Cell Trajectory Inference based on Optimal Transport and a mechanistic stochastic gene expression model

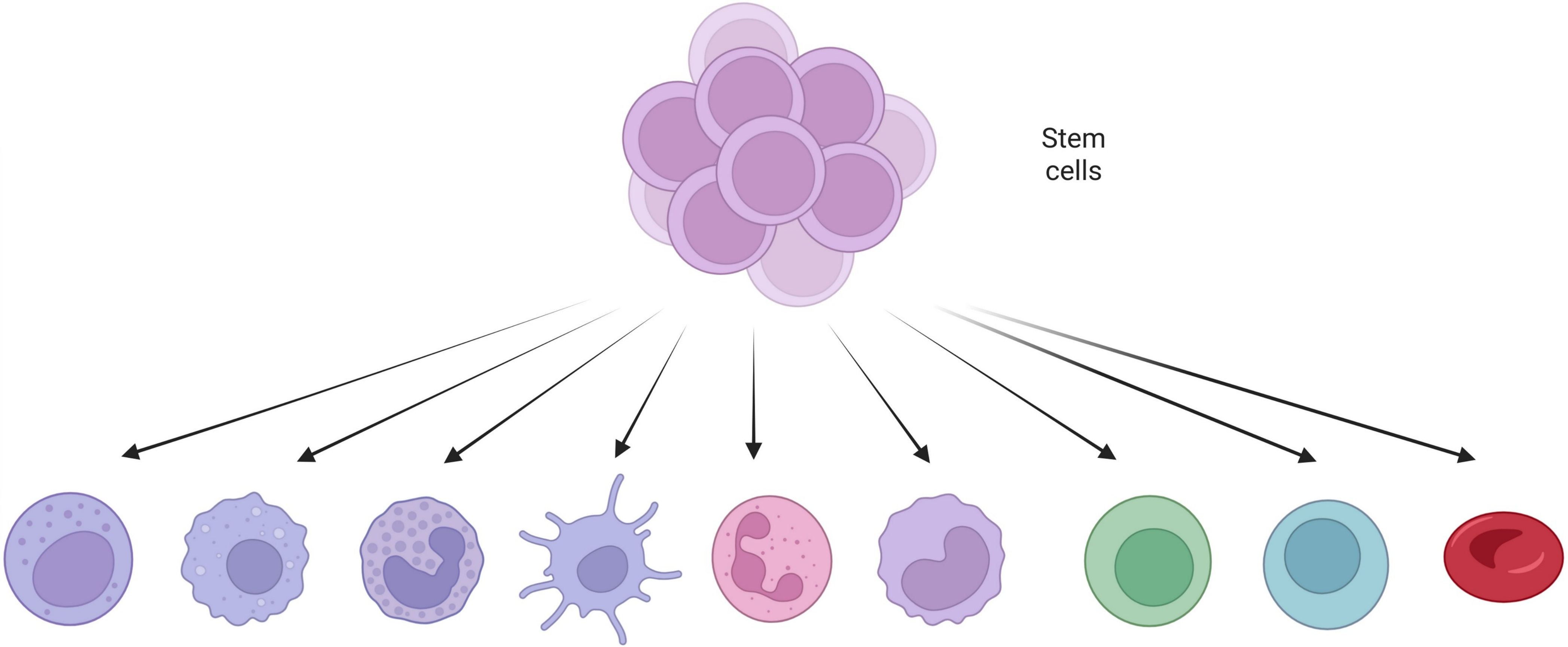
Clémence FOURNIÉ

Supervisors : Fabien Crauste and Olivier Gandrillon

In collaboration with Elias Ventre (INRIA Marseille), Ulysse Herbach (INRIA Nancy) et Aymeric Baradat (ICJ Lyon)

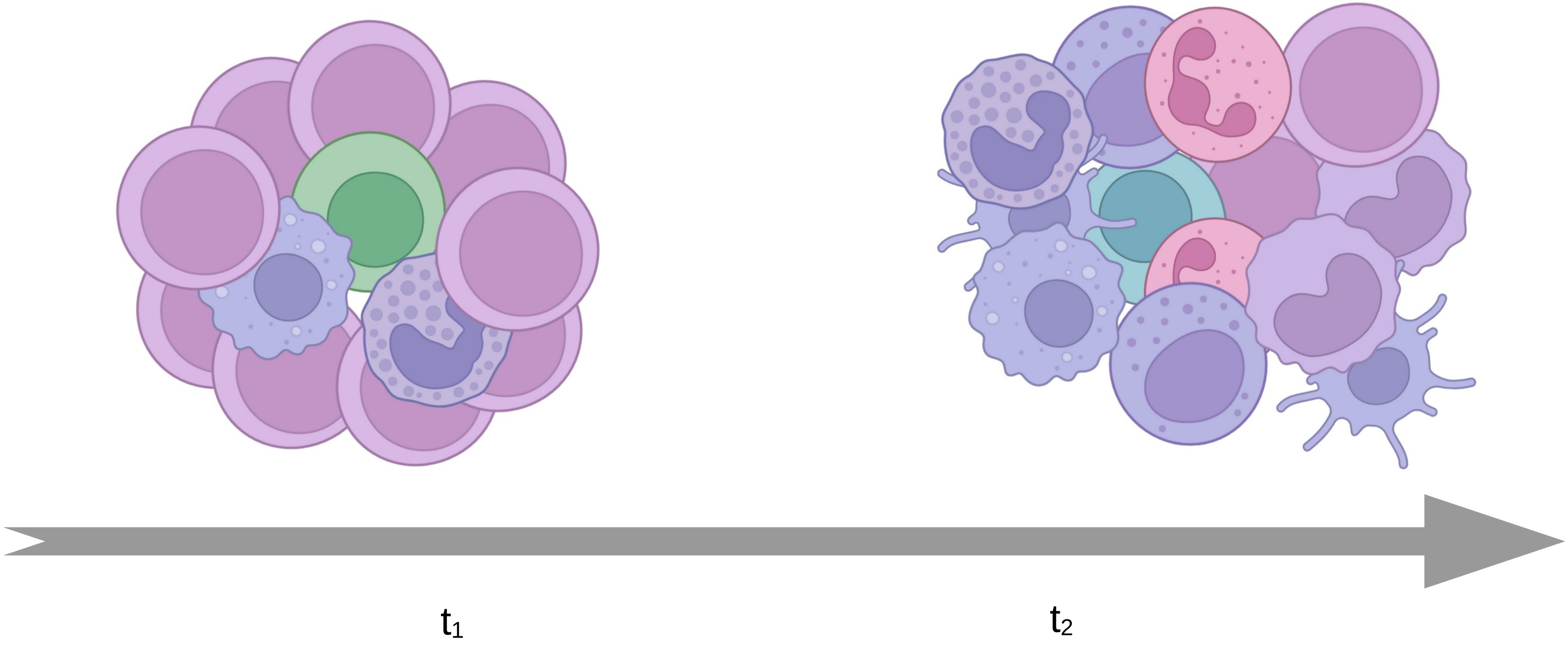
07/11/2025

Cellular differentiation

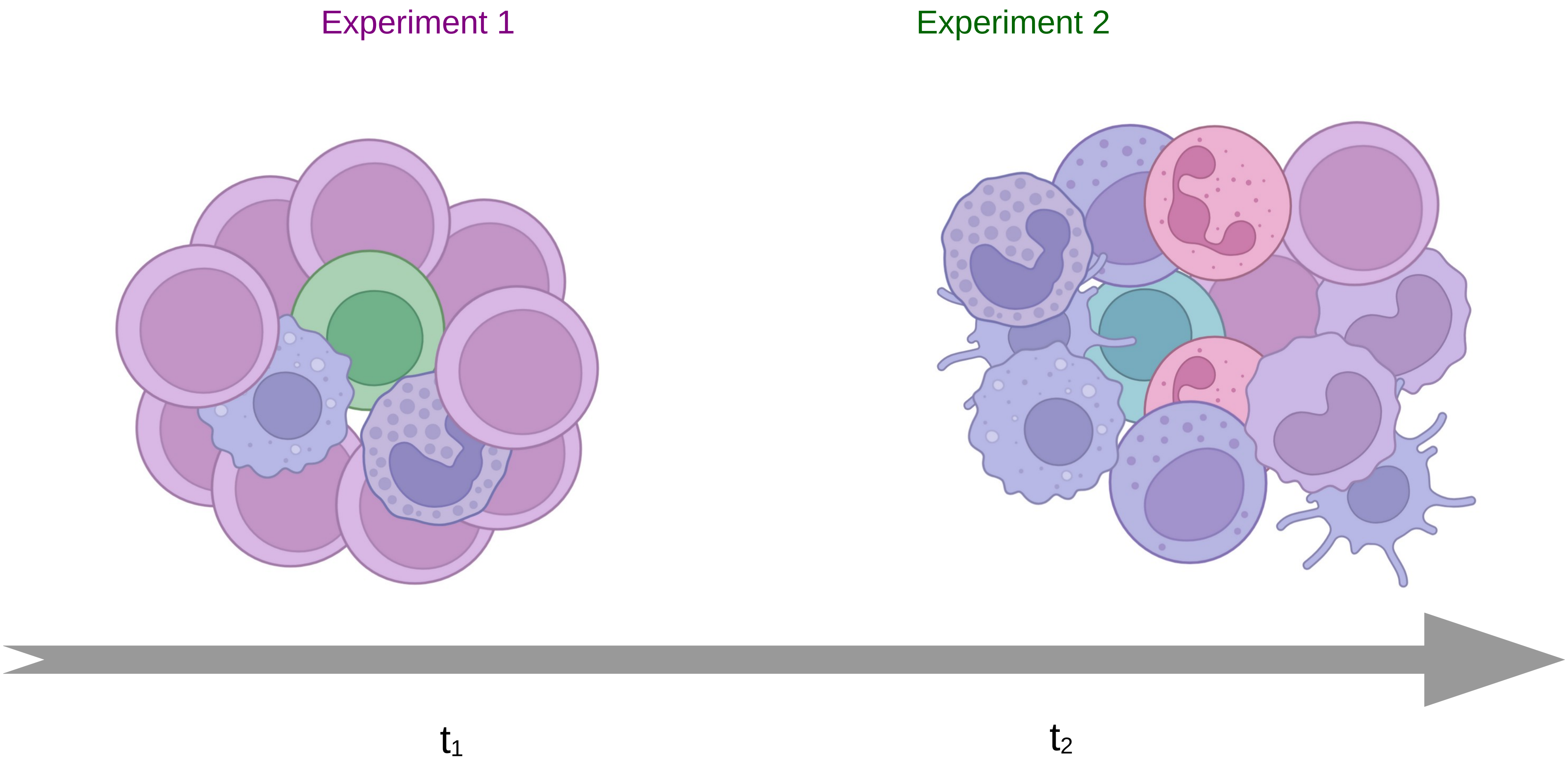


(biorender.com)

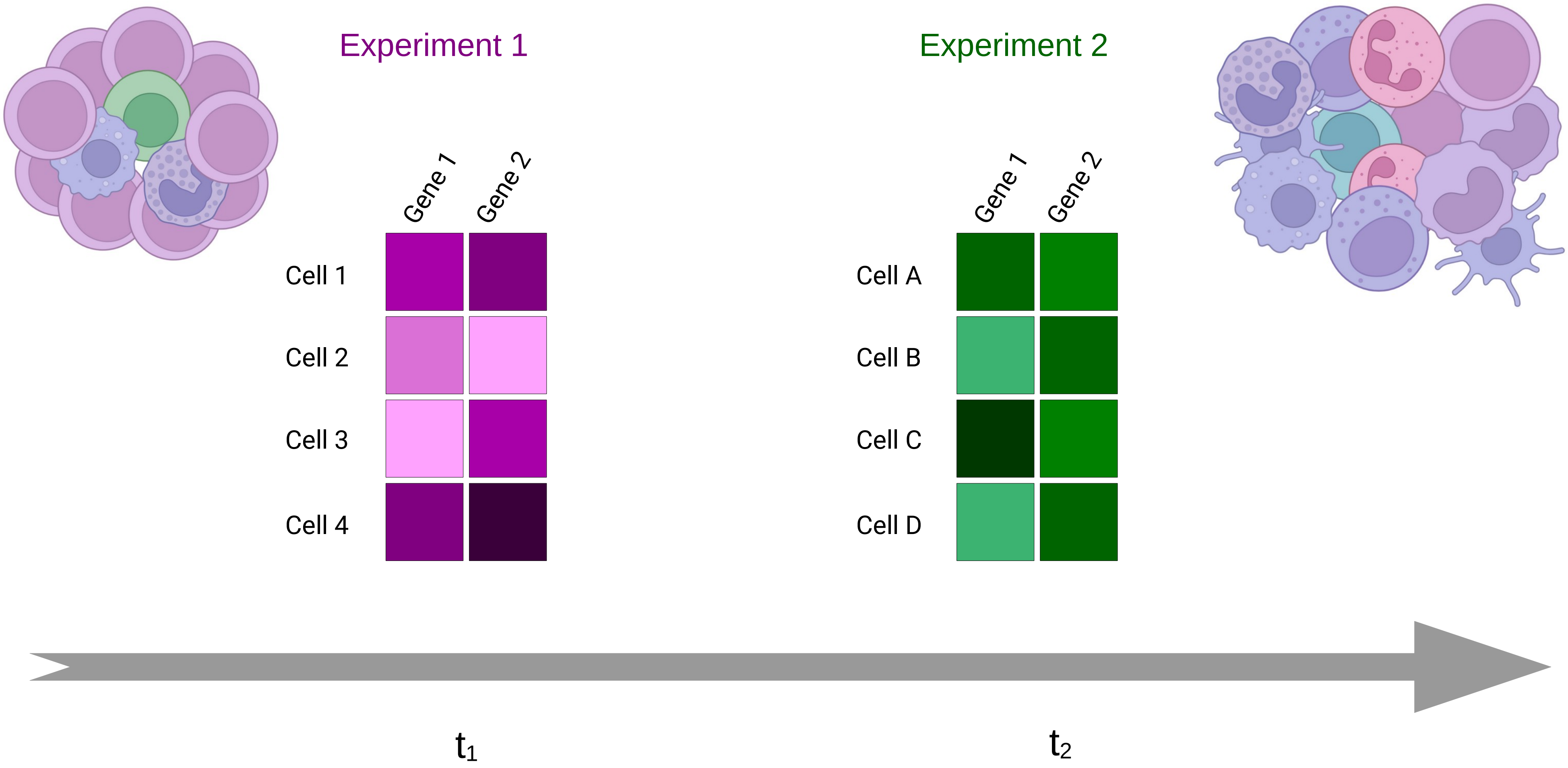
Cellular differentiation



Context

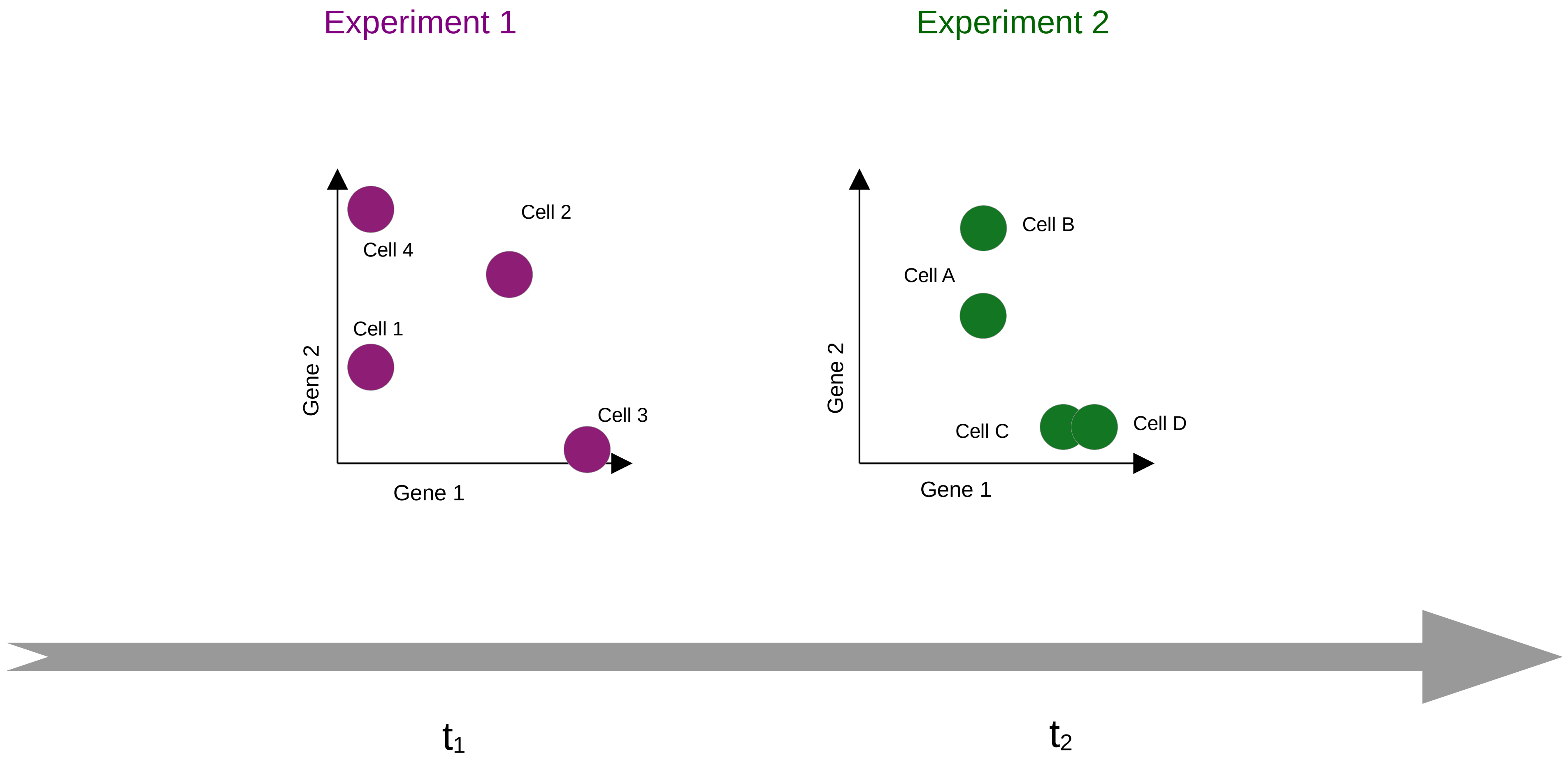


Context

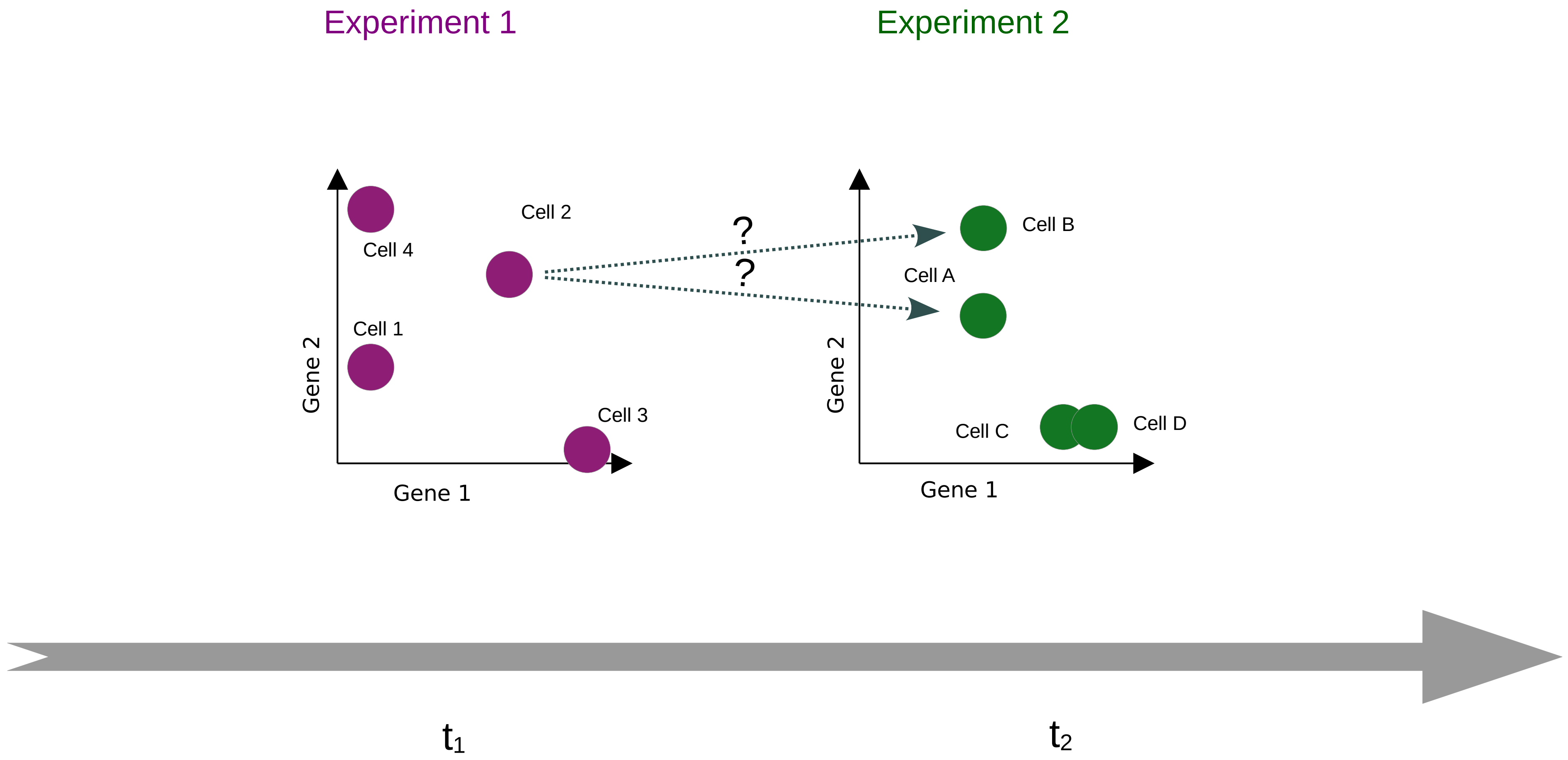


Experiment 1
Gene 1
Gene 2
Cell 1
Cell 2
Cell 3
Cell 4
Experiment 2
Gene 1
Gene 2
Cell A
Cell B
Cell C
Cell D
t_1
t_2

Context

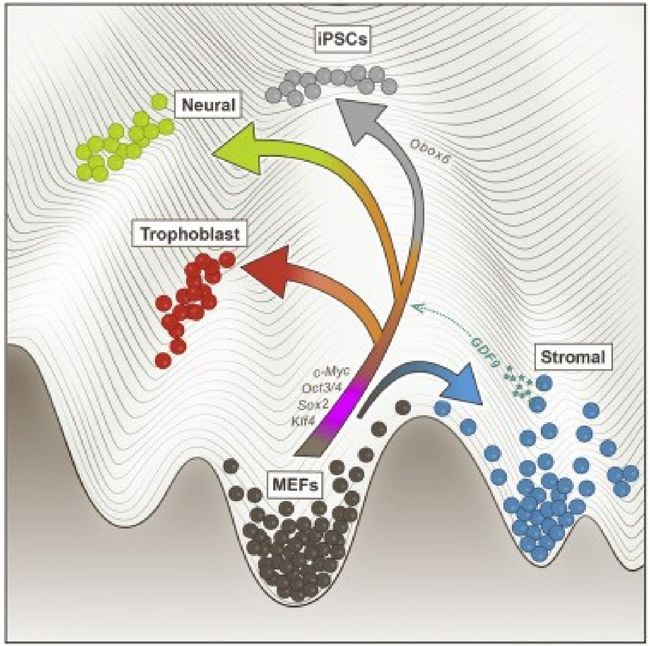

Experiment 1
Experiment 2
Cell 2
Cell 4
Cell 1
Cell 3
Gene 2
Gene 1
Cell B
Cell A
Cell C
Cell D
Gene 2
Gene 1
t1
t2

Context



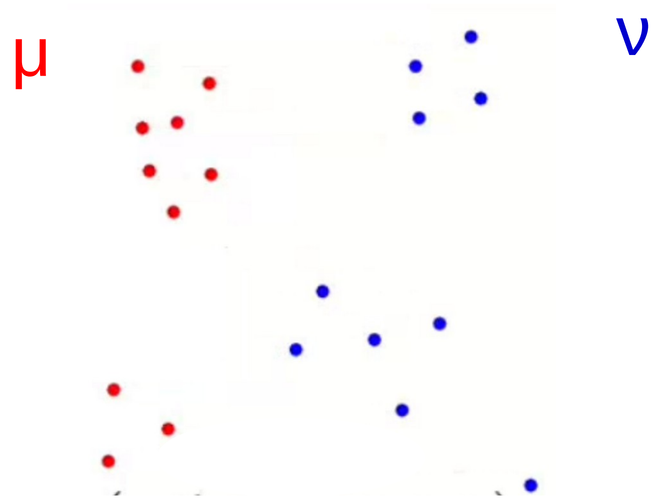
Experiment 1
Experiment 2
Cell 4
Cell 2
Cell 1
Cell 3
Gene 2
Gene 1
?
?
Cell B
Cell A
Cell C
Cell D
Gene 2
Gene 1
t_1
t_2

Optimal Transport: WOT Algorithm



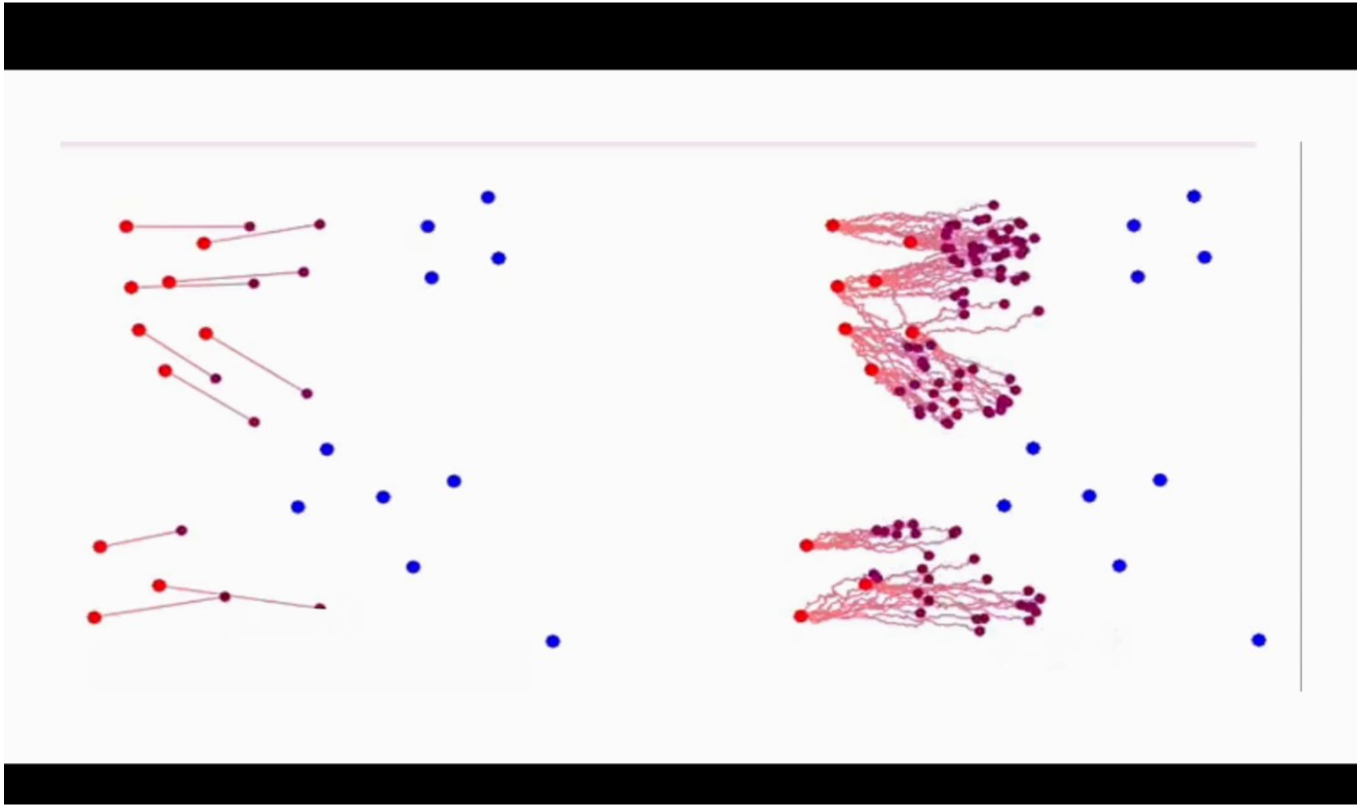
(Shiebinger et al. 2019)

Optimal Transport



Methods: Schrödinger Problem

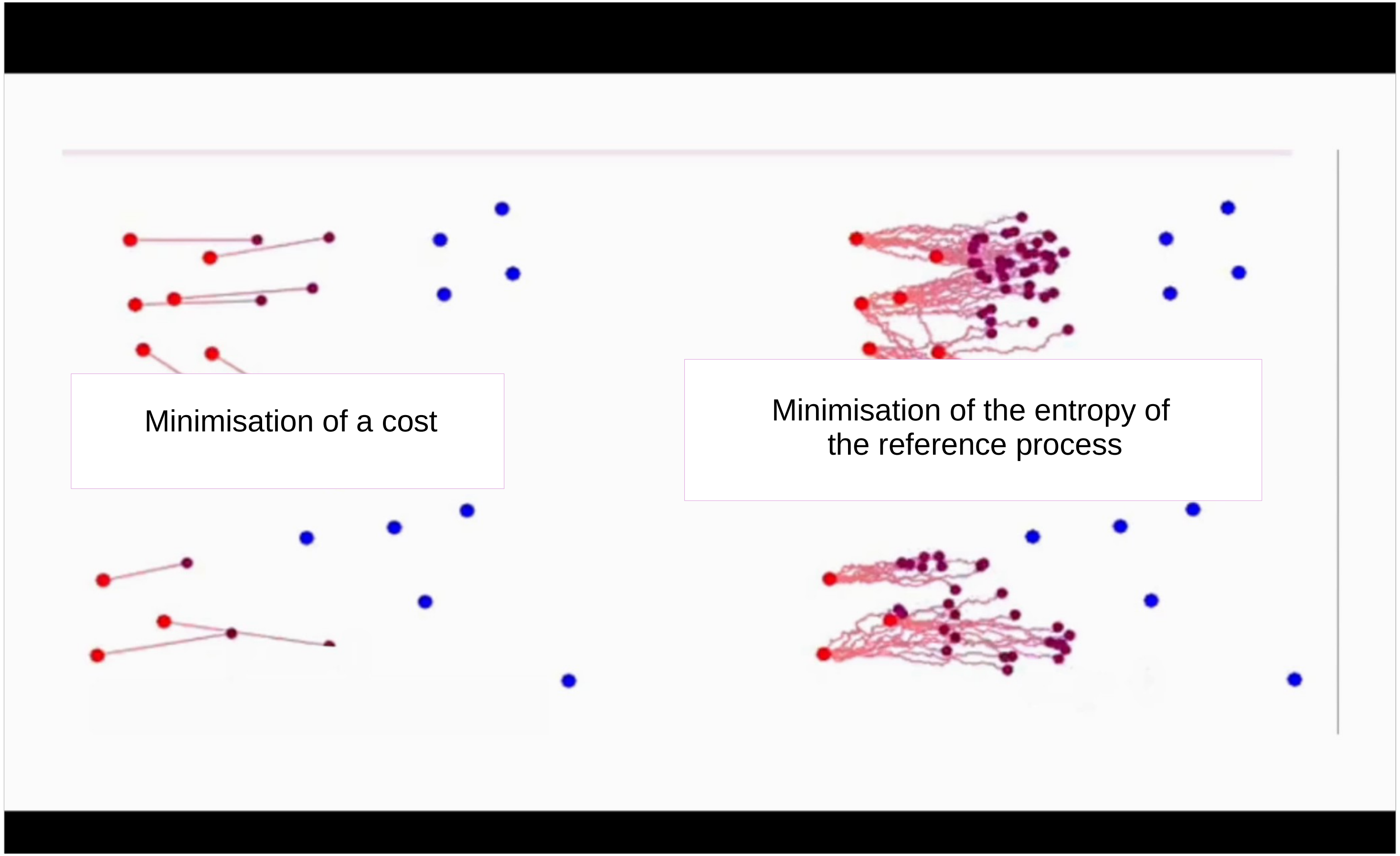
Optimal transport | Schrödinger's Problem



(Gabriel Peyré, X, 2023)

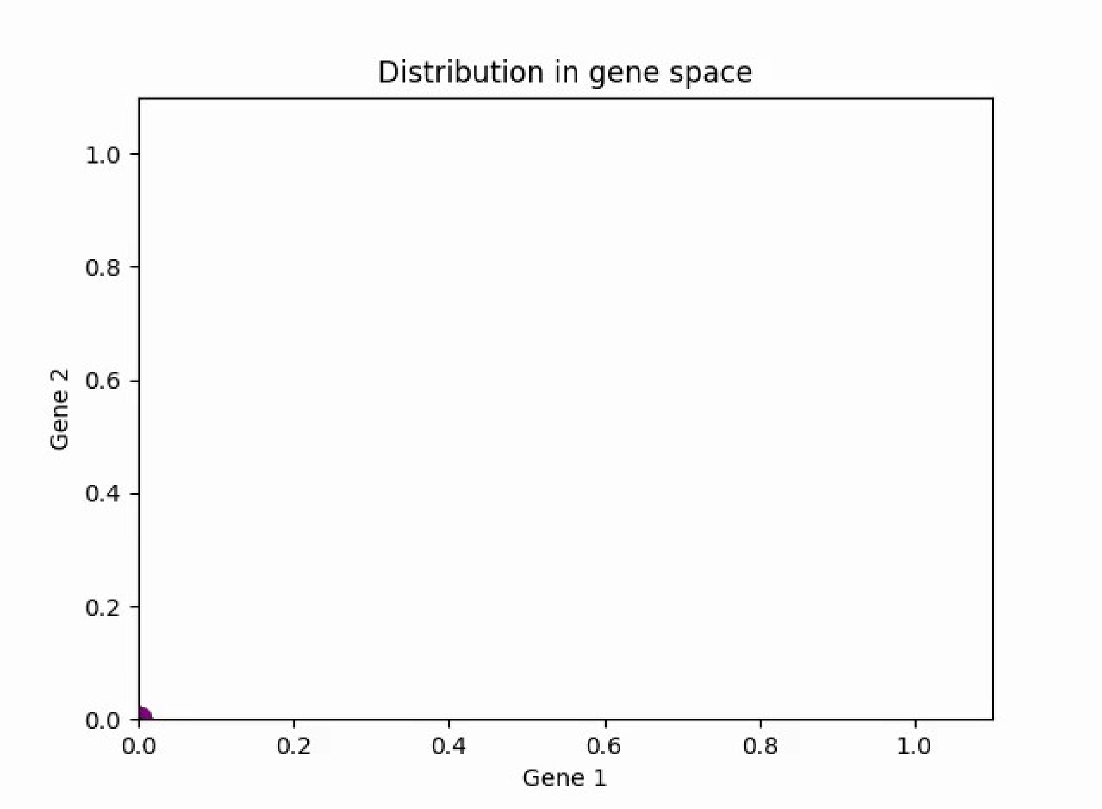
Methods: Schrödinger Problem

Optimal transport | **Schrödinger's Problem**

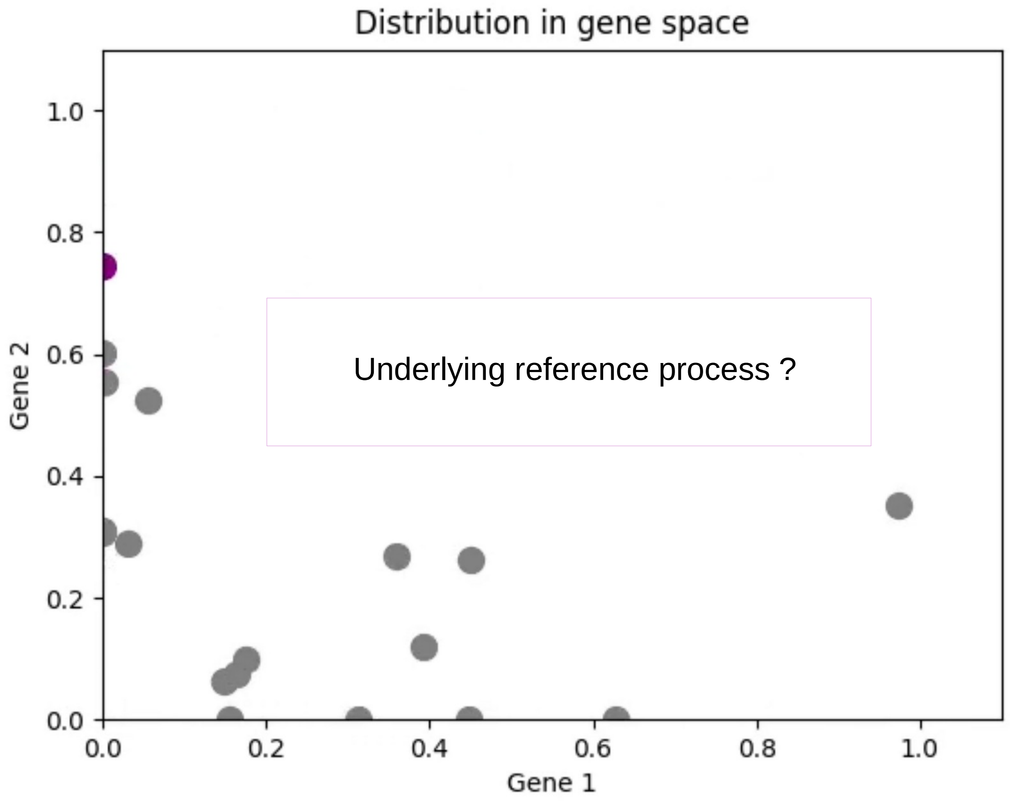


(Gabriel Peyré, X, 2023)

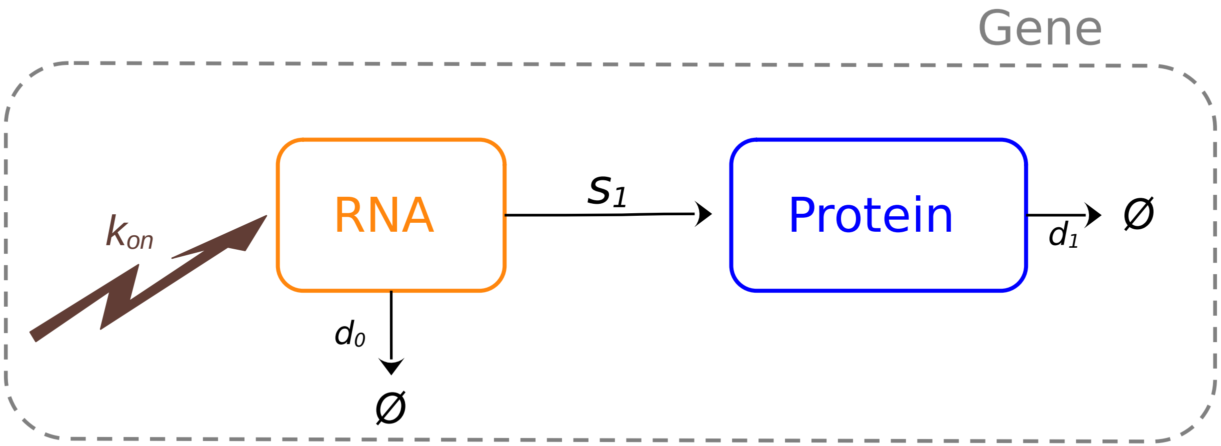
Cells trajectories in 2D



Cells trajectories in 2D



Methods: Bursty Model



Piecewise-deterministic Markov process (PDMP) :

deterministic part + stochastic part

$$\begin{cases} \dot{M}(t) = -d_0 M(t), \\ \dot{P}(t) = s_1 M(t) - d_1 P(t) \end{cases}$$

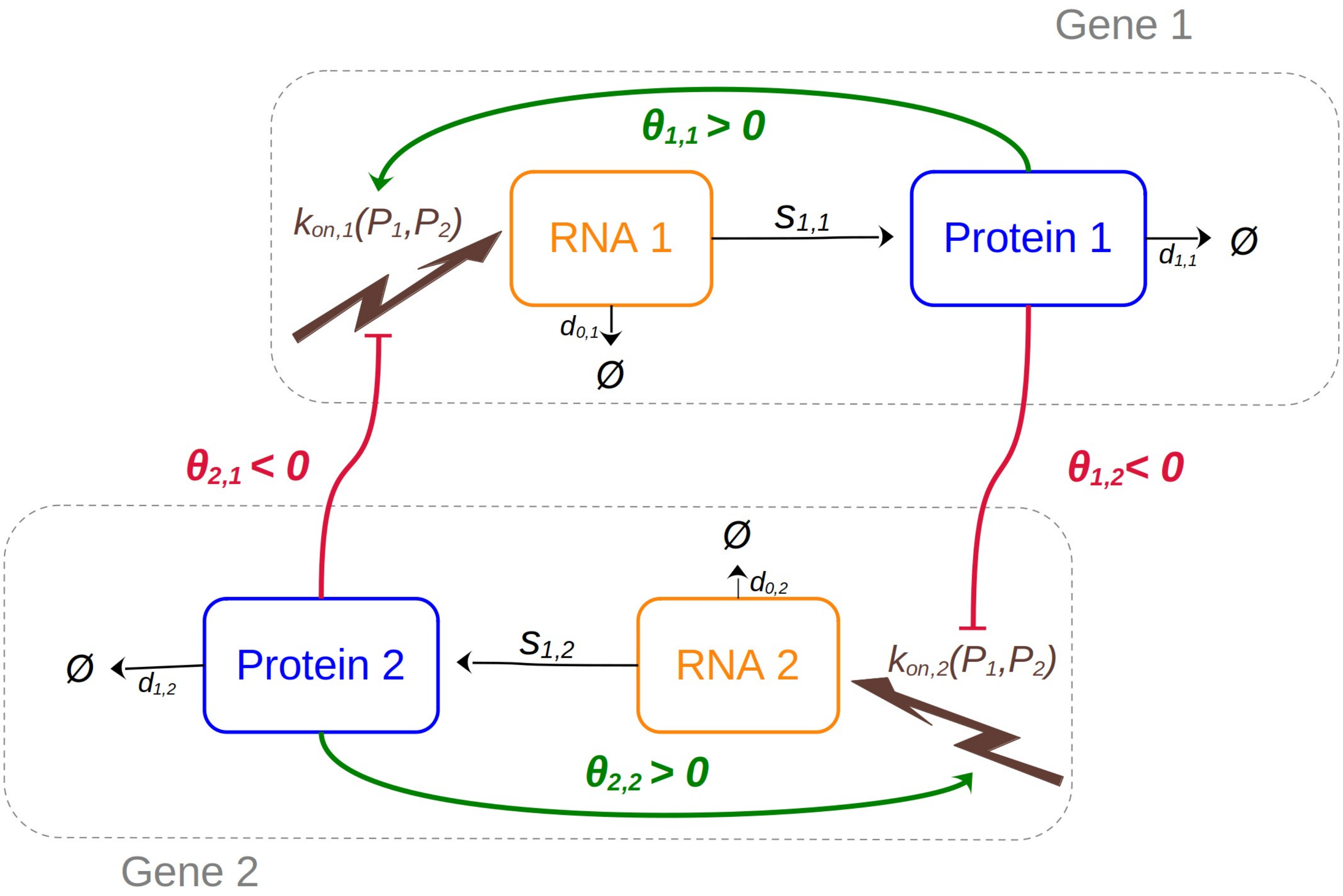
$$k_{on}$$

(Herbach et al. 2022)

Gene regulatory network (GRN) with 2 genes

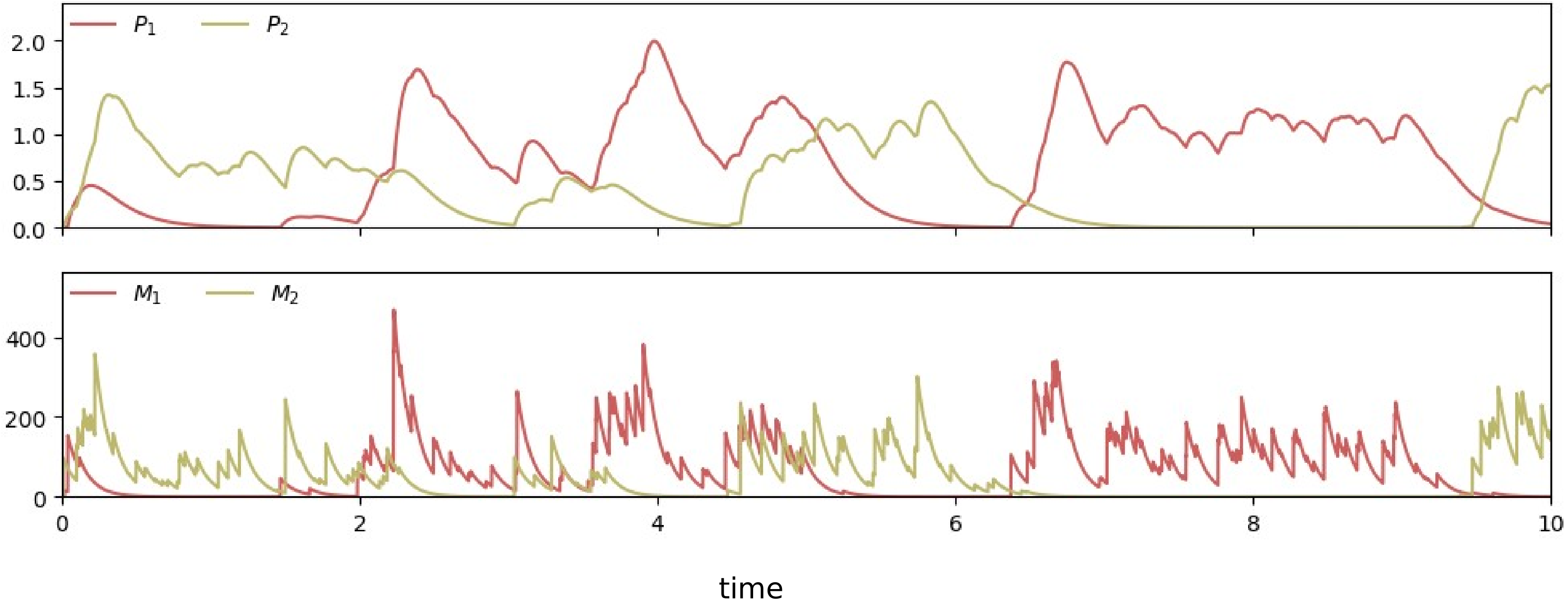
Toggle switch

Methods: Bursty Model
Toggle Switch

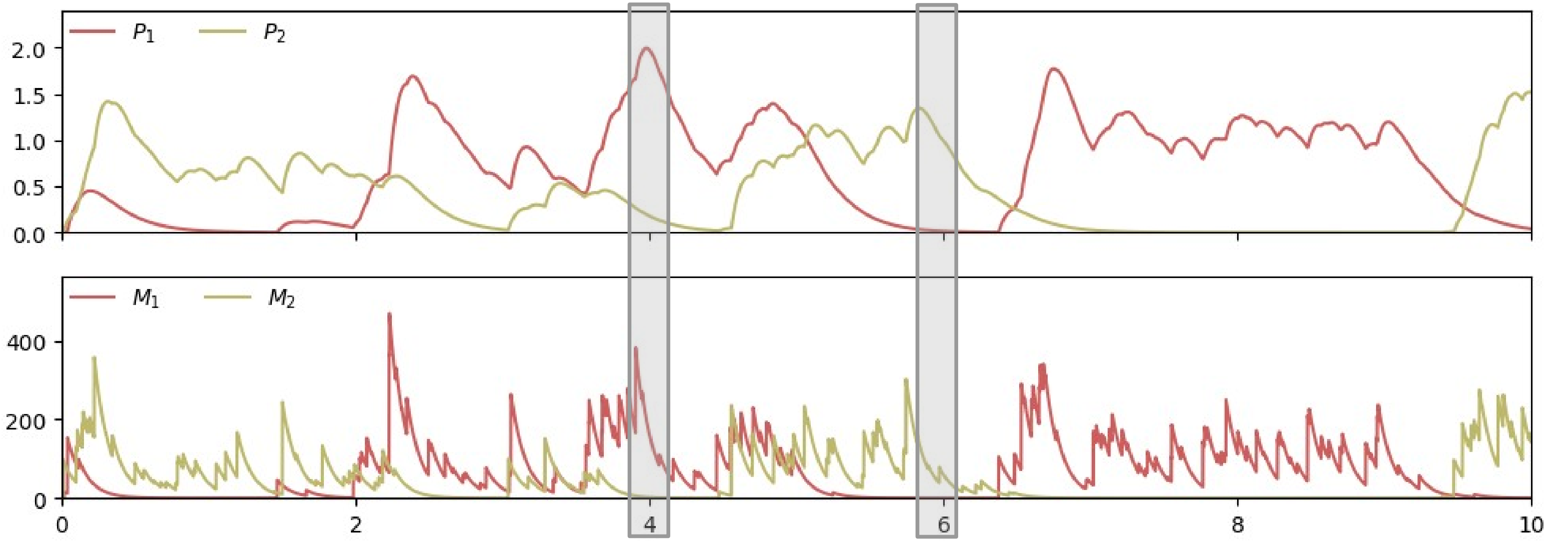


Methods: Simulated data

Evolution of the two proteins (top) and RNA (bottom) quantities over time.
Toggle switch Gene Regulatory Network. Results from HARISSA (Herbach, *2023*).



Methods: Simulated data



t_1

$x_1 = [(P_1,P_2), (M_1,M_2)]$

.

.

$x_N = [(P_1,P_2), (M_1,M_2)]$

t_2

$y_1 = [(P_1,P_2), (M_1,M_2)]$

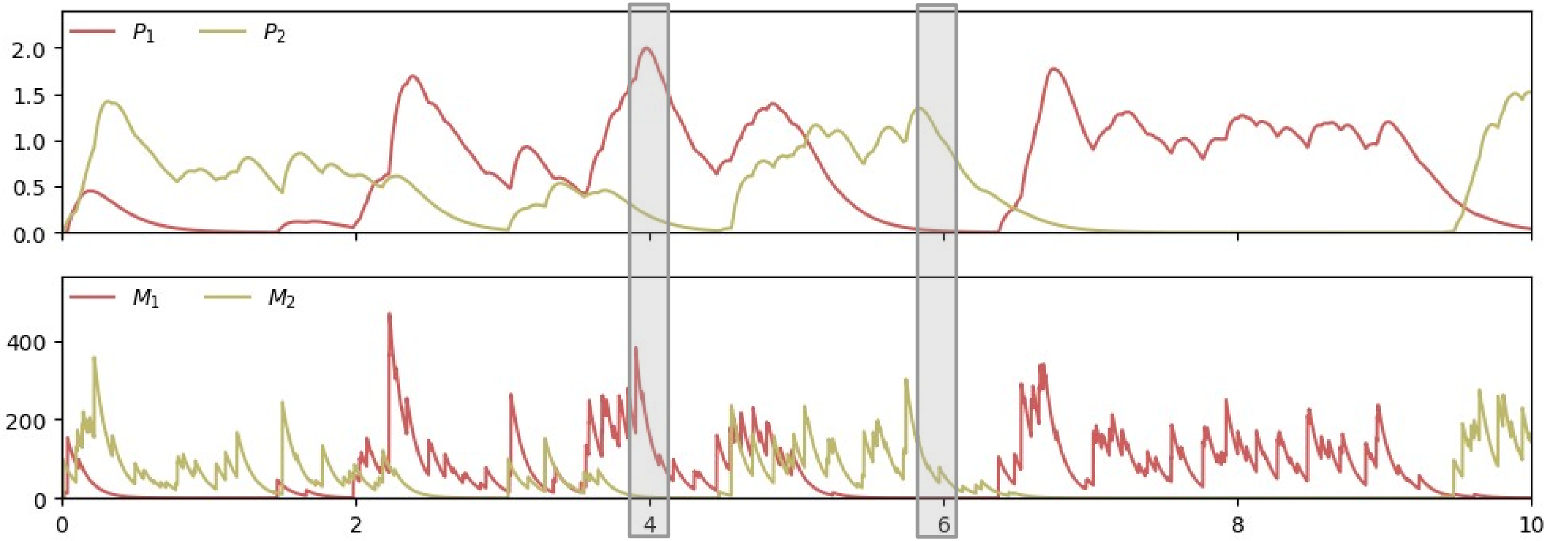
.

.

$y_N = [(P_1,P_2), (M_1,M_2)]$

μ ν

Methods: Simulated data



t_1

$x_1 =$ [(P_1,P_2), (M_1,M_2)]

.

.

$x_N =$ [(P_1,P_2), (M_1,M_2)]

t_2

$y_1 =$ [(P_1,P_2), (M_1,M_2)]

.

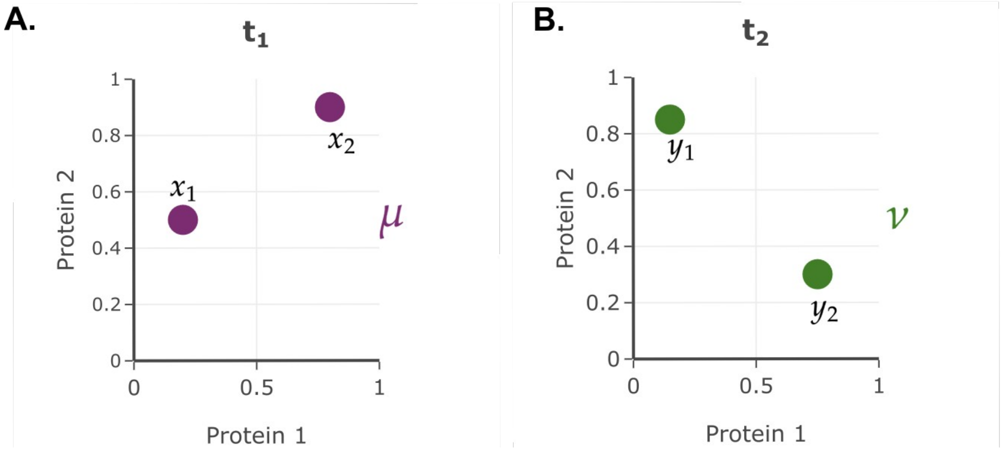
.

$y_N =$ [(P_1,P_2), (M_1,M_2)]

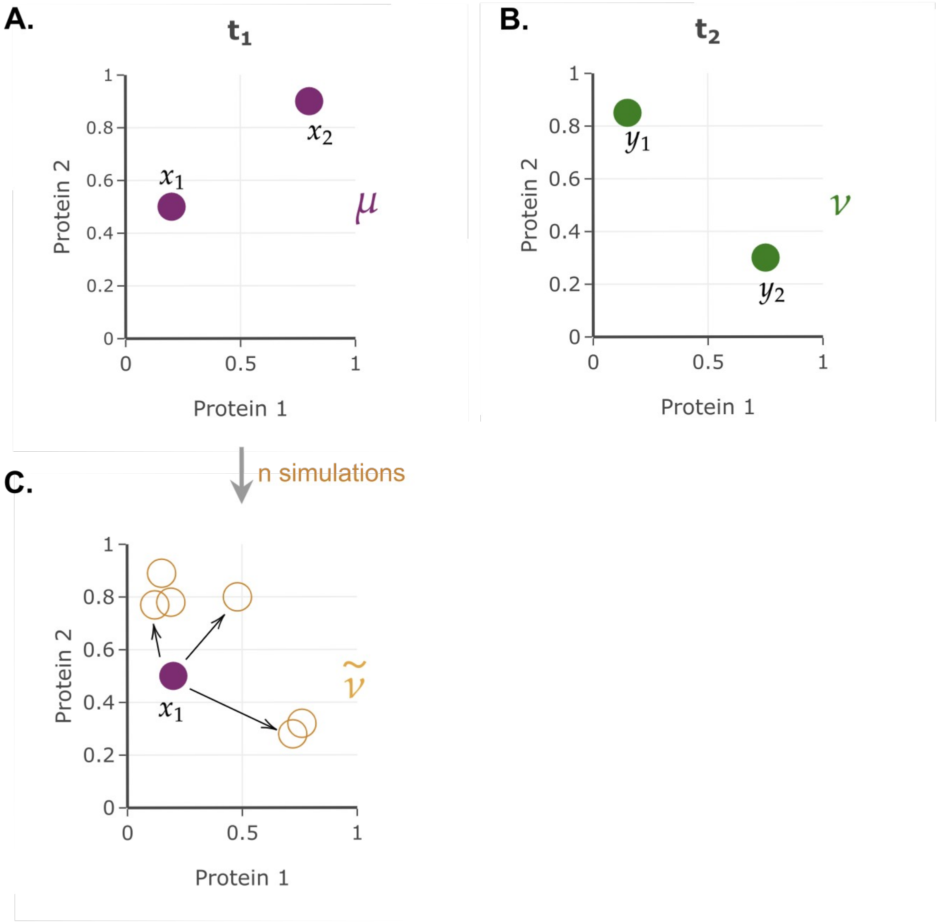
μ

ν

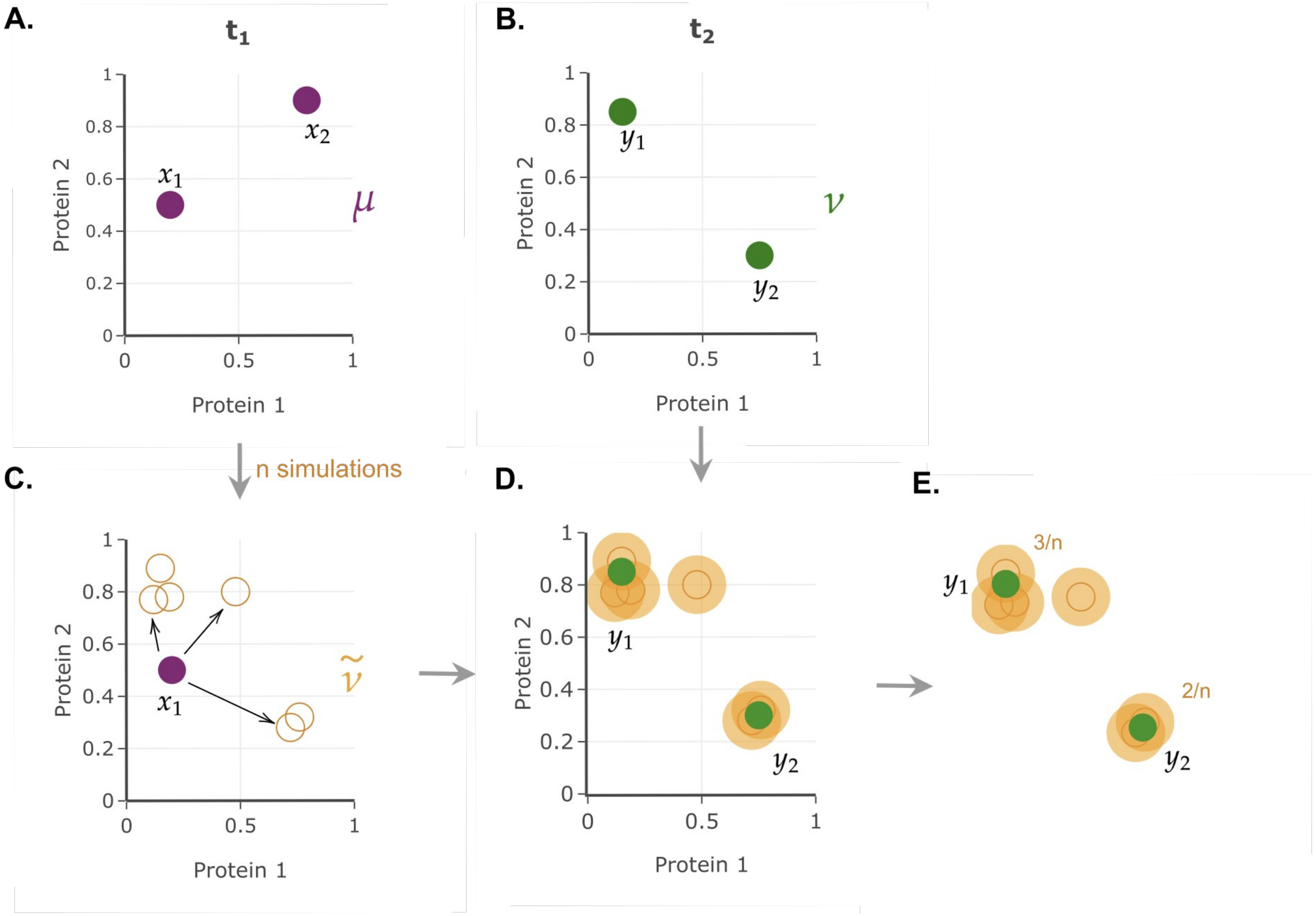
Methods: Approximation of the reference process



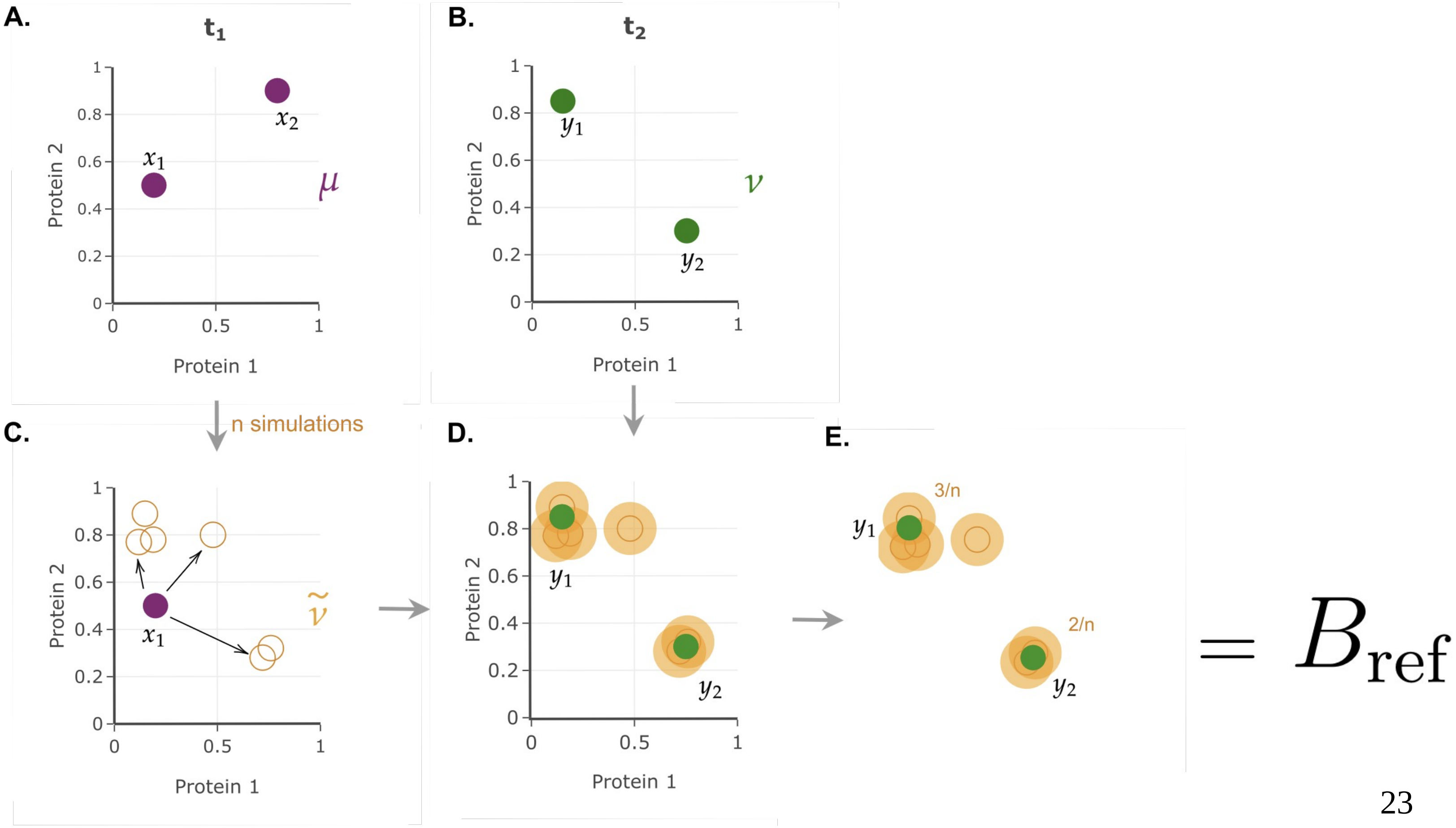
Methods: Approximation of the reference process



Methods: Approximation of the reference process



Methods: Approximation of the reference process



Methods: Schrödinger Problem

$$\boxed{B_{\mathrm{sch}}} := \underset{Q \in \mathcal{P}(X \times Y)}{\arg\min} \{H(Q|B_{\mathrm{ref}}); \ Q(t_1) = u, Q(t_2) = v\}$$

With $H(Q|R) = \sum_{ij} Q_{ij} log\left(\frac{Q_{ij}}{R_{ij}}\right)$

Methods: Schrödinger Problem

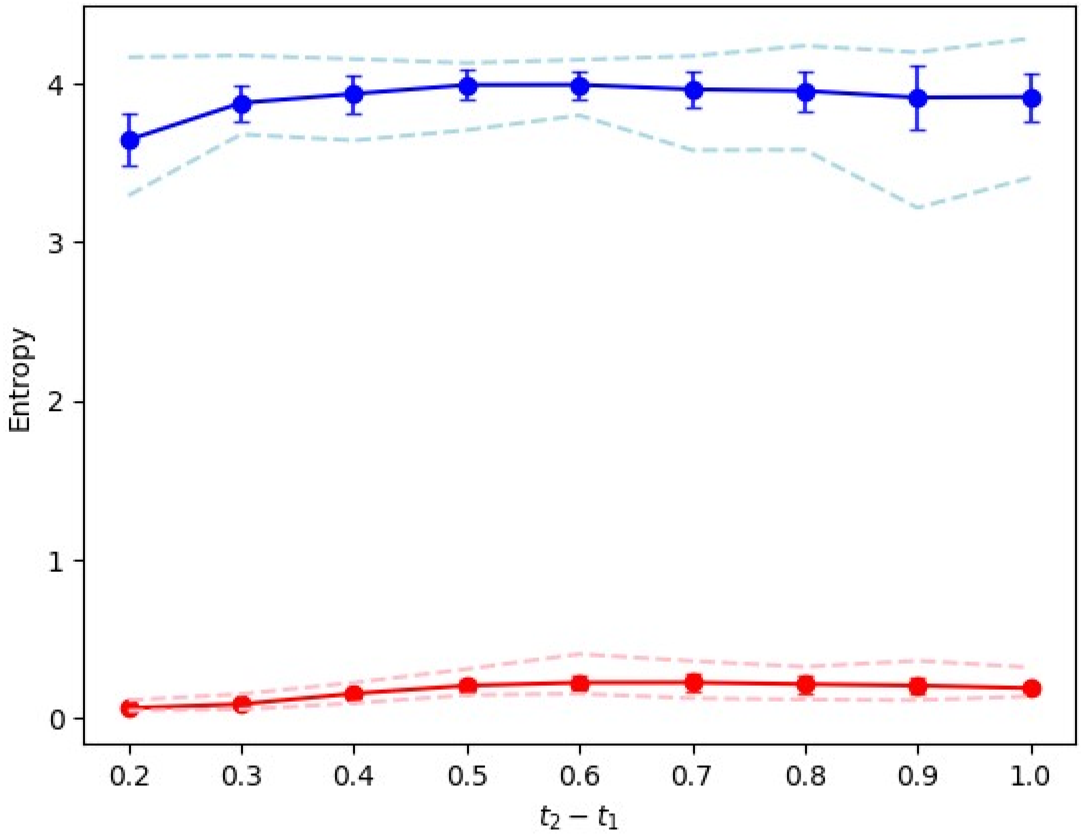
$$D_{\mathrm{sch}} := \underset{Q \in \mathcal{P}(X \times Y)}{\arg\min} \{ H(Q | D_{\mathrm{ref}}); \ \ Q(t_1) = u, Q(t_2) = v \}$$

Methods: Entropy

$$H_{D,B} := H(D_{\mathrm{sch}} | B_{\mathrm{sch}}),$$

$$H_{B} := H(B_{\mathrm{ref}} | B_{\mathrm{sch}})$$

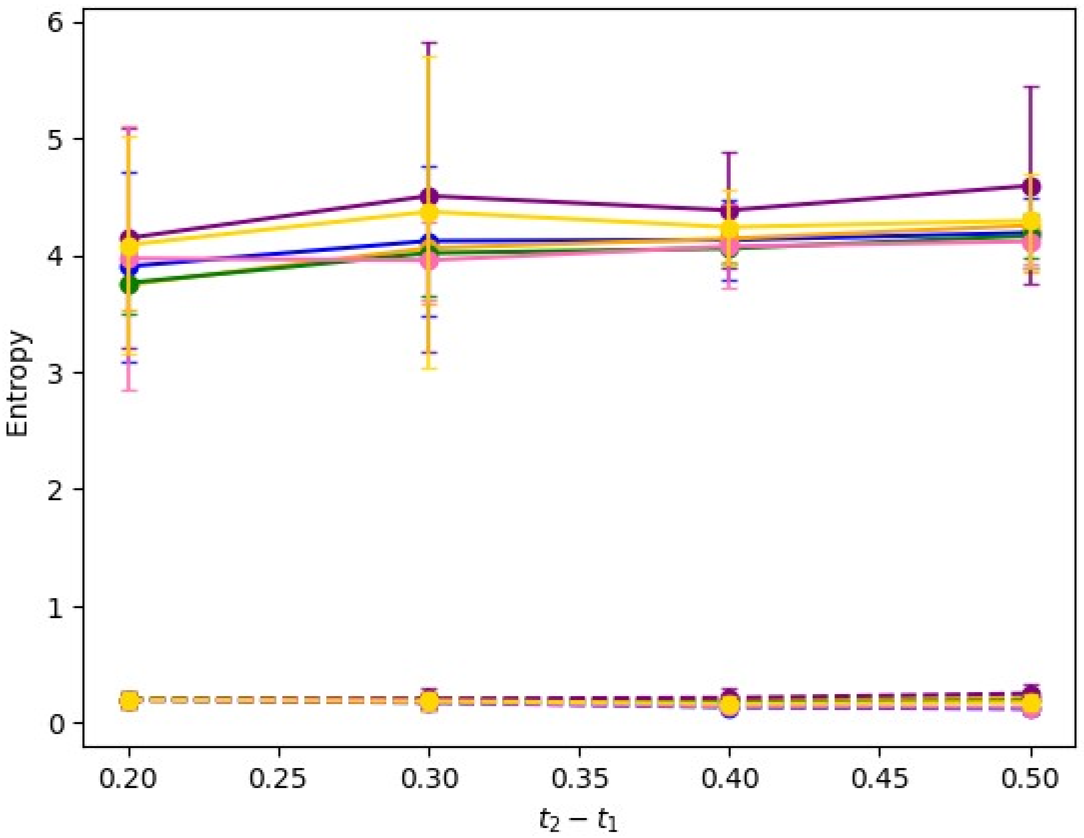
Results: Entropy

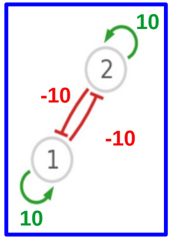


$$H_{D,B} := H(D_{\mathrm{sch}}|B_{\mathrm{sch}})$$

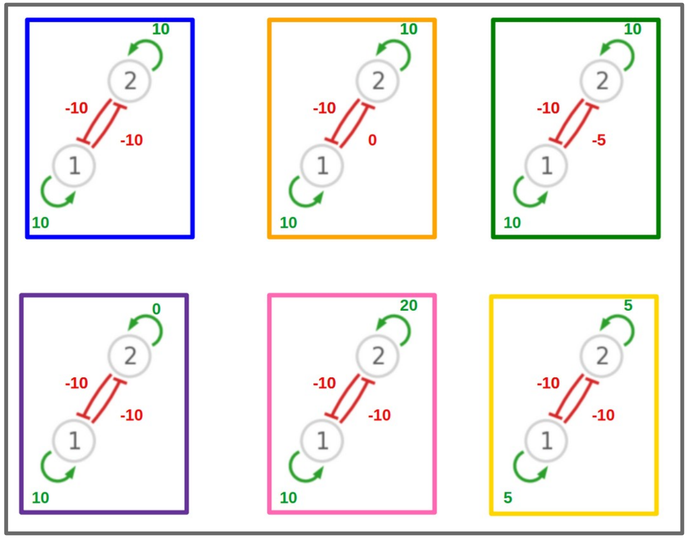
$$H_B := H(B_{\mathrm{ref}}|B_{\mathrm{sch}})$$

Results: Entropy





μ *and* ν



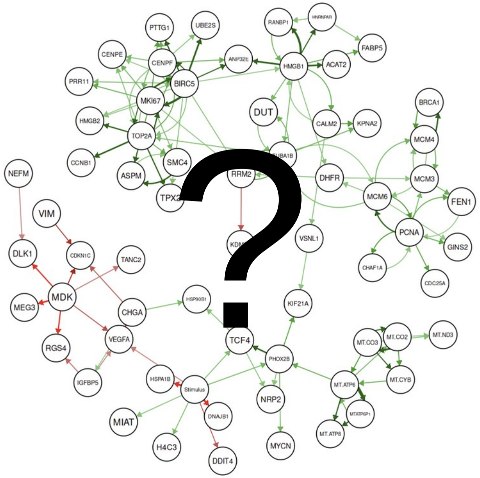
B_{ref}

Discussion

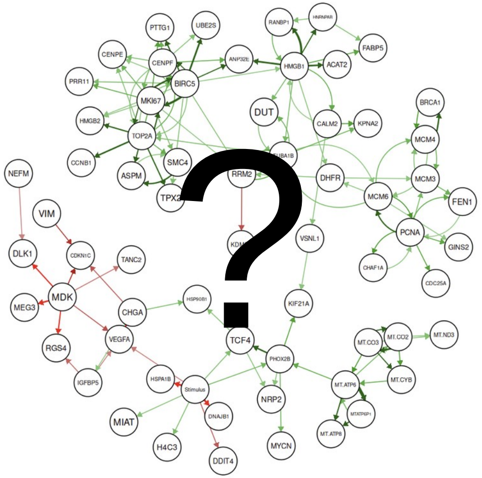
How to extend the model for real data ?

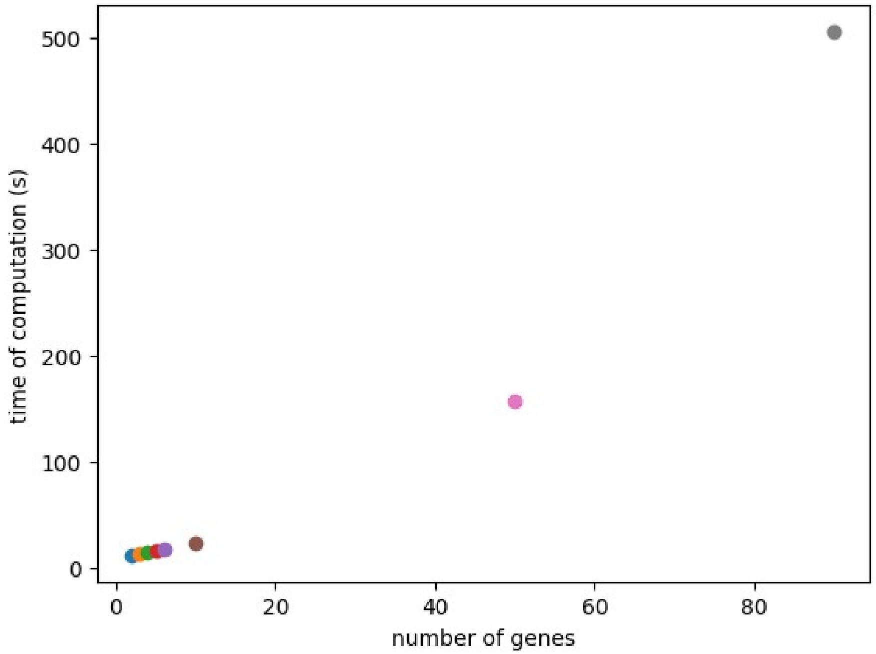
Discussion

How to extend the model for real data ?

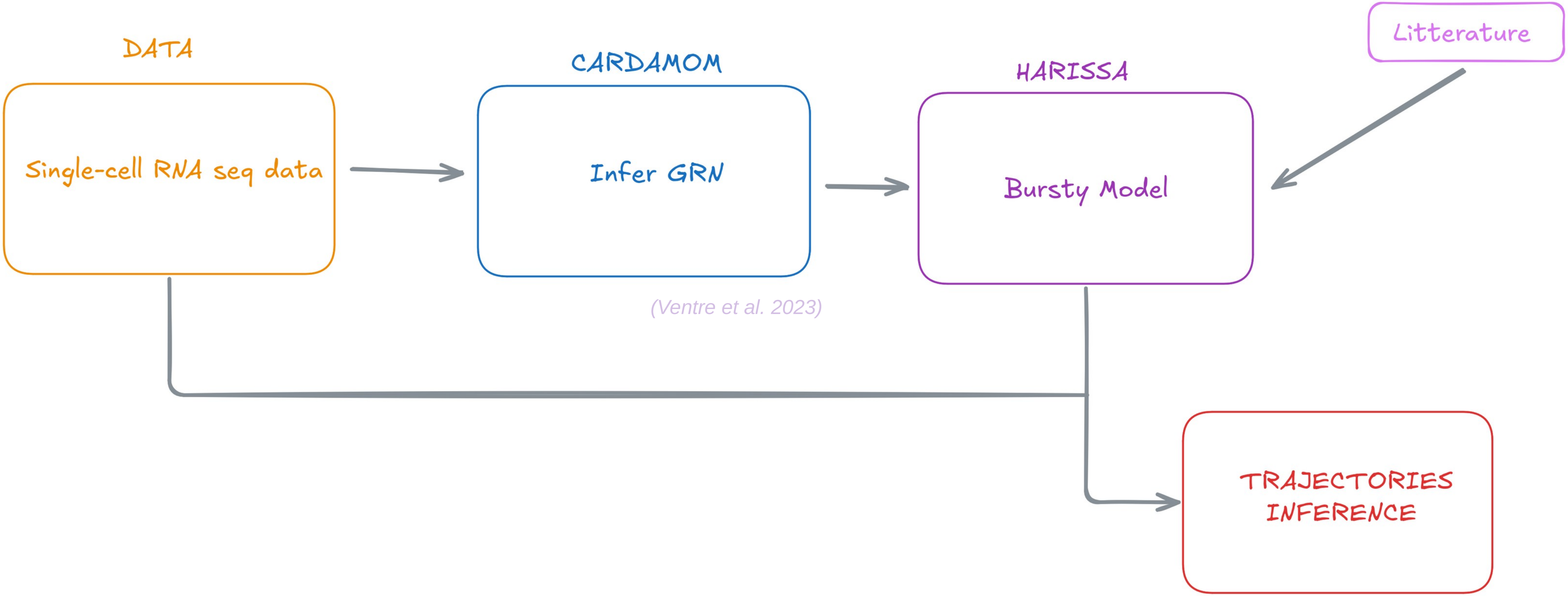


How to extend the model for real data ?





Discussion : Next steps



(Ventre et al. 2023)

Thank you for your attention