Mathematical models to create cardiac digital twins for precision healthcare

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THE PROBLEM

- There are around 7.6 million people living with cardiovascular diseases (CVDs) in the UK
- CVDs cause 27% of all deaths in the UK – one every 3 minutes
- The specific causes require studying the heart from a multiphysics (electrophysiology, mechanics, fluid dynamics) and multiscale point of view (from molecules to whole-organ dynamics)

HOW CAN CARDIAC DIGITAL TWINS HELP?

- A cardiac digital twin (DT) is a virtual representation of the heart of a person
- This representation includes patient-specific data and the known biology and physics of the heart
- DTs allow us to run simulations of a patient’s condition and test multiple treatments
- Create a DT of patient can take months because of the complexity of the process and the number of parameters involved in the biophysics equations

FROM MEDICAL IMAGES TO DIGITAL TWINS

Cardiac computerised tomography (CT)

We applied this pipeline to 20 healthy subjects and made openly available the first cohort of healthy whole-heart models

FUNCTIONAL DIGITAL TWIN

Taking shape into account

- There is a poor understanding of how specific anatomical changes affect different cardiac outputs
- Statistical shape modelling is a mathematical technique to describe complex shapes with a limited set of numbers comparing them to a generated “average” shape
- We applied this technique to our cohort of healthy hearts and used those numbers to link localised changes in anatomy to changes in the simulation of the cardiac function
- We found how small changes in the shape can indicate early indications of hypertension
- We made open-source a synthetic cohort of more than 1000 heart models generated using this technique

IN-SILICO TRIAL OF MEDICAL DEVICES

- Dysynchronous heart failure (HF) is a condition where the two sides of the hearts do not beat at the same time
- Cardiac resynchronization therapy (CRT) is one of the main treatments, where a pacemaker is inserted and the heart is shocked at several locations
- Where to install the CRT electrodes can change between patients and it is not clear if there is an optimal location
- We created DTs of 24 HF patients and 20 healthy ones representing recovered patients
- We tested more than 8000 pacemaker configurations, representing a virtual (or in-silico) trial
- We found that differences in anatomy was more relevant than differences in the electrodes’ locations

ACCELERATING CLINICAL TRANSLATION

- One of the main bottlenecks with DTs is parameter fitting
- Parameter fitting consists of finding the set of parameters that describes best given clinical data
- We developed a pipeline based on Bayesian History Matching and Gaussian Process Emulators to find a reduced parameter space
- We can then reuse that information with new patients reducing drastically the computational load to create DTs

NOW WHAT?

- New modalities, like magnetic resonance imaging (MRI)
- New diseases, like hypertrophic cardiomyopathy (HCM)
- Scale up: can we do hundreds of DTs in a sensible timeframe?
- How can we update DTs with new visits to the hospital?
- Can we add the explicit effect of hormones?

THE PAPERS

| Digital twins and simulations | Taking shape into account | In-silico trial | Bayesian History Matching |

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