Digital Twins and AI for Precision Medicine

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Yale SCHOOL OF MEDICINE

AI Applications in Medicine

- Disease diagnosis, screening, monitoring, and treatment
- Large language models (LLMs)
- Clinical decision support
- Virtual reality and augmented reality
- New drug discovery
- Virtual clinical trials
- Telemedicine
- Human machine interface
- Digital twins for health
- ……

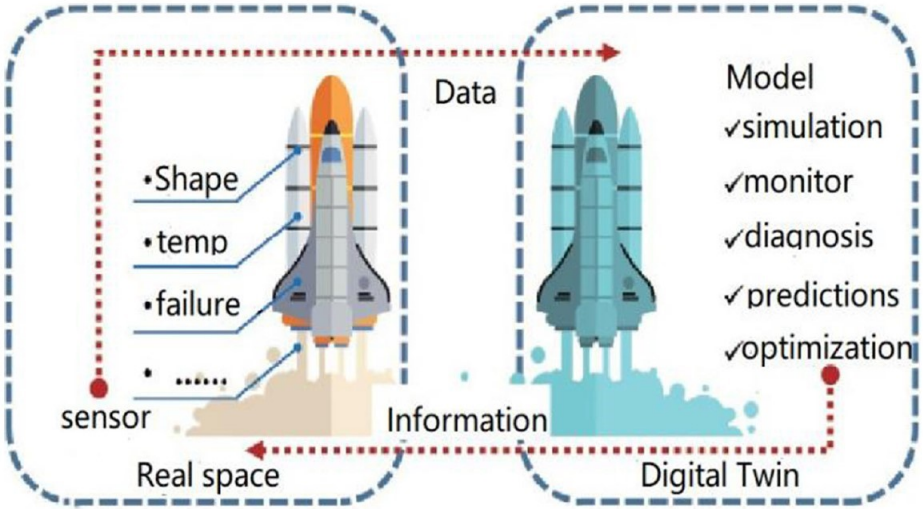
Modern medicine is increasingly becoming a science of information

What is a Digital Twin?

- **A digital representation of a real-world physical system** that serves as the effectively indistinguishable digital counterpart of the original for simulation, integration, testing, monitoring and maintenance

- Used in real time and **regularly synchronized** with the physical system

- Originated from NASA in 2010 to improve physical model simulation of spacecraft



Three Catalysts

- Multimodal data

- Mechanistic & data-driven modeling

Mechanistic Models

$$\frac{\partial C}{\partial t} = \frac{\rho_b}{\varepsilon}\frac{\partial \langle q \rangle}{\partial t} - u\frac{\partial C}{\partial z} + D_z\frac{\partial^2 C}{\partial z^2}$$

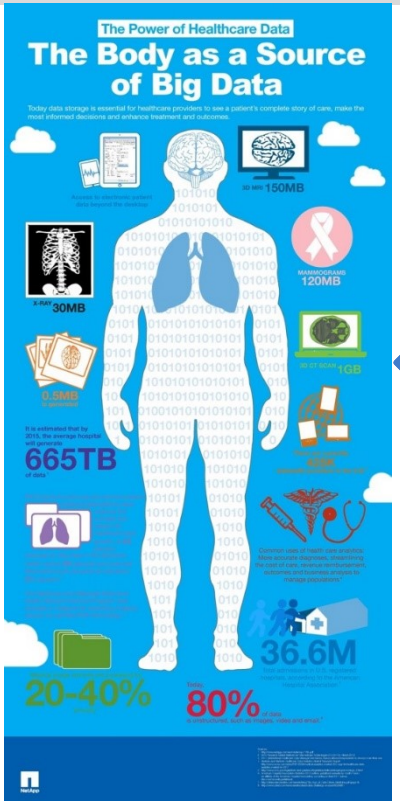
Adsorption Model, ASM Models, etc.

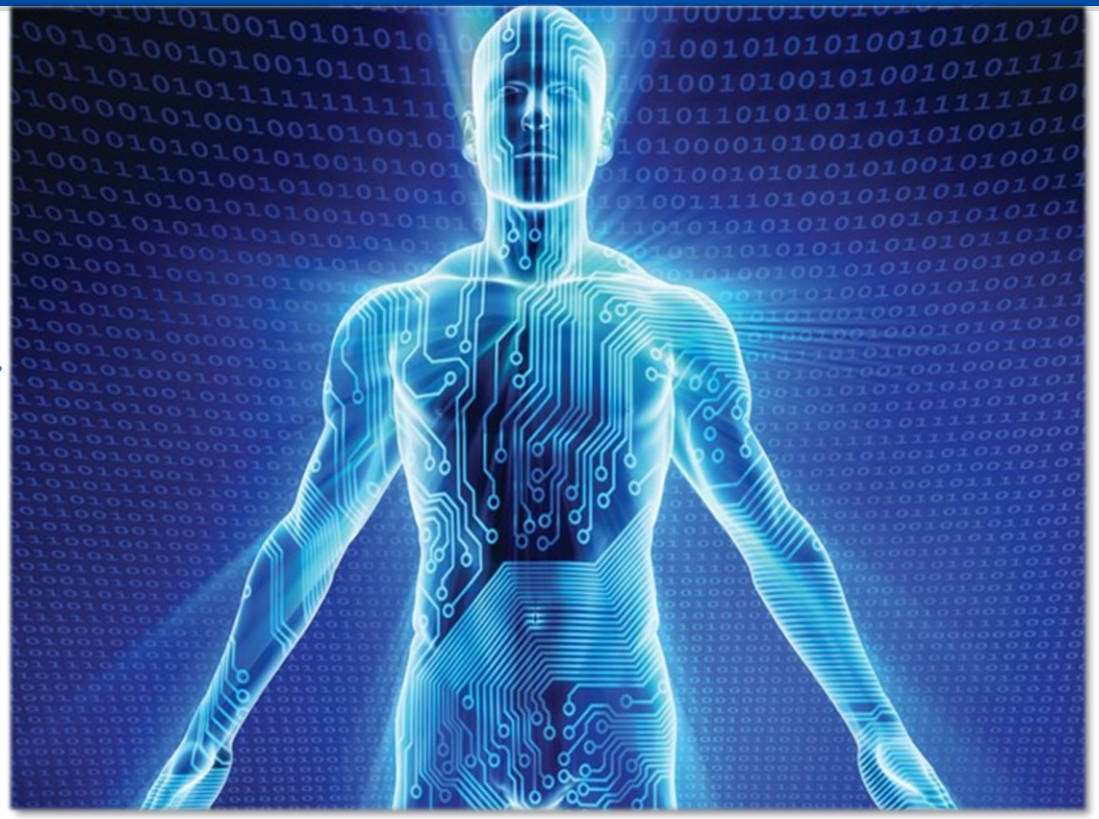
Data-driven Models

Artificial Neural Network, Random Forest, etc.

- High-performance computing

Our Big Idea

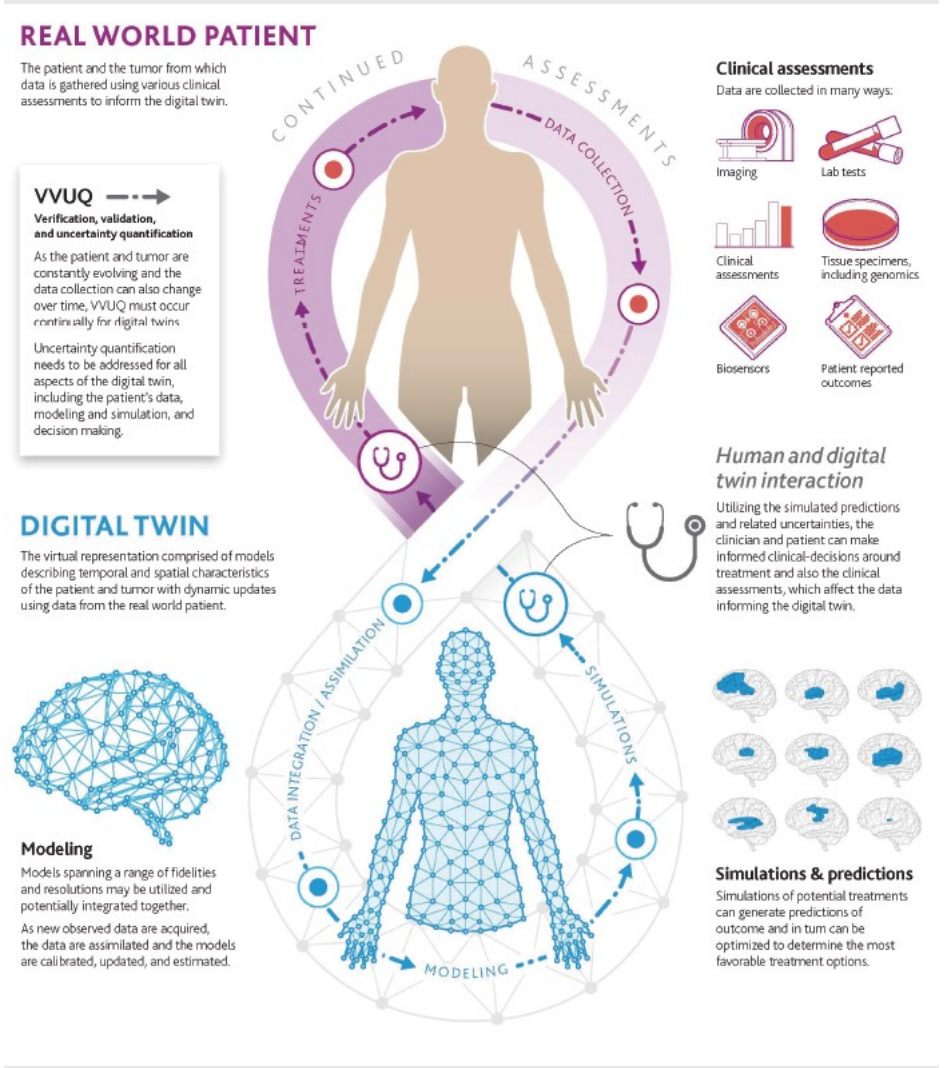

The Power of Healthcare Data
The Body as a Source of Big Data
150MB
MAMMOGRAMS 120MB
30MB
1GB
0.5MB
665TB
36.6M
20-40%
80%



NATIONAL ACADEMIES *Sciences Engineering Medicine*

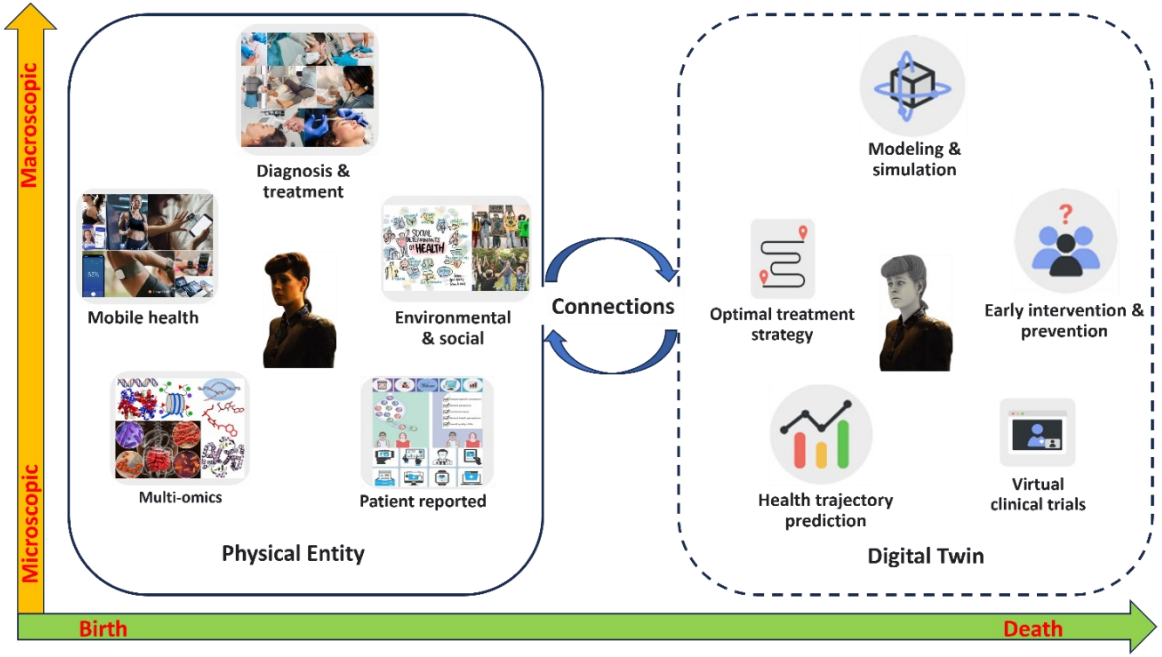
Foundational Research Gaps and Future Directions for Digital Twins

Consensus Study Report



A Human Digital Twin

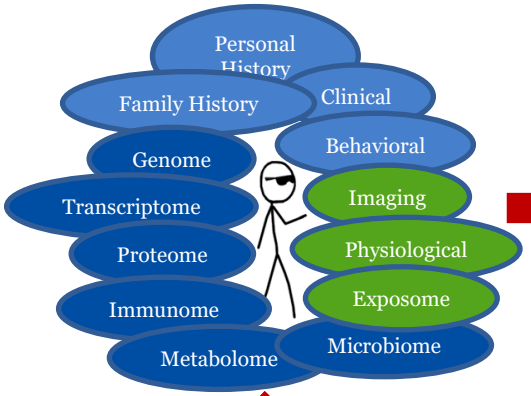
- A dynamic virtual representation of an individual, an organ, or an organ system based on multiscale modeling of multimodal data



Katsoulakis et al, npj Digital Medicine, 7, 77 (2024)

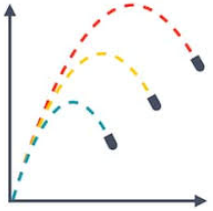
The Big Picture

Personal Phenotypes



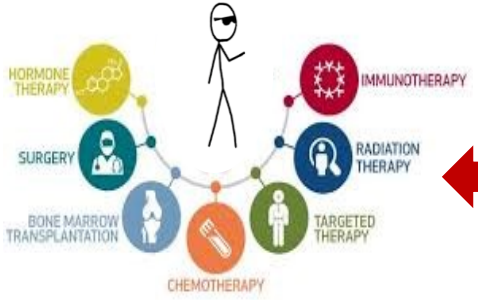
Digital Twin Simulation Using HPC

Personalized Care Trajectories



Shared Decision Making

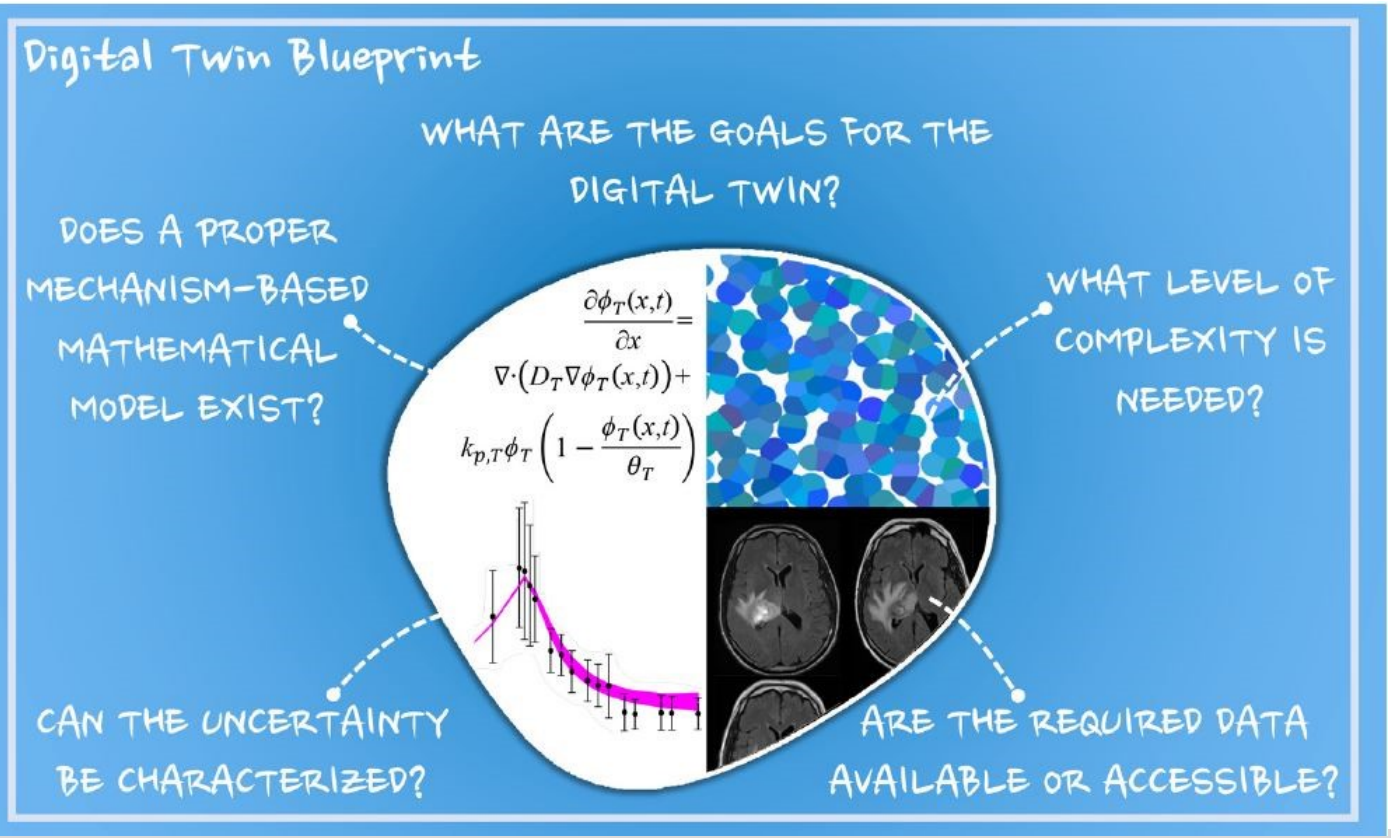
Choose a care path



What Would DT Enable?

- Incorporate genetic, molecular, clinical, environmental, and social factors to predict individual trajectories
  - Identify optimal treatment strategy
- Predict outcomes and side effects throughout one's health trajectory
  - Improve quality of life
- Benchmark clinical performance via virtual control
  - Enable virtual clinical trial
- Early intervention and prevention for general public

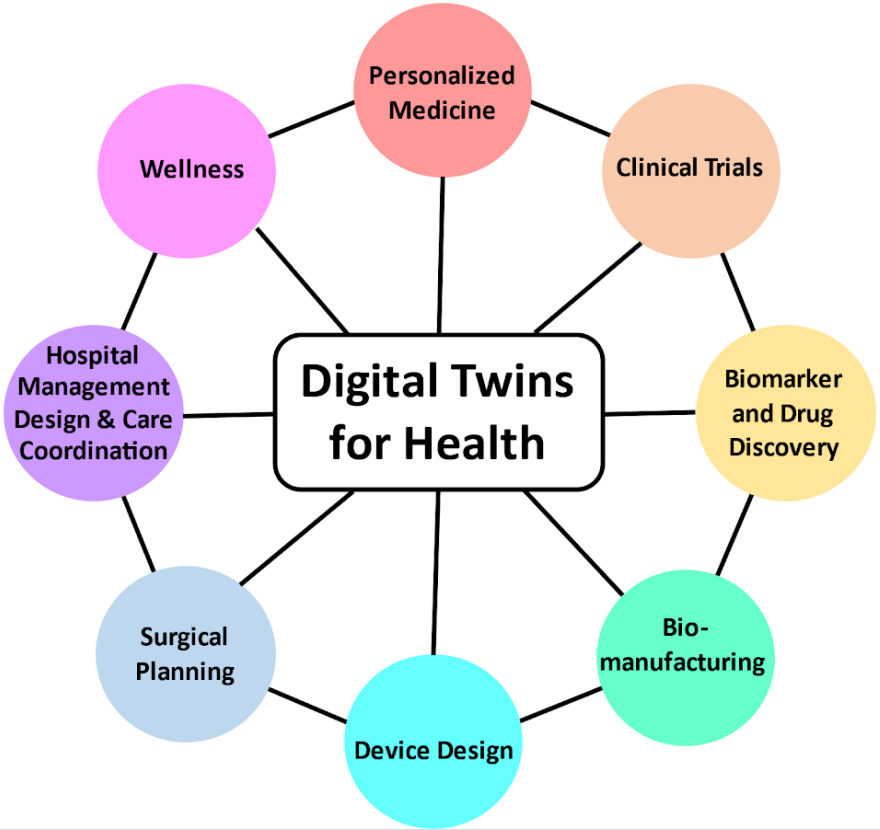
Digital Twin Blueprint



- "All models are wrong but some are useful", George Box
- "Everything should be made as simple as possible, but not simpler", Albert Einstein

Wu et al., Biophysics Rev. 3, 021304 (2022)

Main Applications of DT in Health



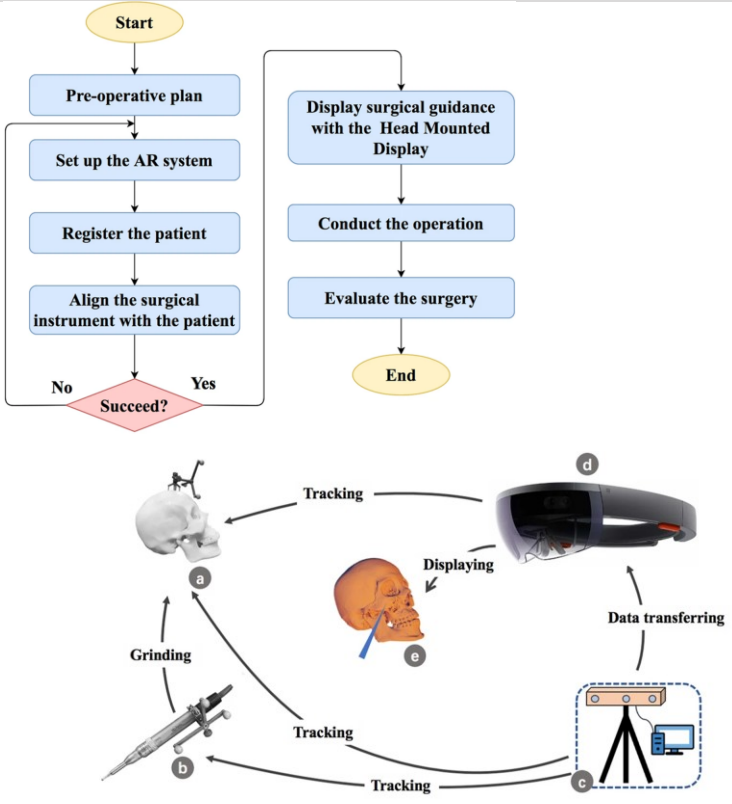
Virtual Clinical Trials

- **Increase the statistical power**
- **Enhance patient recruitment**
  - Targeted selection of right patients and in silico simulation for estimated outcomes
  - Increase the likelihood of success for the proposed trial
- **Help physicians in making adaptive and personalized clinical decision for their patients**

Virtual Drug Testing

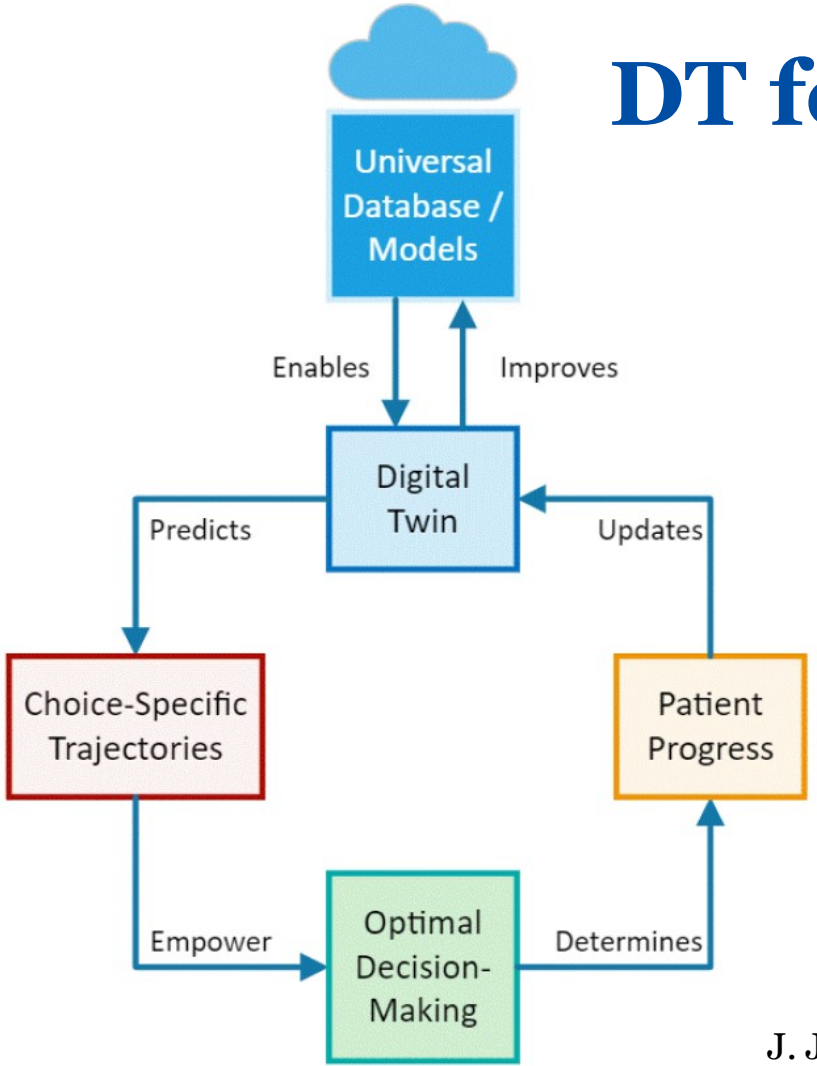
- Testing various candidate drugs against a target protein can be done through computational models
- Candidates can be ranked according to their ability to interact with the target - their binding affinity
- Best candidates then chosen for the patient specific target

DT of a Surgical Patient



Liu et al. Sci Rep 11, 10043 (2021)

DT for Radiation Oncology



Components

- Multimodal patient data
- Multiscale modeling
- High-performance computing

Benefits

- Predicting patient outcomes
- Treatment plan optimization
- Innovative research tools

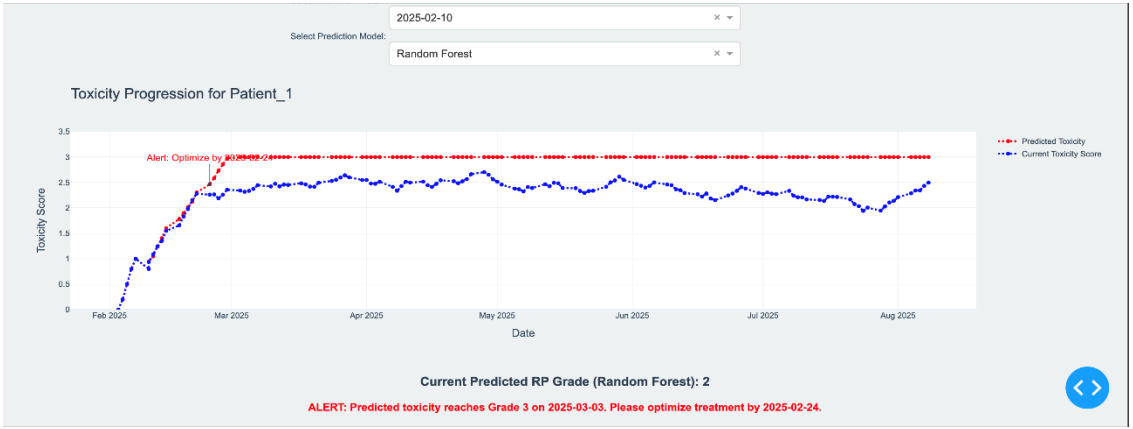
Barriers

- Centralized data commons
- Patient-specific data assembly
- Multiscale modeling

J. Jensen and J. Deng, https://doi.org/10.1145/3543873.3587688

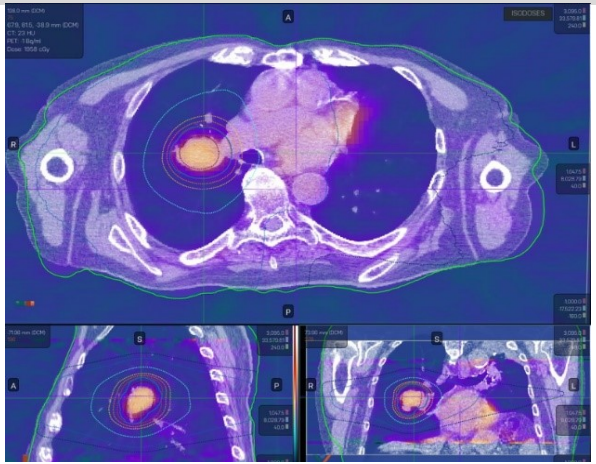
Cancer Patient Digital Twin

- **Patient health prediction**
- **Treatment outcome trajectory**
- **Shared decision-making involving patients**
- **Whole body all organ tracking and monitoring**

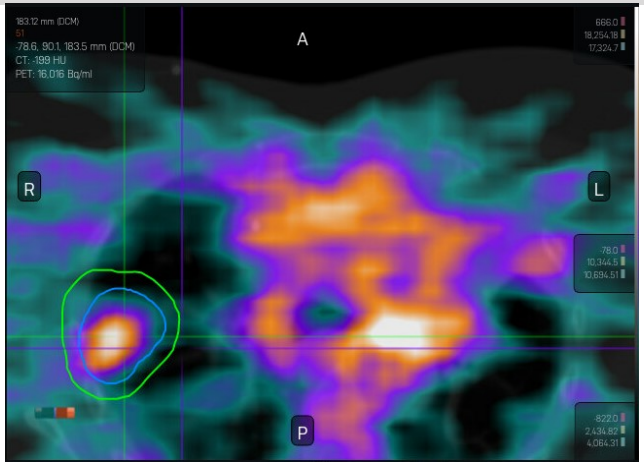


Human body is an all-connected dynamic and open system

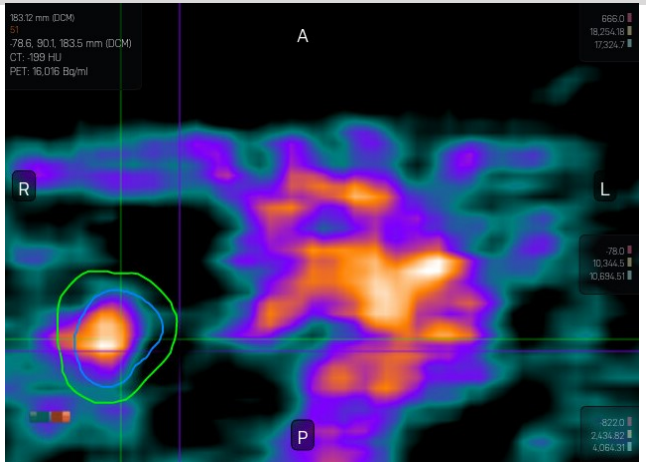
Biology-Guided Radiotherapy



PET/CT merge



PET scan before treatment



PET scan in treatment

A reaction diffusion model including RT-induced cell death

$$\frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho c\left(1 - \frac{c}{k}\right) - R(x, t, Dose)c\left(1 - \frac{c}{k}\right)$$

Develop digital twins to predict NSCLC response to RT *via* integrating ***mechanistic modeling*** with ***patient-specific longitudinal PET scans***

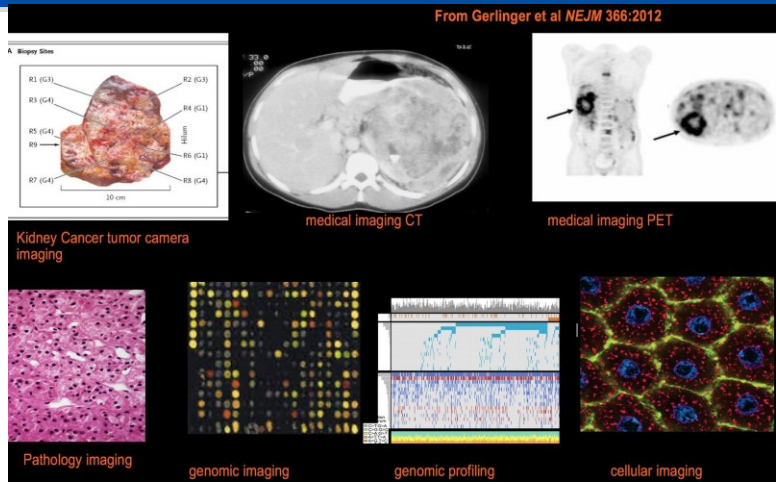
PET scans courtesy of Huixiao Chen, PhD

Challenges

- **Data Acquisition, Integration, Standard, and Quality**
  - Multimodal data acquisition, integration and curation
  - Data standards, quality and accuracy
- **Multiscale Modeling and Simulations**
  - Complex human behaviors with vast dynamic impacting factors and sophisticated causal relations
  - Dynamic biological phenomena at multiscale in space-time
- **Responsible AI**
  - Fairness, transparency (explainability), accountability, robustness, safety, privacy, and security
- **Computing Infrastructure**
  - HPCs, quantum computing, and their access

Multimodal Data Fusion

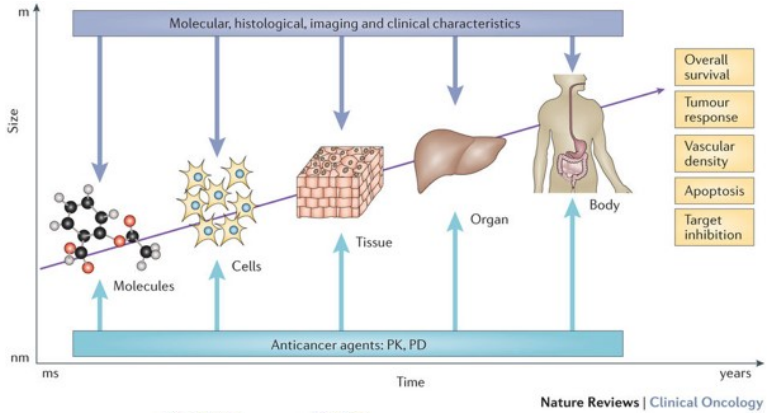
- Functional and molecular imaging
- Radiomics (deep learning-augmented analysis of radiology)
- Liquid biopsies (e.g., circulating tumor cells)
- Whole-slide, highly-multiplexed digital pathology
- Genomic profiling
- Single-cell profiling (e.g., scRNA-seq)
- Patient-derived cell cultures, organoids, & assays
- Intravital imaging (live microscopy within a patient)
- Fitness trackers & wearables
- Implantable sensors

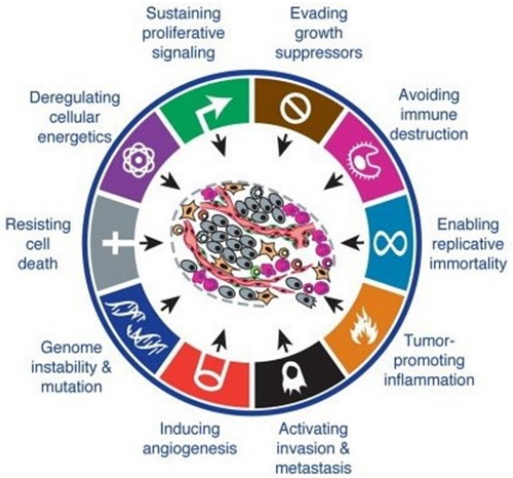


Each technology gives new light on a patient's health state, but it is challenging to coherently *fuse* these together

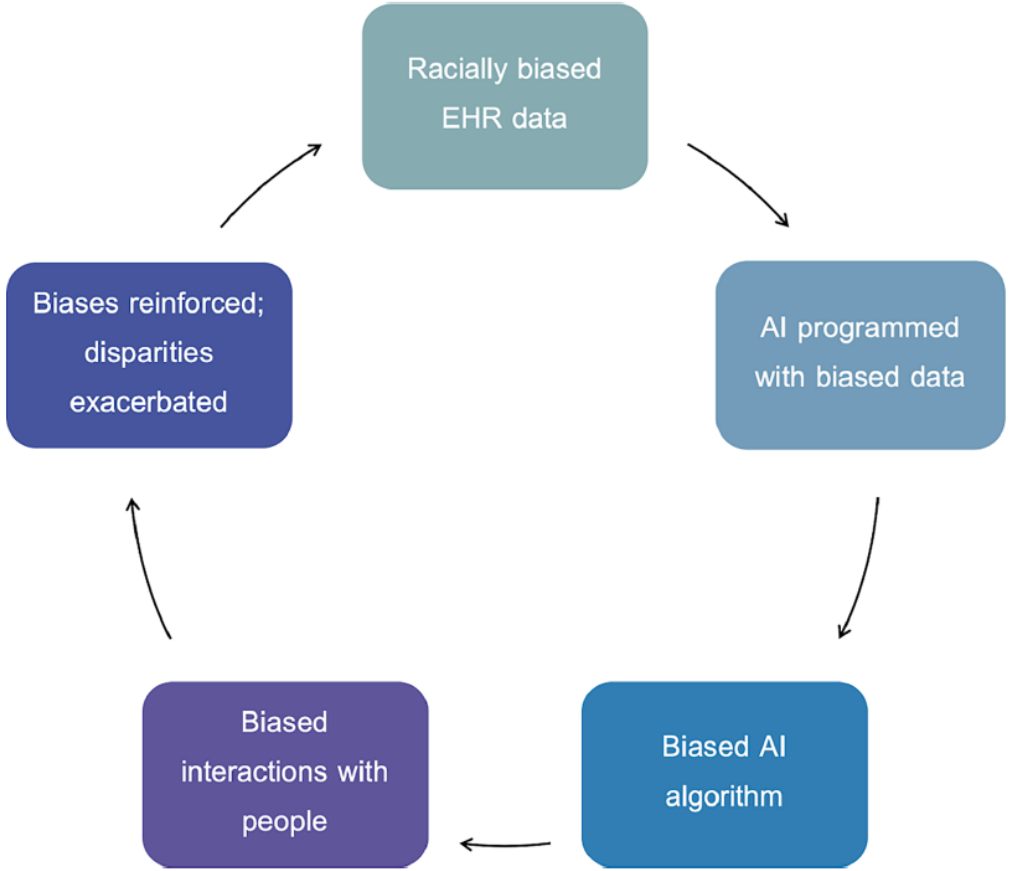
Complex Human Body

- Individual cell processes and dynamics
- Interactions between heterogeneous cells
- Physical constraints (e.g., oxygen diffusion, mechanical barriers)
- Procedures can cause toxicity, resistance, and long-term adverse effects
- Constant interactions with environment
- Social determinants influence one's health and wellbeing across life course
- Many factors involved (e.g., lifestyle, dietary, family history, medication)





Responsible AI



- Require right people, right processes, and right technologies
- Clinical practitioners need to be trained to understand what responsible AI means, what tools and metrics are available to quantify and evaluate responsible AI
- Appropriate technologies need to be used to enforce responsible AI from the beginning to the end for every model, every time

Into the Future

- Artificial General Intelligence (AGI)
  - PhD level intelligent systems/robots (arriving in 2029 or so?)
- Quantum computing
  - > 10^8 times faster than Frontier HPC
- Physical AI or spatial intelligence
  - AI that can see, talk, and do
- Human digital twin from birth to death
  - Fully autonomous as HDT agents
  - Companion and safeguard of one's health

Ability to simulate the future has been a motive for human intelligence evolution

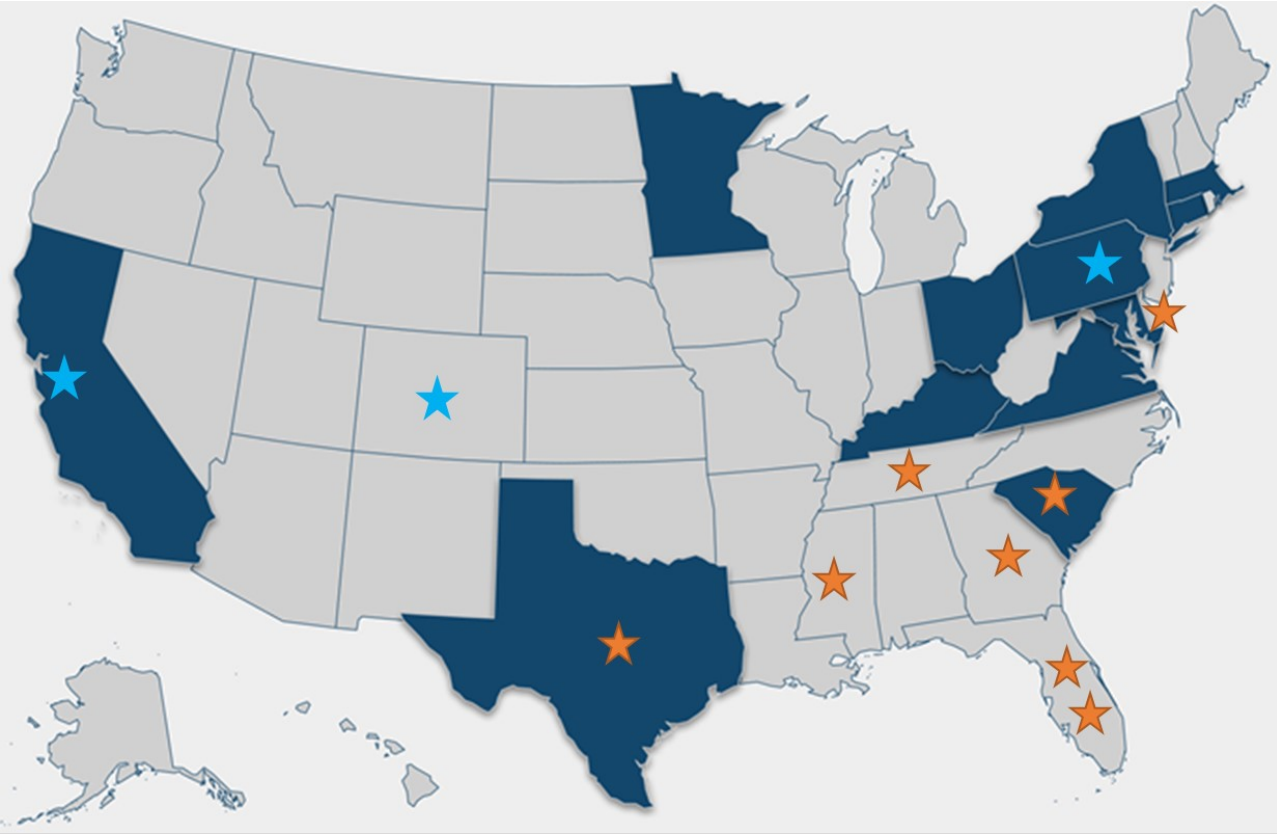
Take Home Messages

- Digital twins have great potential in precision medicine
- Deep understanding of human biology is the key
- Multimodal data integration and multiscale modeling are challenging
- We must tame AI before the arrival of AGI
- Cross-disciplinary collaborations are essential

Acknowledgement

Digital Twins for Health Consortium

Digital Twins for Health Consortium



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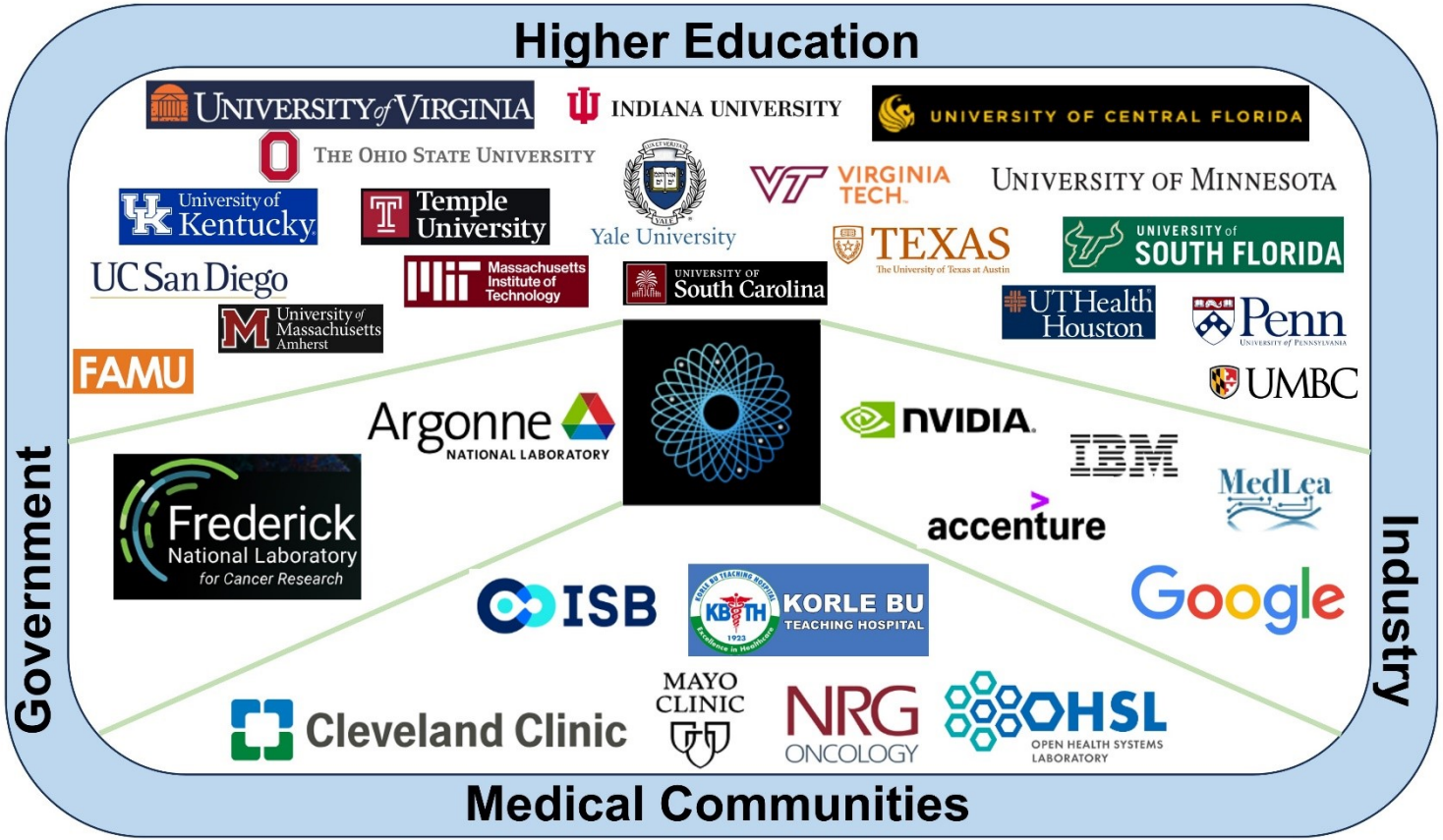
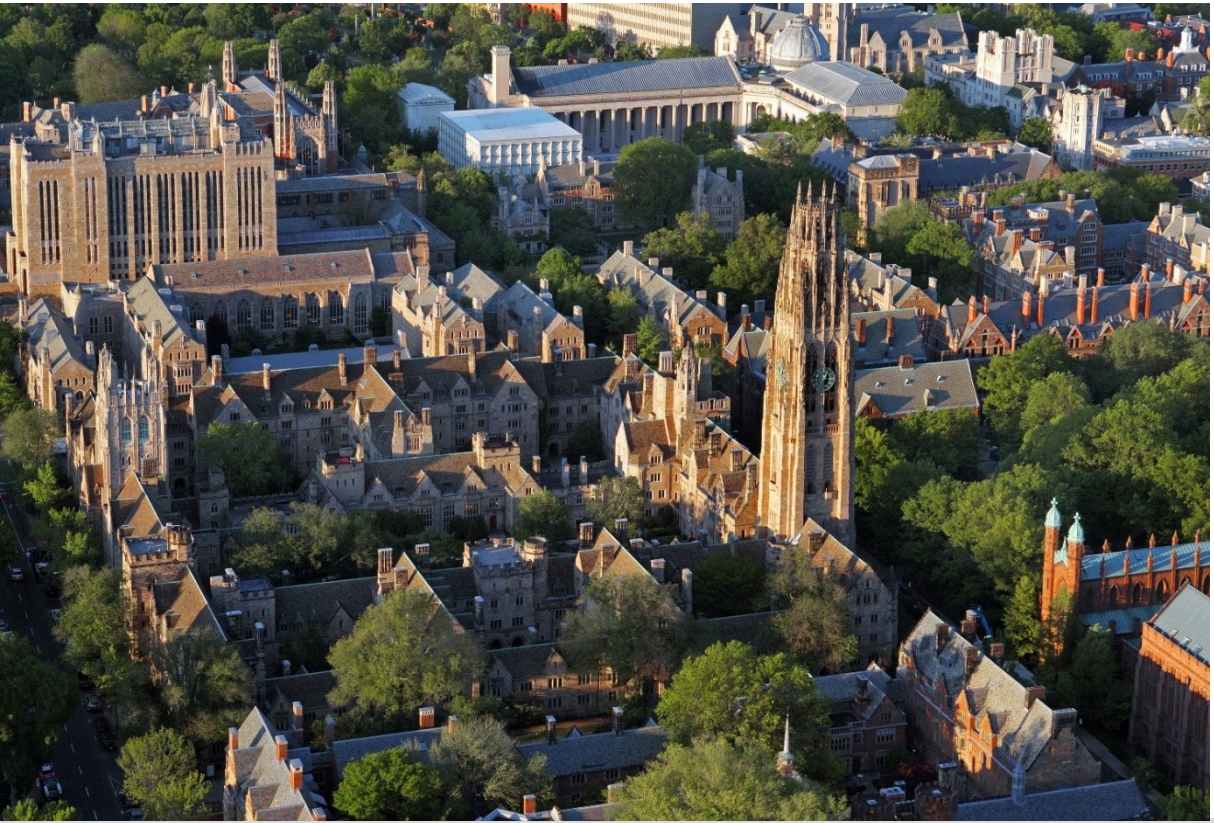
- Mayo Clinic
- IBM
- Accenture

DT4H Ecosystem



https://dt4h.org

Thank You



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