>> digital twins for personalized medicine

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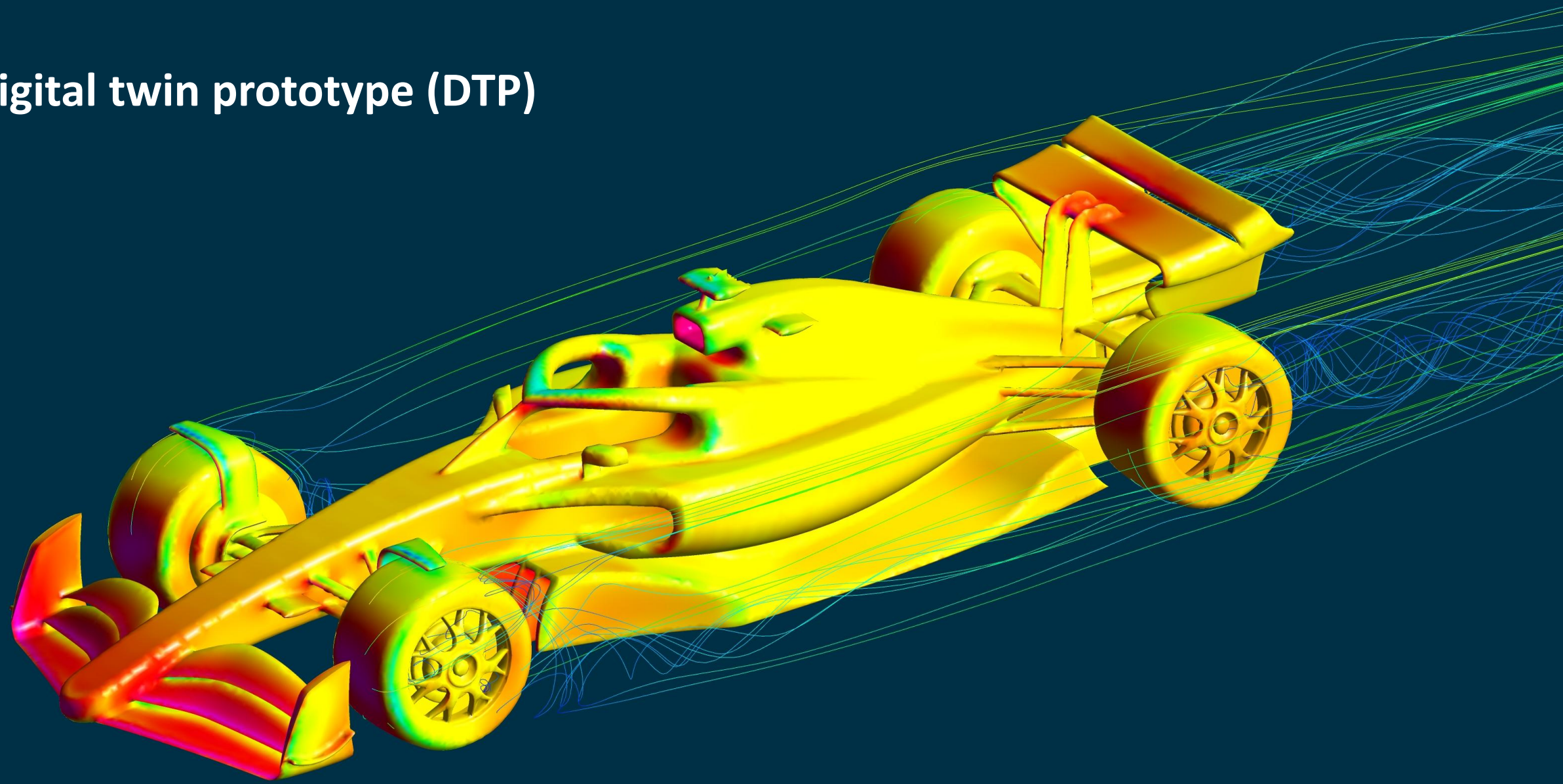
Birth of Digital Twin concept: US Apollo 13 mission in 1970

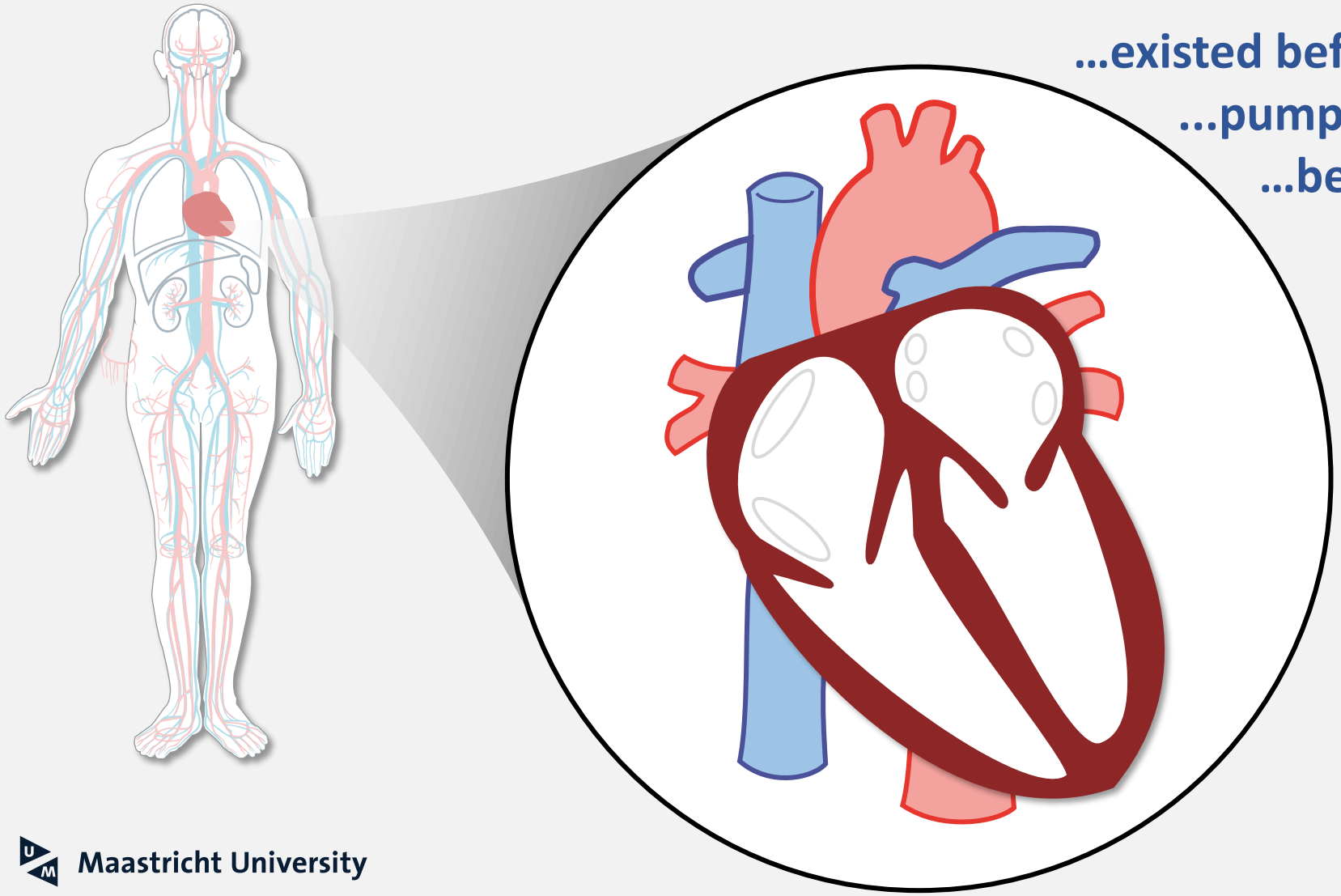
Guo *et al.* Multimedia Tools and Applications (2022)

Digital twin prototype (DTP)



Source: Atif Masood @fetchcfd.com

The heart …



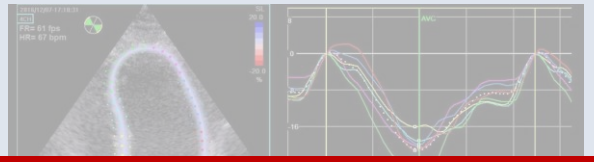
…existed before its digital models/twins

…pumps ~7,500 liters of blood a day

…beats ~100,000 times a day

Biophysical modeling in a nutshell …

OBSERVATIONS



EFFECTS (y)

CAUSES (x)

SYSTEM PROPERTIES

Vascular Resistance

(Flow)

(Pressures)

…

Cardiovascular physiology is complex, dynamic and non-linear

$$y = f(x, t)$$

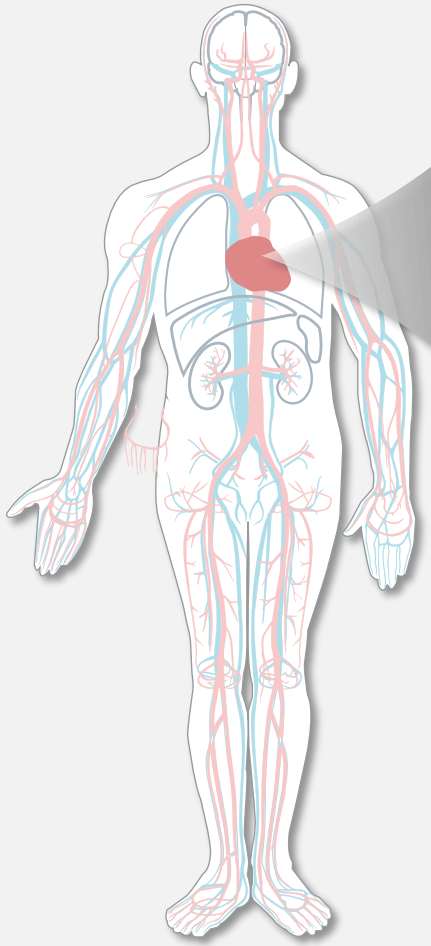
Ohm, Laplace, Bernoulli, Fick, …

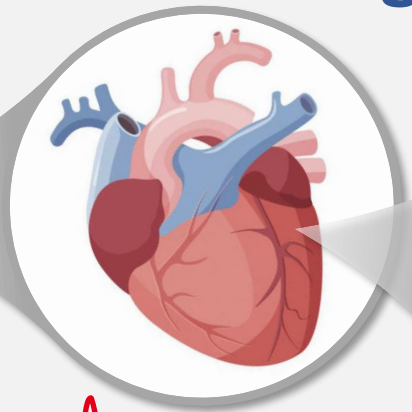
system

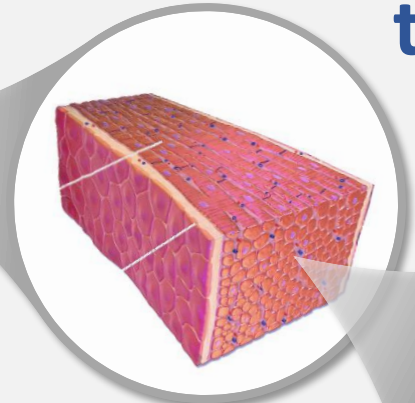
organ

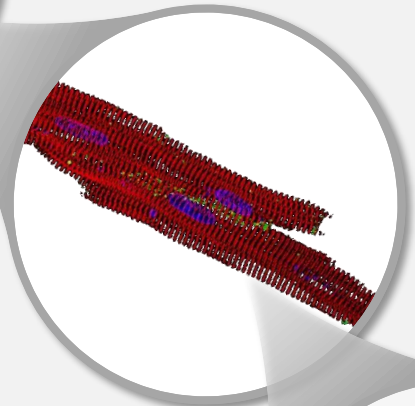
tissue

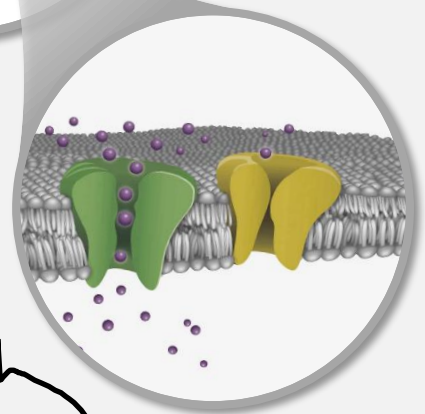
cell











blood flow

pressure

force

$[Ca^{2+}]$

membrane potential

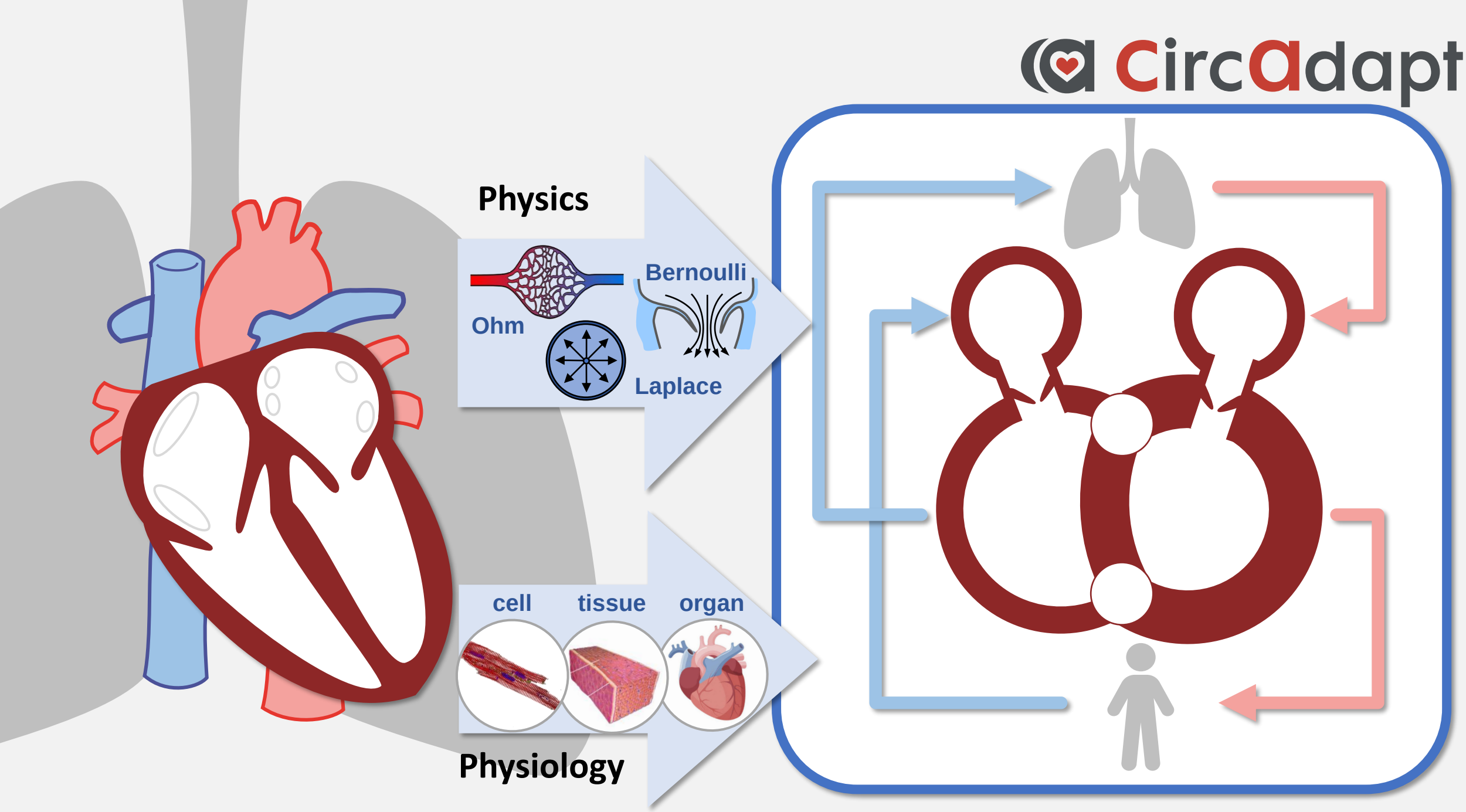
protein

(ion channel, actin, myosin, titin, etc.)

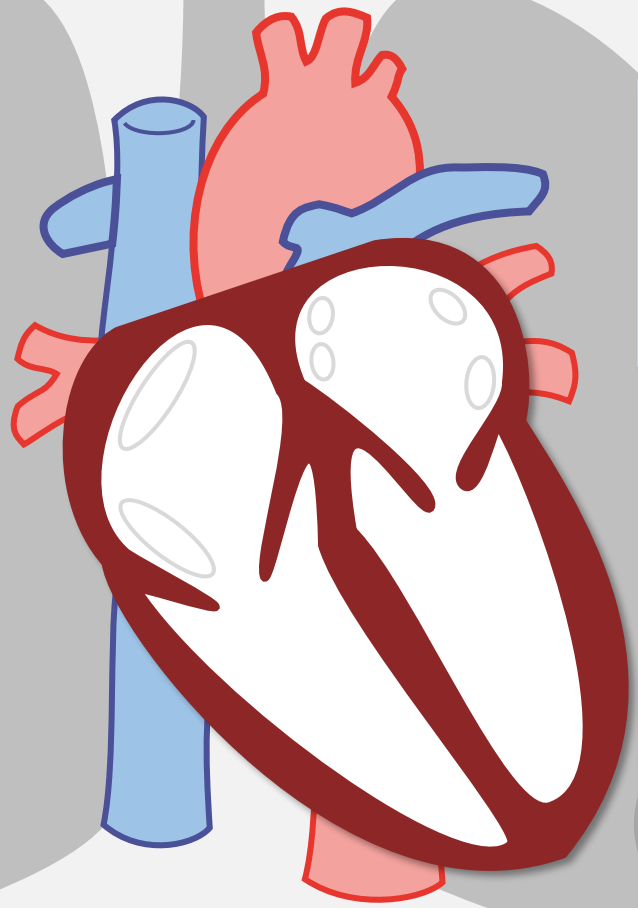
Maastricht University

Niederer S, Lumens J, and Trayanova NA. *Nature Rev Cardiol* 16:100-111, 2019

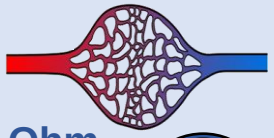
CircAdapt


Physics
Ohm
Bernoulli
Laplace
cell
tissue
organ
Physiology

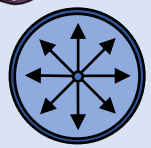
CircAdapt

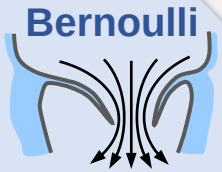


Physics



Ohm

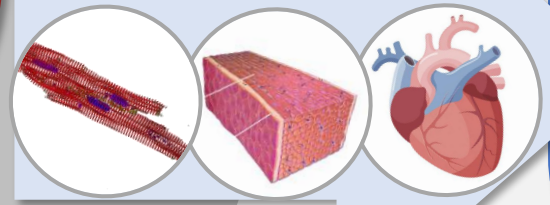




Bernoulli

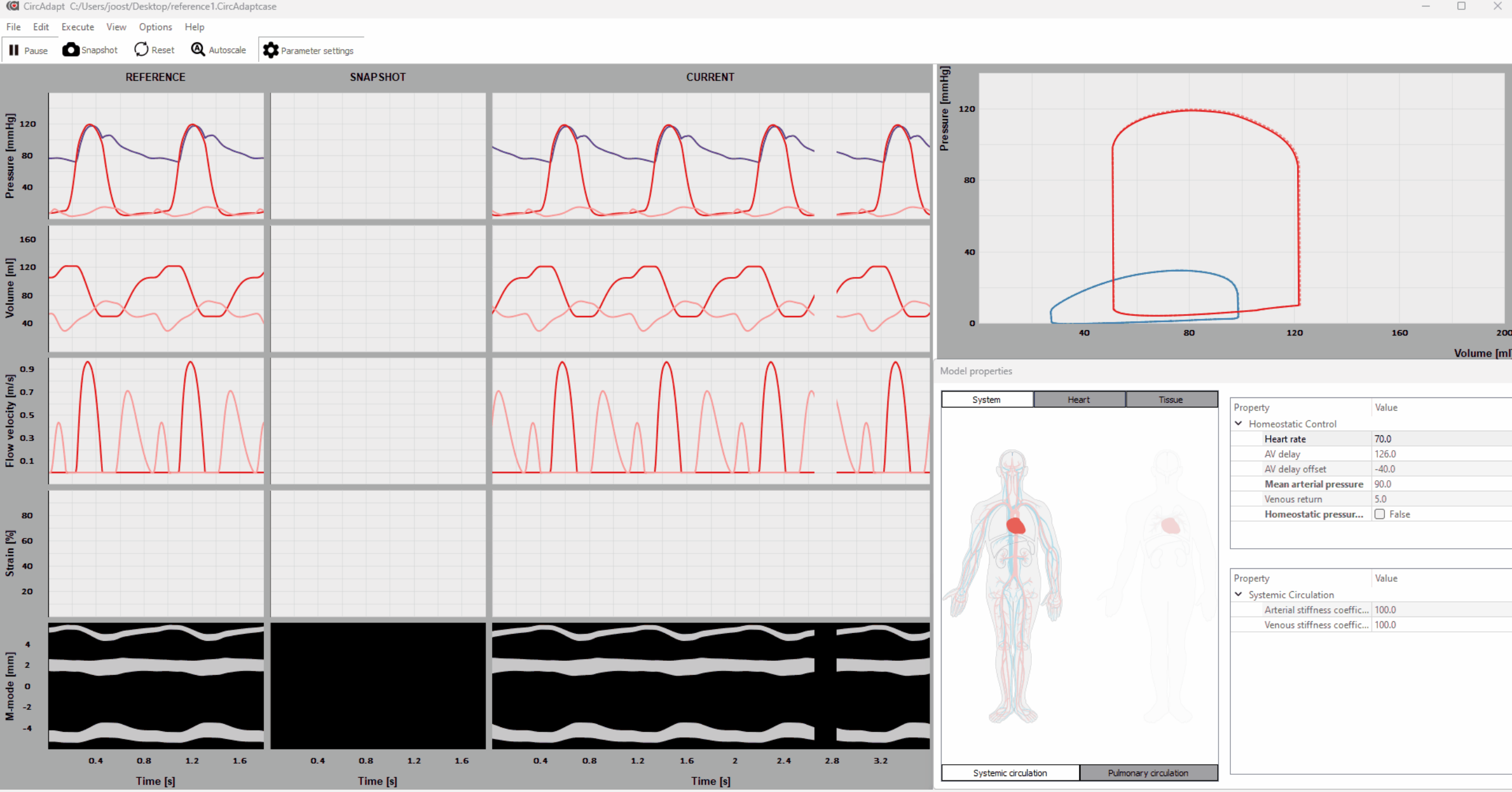
Laplace

cell tissue organ



Physiology

```
199     // Calculate Active stress based on C
200     LNormSe = (Ls - Lsi) / LenSeriesElement;
201     double SfIso = (C     * L) * (1.51*SfAct);
202     double SfRest = 0;
203     if (CRest !=0)
204         SfRest = L* (1.51 * CRest * SfAct);
205
206     // Passive Stress
207     double kk3 = 2 * LsRef / dLsPas;
208     double LfP = Ls / Ls0Pas;
209     double y = exp(log(LfP) * k1);
210     double yTit = exp(log(LfP) * kk3);
211     SfEcm = (y - 1)*(0.0349*SfPas);
212     SfPasT = SfEcm+(yTit - 1)*(0.01*SfAct);
213     double DSfPasDEf = y * (0.0349*SfPas*k1) + yTit * (0.01*SfAct*kk3);
214
215     // Calculate total stress
216     Sf = SfPasT +(SfIso + SfRest)*LNormSe - SfRest;
```

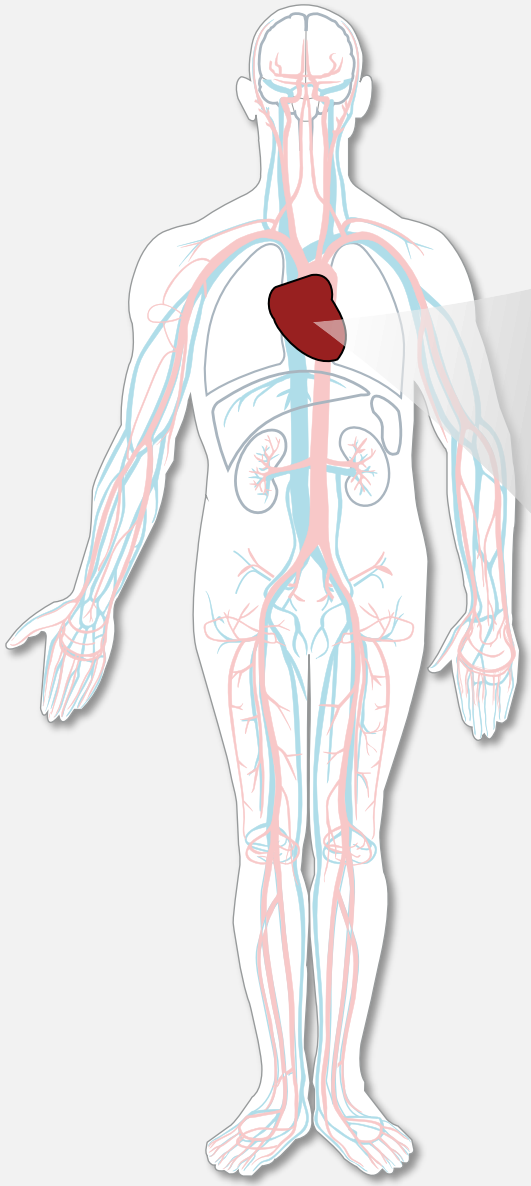


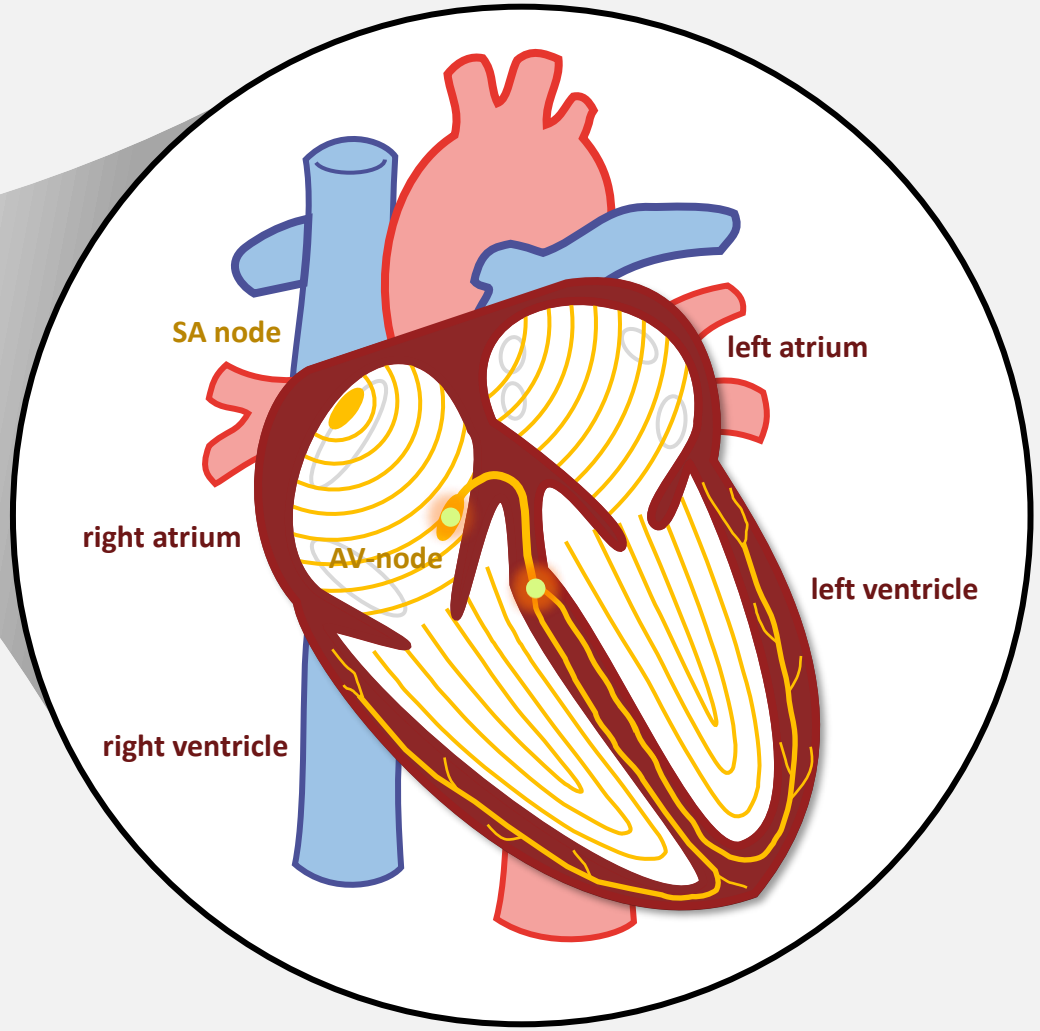
CircAdapt

Arts T *et al.* *Am J Physiol* 2005; **Lumens J *et al.*** *Ann Biomed Eng* 2009; **Walmsley J *et al.*** *PLoS Comp Biol* 2015

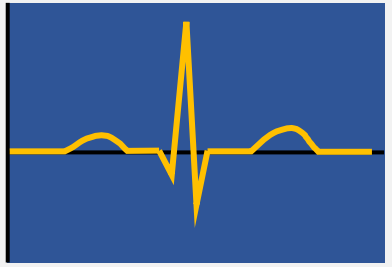
www.circadapt.org

electrical activation of the normal heart

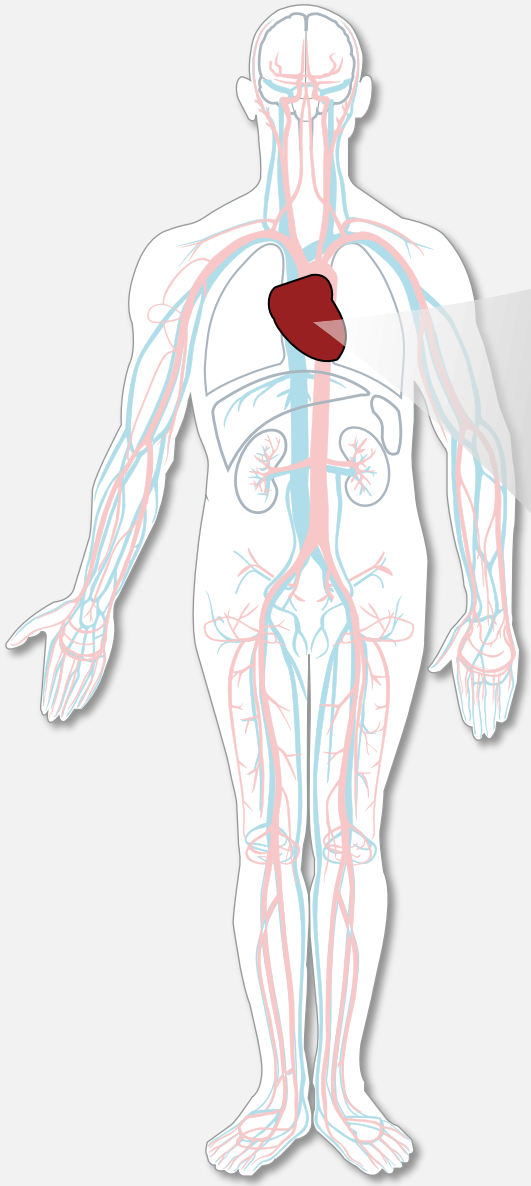


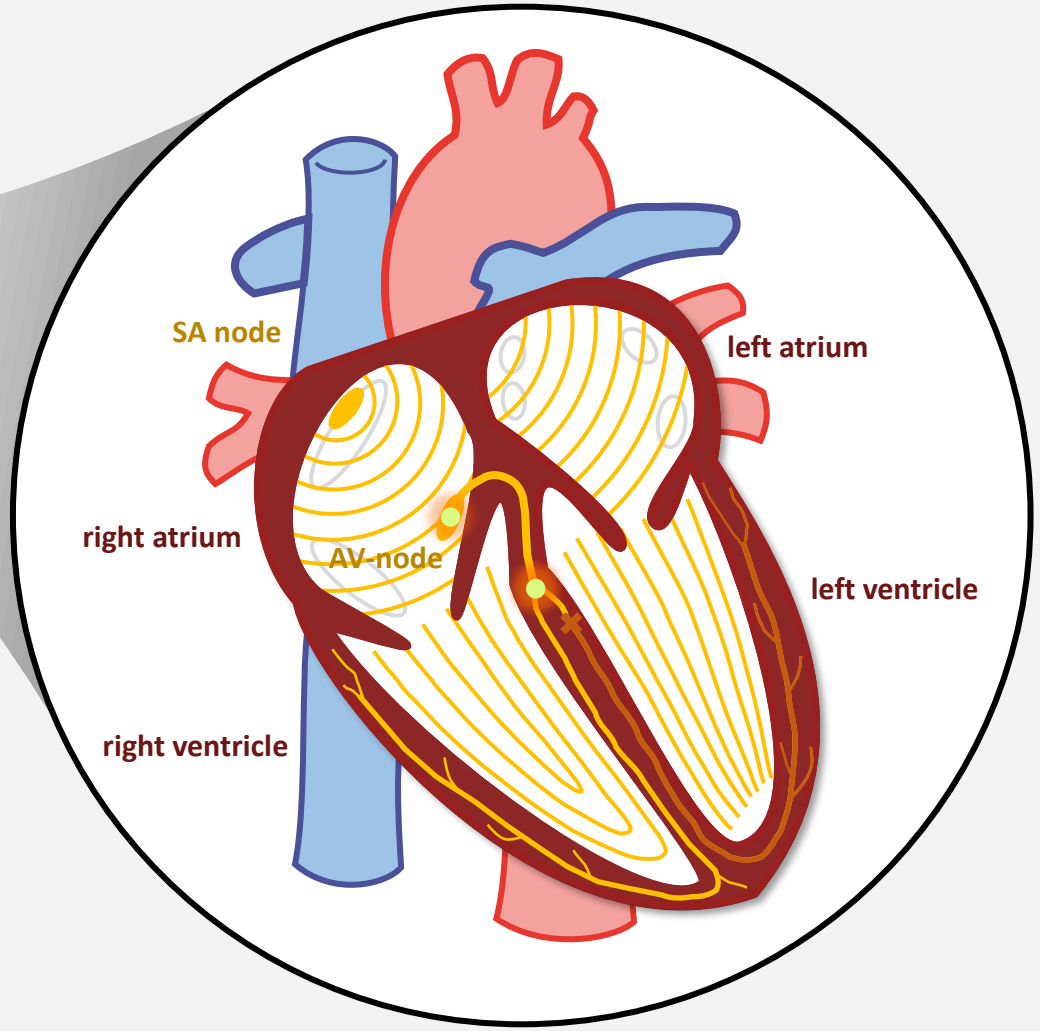


ECG

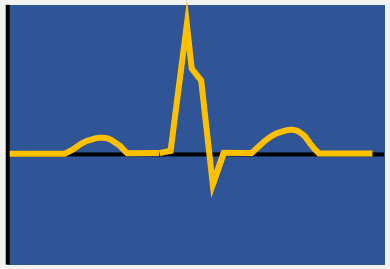


electrical activation disturbed in the failing heart



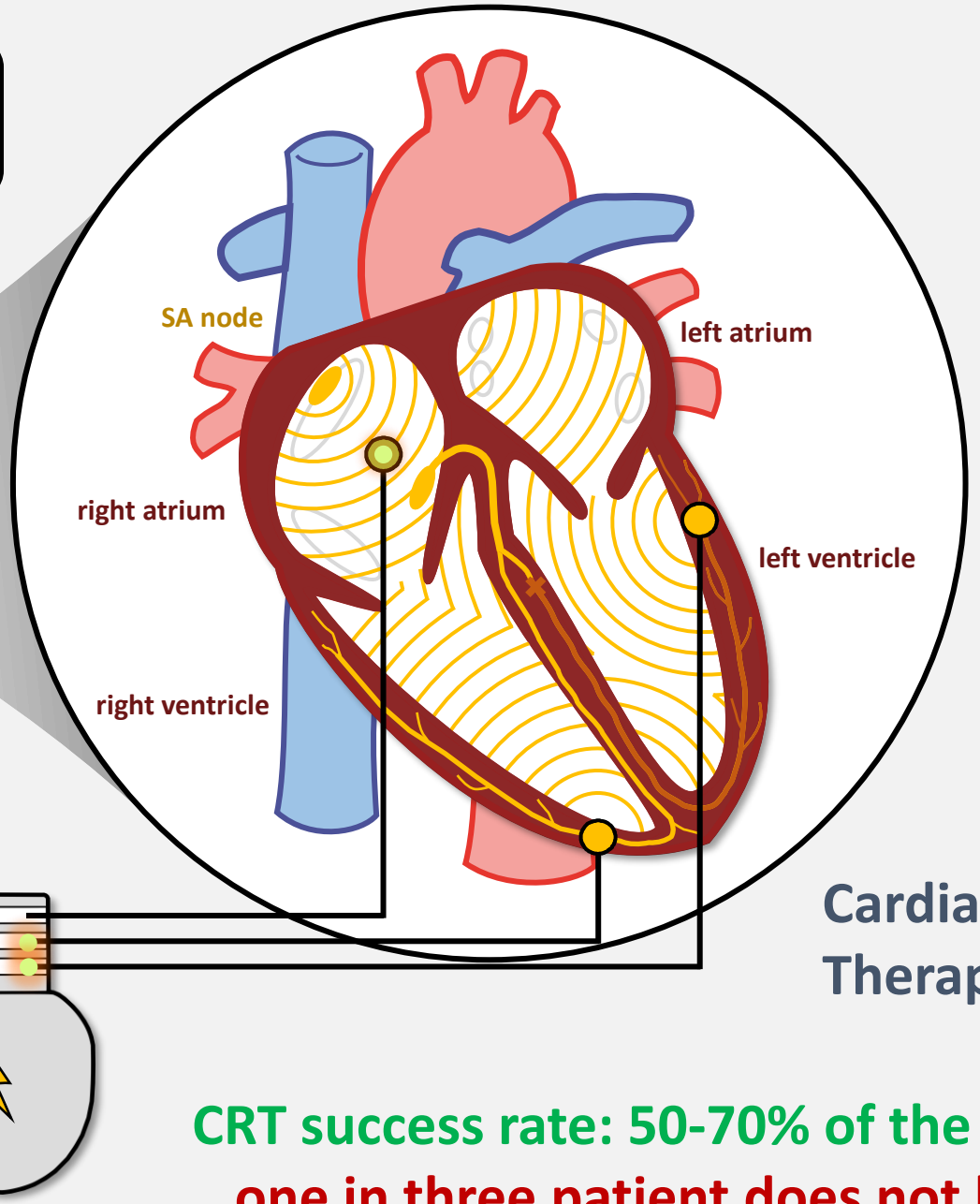


ECG



Left Bundle-Branch Block (LBBB)

heart failure



pacemaker

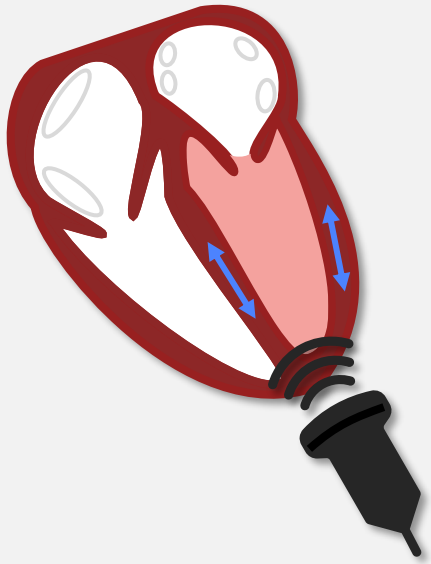
Cardiac Resynchronization Therapy (CRT)

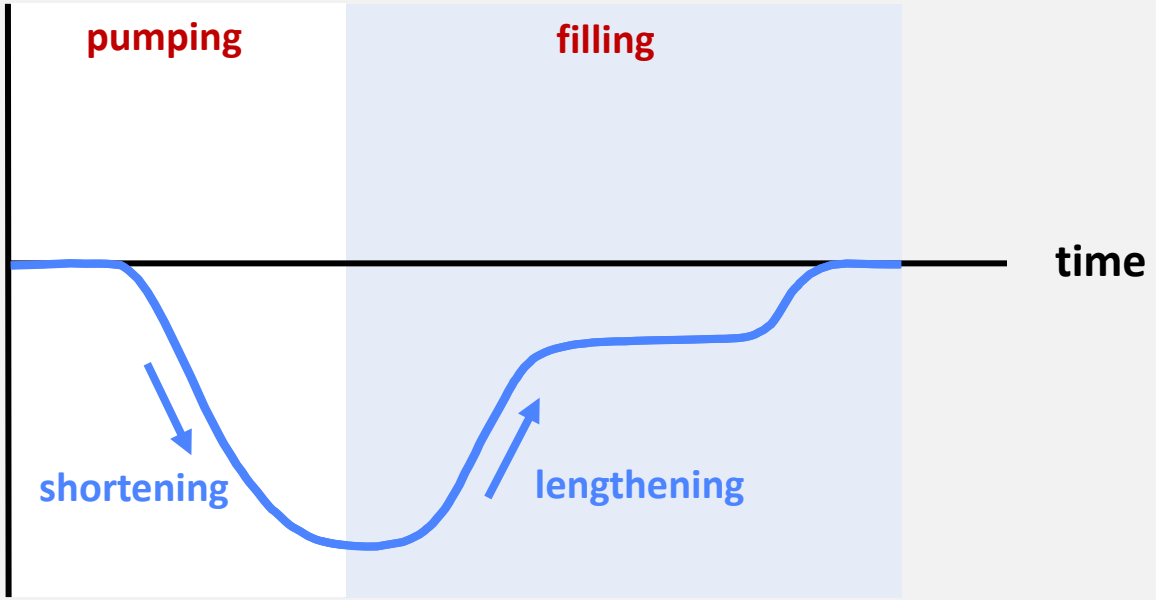
CRT success rate: 50-70% of the patients benefits

...one in three patient does not benefit from CRT

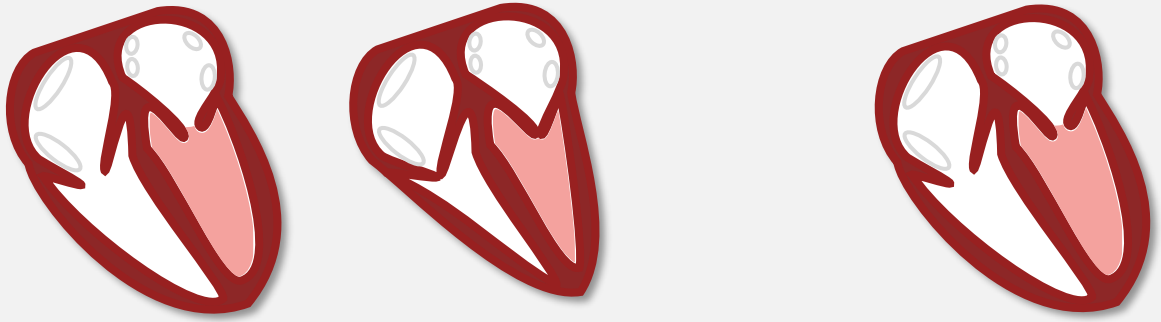
1 cardiac cycle

Deformation of the
left ventricular wall



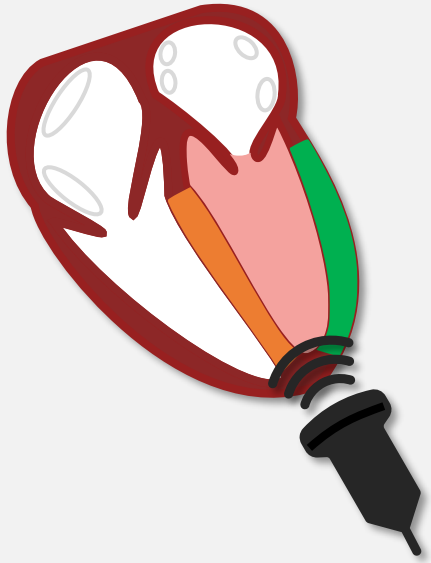


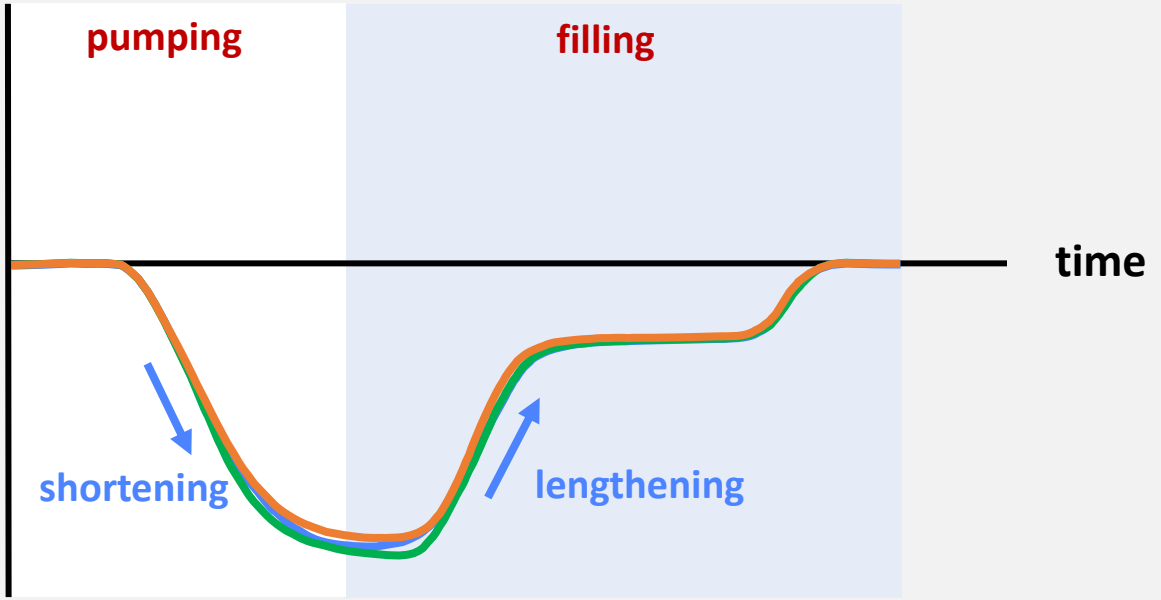
echocardiography



1 cardiac cycle

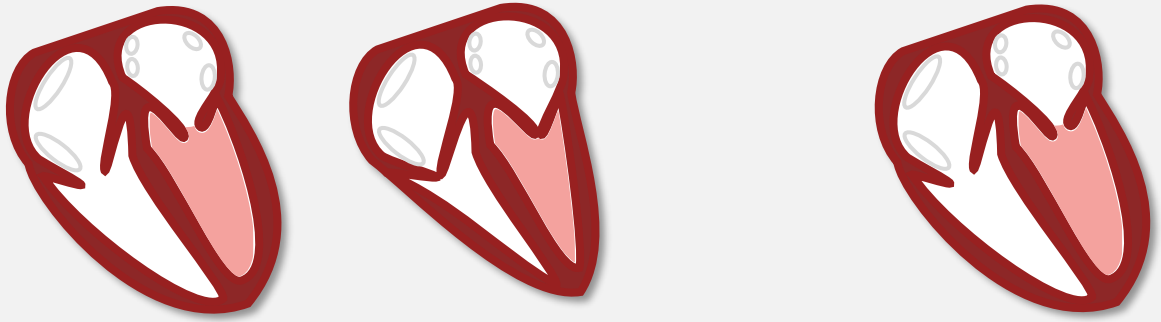
Deformation of the septum and free wall

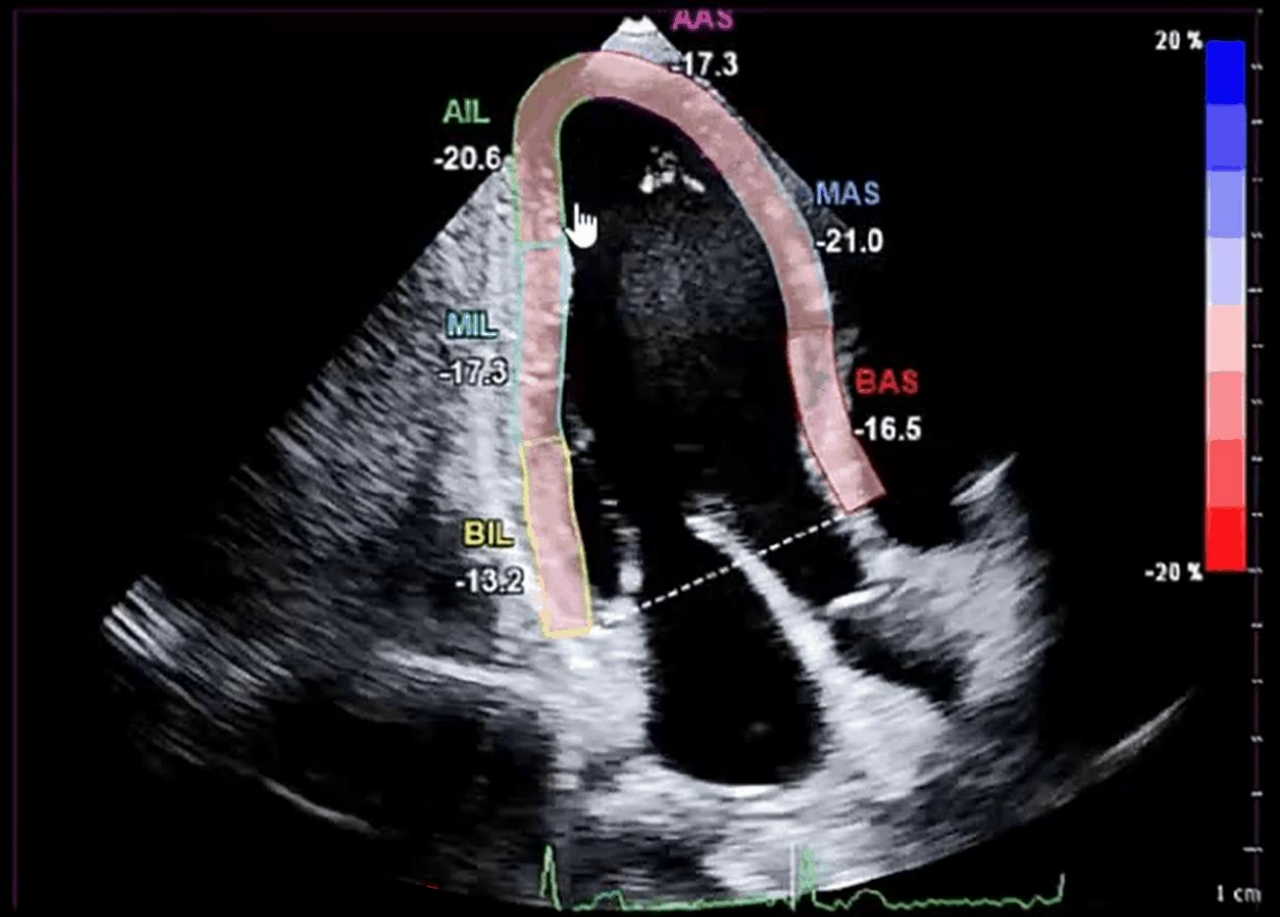


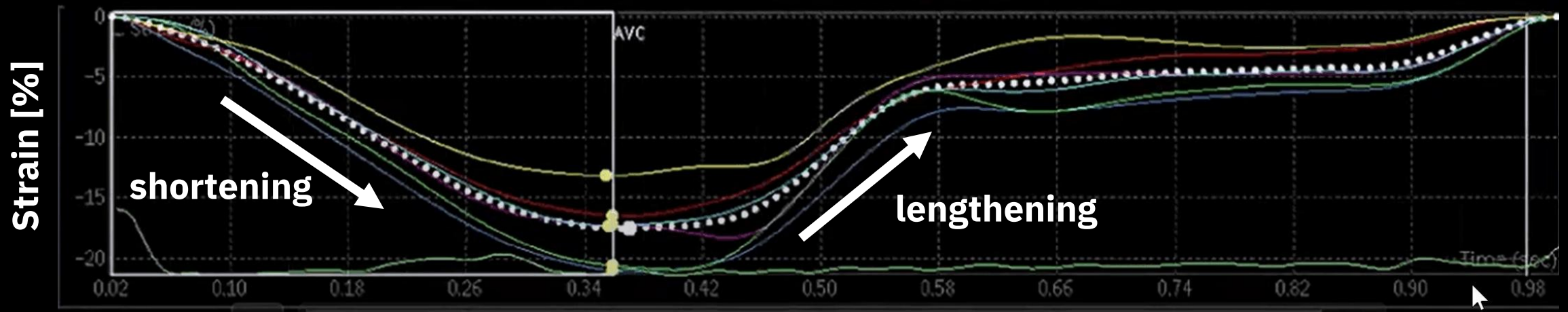


echocardiography

Global pump function of the left ventricle is the result of regional deformation patterns



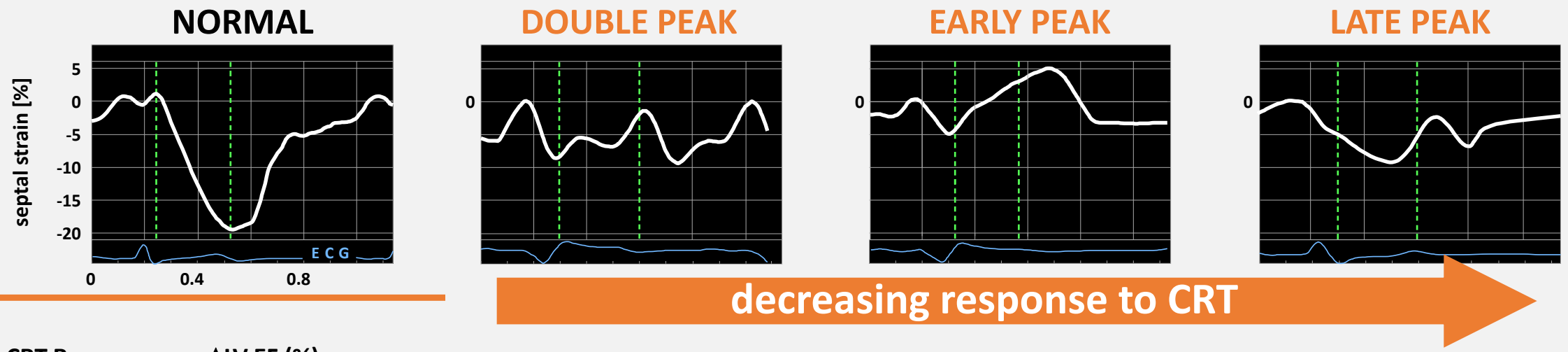

AAS
-17.3
AIL
-20.6
MAS
-21.0
MIL
-17.3
BAS
-16.5
BIL
-13.2
20 %
-20 %
1 cm


Strain [%]
0
-5
-10
-15
-20
AVC
shortening
lengthening
0.02
0.10
0.18
0.26
0.34
0.42
0.50
0.58
0.66
0.74
0.82
0.90
0.98

Septal deformation patterns reveal underlying disease substrates

132 heart failure patients with LBBB

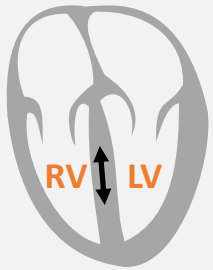
PATIENTS



COMPUTER SIMULATIONS

CRT Response: **ΔLV EF (%)**

ΔLV ESV (%)



synchronous activation

Leenders GE, Lumens J, et al. Circ Heart Fail 2012;5:87-96
Lumens J, Leenders GE, et al. Circ Cardiovasc Imaging 2012;5:491-499

Conclusion I

FORWARD Biophysical models of the human heart and circulation can improve our understanding of (imaging-derived) phenotypic characteristics of the failing heart. Models can be used for hypothesis generation / evaluation.

Fancy stuff, but how can the individual patient benefit from this technology?

Nieuw onderzoek

'Digitale tweeling' uitkomst voor hartpatiënten: kan effect behandeling voorspellen

30 januari 2024 09:08 • Aangepast 30 januari 2024 11:18

Foto ter illustratie, een cardioloog implanteert een pacemaker bij het hart van een patiënt.

Met een 'digitale tweeling' controleren of een pacemakerbehandeling goed werkt voordat die bij de patiënt wordt uitgevoerd: dat kan volgens nieuw onderzoek van Universiteit Maastricht en UMC Utrecht. Met een computermodel wordt dan gecheckt of dit de juiste behandeling voor een hartpatiënt is.

Net binnen

22:06 Toch geen Apple Car meer in de maak: ontwikkeling gestopt

22:01 Suzanne van MAFS mist spanning in huwelijk met Bastiaan: 'Ik wil kunnen stomen'

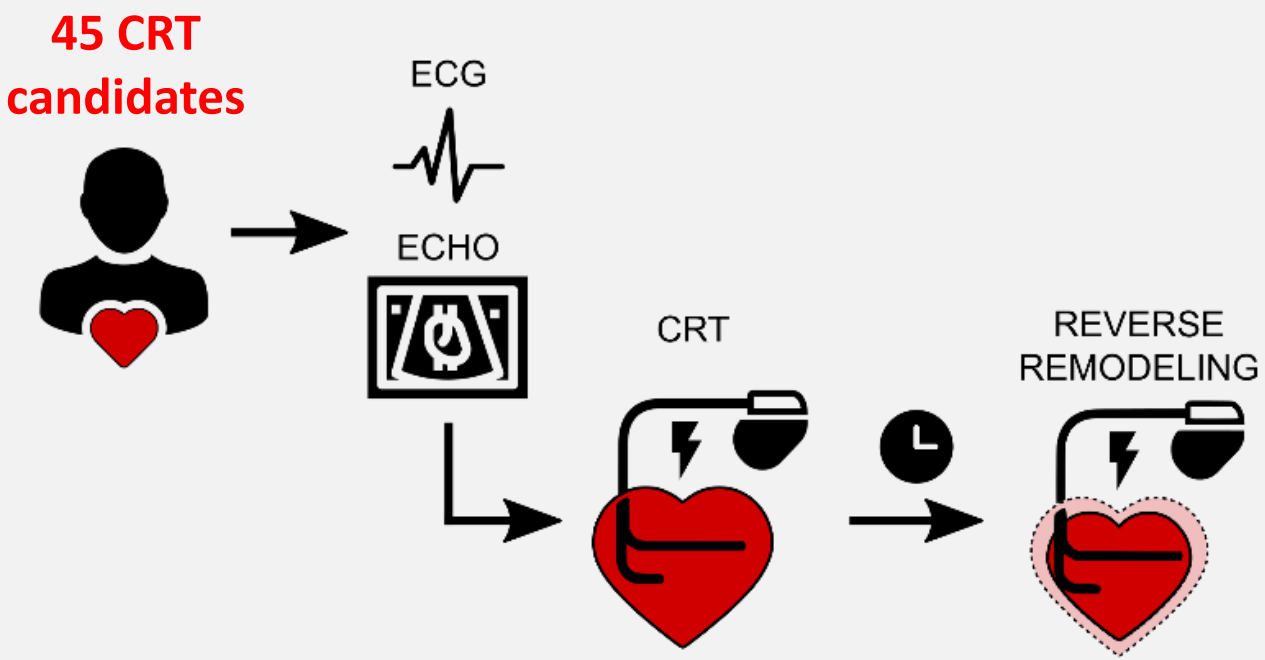
21:53 Duitse voetbalsters voelen dat zij móéten winnen van Oranje

21:27 Man van Lady Gabriella Windsor op 45-jarige leeftijd overleden

20:50 Nederlandse wapens naar Oekraïne: 'Het moet meer en het moet sneller'

Meer nieuws

In silico trial: virtual cardiac resynchronization therapy (CRT) in Digital Twins of heart failure patients



UMC Utrecht

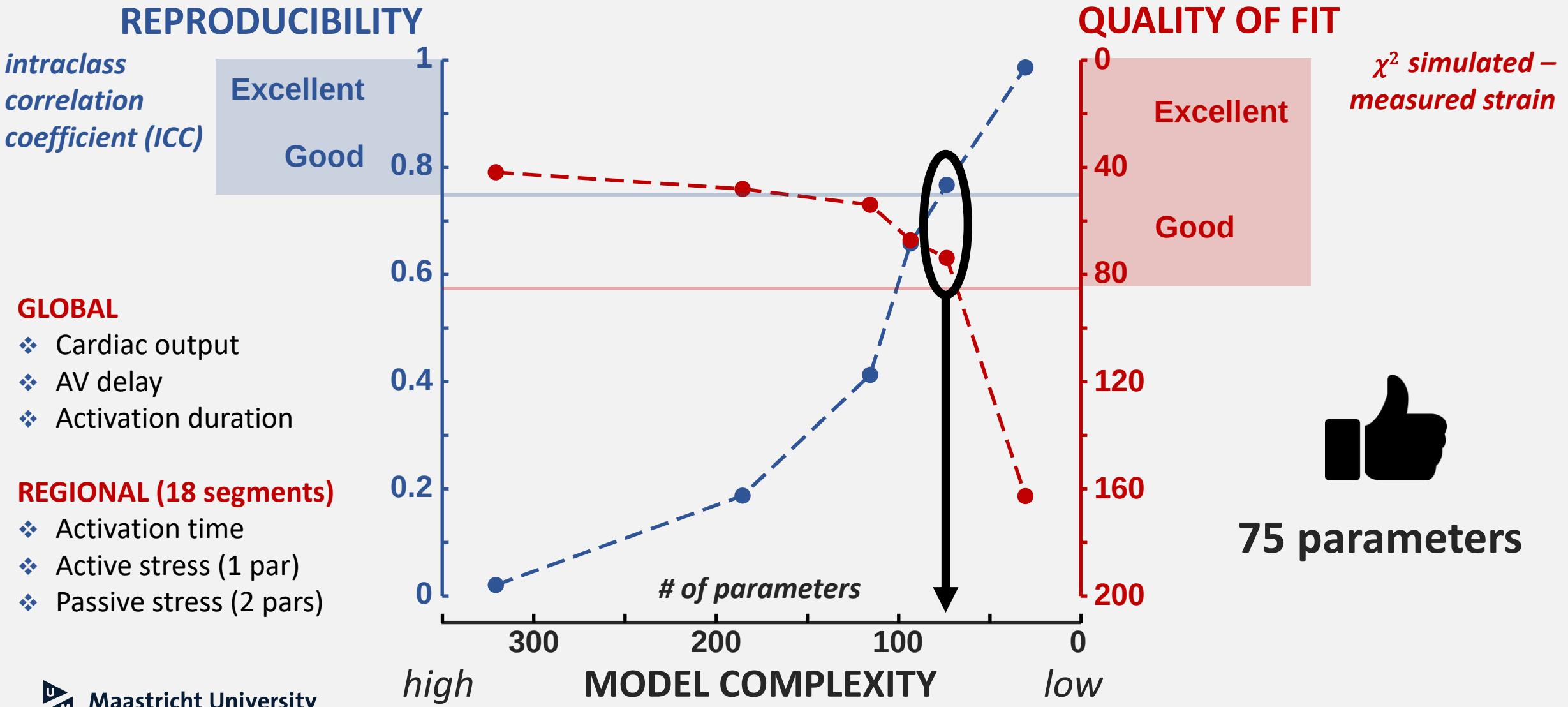
Table 1: Baseline characteristics (n=45).

Age (years)	66 ± 10
Male gender (%, *n*)	62%, 28
QRS duration (ms)	171 ± 21
LBBB morphology[a] (%, *n*)	84%, 38
CRT Class I indication (%, *n*)	82%, 37
Atrial fibrillation (%, *n*)	11%, 5
Ischaemic heart disease (%, *n*)	33%, 15
LVEDV (mL)	217 ± 83
LVESV (mL)	172 ± 81
LVEF (%)	23 ± 9
ACE-inhibitor/AT2 (%, *n*)	93%, 42
Beta-blocker (%, *n*)	67%, 30
Diuretics (%, *n*)	96%, 43
Spironolactone/eplerenone (%, *n*)	51%, 23

Maastricht University

Koopsen et al., *Europace*, 2024;26(1):euae009

Model complexity: reproducibility vs. quality of fit



GLOBAL
- Cardiac output
- AV delay
- Activation duration

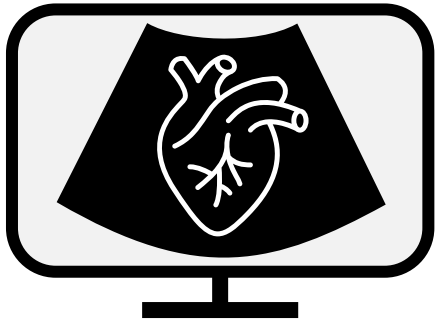
REGIONAL (18 segments)
- Activation time
- Active stress (1 par)
- Passive stress (2 pars)

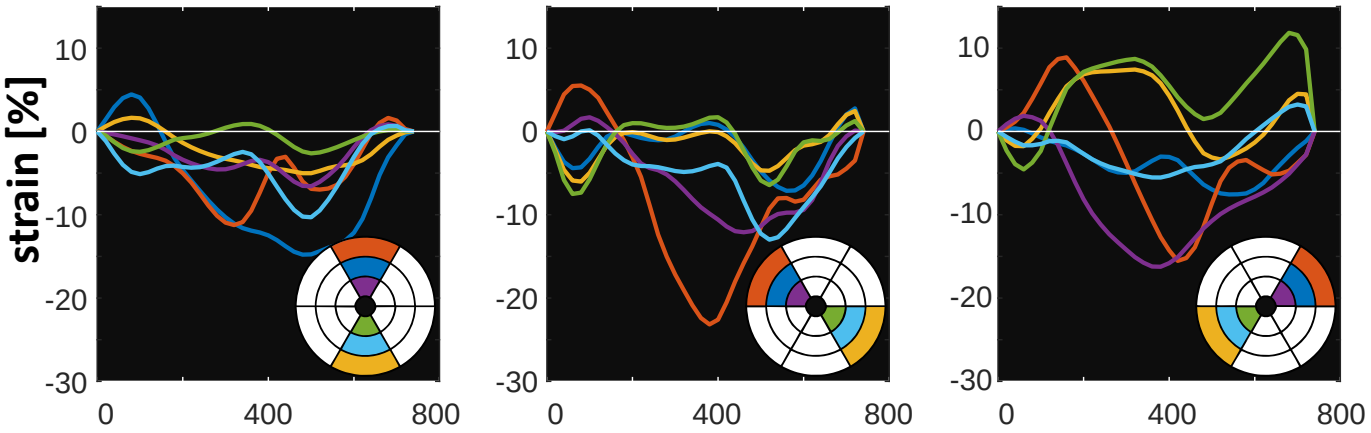
75 parameters

Maastricht University

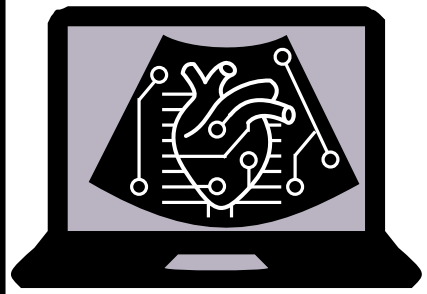
Van Osta et al. *Phil Trans R Soc* (2020), Koopsen et al. *Biomed Eng Online* (2024)

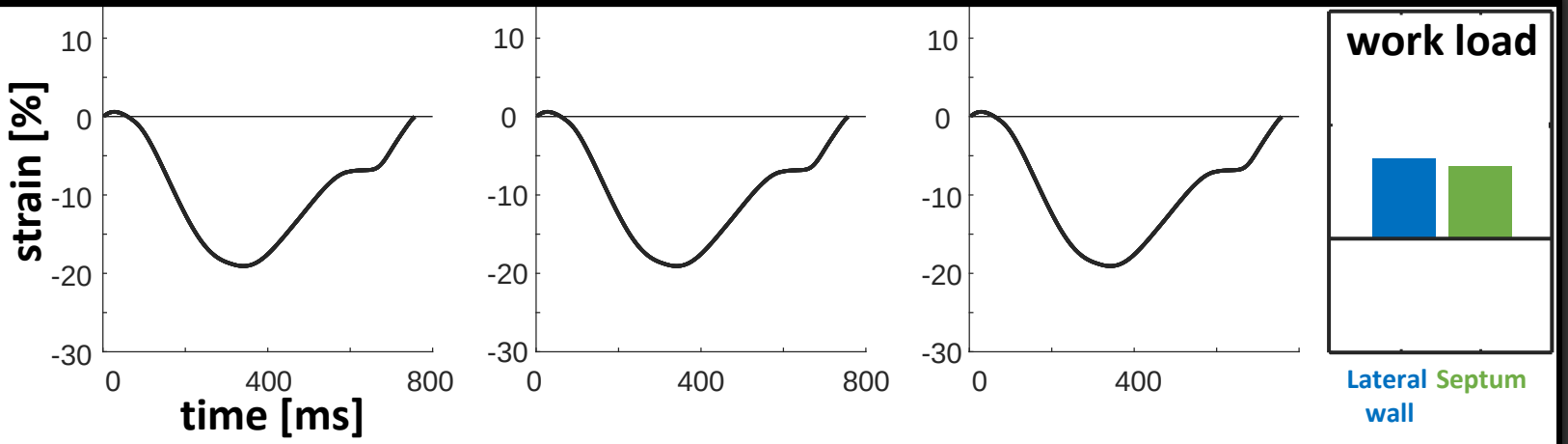
REAL PATIENT





DIGITAL TWIN

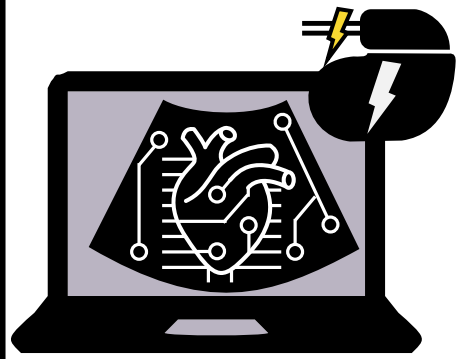




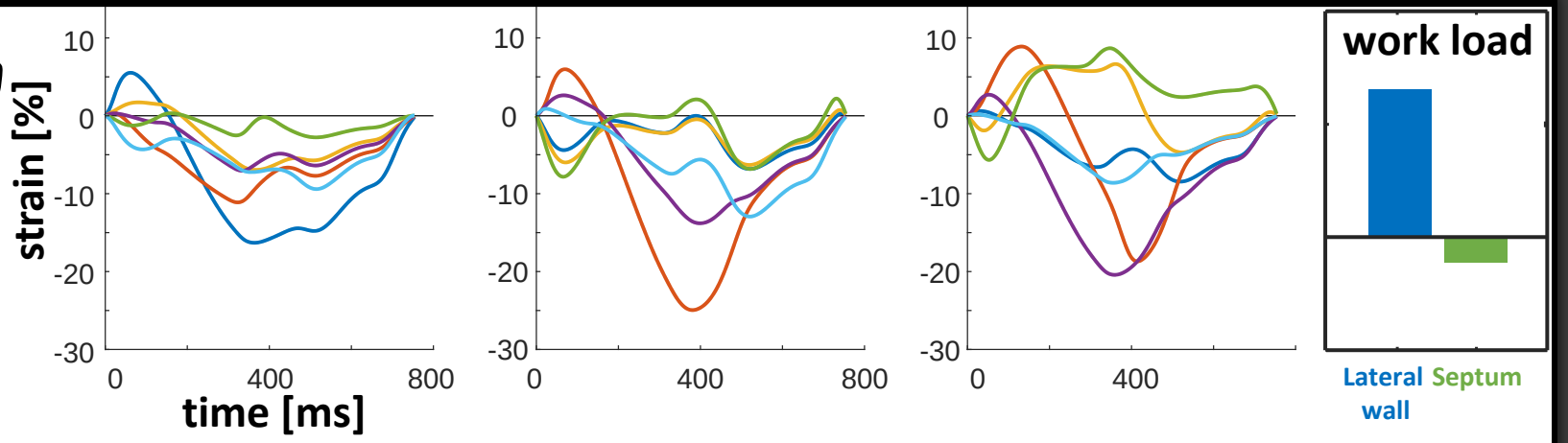
Koopsen et al., *Europace*, 2024;26(1):euae009

REAL PATIENT

virtual CRT



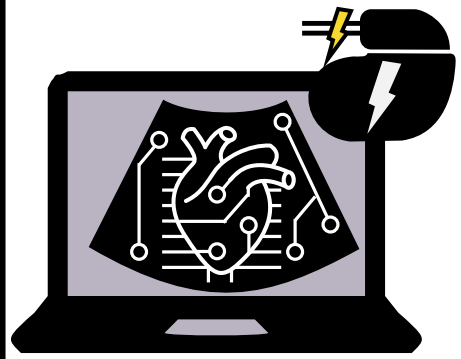
DIGITAL TWIN



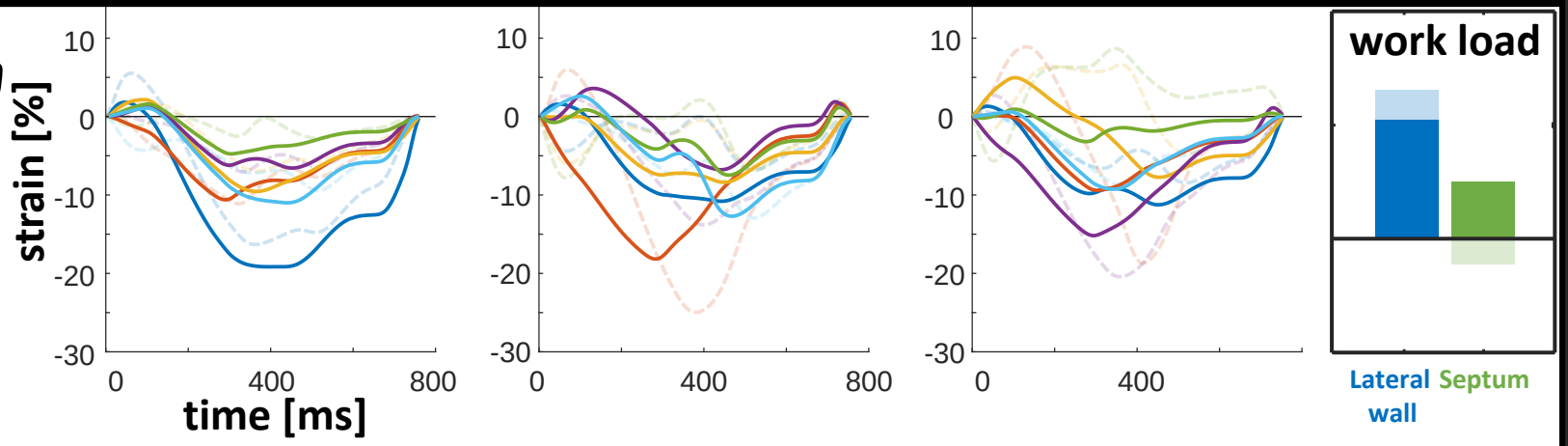
Koopsen et al., *Europace*, 2024;26(1):euae009

REAL PATIENT

virtual CRT



DIGITAL TWIN



Koopsen et al., *Europace*, 2024;26(1):euae009

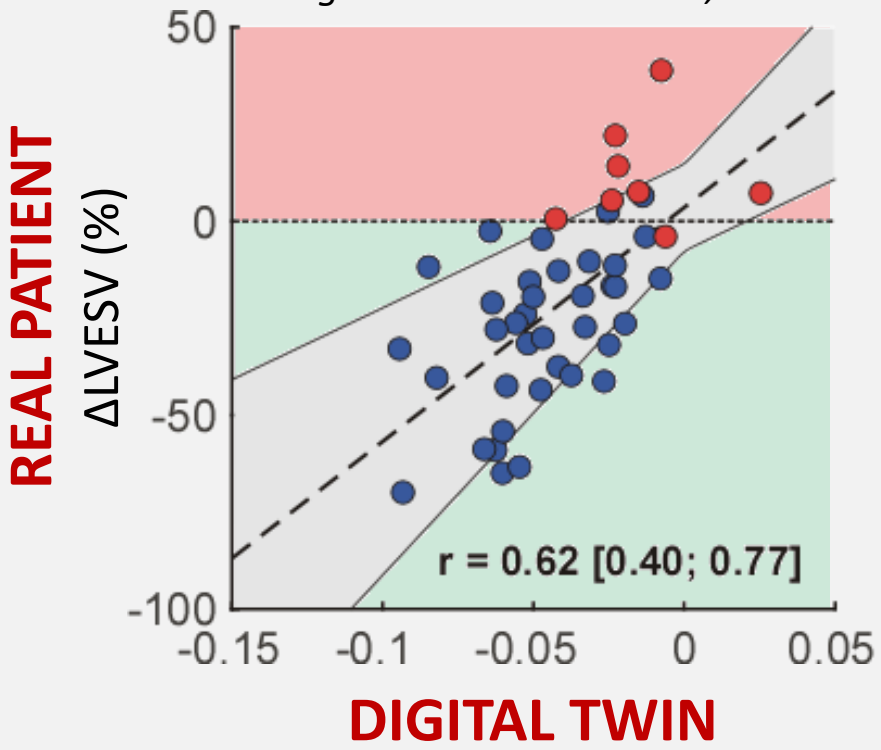
Digital Twins enable CRT response prediction:
a reflection on guidelines

Class I indication

Class IIa/IIb indication

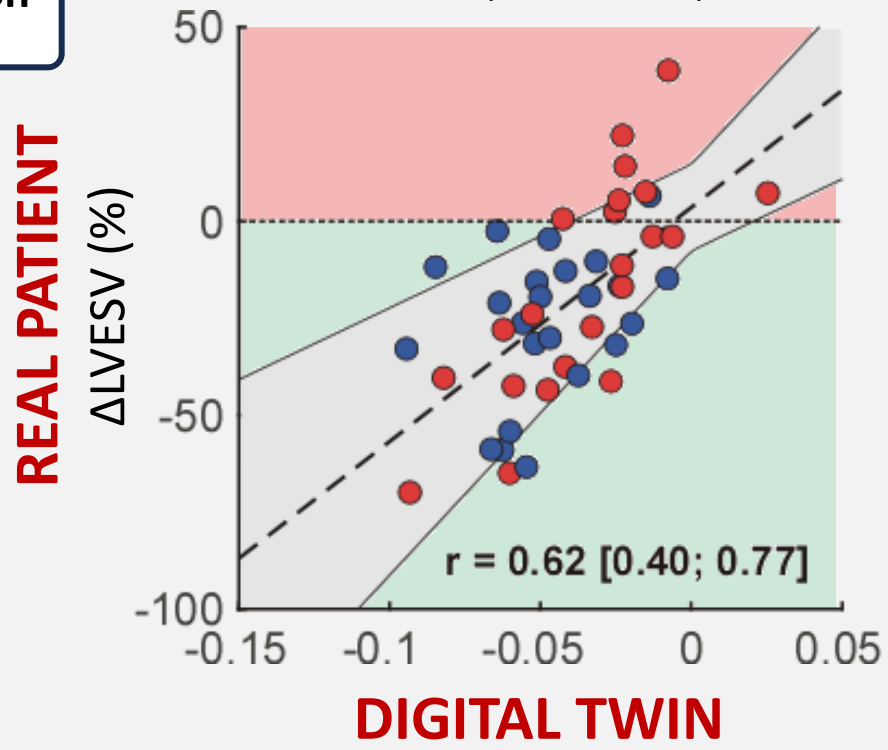
ESC 2013

Brignole et al. Eur Heart J, 2013



ESC 2021

Glikson et al, Eur Heart J, 2021



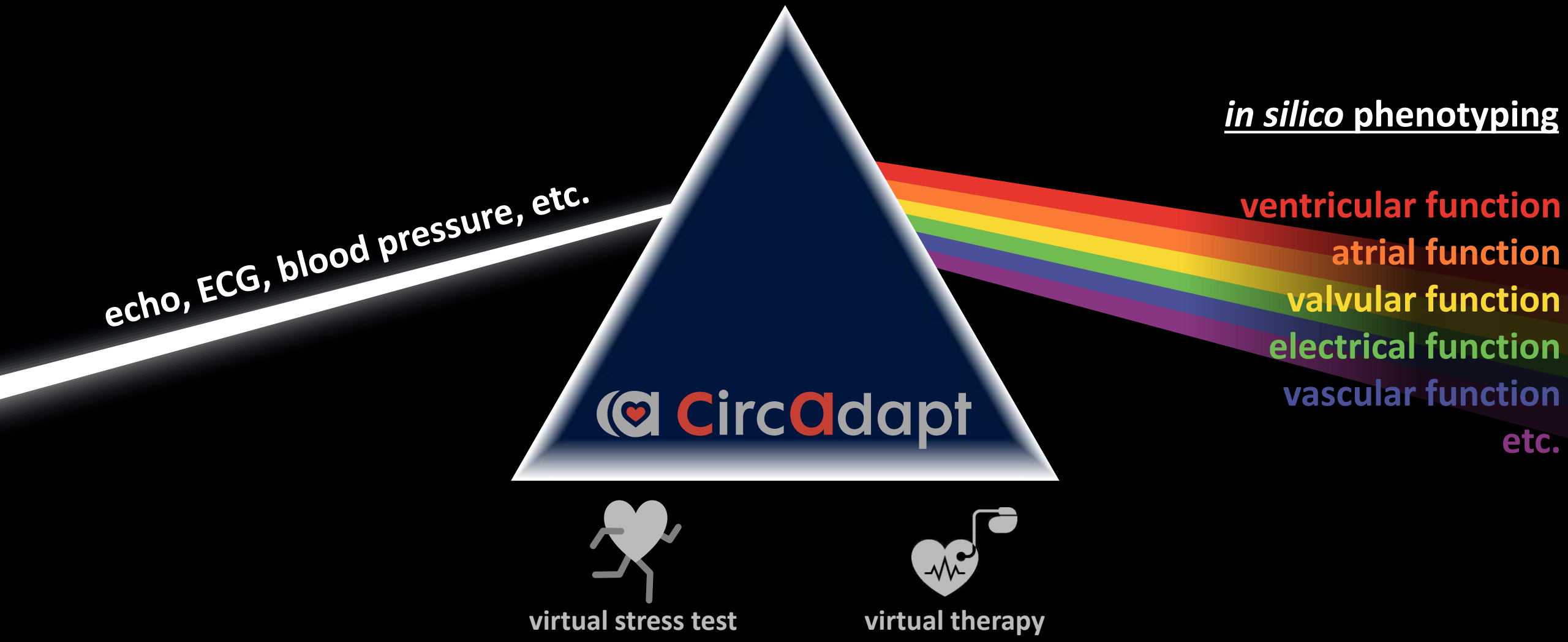
Koopsen et al., *Europace*, 2024;26(1):euae009

Conclusion II

FORWARD Biophysical models of the human heart and circulation can improve our understanding of (imaging-derived) phenotypic characteristics of the failing heart. Models can be used for hypothesis generation / evaluation.

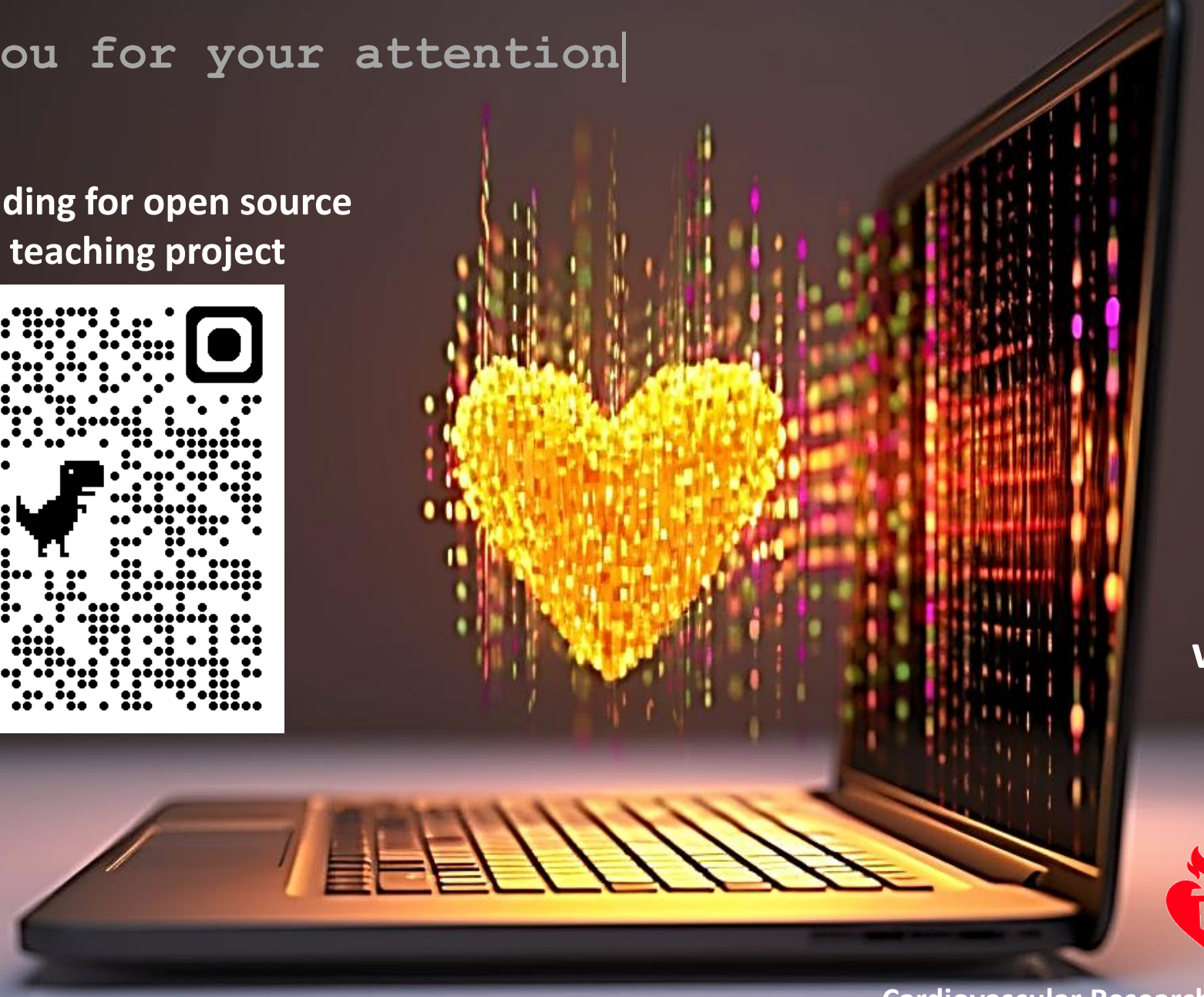
INVERSE Integration of imaging-based diagnostic information in a personalised biophysical model (Digital Twin) can expose ‘hidden’ disease substrates that would remain concealed otherwise and predict therapy outcome.

The patient’s virtual heart is coming to life



Source: Pink Floyd, The Dark Side of the Moon

>> thank you for your attention



UM crowdfunding for open source CircAdapt teaching project

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funded by the dutch heart foundation
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