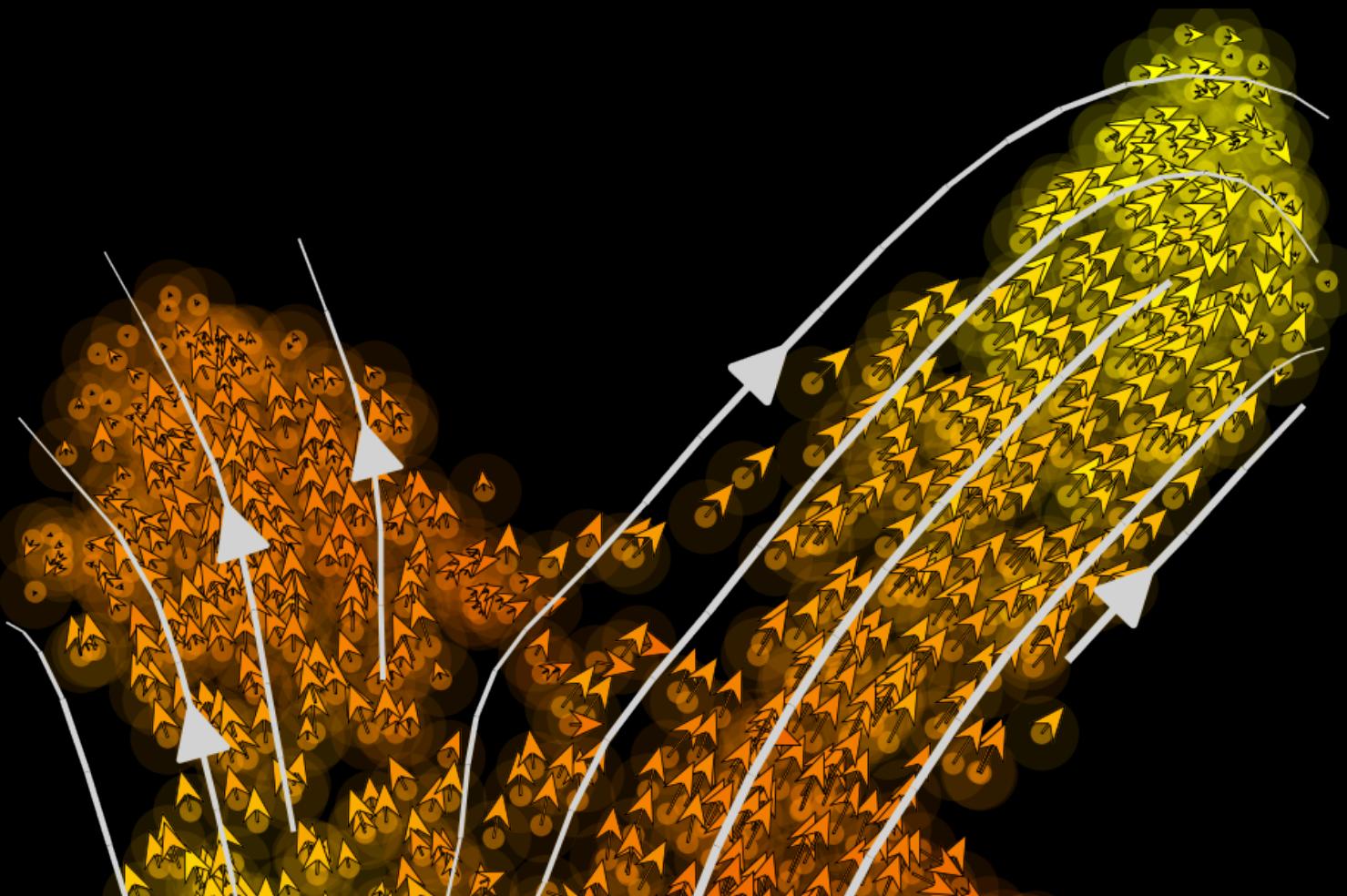


NBIS/SIB single-cell school RNA velocity

Aug 30, 2021

Volker Bergen

vbergen@cellarity.com





MSc Mathematics & MBA Finance

(2011-2017)



PhD Computational Biology

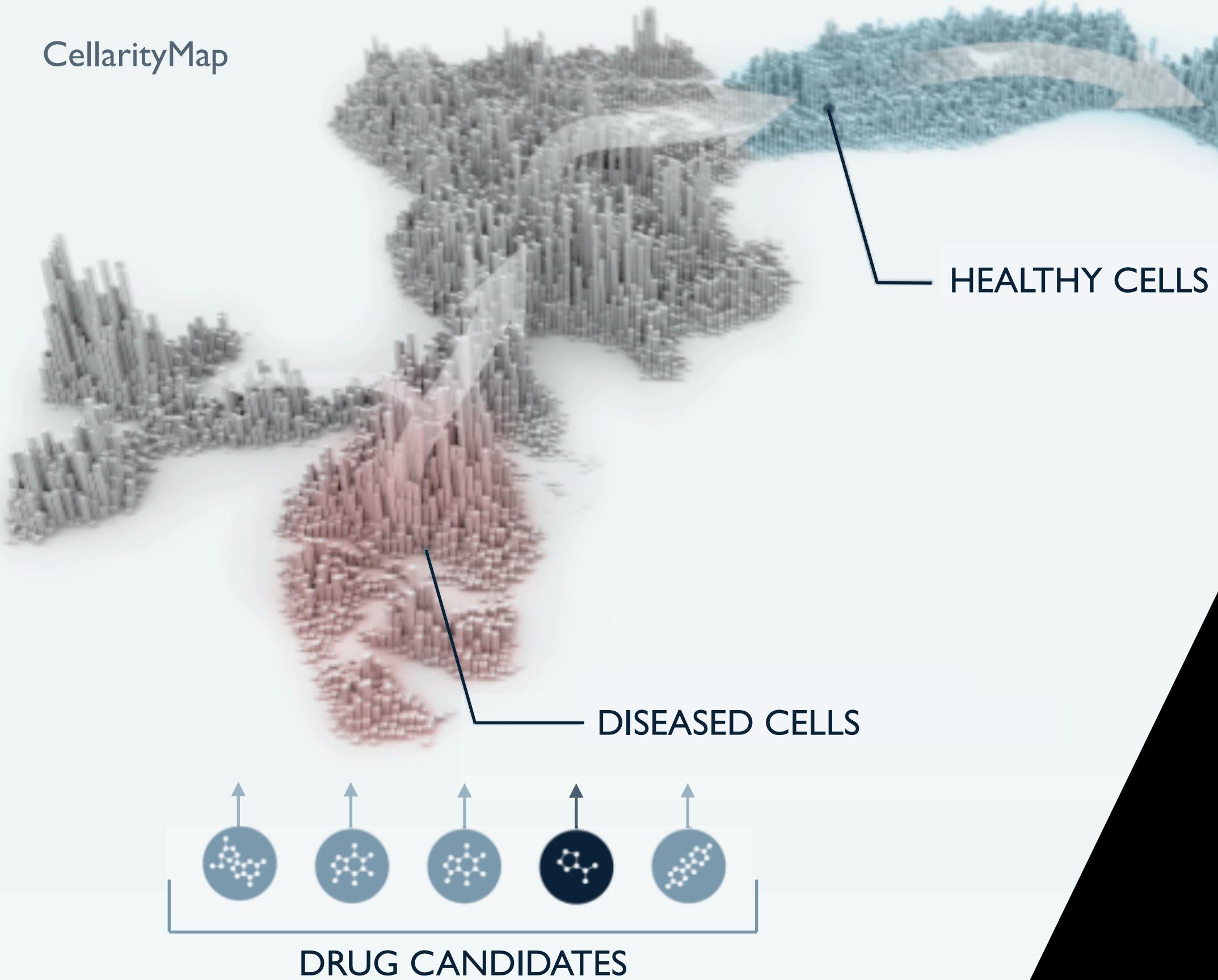
(2017-2020)



ML Scientist & Strategy

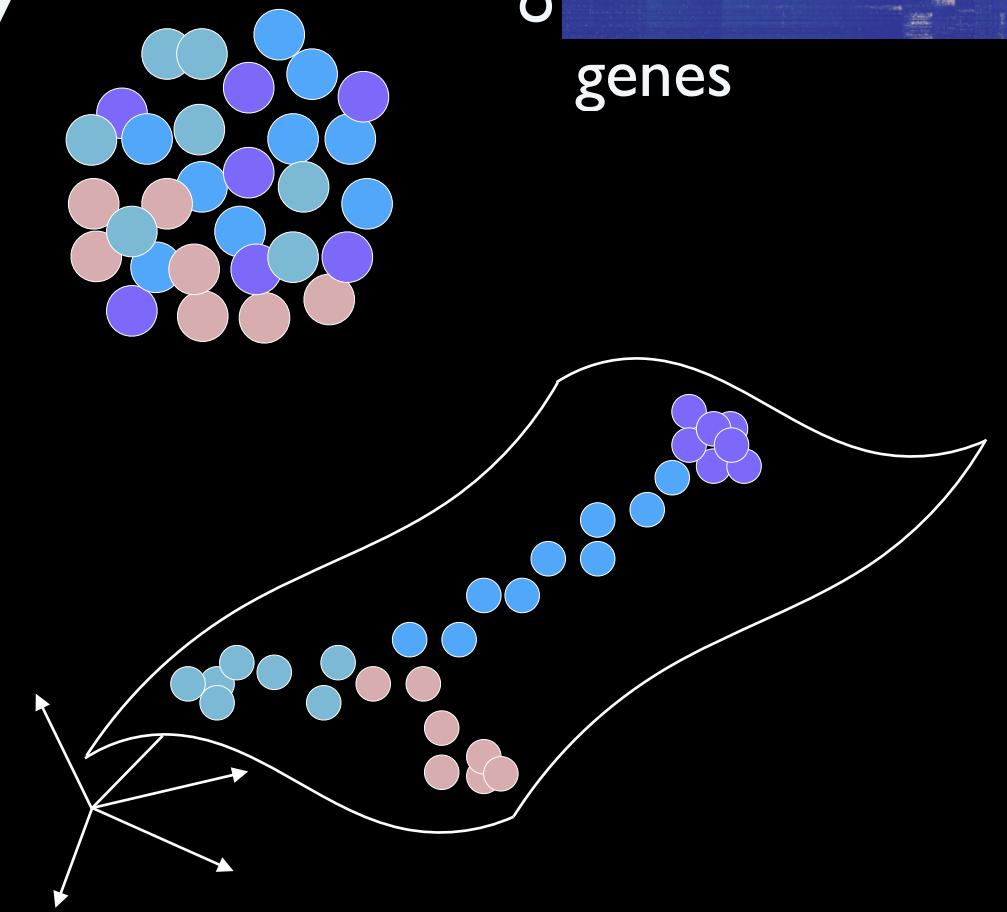
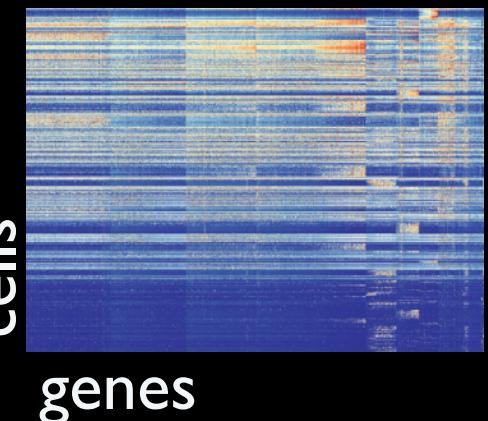
(present)

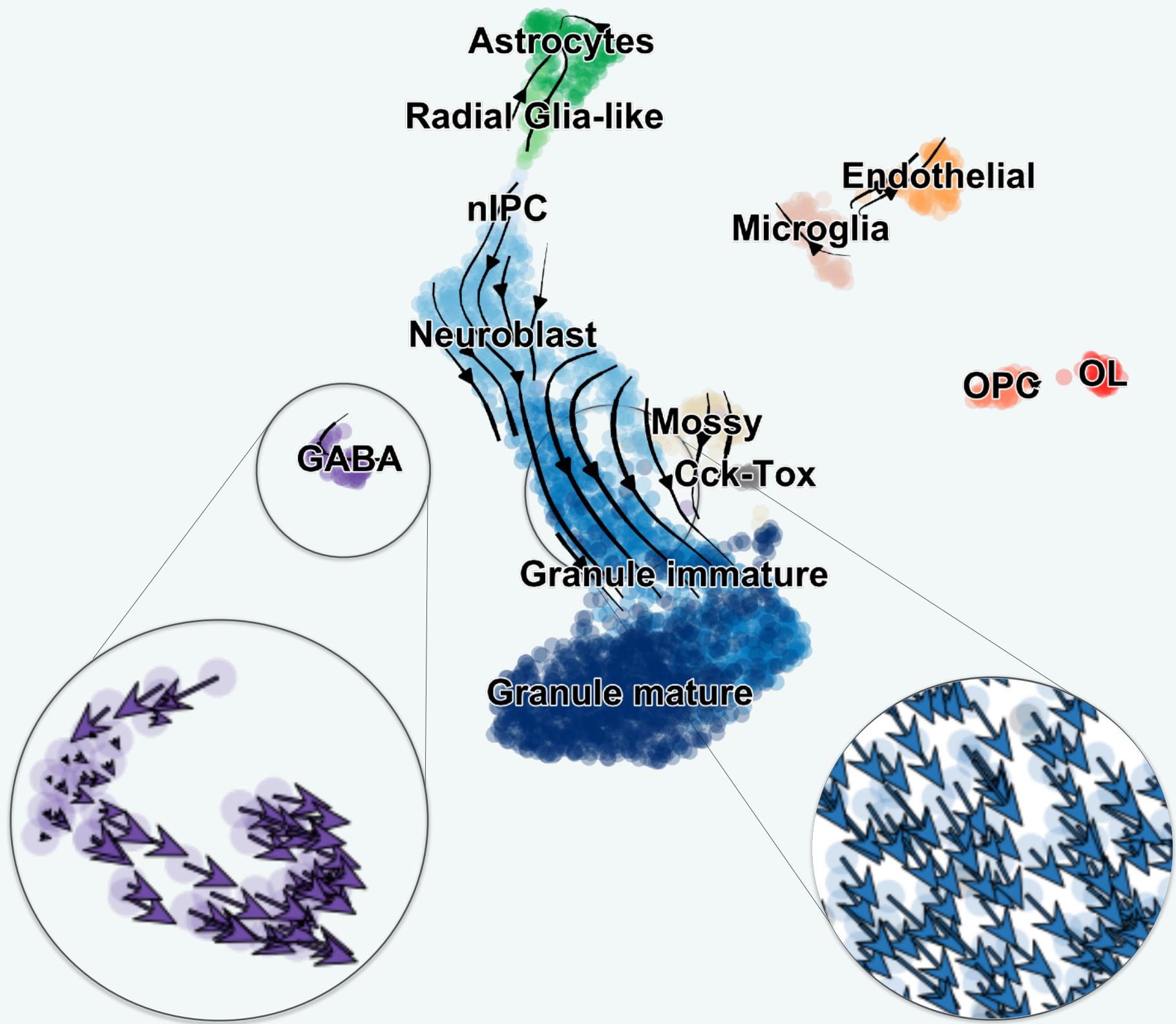
CellarityMap



scanpy

Wolf et al. (2018)





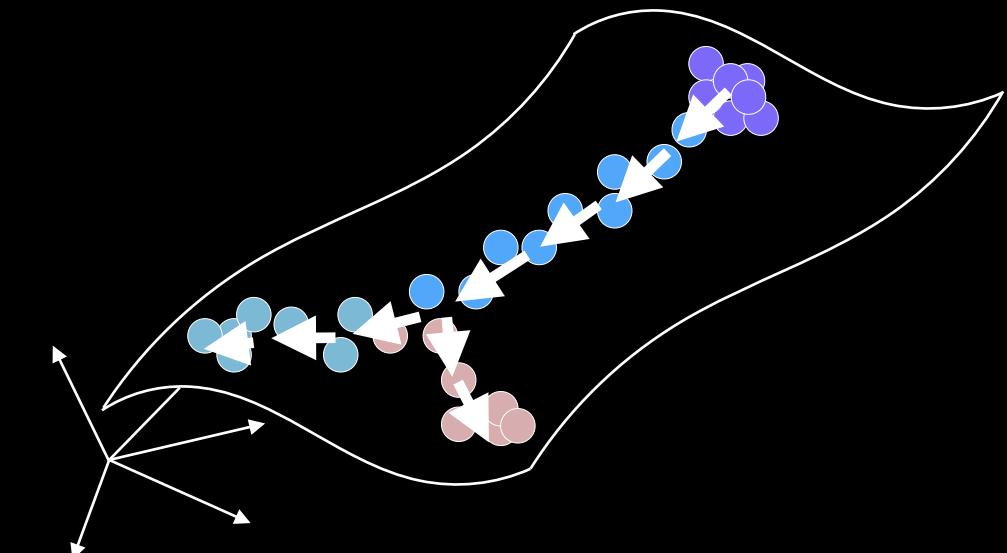
RNA velocity

La Manno *et al.* (Nature 2018)
Bergen *et al.* (Nature Biotech 2020)

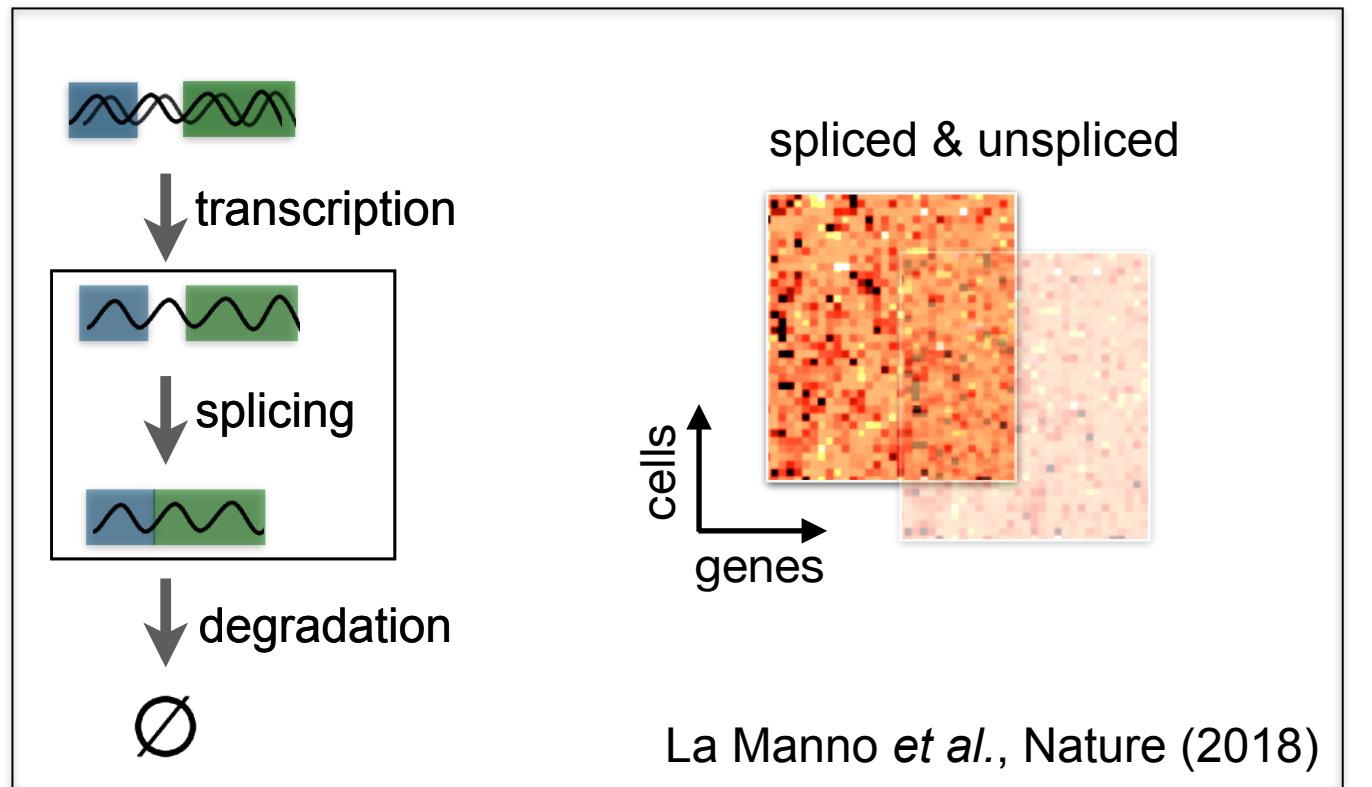
Reviews

Lederer & La Manno (Nat. Biotech 2020)
Bergen *et al.* (MSB, 2021)

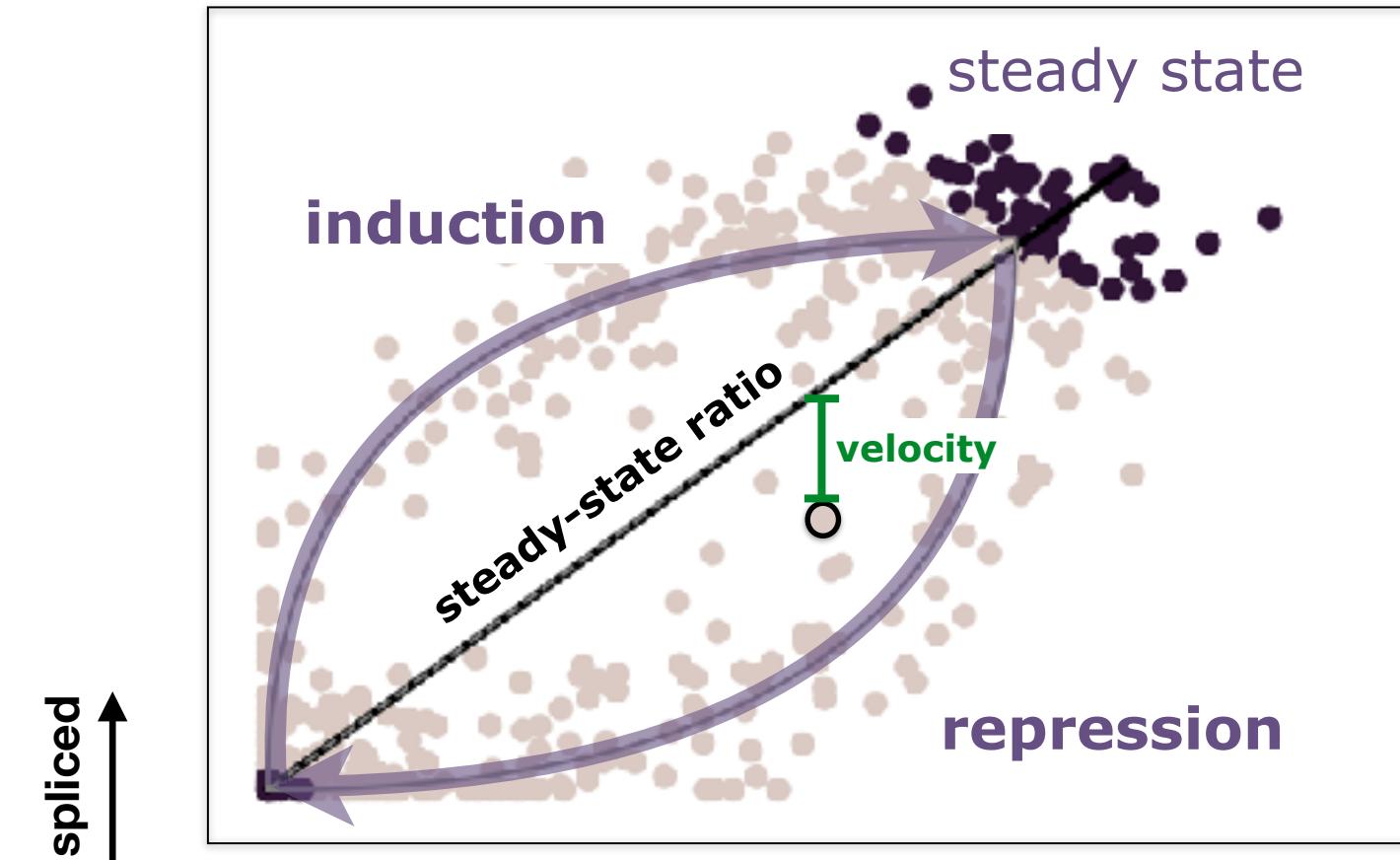
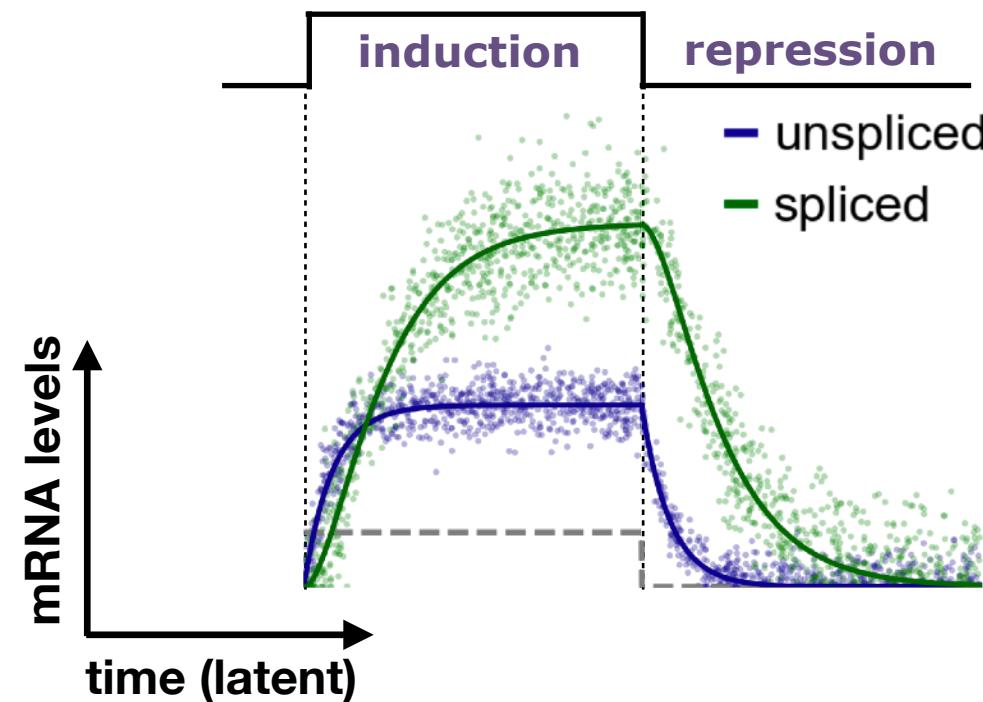
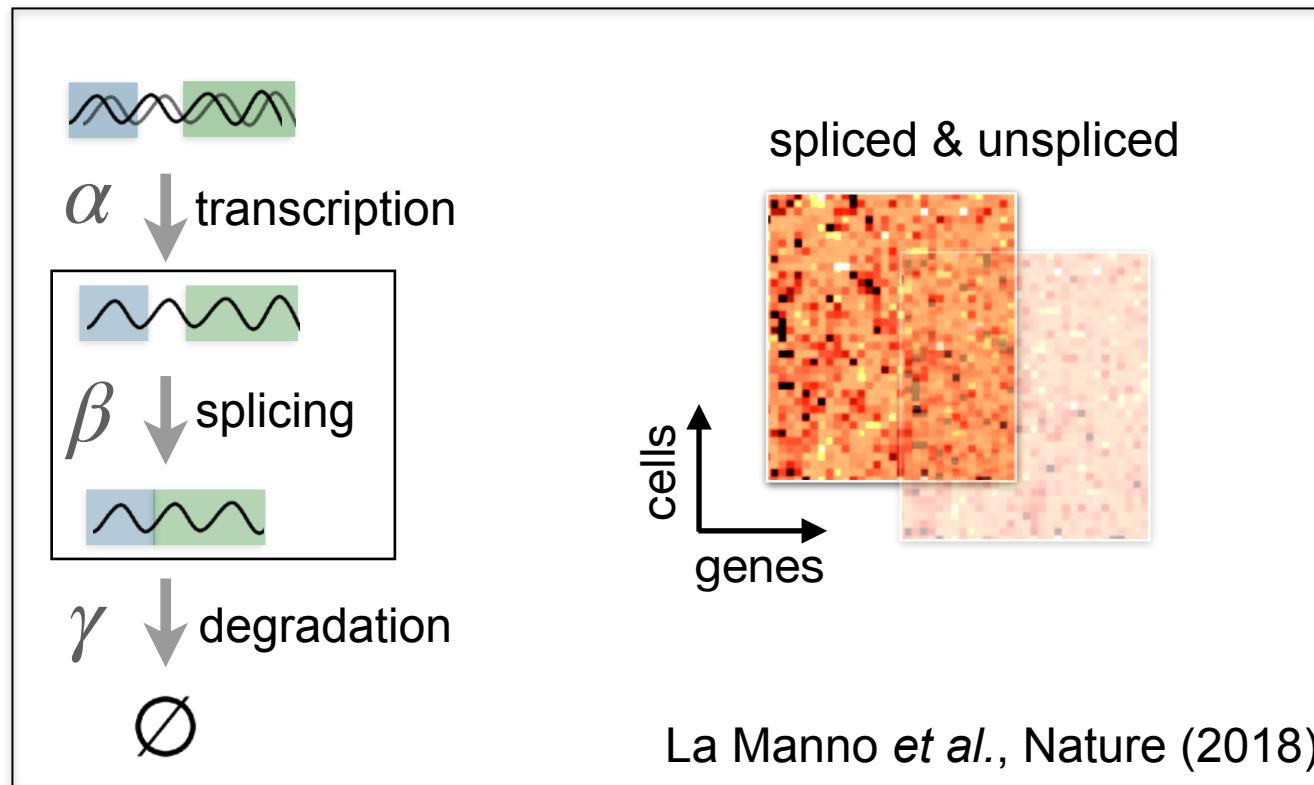
Modeling cellular dynamics with
RNA Velocity



Concept of RNA velocity

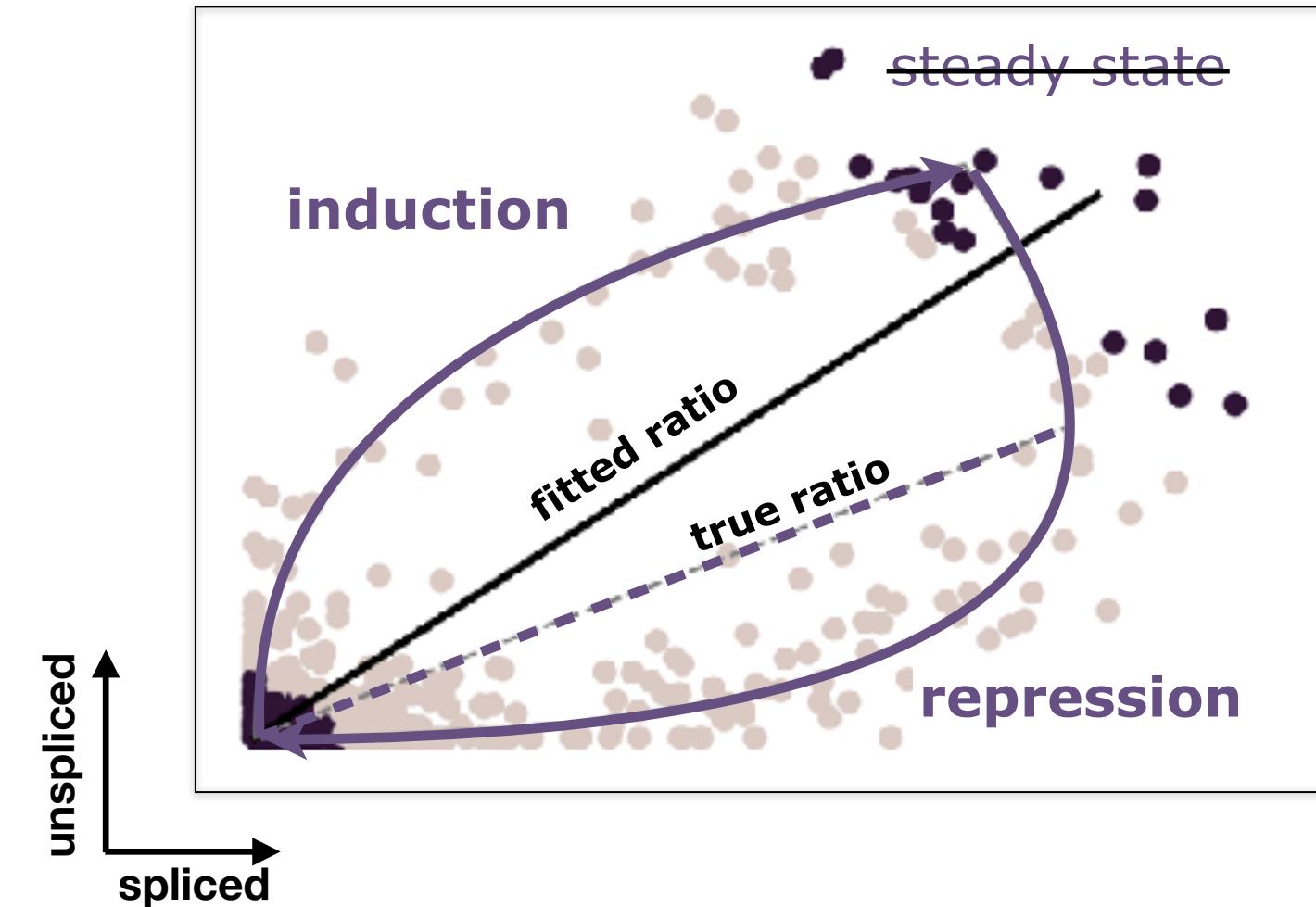
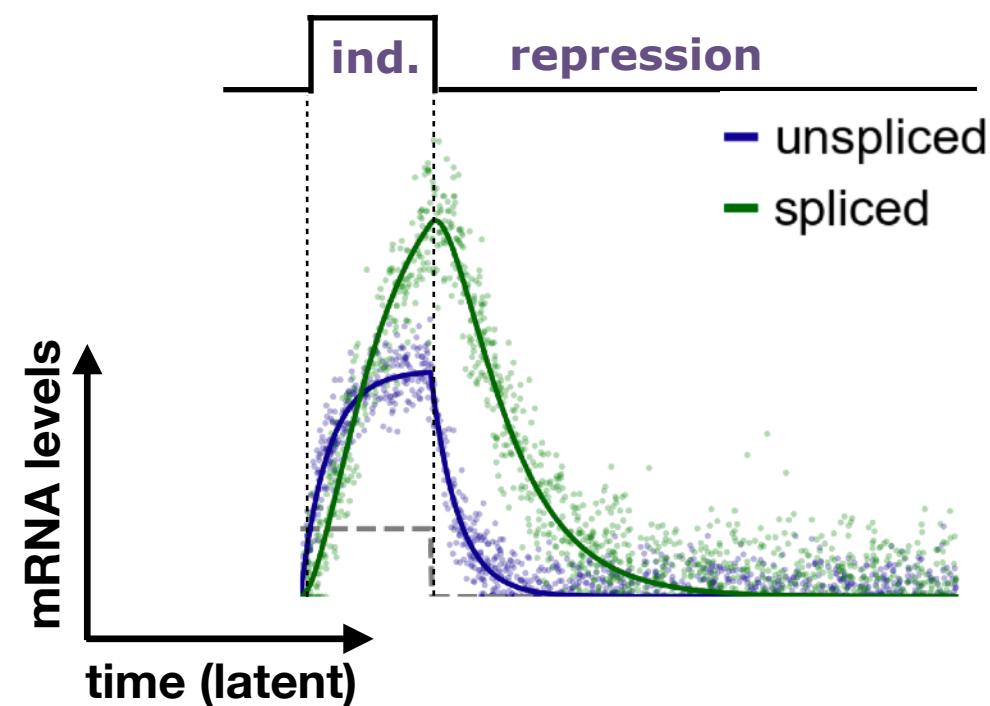
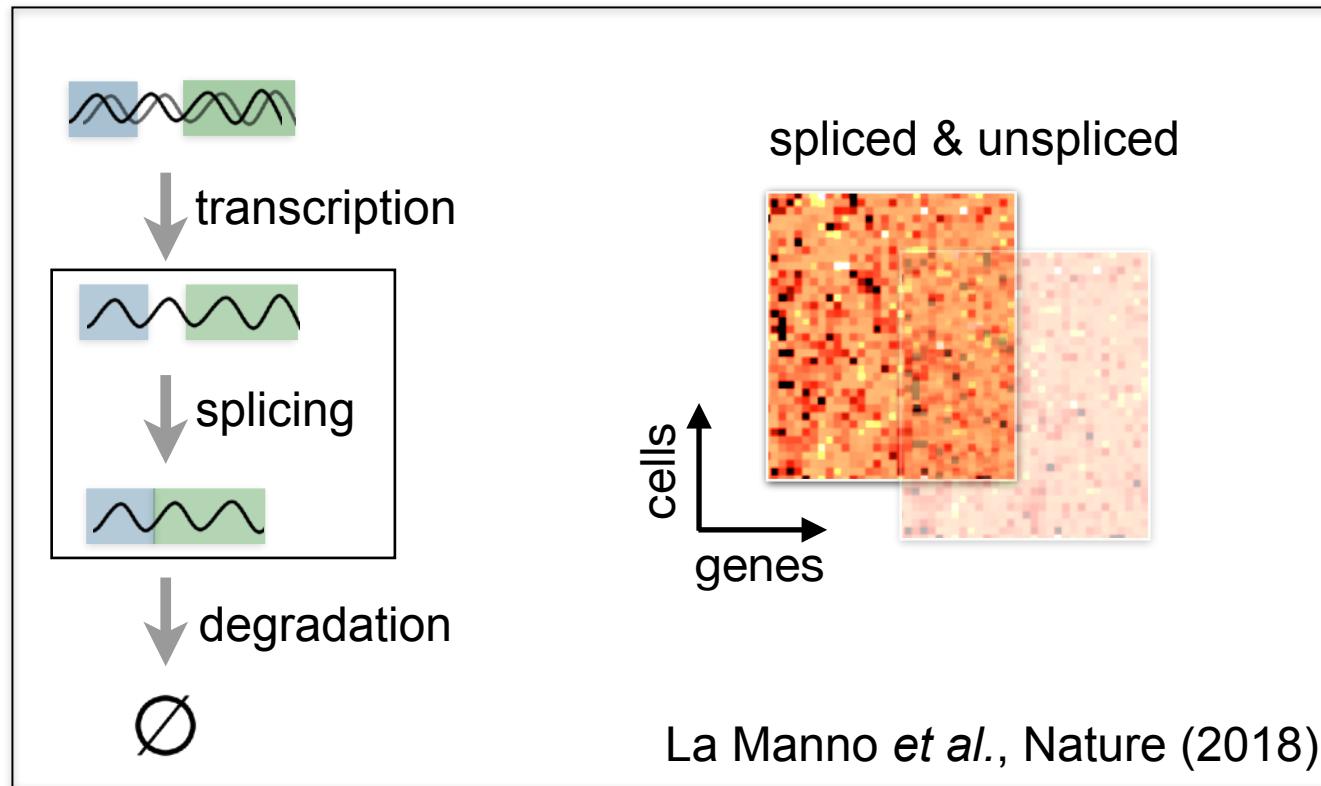


Concept of RNA velocity

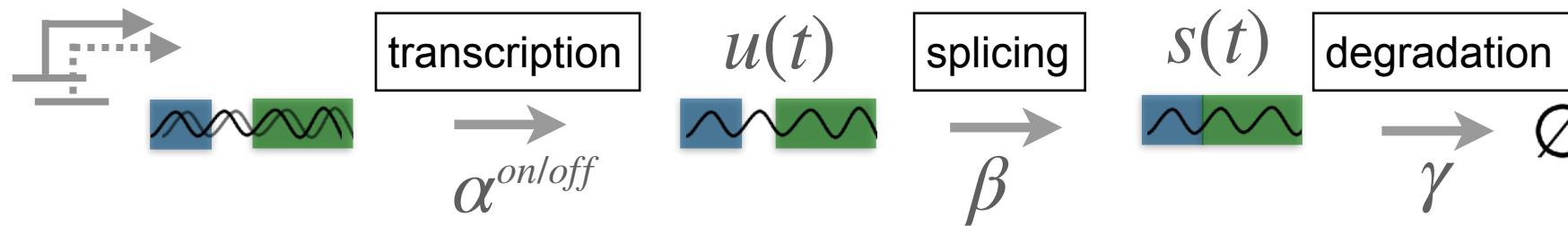


$$\frac{du(t)}{dt} = \alpha - \beta u(t), \quad \frac{ds(t)}{dt} = \beta u(t) - \gamma s(t)$$

Concept of RNA velocity



RNA velocity generalized through dynamical modeling



$$u(t) = u_0 e^{-\beta \tau} + \frac{\alpha}{\beta} (1 - e^{-\beta \tau})$$

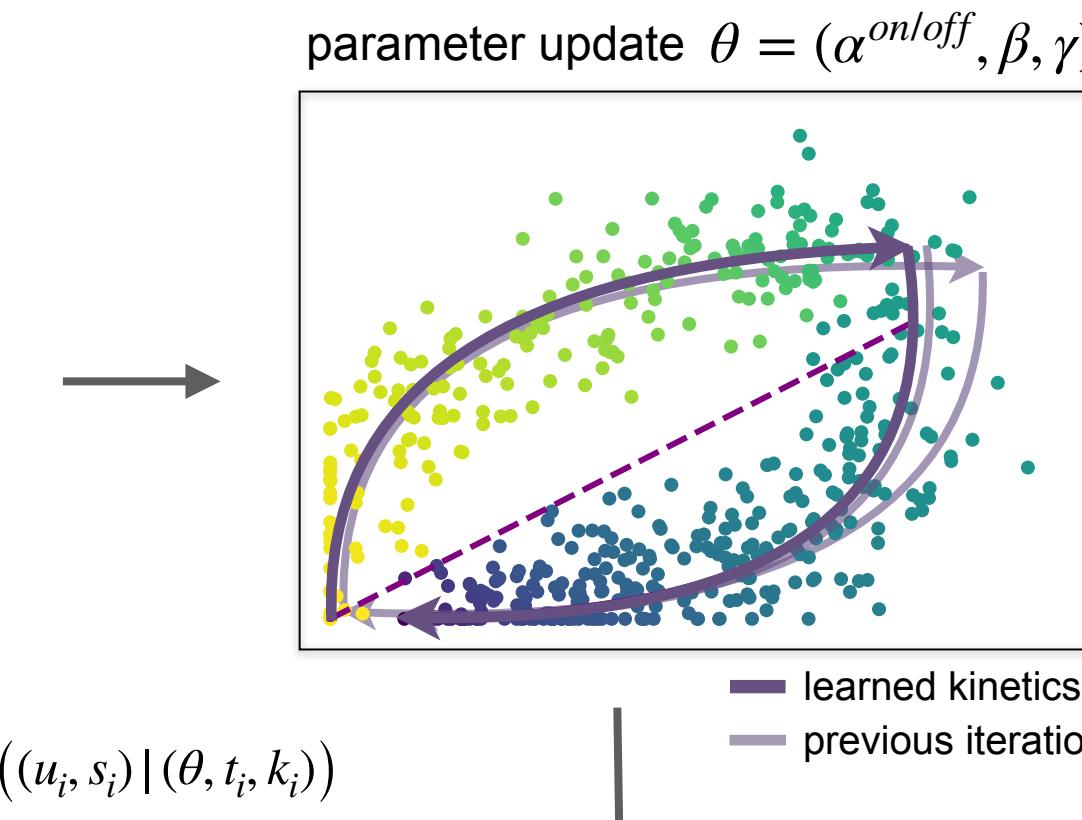
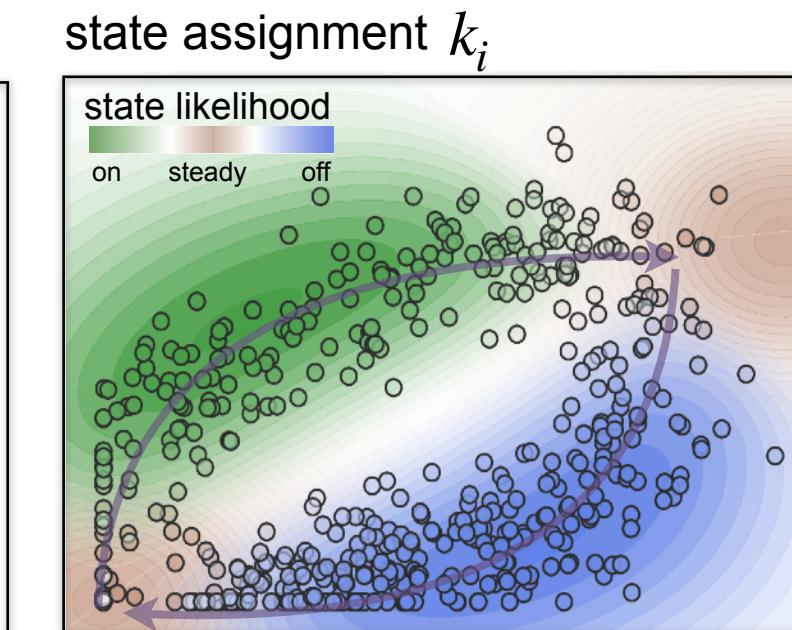
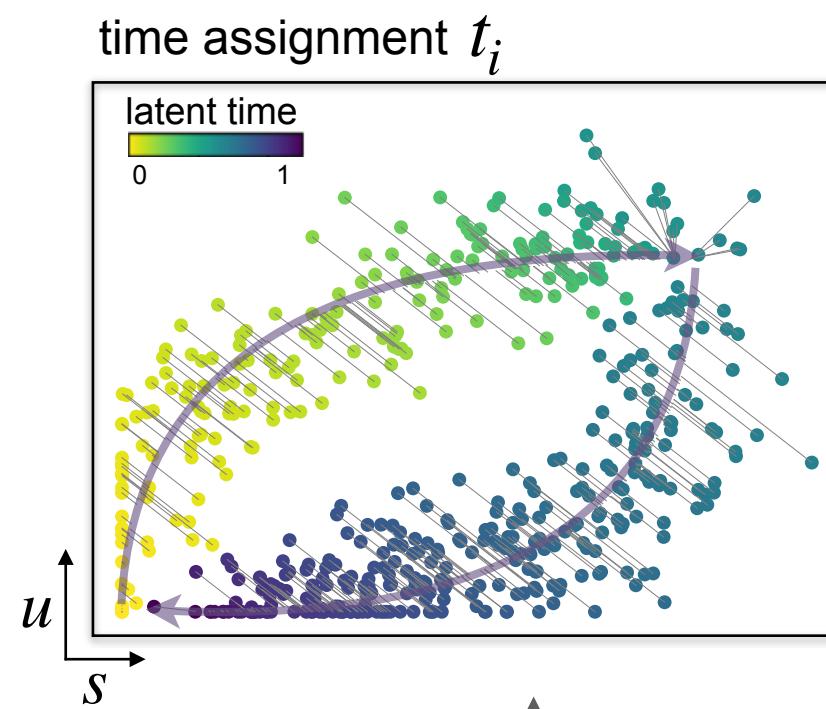
$$s(t) = s_0 e^{-\gamma \tau} + \frac{\alpha}{\gamma} (1 - e^{-\gamma \tau}) + \frac{\alpha - \beta u_0}{\gamma - \beta} (e^{-\gamma \tau} - e^{-\beta \tau}) \quad \tau = t - t_0$$

parameters of **reaction rates**

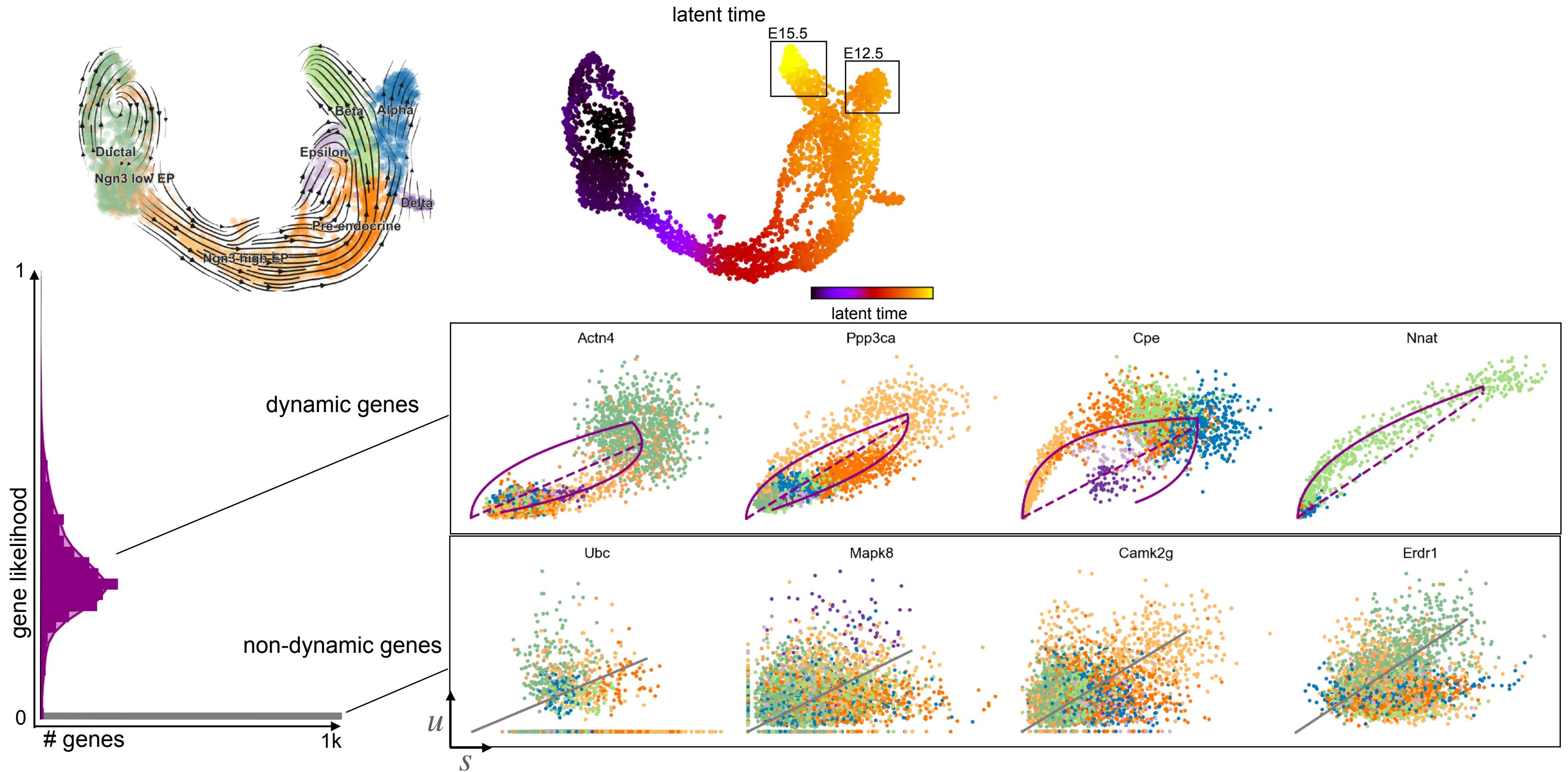
$$\theta = (\alpha^{off}, \alpha^{on}, \beta, \gamma)$$

cell-specific **latent variables**
(switch, time, state)

$$\eta_i = (t_0^{(i)}, t_i, k_i)$$

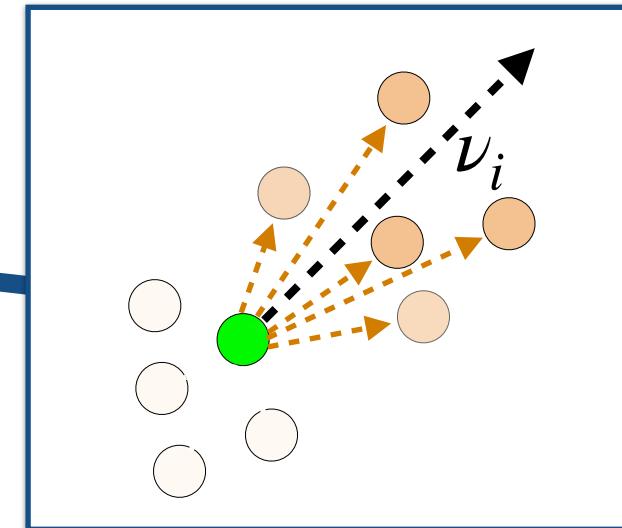
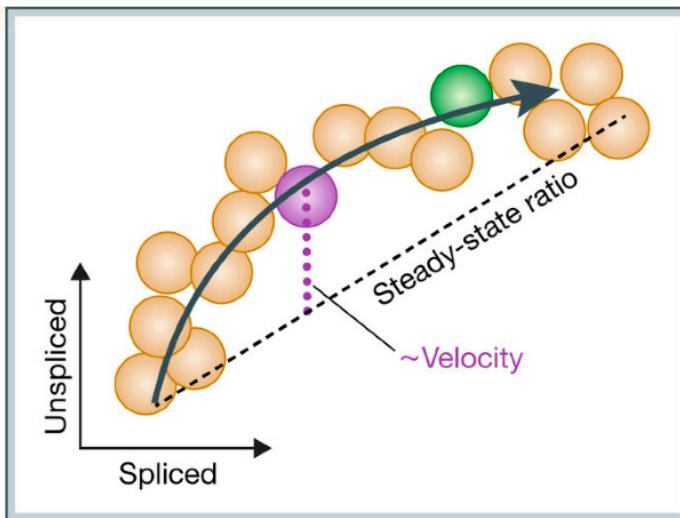


Applications of RNA velocity



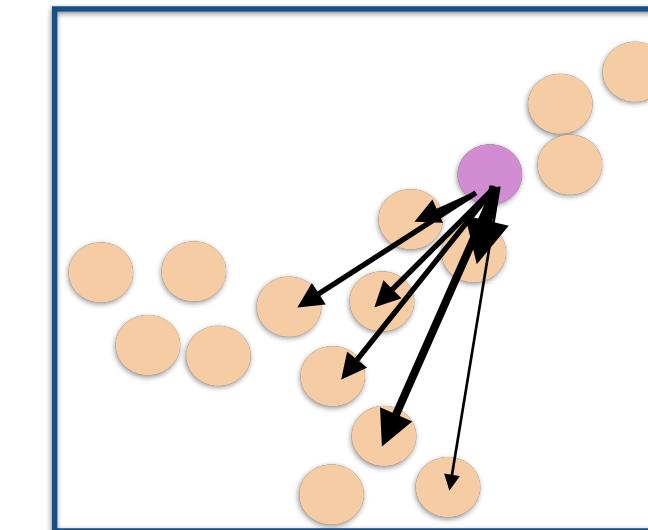
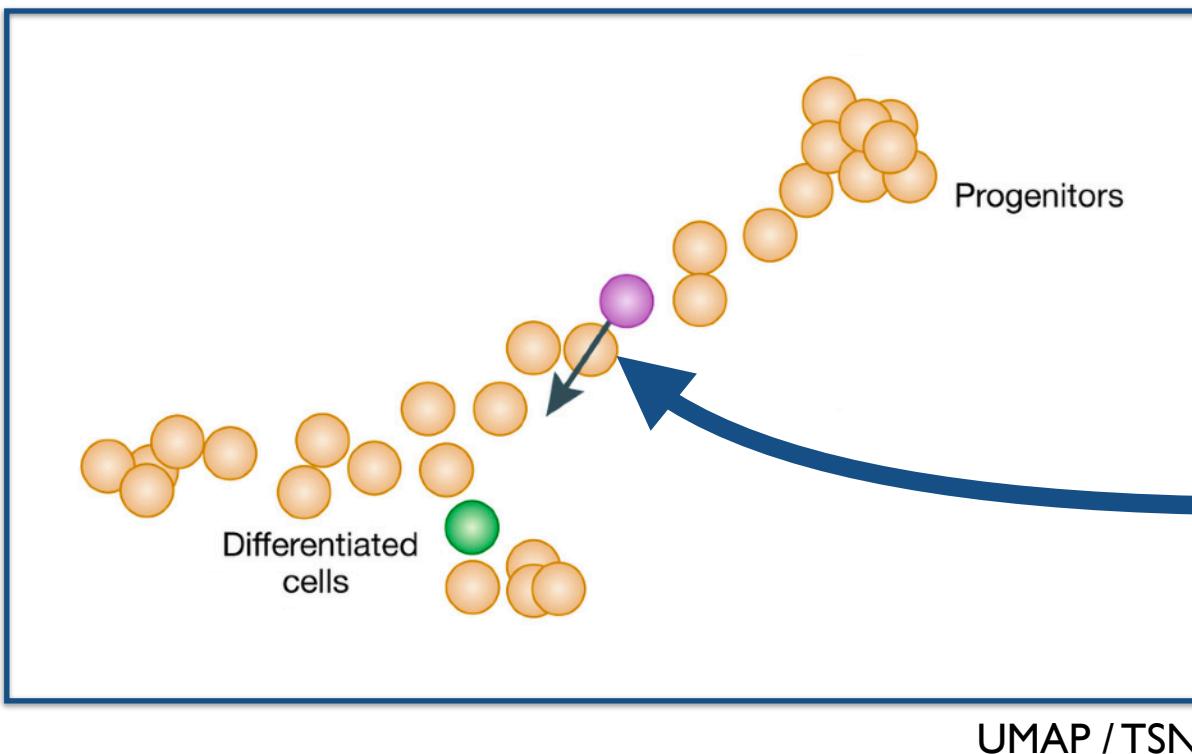
RNA velocity in two dimensions

Compute cell-to-cell transition probabilities by how much the transition correlates with the velocity vector (high-dim)



$$P = \begin{bmatrix} P_{1,1} & P_{1,2} & \dots & P_{1,j} & \dots & P_{1,S} \\ P_{2,1} & P_{2,2} & \dots & P_{2,j} & \dots & P_{2,S} \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots \\ P_{i,1} & P_{i,2} & \dots & P_{i,j} & \dots & P_{i,S} \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots \\ P_{S,1} & P_{S,2} & \dots & P_{S,j} & \dots & P_{S,S} \end{bmatrix}.$$

$$P_{ij} = e^{\rho(\delta_{ij}, \nu_i) / \sigma_i^2}$$

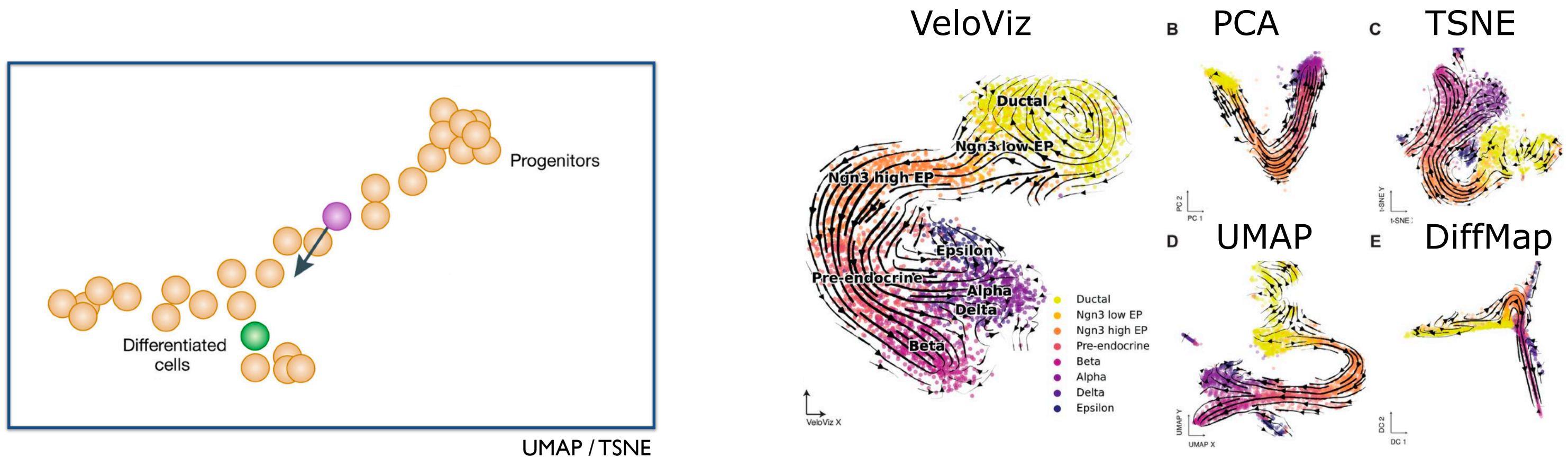


Given the transitions probabilities, compute the expected transition in the lower-dim embedding

RNA velocity - finding a good representation

Topic 1

- What embedding specification best represents the high-dim vector field?
- Can we find other ways to project the data (e.g., parametric UMAP)?

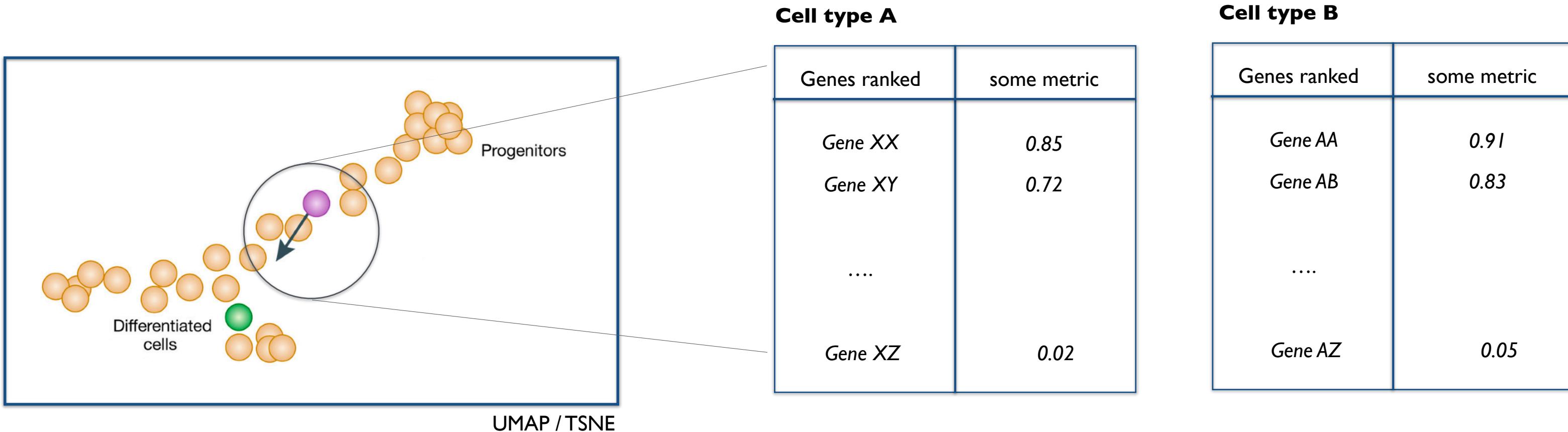


Atta et al. (2021, BioRxiv)

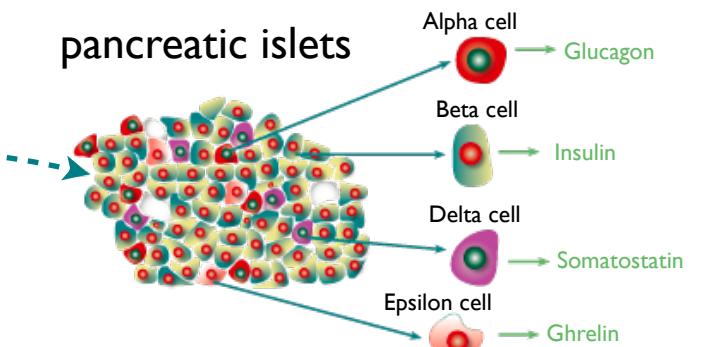
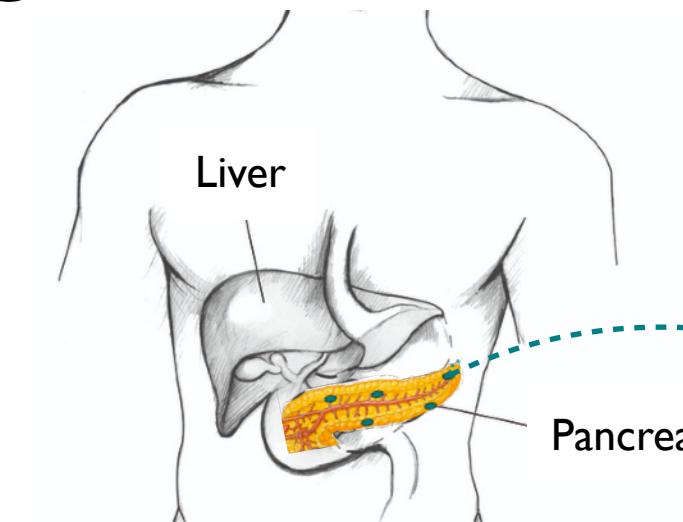
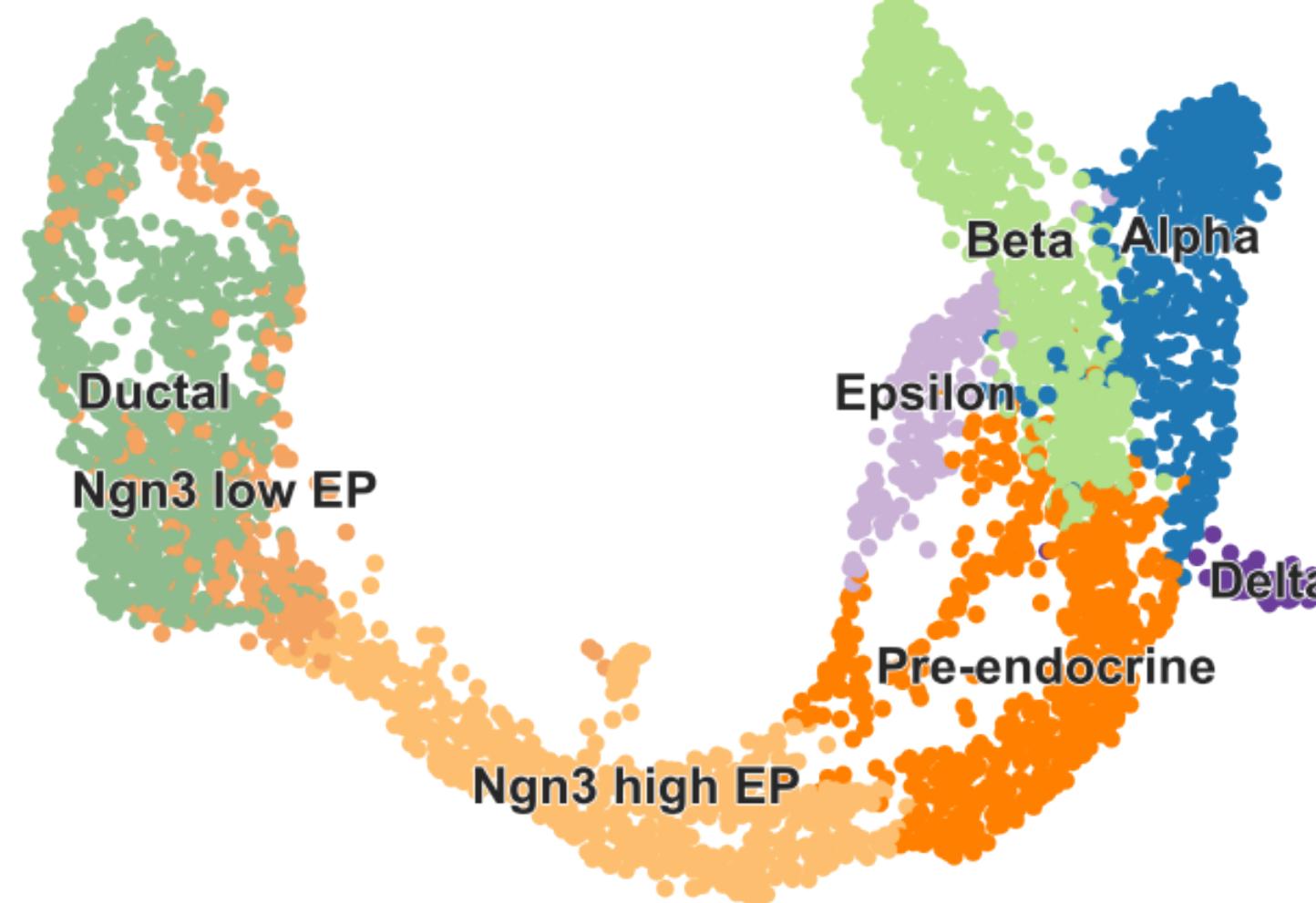
RNA velocity - identifying relevant genes

Topic 2

- What genes are driving the projected arrows in the low-dim manifold?
- Can we systematically identify genes that are important in a particular compartment?

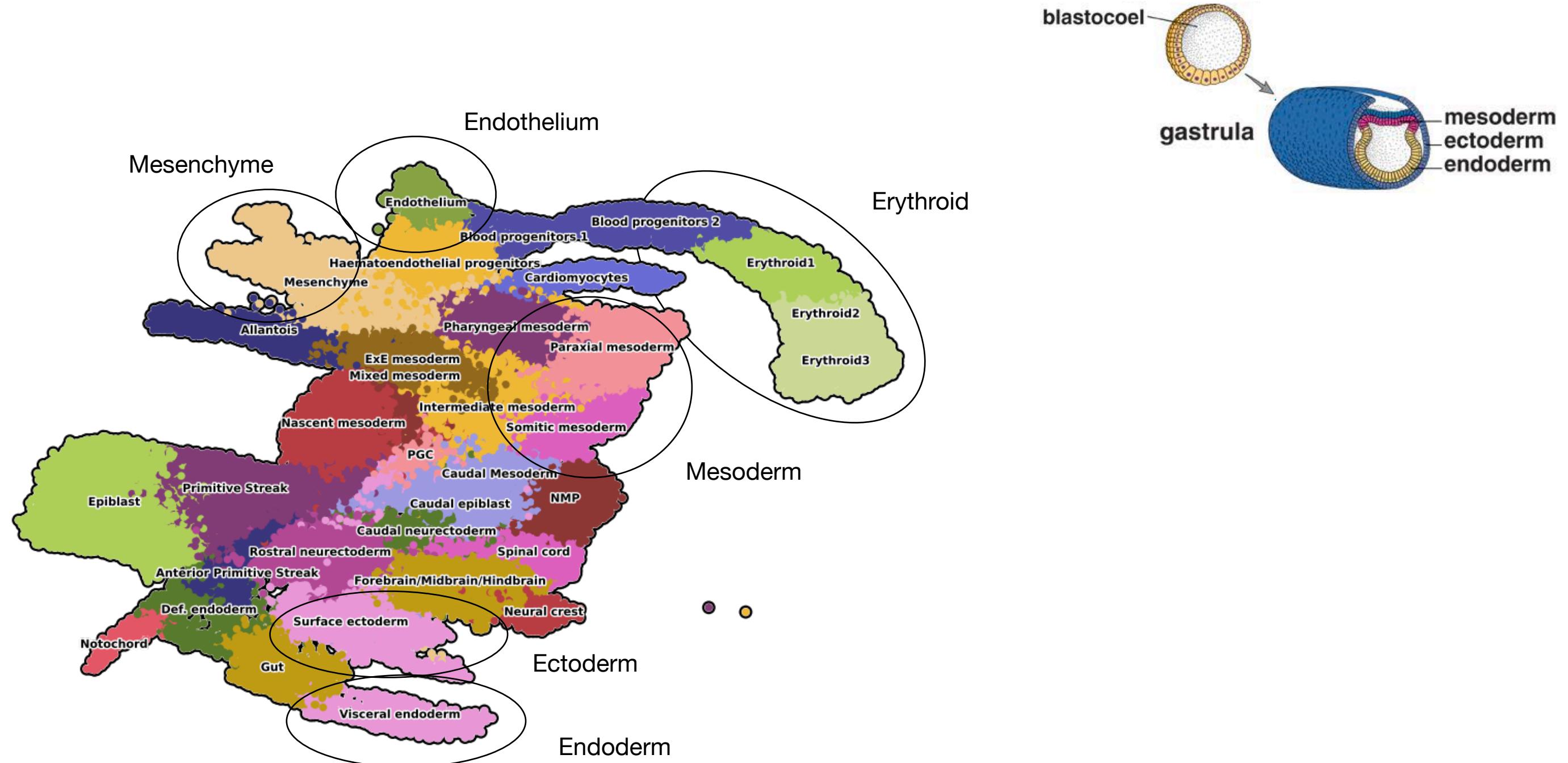


Datasets - pancreatic endocrinogenesis



Bastidas-Ponce *et al.*, Development (2019)
Bergen *et al.*, Nat. Biotech (2020)

Datasets - gastrulation and early organogenesis



Pijuan-Sala *et al.*, Nature (2019)

The scvelo API

```
import scvelo as scv
```

Read the data

```
adata = scv.datasets.pancreas()
```

Preprocessing

```
scv.pp.filter_and_normalize(adata, n_top_genes=2000)
```

```
scv.pp.moments(adata)
```

Velocity estimation

```
scv.tl.velocity(adata)
```

Velocity projection

```
scv.tl.velocity_embedding(adata, basis='umap')
```

Visualization

```
scv.pl.velocity_embedding_stream(adata, basis='umap')
```

The screenshot shows the scvelo.org/api/ documentation page. The left sidebar contains links to MAIN, API, TUTORIALS, PERSPECTIVES, and Getters. The main content area is titled 'Utils' and lists several functions:

- `get_df (data[, keys, layer, index, columns, ...])` - Get dataframe for a specific key.
- `utils.gene_info (name[, fields])` - Retrieve gene information from biotools.
- `utils.cleanup (data[, clean, keep, copy])` - Delete not needed annotations.
- `utils.clean_obs_names (data[, base, ...])` - Clean up the obs_names.
- `utils.merge (adata, ldata[, copy])` - Merge two annotated datasets.
- `utils.show_proportions (adata[, layers, use_raw])` - Proportions of abundance.
- `utils.get_moments (adata[, layer, ...])` - Computes moments for each cell.
- `utils.get_transition_matrix (adata[, vkey, ...])` - Computes cell-to-cell transition matrix.
- `utils.get_cell_transitions (adata[, ...])` - Simulate cell transitions.
- `utils.get_extrapolated_state (adata[, vkey, ...])` - Get extrapolated cell state.
- `utils.convert_to_ensembl ([gene_names])` - Retrieve ensembl IDs for gene names.
- `utils.convert_to_gene_names ([ensembl_names])` - Retrieve gene names for ensembl IDs.
- `utils.leastsq (x, y[, fit, offset, perc, ...])` - Solves least squares $X^*b=Y$.
- `utils.vcorrcoef (X, y[, mode, axis])` - Pearson's/Spearman's correlation coefficient.
- `utils.test_bimodality (x[, bins, kde, plot])` - Test for bimodal distribution.

At the bottom, there are 'Read the Docs' and 'Settings' buttons.