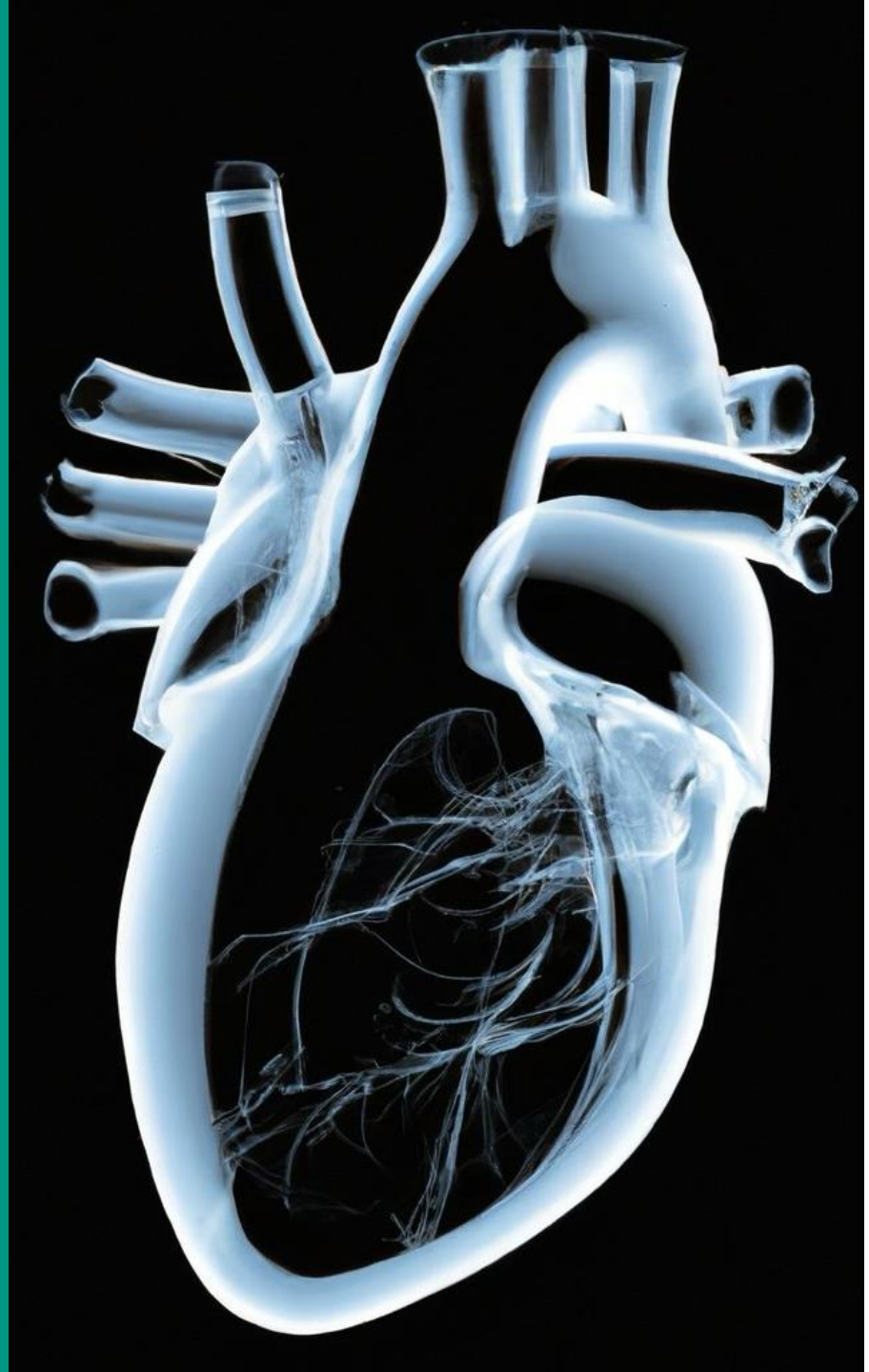
Computational Modelling and Simulation of Cardiac Function Now and Then

Axel Loewe

Institute of Biomedical Engineering (IBT)
Karlsruhe Institute of Technology (KIT)



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Then...

THE ROYAL SOCIETY

Computational modelling of biological systems: tools and visions

By Peter Kohl[1], Denis Noble[1], Raimond L. Winslow[2] and Peter J. Hunter[3]

[1] *University Laboratory of Physiology, Parks Road, University of Oxford, Oxford OX1 3PT, UK*

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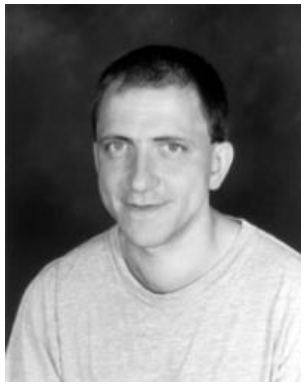

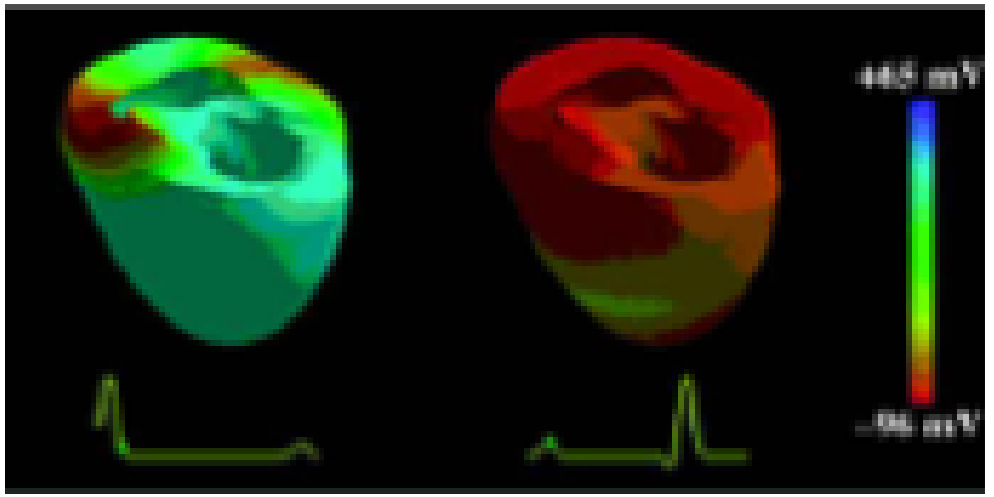

Kohl et al. "Computational modelling of biological systems: tools and visions" PTRSA 2000;358:579-610

Science into the next millennium

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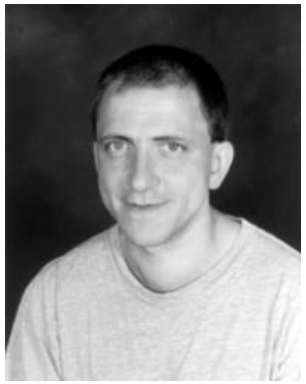

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25 years on

PHILOSOPHICAL TRANSACTIONS A

royalsocietypublishing.org/journal/rsta

Opinion piece

Cite this article: Loewe A, Hunter PJ, Kohl P. 2025 Computational modelling of biological systems now and then: revisiting tools and visions from the beginning of the century. *Phil. Trans. R. Soc. A* **383**: 20230384.
https://doi.org/10.1098/rsta.2023.0384

Computational modelling of biological systems now and then: revisiting tools and visions from the beginning of the century

Axel Loewe[1], Peter J. Hunter[2] and Peter Kohl[3]

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[2]Bioengineering Institute, University of Auckland, Auckland, New Zealand
[3]University of Freiburg, Medical Faculty, Institute for Experimental Cardiovascular Medicine, University Heart Center Freiburg - Bad Krozingen, and Faculty of Medicine, University of Freiburg, 79110 Freiburg, Germany, Freiburg, Germany

AL, 0000-0002-2487-4744; PJH, 0000-0001-9665-4145; PK, 0000-0003-0416-6270

Loewe et al. "Computational modelling of biological systems now and then: revisiting tools and visions from the beginning of the century" PTRSA 2025;383:20230384

Content

1. From then to now
2. Use cases
3. Tools and ecosystems

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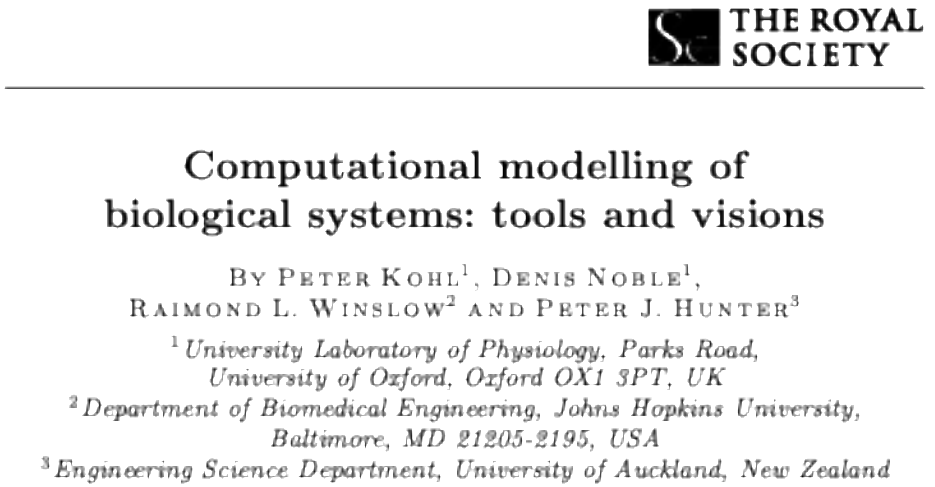
Predicted benefits for society

- Support **decision making**
- Standardization and **individualization** of medical care
- Reduction of morbidity and **mortality**
- Improved **teaching tools**
- **Faster** and more cost-effective research



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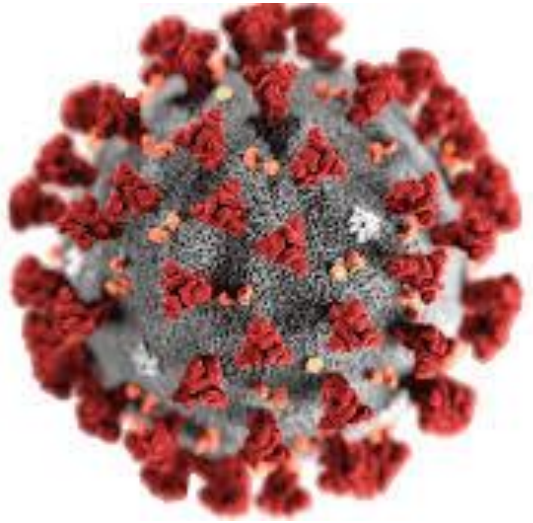

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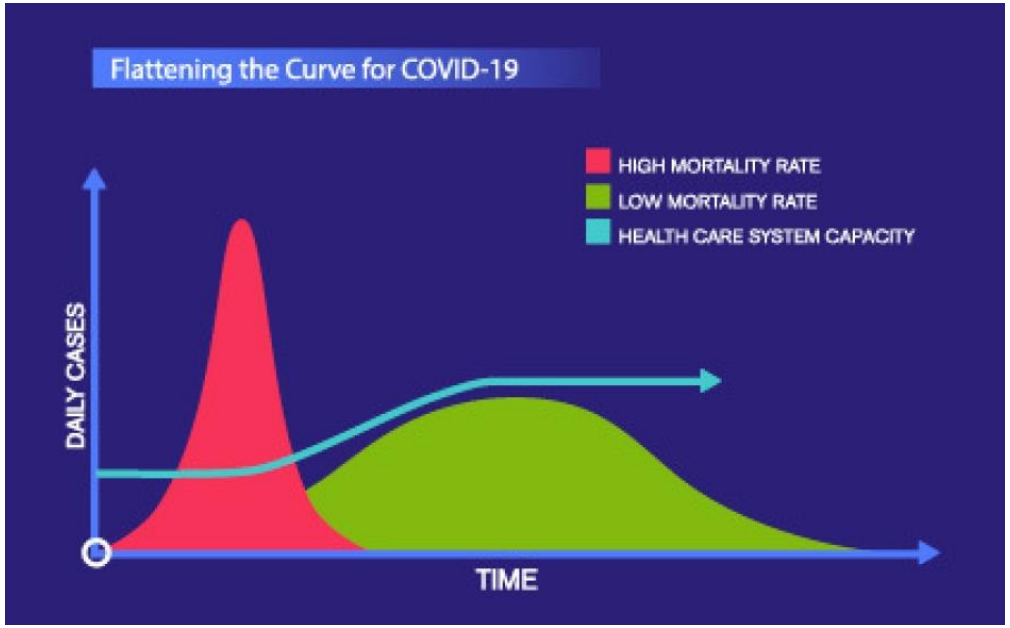

Moran et al. "The future of pandemic modeling in support of decision making: lessons learned from COVID-19" BMC Global and Public Health 2025;3:24

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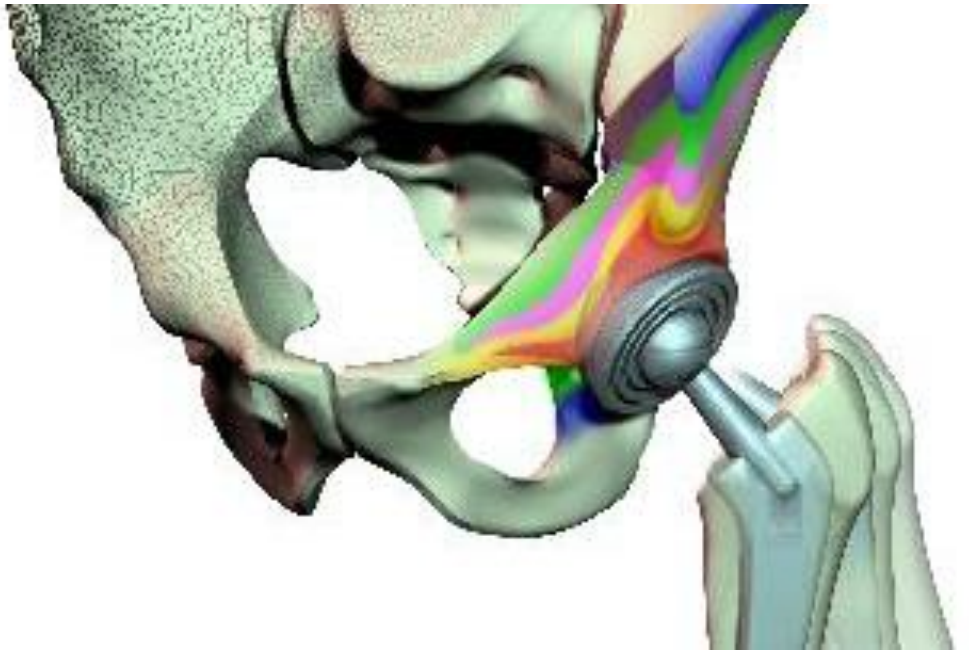

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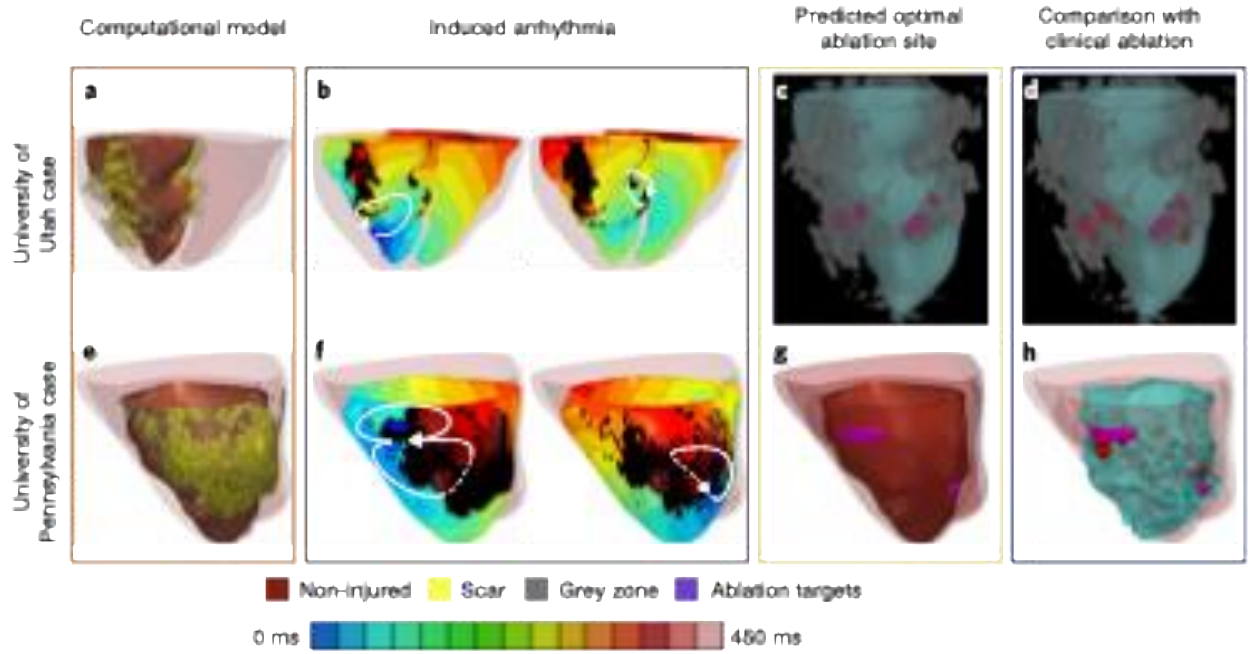

Recruiting

Comparing Pulmonary Vein Isolation to Pulmonary Vein Isolation + OPTIMA Ablation in Patients Undergoing Ablation for Atrial Fibrillation (OPTIMA)

ClinicalTrials.gov ID NCT04101539

Sponsor Johns Hopkins University

Information provided by Johns Hopkins University (Responsible Party)

Last Update Posted 2024-09-20

clinicaltrials.gov

Prakosa et al. „ Personalized virtual-heart technology for guiding the ablation of infarct-related ventricular tachycardia “, Nature Biomedical Engineering 2028;10:732

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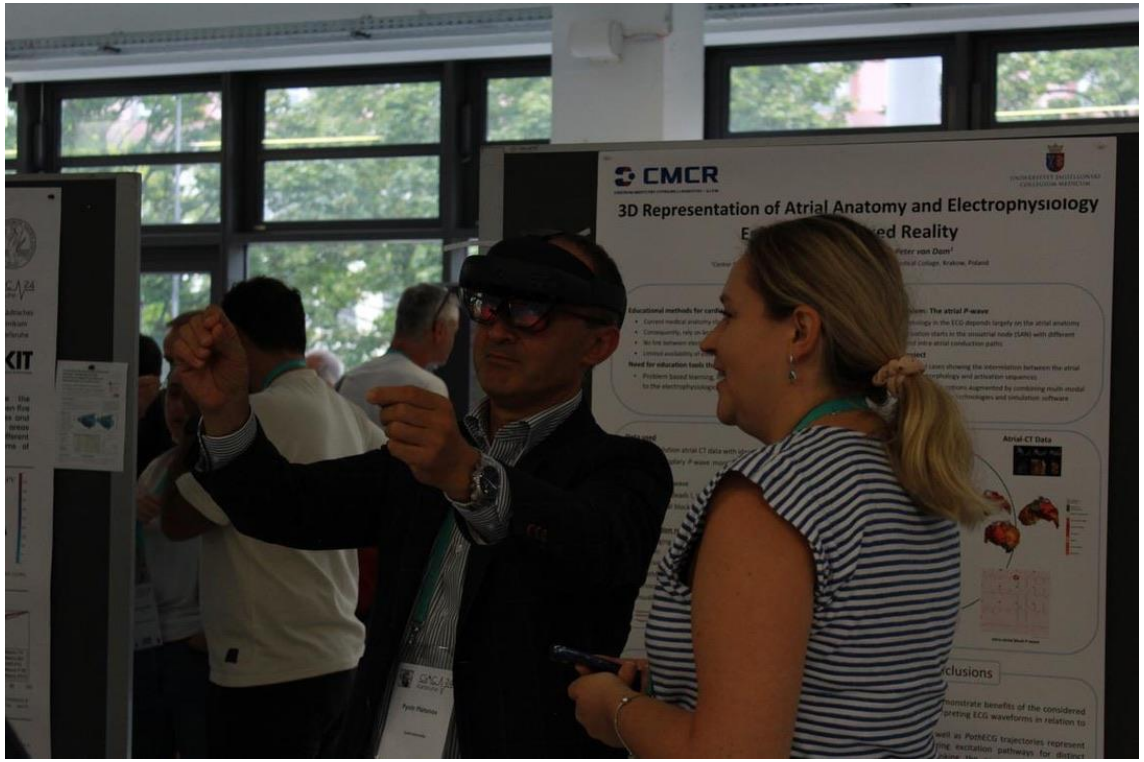


Proniewska et al. „Three-Dimensional Representation of Atrial Anatomy and Electrophysiology Enhanced by Mixed Reality“, Computing in Cardiology 2024;51

How did we get there?

Physiome Project

1990s: **Physiome Project**

“Developing a comprehensive understanding of a healthy human”

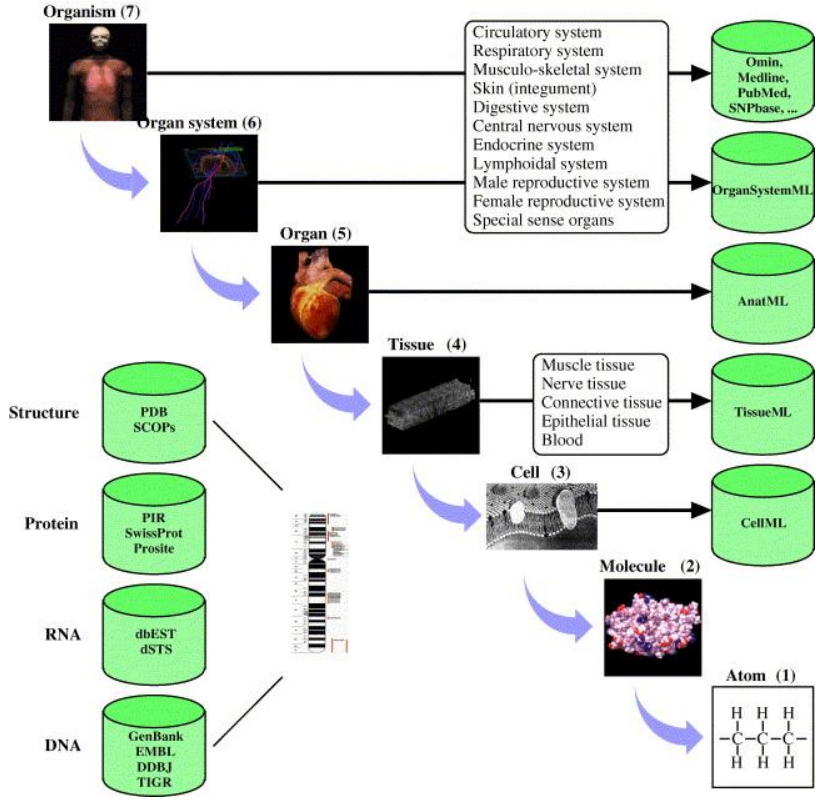
2000s: **Virtual Physiological Human**

Shift from a singular model of ‘the human’ to disease-specific models

2010s: **Personalized models**, variability within cohorts

2020s: **Digital twin, artificial intelligence**

Shared bottleneck: **“big data but small data paradox”**
reliable and relatable high-quality data (as opposed to sheer data quantity)



Hunter „The IUPS Physiome Project: a framework for computational physiology“, Progress in Biophysics and Molecular Biology 2004;85:551-69

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virtualhumantwins.eu

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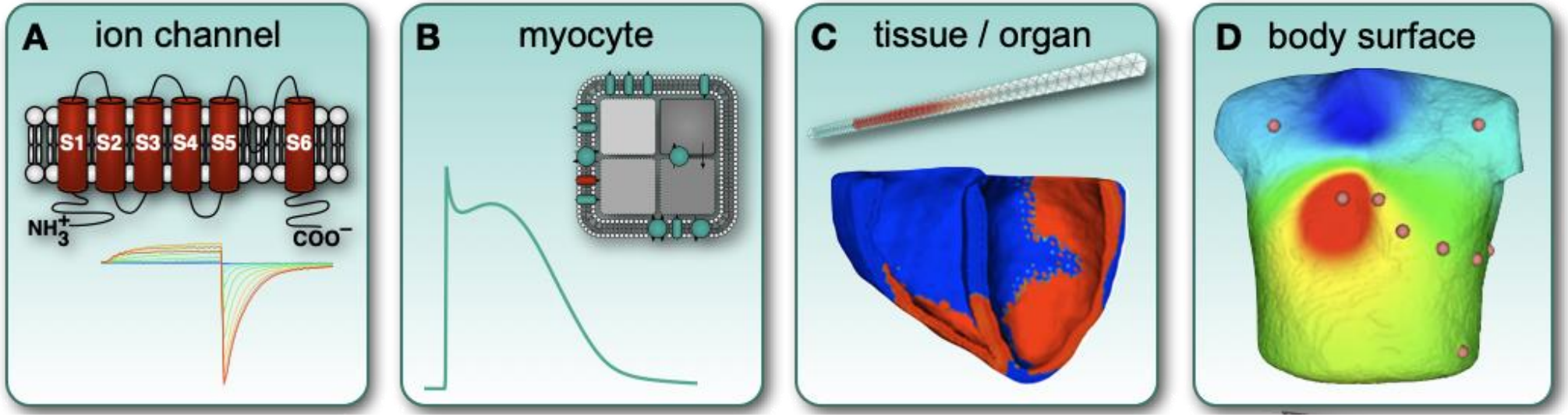
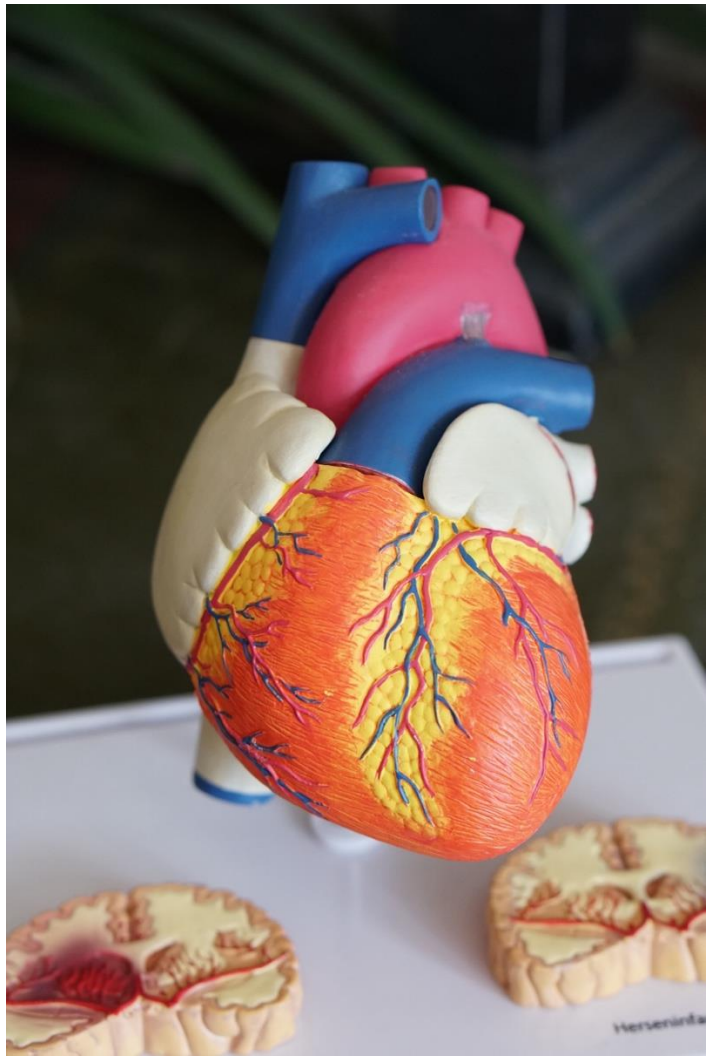
The heart as a multi-scale system



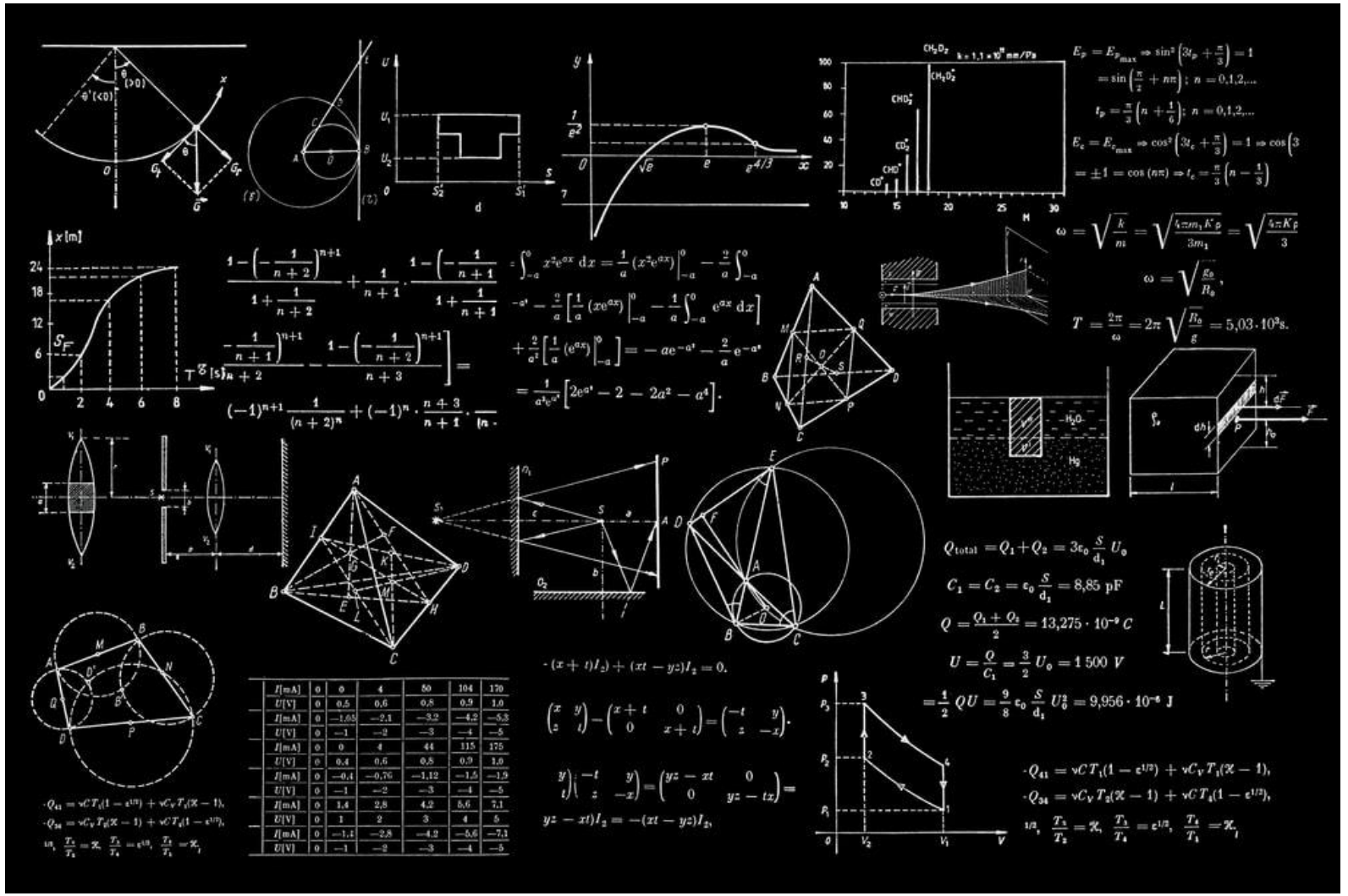
biological level of integration

nanometer micrometer centimeter

How can math help?

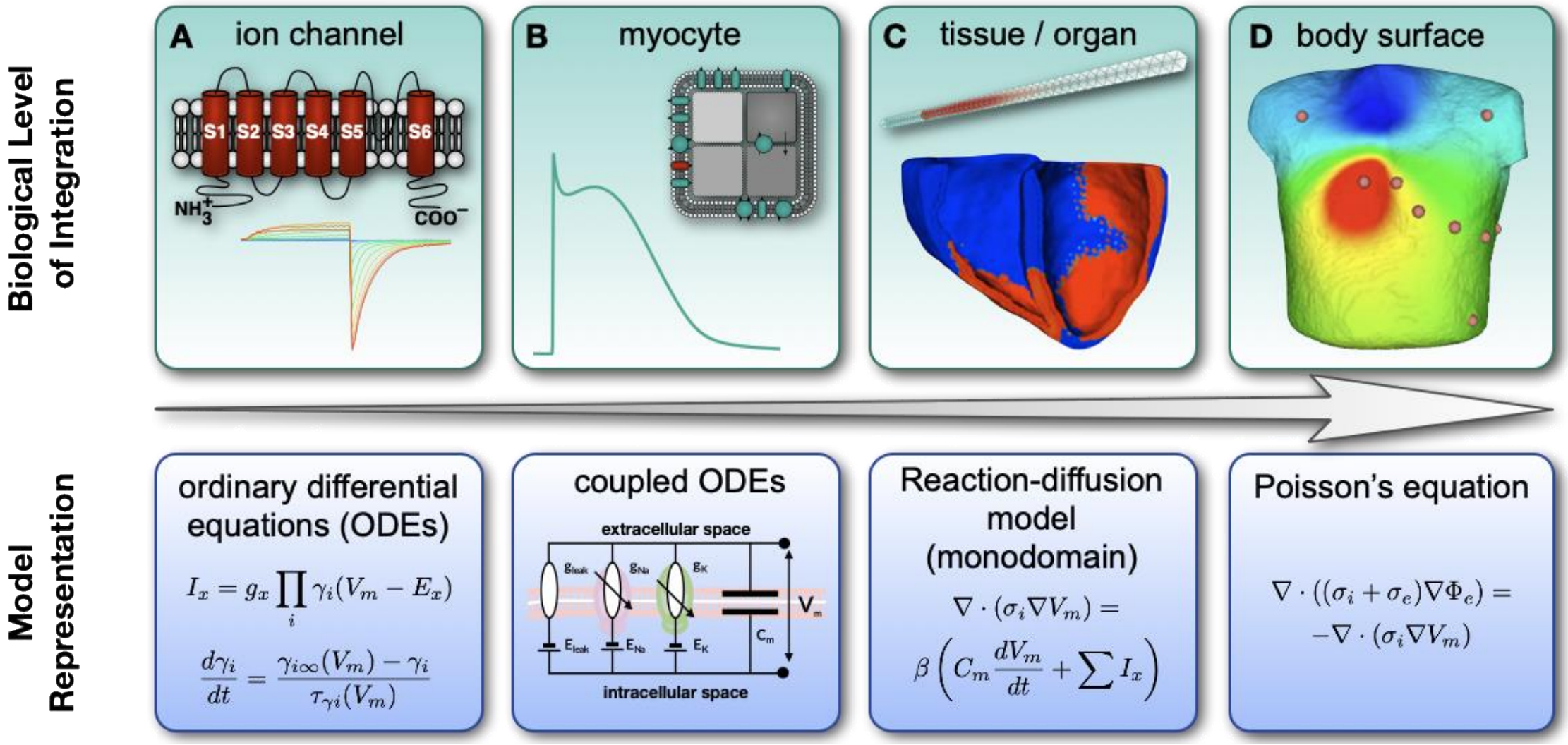


Robina Weermeijer, unsplash.com



Dan-Cristian Pădureț, unsplash.com

Multi-scale system modeling of cardiac electrophysiology



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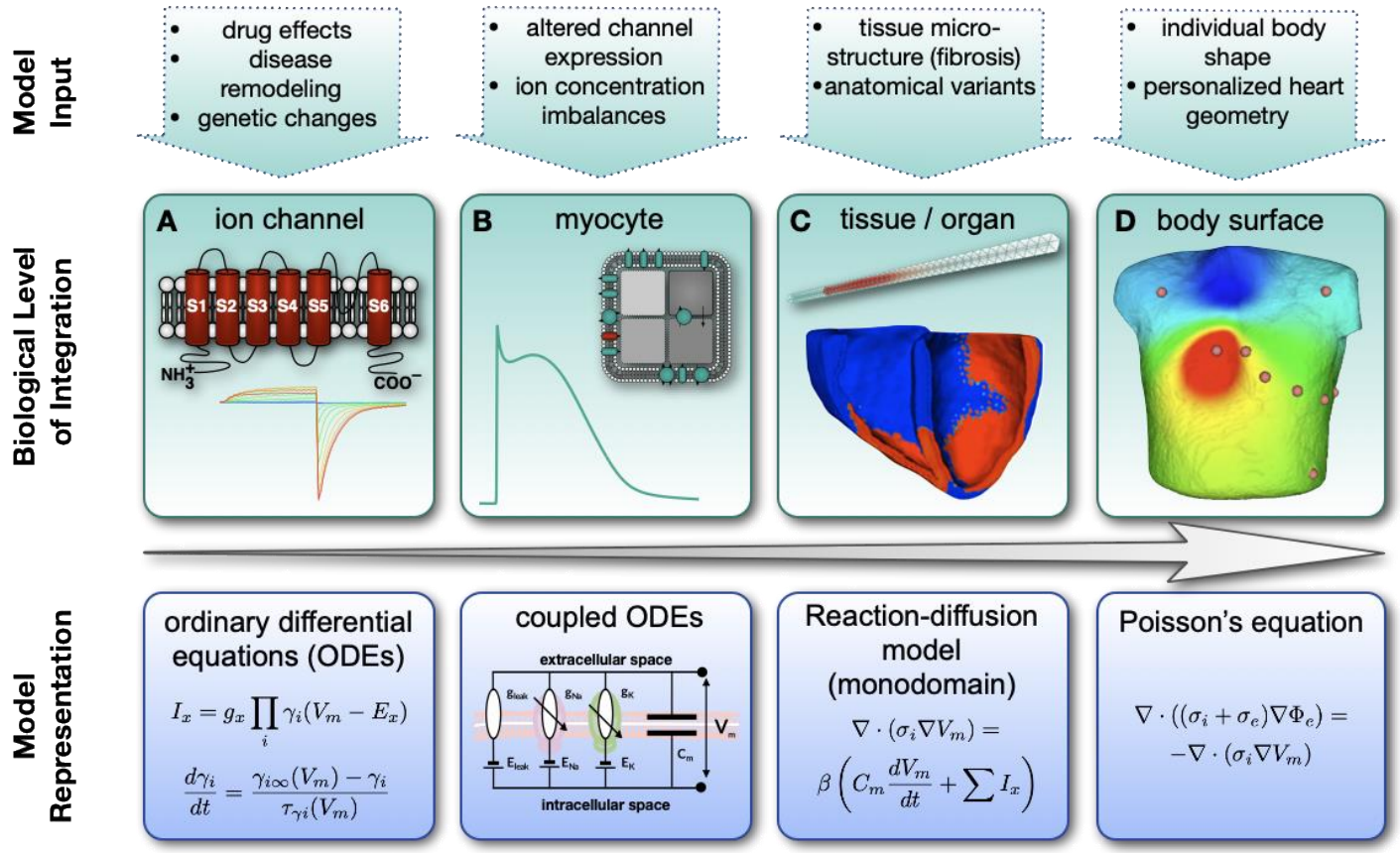

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Computer modeling & simulation

Controlled and **resource-efficient** research environment

- to understand fundamental physiology and pathomechanisms
- to evaluate diagnostic and therapeutic approaches (in silico studies)
- to optimize device design

Personalised medicine through digital twins

Scalable research environment to generate big, quality-controlled dataset for machine learning

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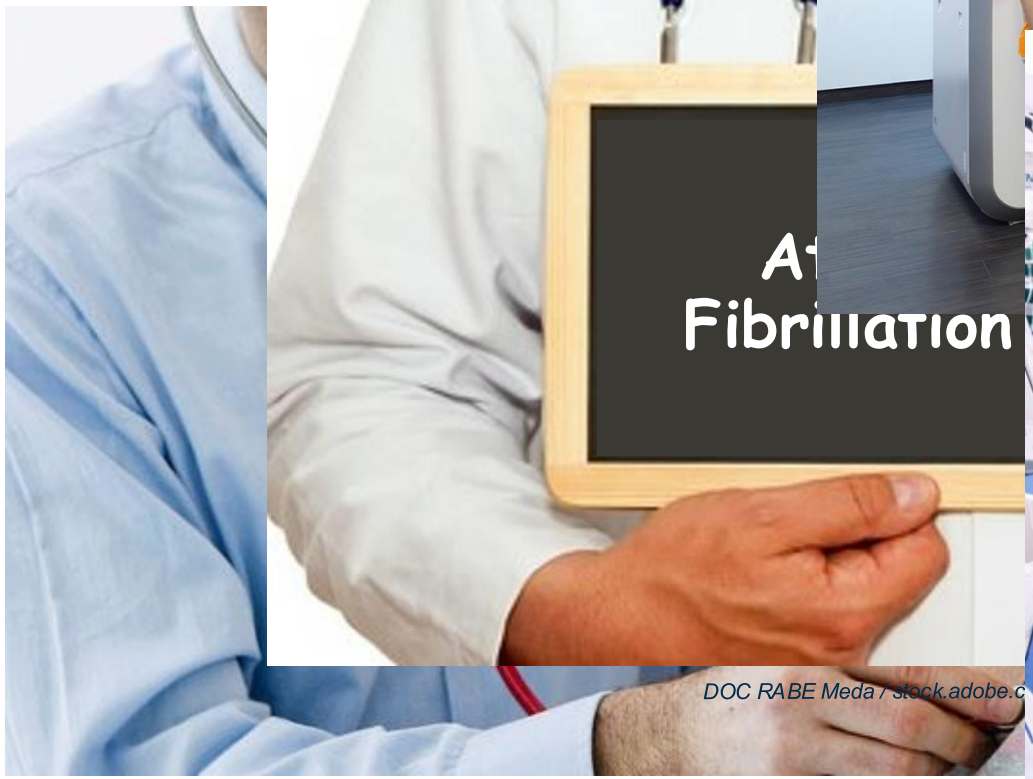
The digital twin visio



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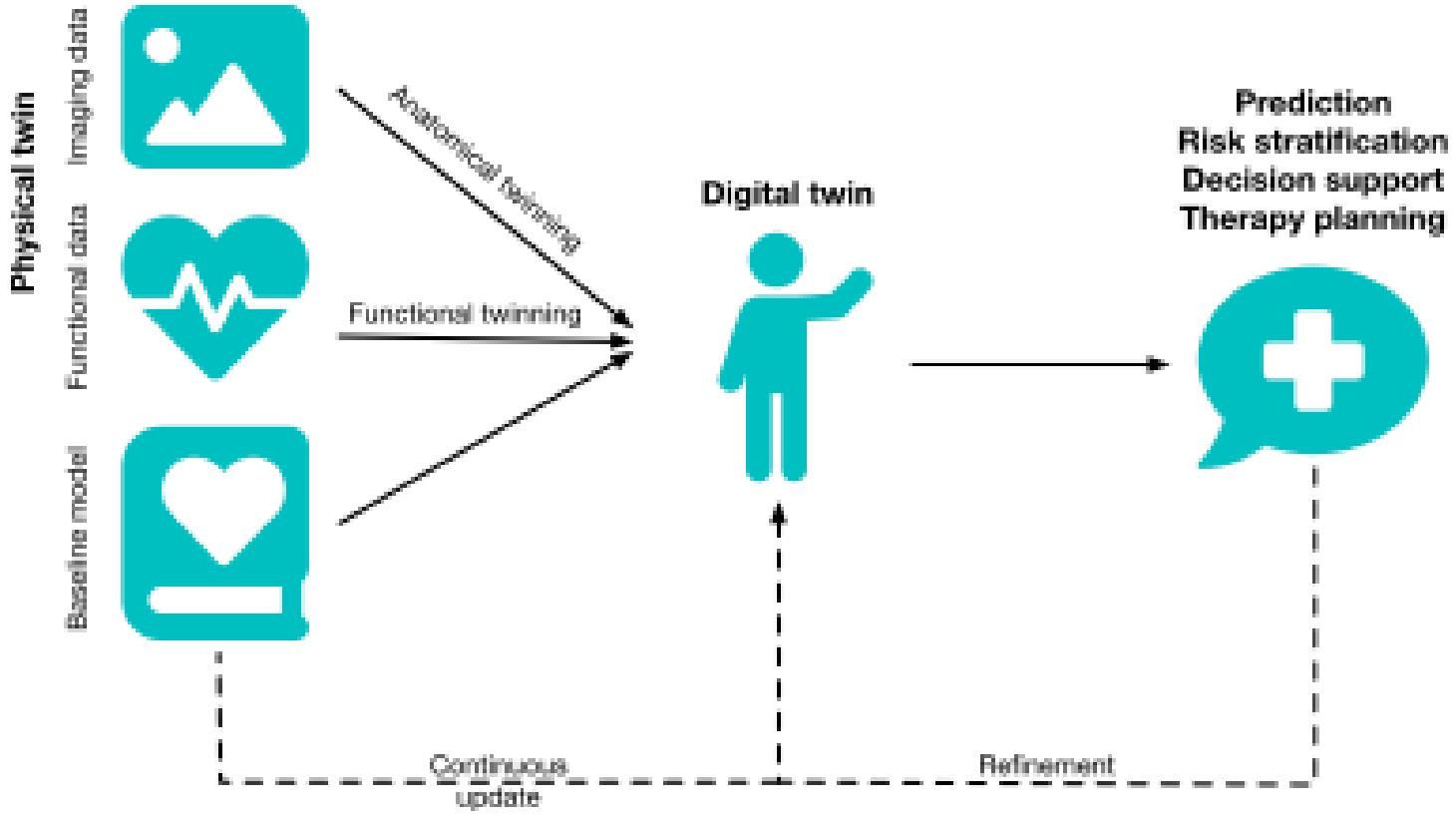
Deutsche Herzstiftung

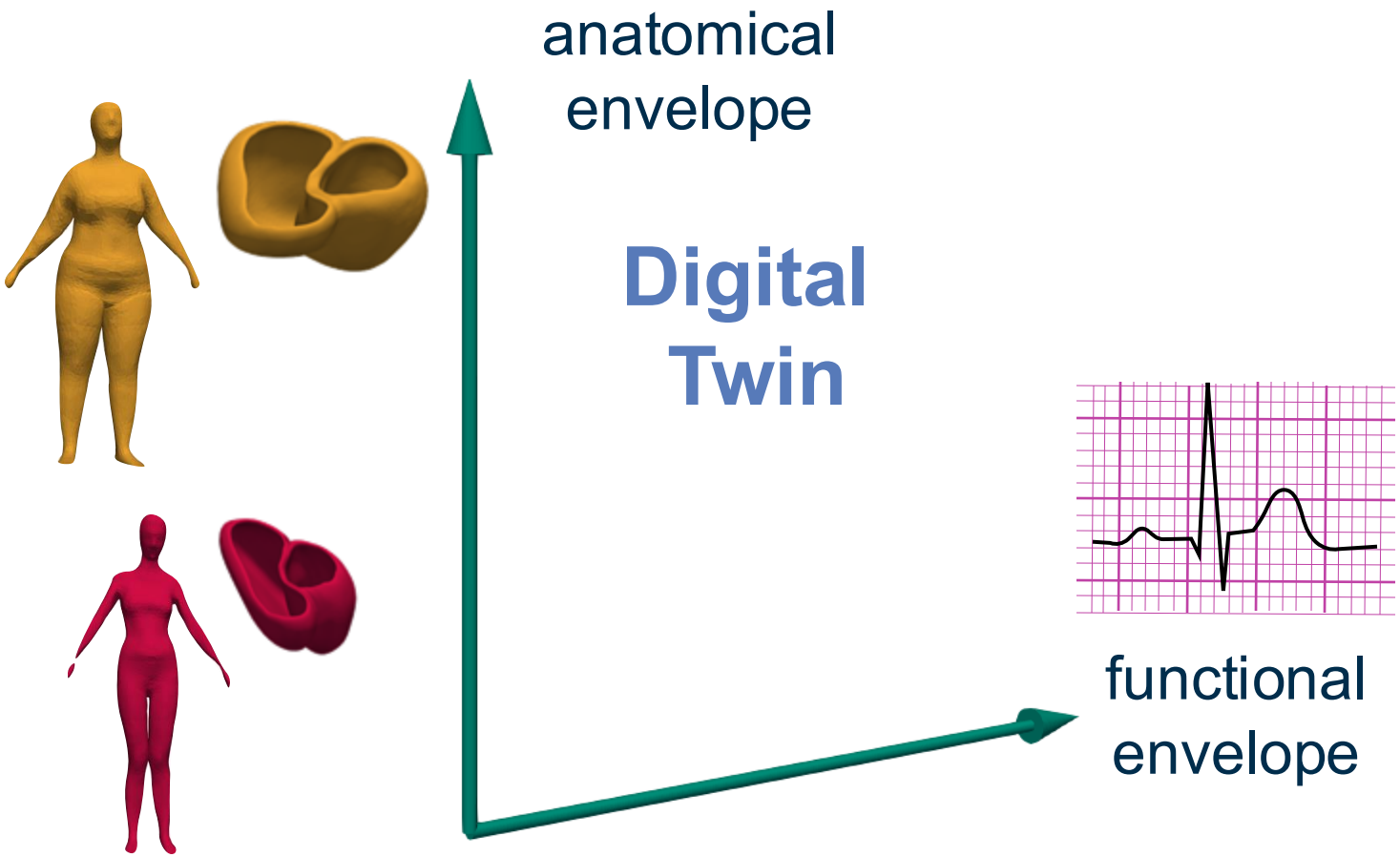
Corral-Acero et al., "The 'Digital Twin' to enable the vision of precision cardiology", Eur Heart J 2020;41:4556-4564

The digital twin vision



Loewe et al. "Cardiac Digital Twin Modeling" in „Innovative Treatment Strategies for Clinical Electrophysiology" 2022

Ensemble simulation spaces



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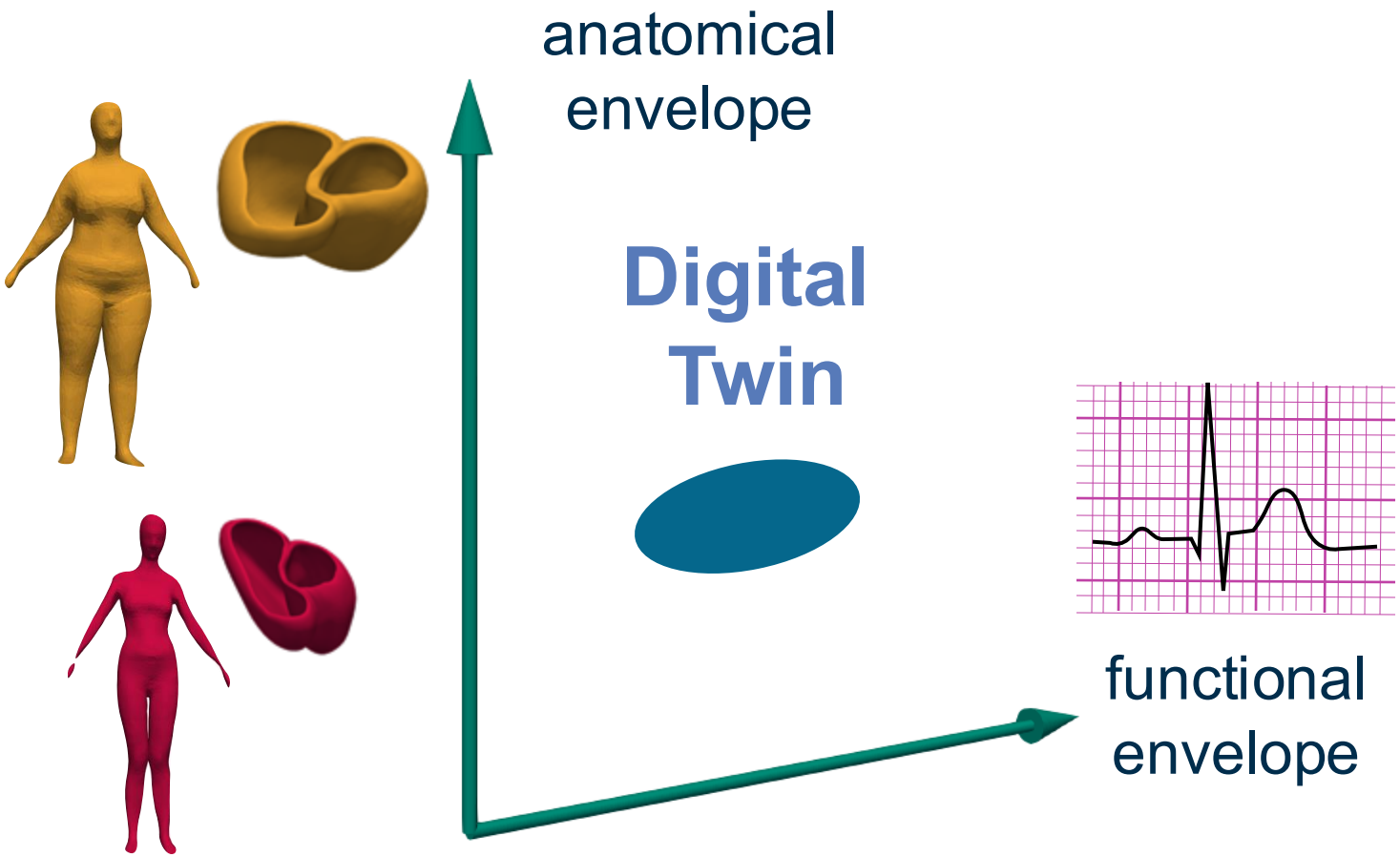

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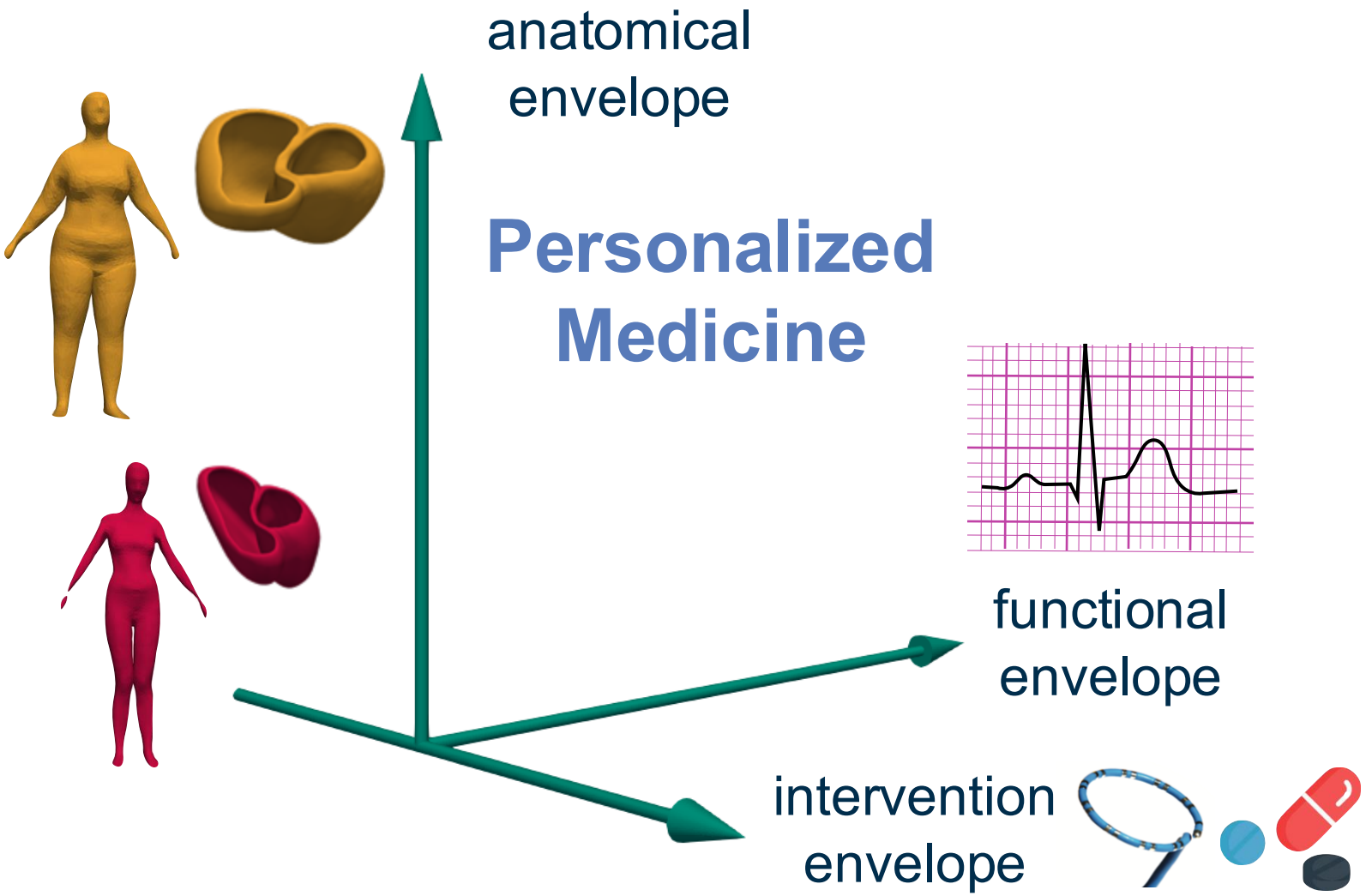

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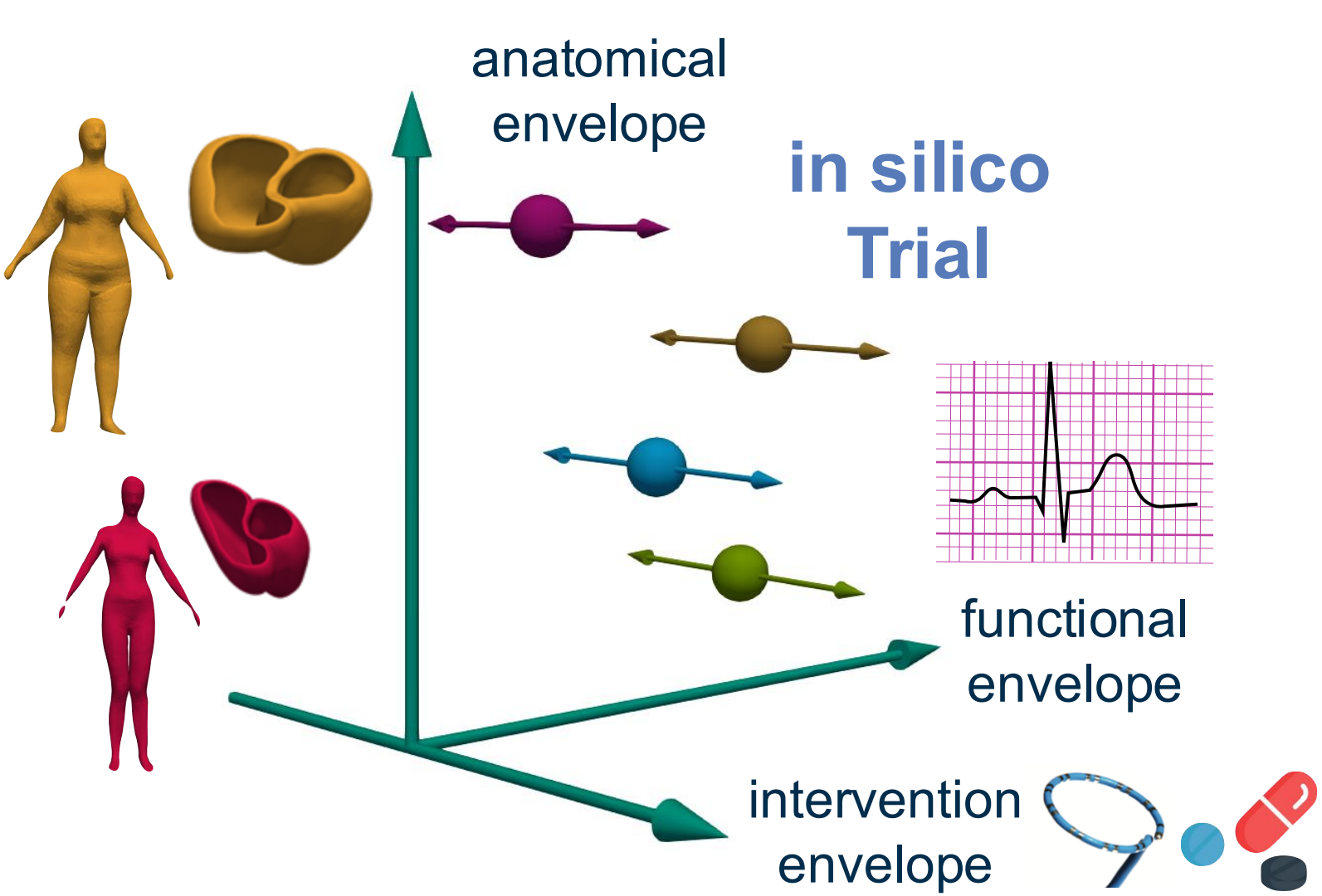

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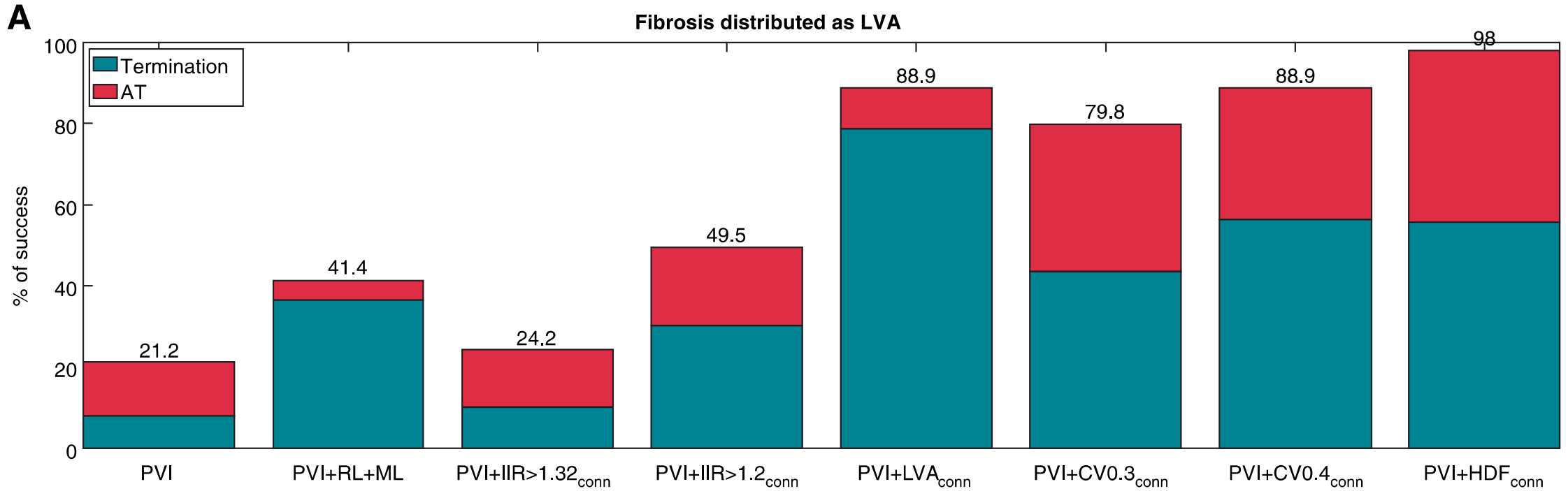
Which personalized atrial fibrillation ablation strategy is optimal?



Azzolin et al., „Personalized ablation vs. conventional ablation strategies to terminate atrial fibrillation and prevent recurrence“, Europace 2023;25:211-22

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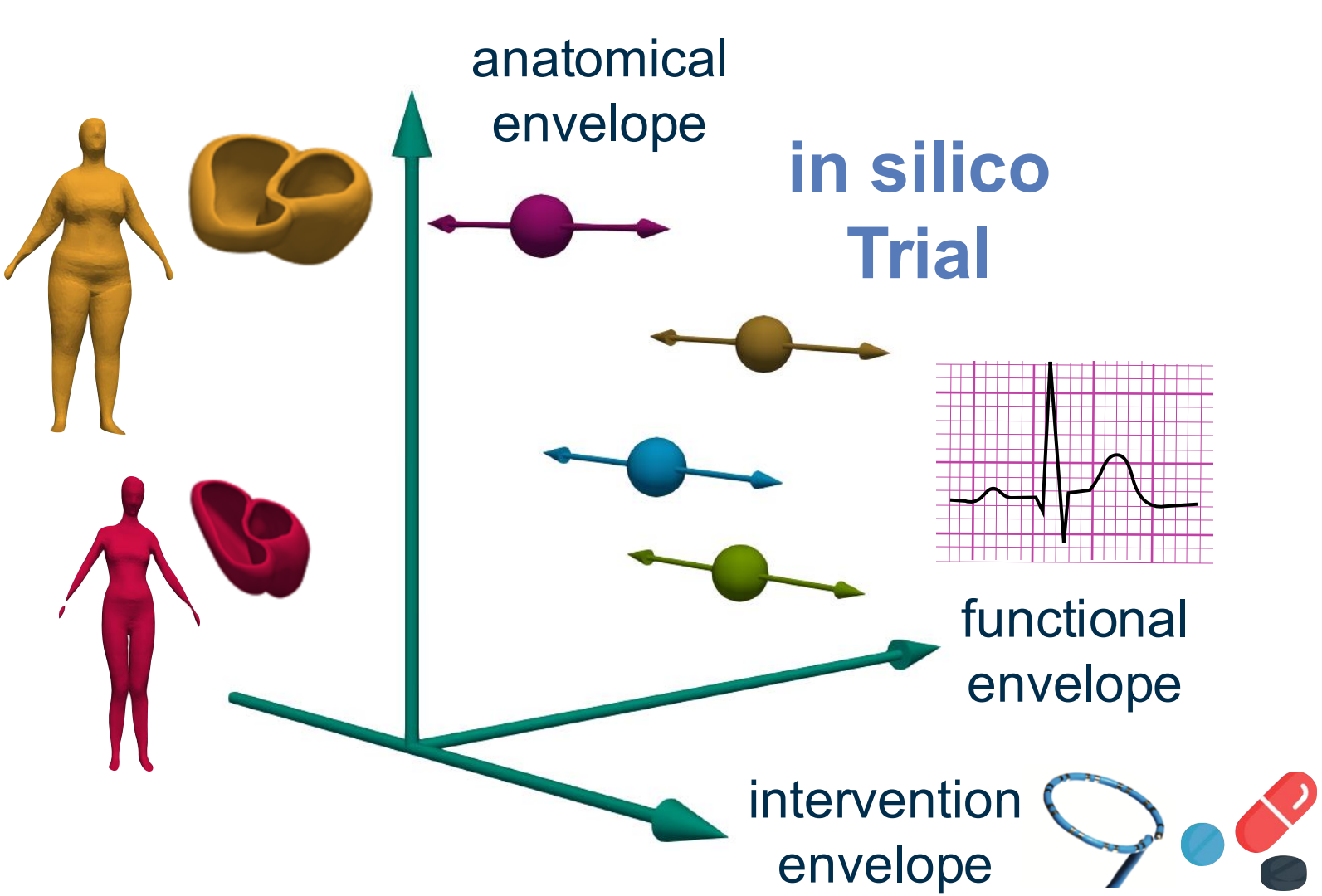

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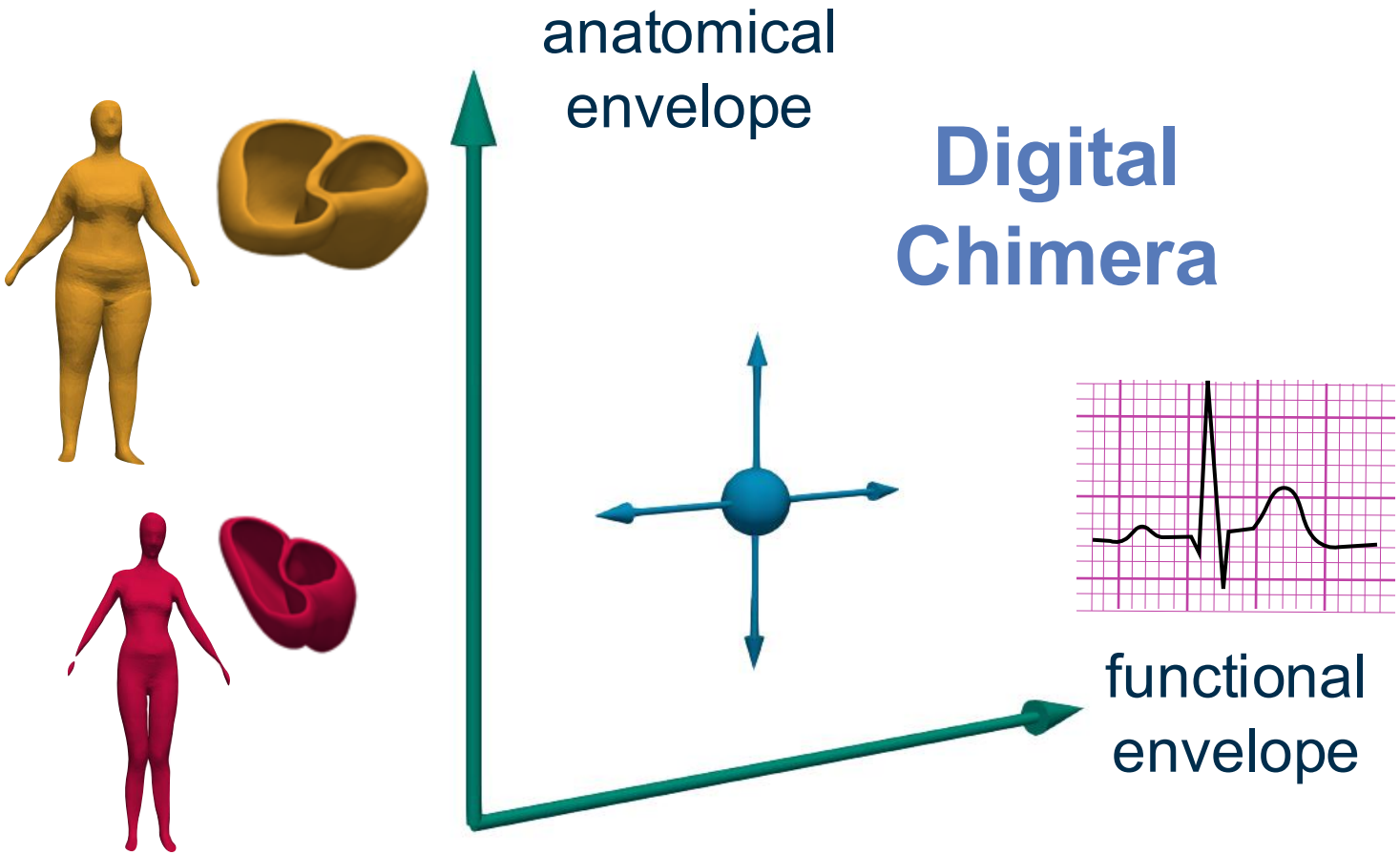

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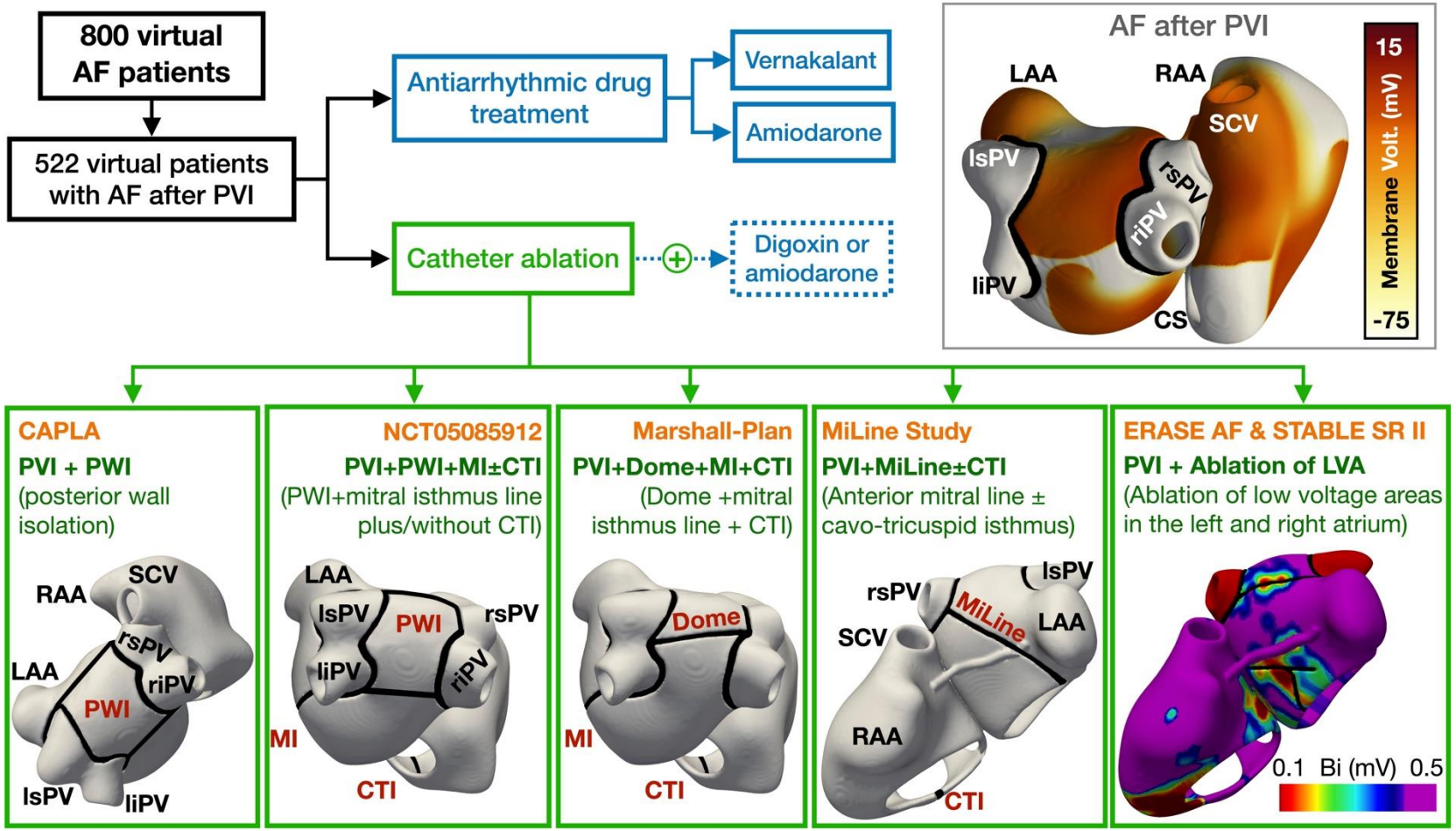
Scaling up from 29 to 800 virtual patients



Dasi et al., "in-Silico TRials Guide Optimal Stratification of ATrIal FIbrillation Patients to Catheter Ablation vs Pharmacological medicaTION: The i-STRATIFICATION Study", Europace 2024;6:euae150

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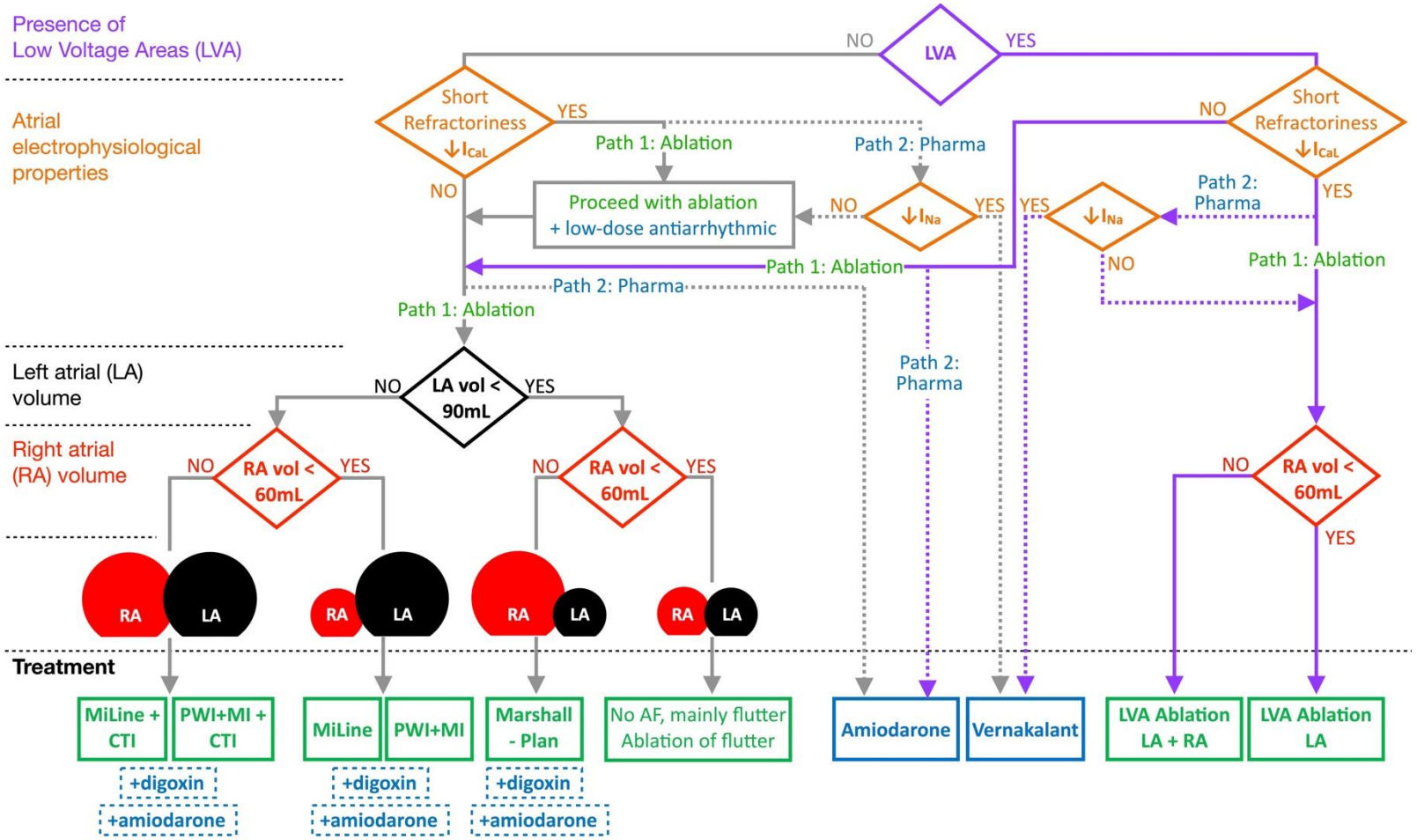

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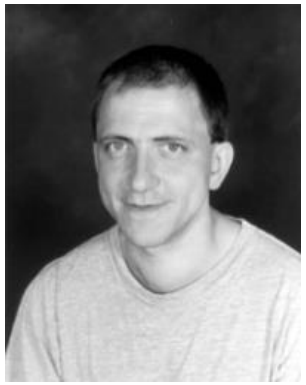

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Reductionism vs. integrationism

"The wise man walks from the village to the top of the nearby mountain and, after a brief and peaceful rest, strides back to the village. There he stays for a short while, before he returns to the mountain, and so on.

Asked why he does this, he replies that he wants to understand his people. But when he dwells inside the village, he can't see the whole of it, and when he is on the summit, he is out of touch with the villagers. So he continues his pilgrimage for eternity."

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Mechanistic vs. data-driven modeling
A new dichotomy?

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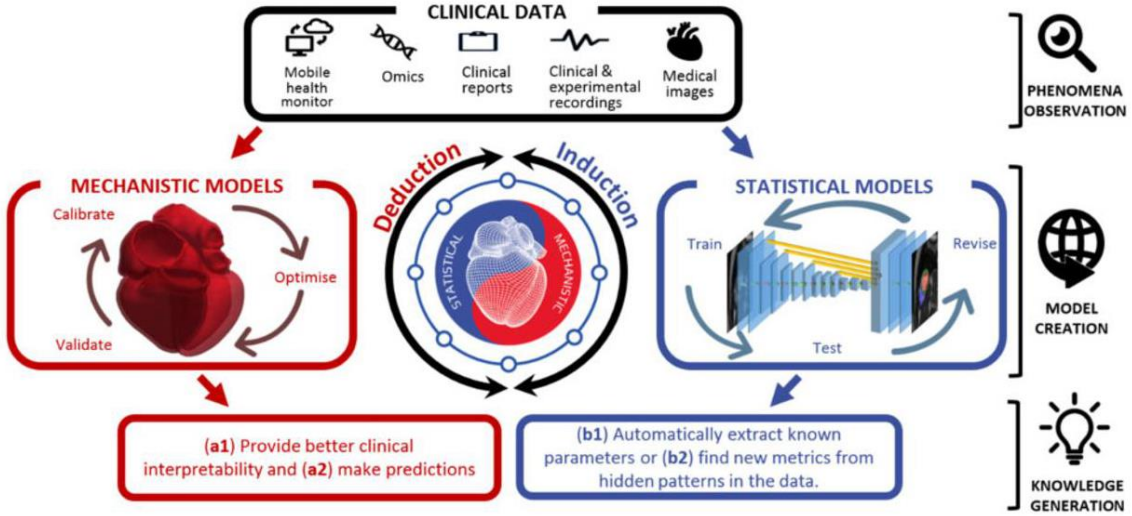

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Open and interoperable ecosystems

Tools & data

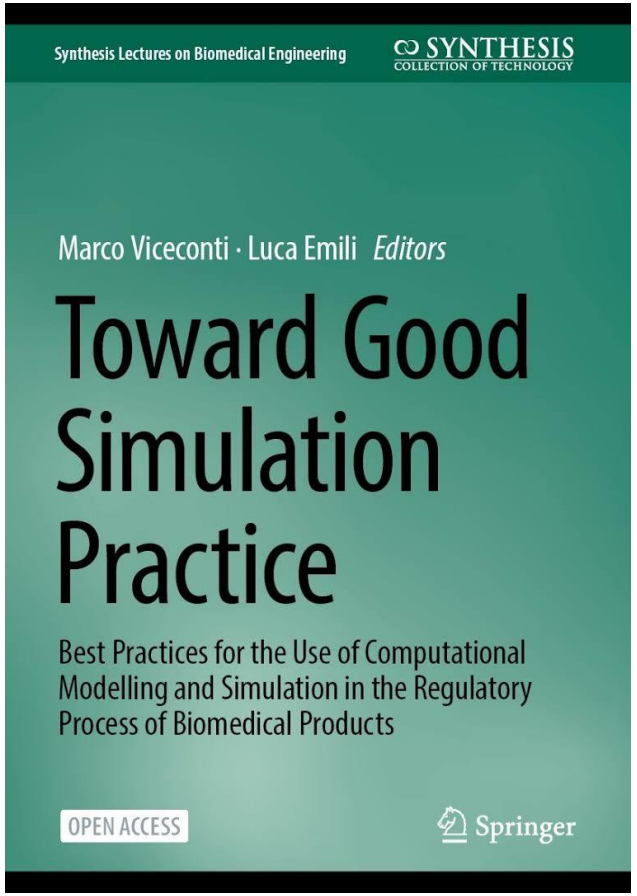
- Standardization (e.g. CellML)
- Findable, accessible, interoperable and reusable (FAIR) and open publication of data, metadata and code
- Reliable and relatable data vs. pure quantity important to go from village to mountain view

Challenges

- Lack of proper incentive and recognition systems (despite commendable efforts to reform research assessment, like DORA and CoARA)
- Disconnect between project funding cycles and expectations for sustained software development

Open Science: collaboration, transparency, and shared resources
→ reproducibility, efficiency and fewer redundant efforts

Communities: EDITH / VPH / HARMONY / openCARP, PhysioNet



Community resources

Program ▾ Authors ▾ Com
FAQ CinC25 Social Media

Tuesday, September 16th

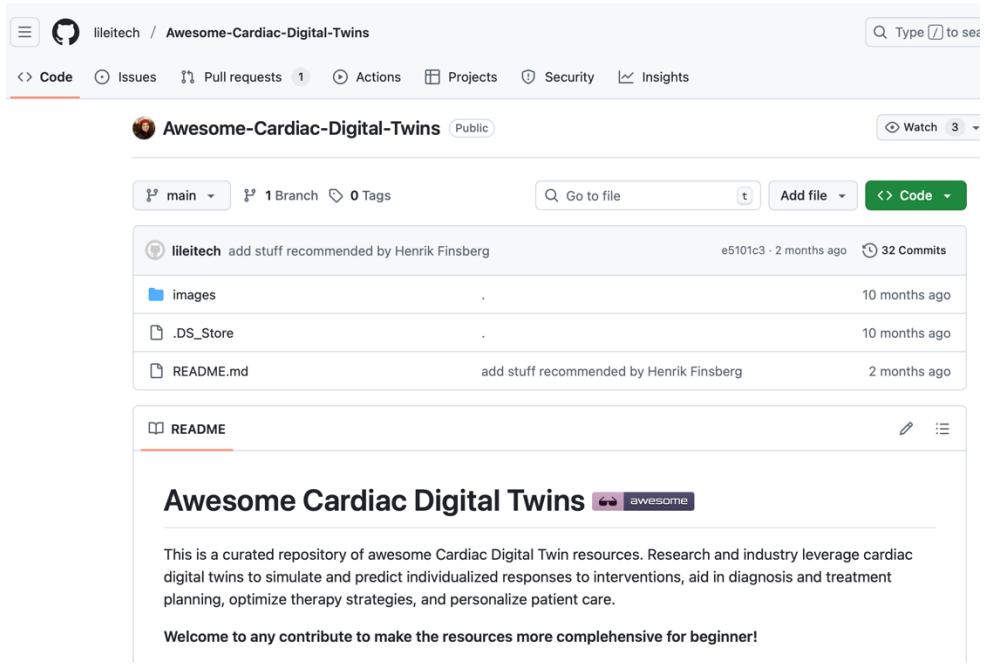
Open Software and Tools for Digital Twins of the Heart (223)

8:30 AM – 9:00 AM

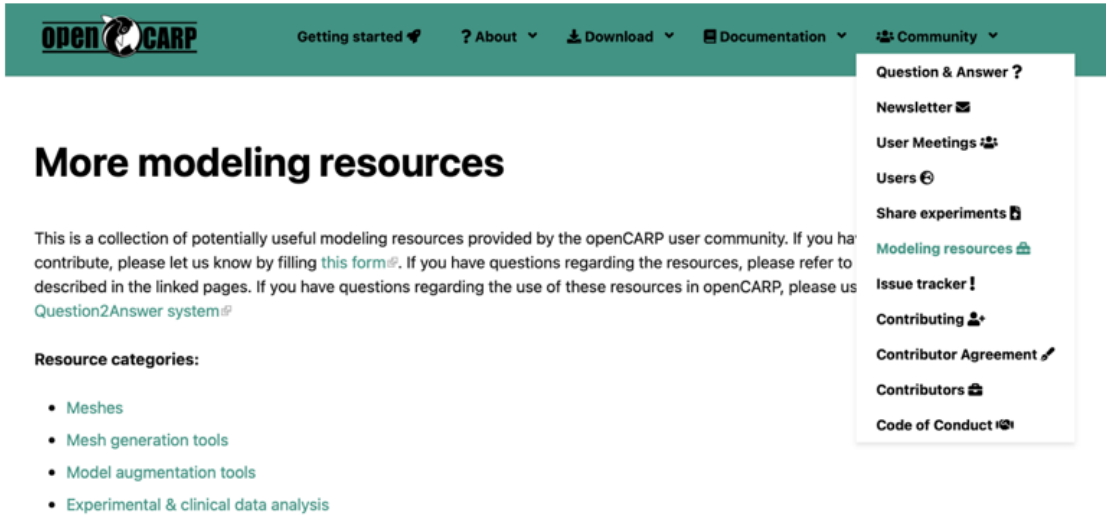
Turquesa 6 Room: Pampa

Description

Authors: Blanca Rodriguez; Rodrigo Weber dos Santos



www.openCARP.org



The road ahead

Advancing modeling methodology

- Multi-physics (electrophysiology, mechanics, fluid, growth, perfusion, metabolism) incl. energetic consistency
- Multi-scale (including subcellular)
- Digital twins: parameter calibration, uncertainty quantification
- Exploiting generative AI and foundation models
- Non-canonical interactions of signals, cells and organs (e.g. immunocardiology)
- More complete and comprehensive models
  ↔ simplification and abstraction for enabling mechanistic insight in knowledge-generating research

Non-technical aspects

- Model validation for additional contexts of use
- Big data but small data (curation, annotation, FAIR & open)
- Ever-growing requirements on the training of researchers (larger labs or intensified collaboration?)
- Communication across disciplines: translation needs translators!

Computer modeling & simulation

Many routes to impact!

Controlled and **resource-efficient** research environment

- to understand fundamental physiology and pathomechanisms
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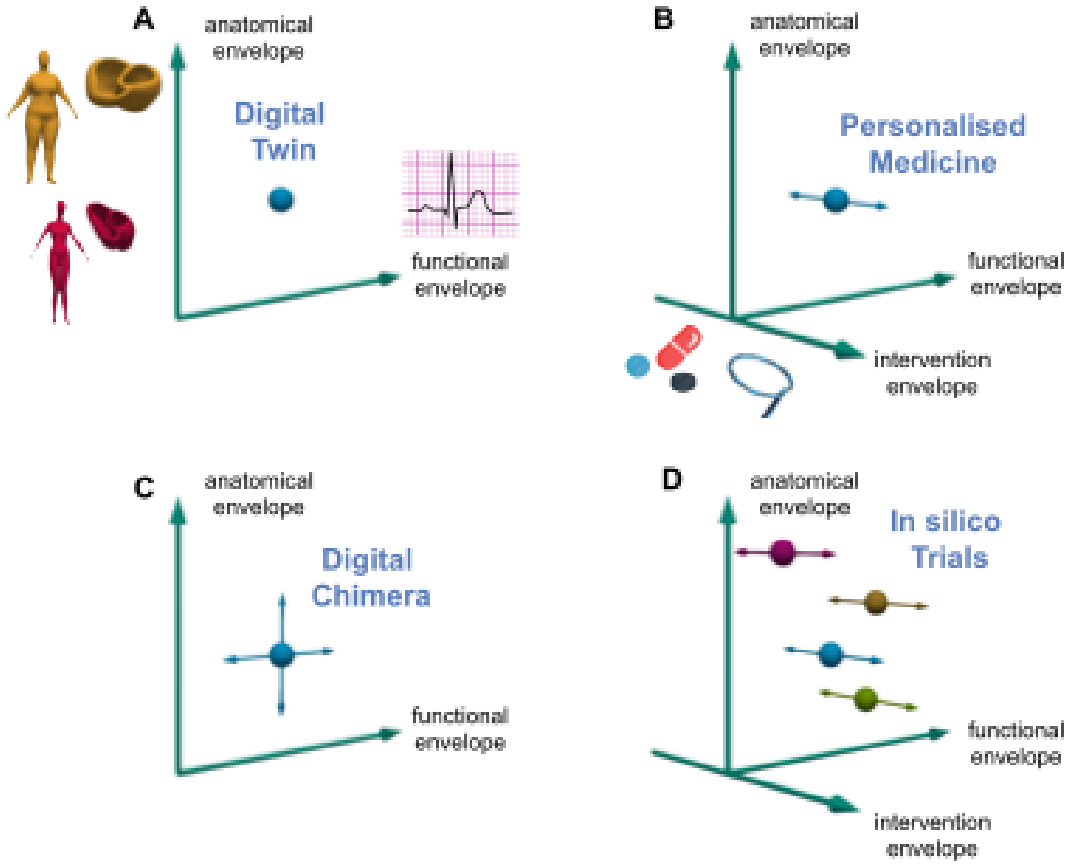
Personalised medicine through digital twins

Scalable research environment to generate big, quality-controlled dataset for machine learning



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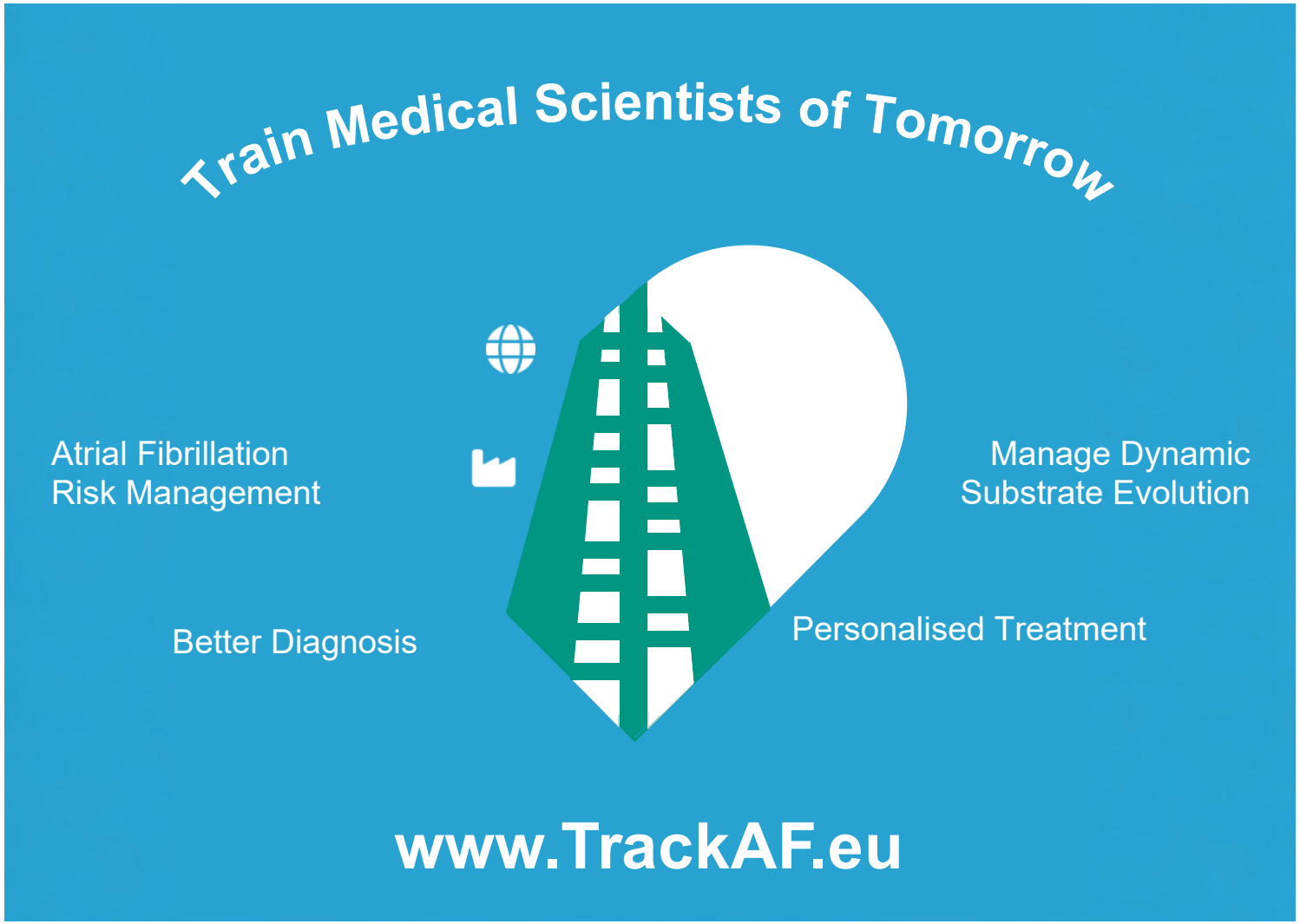

Biomedical Engineering

Clinical Data Science

Biology