

From Code to Cardiology: Open Pipelines Powering Digital Twin Development

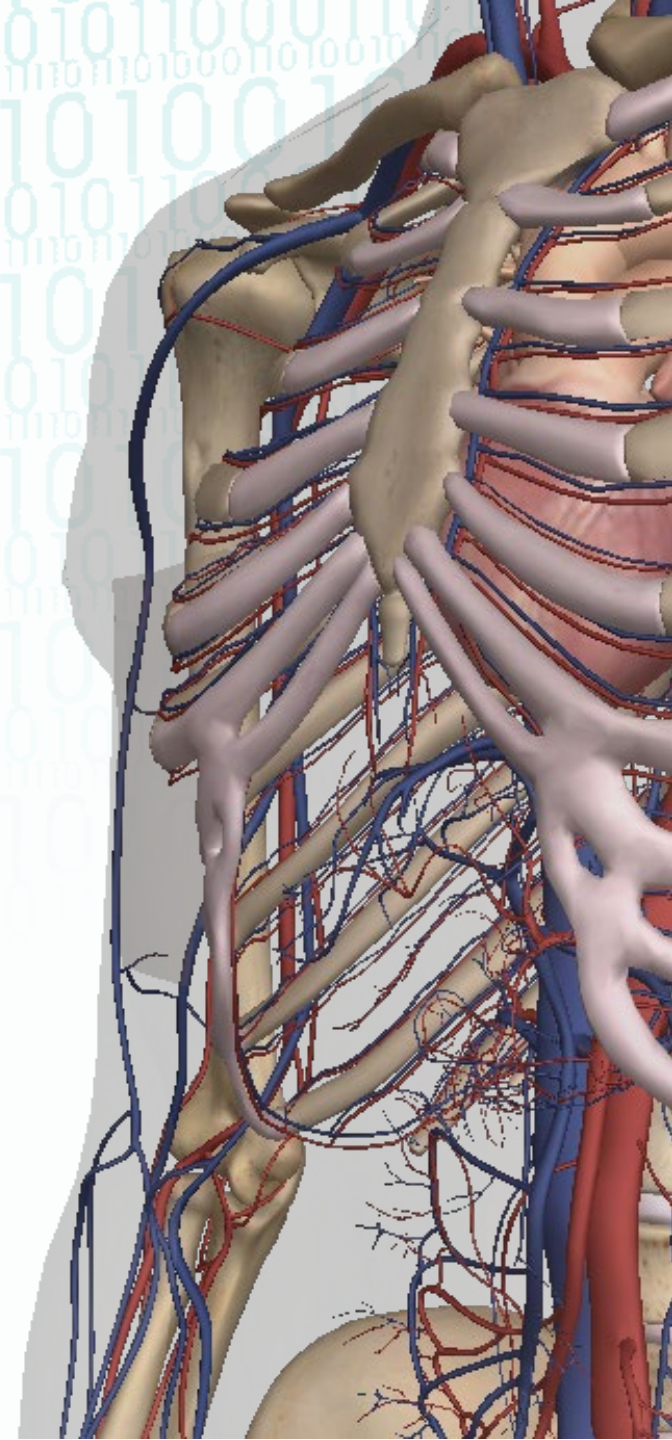
2nd Virtual Human Global Summit

Barcelona — Thursday 23rd October, 2025

Alfonso Bueno-Orovio

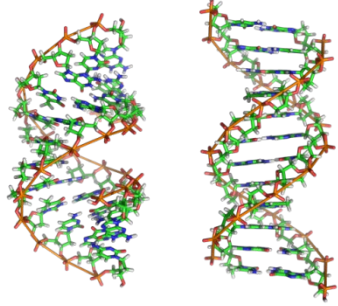
Department of Computer Science, University of Oxford

Contact: alfonso.bueno@cs.ox.ac.uk

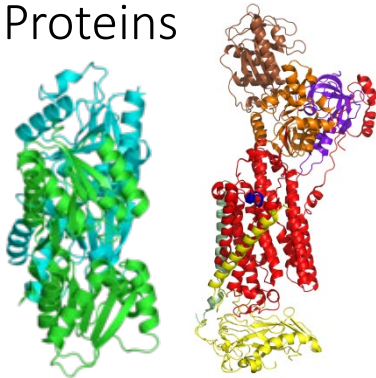


Clinical diagnosis and patient management

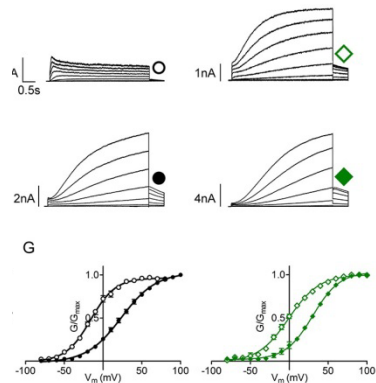
Genetics



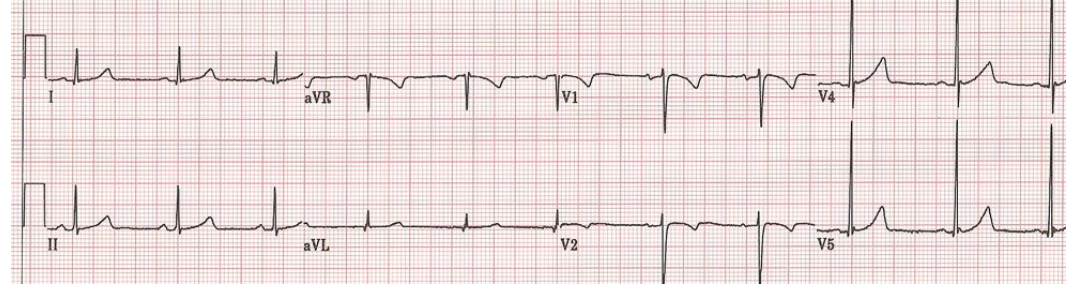
Proteins



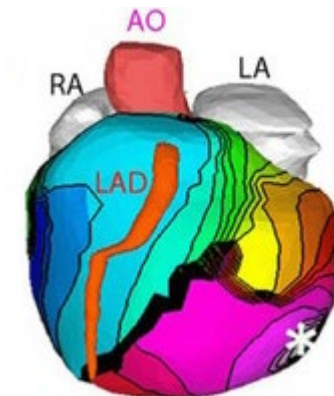
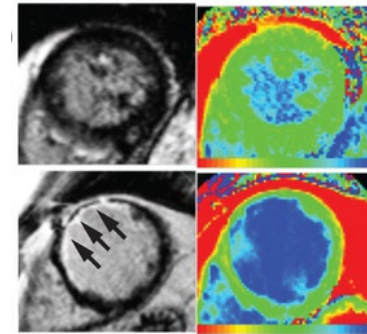
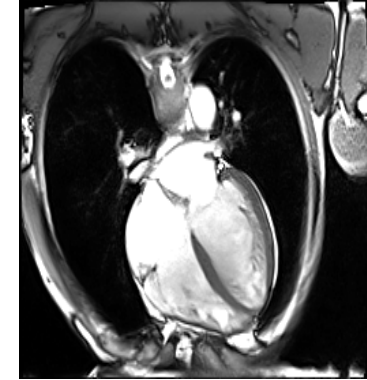
Electrophysiology



Electrocardiogram



Imaging

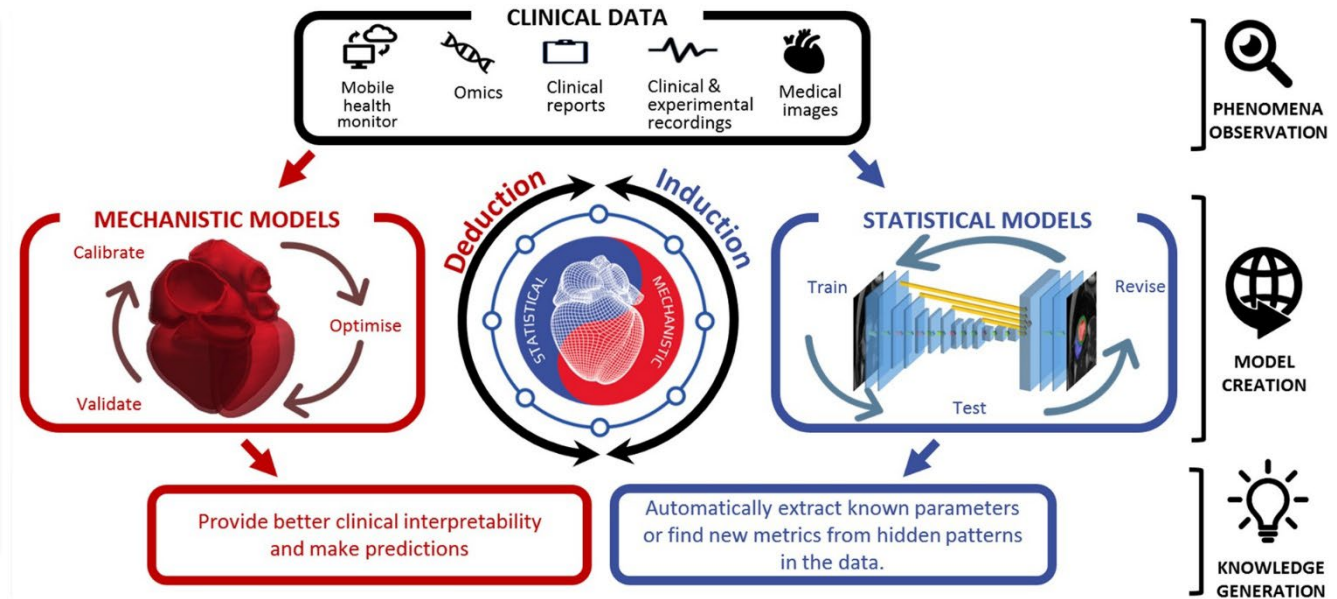


The 'Digital Twin' towards Precision Medicine: PROS

The 'Digital Twin' to enable the vision of precision cardiology

Jorge Corral-Acero¹, Francesca Margara², Maciej Marciniak³, Cristobal Rodero³, Filip Loncaric⁴, Yingjing Feng^{5,6}, Andrew Gilbert⁷, Joao F. Fernandes³, Hassaan A. Bukhari^{6,8}, Ali Wajdan⁹, Manuel Villegas Martinez⁹, Mariana Sousa Santos¹⁰, Mehrdad Shamohammdi¹¹, Hongxing Luo¹¹, Philip Westphal¹², Paul Leeson¹³, Paolo DiAchille¹⁴, Viatcheslav Gurev¹⁴, Manuel Mayr¹⁵, Liesbet Geris¹⁶, Pras Pathmanathan¹⁷, Tina Morrison¹⁷, Richard Cornelussen¹², Frits Prinzen¹¹, Tammo Delhaas¹¹, Ada Doltra⁴, Marta Sitges^{4,18}, Edward J. Vigmond^{5,6}, Ernesto Zacur¹, Vicente Grau¹, Blanca Rodriguez², Espen W. Remme⁹, Steven Niederer³, Peter Mortier¹⁰, Kristin McLeod⁷, Mark Potse^{5,6,19}, Esther Pueyo^{8,20}, Alfonso Bueno-Orovio², and Pablo Lamata^{3*}

Corral-Acero et al., Eur Heart J 2020; 41: 4556-4564



Exploit big data

- Aid healthcare decision making
- Increase clinical interpretability
- Analysis of demographic heterogeneity

Maximise value of data

- Prediction of patient outcomes
- Patient selection for personalised therapy
- Intervention planning

Accelerate evidence

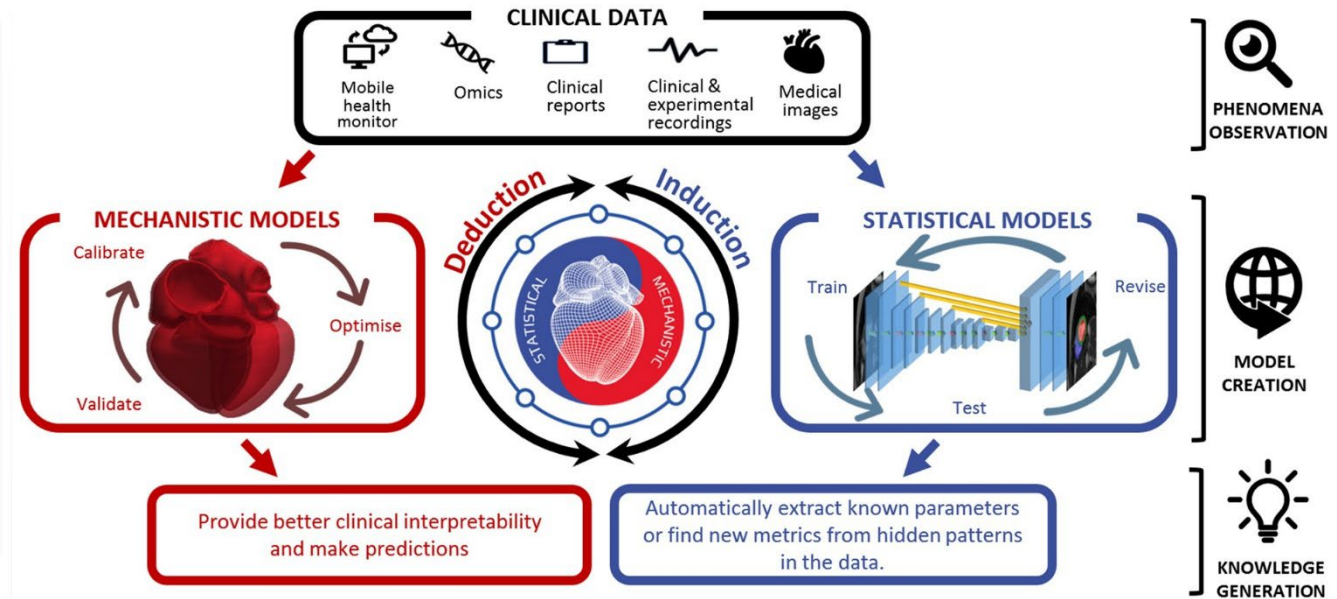
- Integration and augmentation of clinical data
- Mechanistic insights of disease
- Prediction therapeutic targets

The 'Digital Twin' towards Precision Medicine: CONS

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Data integration & personalisation

- Complexity of multi-scale data
- Personalisation gaps for tailoring mechanistic models
- Limited non-invasive biomarkers

Model synergy & validation

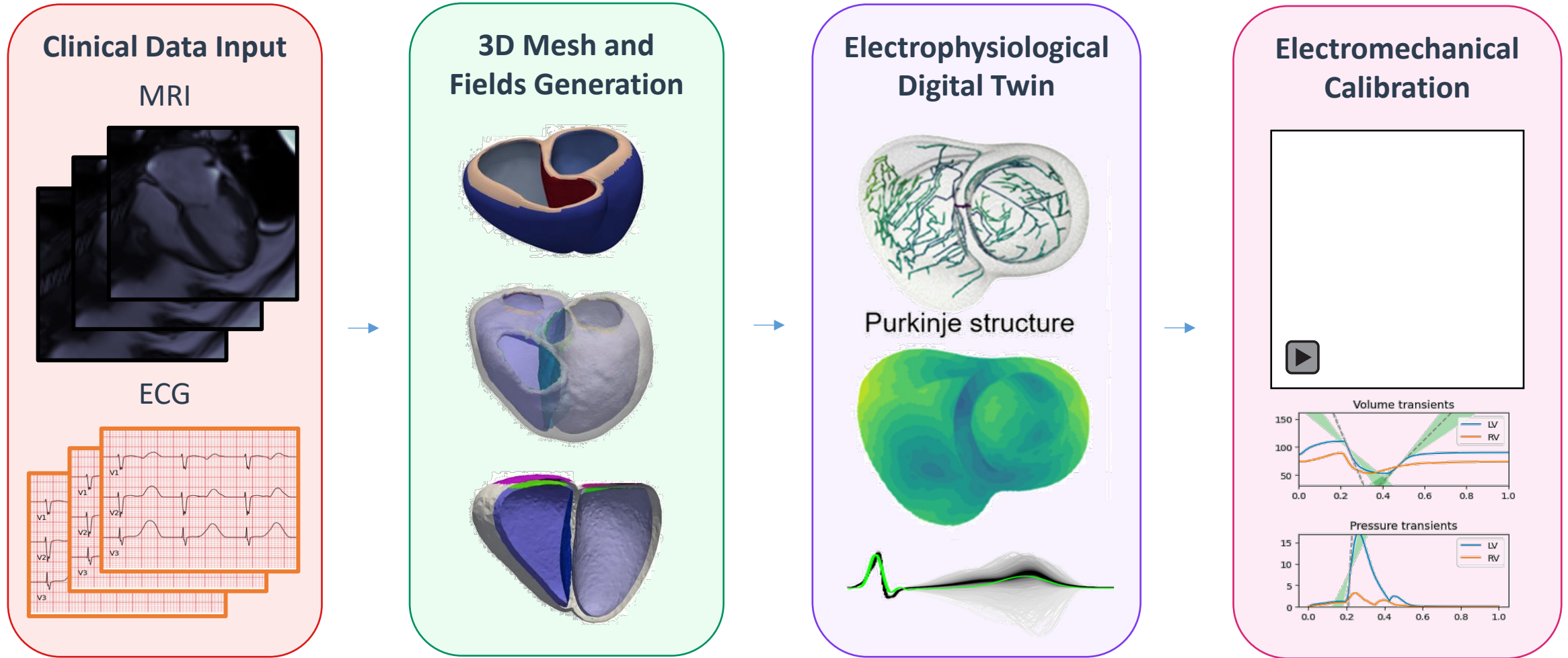
- Mechanistic vs statistical trade-offs
- Validation across populations
- Synthetic populations needed

Clinical & regulatory barriers

- Interpretability and trust
- Bottlenecks in evidence generation
- Regulatory acceptance

Digital Twins/Virtual Humans will only become reality through collective, community-driven innovation

The Oxford Cardiac Digital Twin Pipeline



DOIs:
[10.48550/arXiv/2503/03706](https://doi.org/10.48550/arXiv/2503/03706)
[10.1016/j.media.2024.103361](https://doi.org/10.1016/j.media.2024.103361)
[10.1016/j.compbio.2025.111222](https://doi.org/10.1016/j.compbio.2025.111222)
[10.7554/eLife.106555.1](https://doi.org/10.7554/eLife.106555.1)



[rdoste/
InSilicoHeartGen](https://github.com/rdoste/InSilicoHeartGen)



[juliacamps/
Cardiac-Digital-Twin](https://github.com/juliacamps/Cardiac-Digital-Twin)



[JamesAlecColeman/
sim-based-inf](https://github.com/JamesAlecColeman/sim-based-inf)

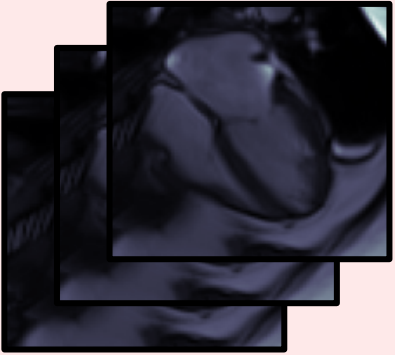


[jennyhelyanwe/
Alya input setup](https://github.com/jennyhelyanwe/Alya_input_setup)

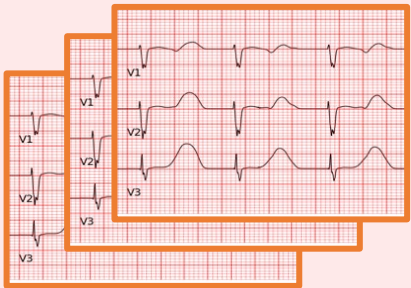
Anatomical 3D reconstruction and synthesis

Clinical Data Input

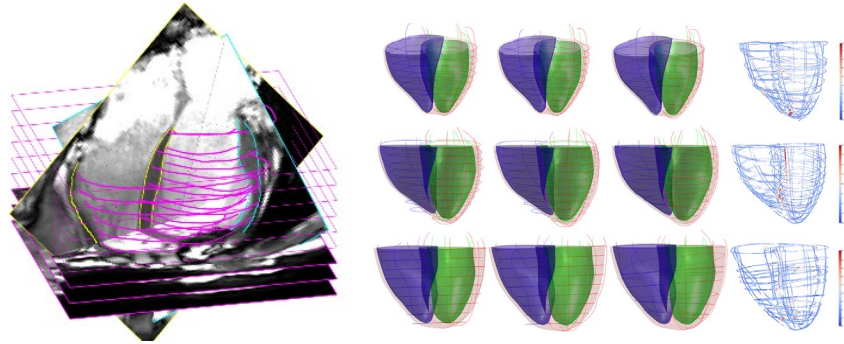
MRI



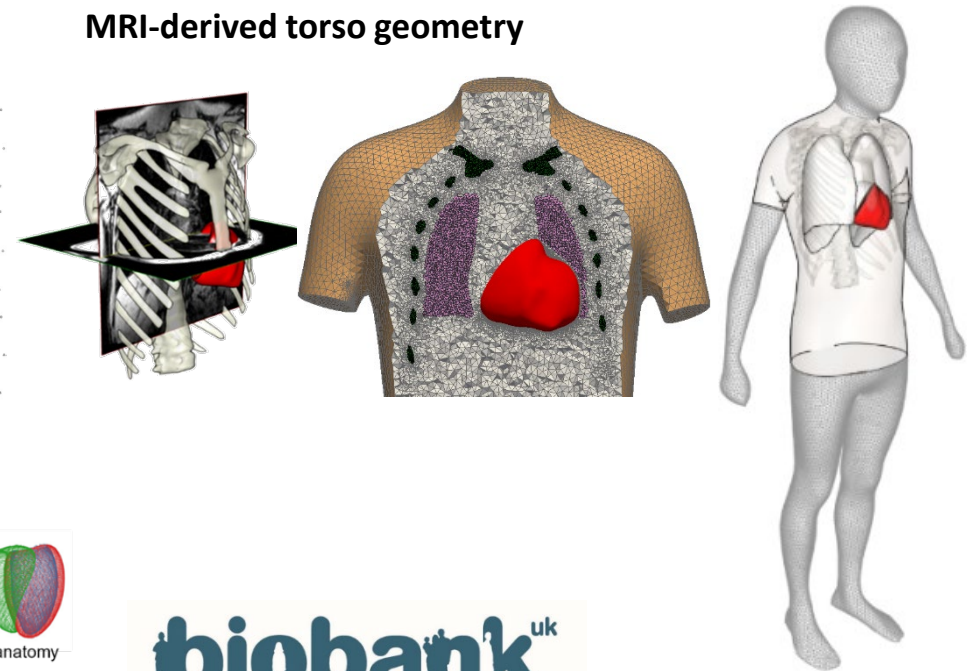
ECG



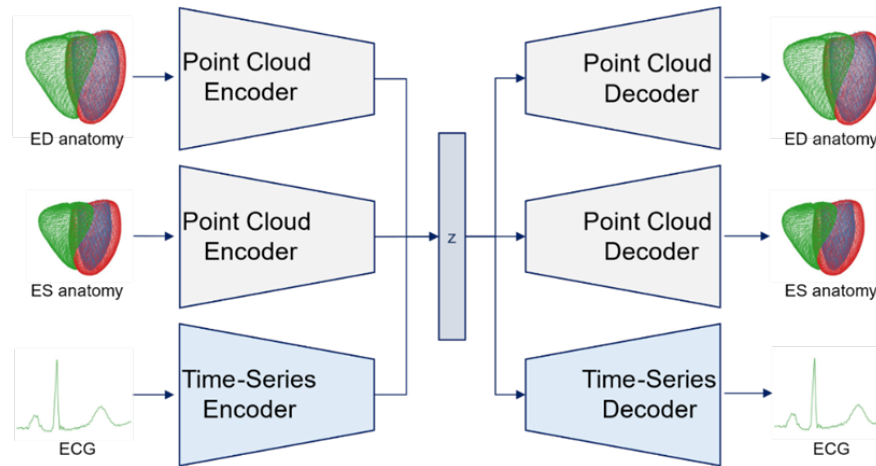
MRI-derived biventricular geometry



MRI-derived torso geometry



Variational autoencoders



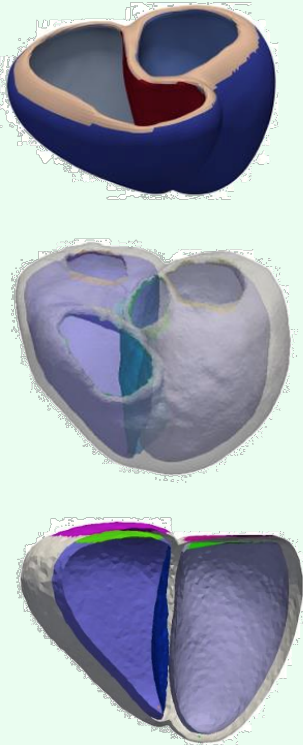
- Generates end-diastole and end-systole anatomies and ECGs
- Virtual patients with specific age, BMI, sex, disease

Towards fully-automated, large-scale *in silico* trials



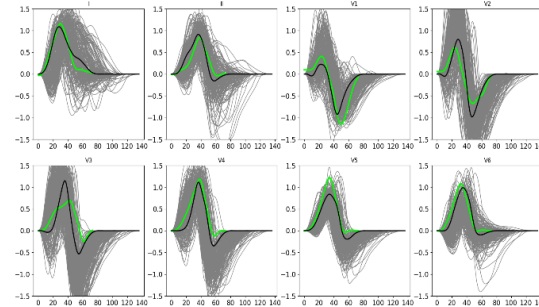
Dr Rubén Doste

3D Mesh and Fields Generation

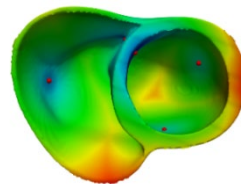


[rdoste/
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Electrophysiology personalisation

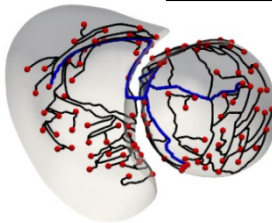


Personalised activation/repolarisation



Camps et al,
Med Image Anal,
2024

Purkinje Tree Generation



Berg et al,
Scientific Reports,
2023



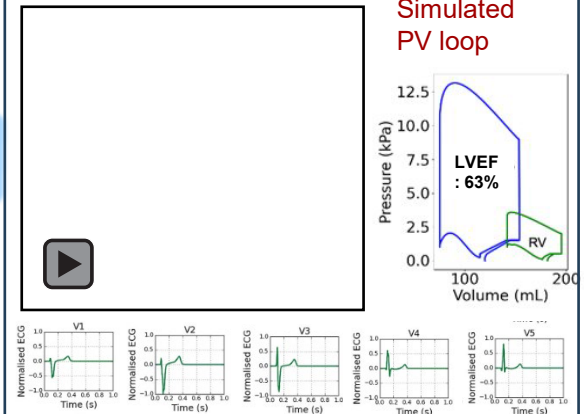
MonoAlg3D

Alya



Centro Nacional de Supercomputación

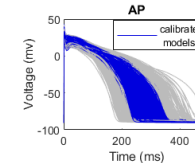
Electromechanical model



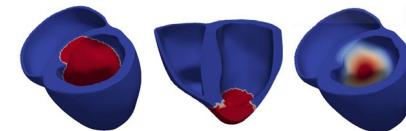
Wang et al, *EP Europace*, 2021

Electrophysiological variability

Calibrated cellular models



Scar/Fibrosis Location



Drug dose

$$I_{\%}(X) = \frac{100}{1 + \left(\frac{X}{IC_{50}}\right)^h} \%$$

Rubén Doste, et al. An automated computational pipeline for generating large-scale cohorts of patient-specific ventricular models in electromechanical *in silico* trials. *arXiv:2503.03706*, 2025.

Functional twinning from ECG recordings

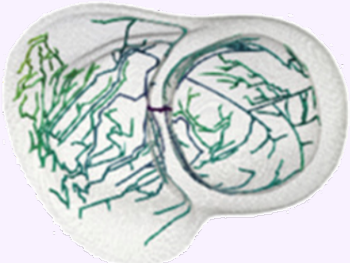


Dr Julià Camps

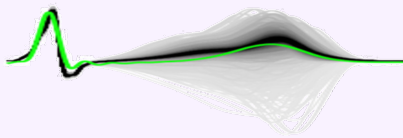
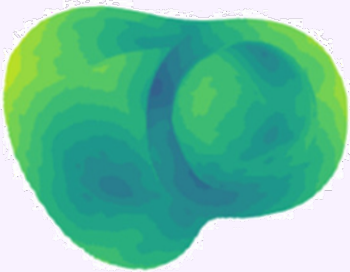


Dr Lucas Berg

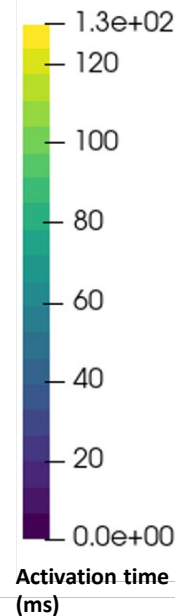
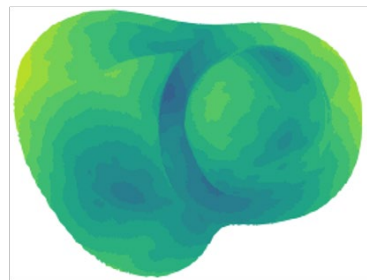
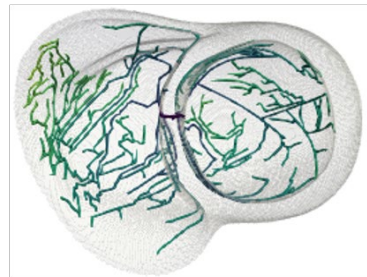
Electrophysiological Digital Twin



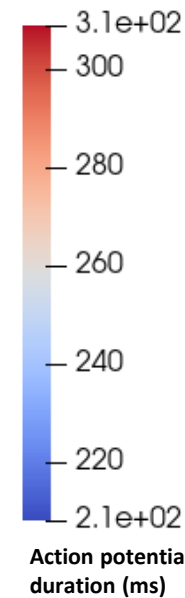
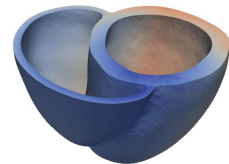
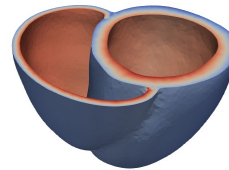
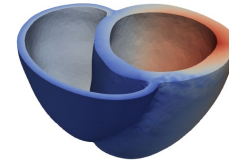
Purkinje structure



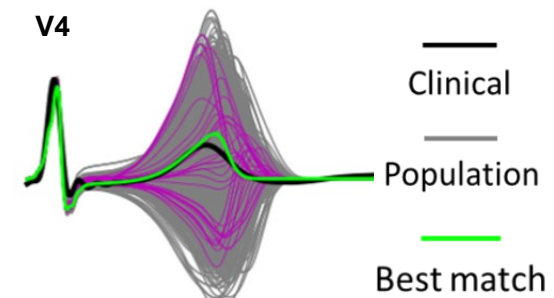
Infer activation from ECG



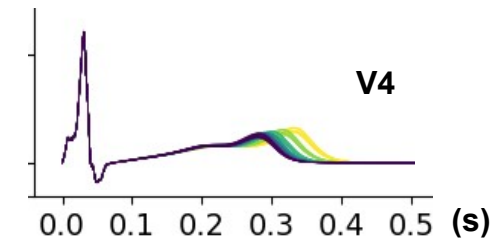
Infer repolarisation from ECG



Account for ECG variability



Simulated response to Dofetilide



[juliacamps/
Cardiac-Digital-Twin](https://github.com/juliacamps/Cardiac-Digital-Twin)

Julia Camps, et al. Inference of ventricular activation properties from non-invasive electrocardiography. *Medical Image Analysis*, 2021.

Julia Camps & Lucas Berg, et al. Digital twinning of the human ventricular activation sequence to clinical 12-lead ECGs and magnetic resonance imaging using realistic Purkinje networks for in silico clinical trials. *Medical Image Analysis*, 2024.

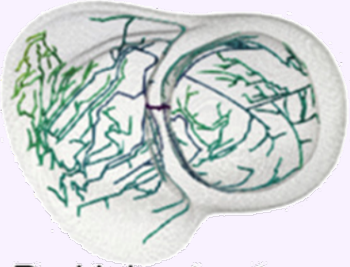
Julia Camps & Zhinuo Jenny Wang, et al. Medical Image Analysis. Harnessing 12-lead ECG and MRI data to personalise repolarisation profiles in cardiac digital twin models for enhanced virtual drug testing. *Medical Image Analysis*, 2025.

Functional twinning from ECG recordings

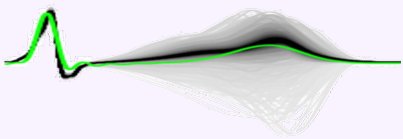
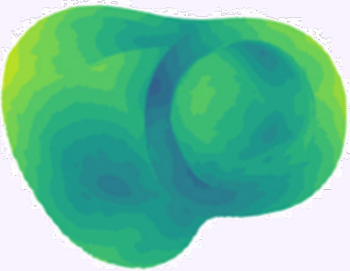


Dr James Coleman

Electrophysiological Digital Twin

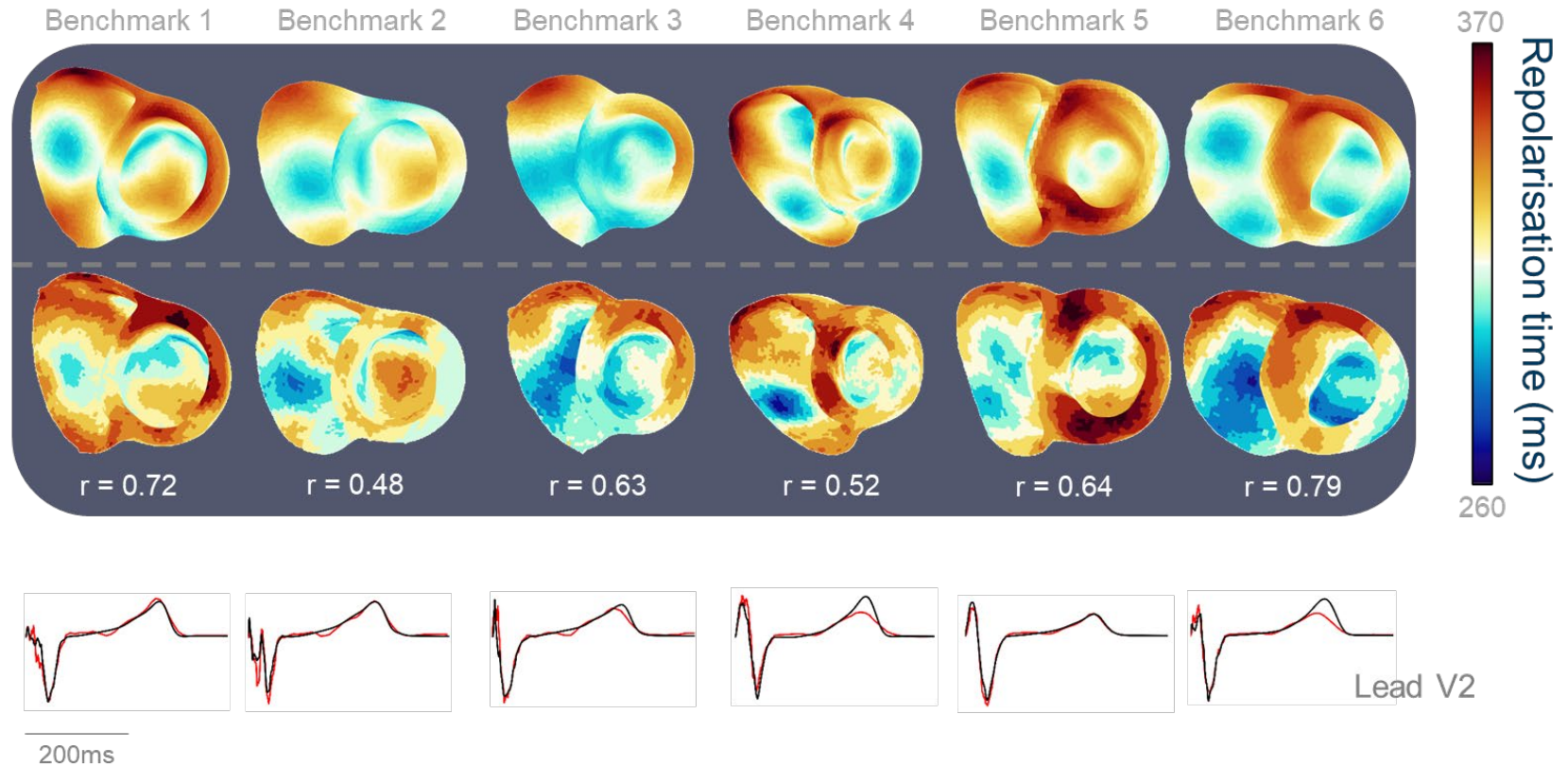


Purkinje structure



**Ground
truth**

**Inferred
from T
wave**



[JamesAlecColeman/
sim-based-inf](https://github.com/JamesAlecColeman/sim-based-inf)

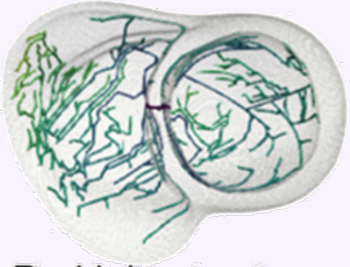
James Coleman, et al. Simulation-based digital twinning of activation and repolarisation sequences from the ECG across healthy and diseased hearts. *Computers in Biology and Medicine*, 2025:198:111222.

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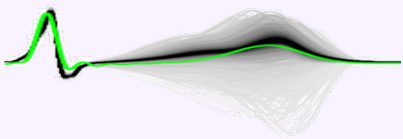
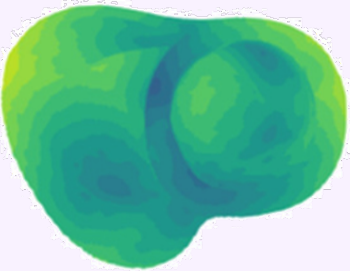


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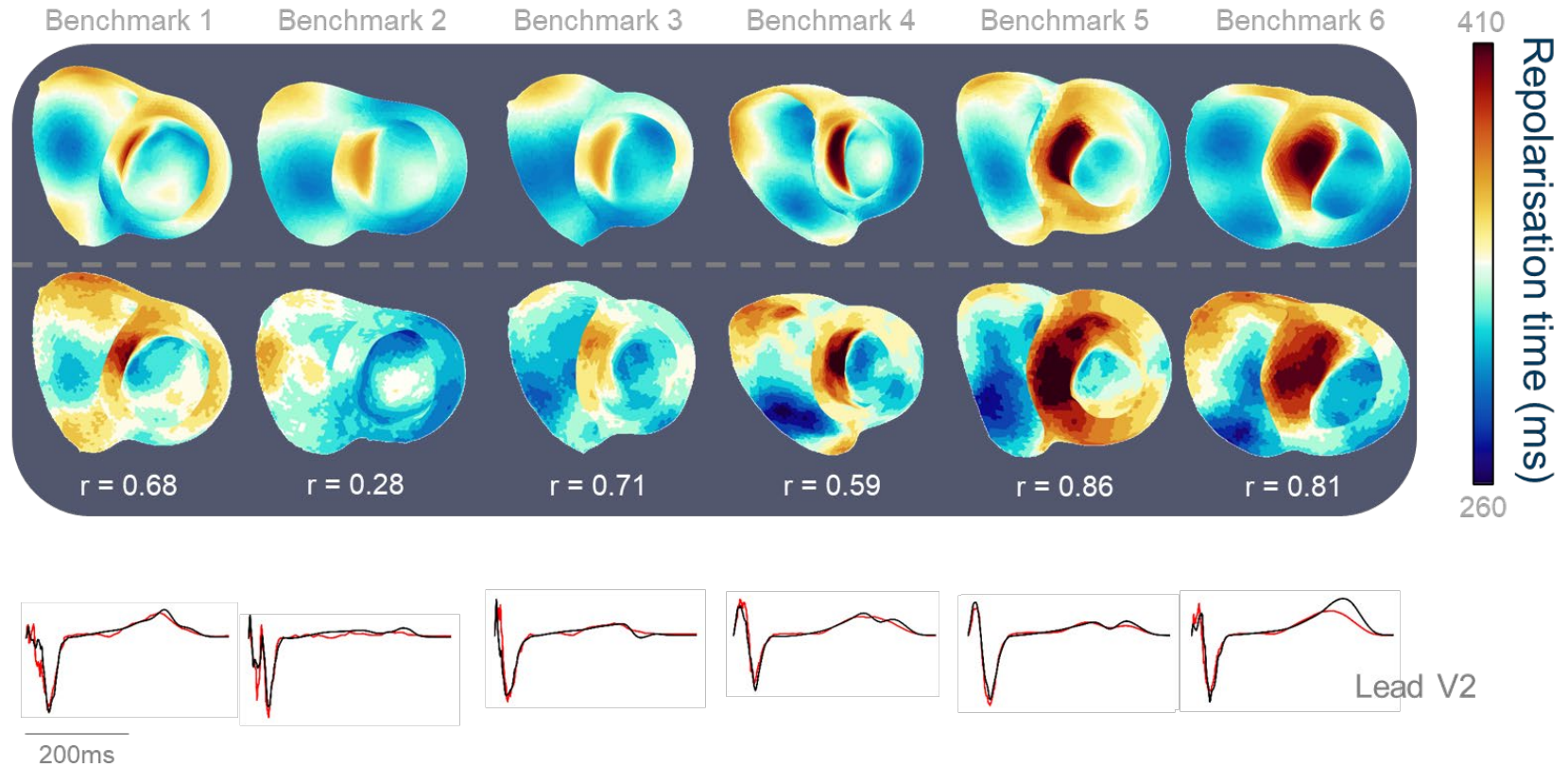


Purkinje structure



**Ground
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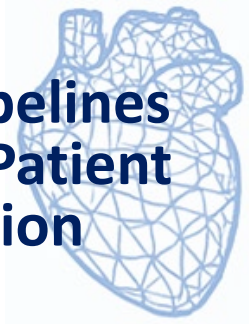


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James Coleman, et al. Simulation-based digital twinning of activation and repolarisation sequences from the ECG across healthy and diseased hearts. *Computers in Biology and Medicine*, 2025:198:111222.

Summary

Scalable Pipelines for Virtual Patient Generation



- ▶ **Automated Mesh Processing:** automated mesh workflows enabling large-scale, simulation ready cardiac models
- ▶ **Large-Scale Cohort Creation:** enable population-wide in silico trials, including synthetic populations for scalable testing

Integration of Multiphysics and Personalisation



- ▶ **Clinical Data Integration:** adaptable pipelines compatible with standard of care (MRI and ECG)
- ▶ **Comprehensive Cardiac Function Analysis:** unified electromechanical simulations with personalised ECG and Purkinje networks

Open Science and Community Resources

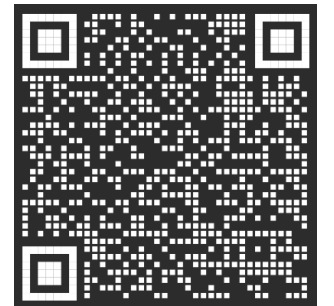


- ▶ **Open-Source Codebases:** modular, extensible tools to foster reproducibility and collaboration
- ▶ **Interoperability:** compatibility with existing platforms, lowering barriers to adoption

Acknowledgments

With outmost thanks to the entire ***Computational Cardiovascular Science Group*** (past and current members) and ***collaborators!***

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https://linktr.ee/oxford_ccs