

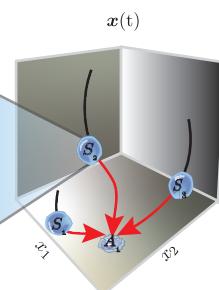
A

MEASURE TRANSCRIPTOMIC STATE / VELOCITY: cscRNA-Seq + tscRNA-Seq

1) Regulatory network in single cells

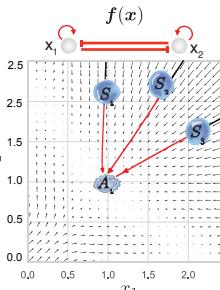
$$\dot{x} = f(x)$$

2) Cell dynamics in high dimension

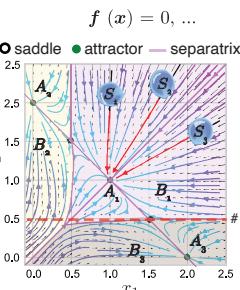


MAP AND CHARACTERIZE VECTOR FIELD OF SINGLE CELLS

3) Velocity vector field of cell dynamics

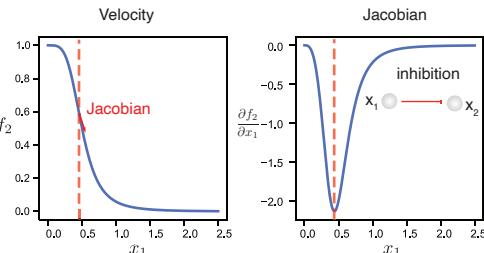
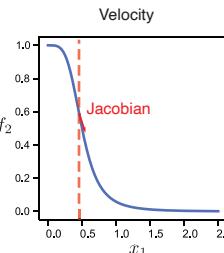
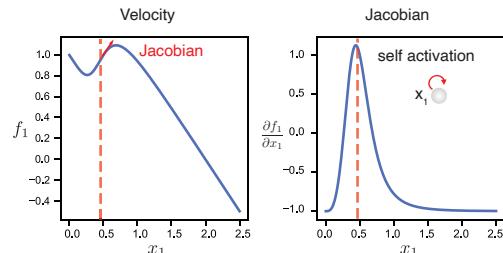
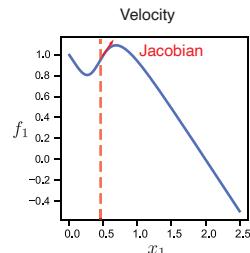


4) Topology of velocity vector field



B

VELOCITY OR JACOBIAN ALONG AN INDICATED LINE REVEALS GENE REGULATIONS



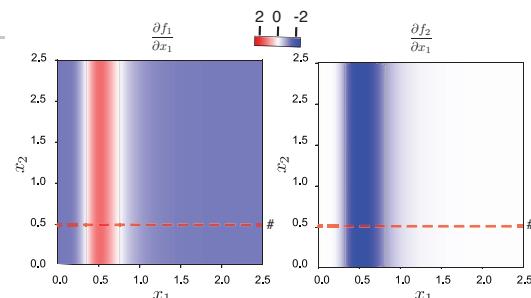
C

STATE DEPENDENT GENE INTERACTIONS: Jacobian matrix

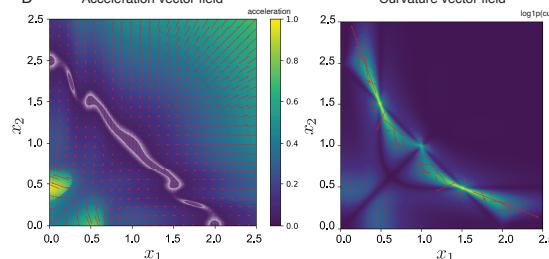


$$\mathbf{J} = \begin{bmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} \end{bmatrix} \quad \begin{aligned} \frac{\partial f_1}{\partial x_1} &= a_1 \frac{n K_1^n x_1^{n-1}}{(K_1^n + x_1^n)^2} - 1 \\ \frac{\partial f_2}{\partial x_1} &= -b_2 \frac{n K_2^n x_1^{n-1}}{(K_2^n + x_1^n)^2} \end{aligned}$$

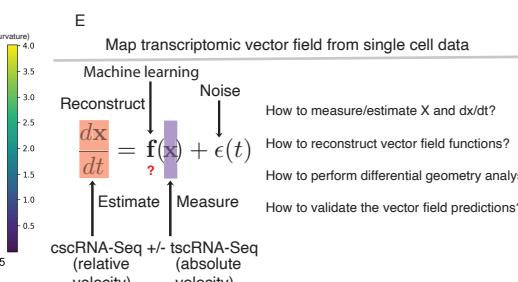
$$K_1 = K_2 = a_1 = a_2 = b_1 = b_2 = 1; N = 4$$



D Acceleration vector field



Curvature vector field



E Map transcriptomic vector field from single cell data

Machine learning

$$\frac{dx}{dt} = f(x) + e(t)$$

cscRNA-Seq (+/- tscRNA-Seq)
(relative velocity)

- How to measure/estimate X and dx/dt ?
- How to reconstruct vector field functions?
- How to perform differential geometry analysis?
- How to validate the vector field predictions?

- Measure
- Estimate
- Noise