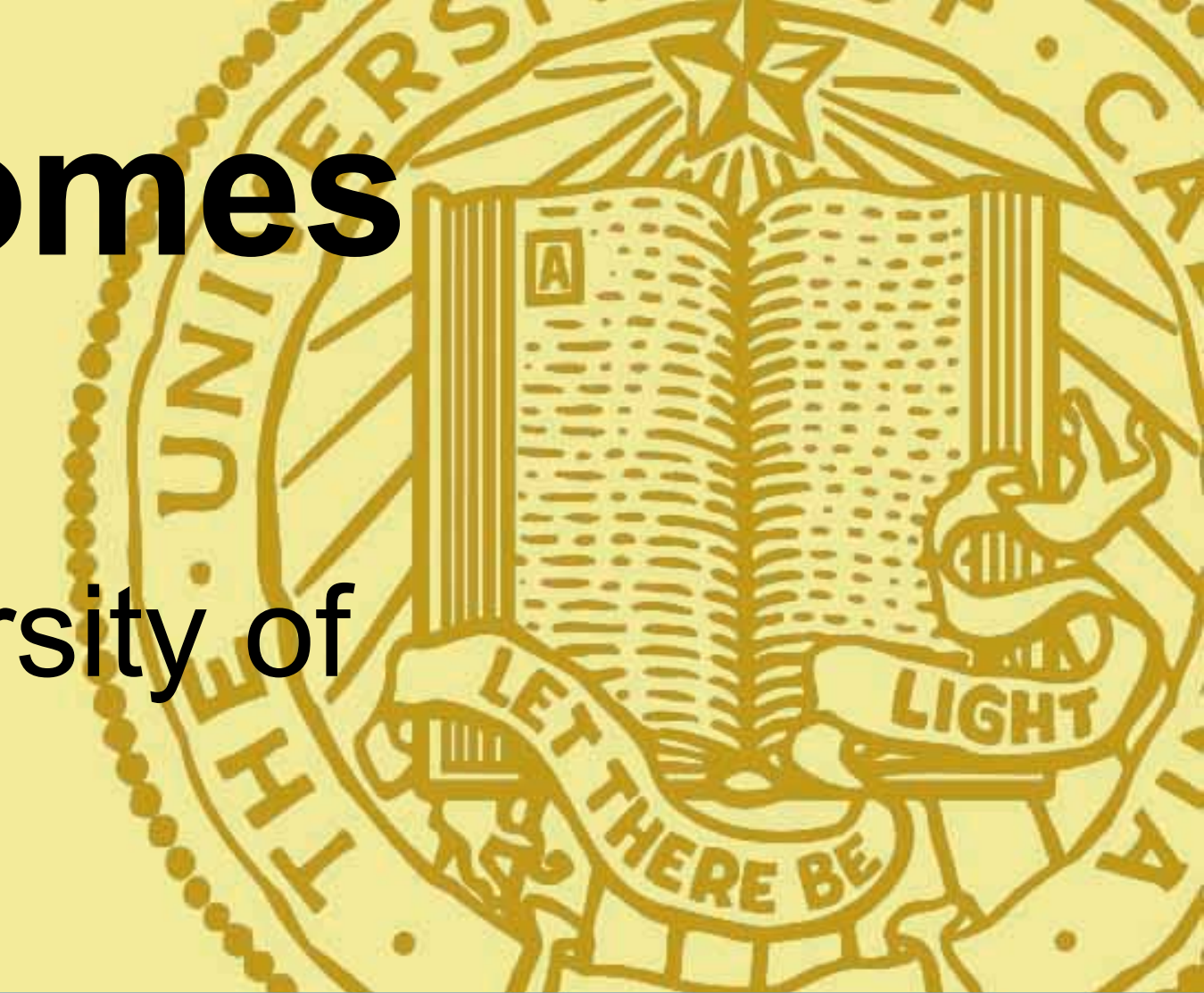


Measuring global shifts of gene networks in single cell transcriptomes

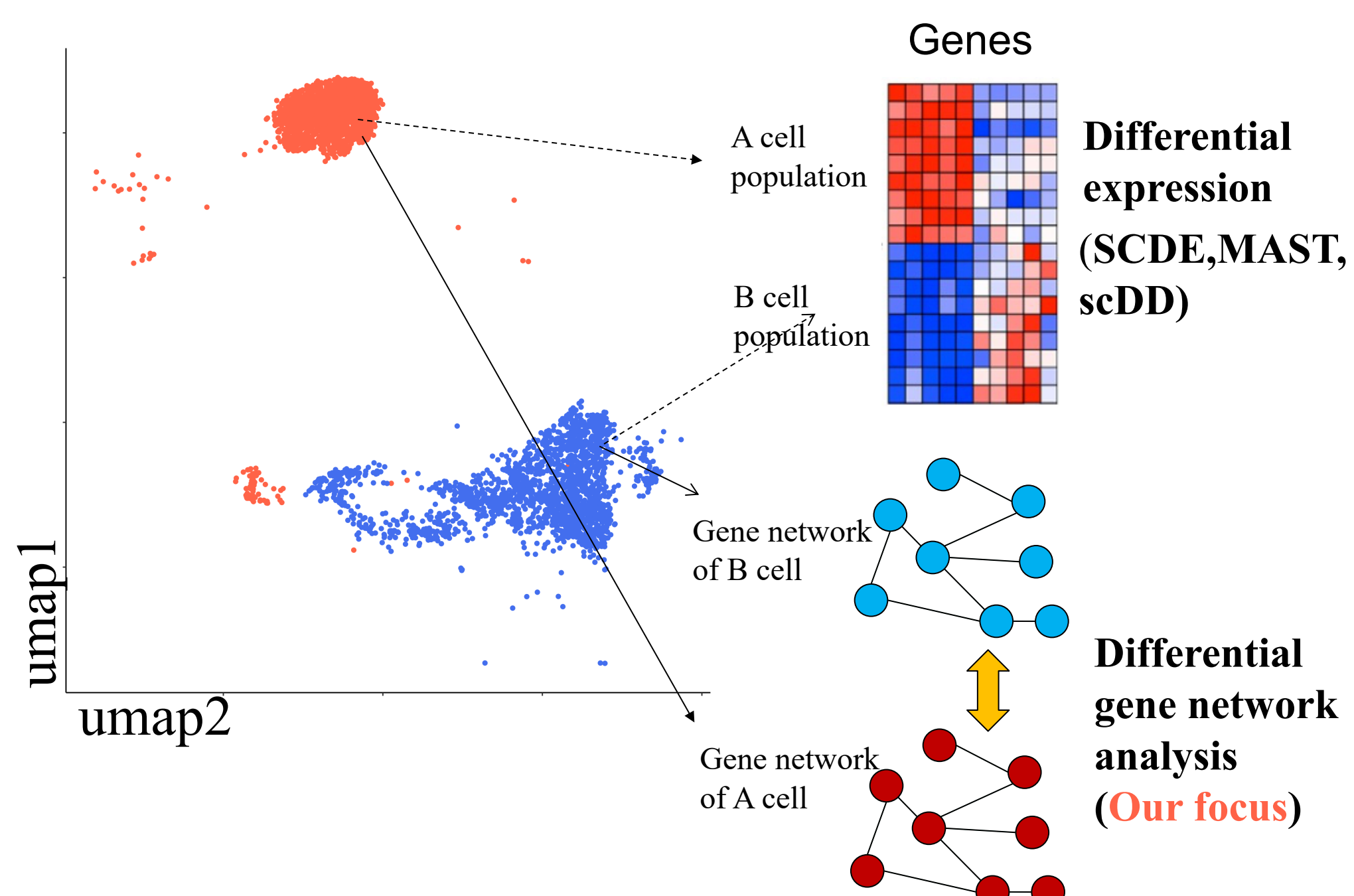
Ruoxin Li^{1,2}, Gerald Quon^{1,2,3}

¹ Biostatistics Graduate Group, ²Genome Center, ³Department of Molecular and Cellular Biology, University of California, Davis, Davis, CA



Motivation

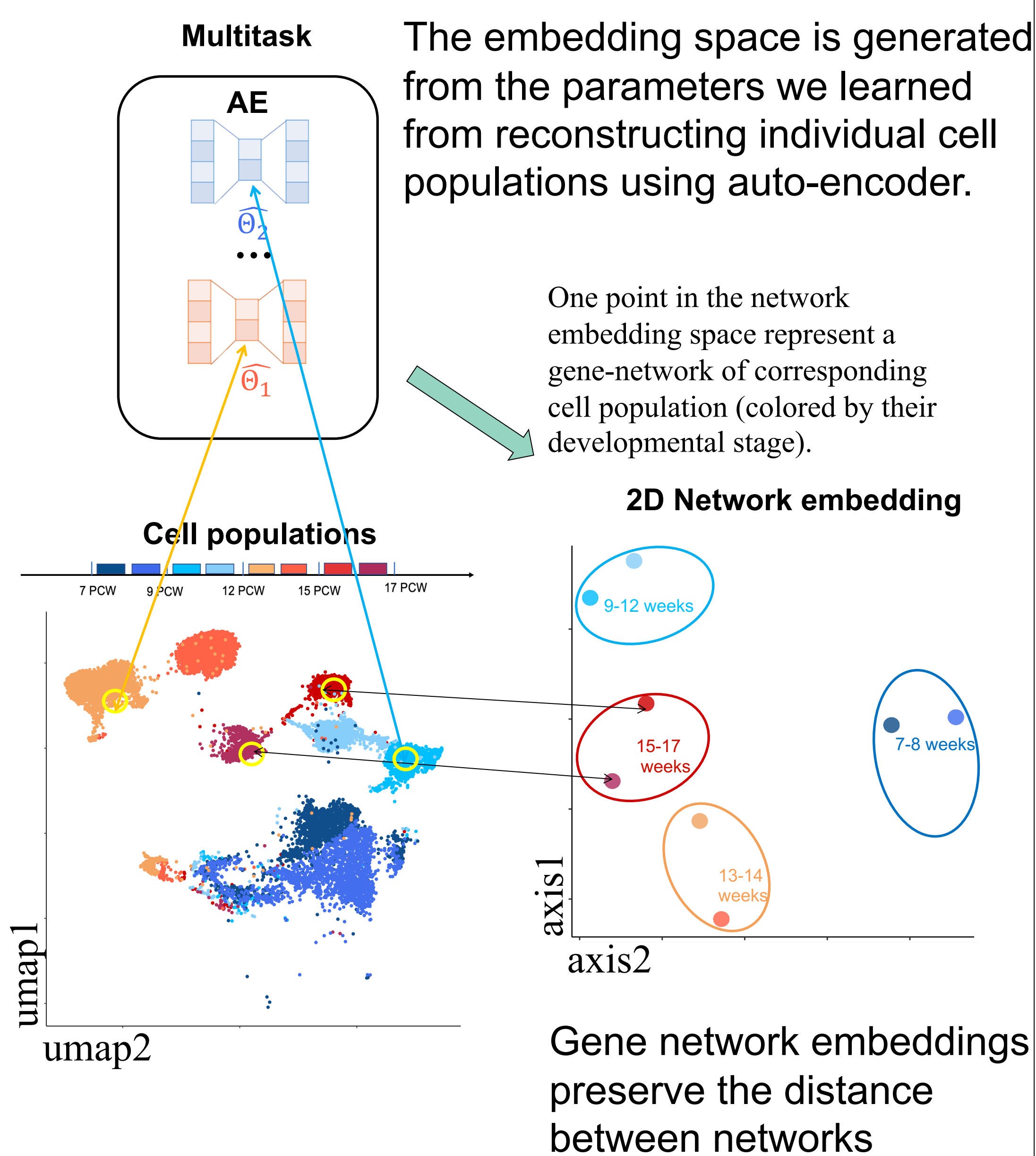
Variation of gene's co-expression pattern



Aim:

1. Gene networks are varying according to development time or experimental conditions. We are aiming to characterize the shifts of gene-networks by measuring their relative distance.
2. We are also interested in which genes are involved in the changes of those networks.

Schematic



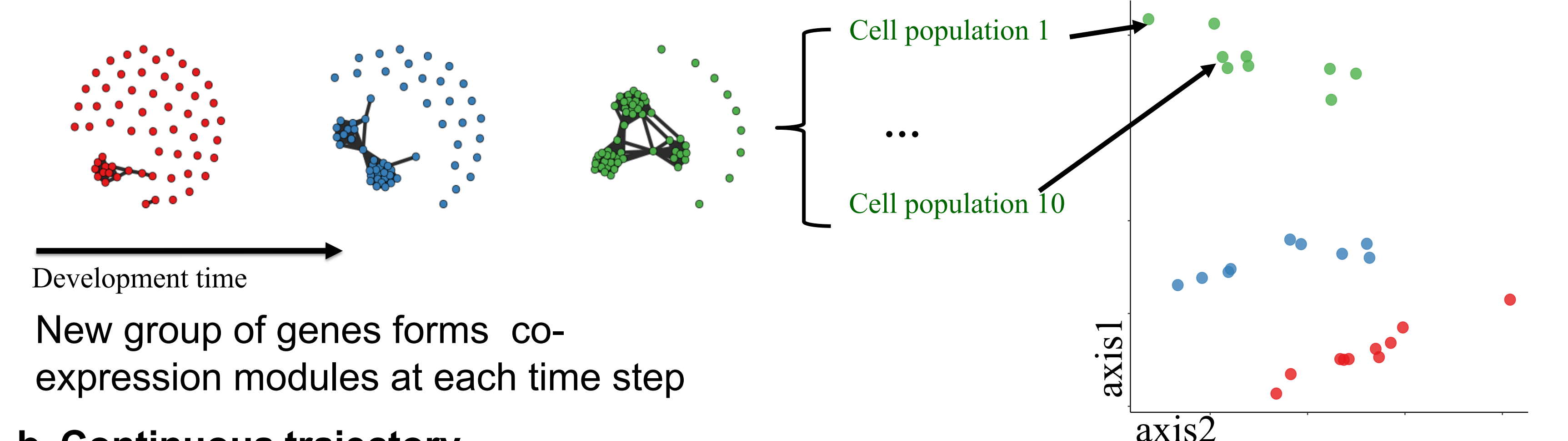
Simulation study of varying gene network trajectories

Goal of simulation study

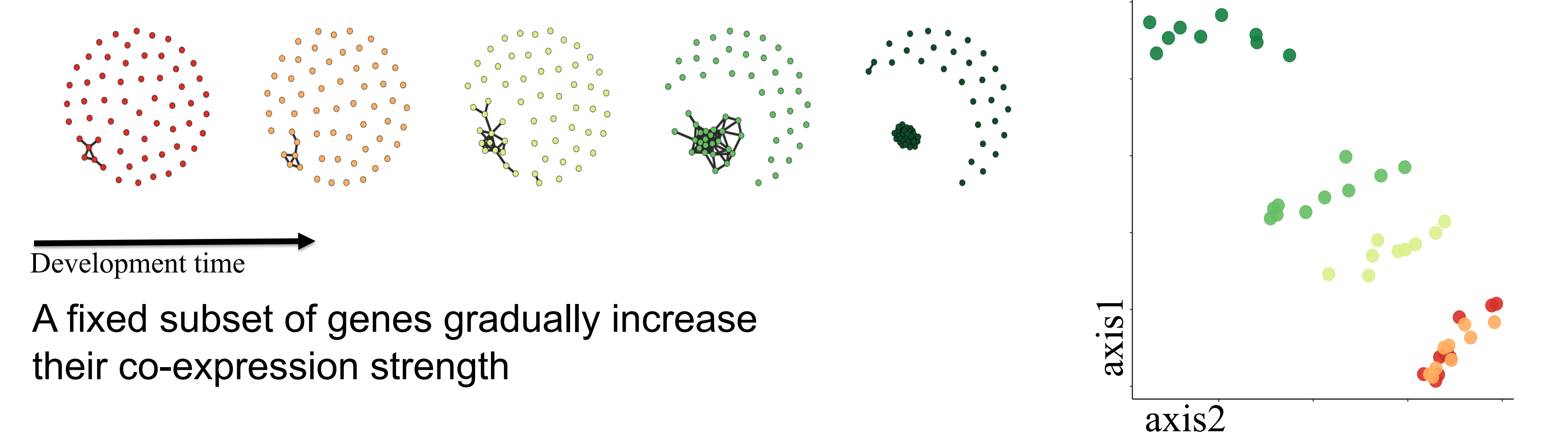
To validate the model, we first simulated scRNA-seq data according to two scenarios of gene network variation: (1) a continuous and (2) a discrete trajectory to represent gene networks that are varying in either slow or fast rate. We verified that our model captured the **'between group distance'** of gene networks in both scenarios.

Network embedding preserves the 'between group distance' between gene networks

a. Discrete trajectory



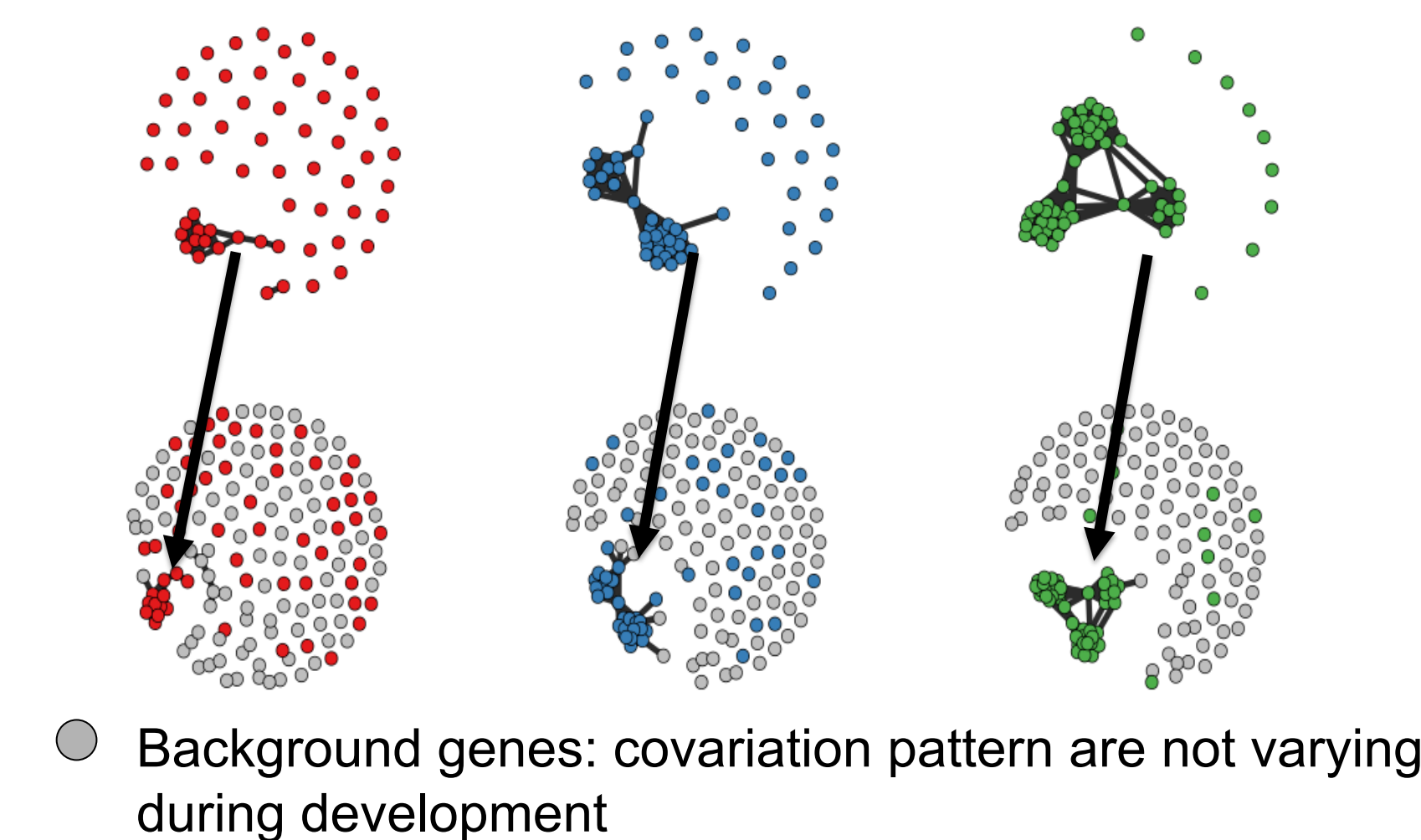
b. Continuous trajectory



Identification of genes involved in the change of network

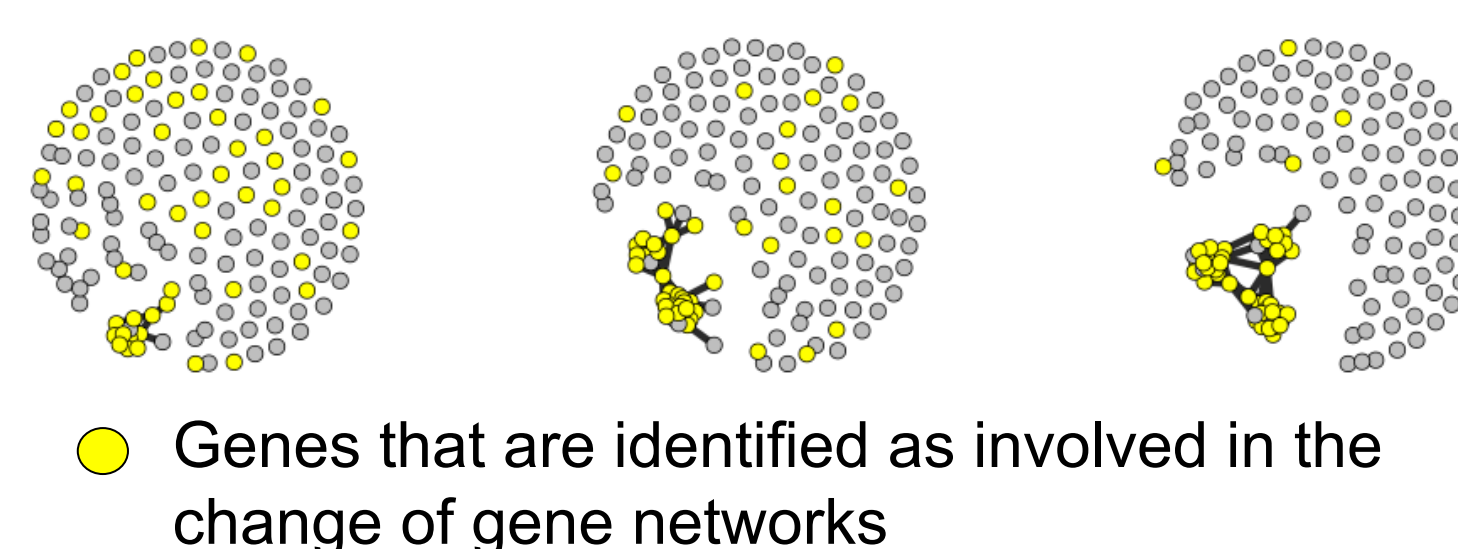
Besides genes in the network trajectory, the simulated genes also include number of **background genes** to test our ability to recover the ground truth genes that are involved in the change of gene networks

Gene network trajectory is a subset of the simulated genomes



In the discrete trajectory, comparing the identified genes and ground-truth genes that are involved in the gene-network trajectory, we obtained jaccard similarity to be 0.70. While for the continuous trajectory, we obtained jaccard similarity to be 0.43. In both scenarios, we were able to recover the ground truth gene set that are involved in the gene network trajectories.

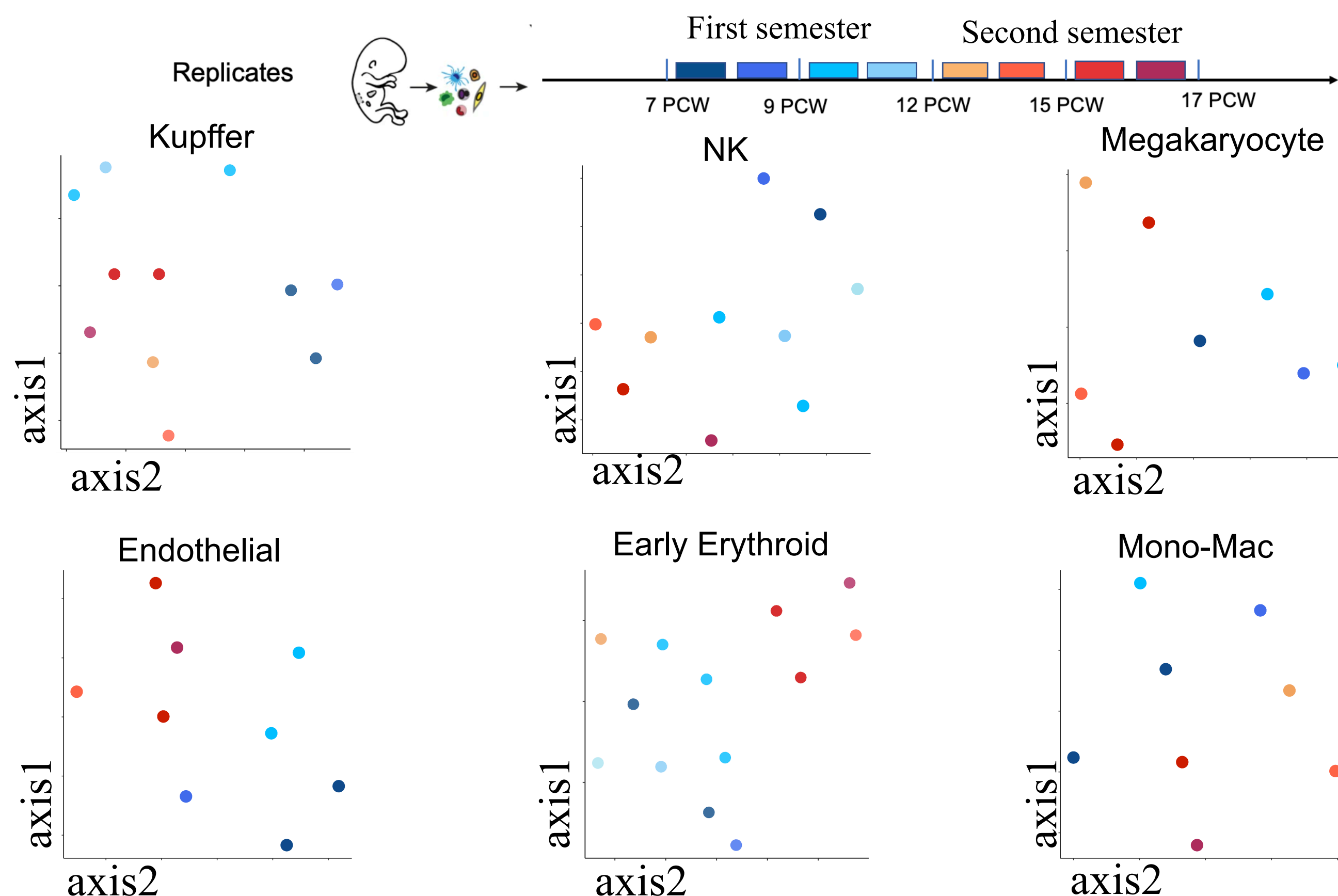
Identification of those genes that are involved in the gene network trajectories



Model validation

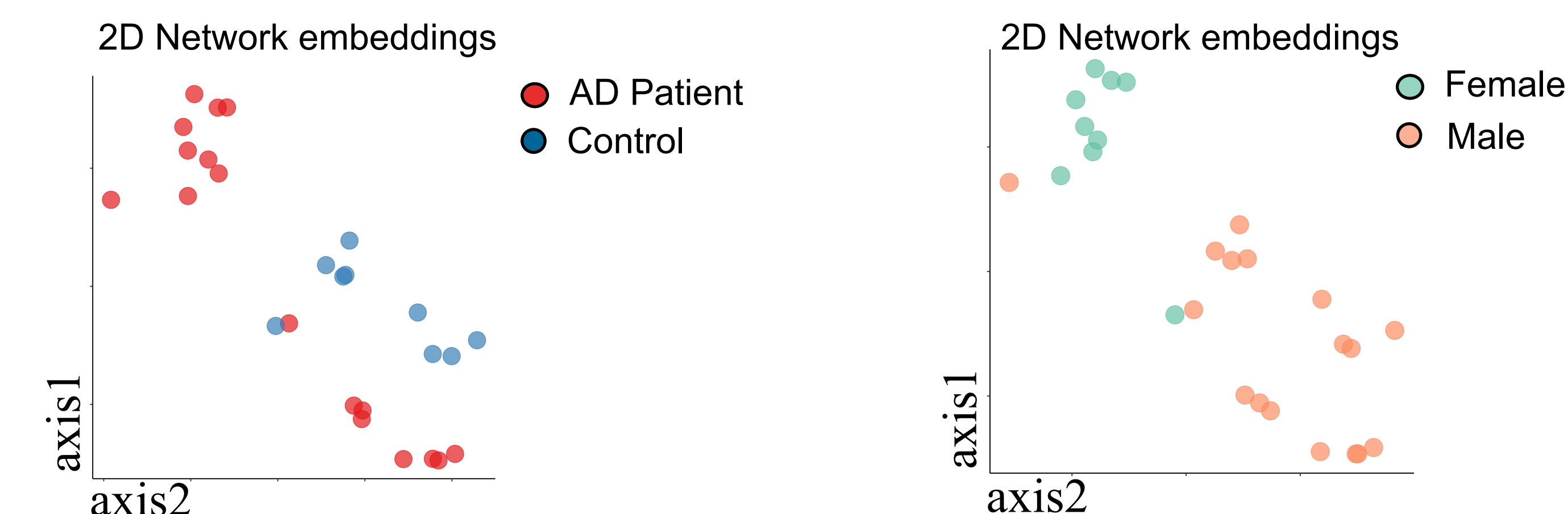
Network embeddings distinguish liver cells from early developmental stage to later [Fetal liver atlas (Popescu et al.)]

The 2D network embeddings separate cell populations of early gestation weeks (first semester: **Blue tone**) from later gestation weeks (second semester: **Red tone**).



Network embeddings distinguish Alzheimer disease from control

Among all the cell populations, 19 were collected from AD patients and 7 were from healthy controls (scRead, Jiang et al). We found clear separation in network embeddings corresponding to AD and control oligodendrocytes. Gender effect of patients also presents in the embedding space.



A number of genes that have been previously implicated in AD pathology were identified, we illustrated some of their structural change in gene networks with Ball-and-Stick representation.

