3000788 Intro to Comp Molec Biol

Lecture 27: Phenomics and precision medicine

Fall 2025

Sira Sriswasdi, PhD

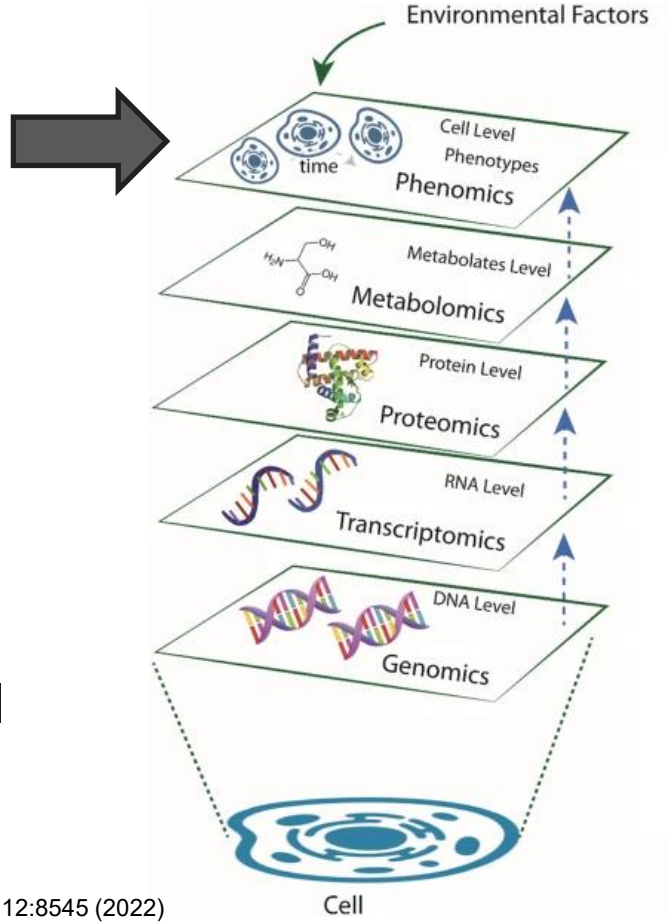
- Research Affairs
- Center of Excellence in Computational Molecular Biology (CMB)
- Center for Artificial Intelligence in Medicine (CU-AIM)

Today’s agenda

- Introduction to phenomics
- Quantitative, high-throughput phenotype profiling
- Applications in biology and medicine

What is phenomics?

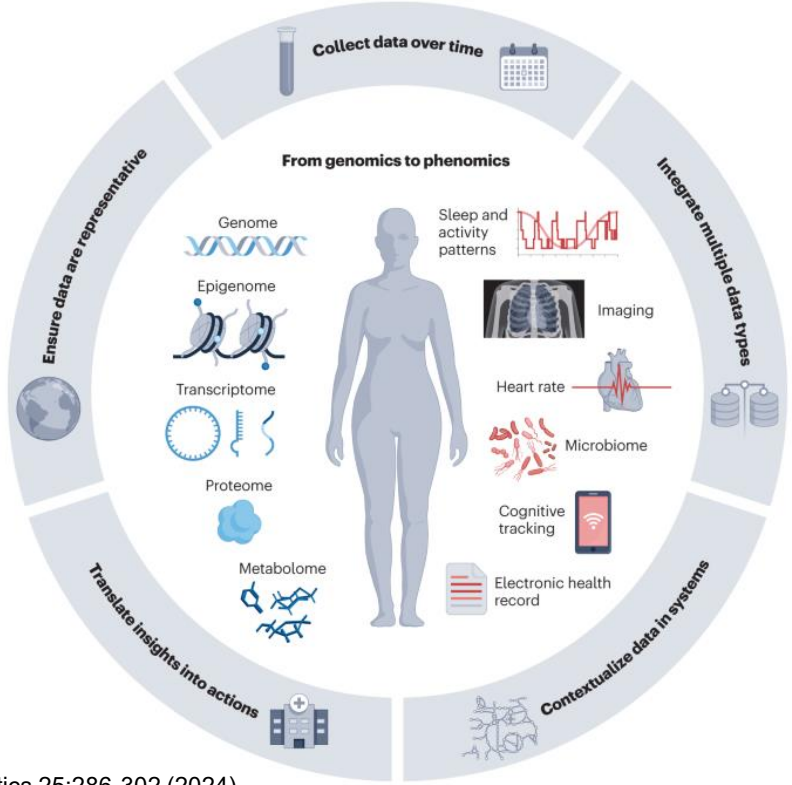
- High-throughput, broad characterization of **phenotypes, phenotype dynamics, and phenotype combinations**
- A single phenotype is usually selected as study target for an omics study
- Combination of molecular and **environmental factors** to explain phenotypes



D'Ozario, M. et al. Scientific Reports 12:8545 (2022)

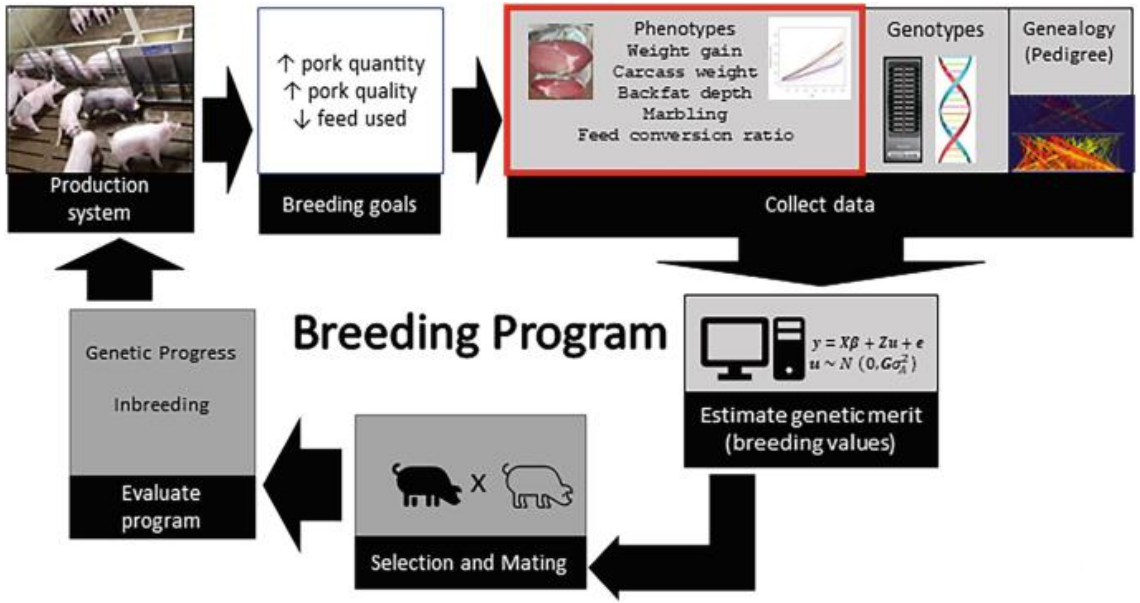
Phenomics in medicine

- Phenotype = clinical measurements (health status)
- Integrating omics data (molecular) with lifestyle and diet (environmental)
- Pinpoint causes of disease and select appropriate treatments



Yurkovich, J.T. et al. Nature Review Genetics 25:286-302 (2024)

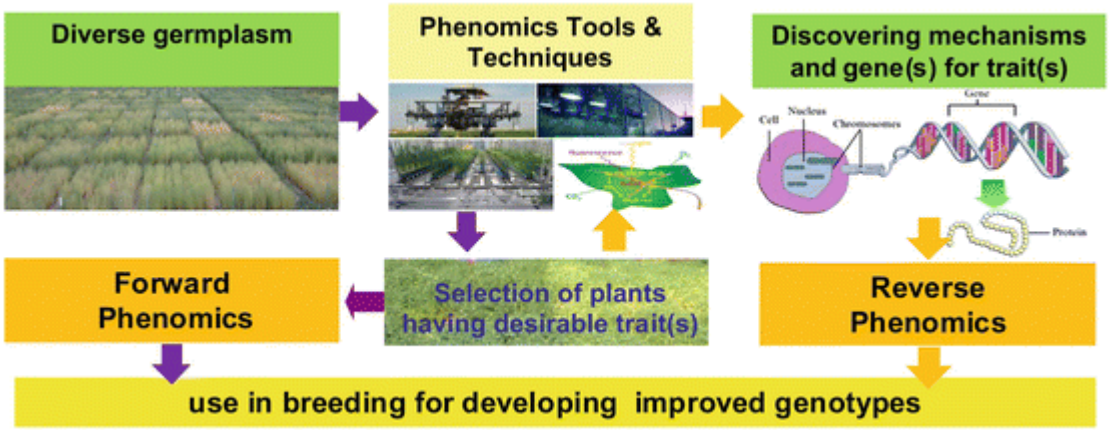
Phenomics in livestock



- Phenotypes ~ health status and **production yield**
- More control over genetic and environmental factors
- More monitoring
- Optimize breeding, food, and production system

Steibel, J.P. “Phenomics in Animal Breeding” Encyclopedia of Smart Agriculture Technologies pp1-8 (2023)

Phenomics in agriculture



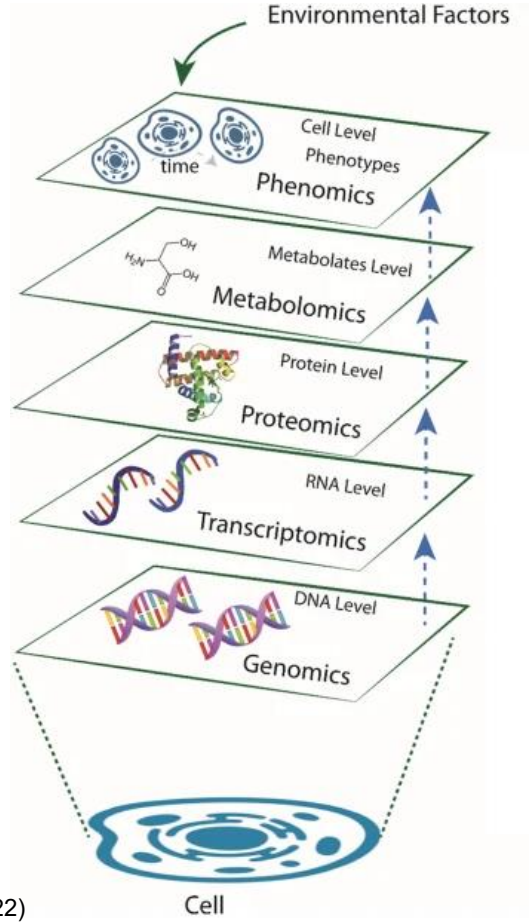
Kumar, J. et al. “Plant Phenomics: An Overview” Phenomics in Crop Plants: Trends, Options and Limitations pp1-10 (2015)

- Phenotypes ~ **resistances**, and **production yield**
- More visual phenotypes
  - Leaf / shoot / root
  - Color / weight / shape
- More experimental options
  - Growth condition
  - Nutrient
  - Disease

Phenomics vs systems biology

- **Systems biology** is the pursuit of bottom-up, mechanistic understanding of biology
  - “What causes phenotype?”

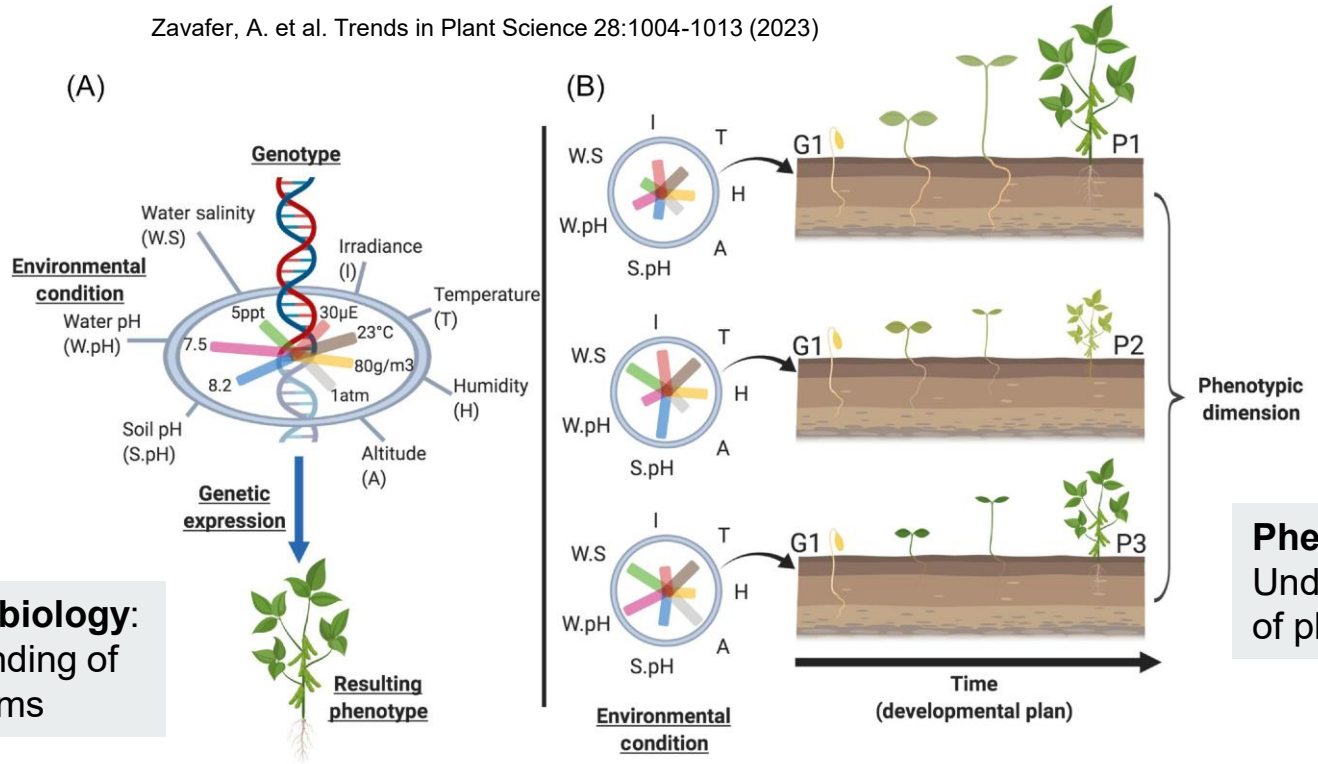
- **Phenomics** is more about top-down understanding of the phenotypes and how to manipulate them
  - “How to change phenotype?”
  - Mechanistic knowledge helps



D’Ozario, M. et al. Scientific Reports 12:8545 (2022)

Phenomics vs systems biology

Zavafer, A. et al. Trends in Plant Science 28:1004-1013 (2023)



Systems biology: Understanding of mechanisms

Phenomics: Understanding of phenotypes

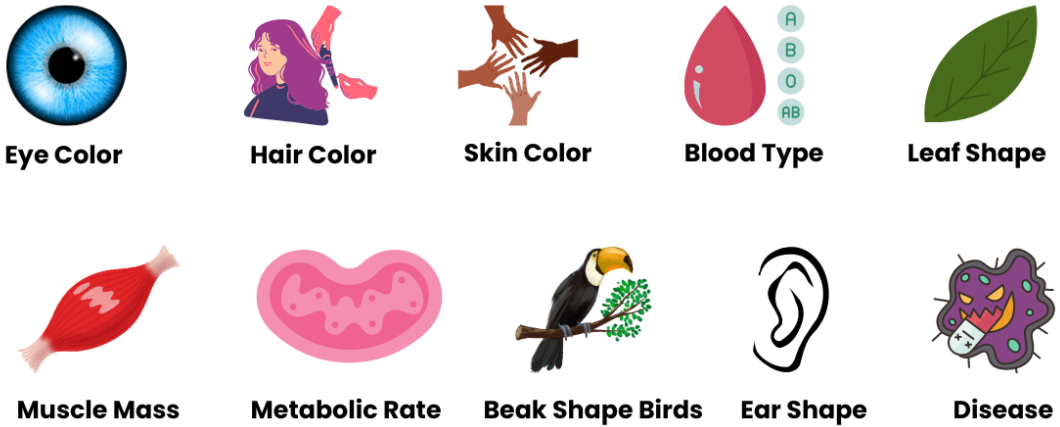
Why phenomics?

- Molecular changes manifest through different phenotypes
- Environmental factors can significantly modify phenotypes
- Lead to applications
  - Personalized medicine
  - Smart breeding
- Complement systems biology and omics analysis

Phenome

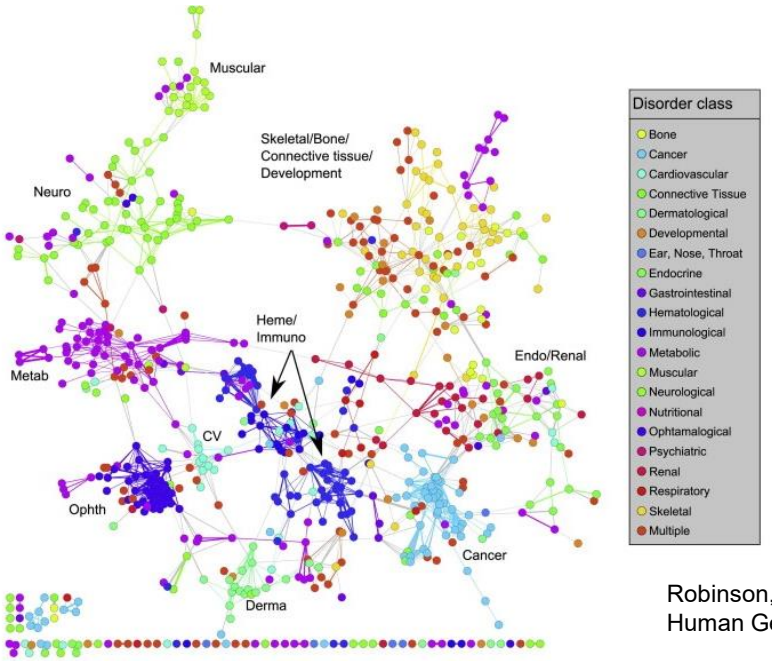
Classes of phenotypes

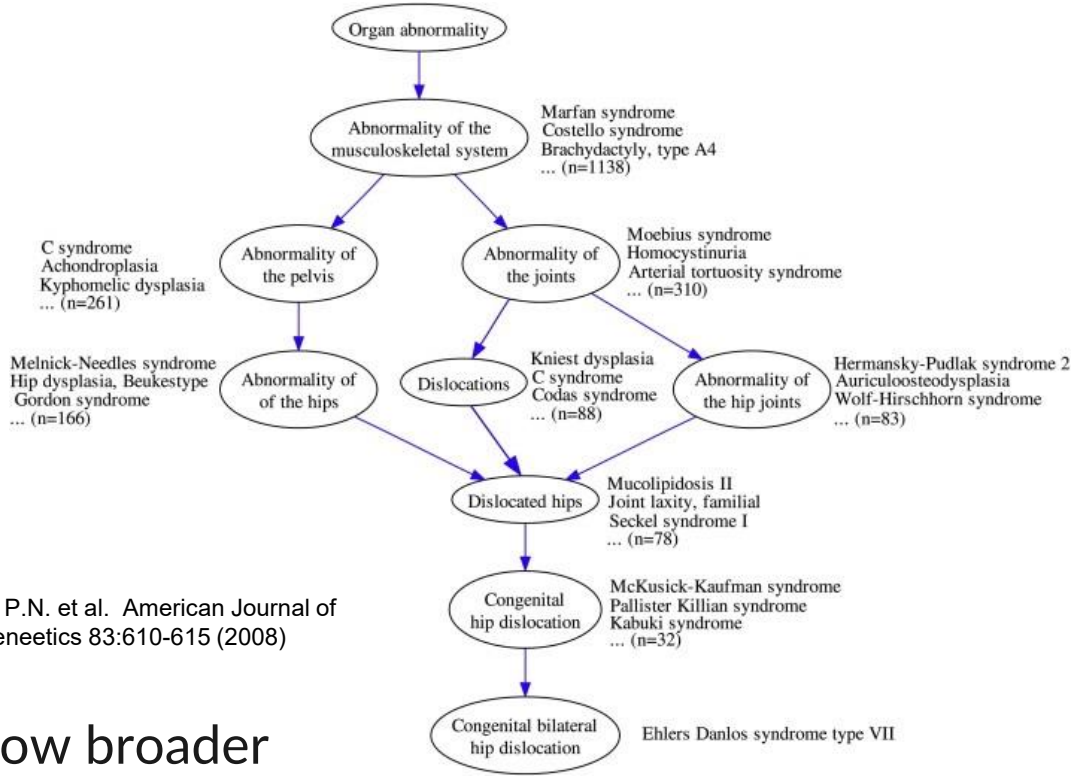
- Physical & morphological
  - Imaging and manual measurements
- Behavioral
  - Monitoring through sensors or videos
- Metabolic & molecular
  - Omics and functional assays



https://www.examples.com/biology/phenotype.html

Human Phenotype Ontology



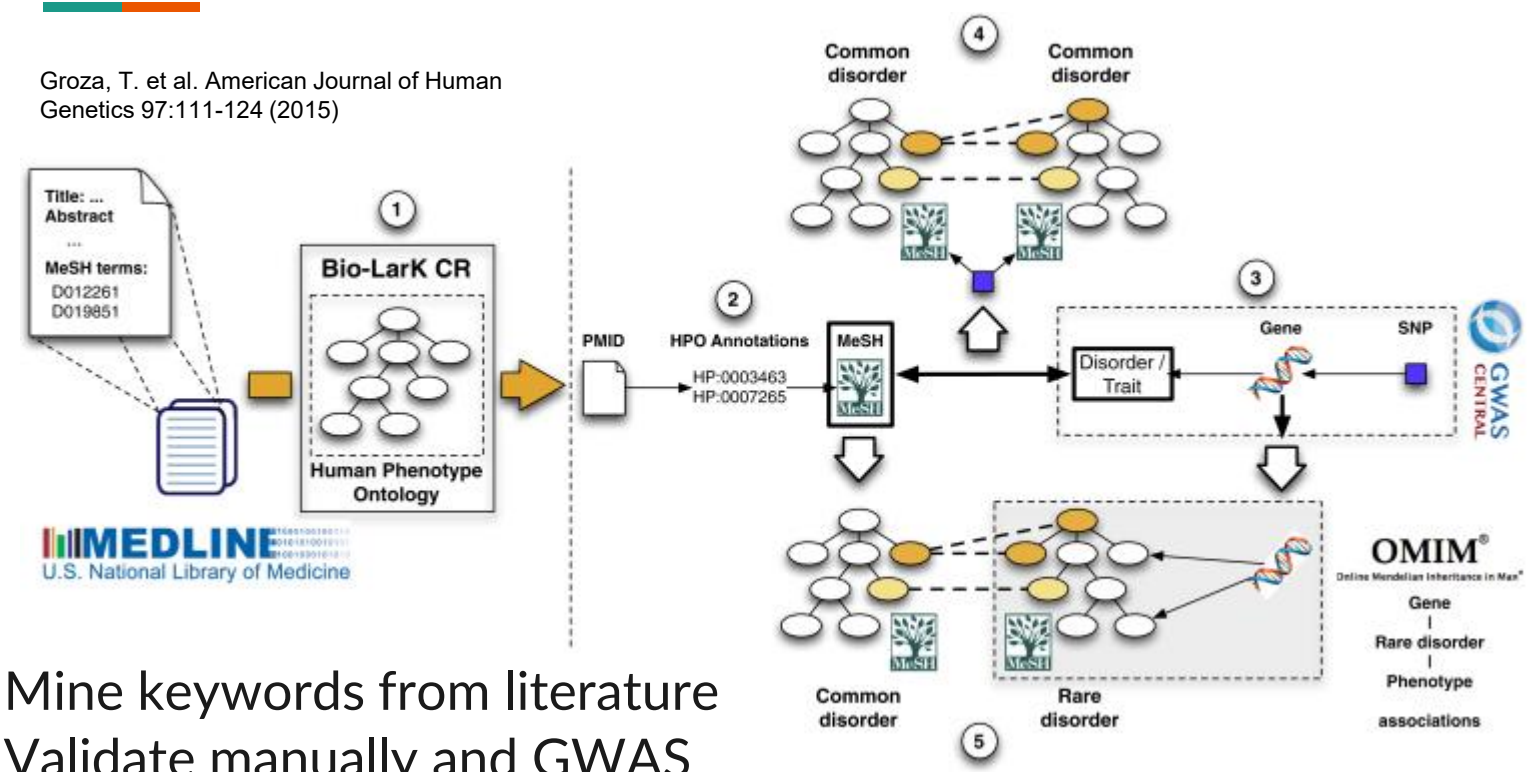


Robinson, P.N. et al. American Journal of Human Geneetics 83:610-615 (2008)

- Initially hereditary diseases, now broader

Curation of human phenotype terms

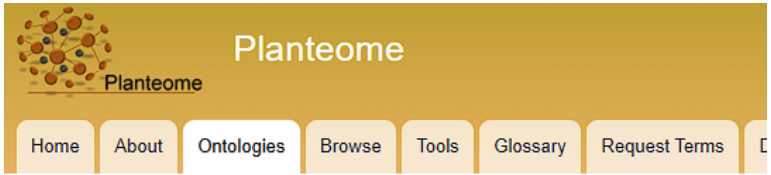
Groza, T. et al. American Journal of Human Genetics 97:111-124 (2015)



- Mine keywords from literature
- Validate manually and GWAS

Open Biological and Biomedical Ontology (OBO)

ID	Title	Description
dpo	Drosophila Phenotype Ontology	An ontology of commonly encountered and/or high level Drosophila phenotypes.
hp	Human Phenotype Ontology (HPO)	The Human Phenotype Ontology (HPO) is a structured and controlled vocabulary for the phenotypic features encountered in human hereditary and...
mp	Mammalian Phenotype Ontology	Standard terms for annotating mammalian phenotypic data.
oba	Ontology of Biological Attributes	A collection of biological attributes (traits) covering all kingdoms of life.
pato	Phenotype And Trait Ontology	An ontology of phenotypic qualities (properties, attributes or characteristics)
vt	Vertebrate trait ontology	An ontology of traits covering vertebrates
wbphenotype	C. elegans phenotype	A structured controlled vocabulary of *Caenorhabditis elegans* phenotypes



Reference Ontologies for Plants:

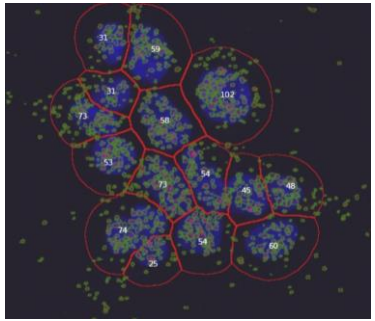
Developed by the Planteome Project:

- Plant Ontology (PO): Download
  - Browse PO: plant anatomical entity
  - Browse PO: plant structure development stage
- Plant Trait Ontology (TO): Browse TO | Download
- Plant Experimental Conditions Ontology (PECO): Browse PECO | Download
- Plant Stress Ontology (PSO): Work in progress

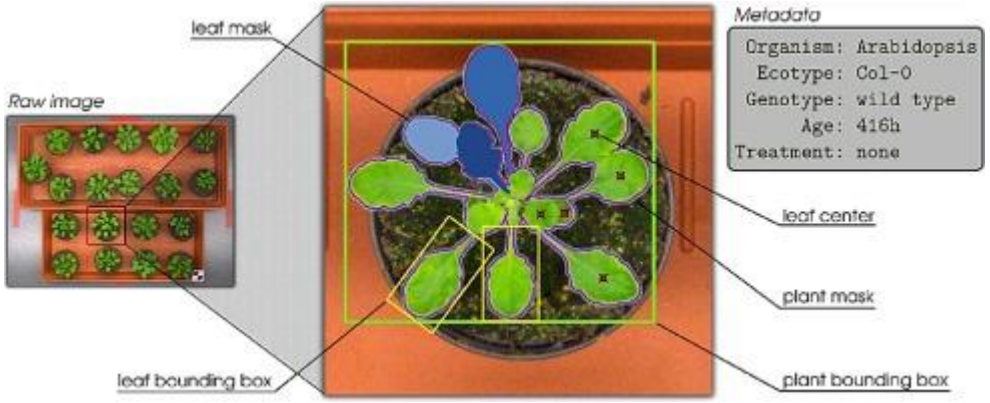
- Community developed collections of standardized terminology
- Facilitate phenomics data sharing and integration

Image-derived phenotypes

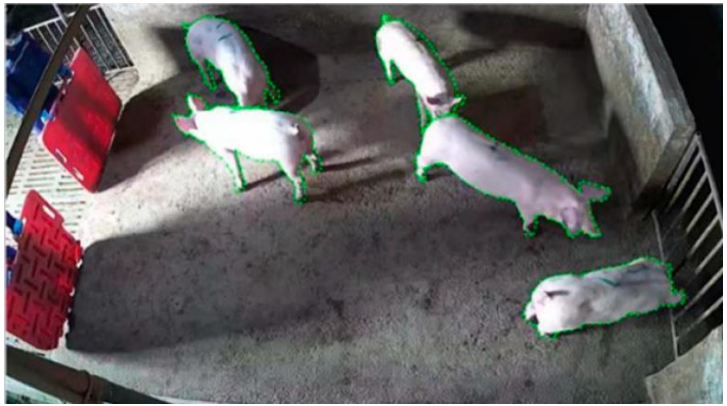
Minervini, M. et al. Pattern Recognition Letters 81:80-89 (2016)



https://cellprofiler.org/previous-examples



- Computer vision techniques enable high-throughput, automated quantification of visible phenotypes
  - Physical & morphological
  - Behavioral

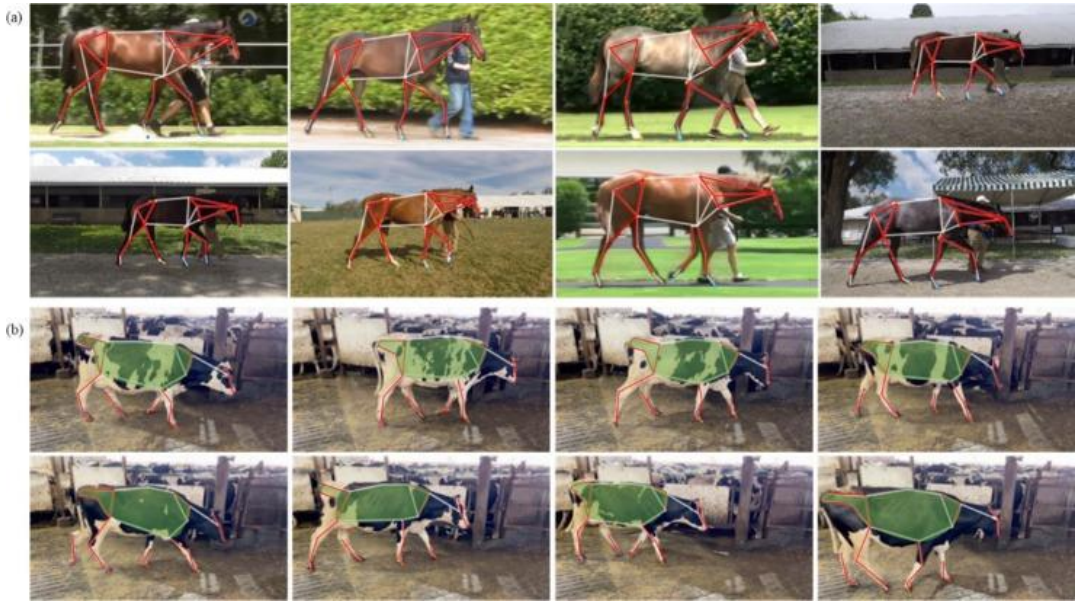


Li, G. et al. Animals 15:1126 (2025)

Animal motion tracking and behavior classification

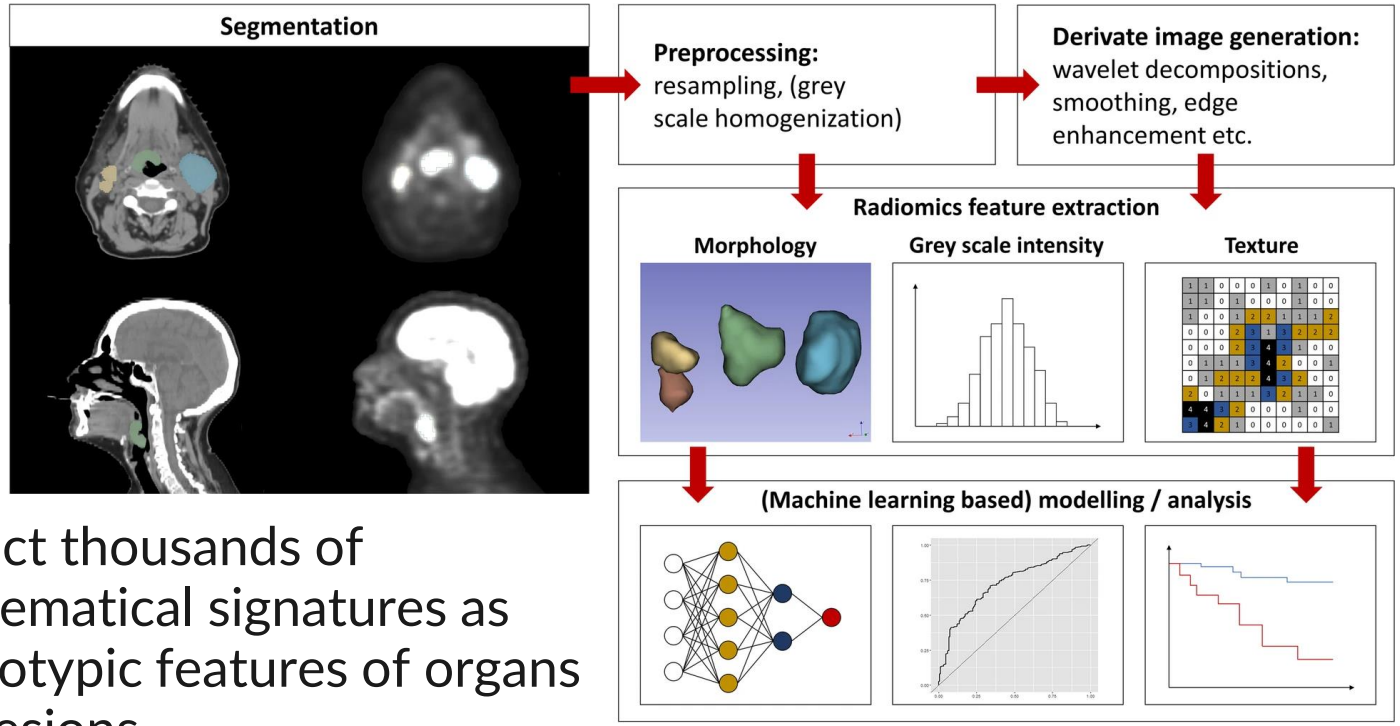
https://www.ultralytics.com/blog/role-of-computer-vision-and-ultralytics-yolo11-in-animal-monitoring

Shumaly, M. et al. Computers and Electronics in Agriculture 237:110560 (2025)



- Identify posture, activity, feeding, as well as social behaviors
- Flag abnormal behaviors, potential sickness

Radiomics: Radiological imaging-based phenomics



- Extract thousands of mathematical signatures as phenotypic features of organs and lesions

Haider, S.P. et al. Cancers of the Head & Neck 5:6 (2020)

The rise of phenomics databases

413,350+ Survey Responses

337,500+ Physical Measurements

312,900+ Genotyping Arrays

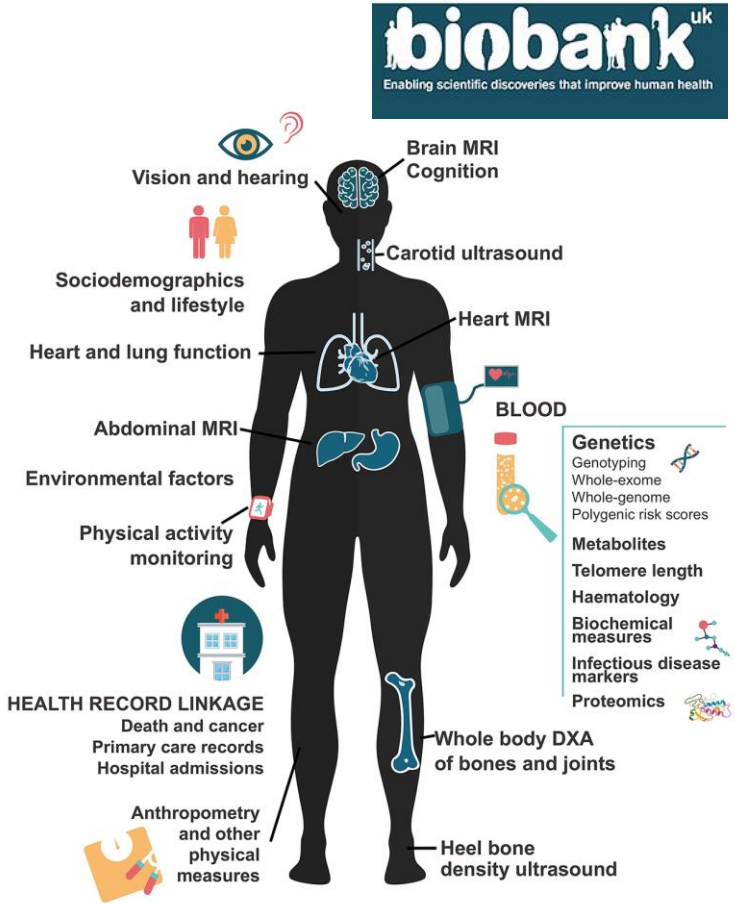
287,000+ Electronic Health Records

245,350+ Whole Genome Sequences

15,600+ Fitbit Records

1,000+ Long-Read Sequences

All of Us RESEARCH PROGRAM



- Omics data alone is not enough to understand the complexity of human phenotypes and diseases
- Addition of questionnaire, medical record, and wearable device

Importance of metadata (and environmental data)

- **Metadata** = details about the context and circumstance of collected data
  - Date & time (including climate and seasonal information)
  - Sample preparation protocols & instrument uses
  - Sample inclusion & exclusion criteria
  - Habitat & growth information (farm, food)
  - Medical history and ongoing intervention

- All these factors can confound data distribution and observable mechanistic associations

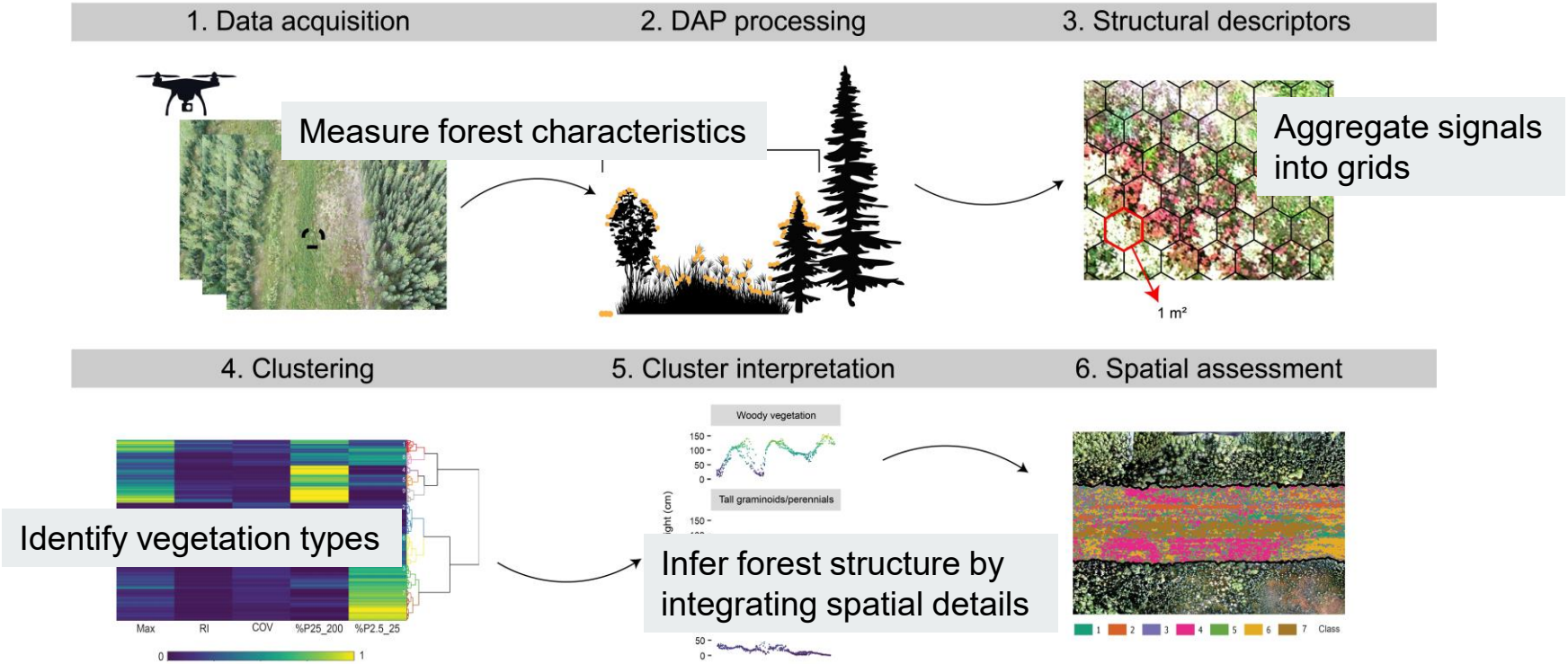
- Lack of metadata can lead to wrong conclusion

High-throughput phenotyping

High-throughput phenotyping assays

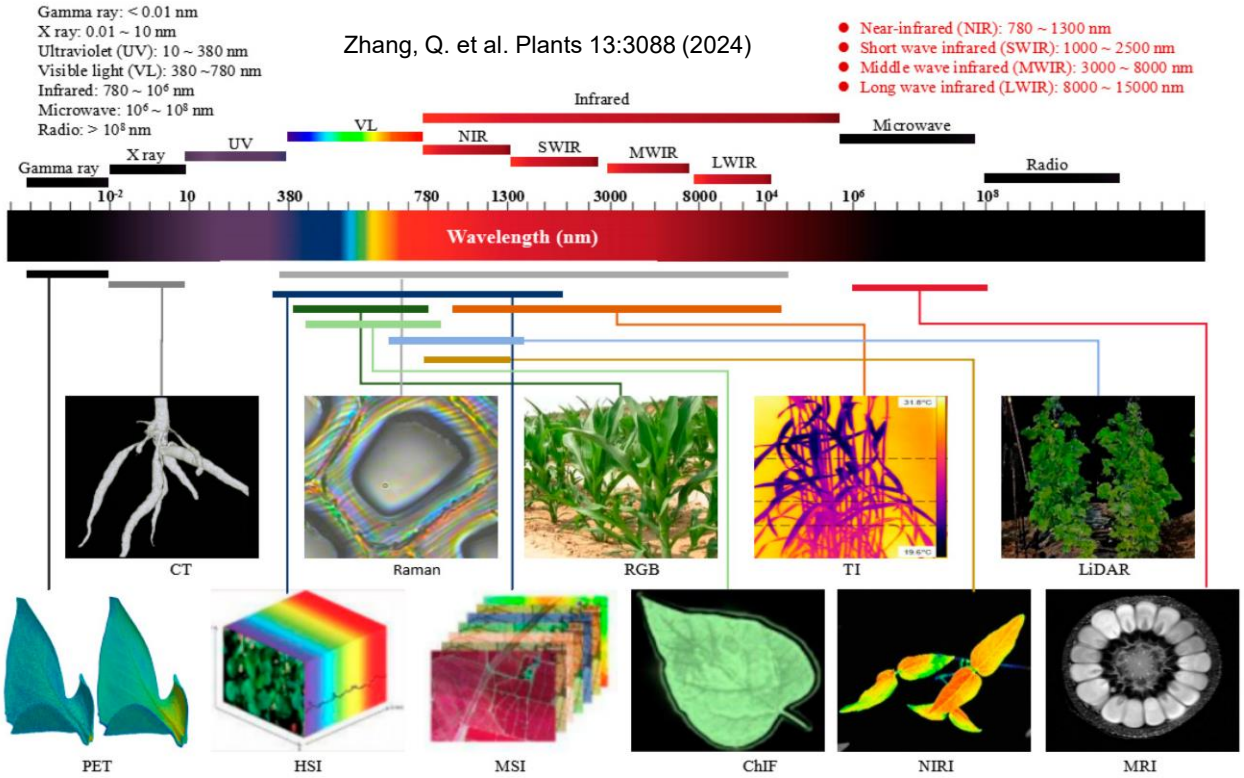
- Omics technology → metabolic and molecular phenotypes
- Static imaging, aided by robots, drones, or handheld technology → physical and morphological phenotypes
- Video monitoring, time-lapsed imaging, wearable devices, IoT sensors → behavioral phenotypes

Spatial forest phenomics via remote sensing



Nuijten, R.J.G. et al. Remote Sensing 13:1942 (2021)

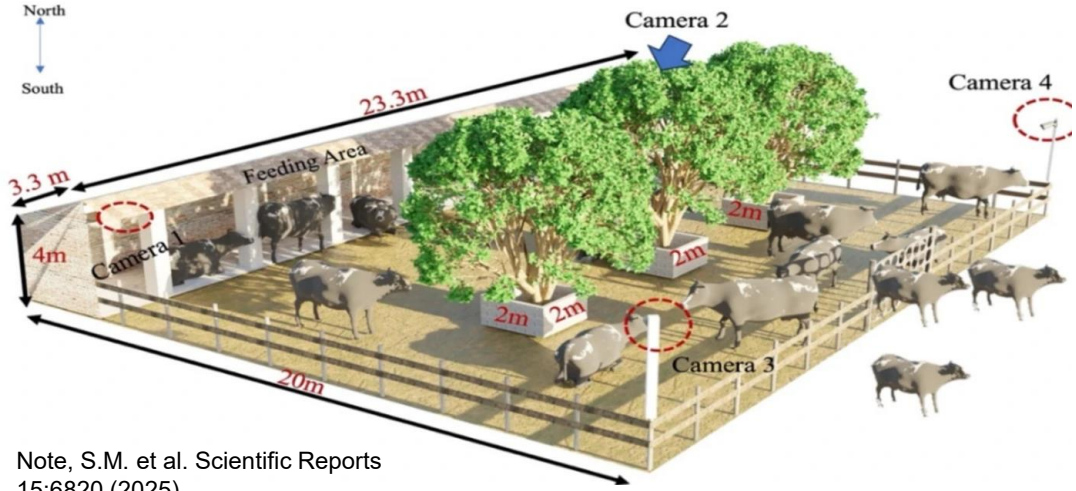
Spectral imaging in plants



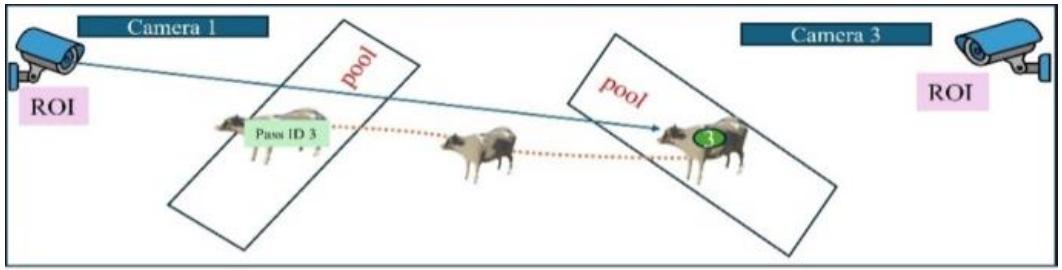
Zhang, Q. et al. Plants 13:3088 (2024)

- Different wavelengths reveal different characteristics
- Hyperspectral (>380 nm) can reveal symptoms of nutrient deficiency

Motion tracking

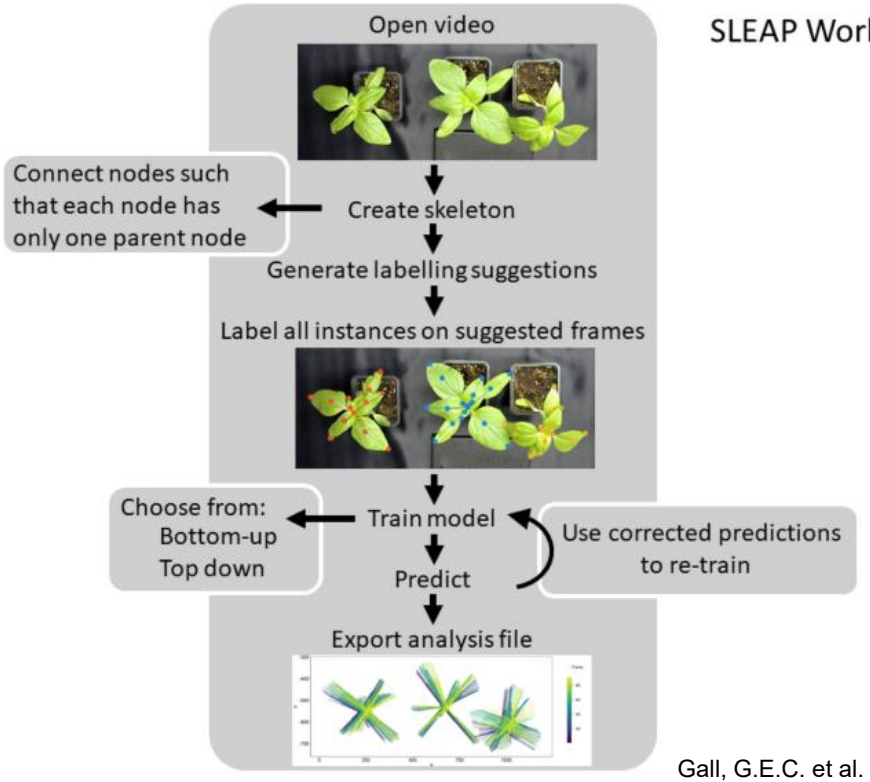


Note, S.M. et al. Scientific Reports 15:6820 (2025)



- Individual animal recognition
- Cross-camera tracking of the same animal
- Coordinate mapping from camera images onto location

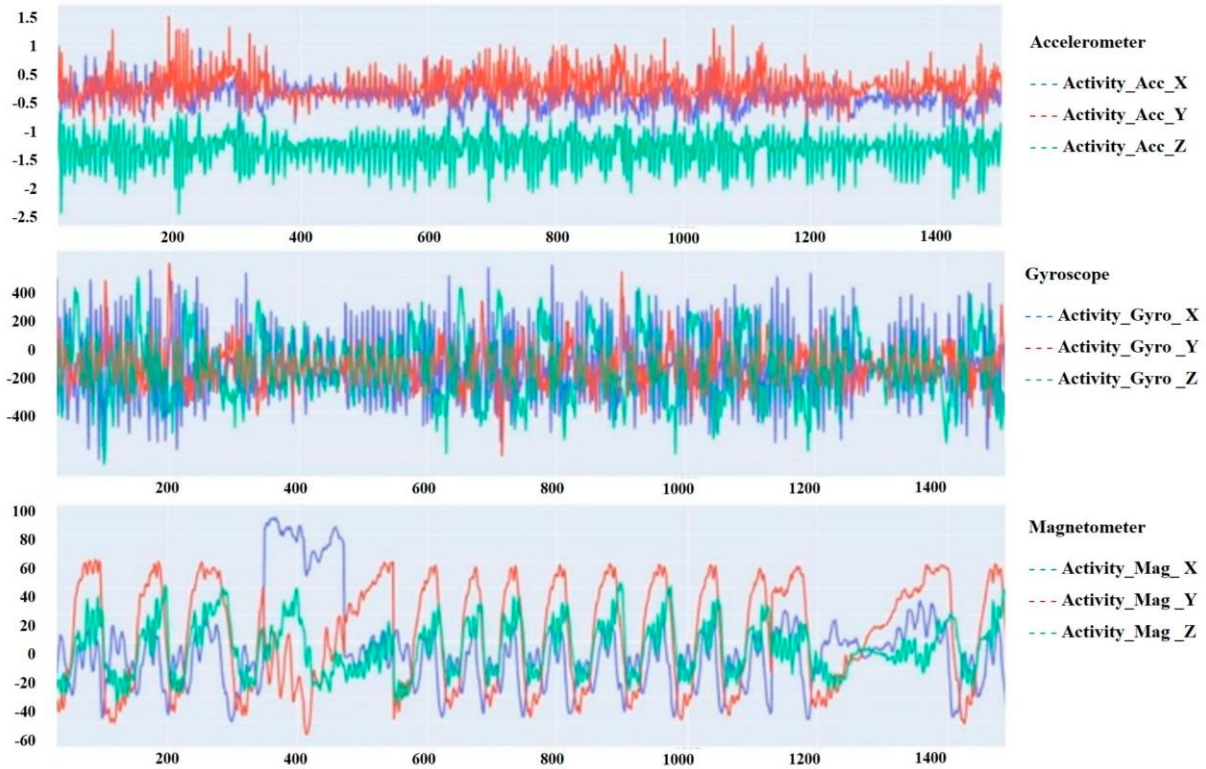
Time-lapsed video



- Stationary camera capturing plant growth
- Measure growth velocity (direction and speed) as phenotypes
- Can also track shape, size, and color changes

Gall, G.E.C. et al. Plant Methods 18:21 (2022)

Sensors and wearable devices



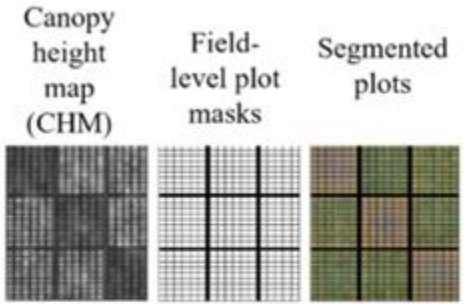
Mozumder, M.A.I. et al. Sensors 24:7436 (2024)

- Use sensors to classify activity types
- Video may be used to train the classification

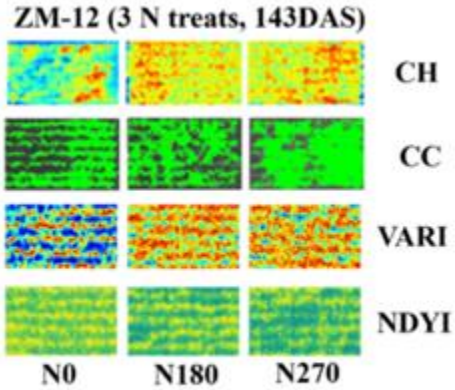
Nitrogen use analysis in wheat

Shen, L. et al. Agronomy 14:1612 (2024)

Orthomosaics of the field experiment



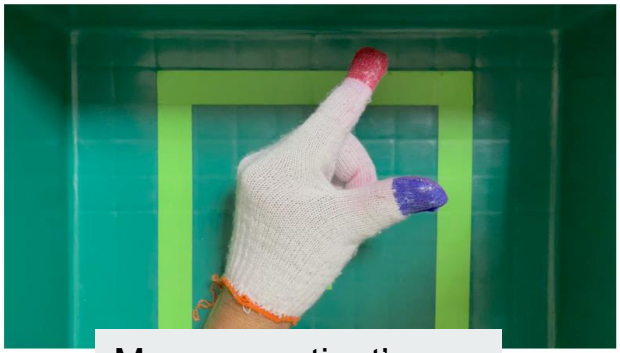
Phenotypic analysis accomplished using the AirMeasurer platform



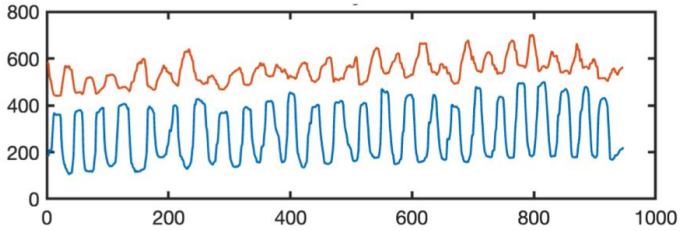
Four plot-based traits analyzed by AirMeasurer

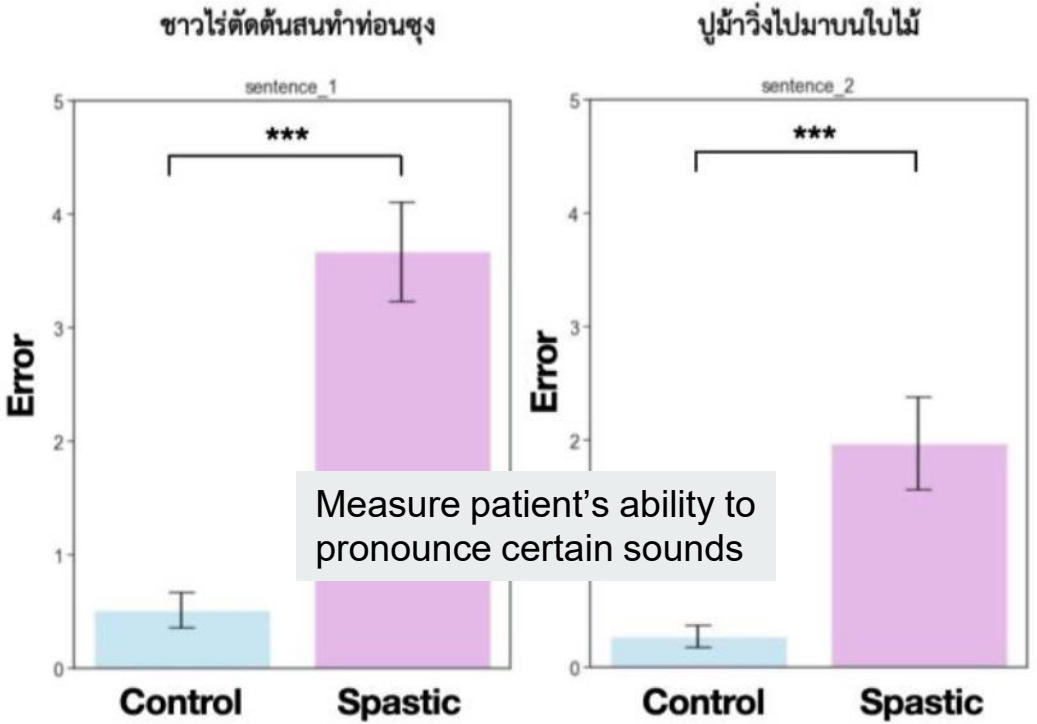
- Different fields with various nitrogen fertilizer amounts
- Photo taken by drone
- Control weather, time-of-day, light condition, location, and height

AI-enabled home-made quantitative phenotypic assays



Measure patient's ability to move fingers





Measure patient's ability to pronounce certain sounds

Credit: Dr. Chaipat Chunharas

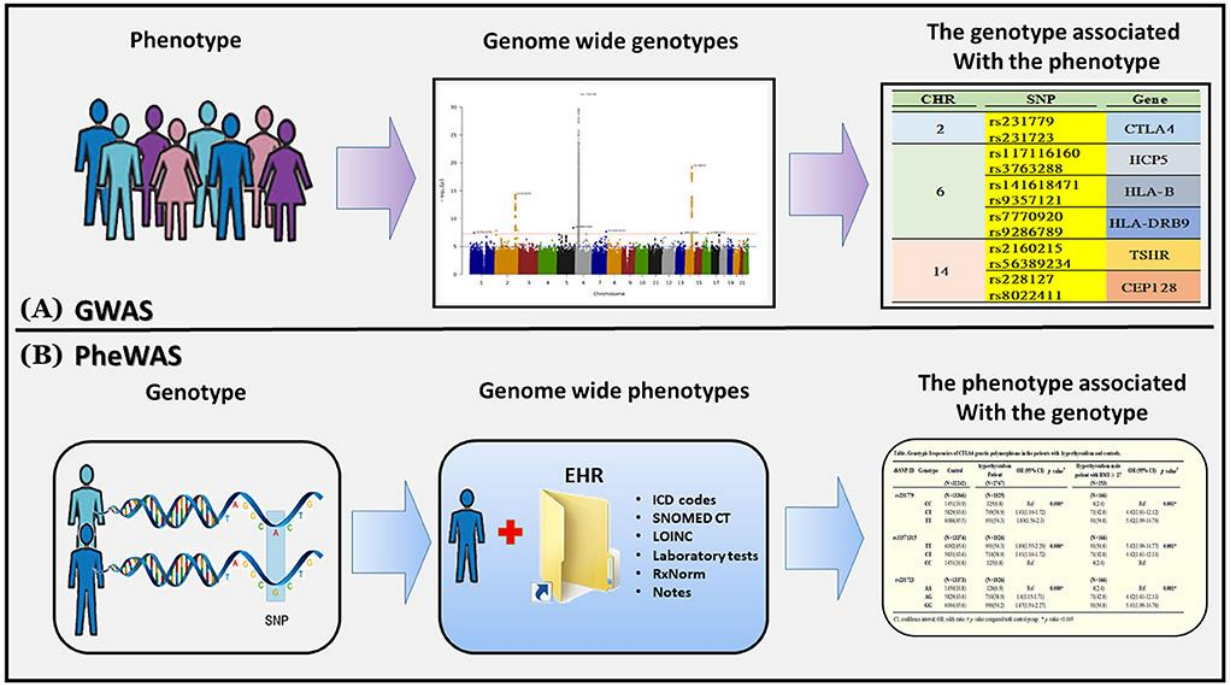
Making sense of phenomics data

Challenges in phenomics analysis

- Multifactorial on both inputs (variables) with outputs (phenotypes)
- Gap of mechanistic knowledge between molecular characteristics and observable phenotypes
- Incomplete information about environmental data → unknown factors
- Incomplete metadata → compatibility across datasets

Phenome-wide association study (PheWAS)

Liu, T.-Y. et al. Frontiers in Medicine 9:830621 (2022)

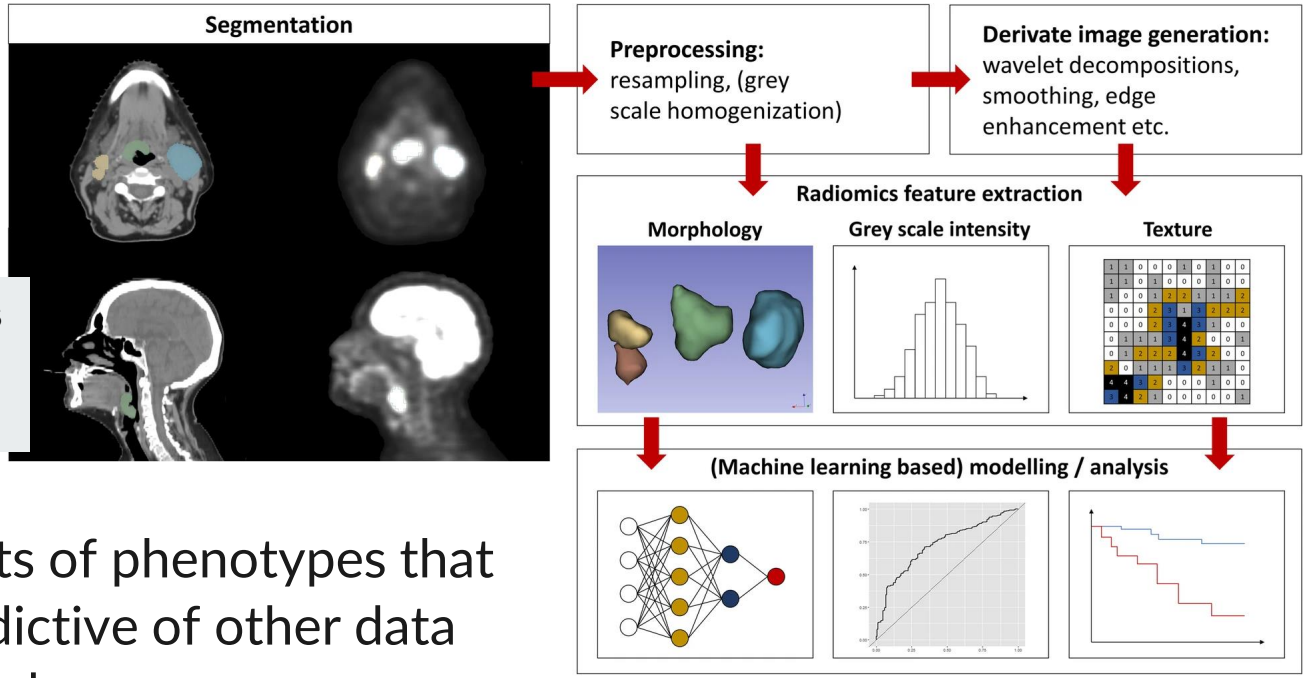


- Flipped GWAS: one genotype vs phenomics

Data-driven feature selection

Shotgun approach: Generate thousands of possible phenotypes

Data-driven: Build models that use phenotypes to predict other types of data



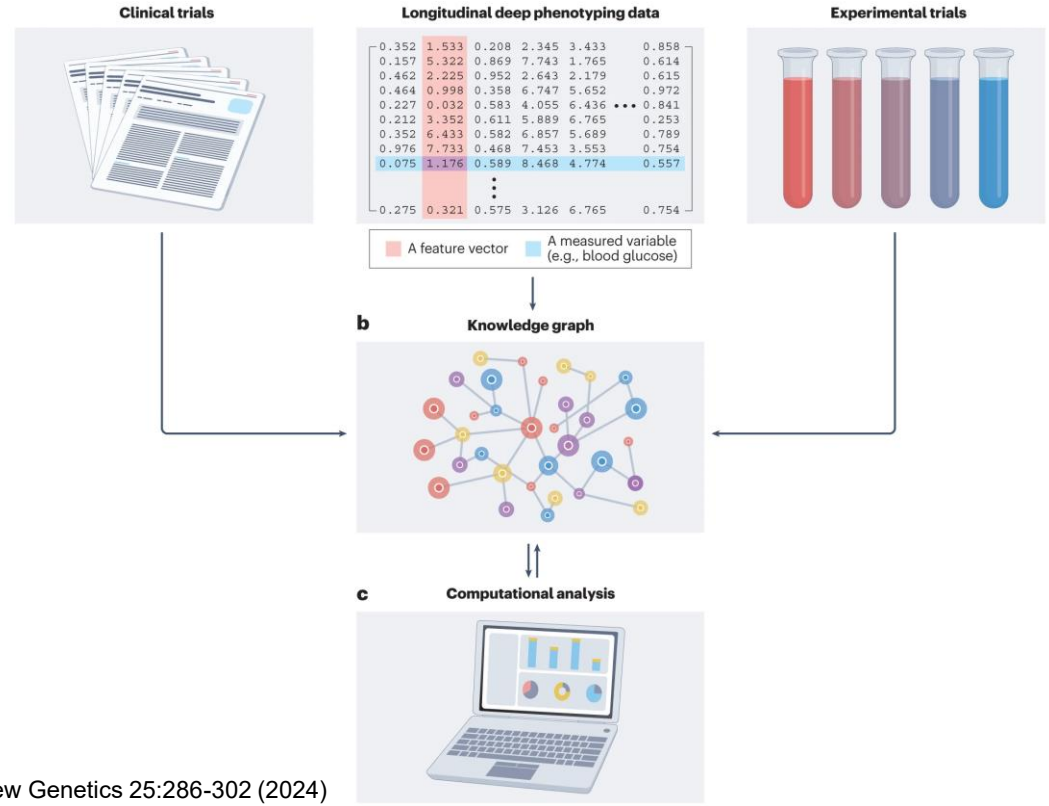
- Identify minimal sets of phenotypes that are associate / predictive of other data
- Image-based biomarkers

Haider, S.P. et al. Cancers of the Head & Neck 5:6 (2020)

Mechanism-guided model building

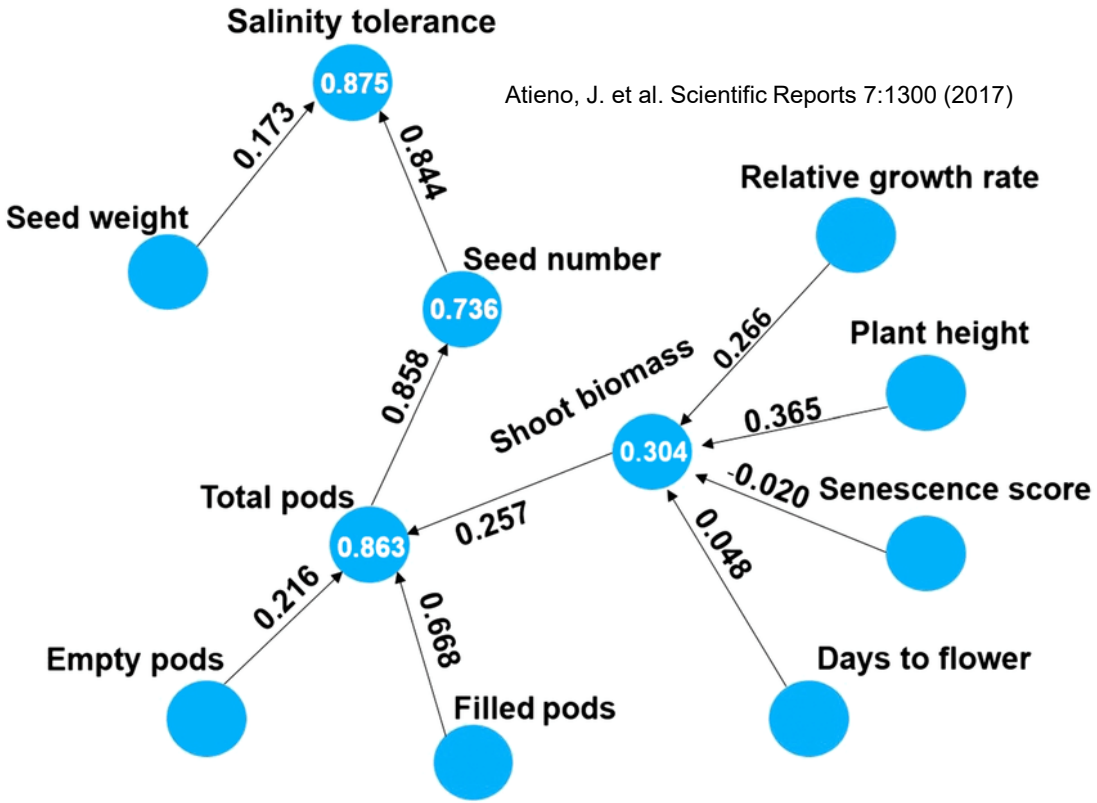
- Constrained data-driven modeling using knowledge graph or causal diagram to force relationships between parameters

- **Example**: biological pathway, protein-protein binding networks



Yurkovich, J.T. et al. Nature Review Genetics 25:286-302 (2024)

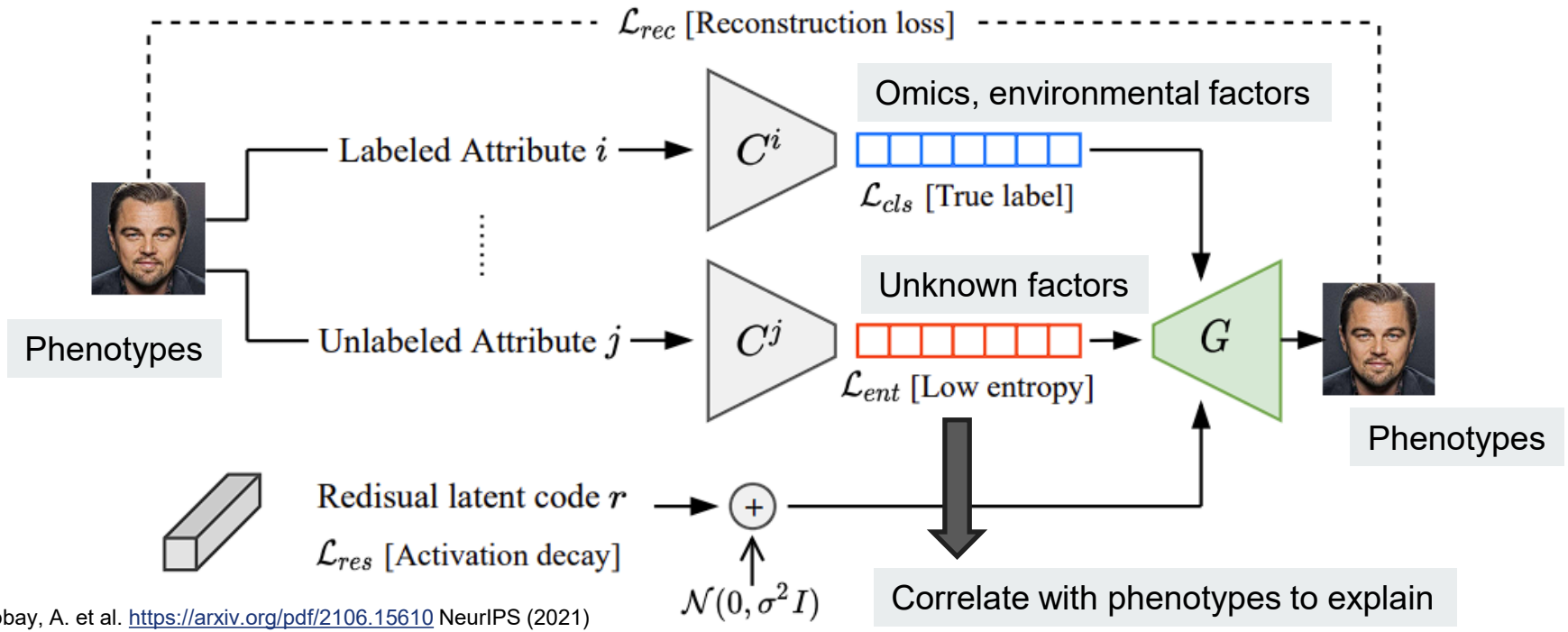
Path analysis



Atieno, J. et al. Scientific Reports 7:1300 (2017)

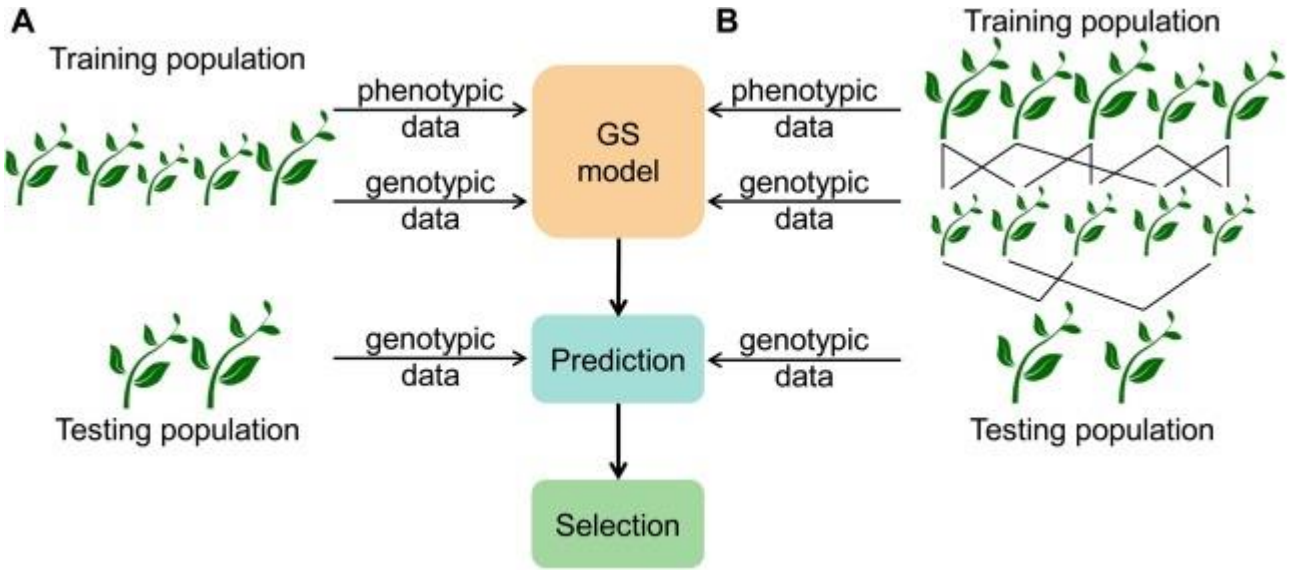
- Decompose direct and indirect effects onto a predefined graph structure
- Upstream nodes are used to predict downstream nodes
- Hierarchical regression

Generative approach to infer unknown factors



Gabbay, A. et al. https://arxiv.org/pdf/2106.15610 NeurIPS (2021)

Phenomics-guided breeding



Tong, H. and Nikoloski, Z. Journal of Plant Physiology 257:153354 (2021)

- Use genotype-phenotype knowledge to select optimal genetic combinations → guide breeding

Summary

- Phenomics focus on understanding and manipulating phenotypes
- Addition of environmental factors on top of omics
- Utilize wide range of assay technology
- Powerful applications in medicine, livestock, and agriculture

Any question?

- See you next time