Multi-Omics Data Analysis

Akhil Jalan

CMMC Special Topics Group Meeting

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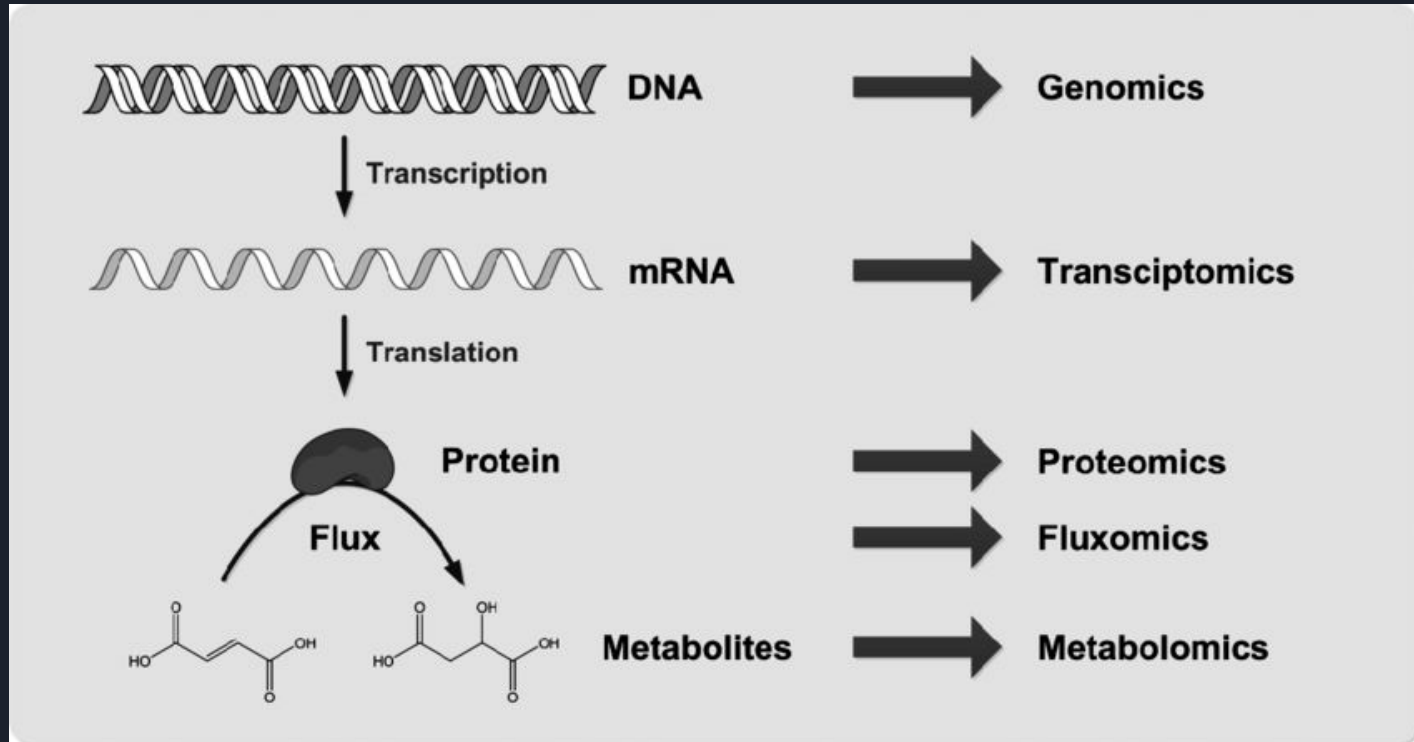
What is **multi-omics data analysis**?

Omics data: Any data related to an "-ome" in systems biology, e.g. the <u>transcriptome, proteome, metabolome, genome</u>, …

Multi-Omics data analysis: Any concerted effort to analyze multiple omics datasets at once

The Central Dogma of Molecular Biology

Source: Gruchattka, Evamaria. Towards a platform organism for terpenoid production–in silico analysis of metabolic networks of potential hosts and in vivo validation. Diss. Dissertation, Dortmund, Technische Universität, 2016, 2016.

Why do multi-omics data matter for cultivated meat?

- The field is inherently **interdisciplinary**
- Can leverage insights from different biological systems in concert
- **Emergent properties** cannot be understood by looking at just one part of an organism

Example: Modeling the skin barrier

Question: How can we model *epidermal skin barrier formation* in silico?

Challenges:

- Multi-scale modeling: Multiple spatial scales involving cells, molecular transport, intra-cellular processes
- Combining discrete (ABM) with continuous (PDE) models

Approach: Combine four modules into an integrated, whole-system model.

Source: **Tasseff**, R., **Aguilar**, B., **Kahan**, S., Kang, S., Bascom, C. C., & Isfort, R. J. (2019). An integrated multiscale, multicellular skin model. bioRxiv, 830711.

Outline of Tasseff et al. modeling approach

(1)Agent-based model of skin cells as ellipsoids

(2) ODE for eukaryotic cell-cycle

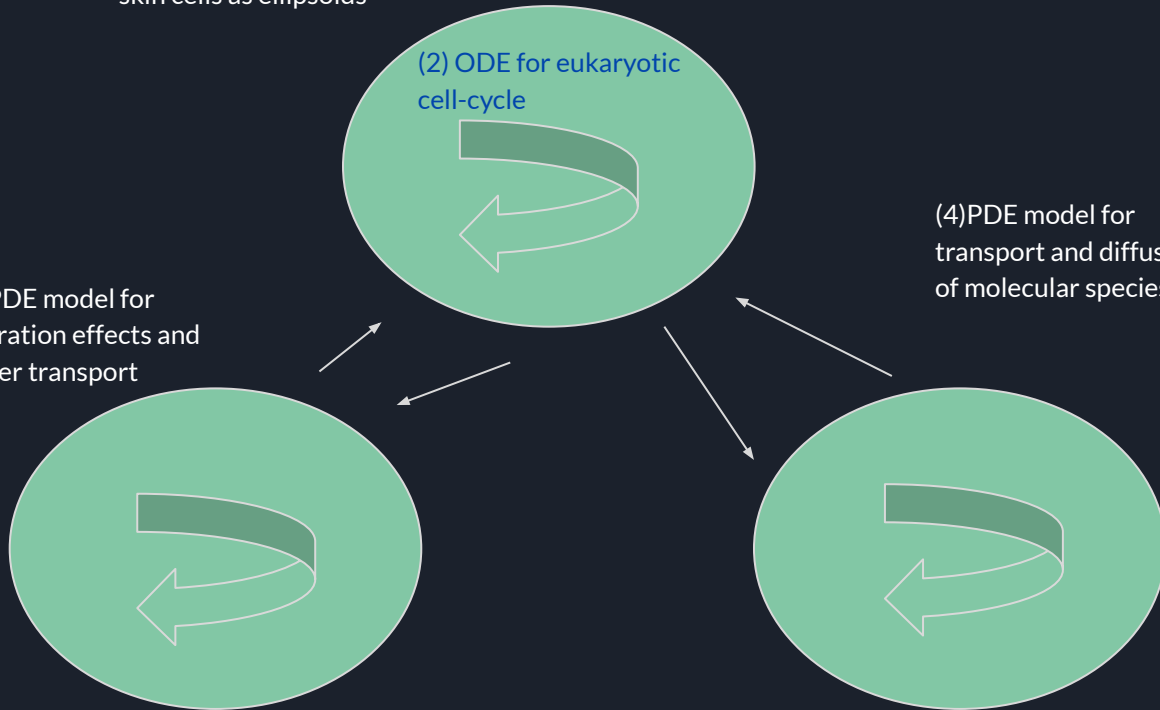(3)PDE model for hydration effects and water transport

(4)PDE model for transport and diffusion of molecular species

Omics involved include:

- Transcriptomics
- Proteomics

Besides omics, they use:

- Fluid mechanics
- Physics of elastic deformation

Lessons from Tasseff et al.

*"While the description of the multiple sub-models can be daunting in itself, **understanding the integration at the needed precision is the most difficult part.** The primary issue at hand is the use of **fundamentally distinct physical concepts, mathematical frameworks and numerical solutions for a single system**…*

*when modeling tissues at cellular resolution, **there is no agreement in the field as to what specific physical or biological concepts should be included and to what level of detail should they be described at**. There is no agreement as to level of flexibility a framework should have, and there is certainly no agreement on an implementation strategy. **We argue the need to identify a set of 'good' models that capture the core physical and biological concepts before we can work on establishing a common ontology or other abstractions** as well as a common set of implementation methods in which the details can be easily communicate."*

- Don't just throw in some model because you can!
- What level of precision is useful?
- What models are actually good for capturing the concepts we care about?

Application: Cell Line Engineering

The Counter

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Lab-grown meat is supposed to be inevitable. The science tells a different story.

by Joe Fassler
09.22.2021, 1:19pm

Tech

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Digging a little deeper...

*"[T]his analysis demonstrated that **inefficient cellular metabolisms with high levels of inhibitor formation will not achieve high cell densities in a large bioreactor**, even with inhibitor removal via perfusion. **Development of highly efficient, immortal cell lines capable of repeatable culture at high density will be required.** This effort should not be underestimated - **even an industrial cell line like CHO, which has enjoyed 60+ years of characterization and optimization, is probably not efficient enough...**"*

Scale-Up Economics
for Cultured Meat

Techno-Economic Analysis
and Due Diligence

David Humbird

DWH Process Consulting LLC
Centennial, Colorado USA

Prepared for Open Philanthropy
San Francisco, California USA

What omics are needed?

Some guesses:

- **Genomics**: Genetic engineering for, e.g. glutamine synthetase (enzyme involved in nitrogen metabolism)
- **Proteomics**: Understanding effects of growth factors in low-cost cell culture media formulations
- **Metabolomics**: Inhibitor production and catabolite secretion

Notice each of these has an accompanying biological network!