virtual patient cohort*

Virtual patient = physiological model + input + BCs

Methodology



Development and validation

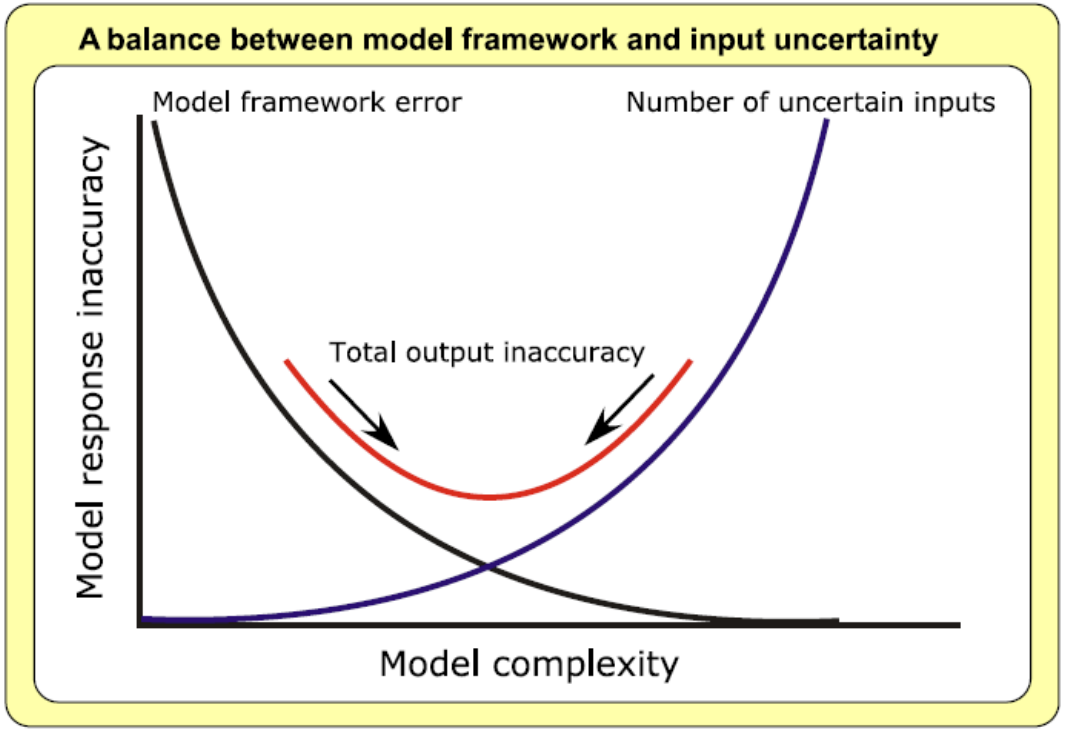


*Develop a **realistic physiological model***

Validation step 1

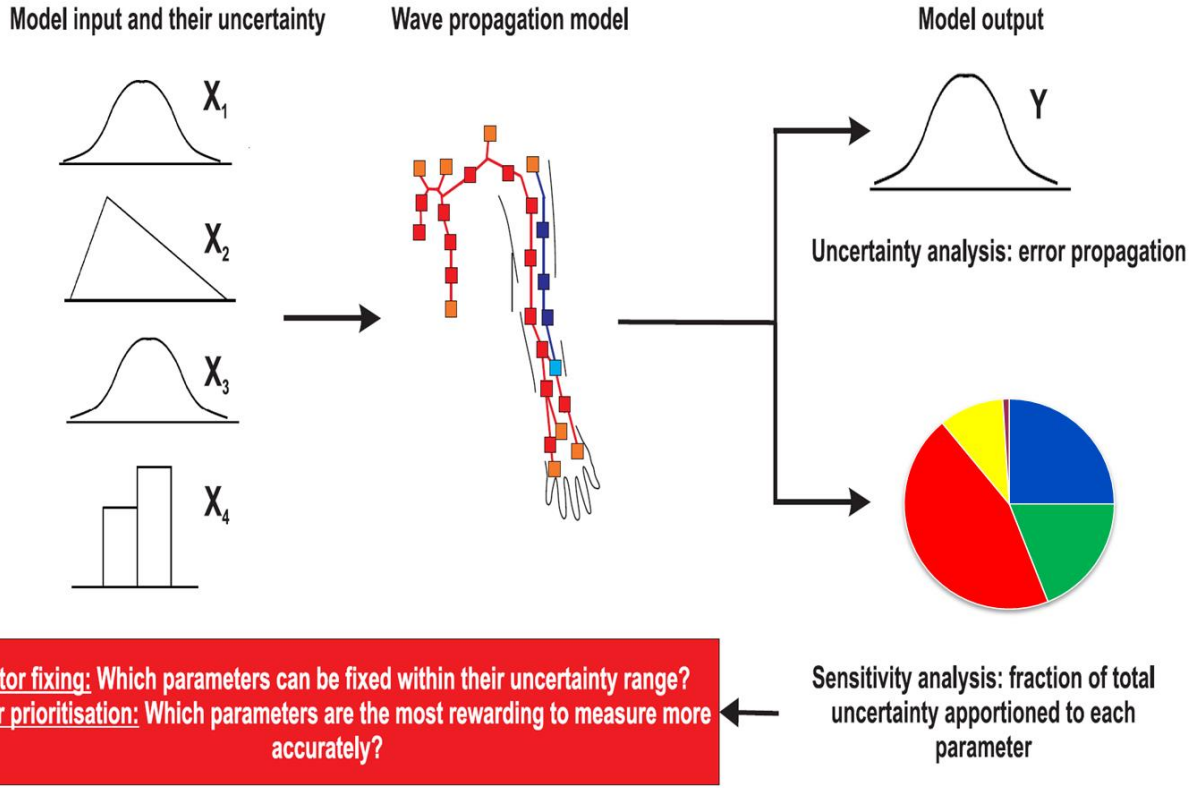
patient level

patient-specific hemodynamics?



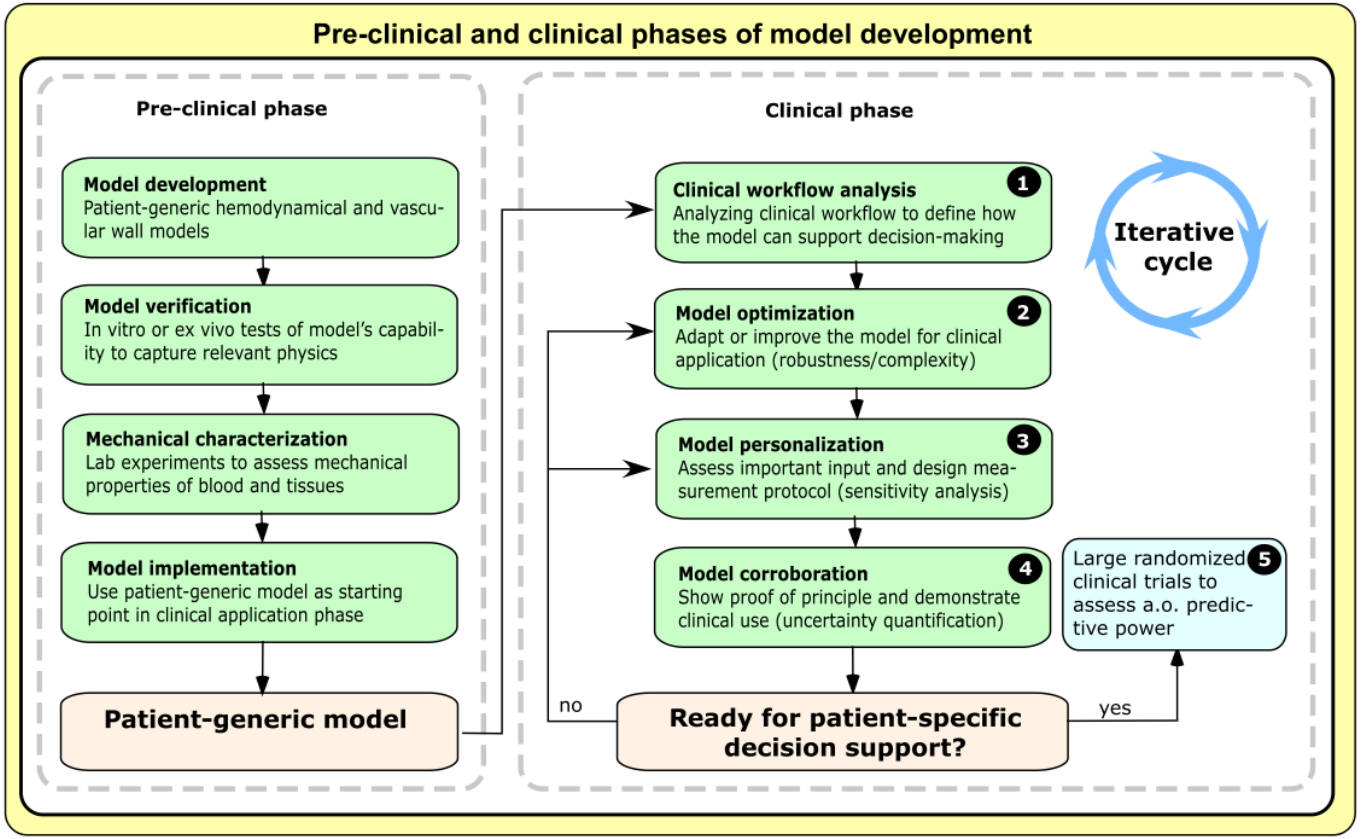
Iterative approach and UQ/SA *in each phase of model development* [2, 3]

Validation step 1



[2,3]

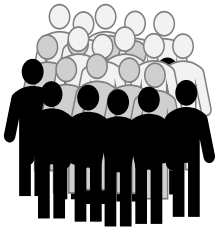
Validation step 1



[2]

Validation step 2

self-validation



similar cohort statistics?

*Evaluate **effect simulations** for multiple individual patients + UQ*

*Assess whether **virtual cohort distributions mimic real cohort** distributions and/or **predefined regions of the output space***

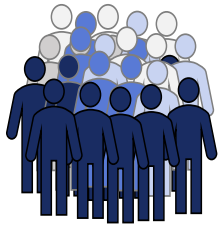
*If **YES**: Move to **cross-validation** step*

*If **NO**: Adapt the **physiological model** and/or **filter** design settings*

[4]

Validation step 3

cross-validation



similar cohort statistics?

*Validate **effect simulations** for multiple individual patients against data from **clinically matched cohorts** (typically by severity score, diagnosis or other patient metric)*

*Assess whether **virtual cohort distributions mimic the real cohort** distributions and/or predefined regions of the output space **for these clinically matched cohorts***

***Apply virtual cohort** for 1) industrial device design/optimization; 2) develop (parameter estimation/image segmentation) algorithms; 3) animal/clinical trial design; 4) educational purposes; 5) virtual clinical trials*

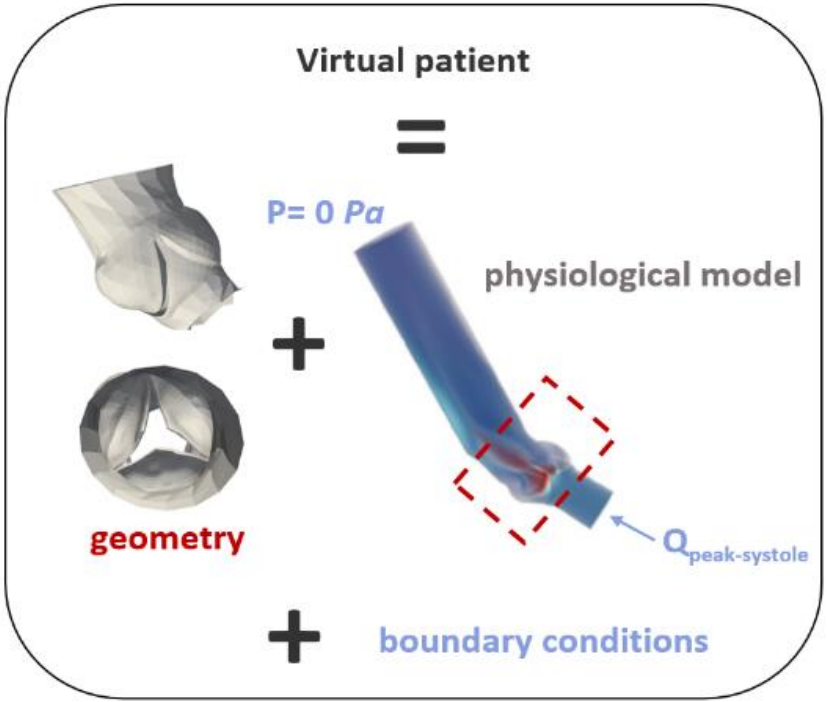
[4]

Preliminary results

Aortic valve stenosis: physiology-driven filtering

SIMCor

The virtual patient

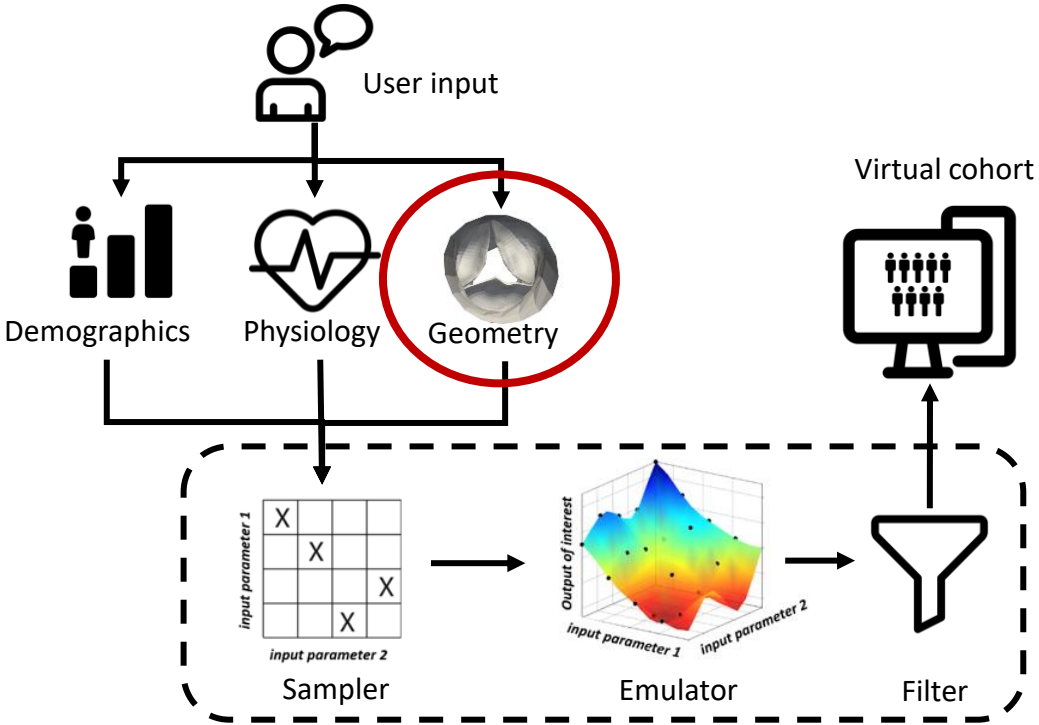


*A **realistic input sample** of an (unknown) population distribution*

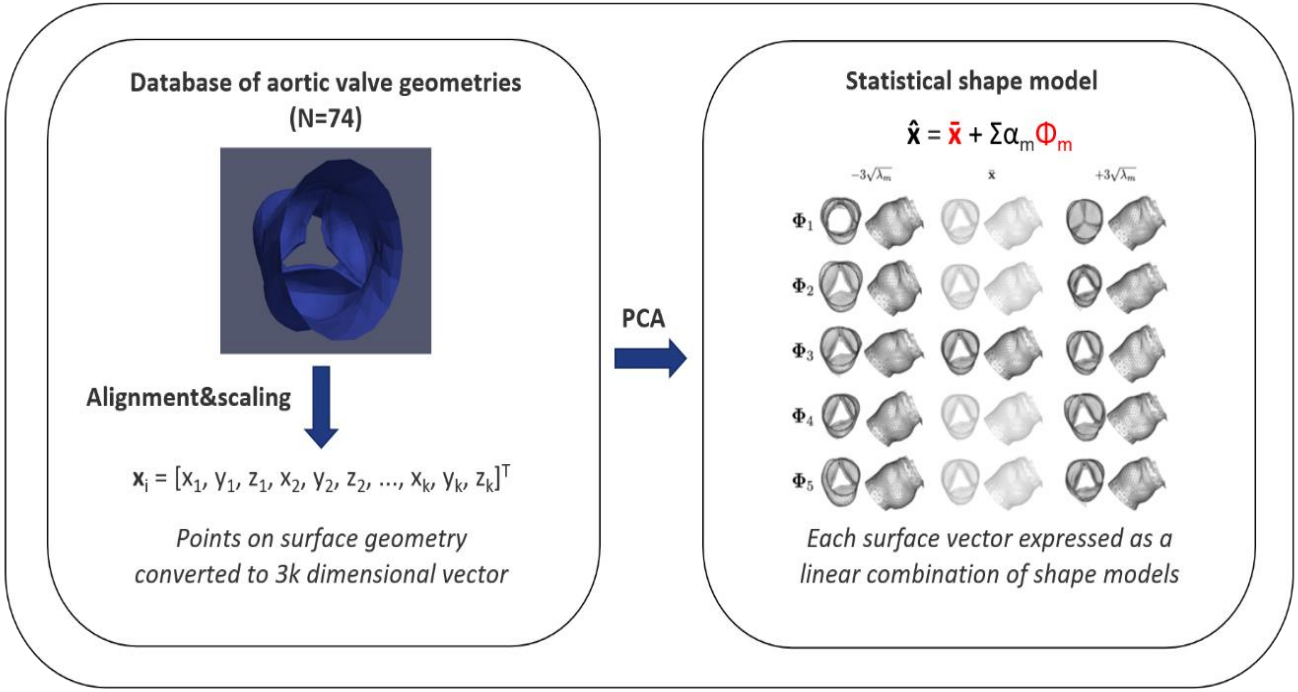
+

A validated ***physiological model***

The virtual cohort generator

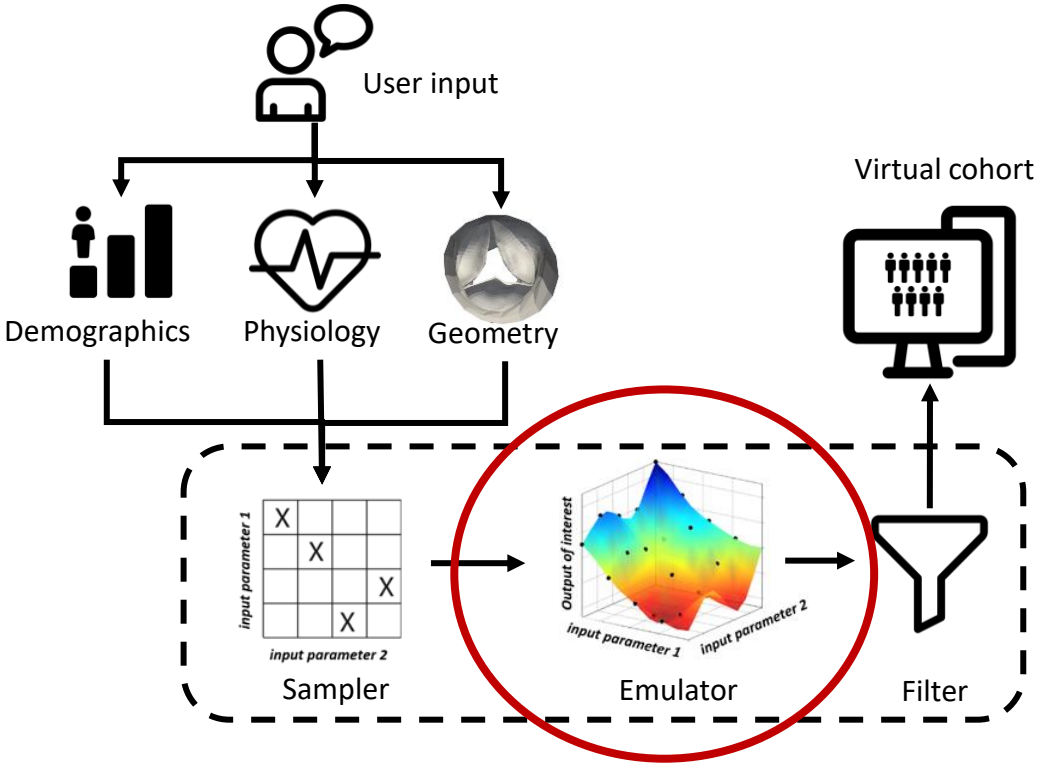


Geometrical input space definition

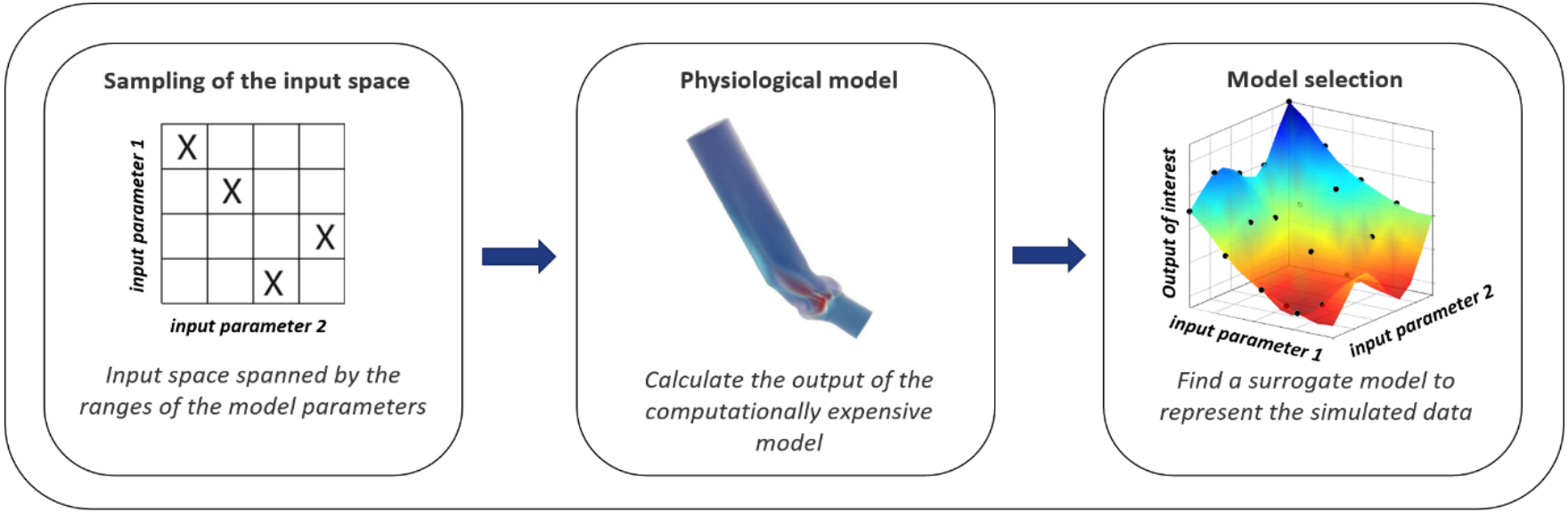


[5, 6]

The virtual cohort generator

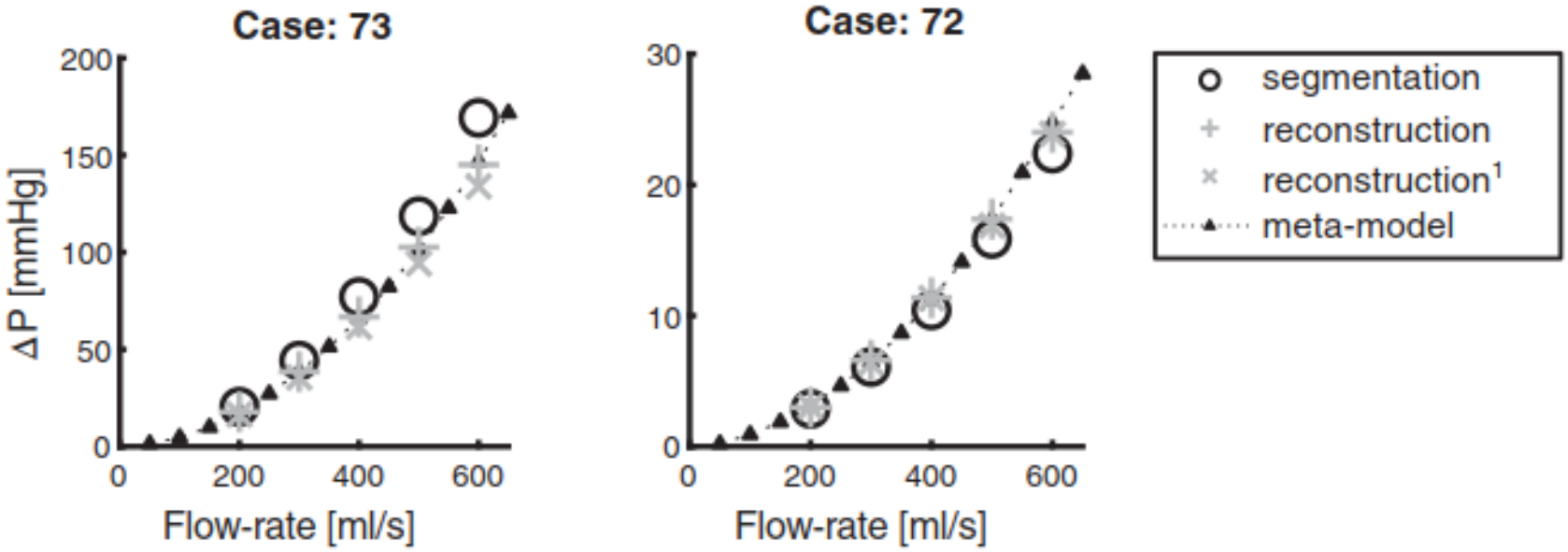


Surrogate model development



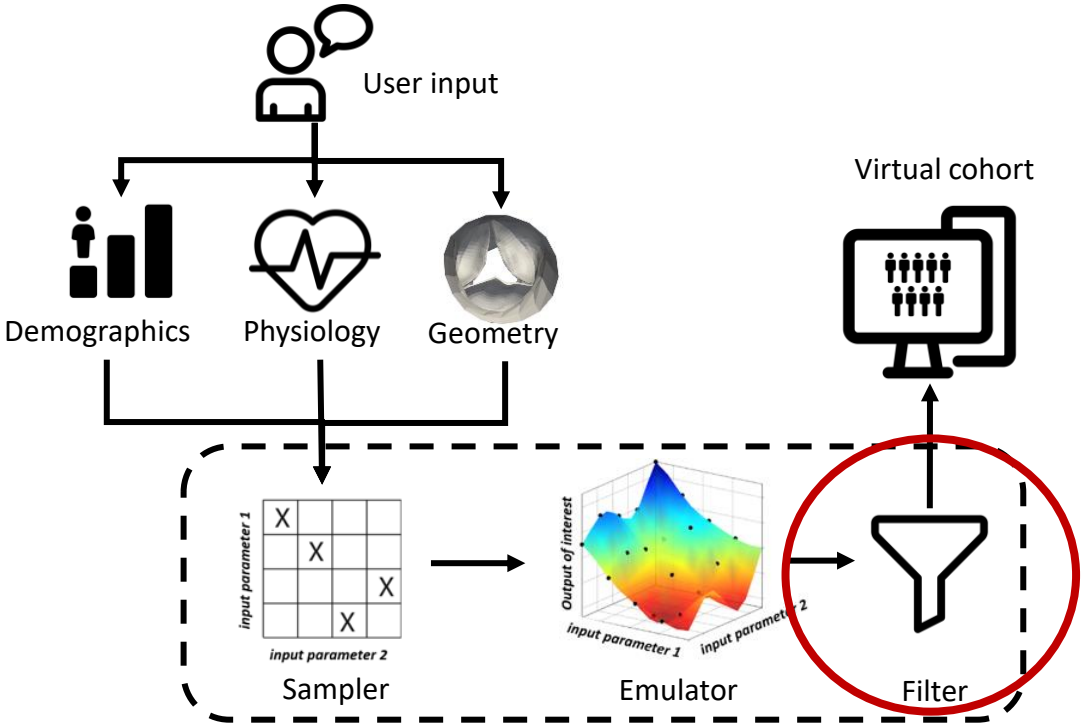
[5, 7]

Surrogate model results

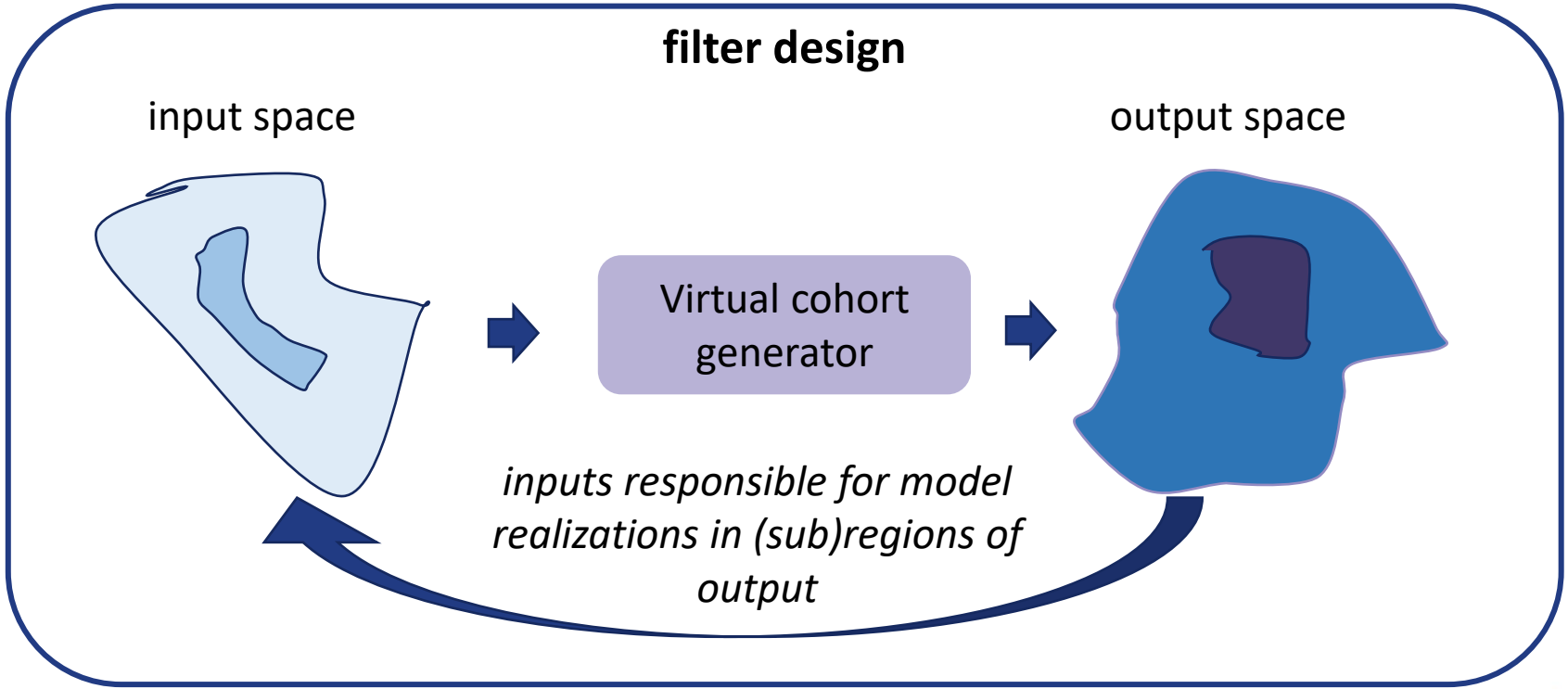


[7]

The virtual cohort generator

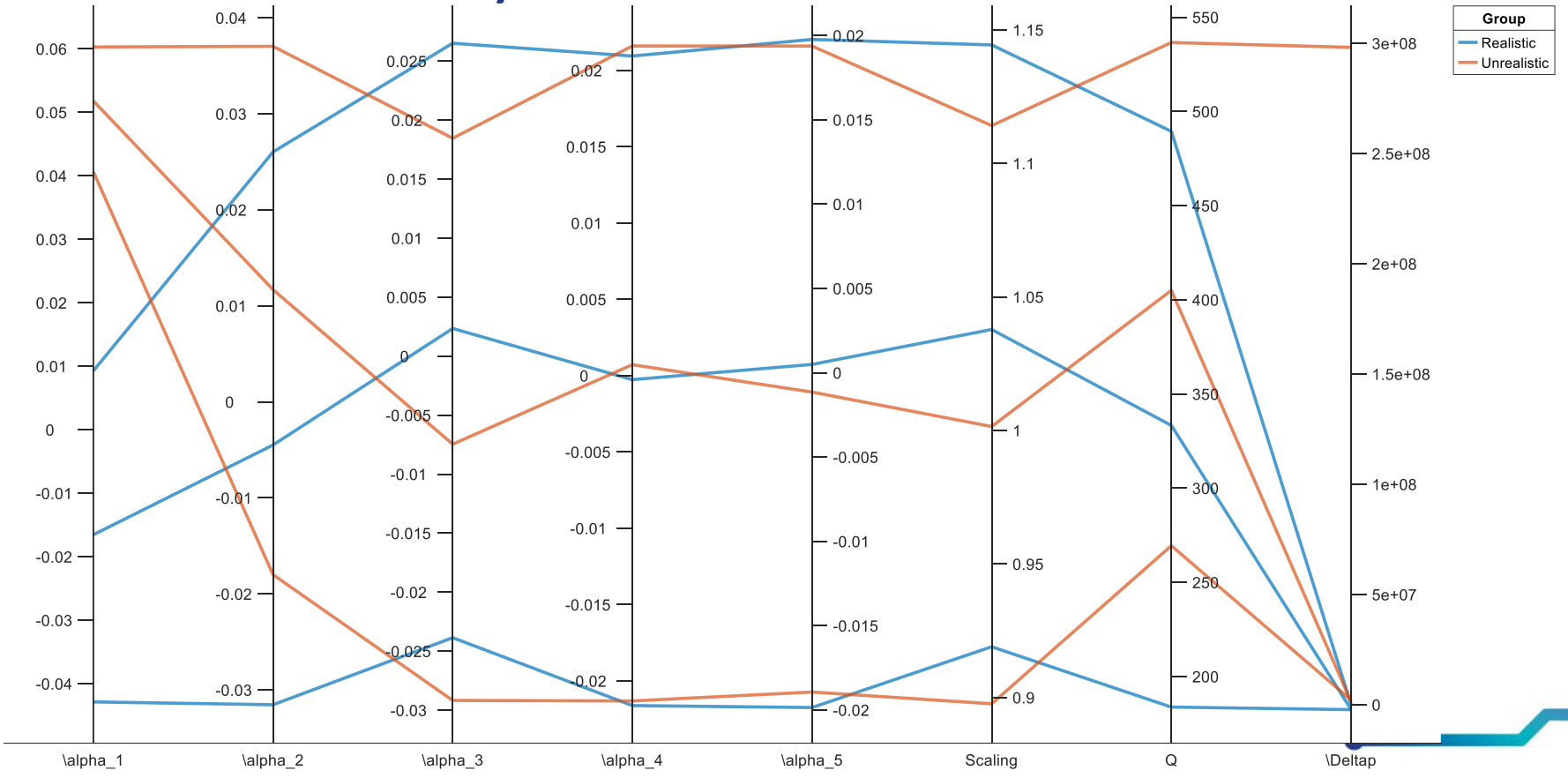


Filter design

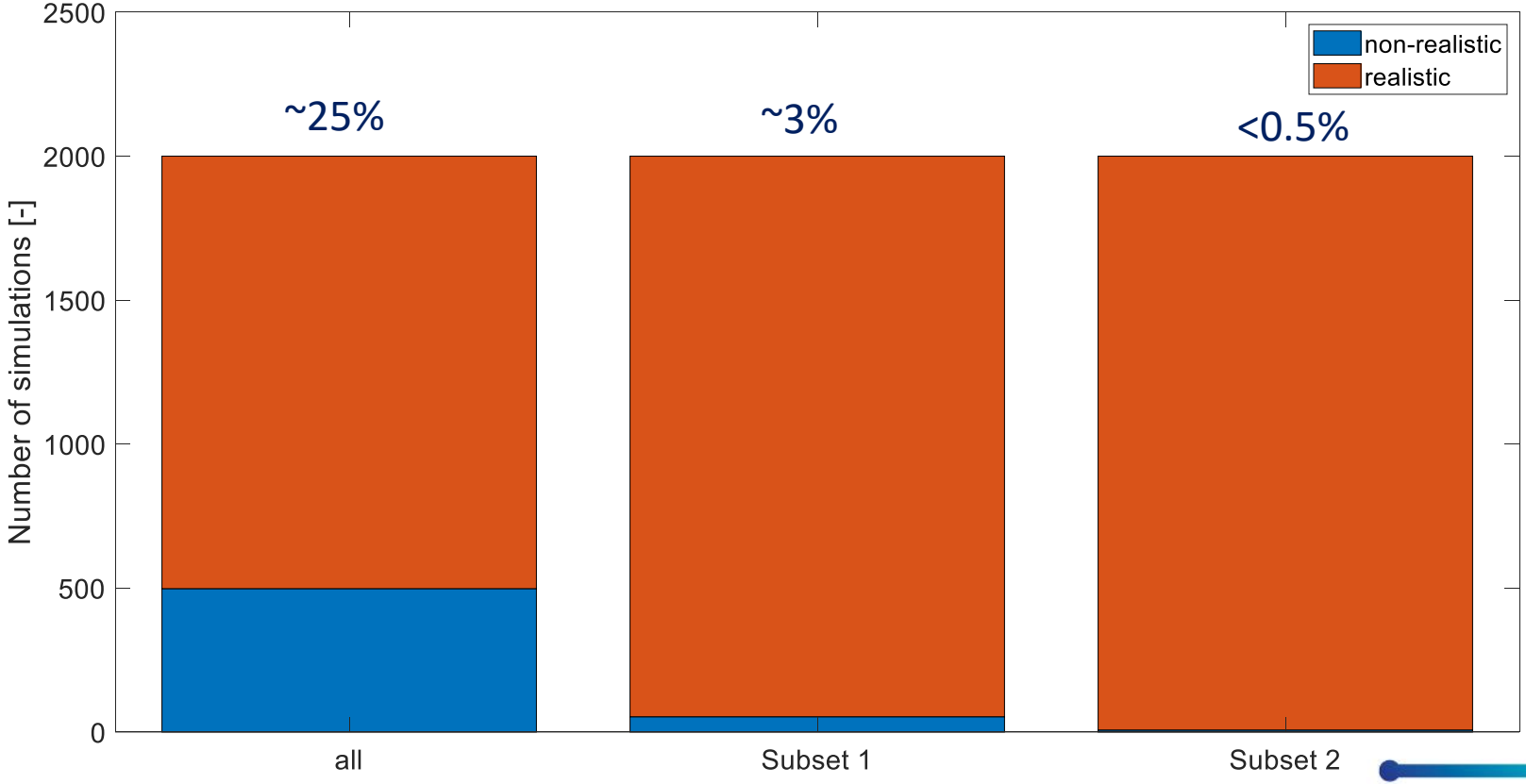


[3,8]

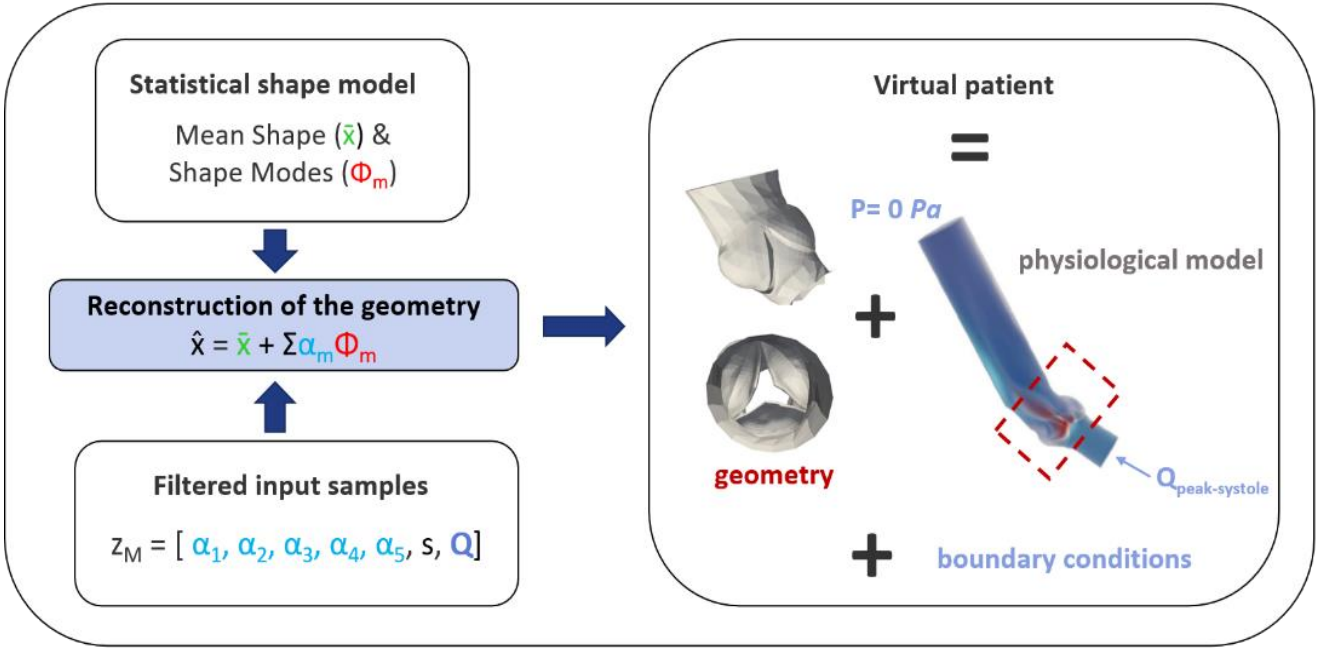
Preliminary results



Preliminary results



The result


Statistical shape model
Mean Shape ($\bar{x}$) &
Shape Modes (Φ_m)
Reconstruction of the geometry
$\hat{x} = \bar{x} + \Sigma\alpha_m\Phi_m$
Filtered input samples
$z_M = [\ \alpha_1, \alpha_2, \alpha_3, \alpha_4, \alpha_5, s, Q]$
Virtual patient
=
P= 0 Pa
physiological model
+
geometry
$Q_{peak\text{-}systole}$
+
boundary conditions

Ongoing work

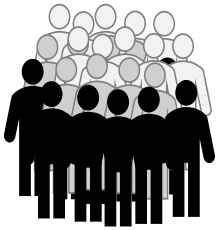
SIMCor

Next iteration

patient level

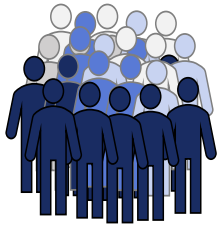
patient-specific hemodynamics?

self-validation



similar cohort statistics?

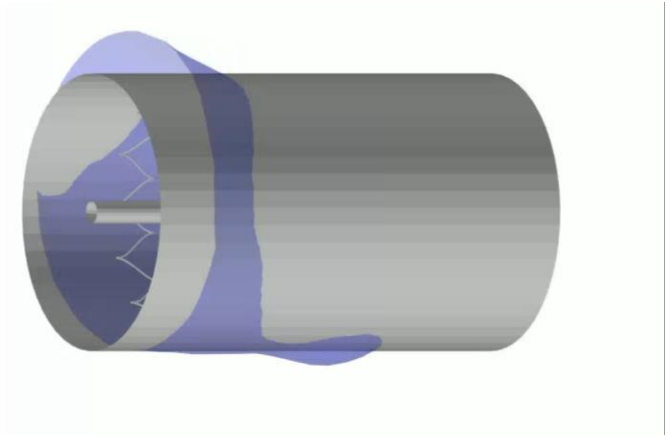
cross-validation



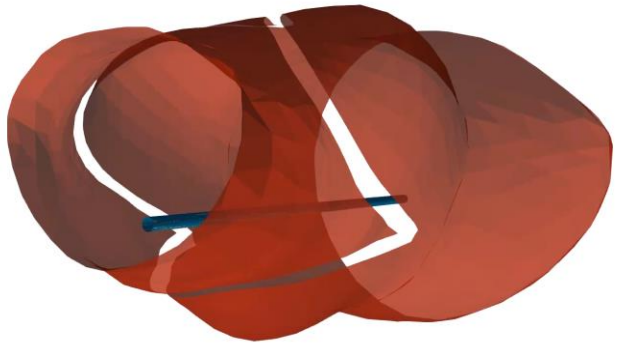
similar cohort statistics?

Next iteration → incorporate ***effect simulations to VCG*** + ***application of VC***

Device-effect simulations



High-fidelity



Fast but reduced-order

Apply different filter strategies

Data-driven

Physiology-driven

Clinically-driven

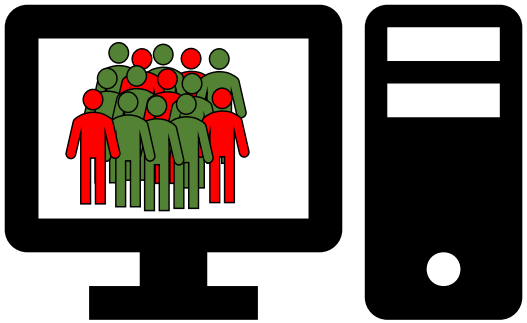
Romero et al. (2021)

Open issues

SIMCor

Open issues

virtual patient cohorts



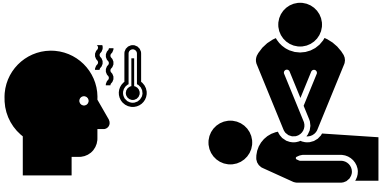
…but based on *engineering metrics*

$\mathcal{L}\{\quad\}$

We need a mapping strategy

***In silico* clinical trial**

hospitalizations

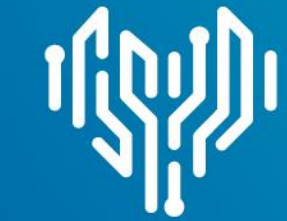


morbidity/mortality

***clinical outcome* criteria**

References

1. https://miro.medium.com/max/713/1*JKN58IlH0uiiWGmSz6R5hA.png
2. Huberts et al. (2018): https://doi.org/10.1016/j.jocs.2017.07.006
3. Saltelli et al. (2008): John Wiley&Sons, Ltd. ISBN: 978-0-470-05997-5
4. Chase et al. (2018): https://doi.org/10.1186/s12938-018-0455-y
5. Hoeijmakers et al. (2019): https://doi.org/10.1016/j.jbiomech.2019.07.010
6. Hoeijmakers et al. (2021): https://doi.org/10.1002/cnm.3518
7. Hoeijmakers et al. (2020): https://doi.org/10.1002/cnm.3387
8. Pianosi et al. (2016): https://doi.org/10.1016/j.envsoft.2016.02.008



Thanks!

Wouter Huberts

w.huberts@tue.nl

wouter.huberts@maastrichtuniversity.nl