eHealth 3.0: Personalized digital twins to capture and use different kinds of clinical knowledge

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Keywords

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1. Introduction

The first generation of eHealth is already a fact: usage of telecommunication to e.g. diagnose patients remotely is now an integrated part of healthcare. We are therefore now in the middle of the second generation of eHealth: artificial intelligence (AI) and machine learning (ML). There are important showcases illustrating that ML can perform diagnosis and image analysis at the level of a trained radiologist, for specific applications [1]. However, ML has critical shortcomings, severely limiting the impact it can have on healthcare. For instance, ML models need the right type of data from thousands of patients to train the models, do not make use of or add to the mechanistic physiological understanding, and are usually developed for a single purpose. ML is therefore often referred to as narrow AI. Mechanistic models overcome these shortcomings, but they take long time to develop, and there are not models available for all relevant processes. In other words, the best approach would arguably be a hybrid approach, combining ML and mechanistic modelling. With such an approach, one could in principle create a digital twin. Digital twins have been used to simulate and predict the behaviour of its physical counterparts in other fields since the early 2000s [2], but remains a non-realized vision in healthcare [3]. Nevertheless, there do exist several kinds of models for different physiological sub-processes and health-related purposes [4–7]. However, no-one has yet combined and personalised these models to fully describe a digital twin for a specific person. We now present a new hybrid approach, combining strengths of ML and mechanistic modelling, and illustrate how this combination can be used to develop digital twins of a specific patient.

2. Methods

Mechanistic models are described using ordinary differential equations (ODEs), which represent mechanistic hypotheses about the physiology in the modelled processes. The machine learning models used are e.g. neural networks. The hybrid modelling is done in different ways depending on the purpose: 1) unmeasured biomarkers are statistically estimated using data from large clinical studies, 2) risk assessments are made using nonlinear mixed-effects modelling, bioinformatics, and ML, 3) simulations of different treatments are done using simulations of ODEs. The first planned use case for this hybrid methodology is to use it in preventative care, specifically in the Health Dialogue – motivational conversation to promote general health and prevent diseases. For this purpose, the hybrid models are trained on data from several prospective cohorts – Whitehall II, SCAPIS, and UK Biobank. The mechanistic models are trained on time series data, longitudinal or short-term, and ML models are trained on multidimensional data and evaluated on known outcomes to get a risk score. The models are then validated on a subset of these data.

3. Results

We have developed and tested models for all of the main organs: brain (4), heart (5), liver (8), fat tissue (6), etc. We have now combined these into an interconnected model, where all organs interact. This world-unique model is multi-level (intracellular biochemistry to whole-body) and multi-timescale (seconds to years). We have developed a first prototype, launched at Almedalen last year, which has since been presented at several keynote presentations. This prototype can simulate some basic variables – such as weight, heart beats, and glucose uptake in fat cells – over years and/or seconds, given certain scenarios such as diet or exercise. It can also calculate a simple risk score for cardiovascular diseases. We are currently developing a more advanced version, which will be tested in clinical usage, in the Health Dialogue, where we hope to increase doctor-patient communication, patient compliance, and preventive actions. We are continuously updating the model based on ongoing and new clinical trials, coming from both healthy controls and different patient groups.

4. Conclusions

We have developed a world-unique and first-of-its-kind digital twin technology, which combines physiological descriptions of all major organs with ML. These models can be personalized and can thereafter be used to simulate how the patient is likely to respond to treatments. The digital twin can also be updated with new data, and is therefore more flexible than traditional narrow AI ML approaches; our hybrid model can be incorporated and re-used for a much wider variety of tasks in healthcare. For these reasons, our digital twins can lay the foundation for a more general-purpose AI in healthcare, and can be said to represent a third generation of eHealth: eHealth 3.0.

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