Tampere University

Digital Twins in Healthcare: New Opportunities?

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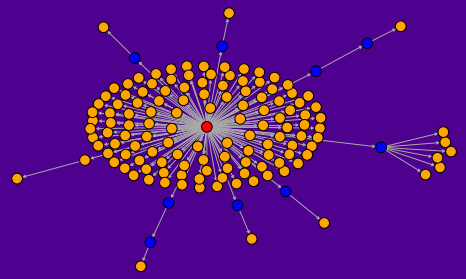


EHTEL webinar

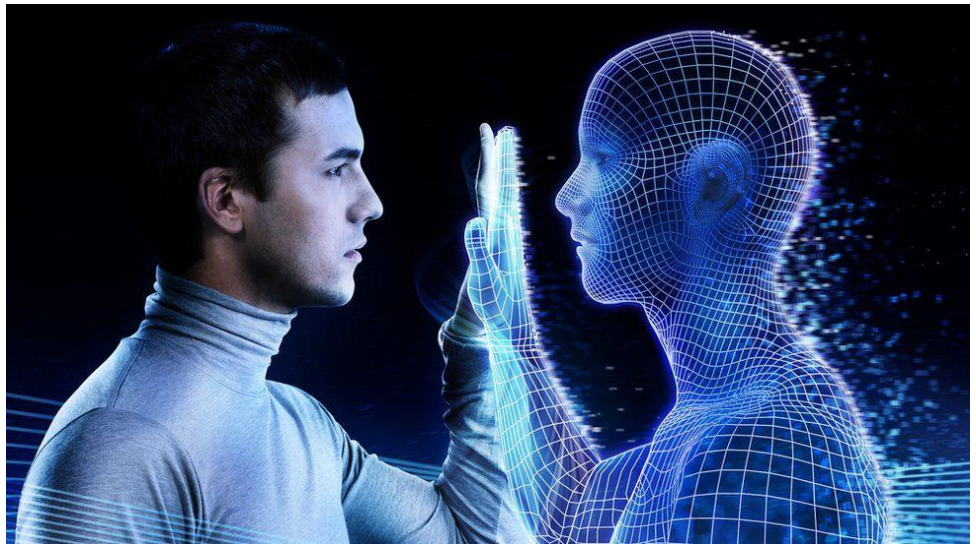
Overview

Content:

1. Origins of digital twins
2. What are digital twins?
3. Multidisciplinary applications

Background

4. **Main advantage(s)** of Digital Twins
   - Testing Virtual interventions
5. Summary

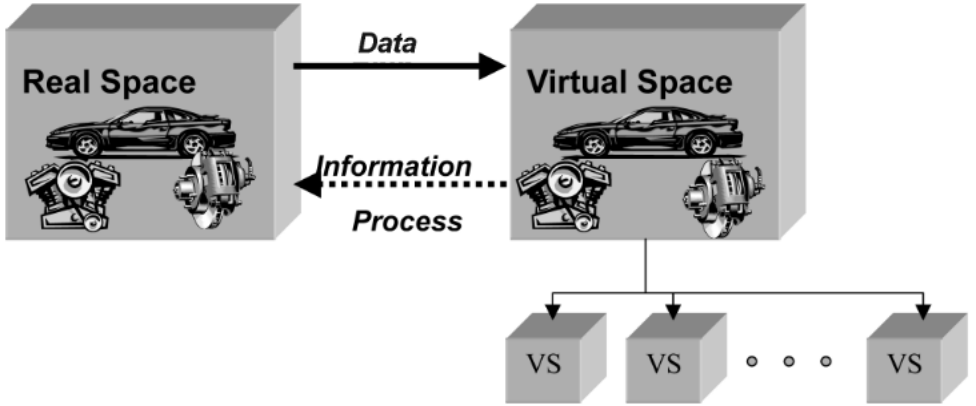


Good visualization yet misleading impression.

Origins of a digital twin

Michael Grieves is widely recognized as the first to describe the concept of a digital twin in more technical terms although also he did not provide a formal definition.

Grieves, M.W. Product lifecycle management: The new paradigm for enterprises. Int. J. Prod. Dev. **2005**, 2, 71–84



Originally called:
Mirrored Spaces Model (MSM)

Gelernter, D. **Mirror Worlds**: Or the Day Software Puts the Universe in A Shoebox… How It Will Happen and What It Will Mean; Oxford University Press: Oxford, UK, **1991**

Virtual alternatives

↓

Multiple digital twins

What are digital twins?

First definition of a DT by NASA (**2012**):

“The Digital Twin is an integrated multiphysics, multiscale, probabilistic simulation of an as-built vehicle or system that uses the best available physical models, sensor updates, fleet history, etc., to mirror the life of its corresponding flying twin”.

Descriptive list: In the manufacturing and engineering literature there are many more similar definitions.

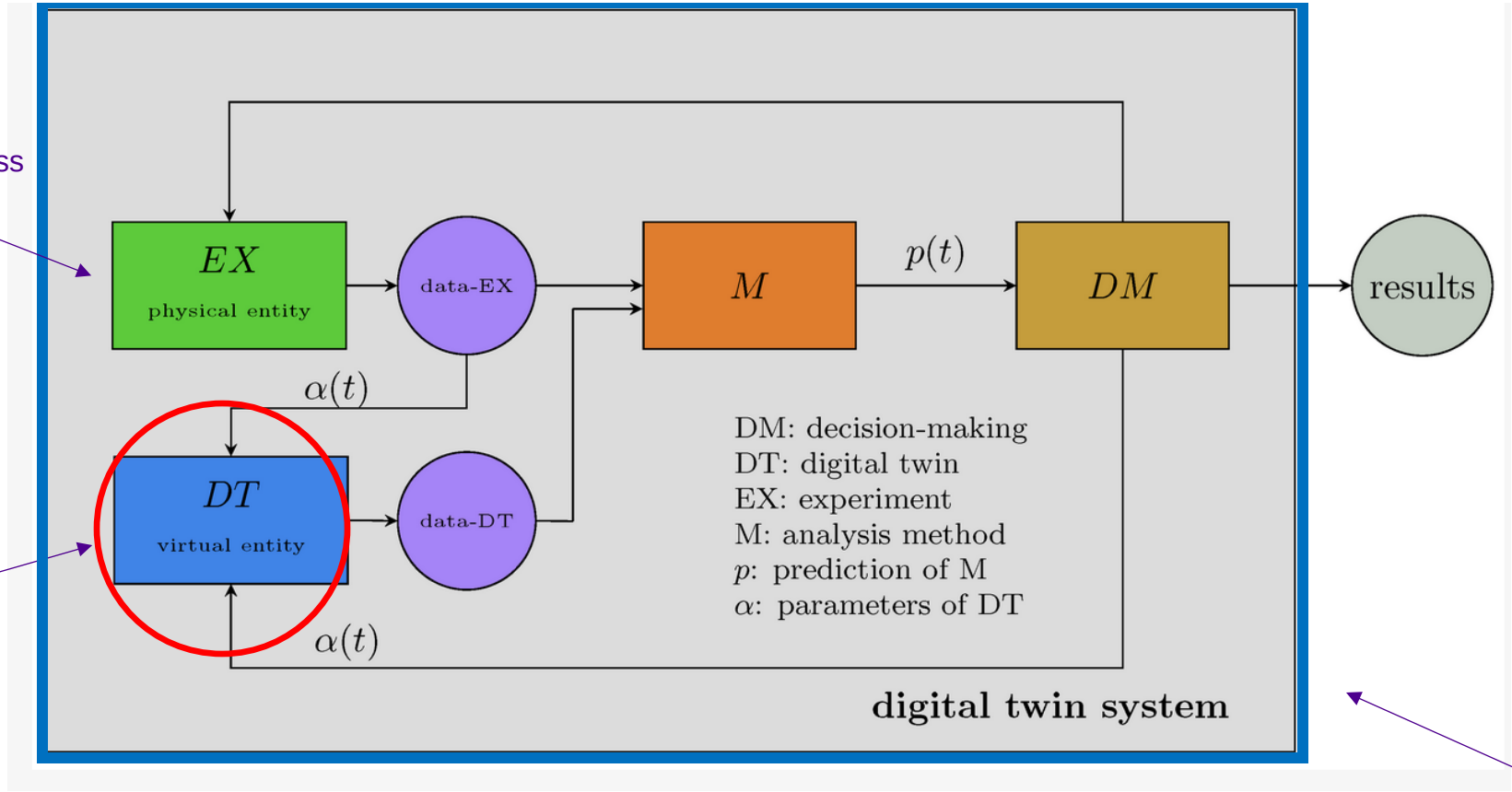
Our approach: Data science-based definition based on functional relations between data

Emmert-Streib, Frank. "Defining a Digital Twin: A Data Science-Based Unification." *Machine Learning and Knowledge Extraction* 5.3 (**2023**): 1036-1054.

Emmert-Streib, Frank, and Olli Yli-Harja. "What is a digital twin? Experimental design for a data-centric machine learning perspective in health." *International journal of molecular sciences* 23.21 (**2022**): 13149.

DTS is given by functional relations whereas a DT is just a part of it.

- Manufacturing process
- Product design
- Patient



Digital twin (DT)

Digital twin system (DTS)

What-If scenarios
(different hypothesis) → Multiple digital twins

Examples for applications

- Manufacturing
- Engineering

Classic applications (~ 2005)

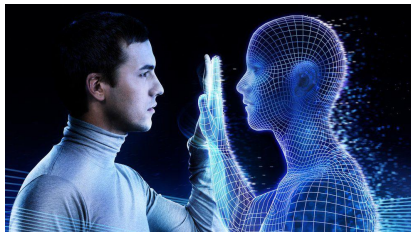
- Immunology
- Oncology
- Urban development
- Supply chain management
- Climate research

Recent applications (~ 2018)

Shrivastava, C., Berry, T., Cronje, P. *et al.* Digital twins enable the quantification of the trade-offs in maintaining citrus quality and marketability in the refrigerated supply chain. *Nat Food* **3**, 413–427 (2022).

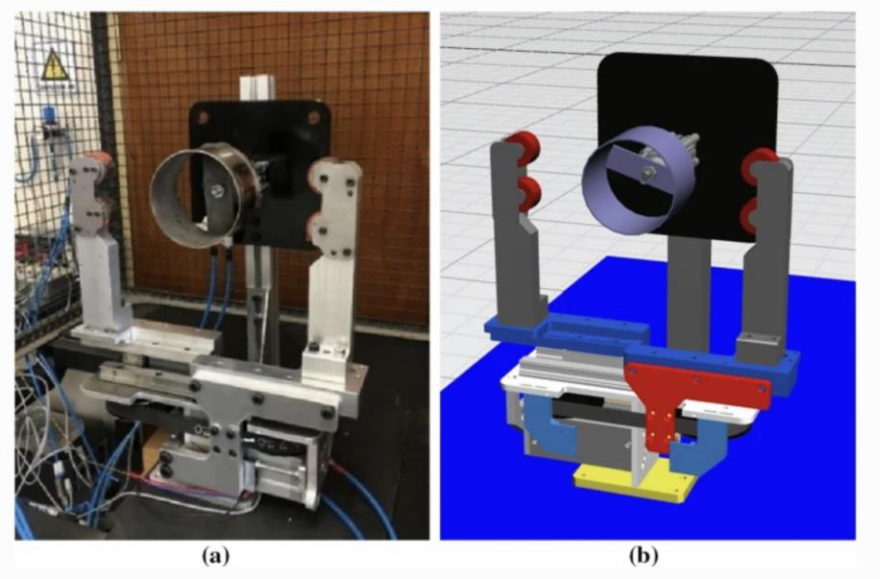
Bauer, P., Stevens, B. & Hazeleger, W. A digital twin of Earth for the green transition. *Nature Climate Change.* **11**, 80–83 (2021)

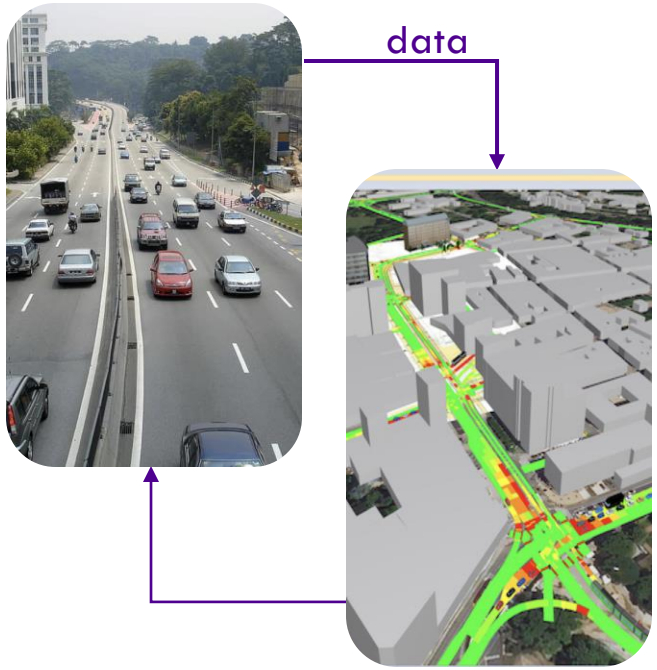
Zooming out: Bigger picture



Applications in Manufacturing and Engineering

Mechanistic models of physical objects → "See" what is happening (pictures, videos)



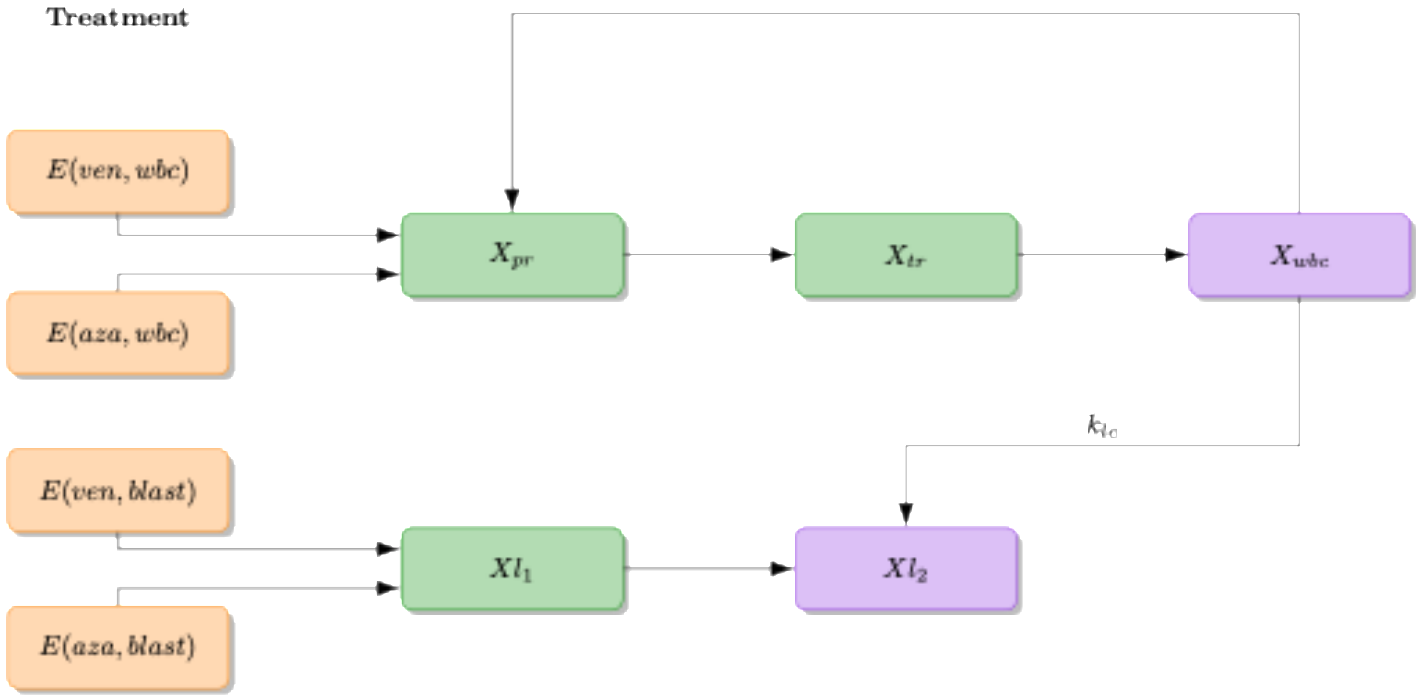


- Manufacturing
- Urban planing
- Engineering

AML-DT:

Acute Myeloid Leukemia

Regulatory network



System of ODEs

Observed variables

Unobserved variables

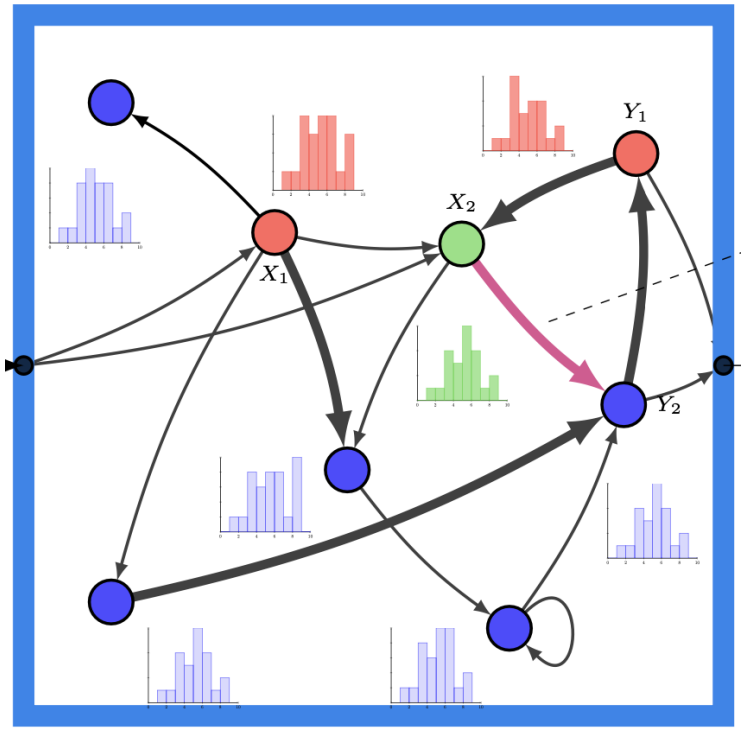
$$\dot{X}_{pr} = -k_{tr}X_{pr} + k_{tr}(1 - E(ven, wbc) - E(aza, wbc))\left(\frac{B}{X_{wbc}}\right)^{\gamma}X_{pr}$$
$$\dot{X}_{tr} = k_{tr}(X_{pr} - X_{tr})$$
$$\dot{X}_{wbc} = k_{tr}X_{tr} - k_{wbc}X_{wbc}$$
$$\dot{X}_{l1} = (2 * a_1 * k_{lc} - 1) * p_1 * X_{l1} - p_1 * (E(ven, blast) + E(aza, blast) * X_{l1}$$
$$\dot{X}_{l2} = 2 * (1 - a_1 * k_{lc}) * p_1 * X_{l1} - d_2 * X_{l2}$$

$$k_{lc} := \frac{1}{(1 + c_1 * X_{wbc} + c_2 * X_{l2})}$$
$$E(ven, wbc) = slope_{ven_{wbc}} * ln(1 + X(ven, central))$$

Zhang, et al. "Digital Twin Models for Predicting Venetoclax and Azacitidine-induced Neutropenia in Patients with Acute Myeloid Leukemia", npj Digital Medicine, submitted.

Zooming out: Bigger picture

Complex systems of physical objects → Abstract characterization (networks, graphs etc)



Complex systems are spacially and temporally simplifications/abstractions of real-world systems.

- Epidemiology
  - SIR (**S**usceptible, **I**nfectious, or **R**ecovered)
  - SEIR
- Economics
  - Supply chains
  - Trading
- Biology, Health, Medicine, Pharmacogenomics
  - Gene regulatory networks
- Climate research

Simulation of dynamical behavior (e.g. corresponding to gene activity)

What is new?

A Look Back at the Science of Data Analysis

1. Phase: Statistics
- Started in 18th century
- Systematic collection of demographic and economic data by states
- Purpose: **Summarization** of data

2. Phase: Big data
- Started in 1990s (human genome experiment)
- Data-driven statistical and machine learning models
- Purpose: Making **predictions**

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3. Phase: Digital twins
- Started in 2000s
- Purpose (multiple): Studying **virtual interventions** → Testing "What-If" scenarios

New and different capability!

Cumulation of capabilities

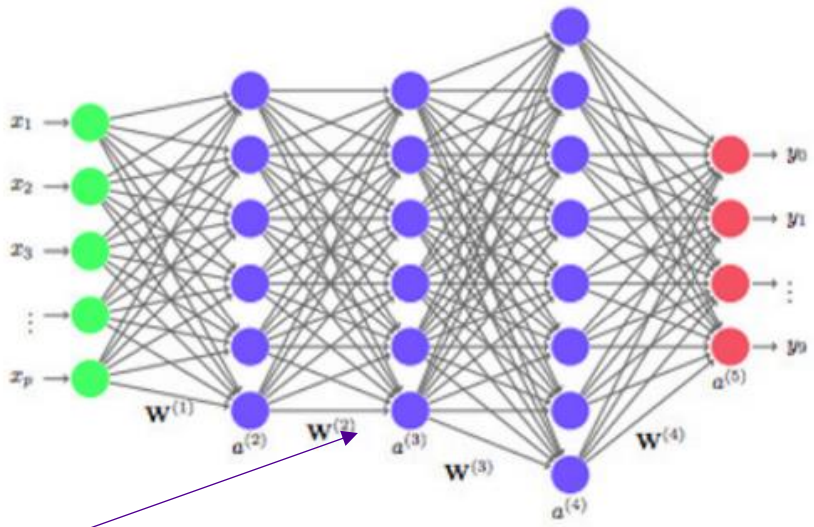
Time

Advantages of digital twins: Virtual Interventions

Typical prediction model

Deep learning neural networks

Data
Historic events



Prediction
Copy history

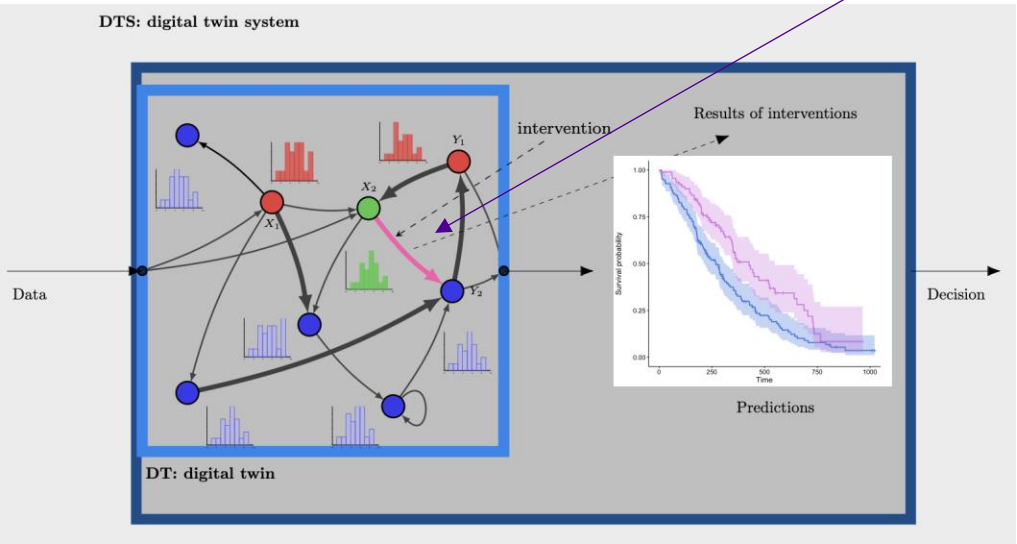
Components have no meaning! ⟵ Black box model

Advantages of digital twins: Virtual Interventions

Digital twin model

New event: Administration of a drug changes protein-protein interaction

Mechanistic model



Data
Historic events

Prediction
Copy history

What-If scenarios

Effect of Interventions

New feature of Digital twins

Components have a meaning! ⟵ Interpretable model

One can not only make predictions but also study **effects** of **virtual interventions** (e.g. **testing drugs**).

Summary

- **Digital twin** is like a **Matryoshka doll** (many components + multiple purposes).
- Digital twins in health **focus on specific health-related aspects** rather than representing the entire organism
- Main **advantages** of digital twins:
  - Virtual interventions → testing drugs or treatment options
  - Become more "useful" over time (via learning) → better predictions
- Examples in health:
  - Testing drugs (decision support)
  - Testing hospital policies (health economics)
- Beyond a digital twin: **Complexity data science** → **Methodology**

Emmert-Streib, Cherifi, Kauffman and Yli-Harja, Moving Beyond Simulation and Learning: Unveiling the Potential of Complexity Data Science, PLoS Complex Systems, 2024.

Emmert-Streib, Cherifi, Kaski, Kauffman and Yli-Harja, Complexity Data Science: A spin-off from digital twins, PNAS Nexus, accepted.

Emmert-Streib, Hood, Yli-Harja, A new paradigm for P4 medicine: digital twins, in preparation.

Tampere University

Thank you!

Prototype System for acute myeloid leukemia (AML) Digital Twins (2023 – 2028)

- Ilya Shmulevich, Institute for Systems Biology, USA
- Caroline Heckman, Institute for Molecular Medicine Finland
- Mika Kontro, Institute for Molecular Medicine Finland
- Heikki Kuusanmäki, Institute for Molecular Medicine Finland
- Boris Aguilar, Institute for Systems Biology, USA
- Guangrong Qin, Institute for Systems Biology, USA
- Olli Yli-Harja, Tampere University, Finland
- Amer Farea, Tampere University, Finland
- Jerome Chandraseelan, Tampere University, Finland

Funding:

ACADEMY OF FINLAND

NIH National Institutes of Health
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