Cell Trajectory Inference based on Schrödinger problem and a mechanistic stochastic gene expression model

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Supervisors : Fabien Crauste
and Olivier Gandrillon

18/03/2026

Slides available : https://clemencefournie.pages.math.cnrs.fr/

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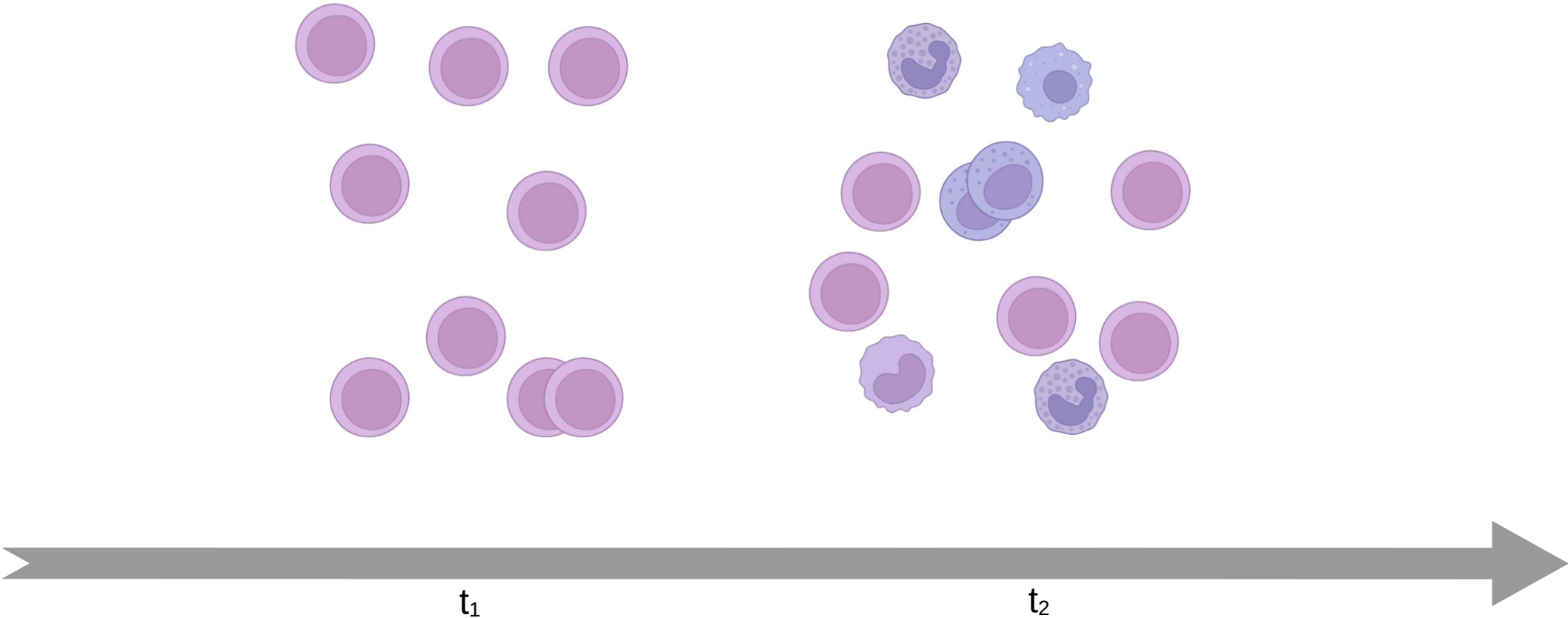
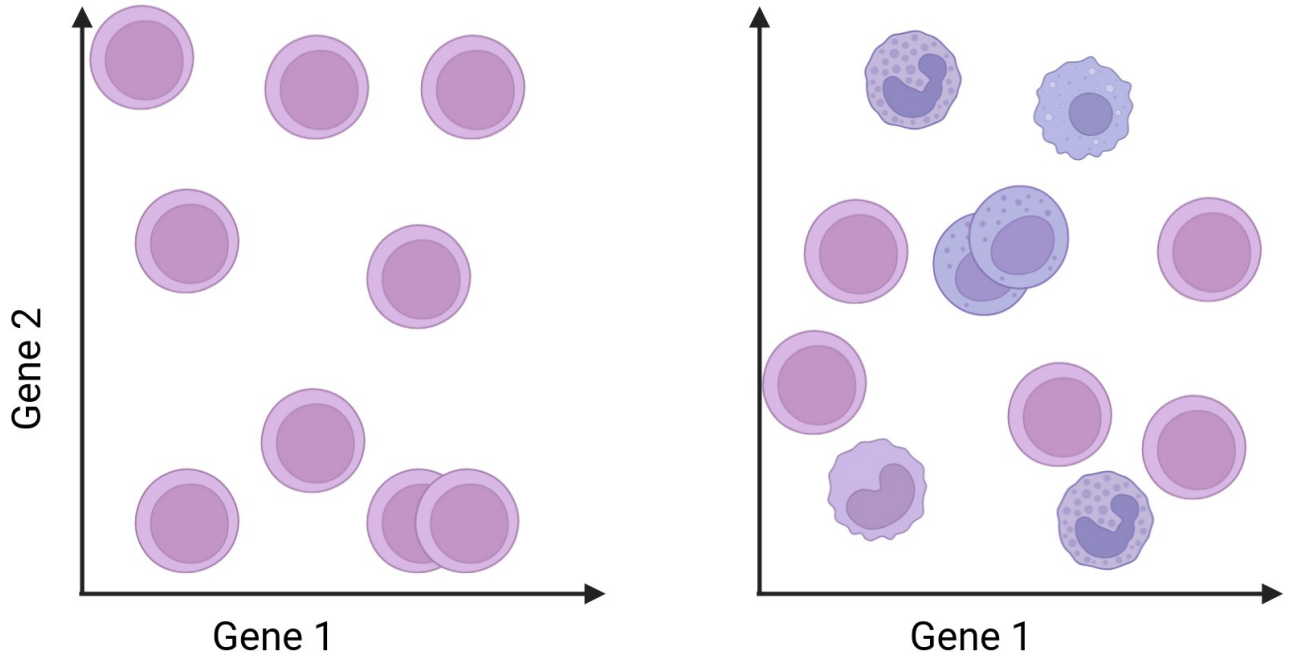
Clémence Fournié, Elias Ventre, Ulysse Herbach, Aymeric Baradat, Olivier Gandrillon, Fabien Crauste, Preprint, 2025.

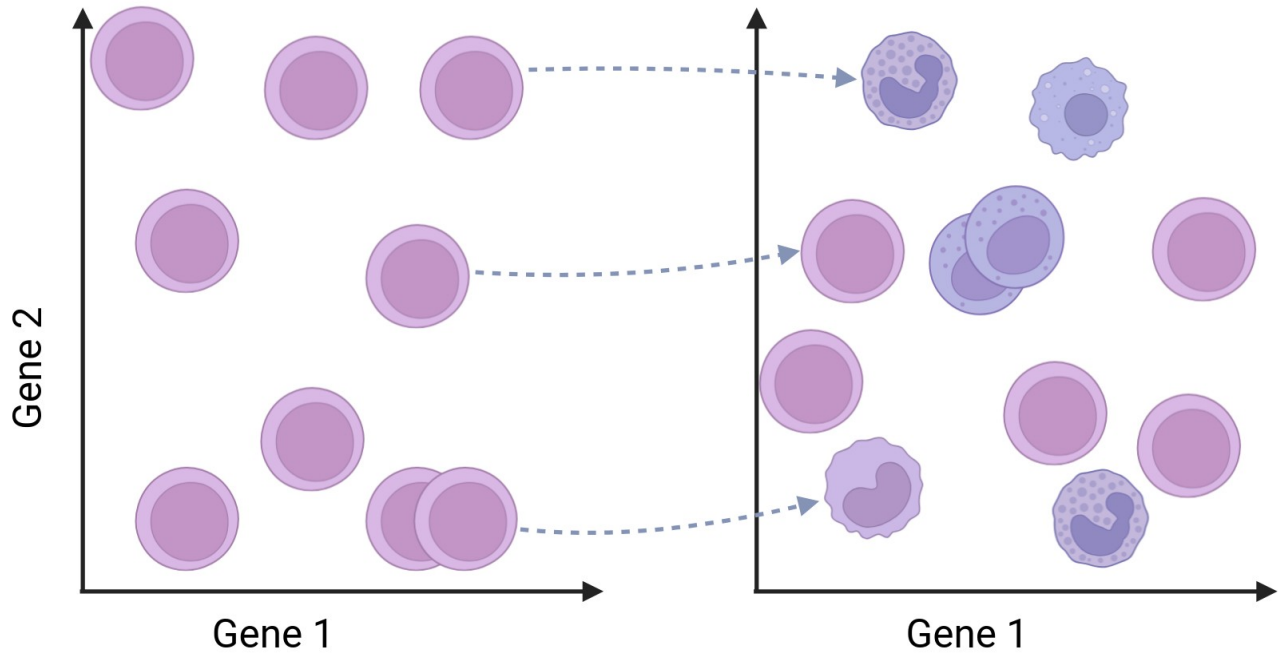
scRNA-seq Data Set



Gene Space



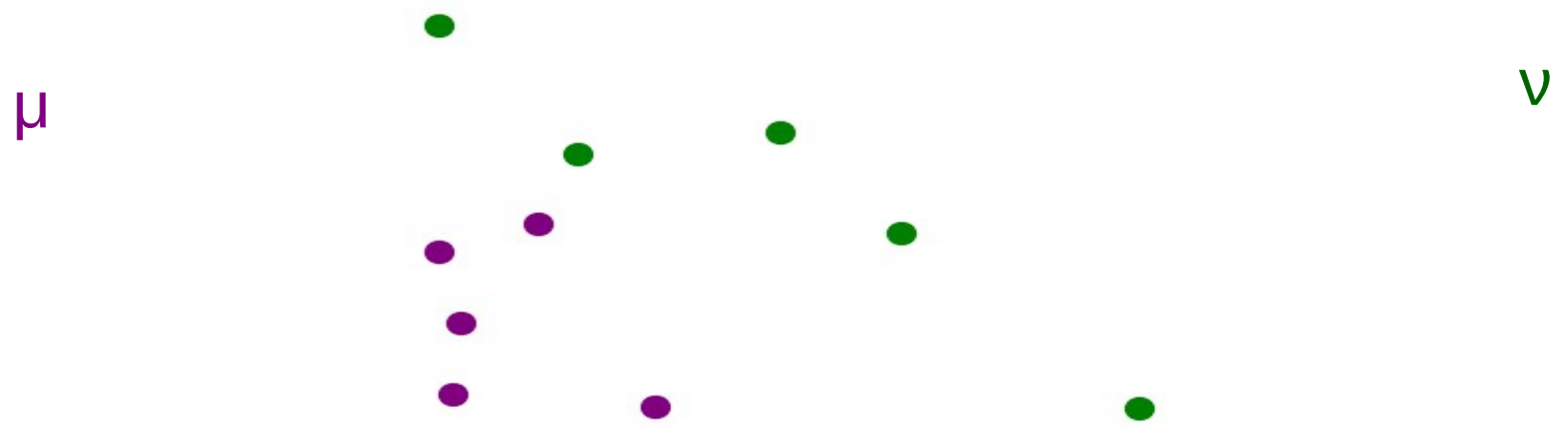
Trajectories Inference



(Idea from Shiebinger et al. 2019)

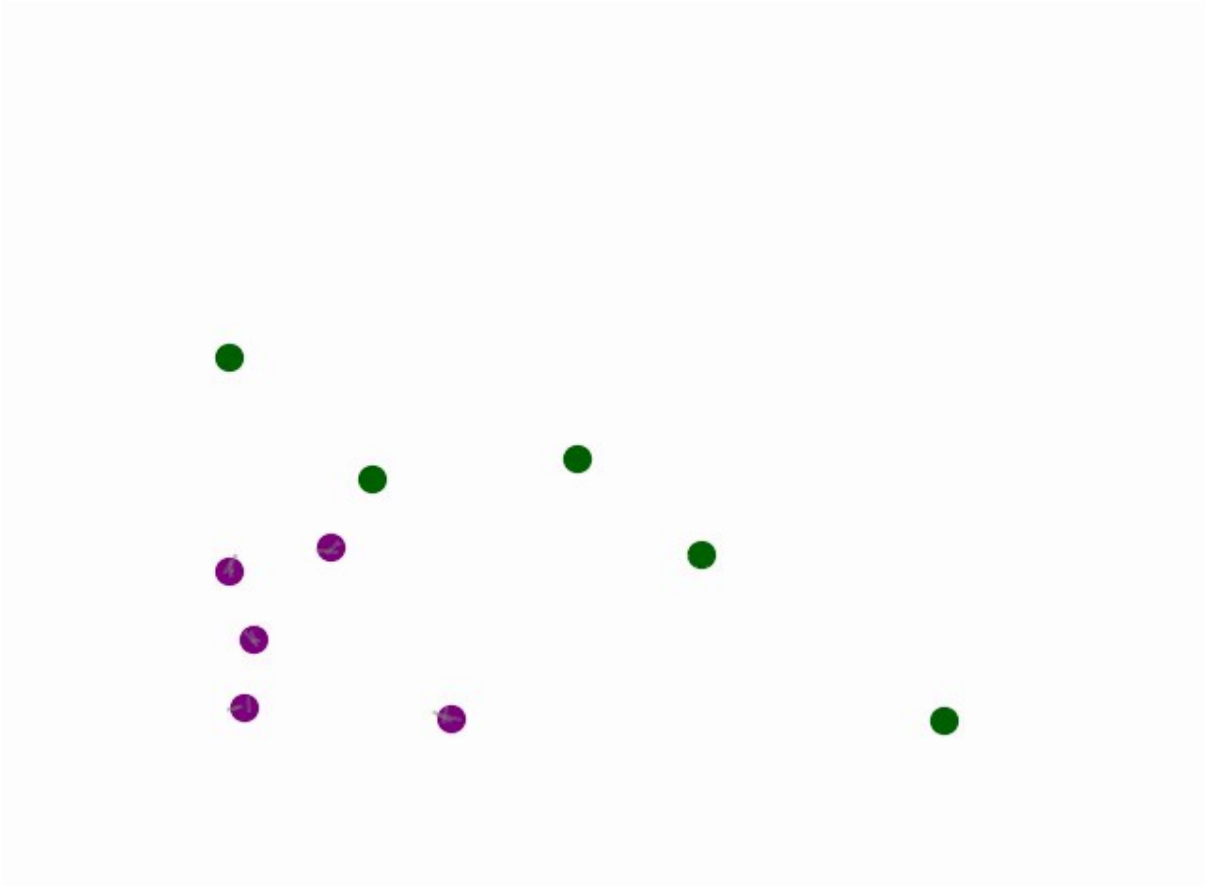
(biorender.com)

Trajectories Inference - Schrödinger Problem



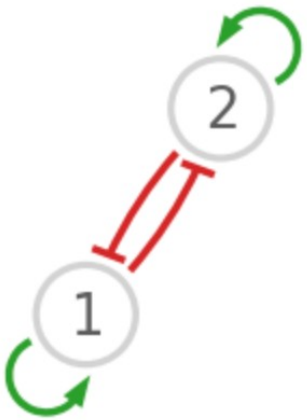
Schrödinger Problem – Diffusive Process

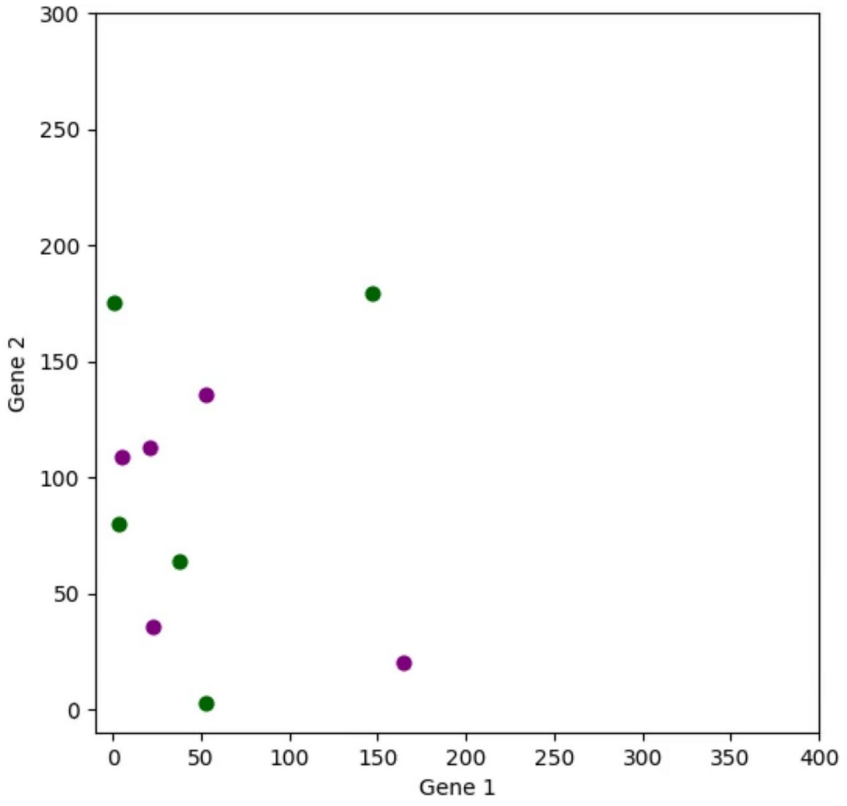
μ



ν

Gene Regulatory Network
toggle-switch





μ

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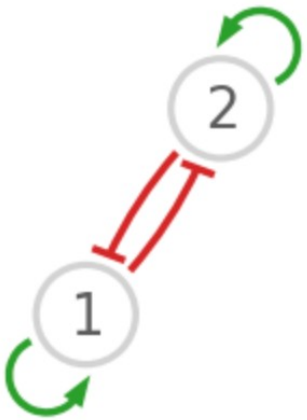
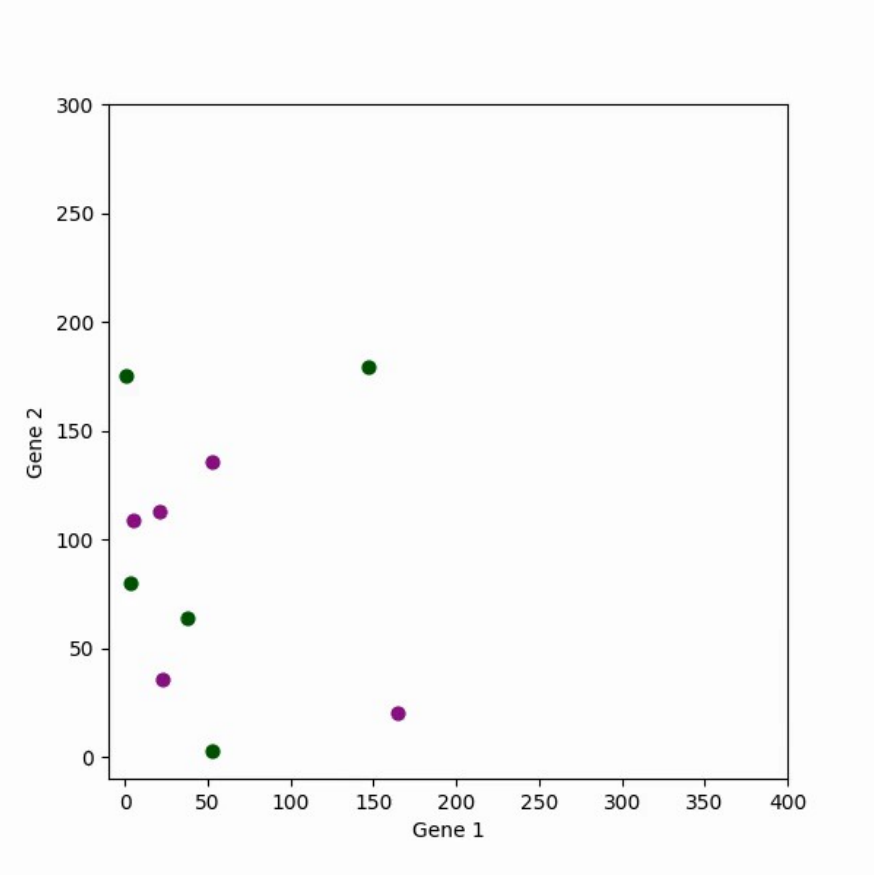


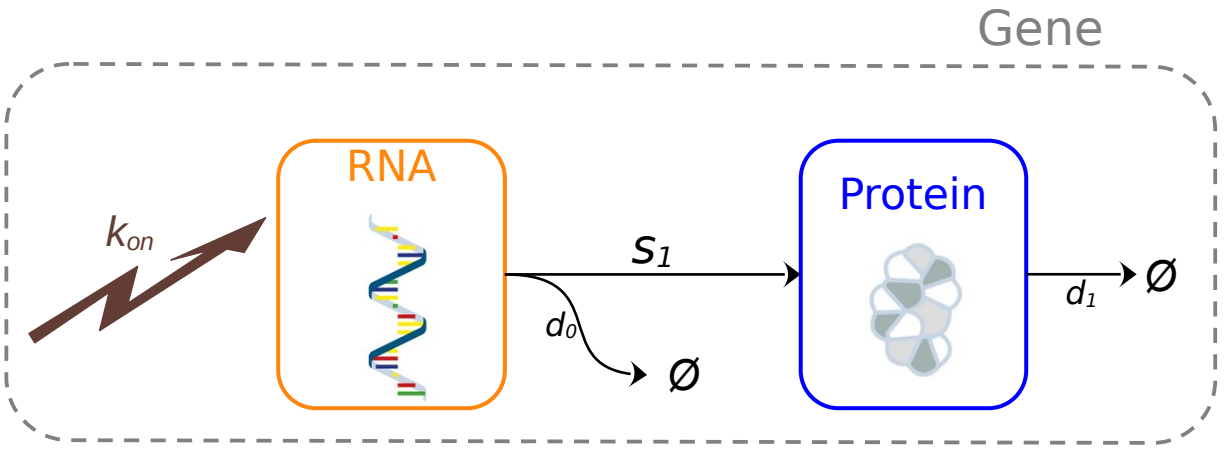
μ



ν

Mechanistic Stochastic Gene Expression Model

Bursty model

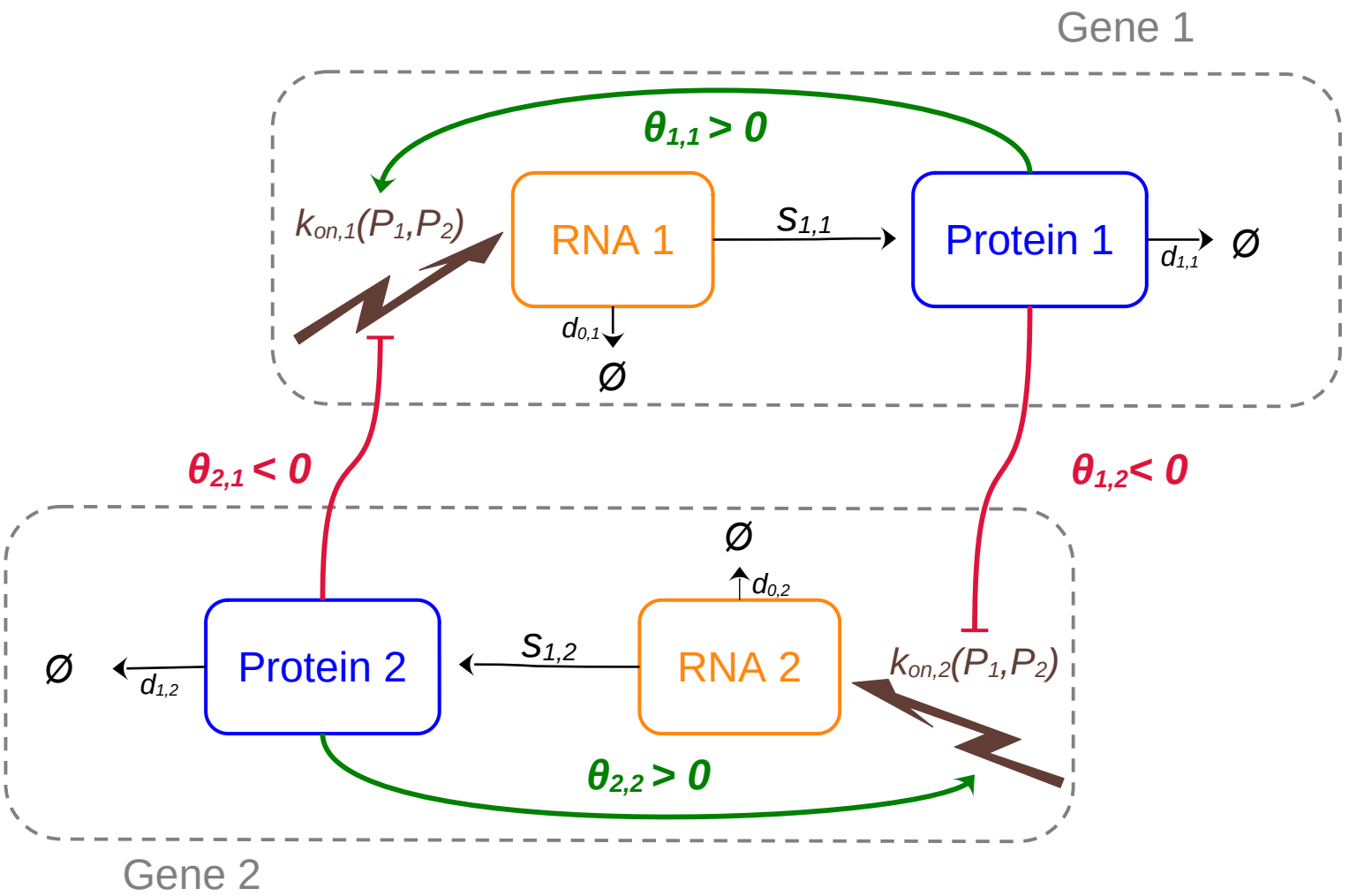


$$k_{on,i}(P_1,\ldots,P_G) = \frac{k_{0,i} + k_{1,i}\exp(\beta_i + \sum_{j=1}^{G}\theta_{ji}P_j)}{1 + \exp(\beta_i + \sum_{j=1}^{G}\theta_{ji}P_j)}$$

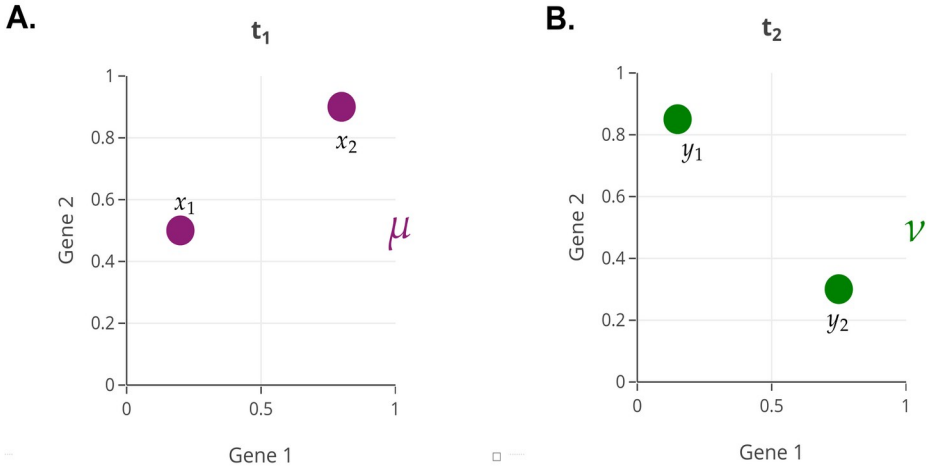
$$\begin{cases} \dot{M}(t) = -d_0 M(t), \\ \dot{P}(t) = s_1 M(t) - d_1 P(t). \end{cases}$$

(Herbach et al. 2022)

Bursty Model
toggle-switch



Methods: Approximation of the reference process



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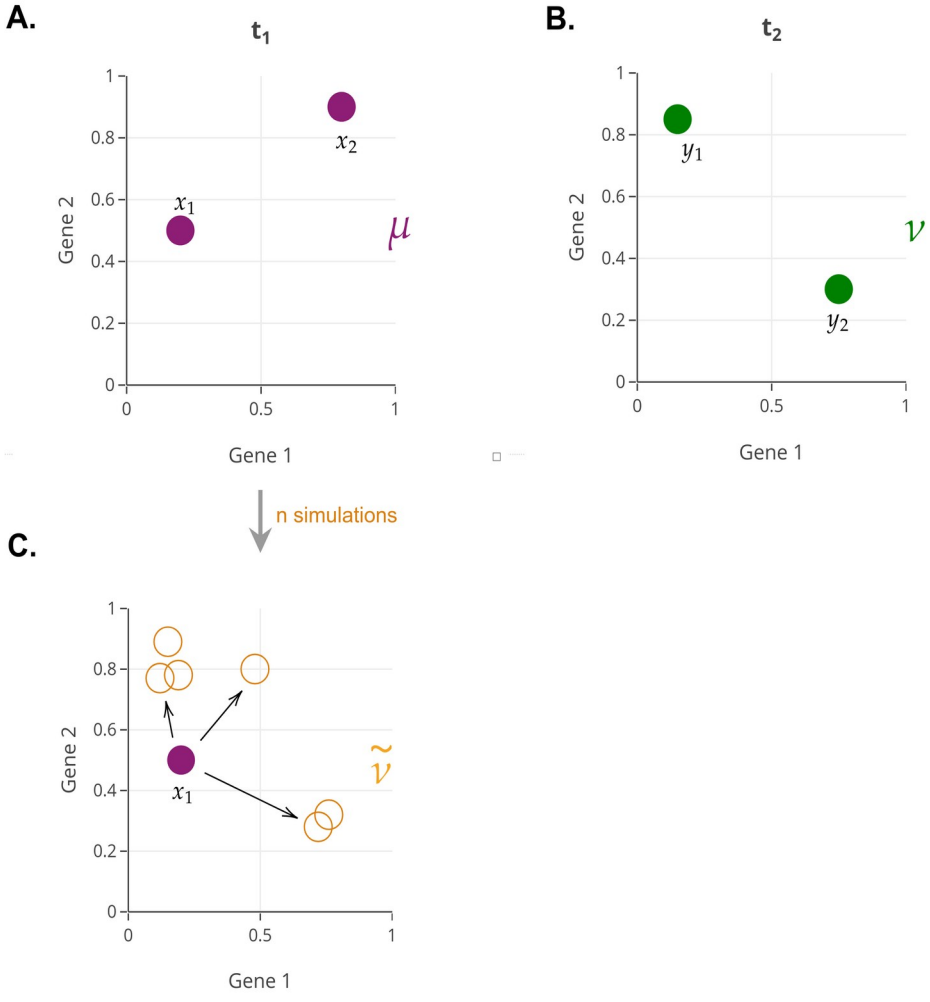

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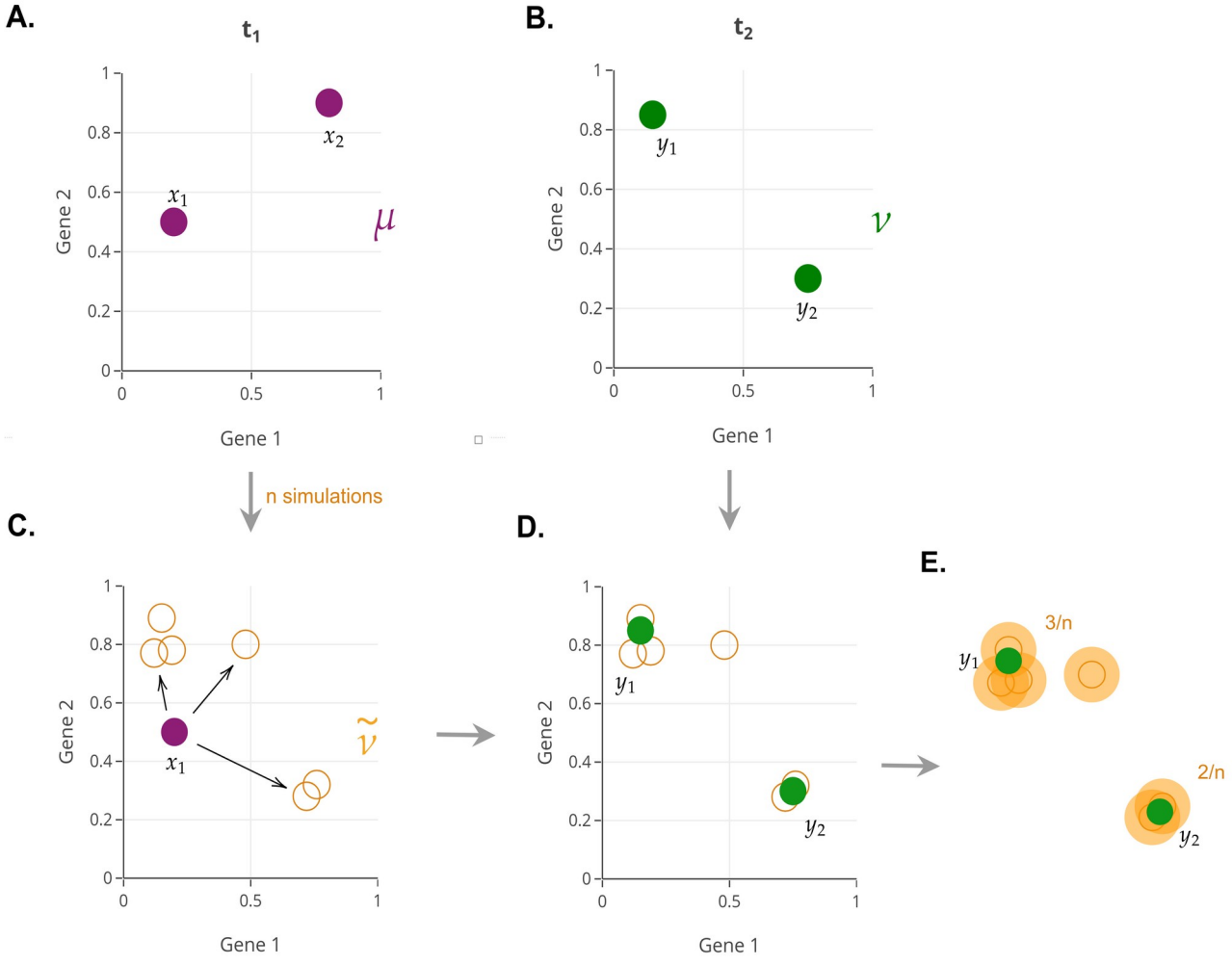

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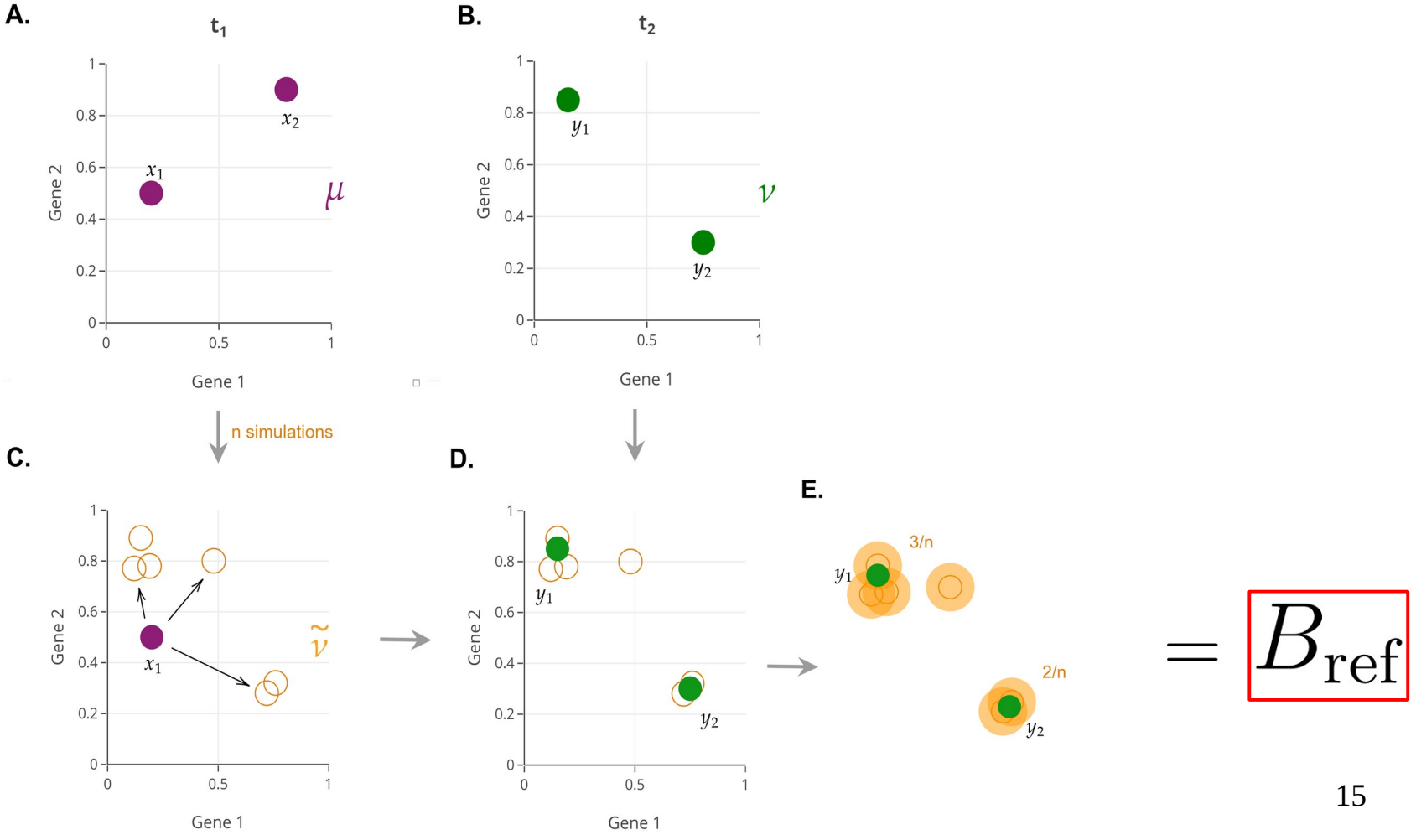


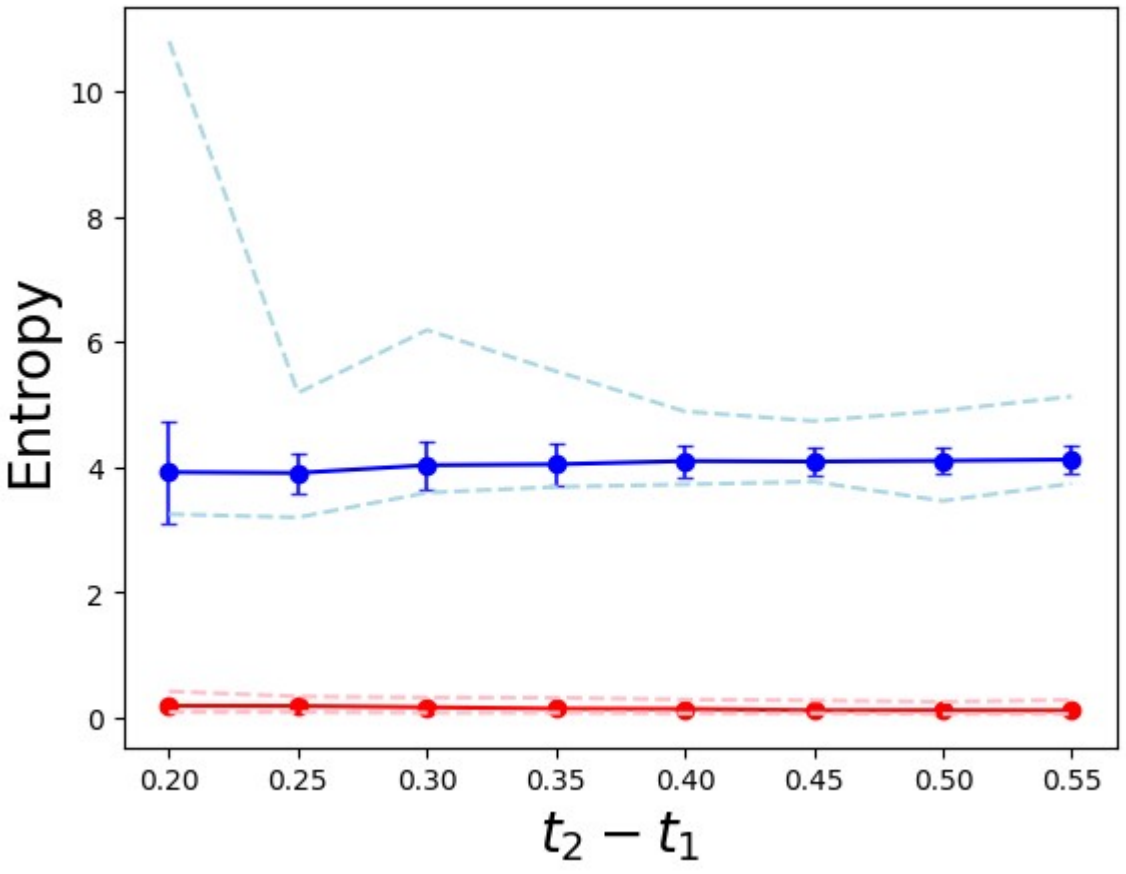
$$= B_{\text{ref}}$$

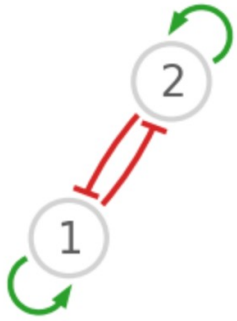
Methods: Schrödinger Problem

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

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

Results: Toggle-switch



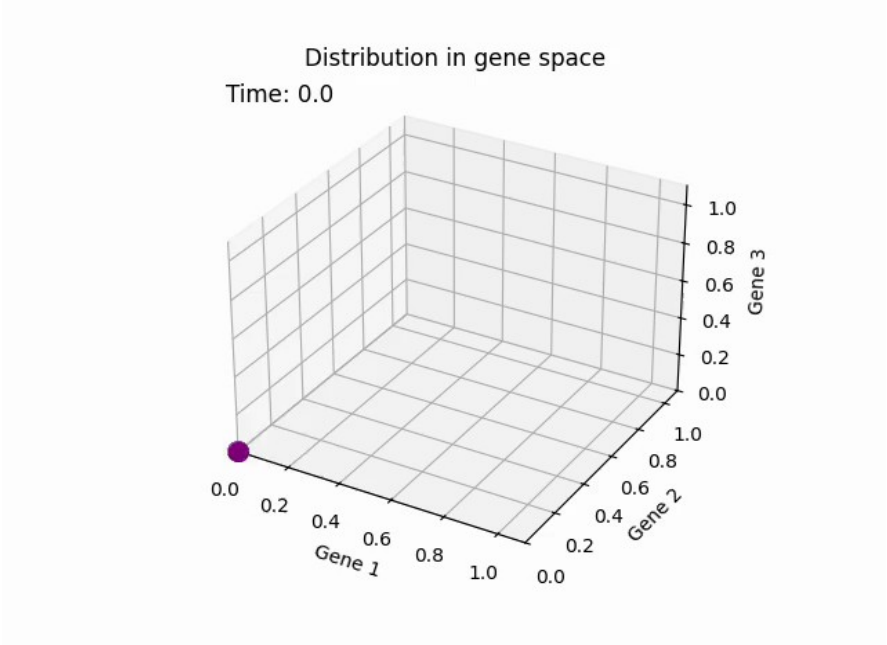


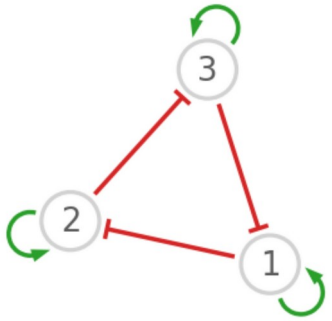
Bursty model vs Diffusion

Bursty model vs “ground truth”

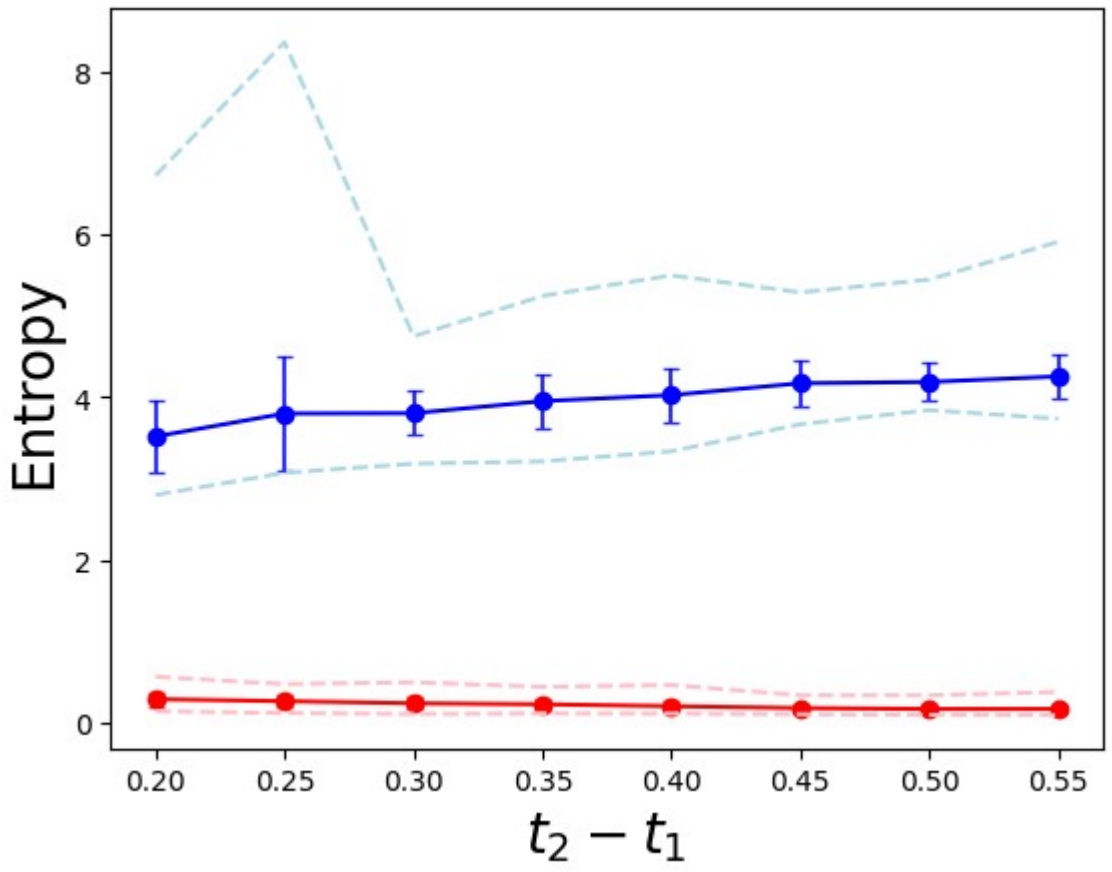
The smaller the entropy, the better the Bursty model

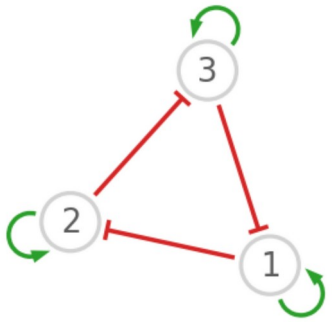
Gene Regulatory Network
Repressilator





Results: Repressilator





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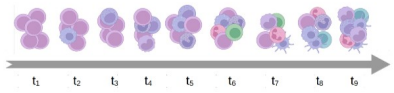
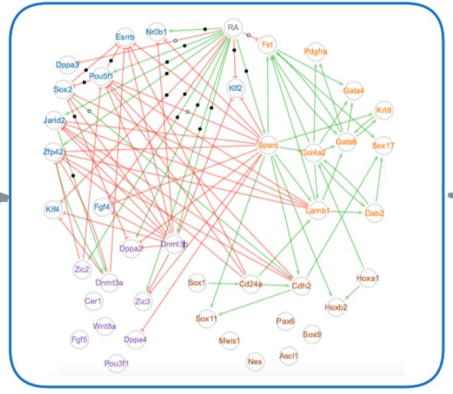
Discussion

Sc RNA seq DATA



Gene Regulatory Network Inference



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TRAJECTORIES INFERENCE

EVALUATION

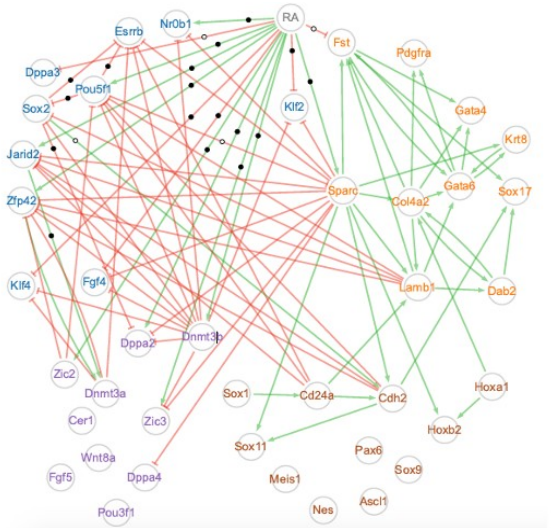
Thank you for your attention

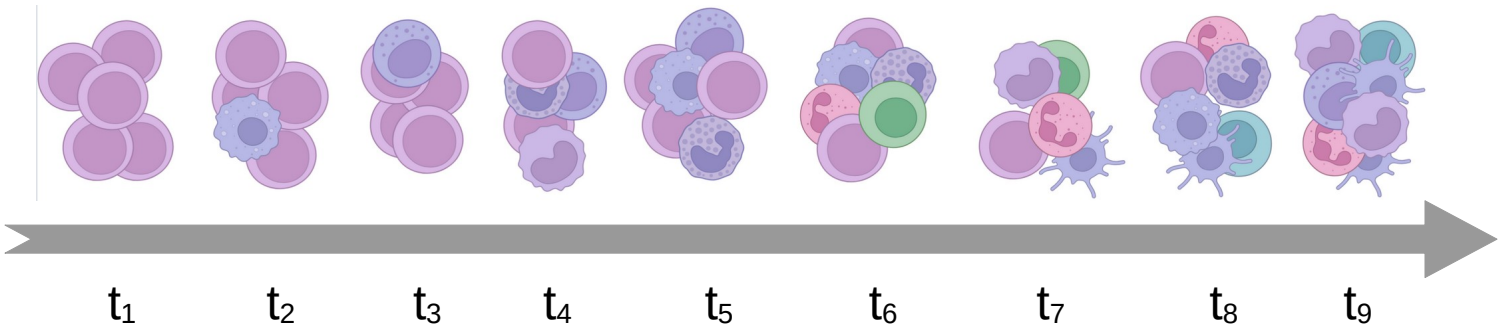
Contact: clemence.fournie@math.cnrs.fr

Gene Regulatory Network

scRNA-seq of a retinoic acid-induced differentiation of mouse embryonic stem cells

(Semrau, 2017)

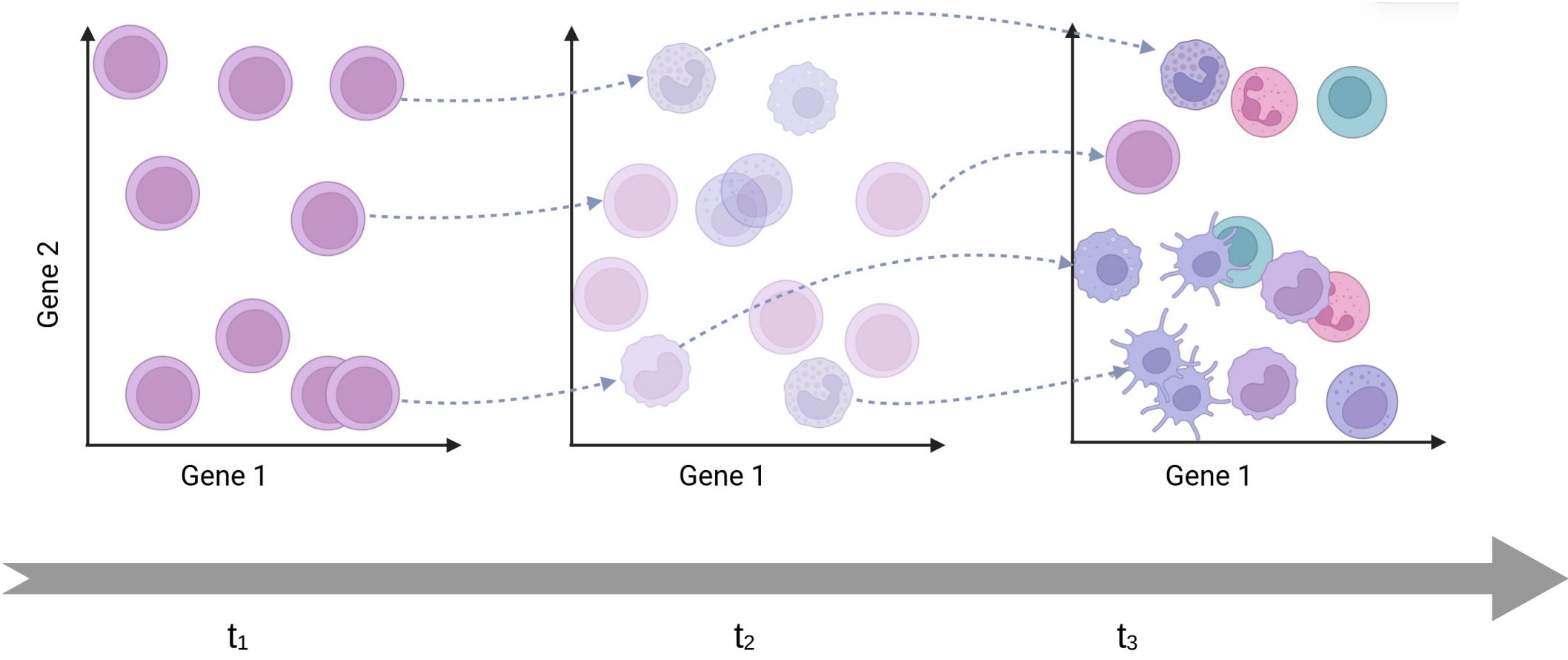




(Ventre et al, 2023)

(biorender.com)

Interpolation



Results: Interpolation