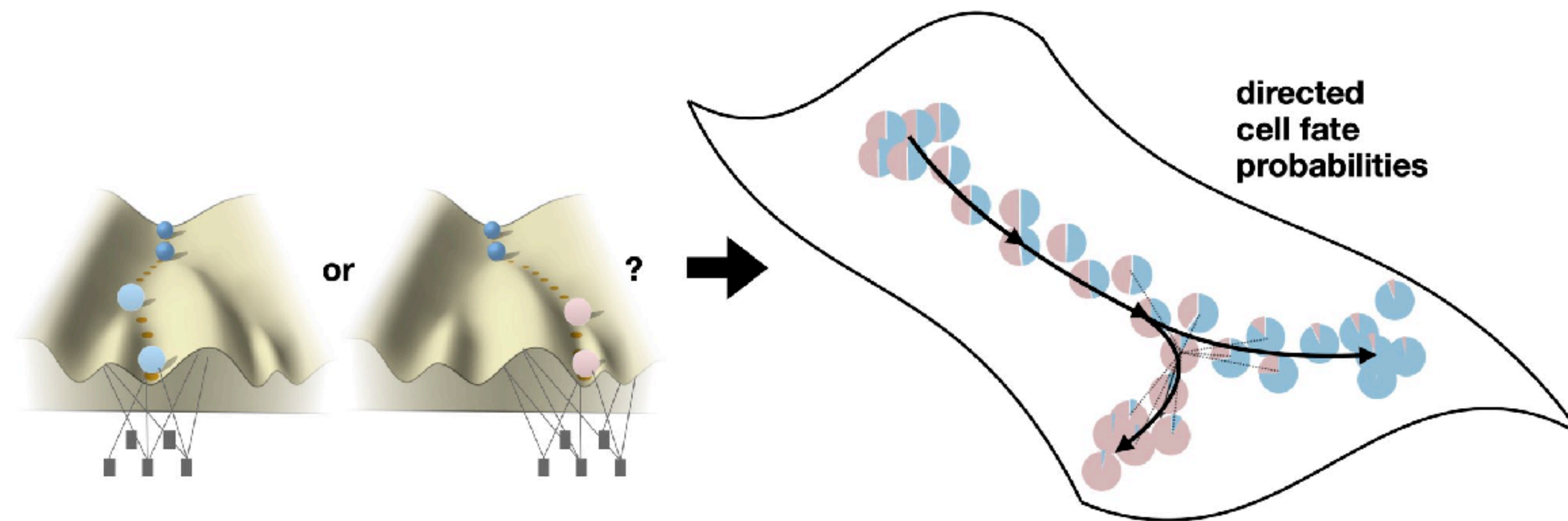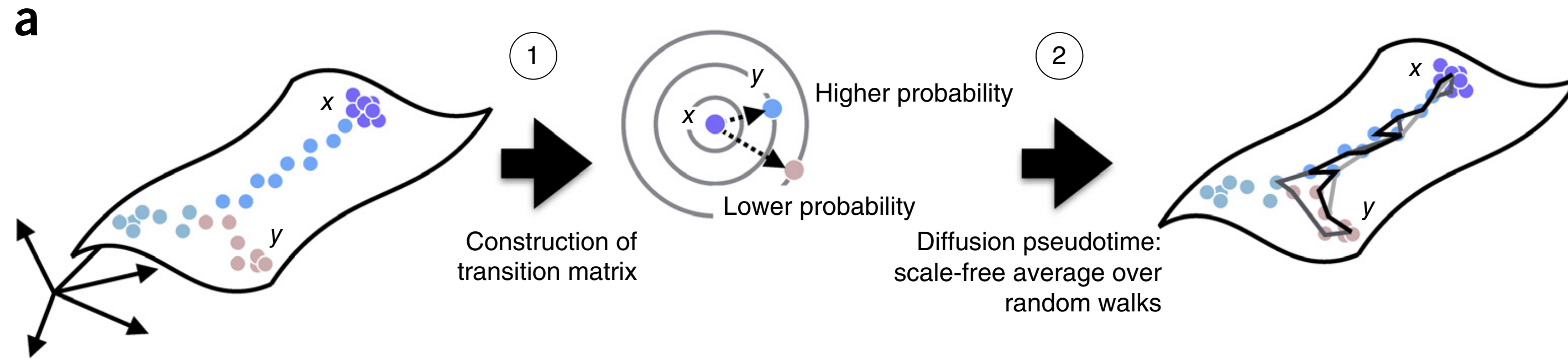# CellRank for directed single-cell fate mapping

Marius Lange[1,2], Volker Bergen[1,2], Michal Klein[1], Manu Setty[3], Bernhard Reuter[4,5], Mostafa Bakhti[6,7], Heiko Lickert[6,7], Meshal Ansari[1,8], Janine Schniering[8], Herbert B. Schiller[8], Dana Pe'er[3]*, Fabian J. Theis[1,2,9]*
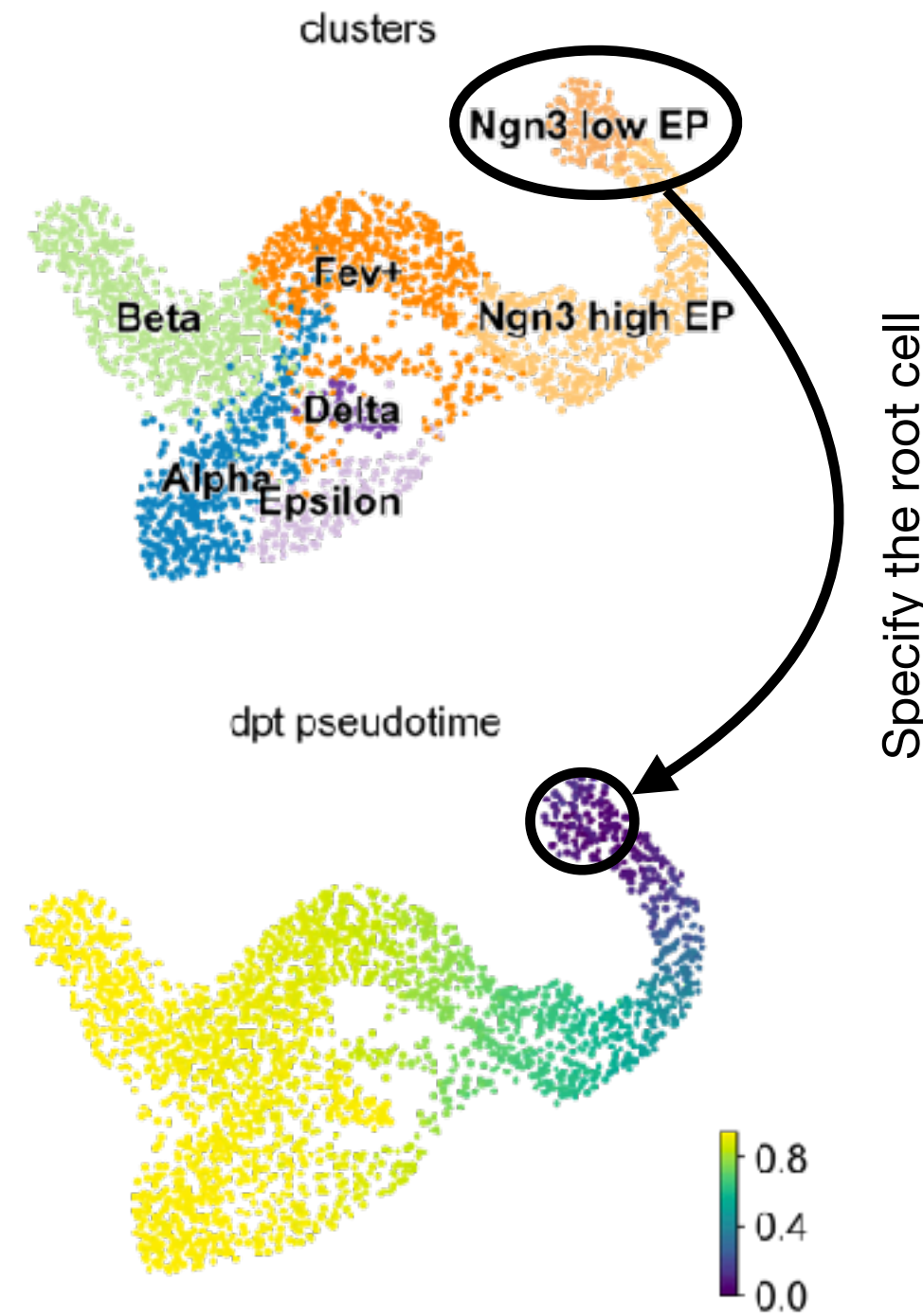
Institute of Computational Biology, Institute of Diabetes and Regeneration Research and Institute of Lung Biology and Disease @ Helmholtz Munich, Program for Computational and Systems Biology @ MSKCC New York, Department of Computer Science @ University of Tübingen

cellrank.org

directed cell fate probabilities

10.1101/2020.10.19.3

Emerging technologies in single-cell research virtual edition 2020

Single cell RNA-seq and computational tools uncover lineage relationships

a

① Construction of transition matrix

Higher probability

Lower probability

② Diffusion pseudotime: scale-free average over random walks

Works **really** well for normal development

clusters

Ngn3 low EP

Beta   Fev1   Ngn3 high EP

Delta
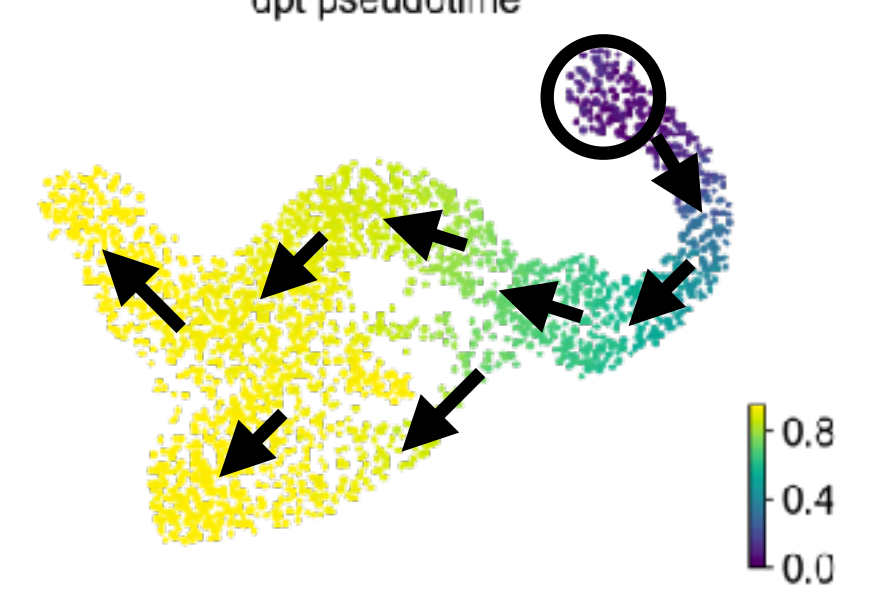
Alpha   Epsilon

dpt pseudotime

Specify the root cell

0.8
0.4
0.0

perturbed conditions

regeneration, reprogramming, etc

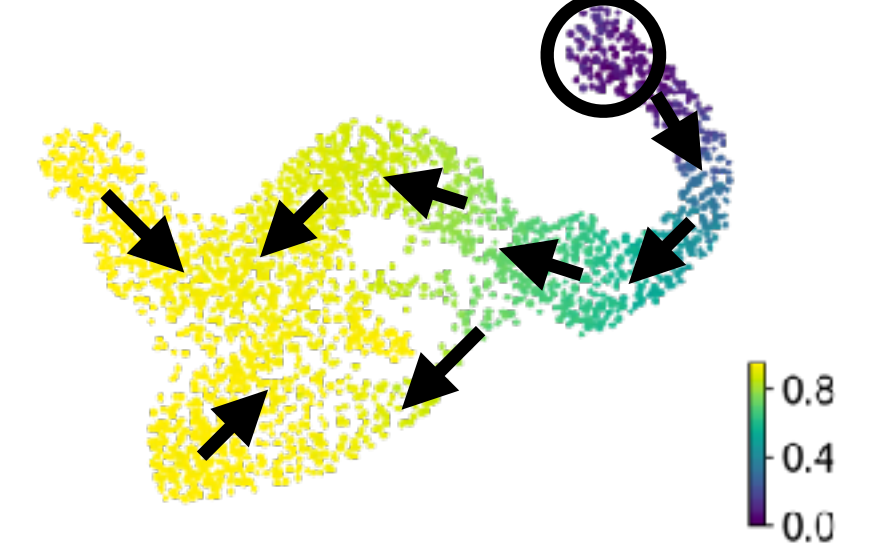Challenges under **perturbed** conditions

Uncertain initial/terminal states

dpt pseudotime

Uncertain directions

dpt pseudotime

0.8
0.4
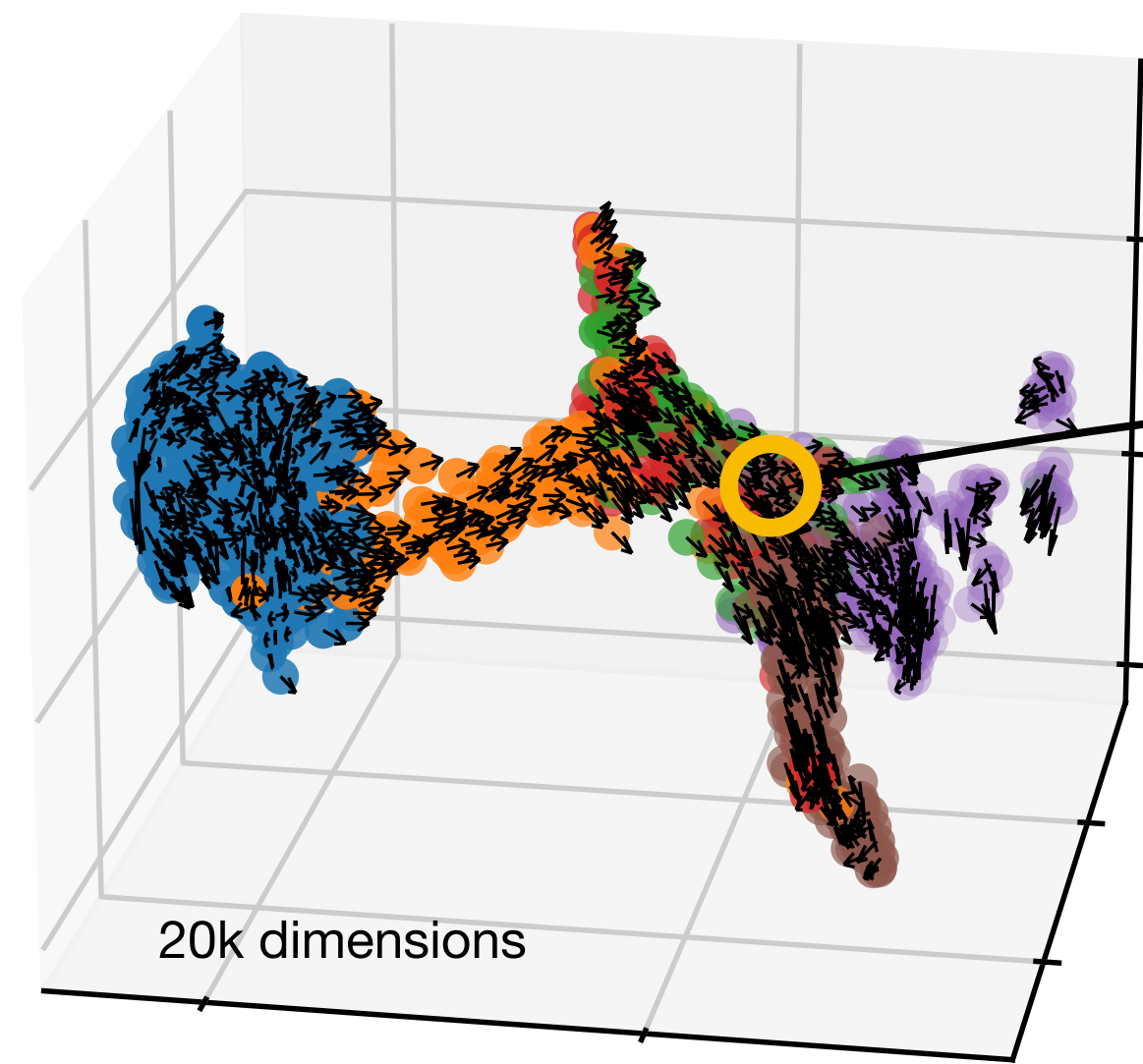0.0

or

or

0.8
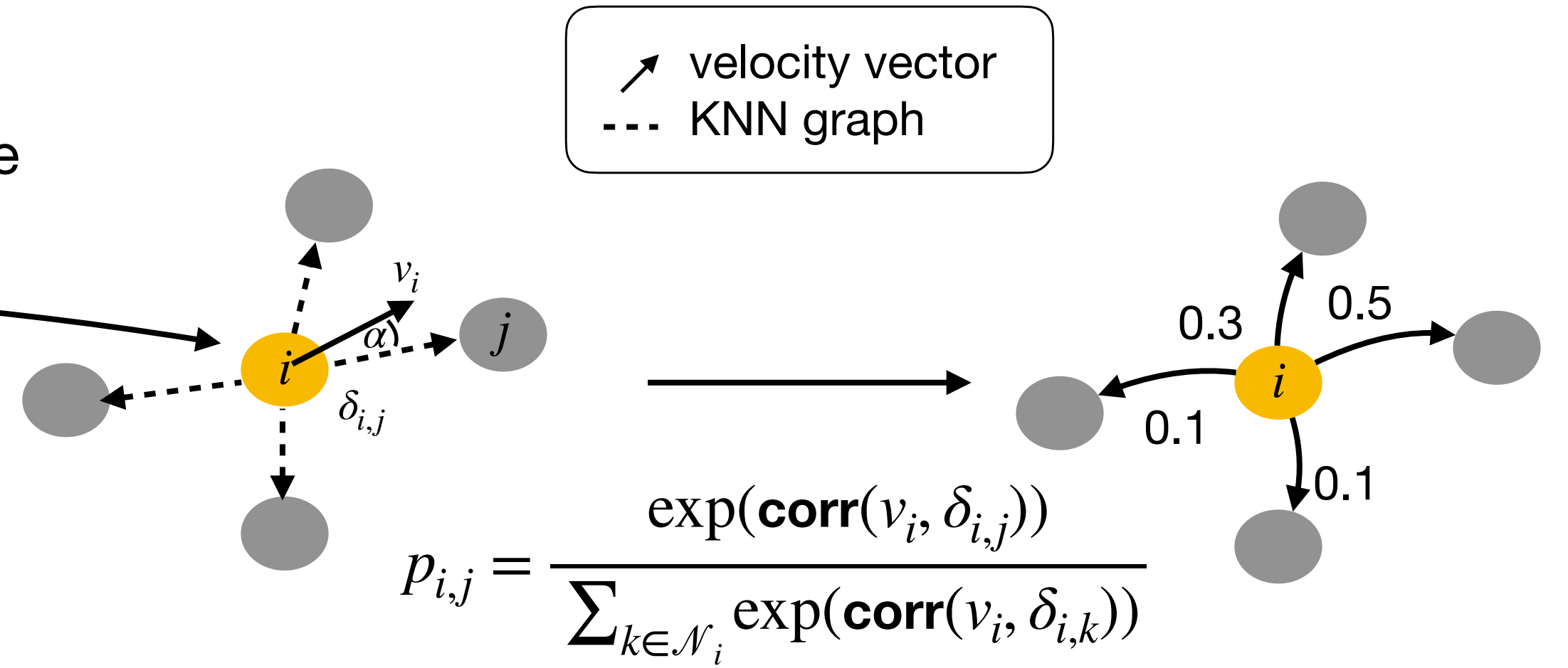0.4
0.0

0.50
0.25
0.00

0.8
0.4
0.0
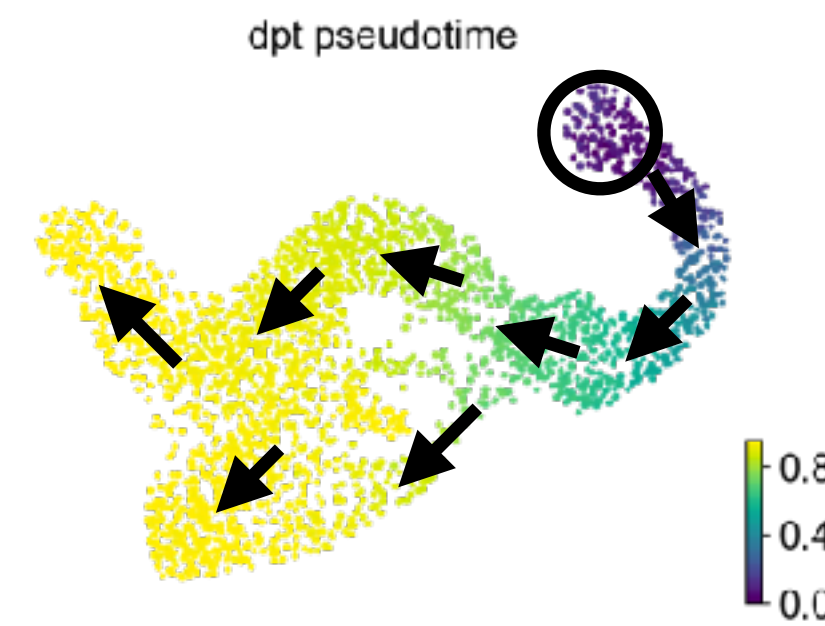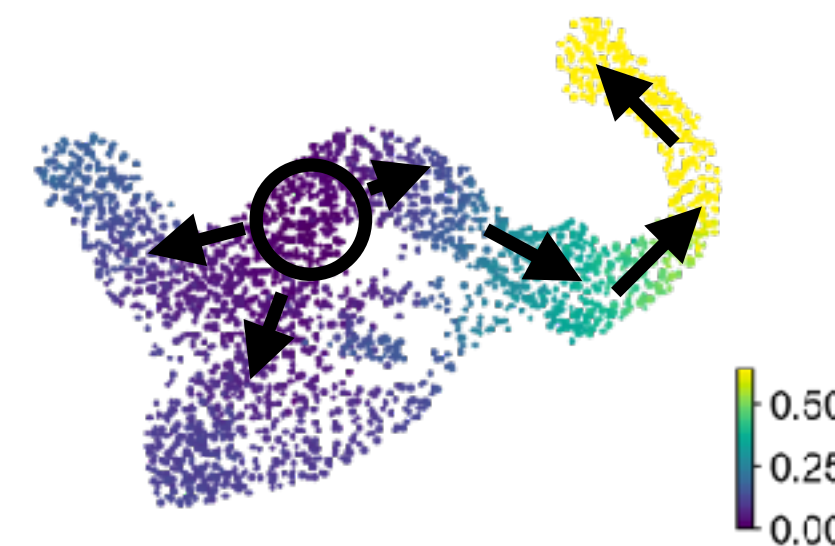
Top panel taken from Haghverdi et al., Nature Methods (2016)
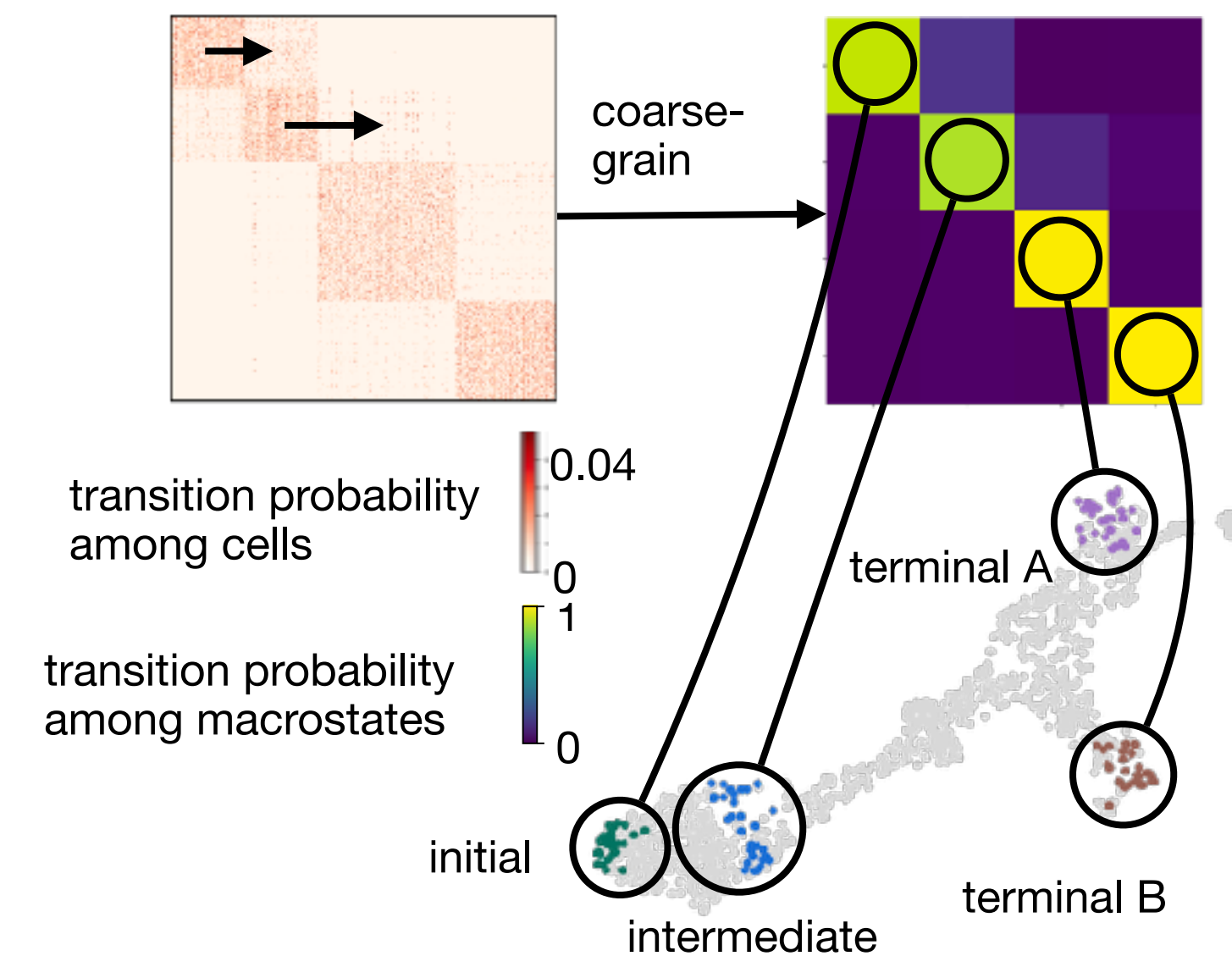**Data from Bastidas-Ponce et al., Development (2019)**

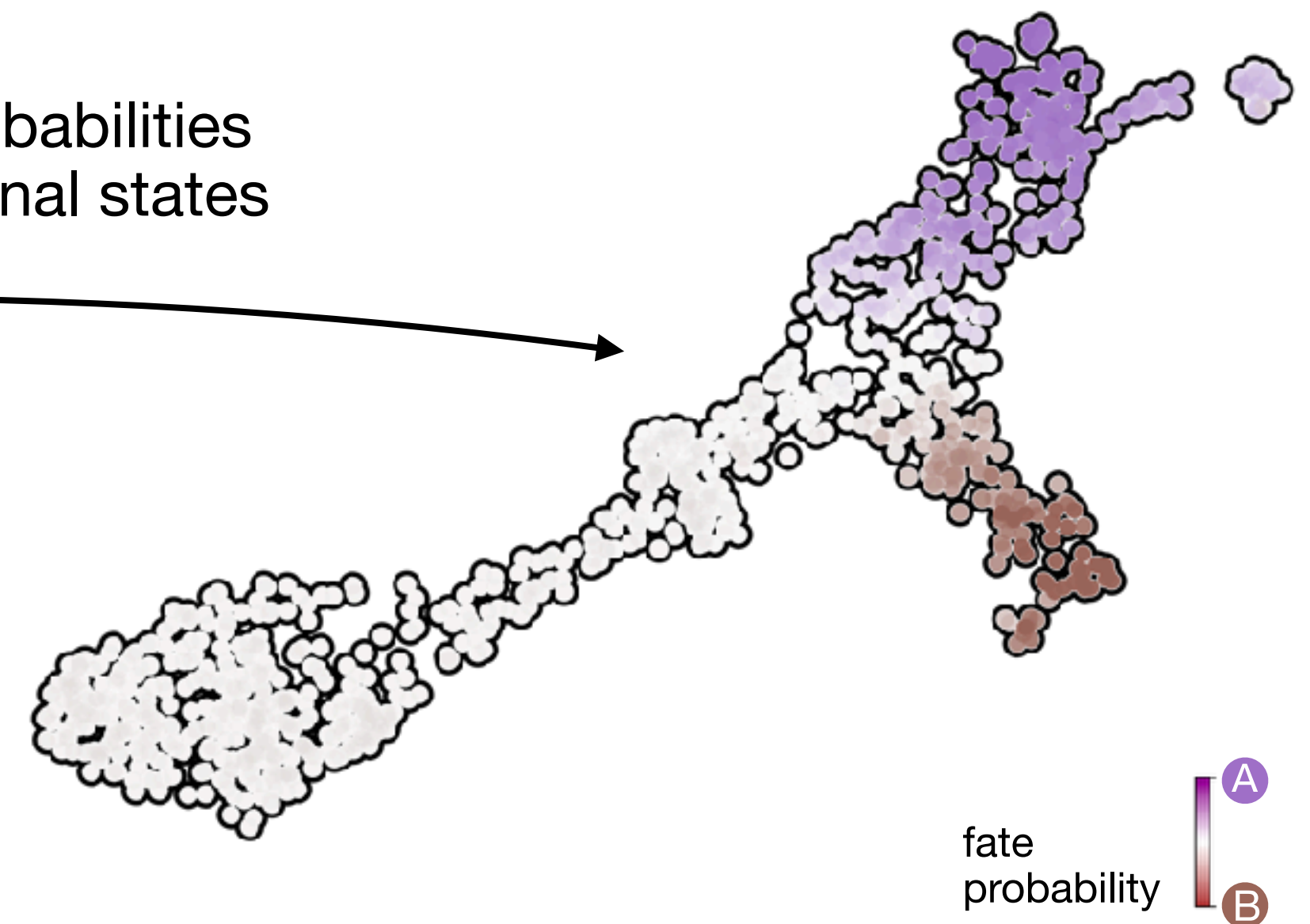# CellRank combines RNA Velocity with transcriptomic similarity to robustly model cellular fate establishment

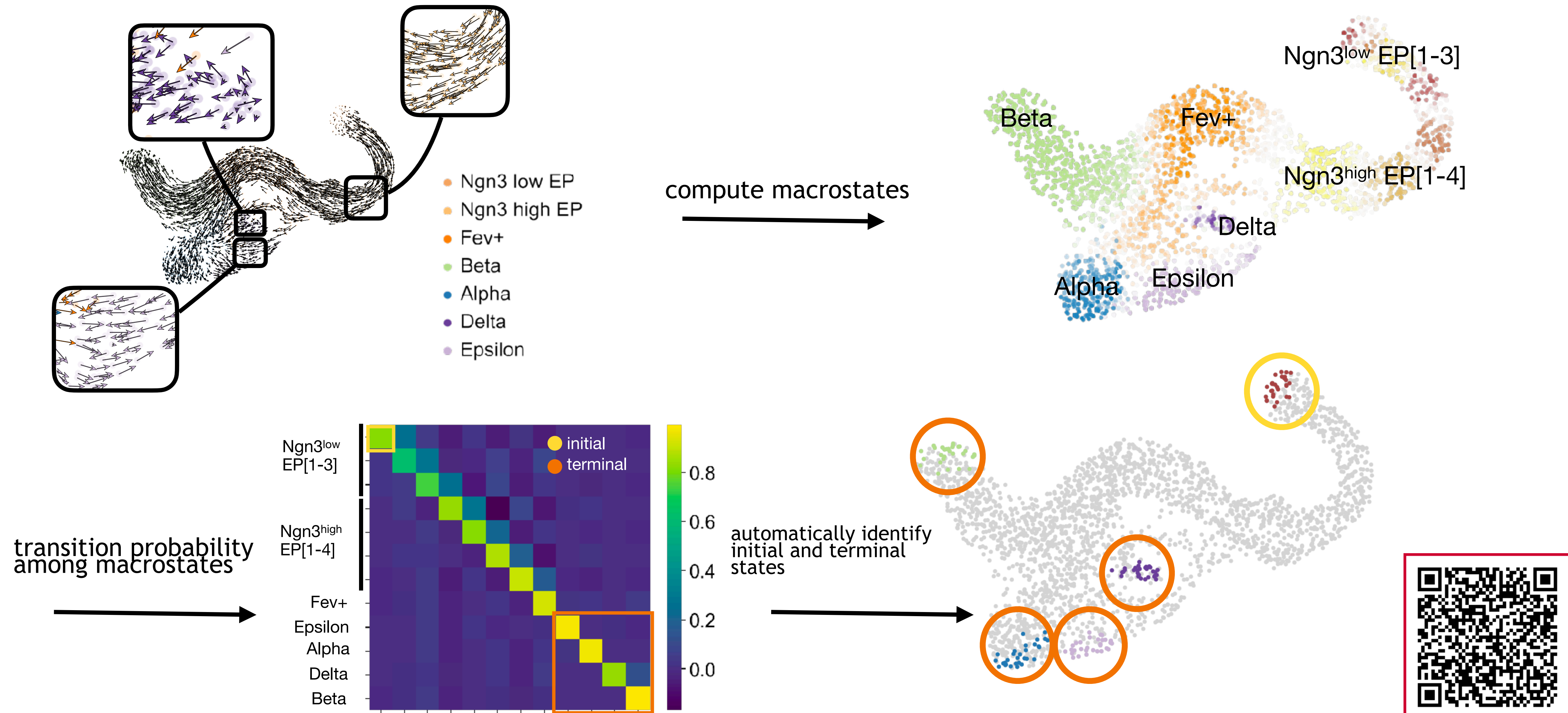for each cell i, combine velocity with similarity to define transition probabilities

velocity vector

--- KNN graph

v_i

j

α

$\delta_{i,j}$

i

0.3   0.5

i

0.1   0.1

$$p_{i,j} = \frac{\exp(\mathbf{corr}(v_i, \delta_{i,j}))}{\sum_{k \in \mathcal{N}_i} \exp(\mathbf{corr}(v_i, \delta_{i,k}))}$$

20k dimensions

Coarse-grain the large transition matrix to reduce the system to it's essence

coarse-grain

Compute fate probabilities towards the terminal states

transition probability among cells

0.04

0

transition probability among macrostates

1

0

terminal A

initial

intermediate

terminal B

A

B

fate probability

CellRank delineates fate choice in pancreatic development

Please see our manuscript for the full story!