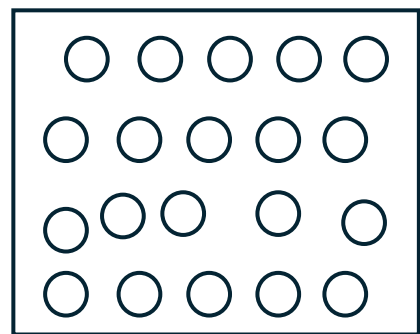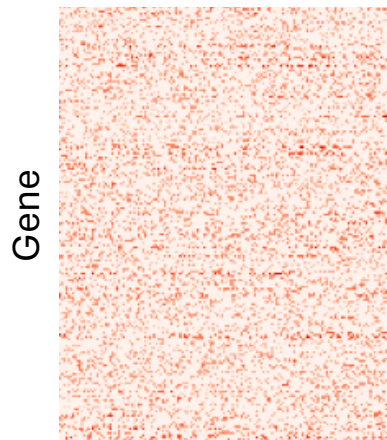**A** Input: ST data

Spatial locations of cells

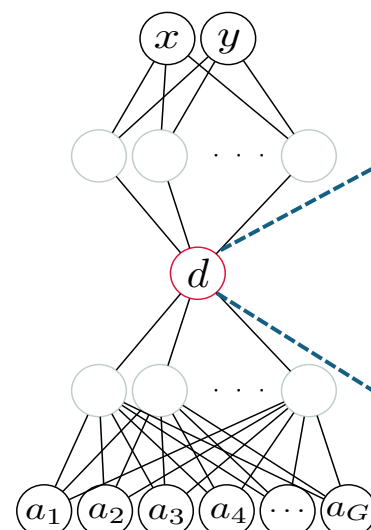Gene expression matrix

Cell

Gene

B GLACIER 🏔️
(Granger-Led Analysis of Cellular Isodepth and Expression Regulation)
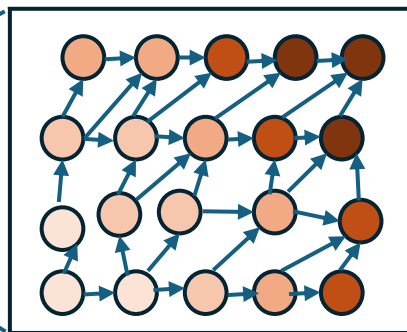
1. Create spatial DAG using topographic map of tissue slice
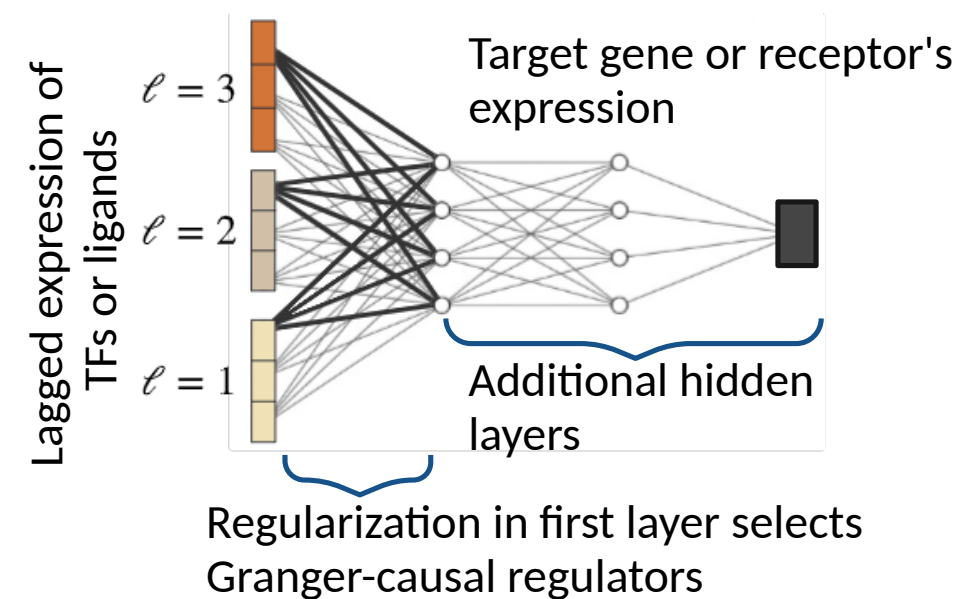
Input: spatial coordinates

x y

d

Spatial DAG

Isodepth

a_1 a_2 a_3 a_4 $\cdots$ a_G

Output: gene expression

2. DAG-structured Granger causal inference

Lagged expression of TFs or ligands

$\ell = 3$

$\ell = 2$

$\ell = 1$

Target gene or receptor's expression

Additional hidden layers

Regularization in first layer selects Granger-causal regulators

C Output: cellular interactions

TF

Expression

Target gene

Isodepth

Ligand

Expression

Receptor

Isodepth