Research towards virtual human twins

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Outline

- Virtual Physiological Human (VPH), digital twin, Virtual Human Twin (VTH)
- Motivation
- VHT from computer science perspective
- Features of the platform for VHT
- Demonstrator architecture
- Example application
- Summary and future work

VPH, digital twin, Virtual Human Twin

- **VPH - *Virtual Physiological Human***, sometimes *in silico medicine* - a field involving the use of individualized computer simulations based on physiology in aspects of prevention, diagnosis, prognostic assessment and treatment of disease and biomedical product development

- ***A digital twin*** - a digital representation of a physical object, person or process, placed in context in a digital version of its environment

- **VHT - *virtual human twin*** - an integrated, multi-scale, multi-temporal and multi-disciplinary representation of quantitative human physiology and pathology (EDITH project definition)

Role of VHT

- Vision: digital twins of humans, from cells and tissues to organs and entire bodies

- A digital twin may help to
    - predict the risk of disease,
    - plan and control medical treatment,
    - take part in virtual drug tests,
    - propose changes in diet and lifestyle,
    - identify therapies that improve well-being and prolong life

- With VHT a real personalised medicine may be possible

Selected institutions and projects in computational medicine

- VPH Institute - https://www.vph-institute.org/
  an international non-profit organization whose mission is to ensure that VPH is fully realized, widely adopted and used effectively in both research and clinics

- CompBioMed - https://www.compbiomed.eu/
  Center of Excellence financed by the European Commission (H2020), focused on the use and development of computational methods in biomedical applications

- EDITH - https://www.edith-csa.eu/edith/
  European Commission project (Digital Europe); its goal is to define a roadmap for moving from single-organ systems to a fully integrated, multi-scale, multi-organ, whole-body twin, driven by data and knowledge

- Sano Centre for Computational Personalised Medicine International Research Foundation - https://sano.science/

EDITH – European Virtual Human Twin
https://www.edith-csa.eu/

EDITH's main objective: to frame an inclusive ecosystem of digital twins in healthcare within the EU Member States and associated countries through:

- a comprehensive roadmap of the current landscape
- implementation a federated cloud-based repository
- gathering human digital twin resources: models, data sets, algorithms, practices
- designing the architecture of a simulation platform to facilitate the transition towards the use of comprehensive Virtual Human Twin (VHT) models in personalised medicine

Main Cyfronet task: elaboration of a demonstrator of such a simulation platform.

VHT from computer science perspective

- A set of software modules implementing human physiology models which can simulate human body processes
- A set of data which represents the specific patient in relation to a specific condition or treatment process
- Simulation modules may be run on different compute resources: local servers, clouds, HPC.
- The data is not typically restricted in any manner, it may include:
    - unstructured textual data
    - binary data
    - structured repositories
    - free-text descriptions

Basic VHT requirements

- A system agnostic to the supported classes and formats of data items, to support a comprehensive data repository where various data items may be queried, retrieved and fed into the computational models which constitute the simulation workflow

- Access to a computational infrastructure such as:
  - standalone servers for small-scale simulations
  - cloud computing infrastructures for simulations in which a moderately sized set of data is processed using complex algorithms
  - High Performance Computing for scale-out studies which involve processing large amounts of data and "parameter study" types of computations

Platform features (1/2)

- Model versioning - previous versions of the model are stored and may be referred to if needed
- Repeatable runs
  - **Repeatability** – same team, same experimental setup; a researcher can reliably repeat own computation
  - **Replicability** - different team, same experimental setup; an independent group can obtain the same result using the author's own artifacts
  - **Reproducibility** - different team, different experimental setup; an independent group can obtain the same result using artifacts which they develop completely independently
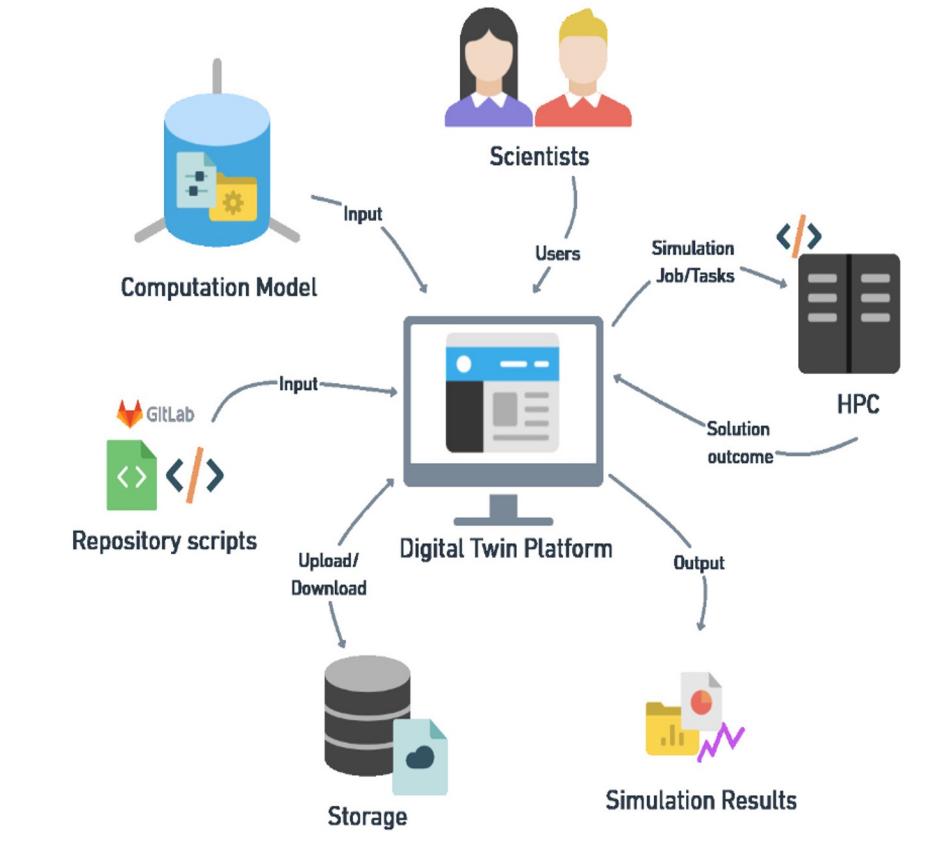
Platform features (2/2)

- **Coherent and manageable** to enable a group of scientists with various backgrounds to run digital experiments
- The system should enable execution of computational models controlled by a set of scripts with a **versioning system** enabling **collaborative editing and tagging** specific versions that may be later selected to suit the researchers' need
- The system should allow **streamline access** to compute infrastructures
- Models need to operate on data stored in a storage backend
- The platform should provide a straightforward way **to display, download and analyze** simulation results
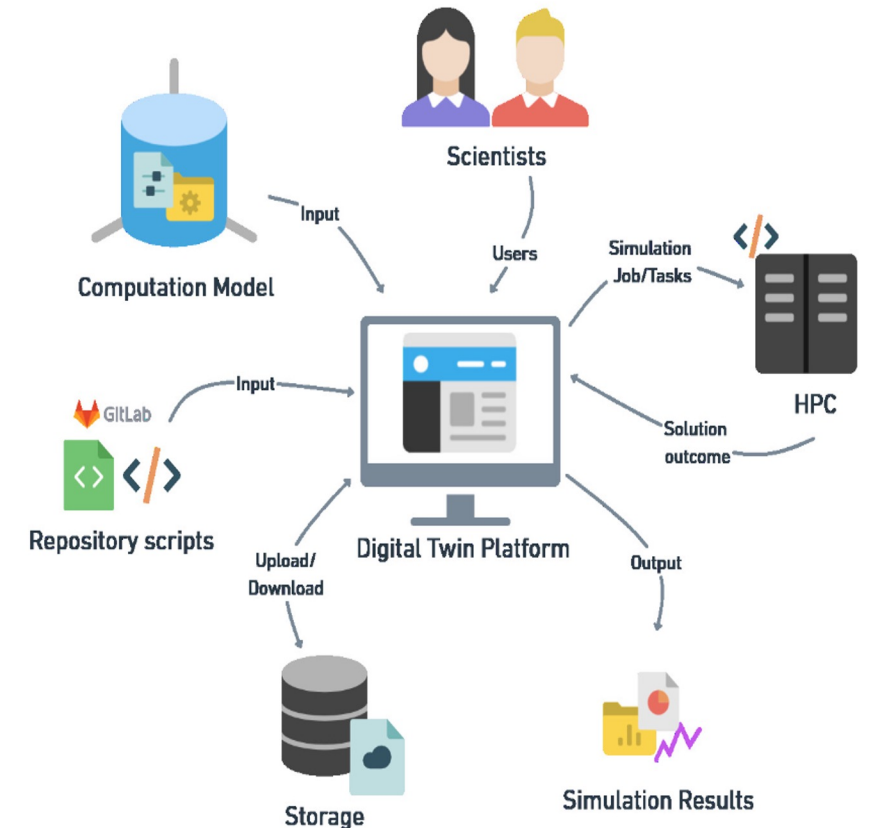
EDITH demonstrator – extended MEE

- Model Execution Environment (MEE) is a specialized HPC high-level service to manage data and computations in the context of a patient cohort
- MEE is the result of EurValve, PRIMAGE, and In Silico World (ISW) EU projects
- In EDITH MEE was extended based on requirements of a set of models and applied to validate virtual human twin idea
- MEE hides the complexity of the underlying infrastructure and introduces a unified way for patient/case data to be stored and maintained

Usage example - the BoneStrength application

Osteoporosis: bone metabolism disorder; causes bone mineral mass loss, bones become more fragile and prone to fracture
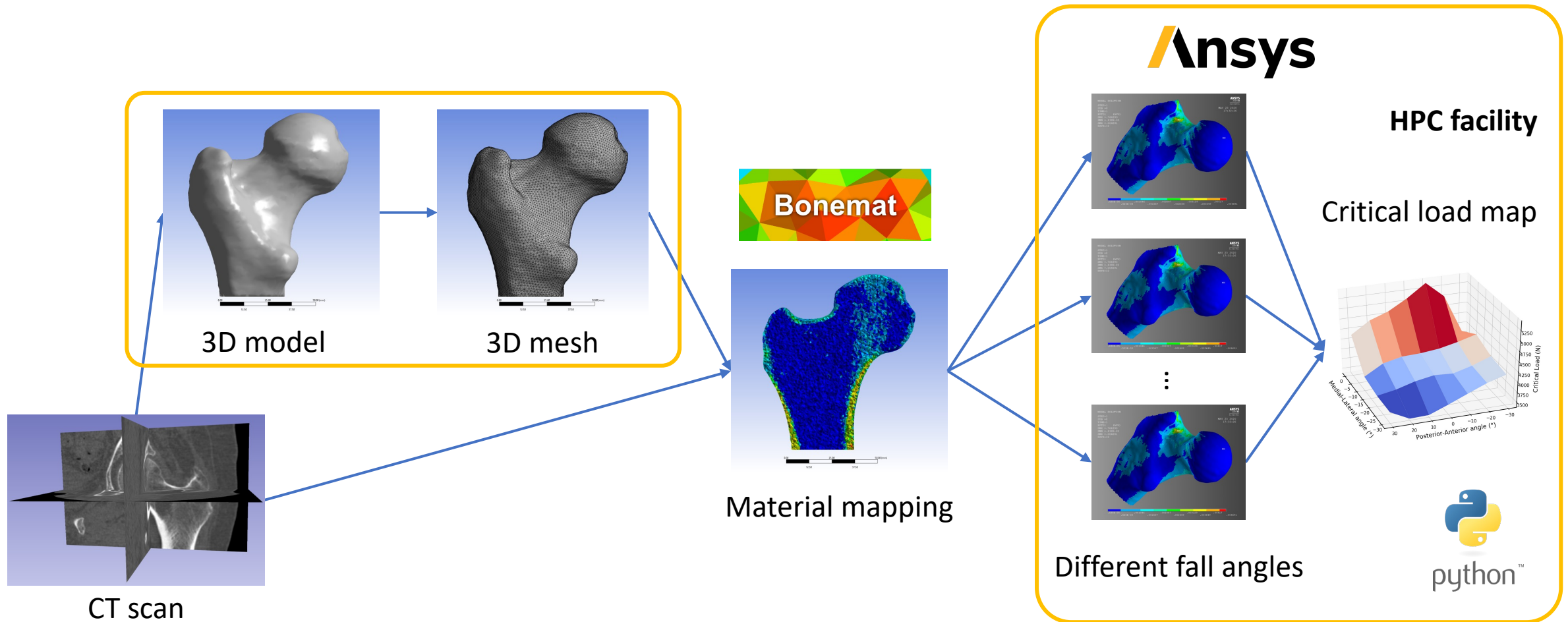
- mainly affects post-menopausal women

- about 3M fragility fractures in Europe every year (1-year mortality after fragility fracture at around 20%)

- osteoporosis drugs require long times to show effects
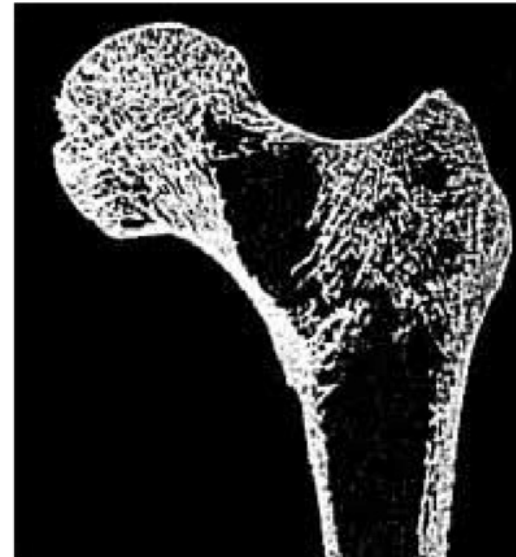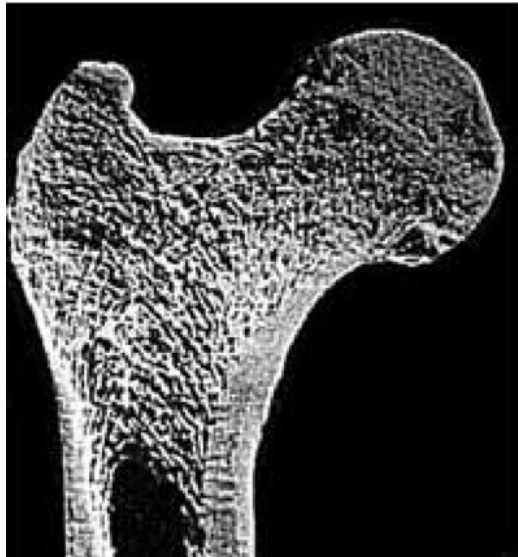
Healthy Osteoporotic

The BoneStrength workflow

CT scan

3D model

3D mesh

Bonemat

Material mapping

Ansys

HPC facility

Different fall angles

Critical load map

python

The BoneStrength application campaign

- The full BoneStrength campaign involved 7628 simulated falls
- Each fall requires between 1 and 2 hours to simulate to completion on a cluster node, HPC computing was provided by the Ares cluster at ACC Cyfronet
- The first cohort (0 g/cc/year) was successfully simulated, obtaining an incidence of 0.66% per year (69 fractures for 1044 patients in 10 years follow up)
- For the second cohort (resorption rate of 0.003 g/cc/year) predicted incidence was 0.89% per year (92 fractures for 1035 patients in 10 years follow up, given that for 9 patients simulations failed)
- Lastly, in the third cohort (resorption rate of 0.0064 g/cc/year) fracture incidence was 1.13% per year (116 fractures for 1028 patients in 10 years follow up)

In each case, we can successfully simulate at least 1000 patients, which is the common sample size for Phase III clinical trials.

Vision of personalised medicine

- Informed, empowered, engaged and responsible citizens
- Conscious, empowered, committed and responsible health care providers
- Health systems enable personalized, optimized health promotion and disease prevention, diagnosis and treatment for the benefit of patients
- Access to health information to optimize treatment, care, prevention and research
- Economic value by establishing a new generation of health care

Vicente, A. M., Ballensiefen, W. & Jönsson, J.-I. How personalised medicine will transform healthcare by 2030: the ICPerMed vision. J. Transl. Med. 18, 180 (2020), https://doi.org/10.1186/s12967-020-02316-w

Summary and future work

- VHT is a contribution to change medicine from a discipline based on the past experience to medicine led by scientific activities and similar to engineering
- Extended MEE as the EDITH demostrator is released on the open-source license - https://gitlab.com/cyfronet/mee)

- **GEMINI** - *A Generation of Multi-scale Digital Twins of Ischaemic and Haemorrhagic Stroke Patients:* Our role: elaboration of good practices to produce complex medical computer and next simulation experiments with virtual twin models run for a large cohort of patients on the ACC Cyfronet AGH infrastructure
- **Meetween:** new solutions for language-free collaboration between people using comprehensive, integrated algorithmic capabilities offered by fundamental models and self-supervised training on large data sets, and, as a result, we expect that AI solution will considerably enhance virtual human twins

Acknowledgements

Additional reading

- EDITH project VHT Roadmap available at https://www.edith-csa.eu/

- About virtual human twin in a popular way:
  - Peter Coveney, Roger Highfield: *Virtual You. How Building Your Digital Twin will Revolutionize Medicine and Change Your Life*, Princeton University Press, 2023
  - Marian Bubak, *Cyfrowi bliźniacy i medycyna przyszłości*, lecture at Copernicus Center, 21.09.2023, available on YouTube via https://sano.science/popularization-of-computational-medicine/

- About Sano Centre achievements:
  - Sano website - https://sano.science/
  - Tygodnik Powszechny 29.11.2023
  - Tygodnik Powszechny 13.03.2024