# Building around a model: Cancer Digital Twin (CDT)

Presenter: Carlos F Lopez
Institution: Altos Labs
(These are my opinions and not those of Altos Labs).

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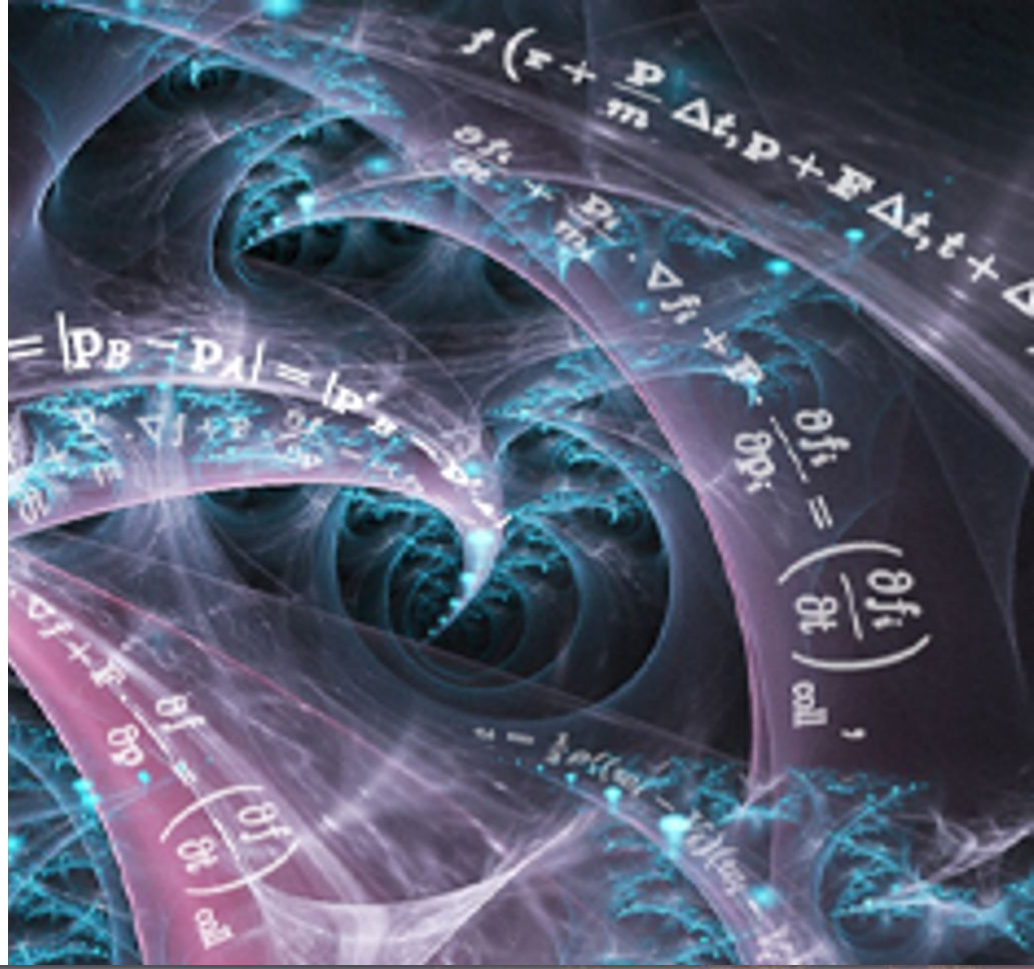
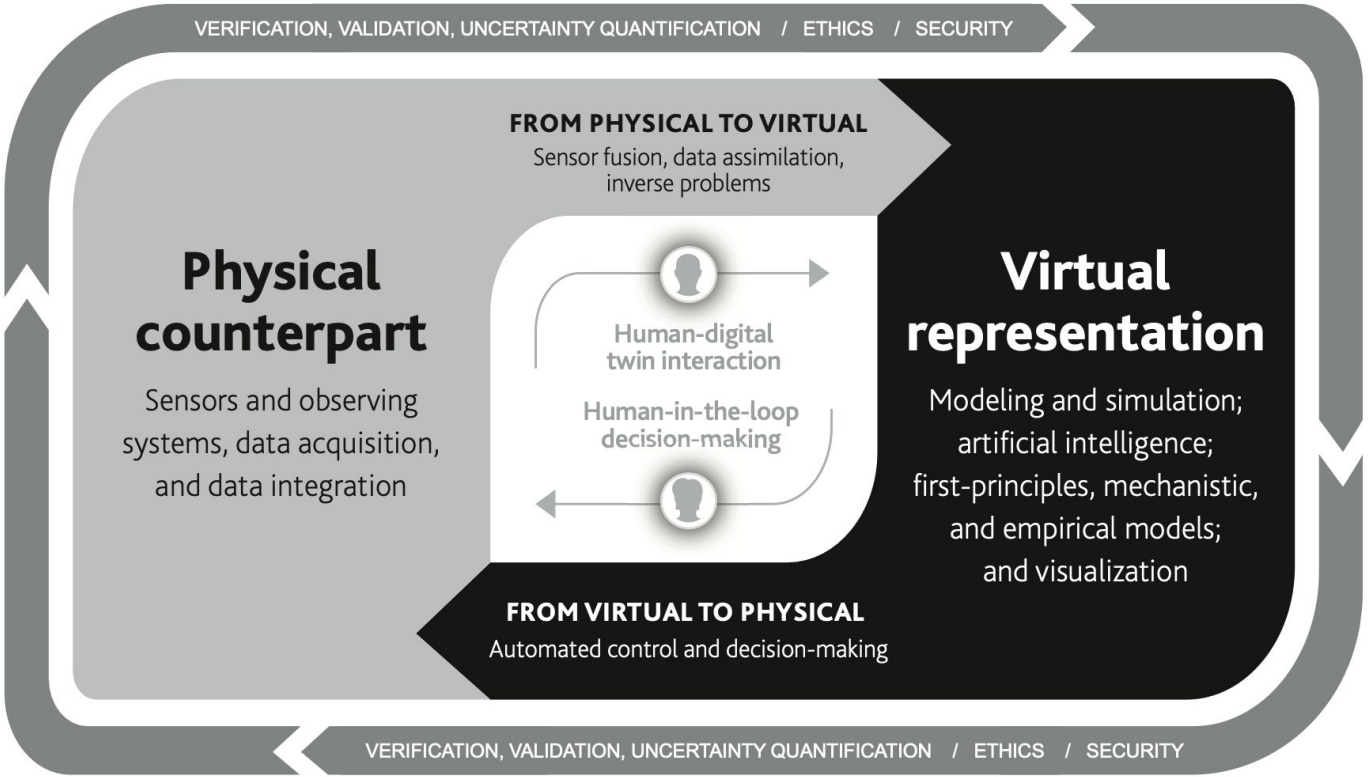


# Filling in the “Loop Diagram”

A digital twin is a set of virtual information constructs that mimics the structure, context, and behavior of a natural, engineered, or social system (or system-of-systems), is dynamically updated with data from its physical twin, has a predictive capability, and informs decisions that realize value. The bidirectional interaction between the virtual and the physical is central to the digital twin.

- Task: Cast a particular BDT project into NASEM Loop

# “Loop Diagram” for cancer




- Hypothesis: Cancer could be treated as a chronic disease with BDT.
- Take advantage of the explain / predict PV-VP loop!

# “Fit for purpose” => What is the problem?

Can we explain and predict cancer emergence and response to treatments to avoid drug resistance?

- Most cancer patients develop some sort of drug resistance.
- ~ 10 million deaths/year world-wide
- Heterogeneous disease (insults and functional response)
- ~50% death within 10 years (varies by type)
- Treatment: chemotherapy, radiation, some targeted therapies.

- Biology/Compute/Action time scale
  - Decision Timeframe = Months to years

# Why a BDT for this problem?

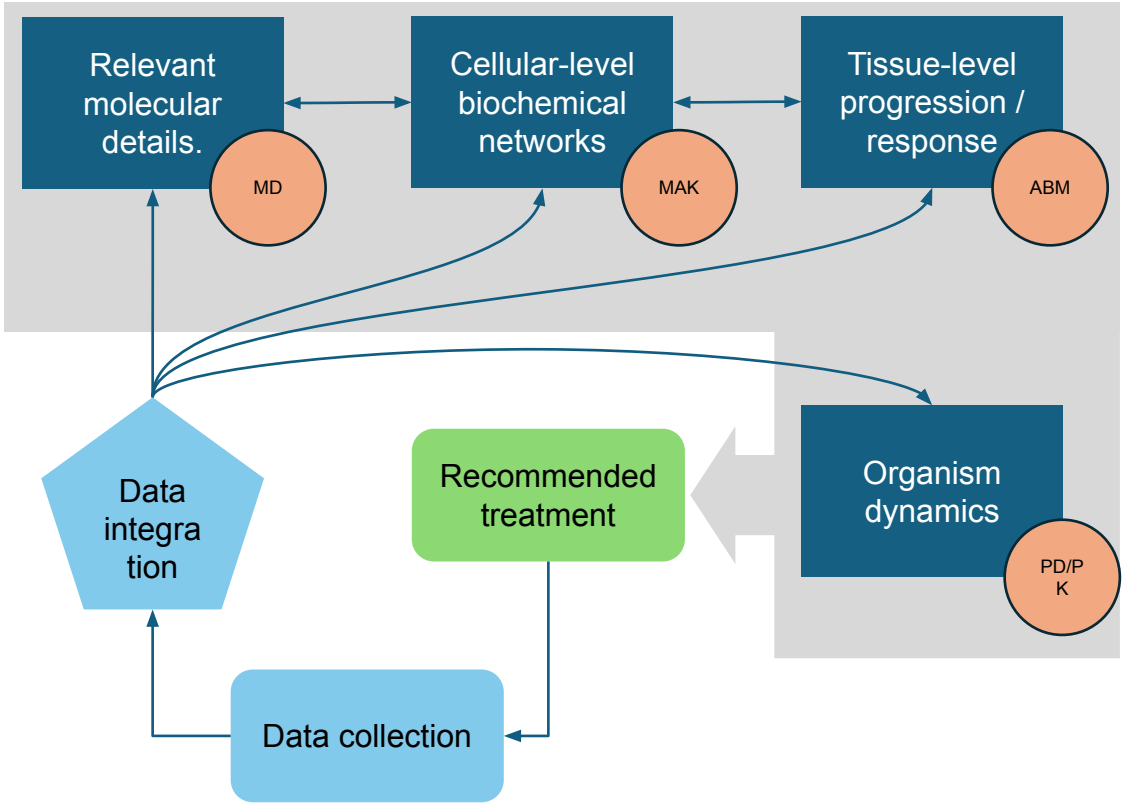
- Each cancer is different.
  - Patients treated as “average” when each patient exhibits unique disease features.
  - Personalized medicine would integrate a digital twin for each patient.
  - Multiscale: from cells to whole organism.

- Continuous Adaptive Control Problem
  - Updatable treatment - response - progression model.
  - Data across many modalities and scales.
  - AI / ML possibilities with available data.

- This model/patient paradigm requires capabilities offered by biomedical digital twins.
  - Establish real-virtual counterparts

# Virtual asset? Chronic Cancer Digital Twin (CCDT)

- What methods and what level of detail?
- From organism to cells, back to organism.
- Organs?
- PD/PK + ABM + MAK + MM/MD?



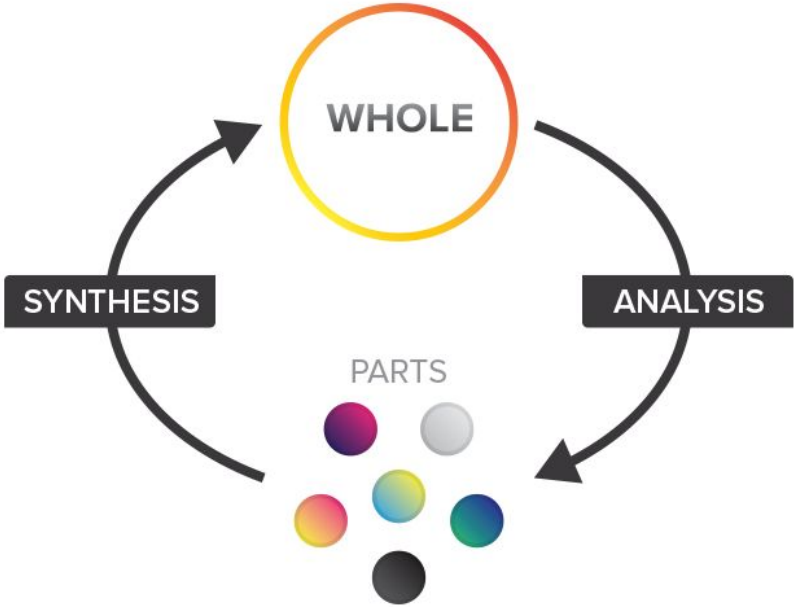
# Physical Asset/bidirectional data link?

- Collect human data, multiple scales / modalities
- Build temporal resolution in all datasets.
- Pass data to model, calibrate model to data, simulate treatment in model, return results to human level, update model as needed.
  - Modalities
    - Existing assays (blood, biopsies, MRI, tissue culture, etc)
    - **AI/ML methods to link modalities to molecular details.**
    - **AI/ML methods to build generalizable models (e.g. foundation model of Breast Cancer).**

https://www.shutterstock.com/search/biomedical-machine

# Verification, Validation, Uncertainty Quantification

- Verification:
  - Necessary at each scale but also at whole organism level.
  - Hermeneutic problem!
- Validation:
  - Necessary at each scale but also at the whole organism level!
  - Did organism respond as expected? Did parts respond as expected?
- Uncertainty Quantification:
  - Bayesian methods.
  - AI/ML methods (e.g. analyze models and data in latent spaces).




https://uxbooth.com/articles/hermeneutics-for-designers/

# What to do with the virtual twin output?

Decision-making/Human in the loop(AI?) (control step)

- Track individuals with cancer risk.
- Prevent cancer development?
- Formulate best treatment for individual patient.
- Set monitoring schedules.
- Collect data needed to update / expand BDT.

- Human in the loop: Will require MD and PhD to work together and make decisions about treatment.
- Bring more biology to physics, more physics to biology.
- Proof of concept?
- Use existing data?

# Security/Privacy/Ethics Issues ?

- Low?
  - Patient information will be protected by medical records standards.
  - AI models will eventually contain all known data about humans in cancer and could be used as generative models.
  - How generalizable are these models?
  - Defining the multiscale communication with rigorous mathematics is key!

# Summary

- Fit-for-purpose: Clearly defined + circumscribed problem for a given cancer type (e.g. breast)
- Virtual Asset: Iterative refinement, bidirectional communication
- Physical Asset: Develop novel methods for multiscale integration in biology along with standardized metrics at each scale.
- Trustworthiness (VVUQ)
  - explain, capture, predict real-world temporal biology?
  - being small, start small, expand.
- Security and Ethics: for patient, low risk. IP unclear.