How to Build the Virtual Cell with Artificial Intelligence: Priorities and Opportunities

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Literature Report

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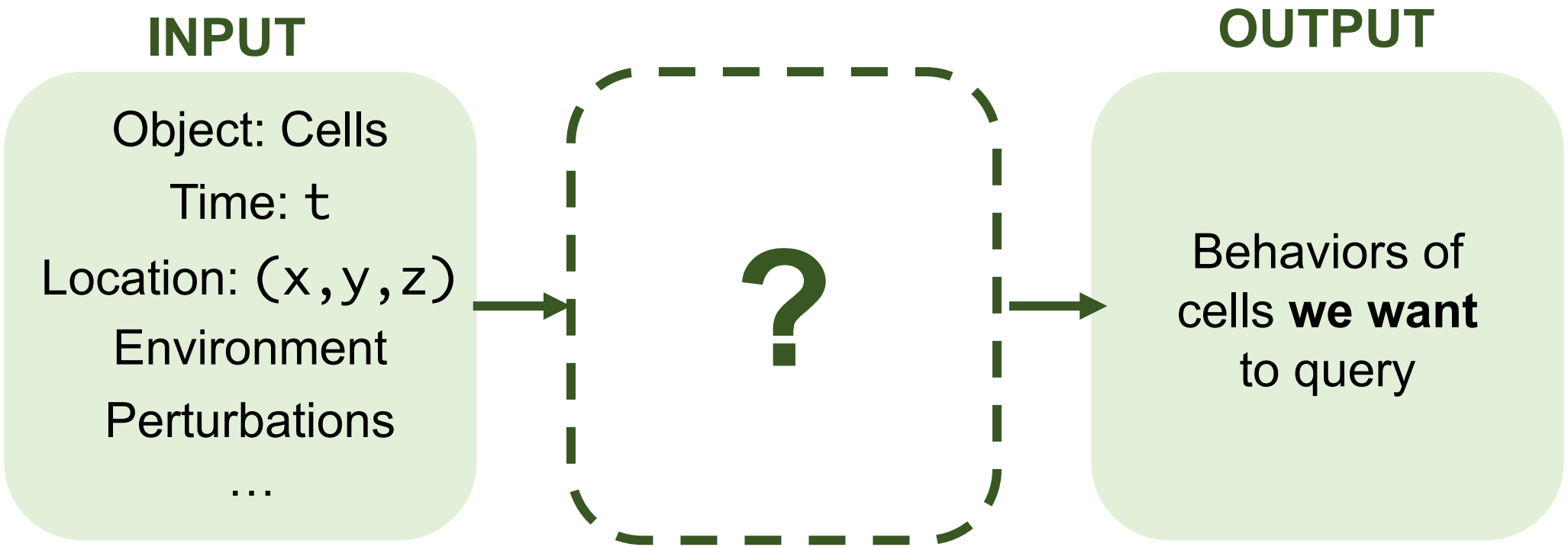
GOAL

How to Build the **Virtual Cell** with Artificial Intelligence

➢ **Definition**

“simulator of cells and cellular systems under varying conditions and changing contexts”

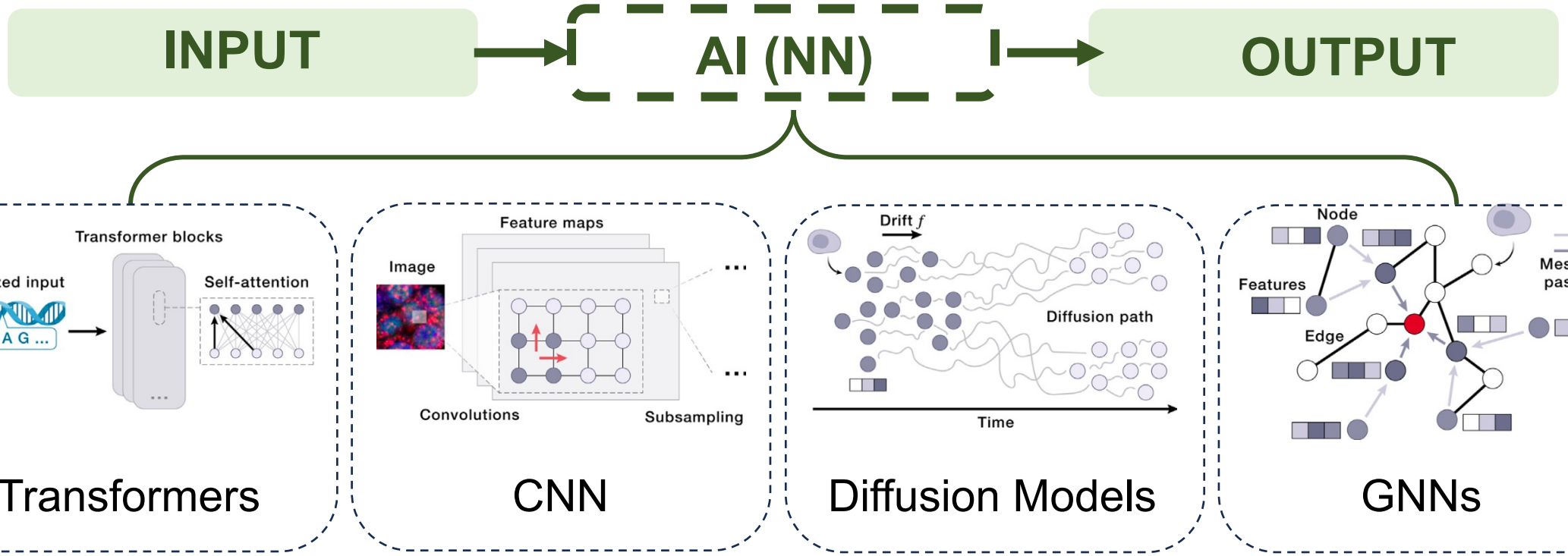


TOOL

How to Build the Virtual Cell with **Artificial Intelligence**

➢ Definition

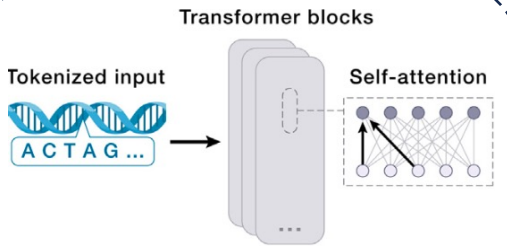
the ability of machines to **perform tasks** that **require human intelligence**



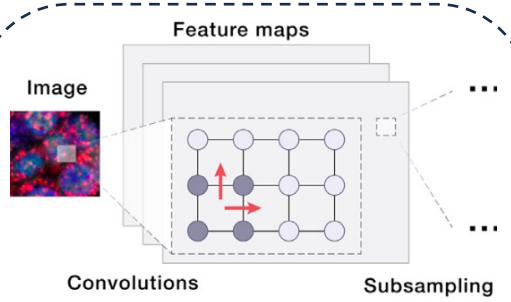
Artificial Intelligence (AI) → Machine Learning (ML) → Deep Learning (DL) → Neural Networks (NN)

TOOL

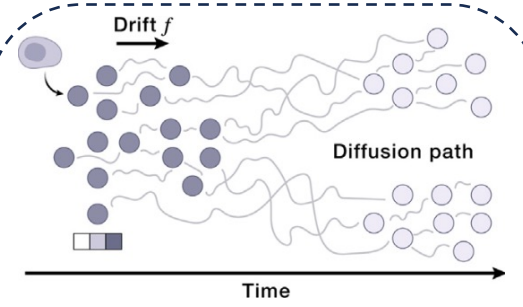
How to Build the Virtual Cell with **Artificial Intelligence**



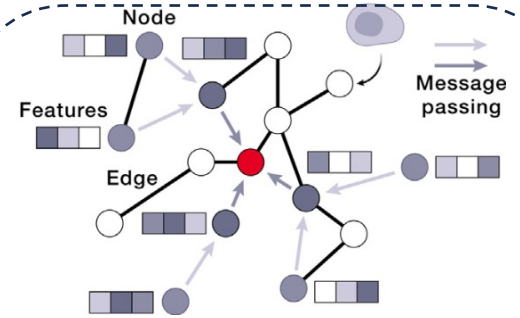
Transformers
sequences
→multimodalities



CNN
regular “network”
e.g. images



Diffusion Models
data generation
e.g. time trajectory



GNNs
node + edge objects
e.g. protein structure

TOOL

How to Build the Virtual Cell with **Artificial Intelligence**

Transformers | **CNN** | **Diffusion Models** | **GNNs**

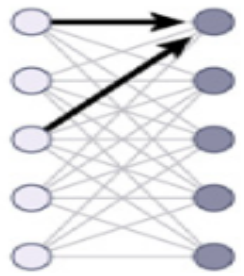
Raw Data —(**Primary coding**)→ **Primary Embedding** —(**Nueral network**)→ **Latent Space Embedding**

TANSFORMER

Gene Expression —(**Simple Mapping**: Linear projection or **table lookup**)→ **token embedding** —(**e.g. self-attention**)→ **contextual embedding**

Gene A, B, C, D, E
[5.2, 0.0, 1.8, 3.3, 7.1]

Gene A (5.2) → [0.4, 1.1, -0.2]
Gene B (0.0) → [0.0, 0.0, 0.0]
Gene C (1.8) → [0.3, 0.2, 0.1]
Gene D (3.3) → [0.6, 0.7, -0.1]
Gene E (7.1) → [1.0, 1.2, 0.4]



× n layers

[[0.48, 0.90, 0.03],
[0.10, 0.05, 0.12],
[0.30, 0.35, 0.25],
[0.52, 0.60, 0.10],
[0.95, 1.00, 0.60]]

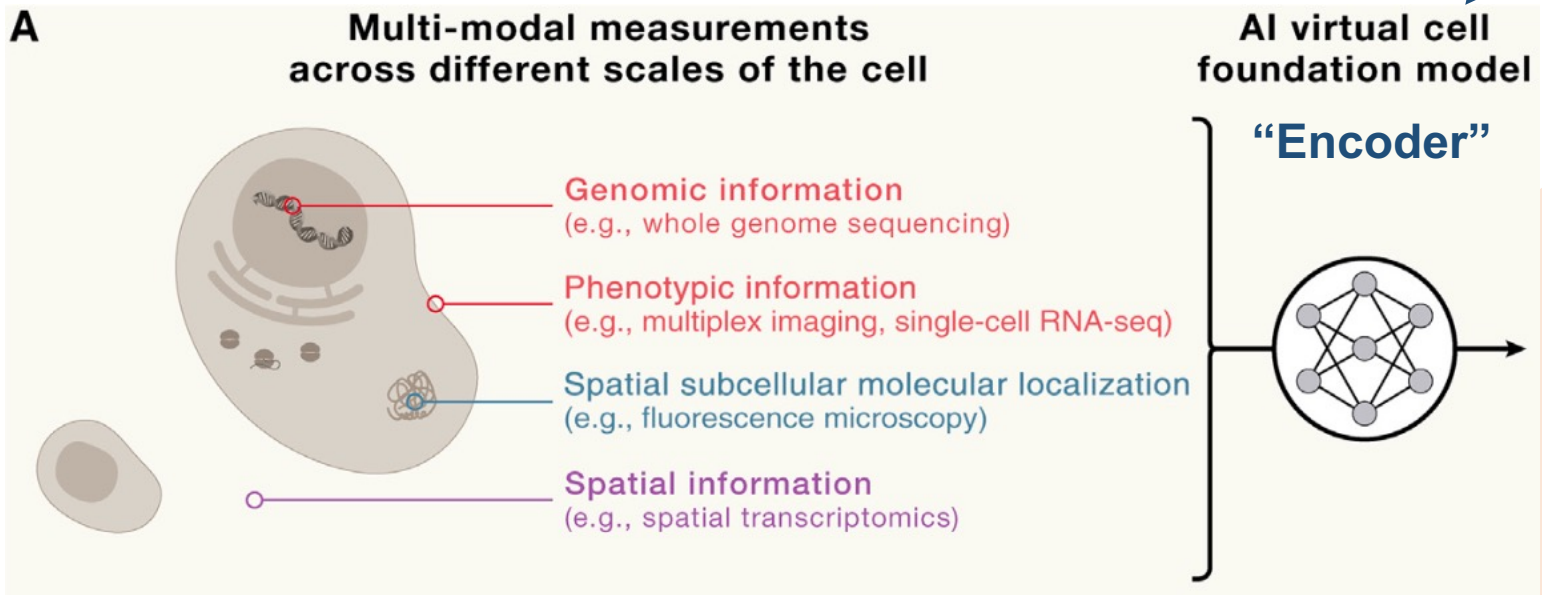
mean pooling↓
[0.47, 0.58, 0.22]

➢ **Embedding**: a representation for computation
① numerical ② preserve structure ③ enable further manipulation

Method

How to Build the Virtual Cell with Artificial Intelligence

Raw Data → Primary coding → Primary Embedding → Nueral Network → Latent Space Embedding



✓ Multi-modality
✓ Biological structures

URs
- Molecular
- Cellular
- Multicellular

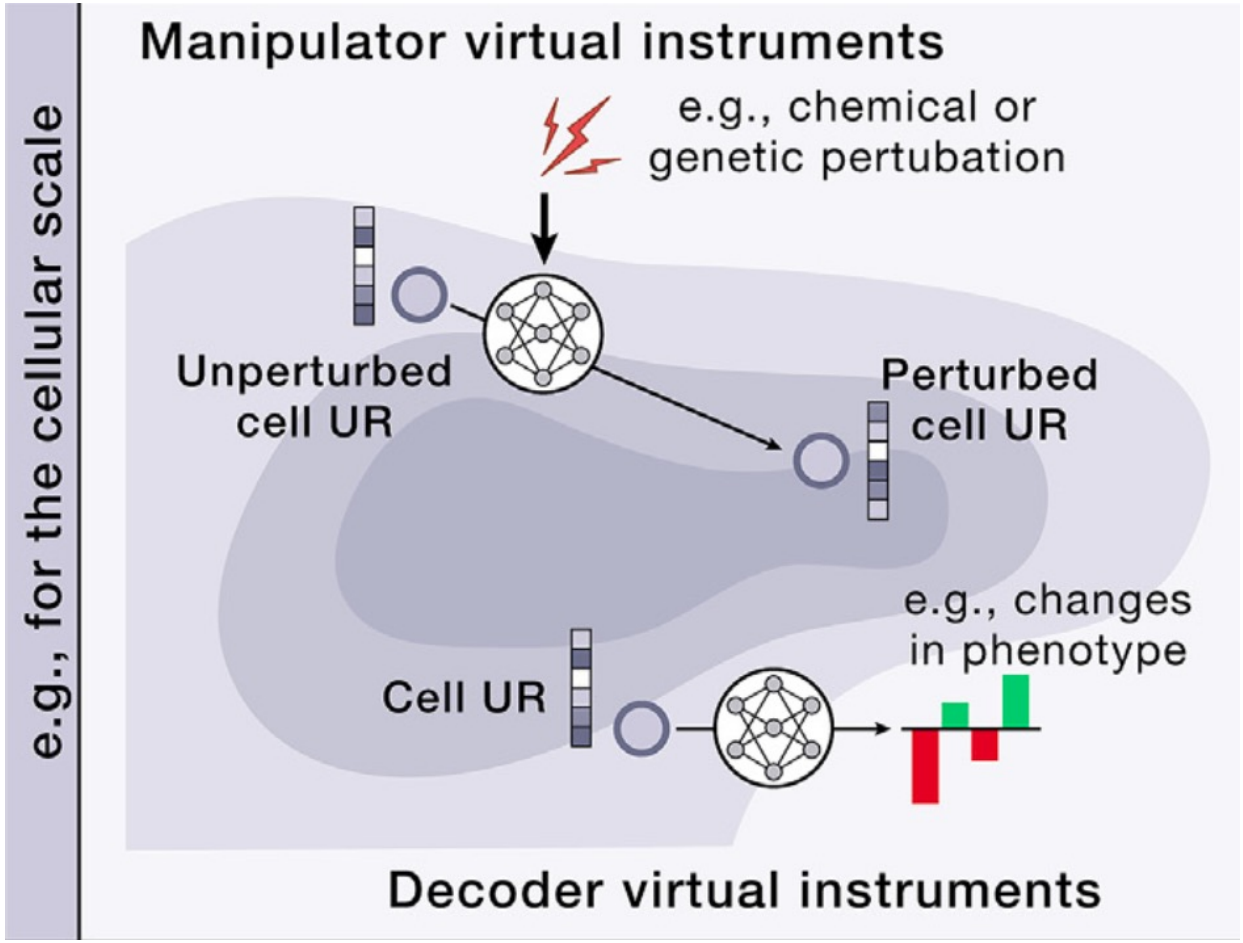
UR abstraction ↓ Physical scales

➢ **Universal Representations (URs)**

"**embeddings** produced by a **multi-modal** AIVC **foundation model**"

How to Build the Virtual Cell with Artificial Intelligence

Raw Data → **AIVC Foundation Model** → **UR** → **Neural Network** → **Cells Behavior**



➢ Virtual Instruments (VIs)

Neural networks that take URs as input and produce a desired output

pre UR [0.47, 0.58, 0.22]

↓ **Manipulator VI**
e.g. drug administration

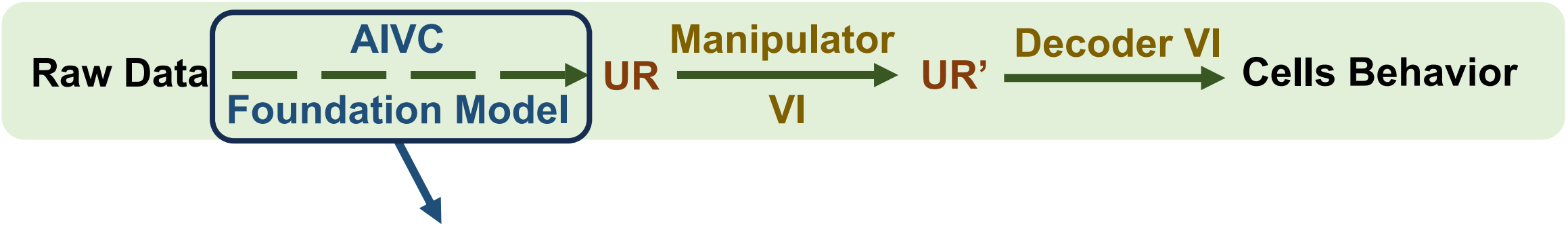
pro UR [0.97, 0.04, 0.23]

↓ **Dcoder VI**

Human understanderble

Gene A, B, C, D, E
[4.9, 30.0, 1.7, 17.8, 0.7]

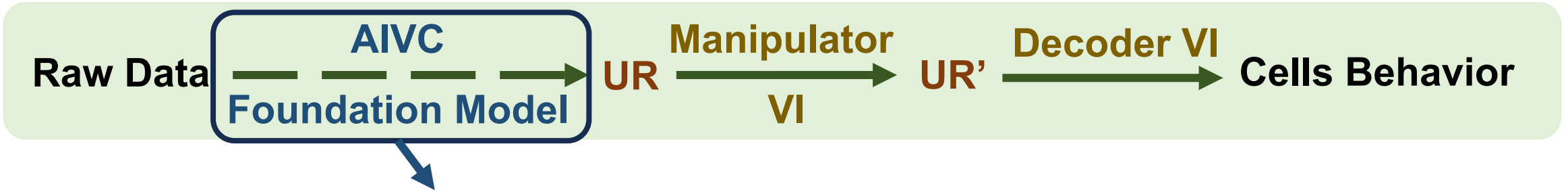
AIVC: Priorities and Opportunities



➢ **Tool Building:** Architectures for **multi-modal biological** data

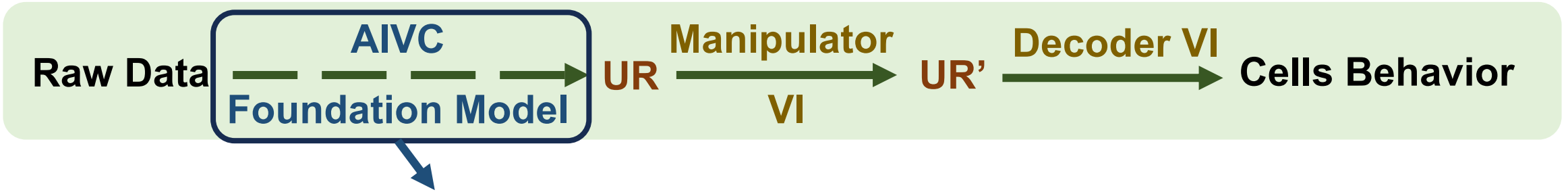
- "**Interconnection** of many large models to **capture everything** in UR" ---- Charlotte Bunne
- Self-consistent across scale, modality, and context
- **LACK!** DNA ≠ texts, medical images ≠ images

AIVC: Priorities and Opportunities



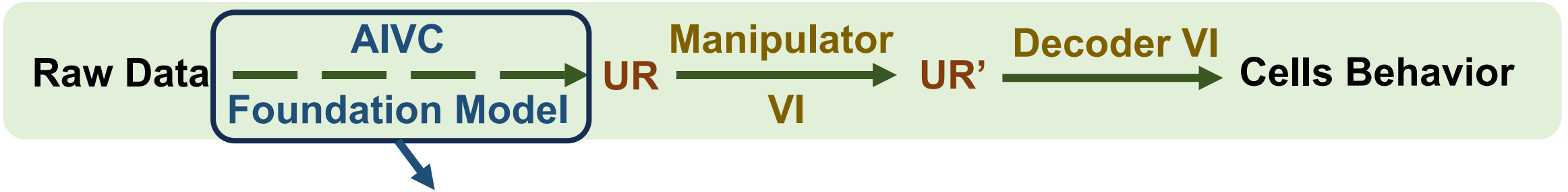
- **Tool Building:** Architectures for **multi-modal biological** data
- **Data Collection**
  - Multi-modal, multi-scale, multi-dimension (t, x), multi-species
  - **Information amount**: short read 14 pb > 1,000×dataset used to train ChatGPT **Redundant?**
  - **Perturbation**: large **combinatorial space**; in vivo? → organoid…

AIVC: Priorities and Opportunities



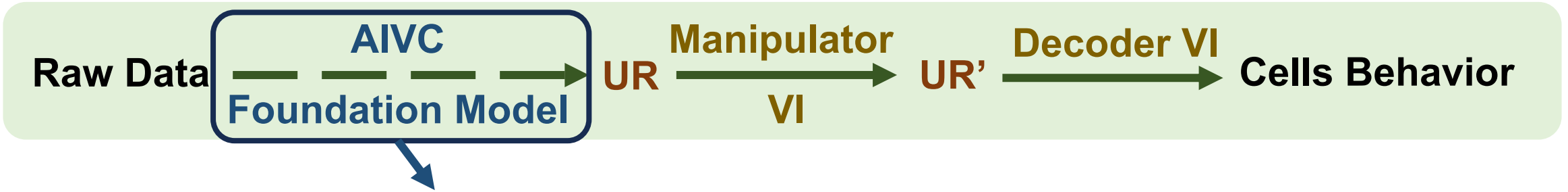
- **Tool Building:** Architectures for **multi-modal biological** data
- **Data Collection**
- **Model Evaluation**
  - Generalizability
  - Discovering new biology, ↑understanding

AIVC: Priorities and Opportunities



- **Tool Building:** Architectures for **multi-modal biological** data
- **Data Collection**
- **Model Evaluation**
- **Interpretability VS Utility**
  - Modular structure enable pinpointing
  - Project result to **interpretable space** (decoder VI)

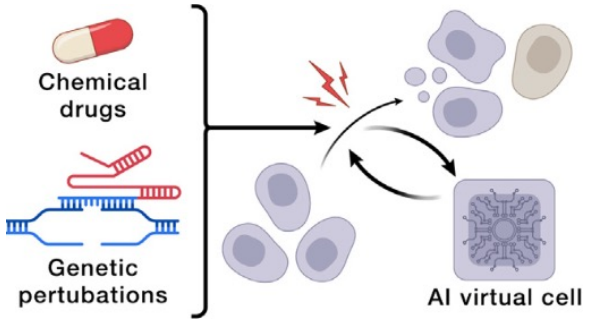
AIVC: Priorities and Opportunities



- **Tool Building:** Architectures for **multi-modal biological** data
- **Data Collection**
- **Model Evaluation**
- **Interpretability VS Utility**
- **Community**: non-expert interface, for collaboration!
- **Humanity Consideration**: diversity, privacy, ethics…

AIVC: Priorities and Opportunities

Raw Data --▸ **UR** — **VI** —▸ **Cells Behavior**



➢ Predict Response

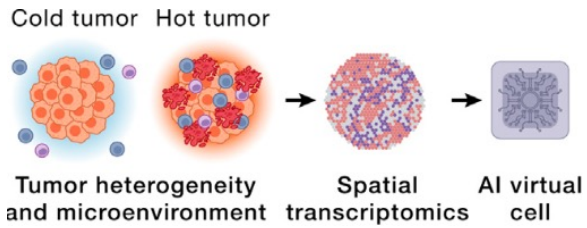
Cell state 1
e.g. expression profile

Engineering
- Cell therapy
- Drug delivery

Cell state 2 (Response)

Optimization

➢ Unlock Biological Laws



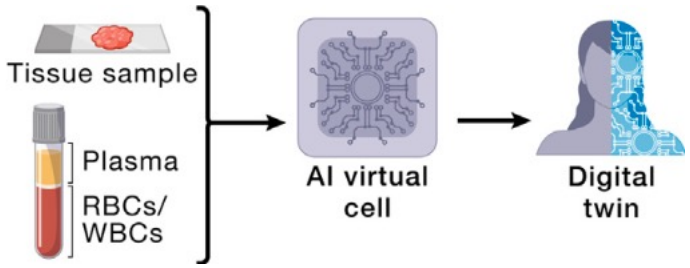
Tumor spatial **omics +**
Microenvironment **conditions**

Laws of tumor
Heterogeneity insights
Pan-cancer markers

"Machine Learning is the formalism through which we understand high dimensional data."

AIVC: Priorities and Opportunities

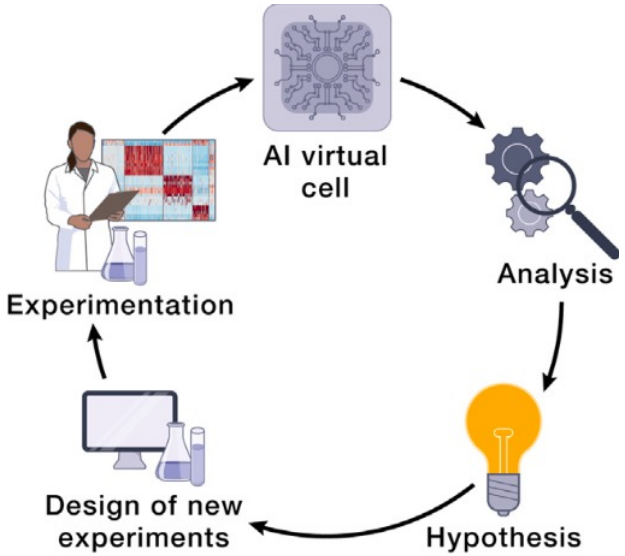
Raw Data --▸ **UR** —VI—▸ **Cells Behavior**



➢ Digital Twin

Patient samples
(easy access)
e.g. blood, images etc.

—▸ **Digital twin**
(inaccessible cell types)
→ personalized simulations



➢ Guide Experiments

Cellular system state —intervention—▸ **Result with confidence**

Gene A, B, C, D, E
[5.2, 0.0, 1.8, 3.3, 7.1]

Gene A, B, C, D, E
[4.9, 30.0, 1.7, 17.8, 0.7]
Possibility = 0.0001

Low!
Test it!

New Biology or
Model Optimization

◂—

- Generate **hypothesis**
- Identify **valuable data** to collect

"Everything we do in science is hypothesis driven"

AIVC: Priorities and Opportunities For us!

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- 42-author 50-institute blueprint
- A **roadmap** for a once-vague dream
- Require interdisciplinary collaboration
- BOLD! **Doable**?
- **Together**, I believe **YES!**

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