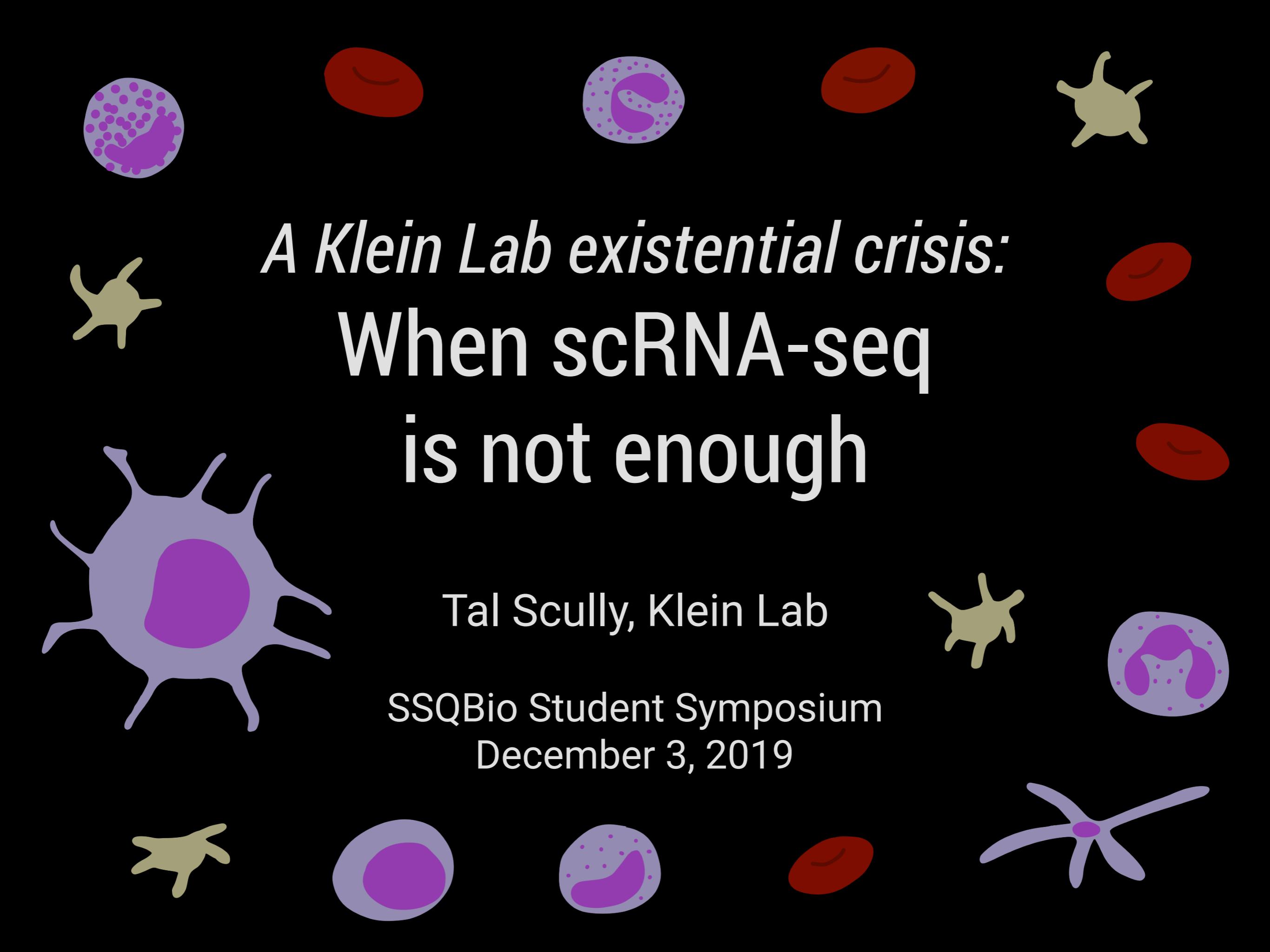


EPIGENETICS AND FATE CHOICE IN HEMATOPOIESIS

Tal Scully, Klein Lab

SSQBio Student Symposium
December 3, 2019

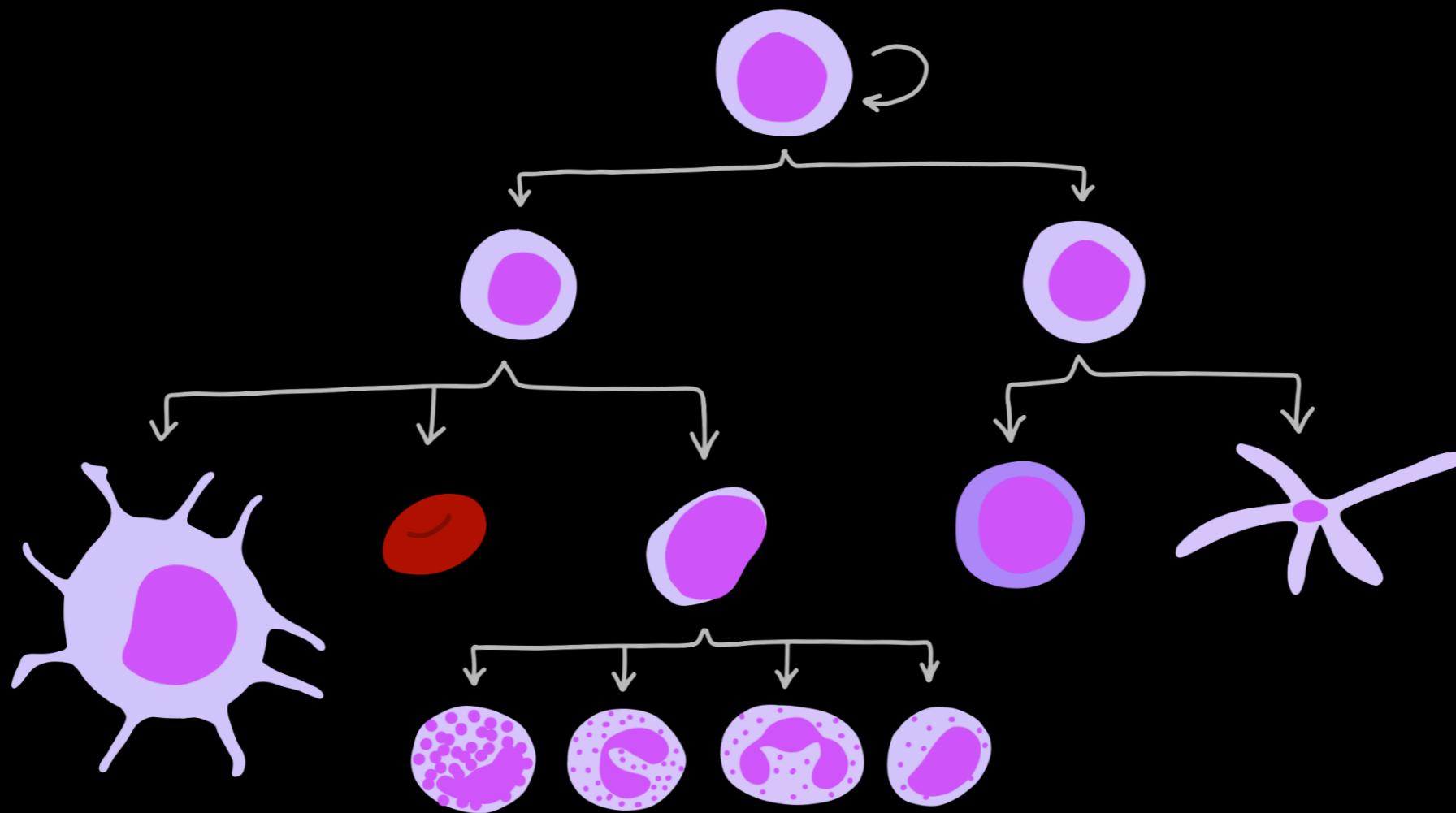


A Klein Lab existential crisis: When scRNA-seq is not enough

Tal Scully, Klein Lab

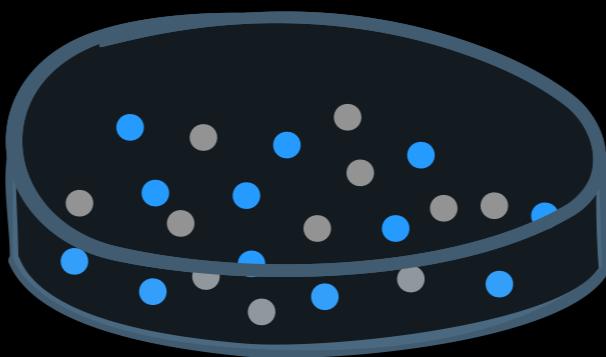
SSQBio Student Symposium
December 3, 2019

Hematopoiesis can reveal the fundamental principles of fate choice

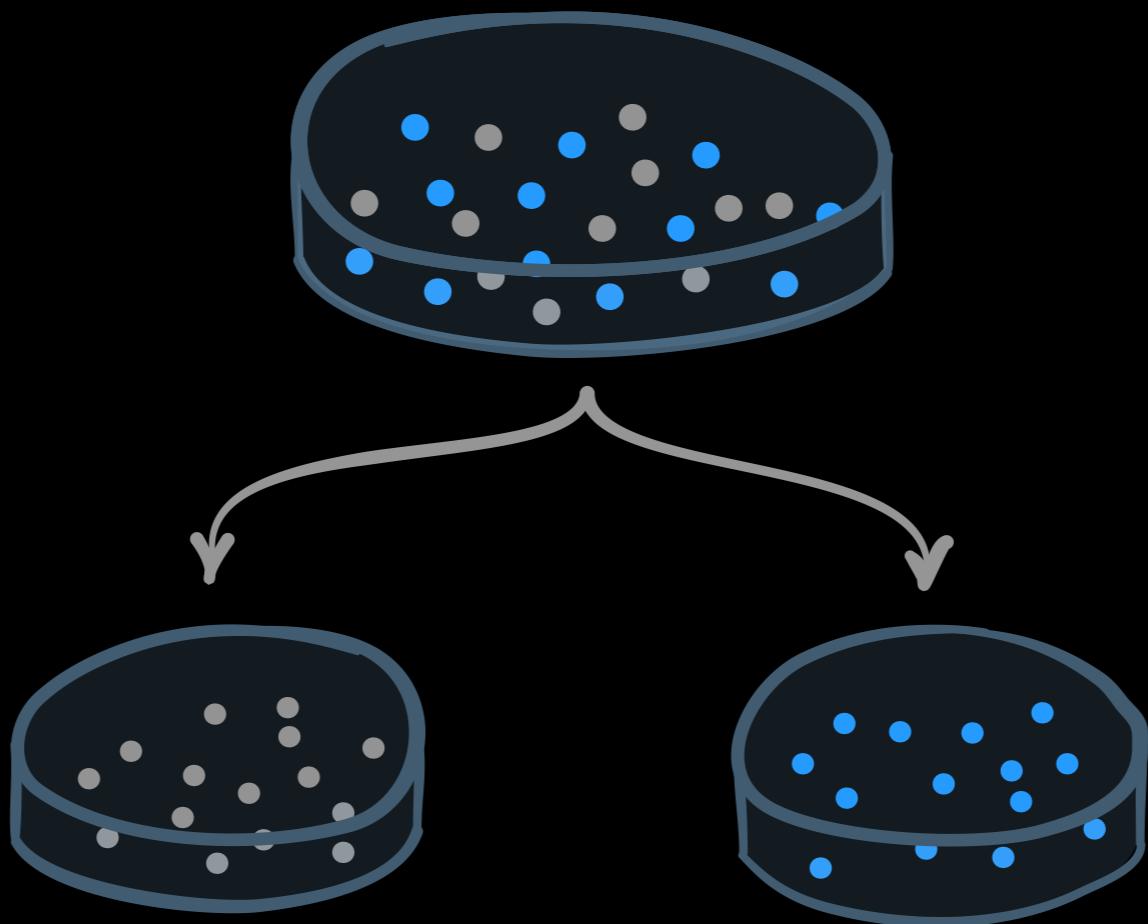


1. What is the order of fate decisions?
2. How are fate decisions molecularly implemented?

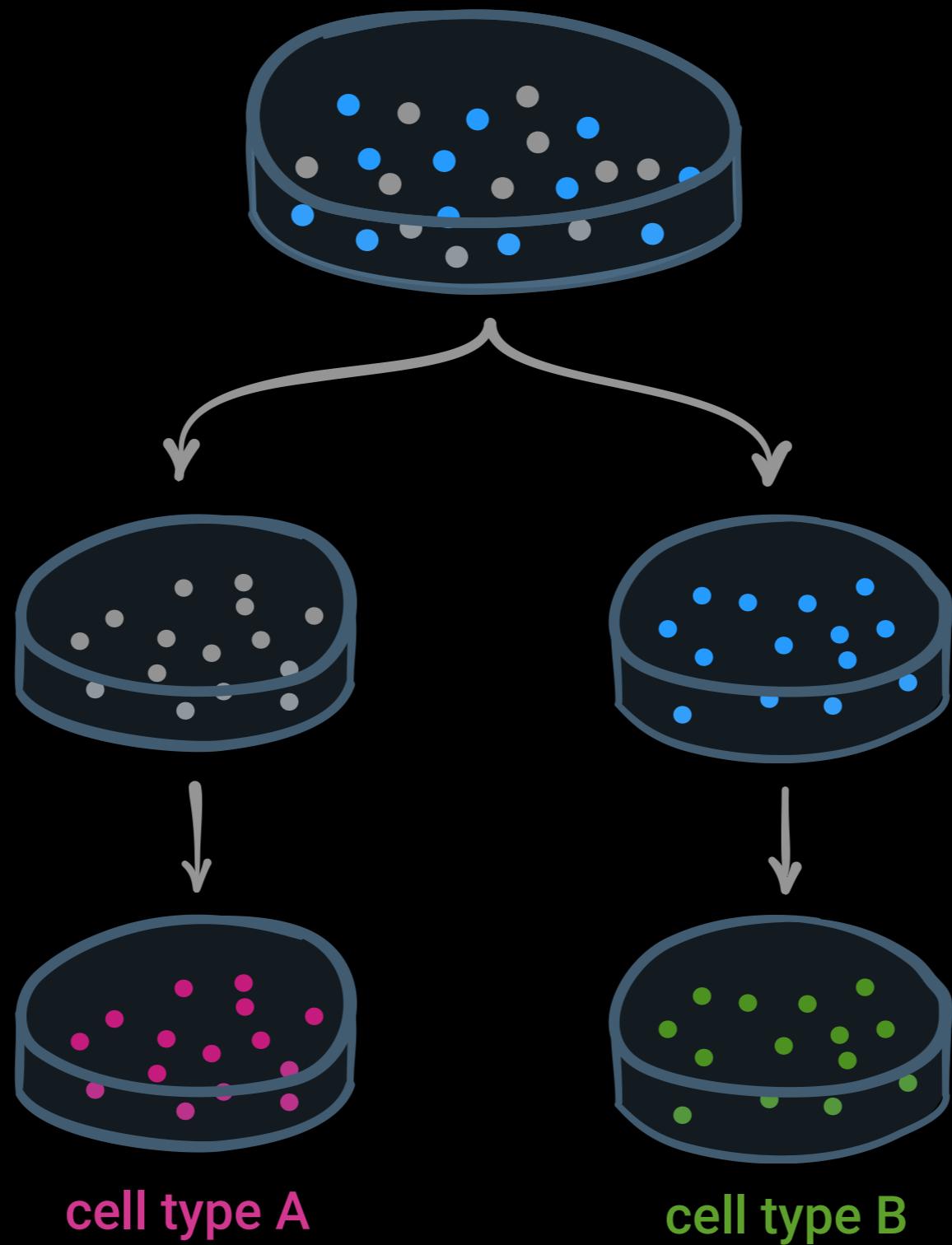
If we identify a biasing factor, we can predict fate choice



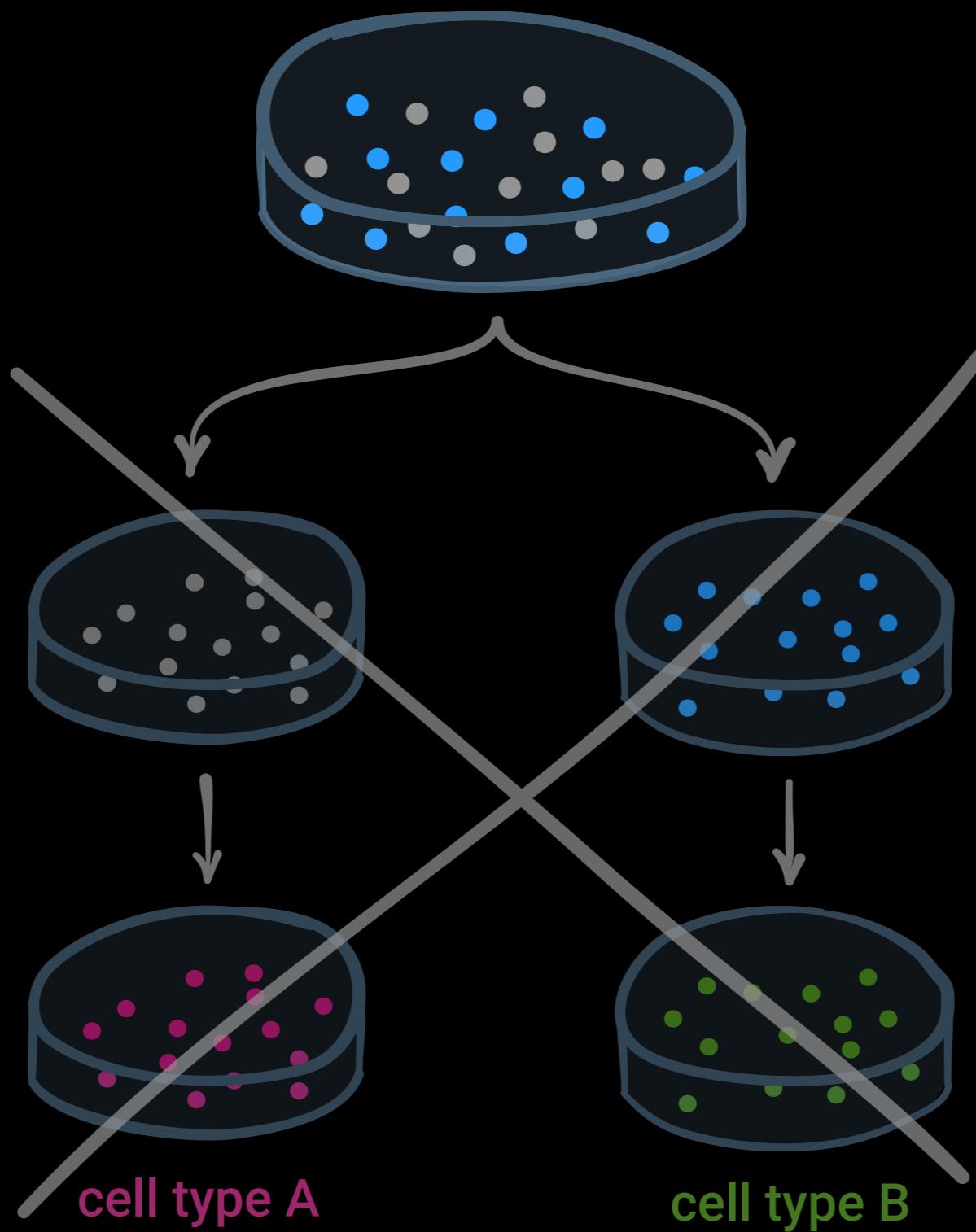
If we identify a biasing factor, we can predict fate choice



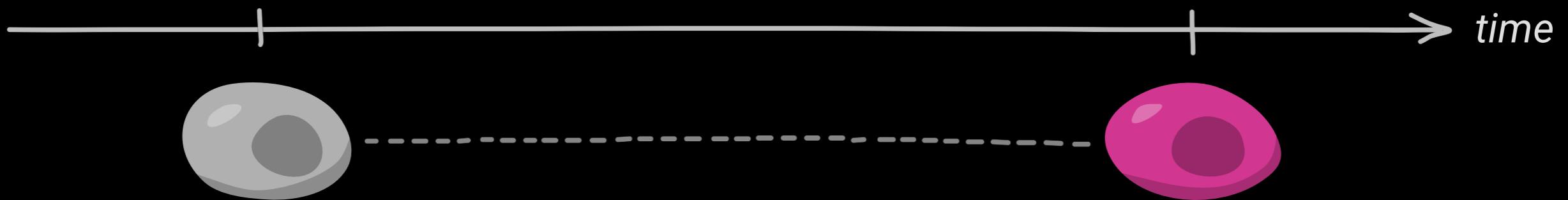
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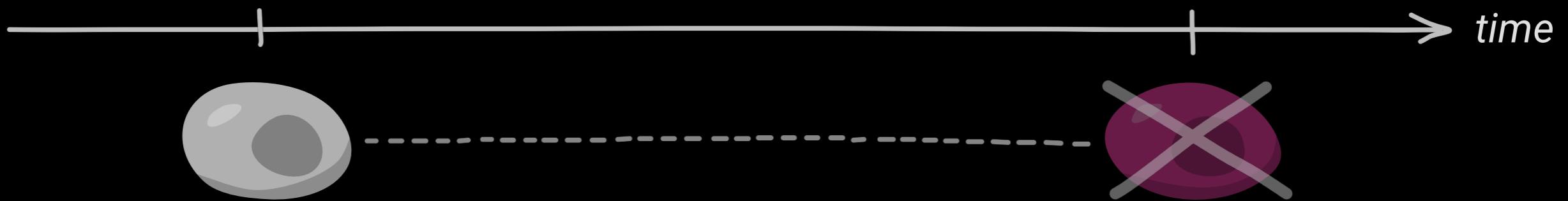
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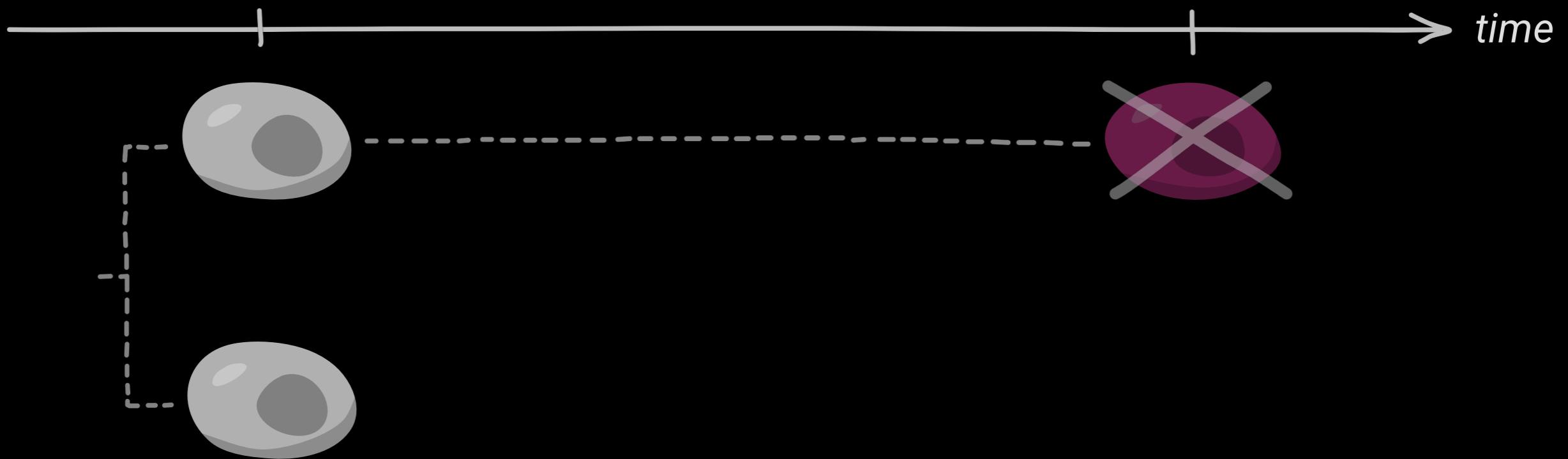
Sister cell tracking connects early cell states to mature fates



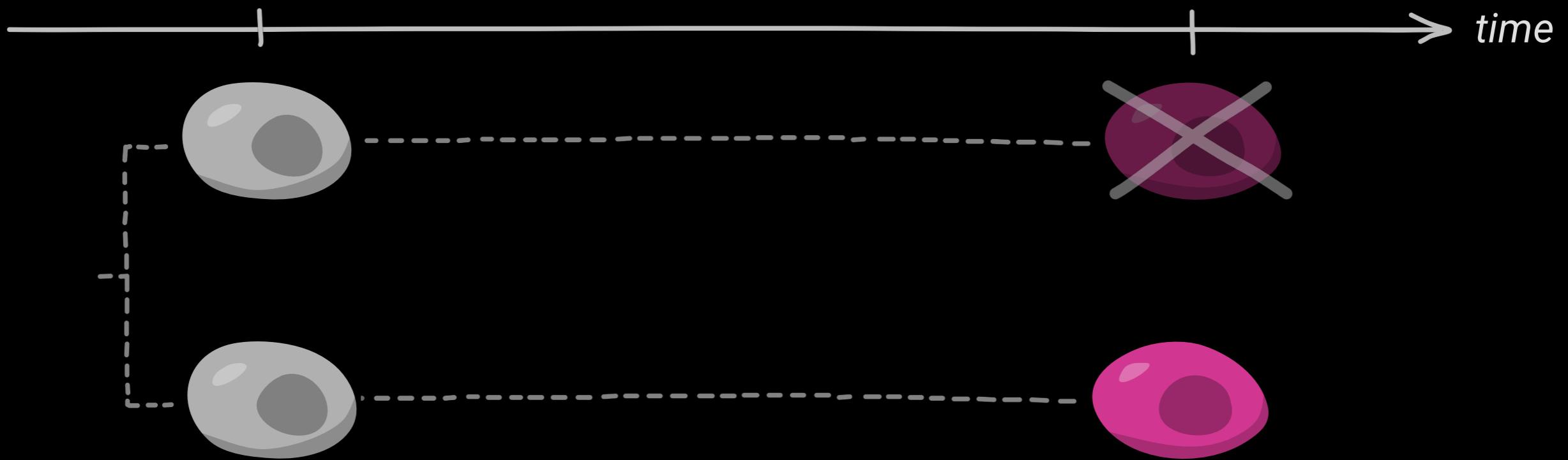
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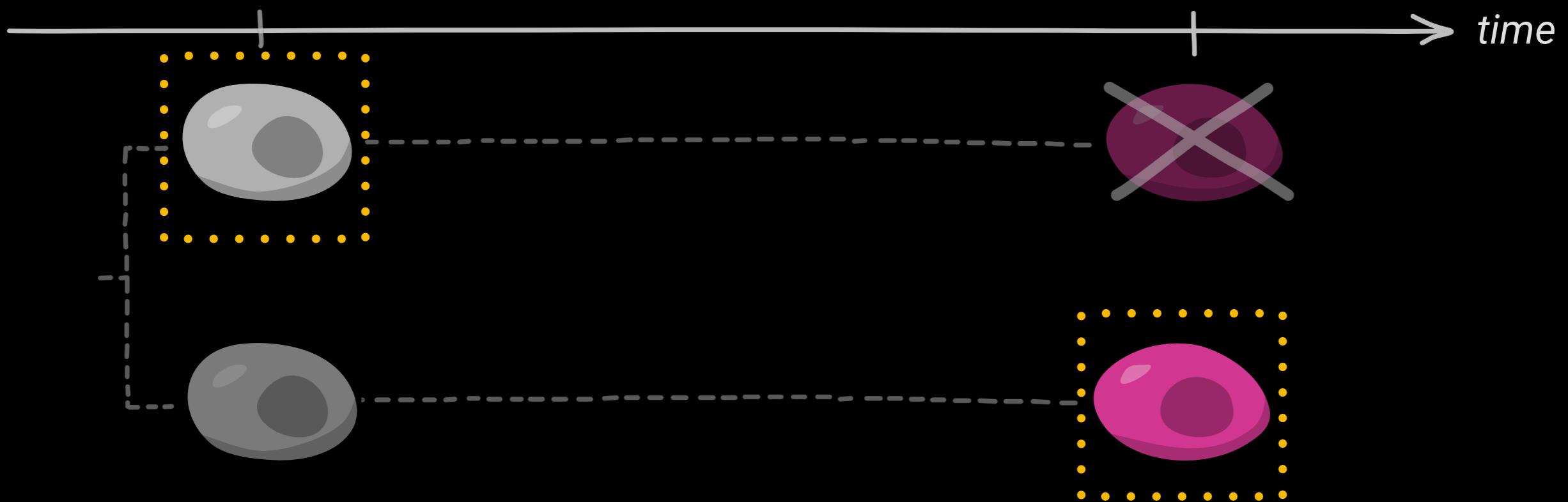
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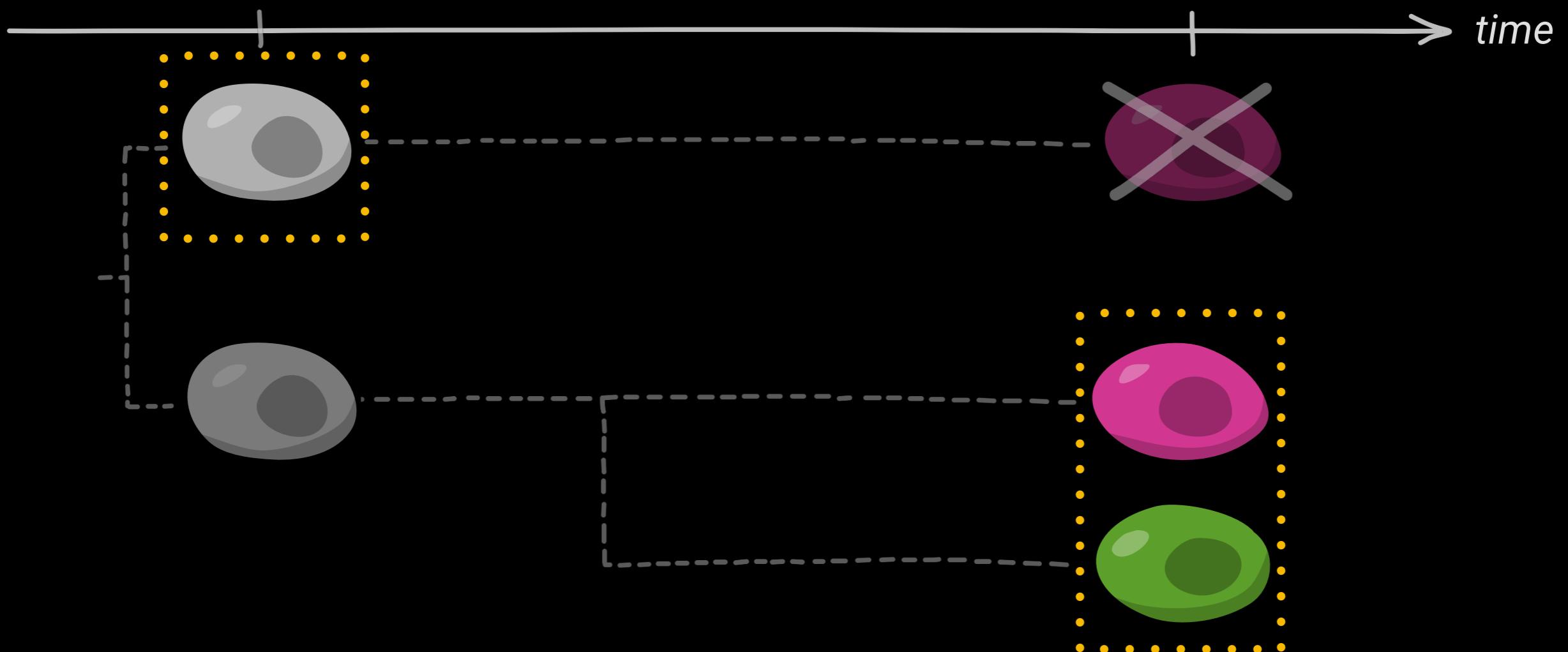
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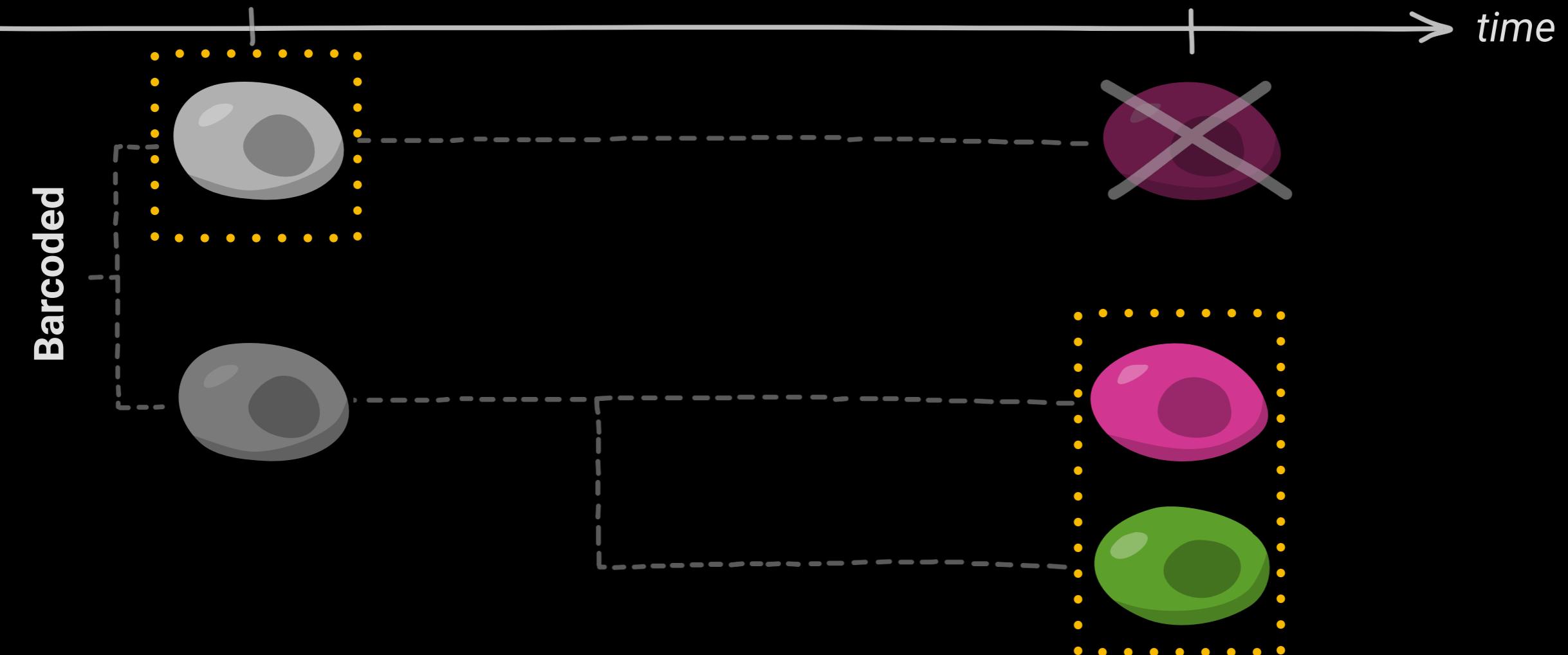
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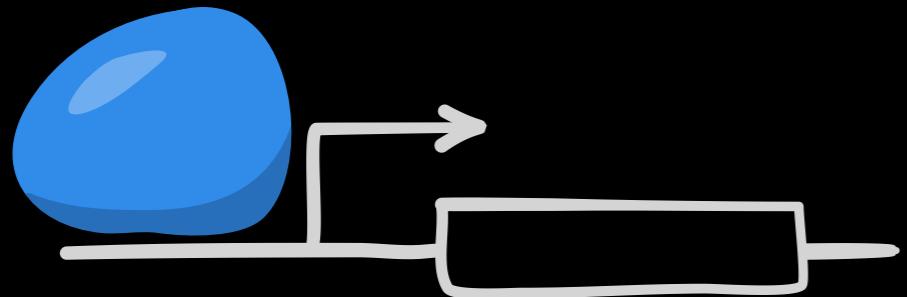
Sister cell tracking connects early cell states to mature fates



What molecular components bias fate?

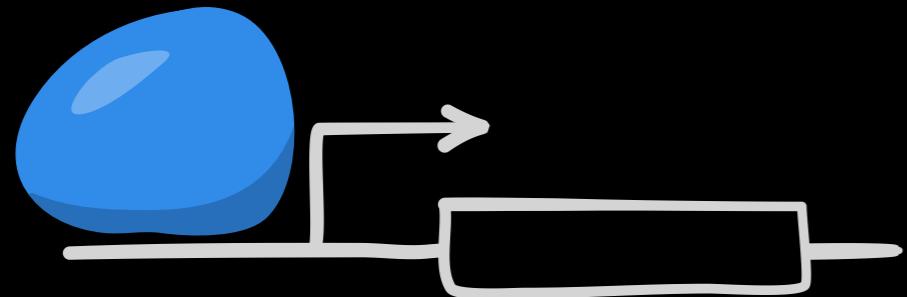
What molecular components bias fate?

Transcription

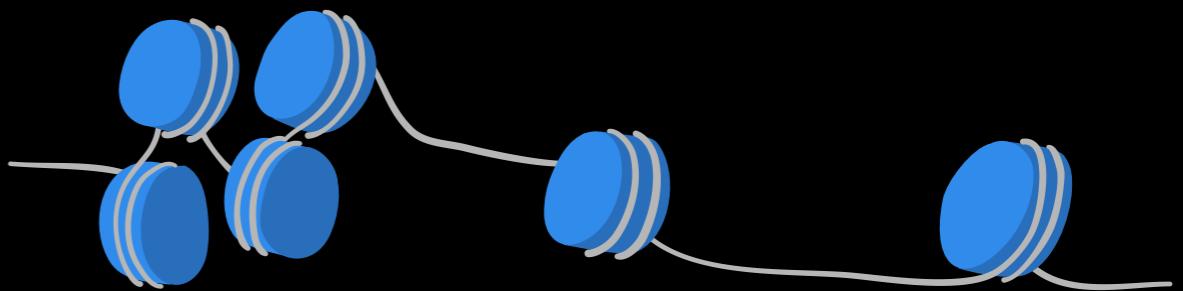


What molecular components bias fate?

Transcription

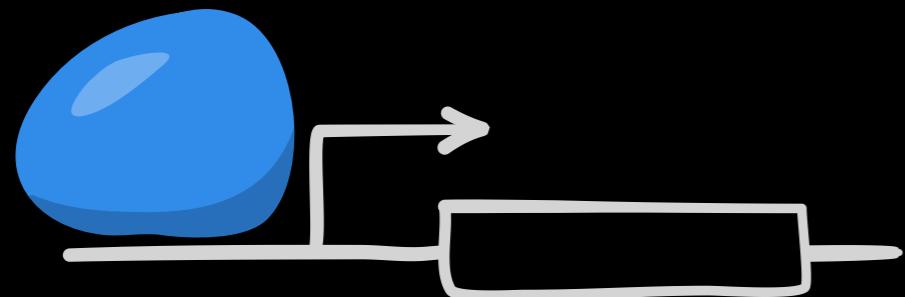


Chromatin

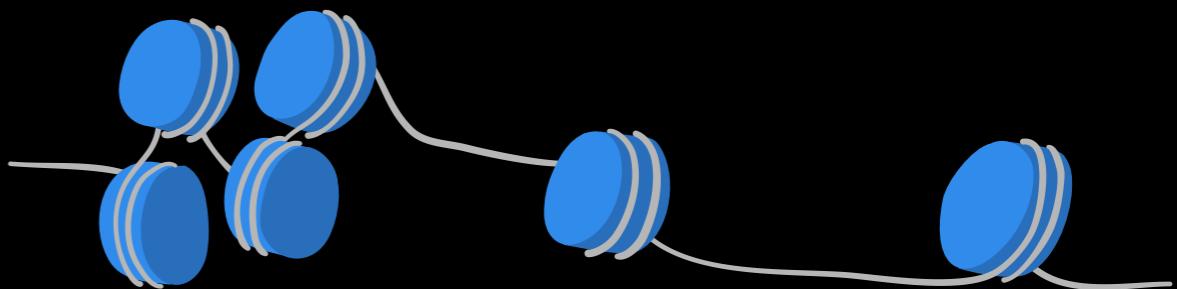


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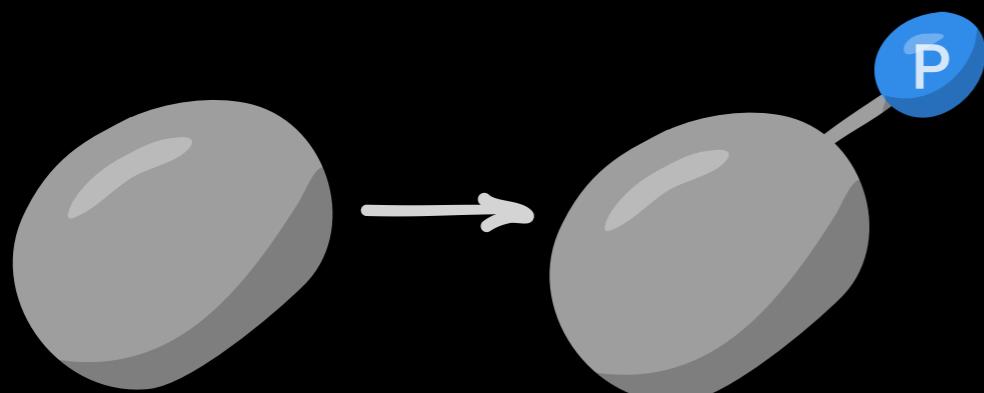
Transcription



Chromatin

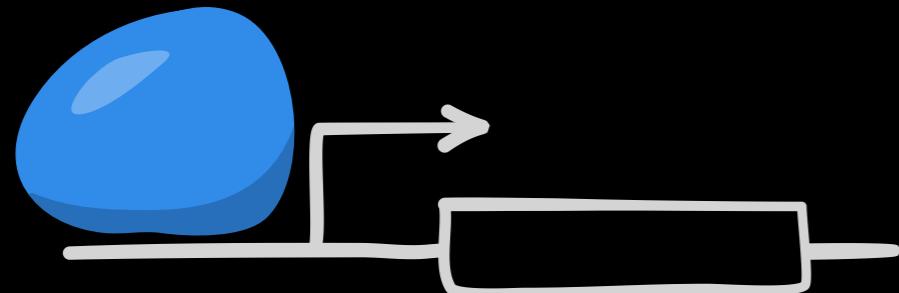


Post-translation

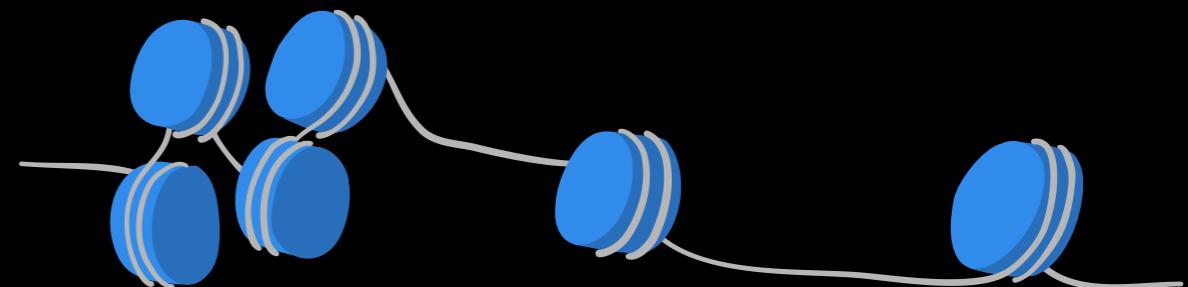


What molecular components bias fate?

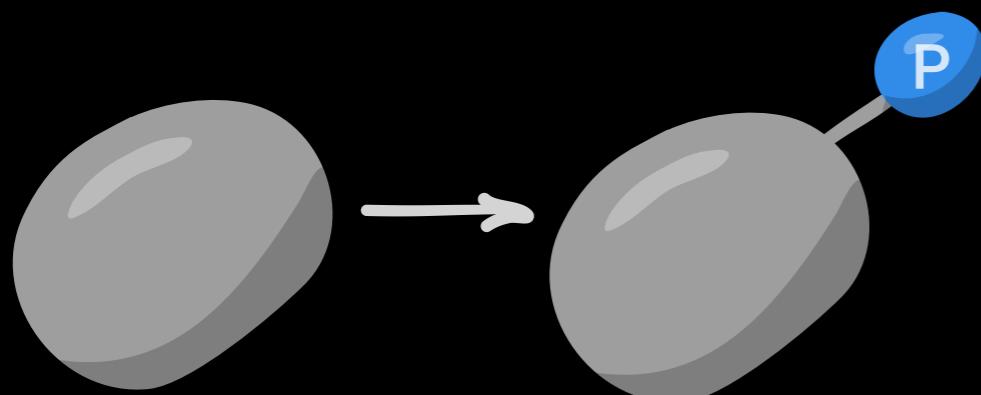
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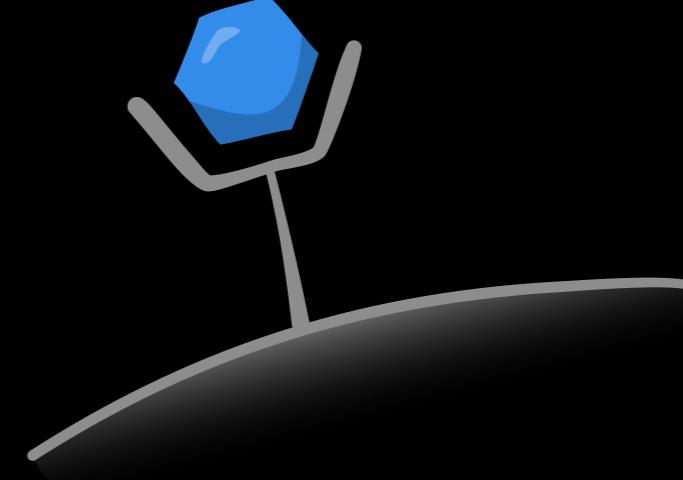
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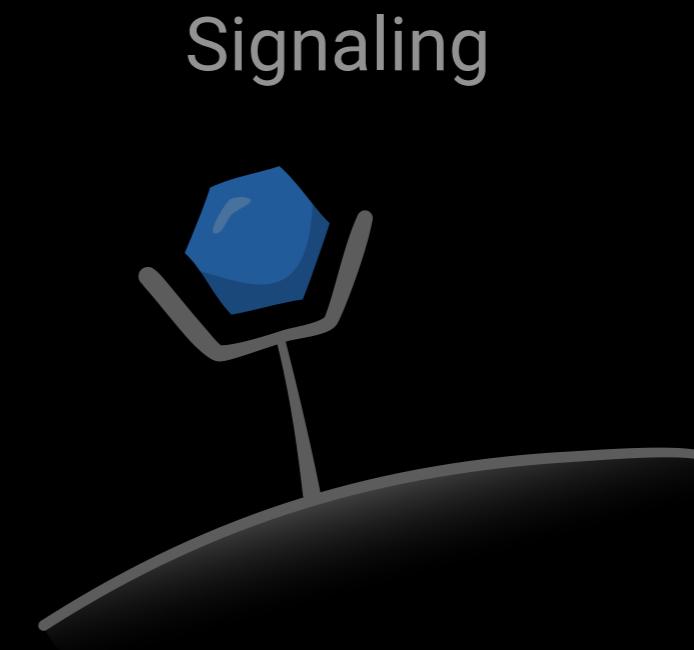
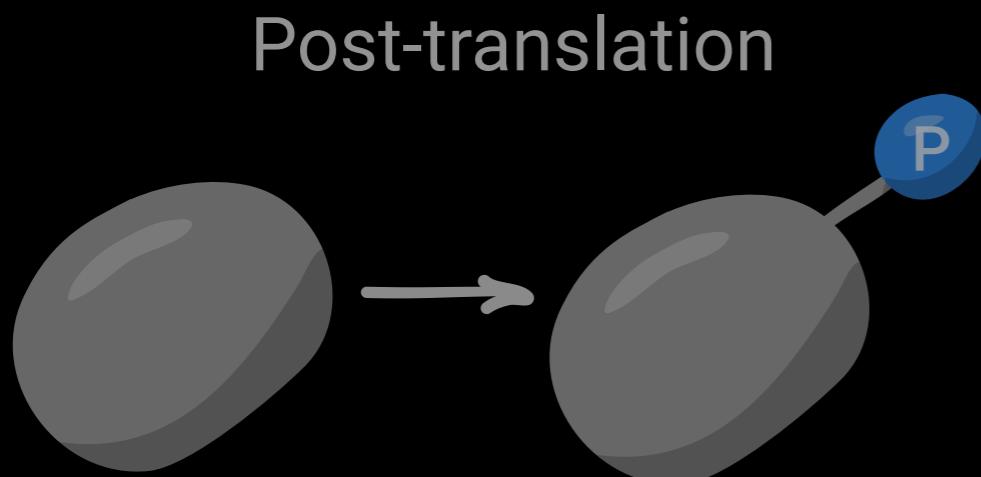
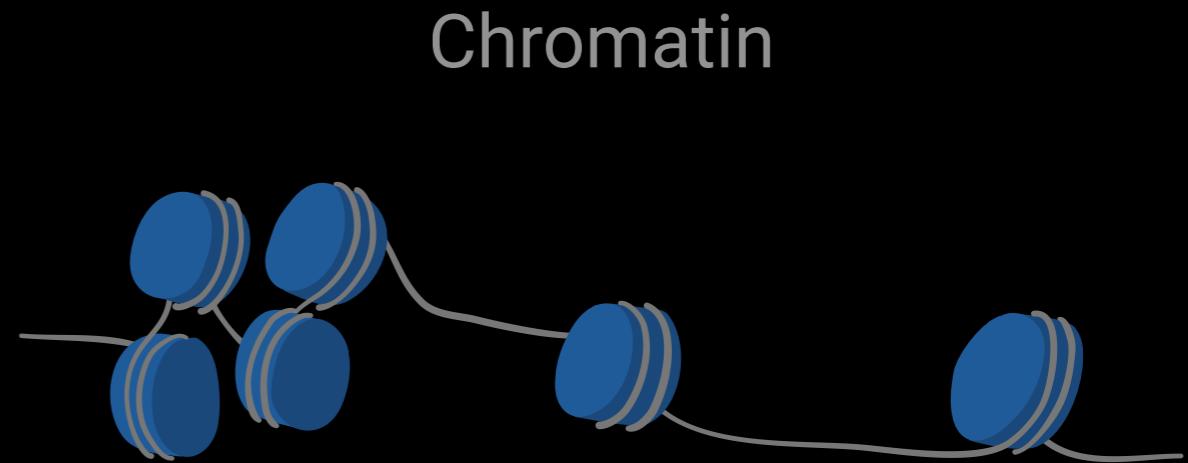
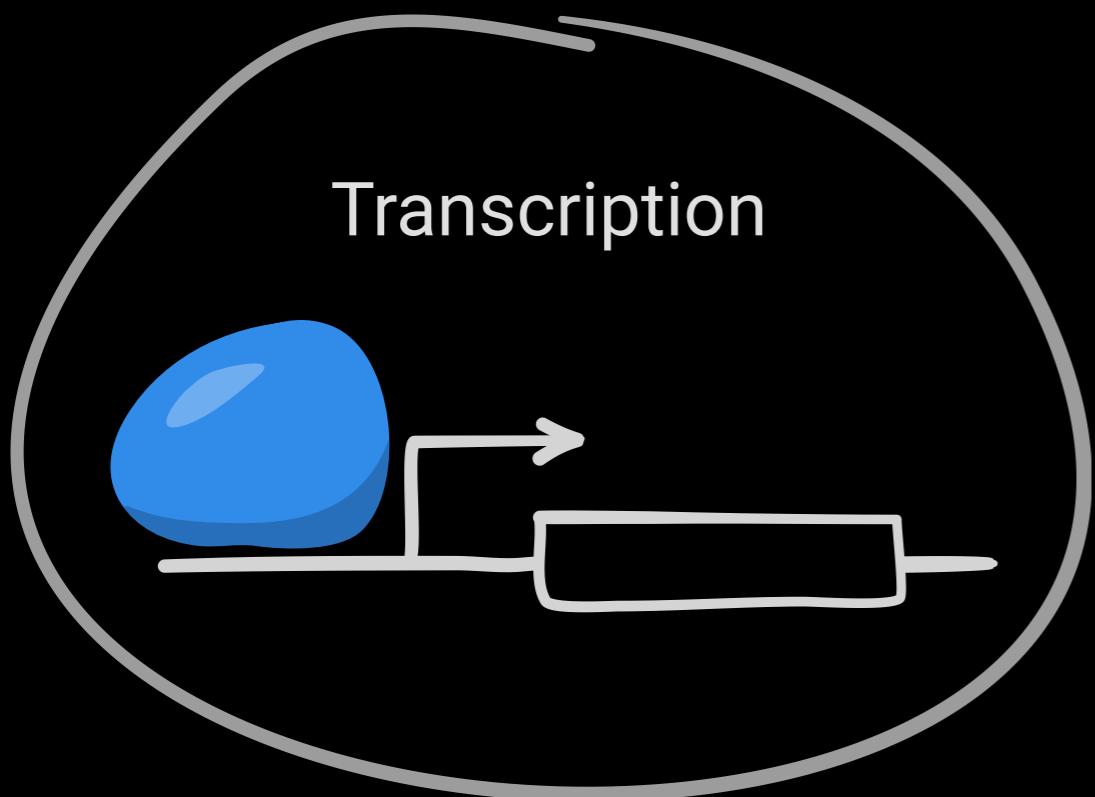
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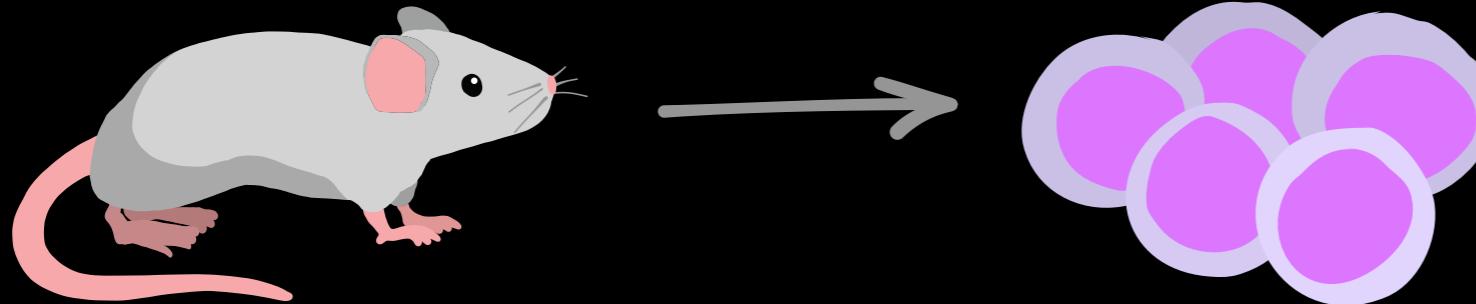
Signaling



What molecular components bias fate?

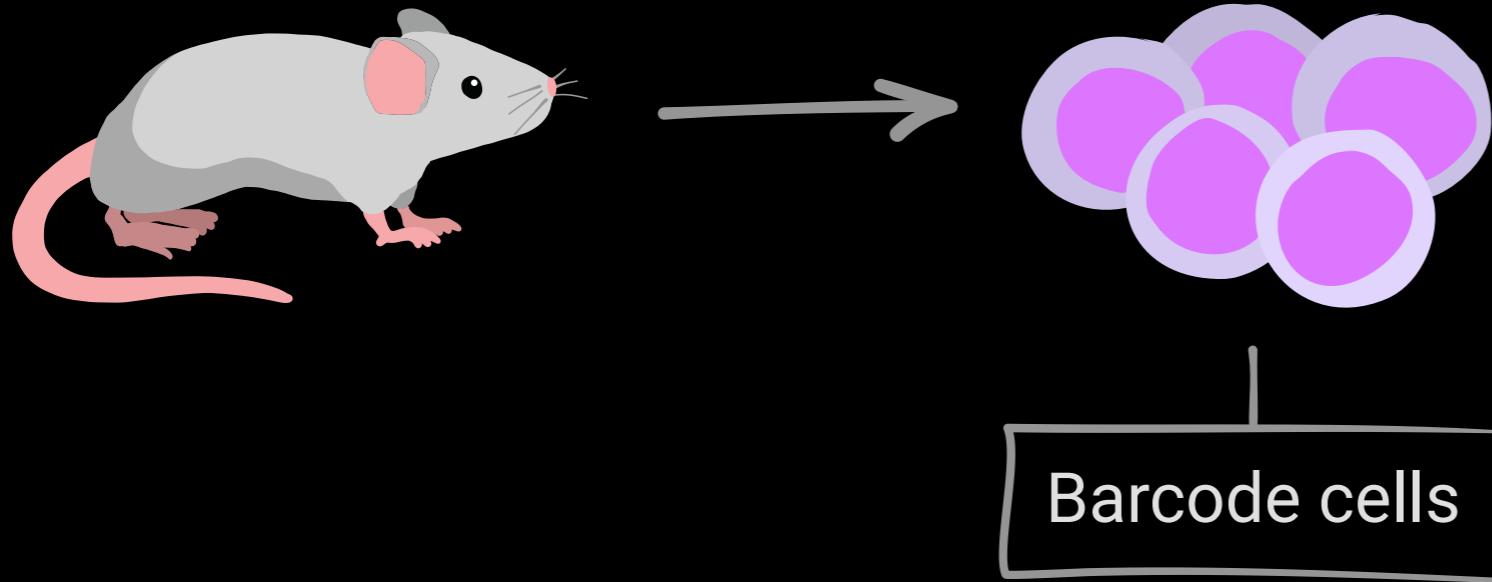


scRNA-seq was combined with sister cell tracking



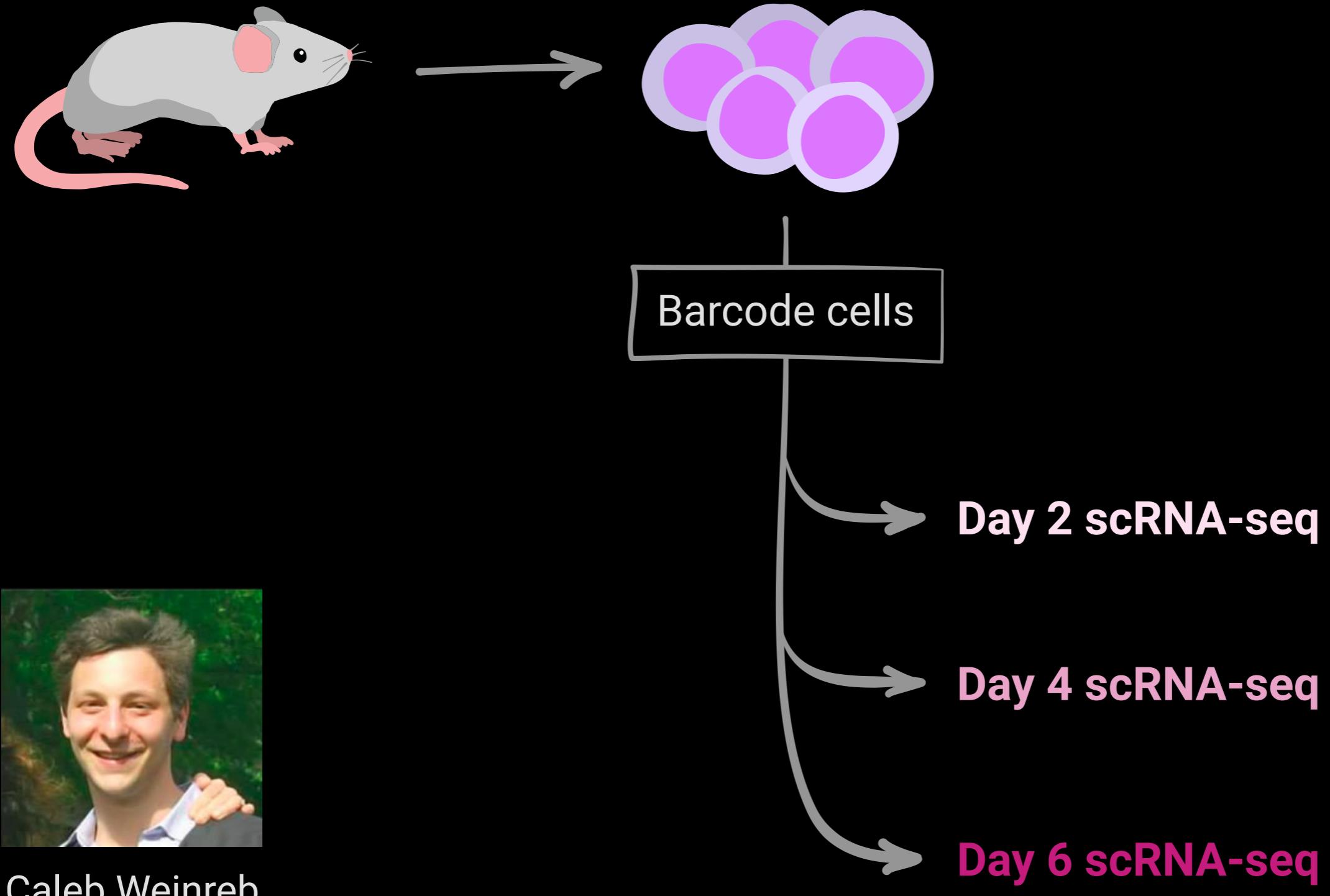
Caleb Weinreb

scRNA-seq was combined with sister cell tracking

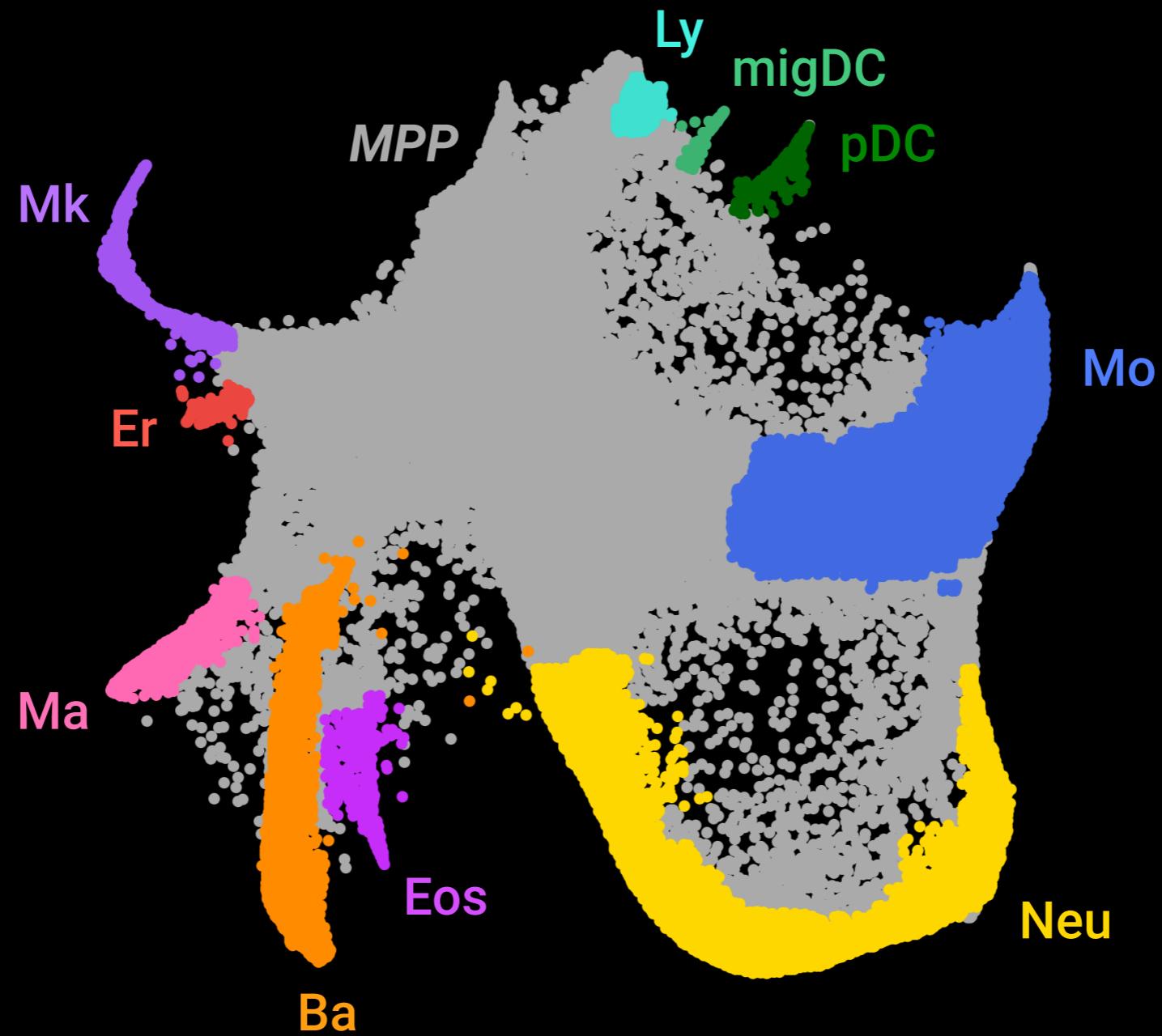


Caleb Weinreb

scRNA-seq was combined with sister cell tracking



scRNA-seq reveals progenitor and mature cell states



SPRING plot of hematopoiesis

Similar cells often appear committed to different fates

clone 1

Day 2

Day 4

Day 6



Similar cells often appear committed to different fates

<i>clone 1</i>	<i>clone 2</i>
Day 2	Day 2
Day 4	Day 4
Day 6	Day 6



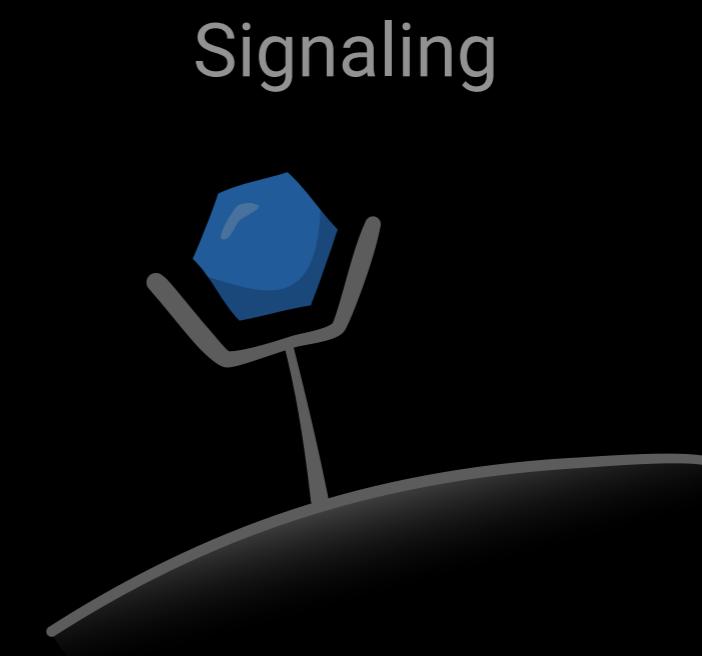
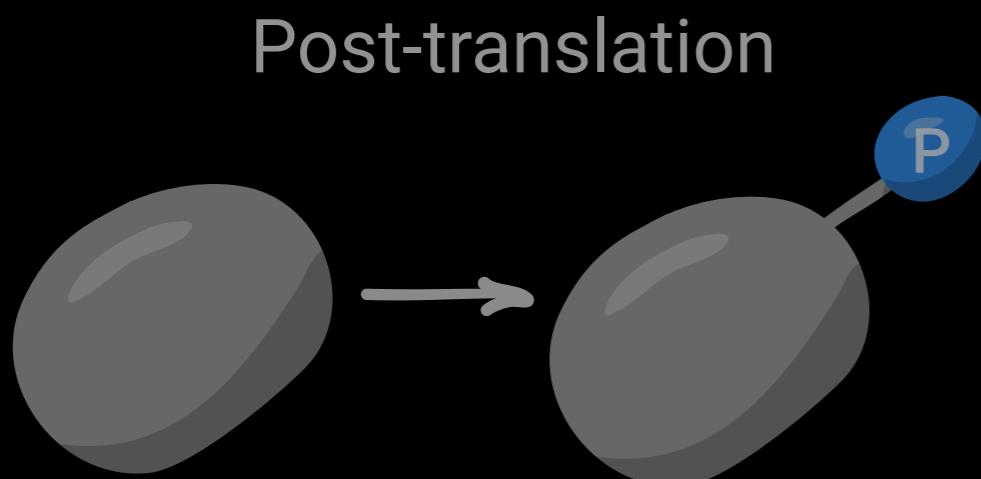
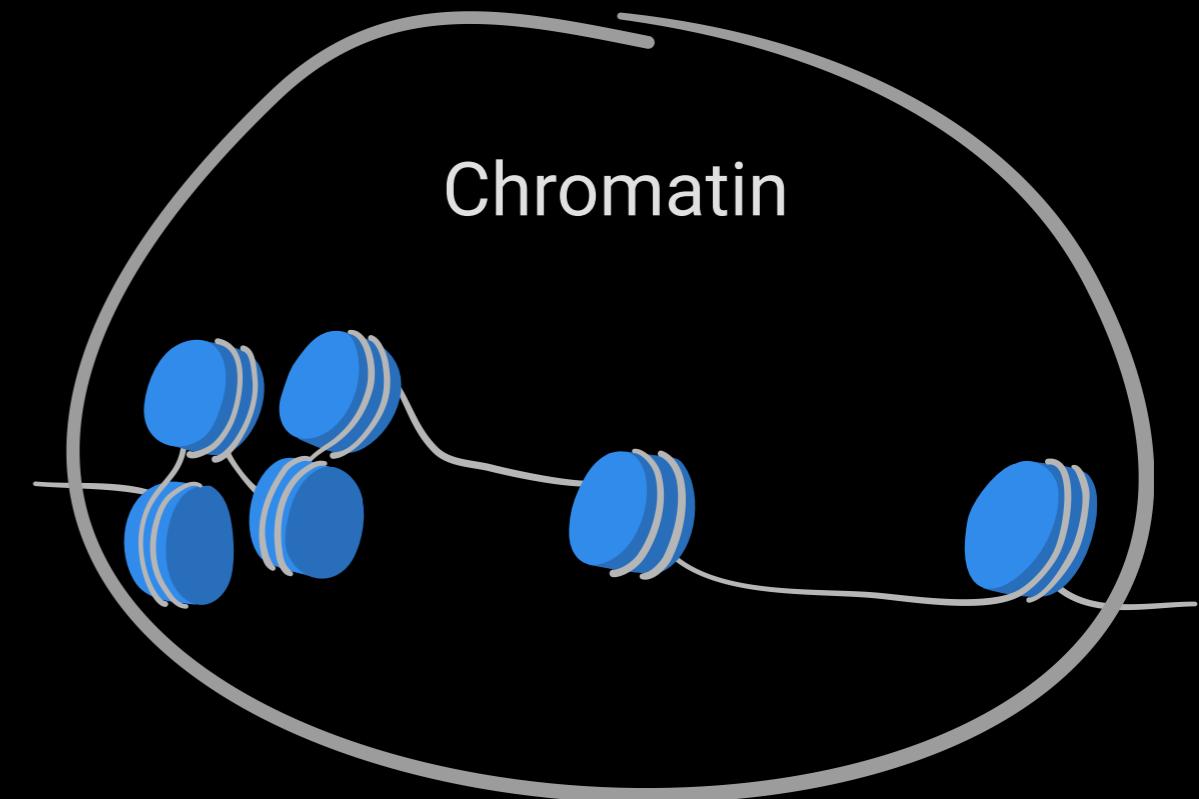
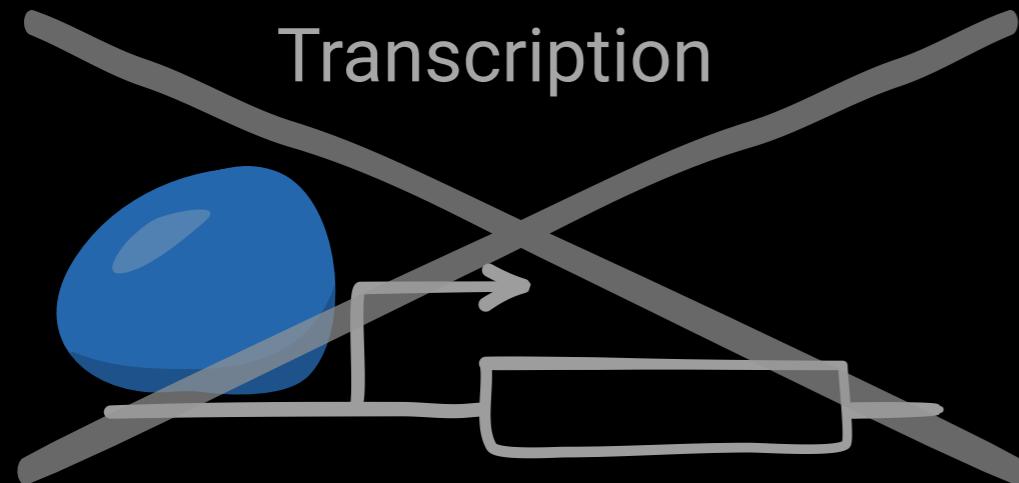
Similar cells often appear committed to different fates

<i>clone 1</i>	<i>clone 2</i>
Day 2	Day 2
Day 4	Day 4
Day 6	Day 6



What is controlling fate commitment?

What molecular components bias fate?



Epigenetics may explain stem cells' fate bias "memory"

Yu et al. 2016: "Epigenetic Memory Underlies Cell-Autonomous Heterogeneous Behavior of Hematopoietic Stem Cells"



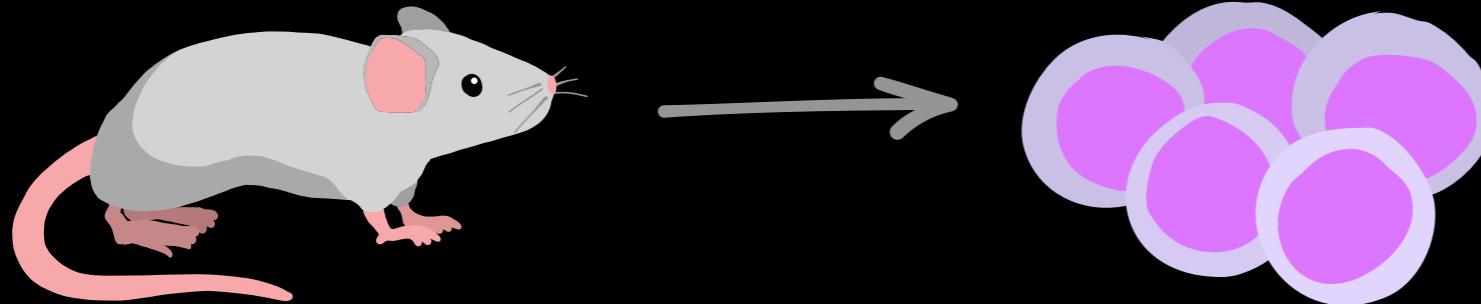
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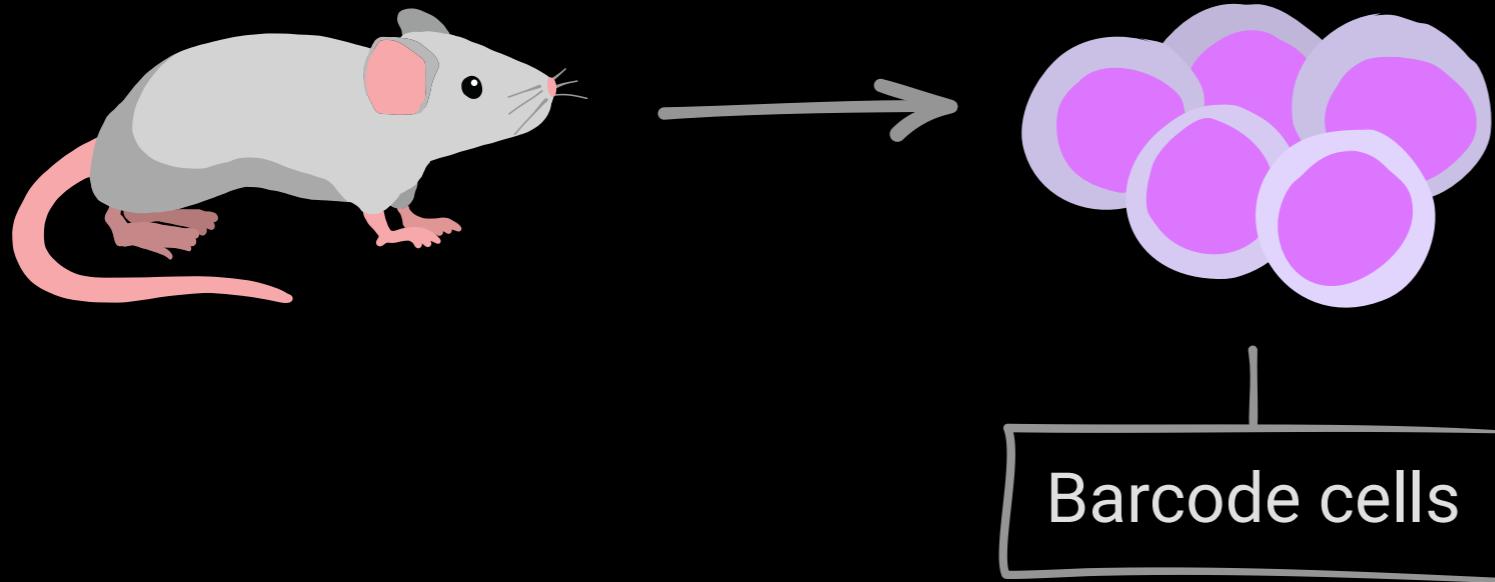


Stem cell bias correlated with epigenetic factors

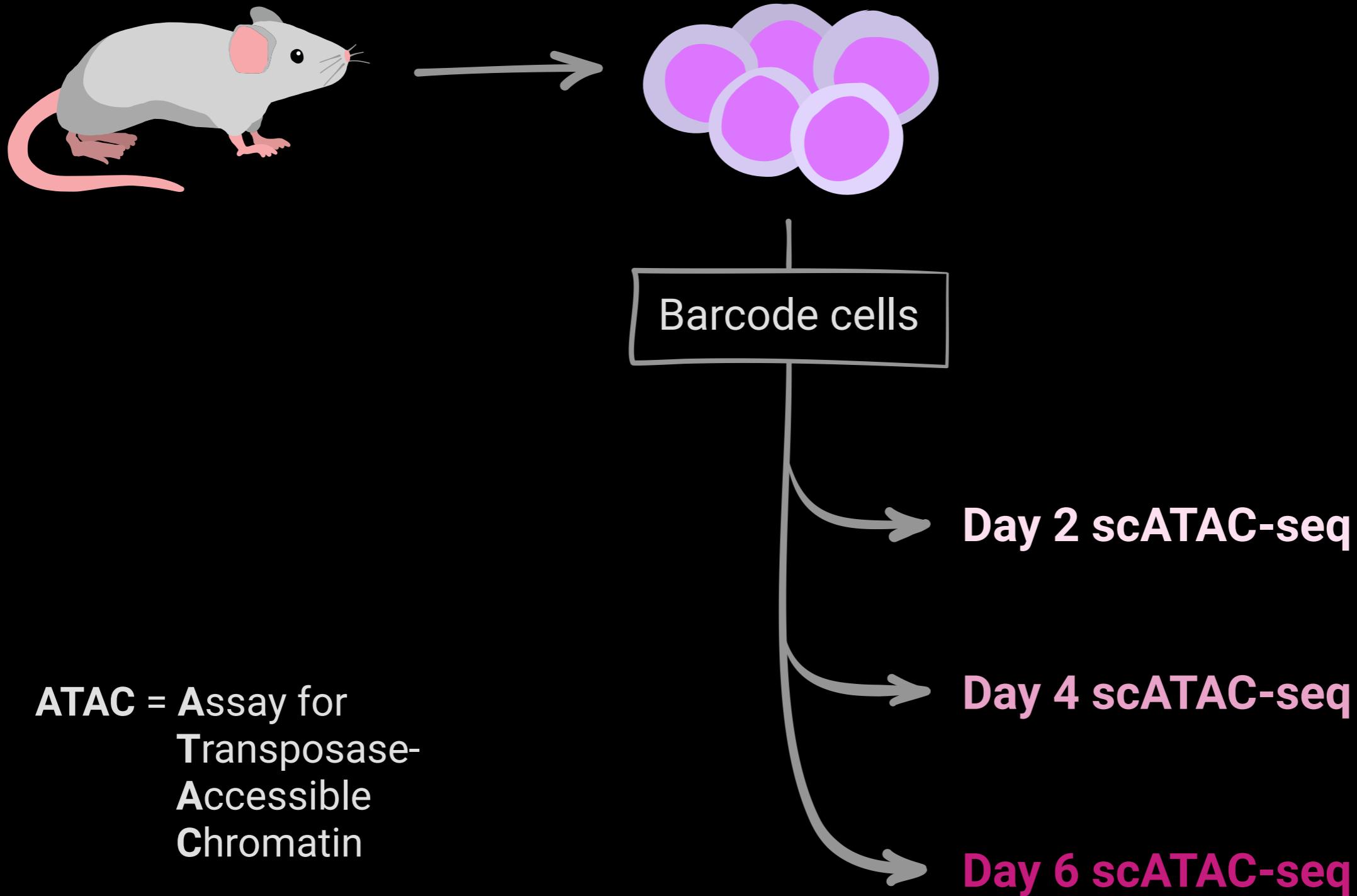
scATAC-seq with sister cell tracking will connect early chromatin states to cell fate



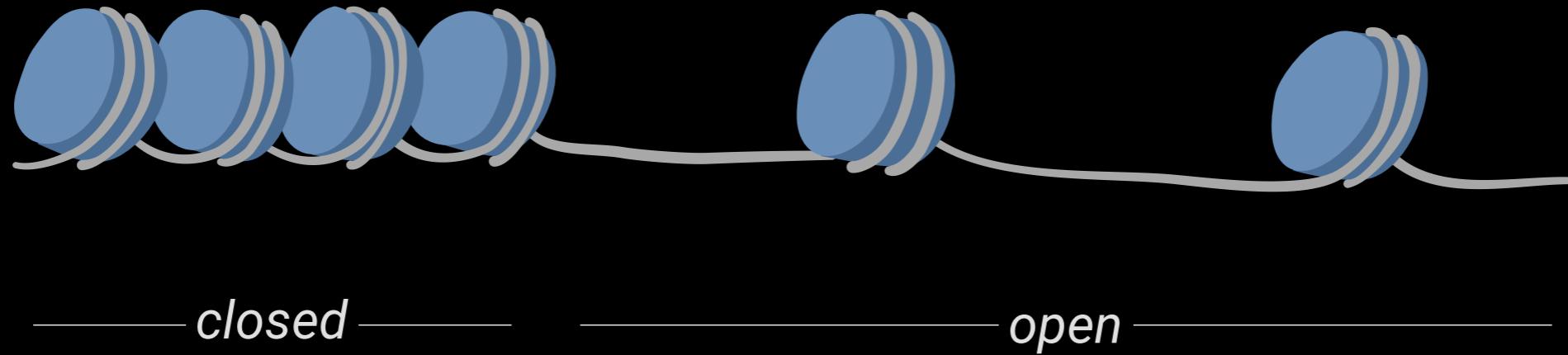
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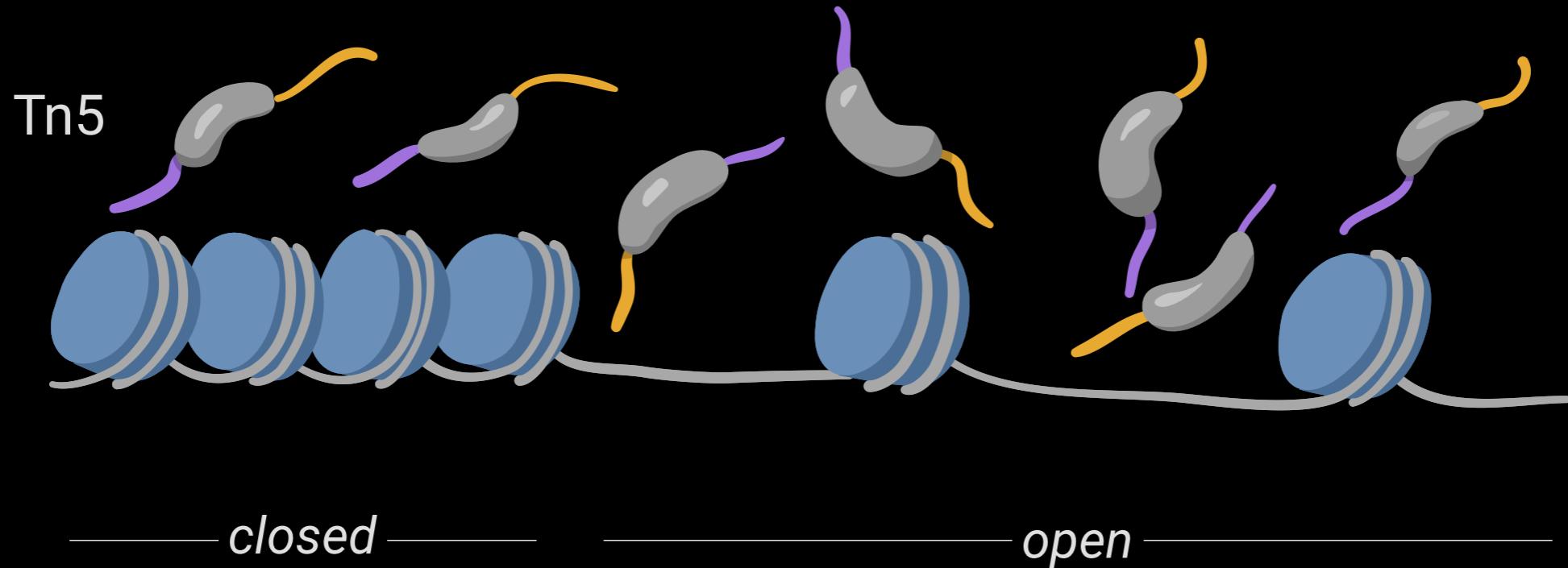
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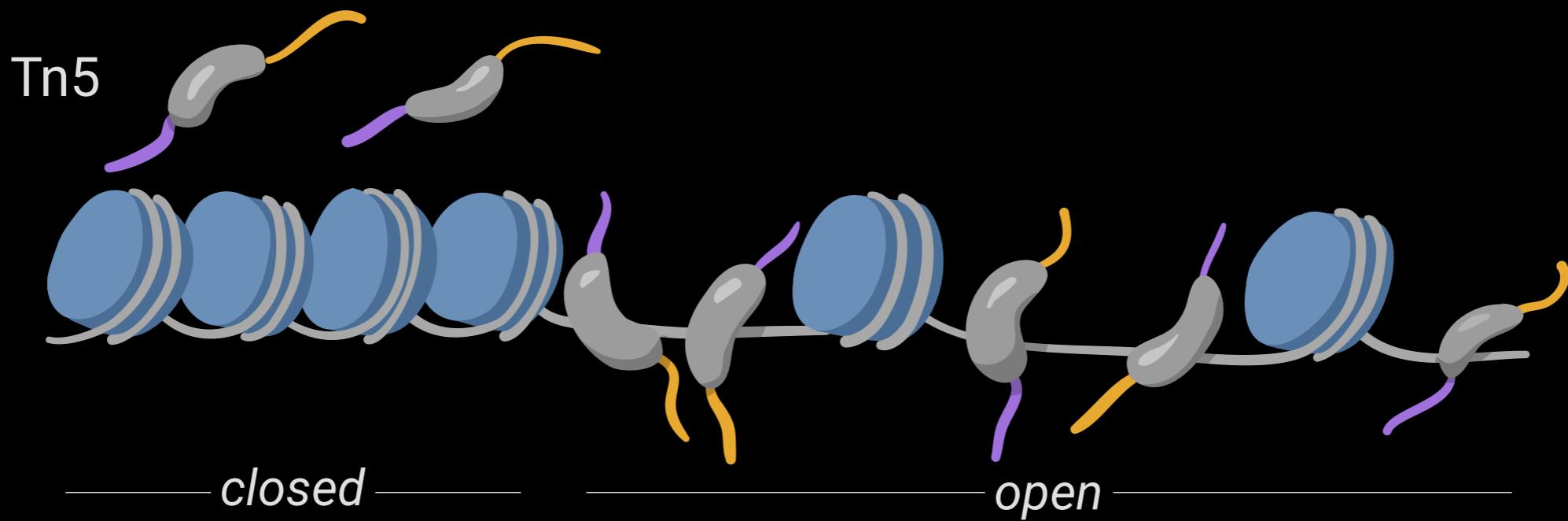
scATAC-seq reveals the chromatin accessibility of single cells



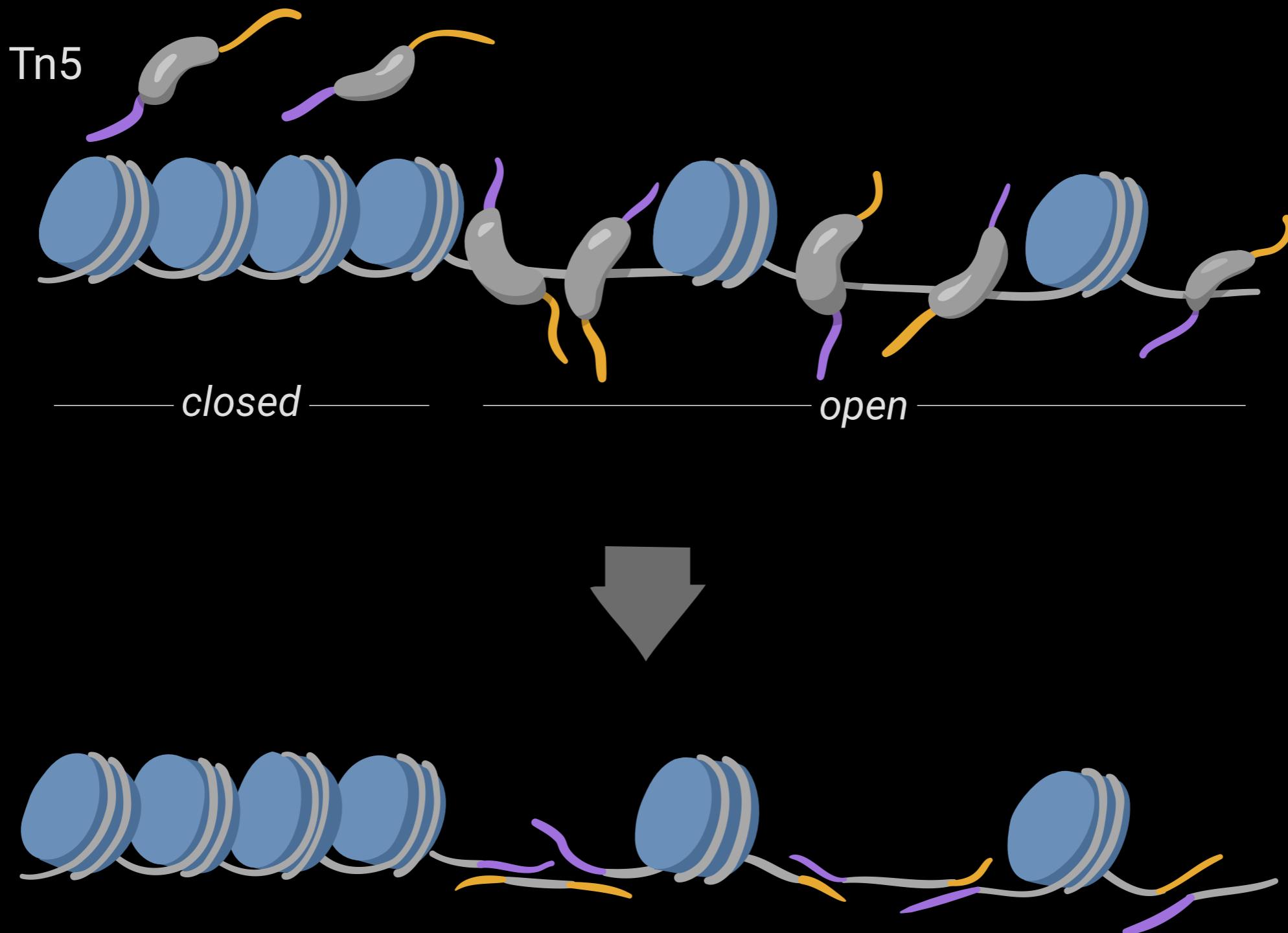
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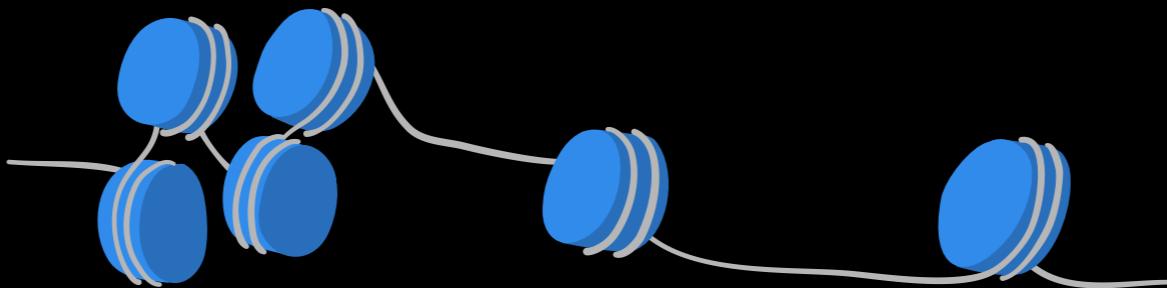


scATAC-seq reveals the chromatin accessibility of single cells



My aims are...

1. Combine lineage tracing with epigenetic assays.
2. Identify early epigenetic events that bias fate.
3. Establish how predictive epigenetic information is.



Acknowledgements

Klein Lab

Allon Klein
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Nikit Patel
Qiu Wu
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Sam Wolock
Yuheng Lu

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G2 cohort

