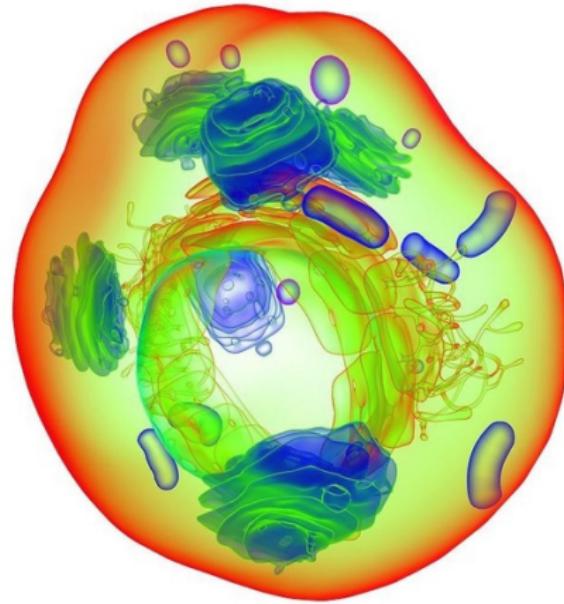


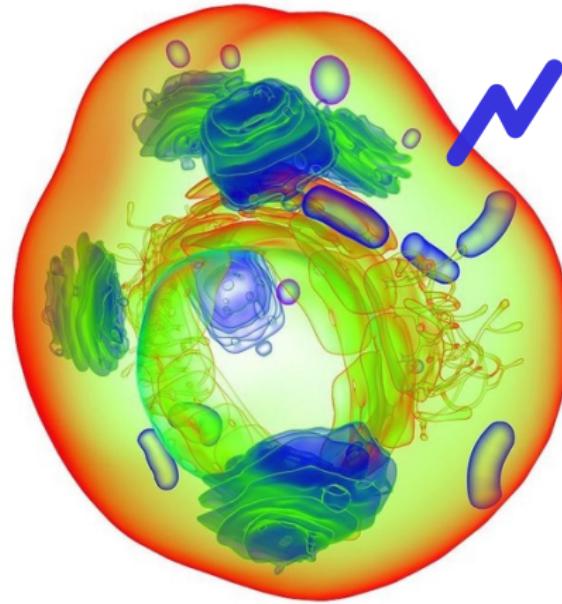
# Modelling single-cell dynamics with trajectories and gene regulatory networks

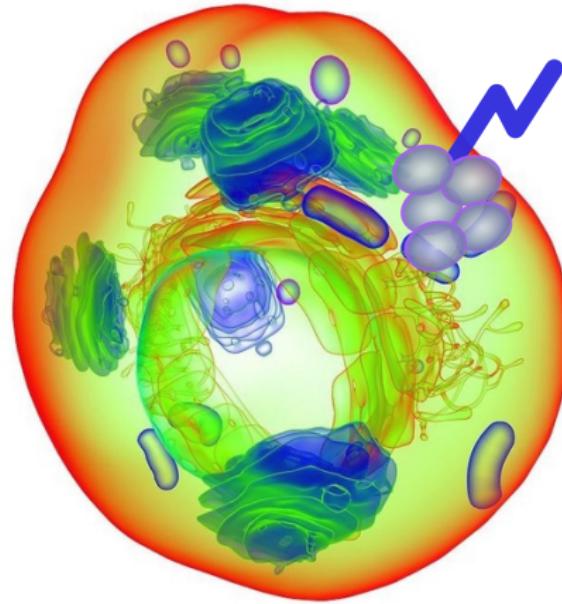
Robrecht Cannoodt

16 december 2019



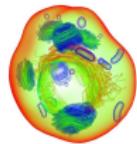






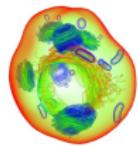
# Hoe maken cellen eiwitten aan?

Cel

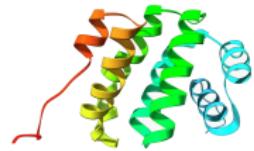


# Hoe maken cellen eiwitten aan?

Cel

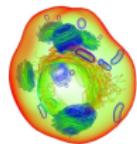


Eiwit

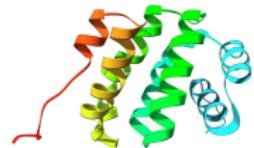


# Hoe maken cellen eiwitten aan?

Cel



Eiwit



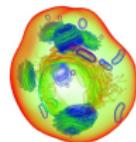
Restaurant



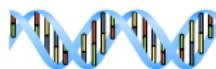
Sushi

# Hoe maken cellen eiwitten aan?

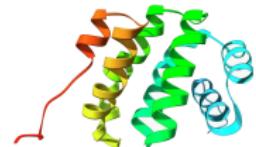
Cel



DNA



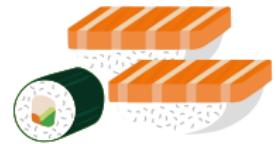
Eiwit



Restaurant



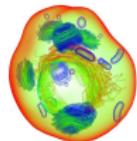
Kookboek



Sushi

# Hoe maken cellen eiwitten aan?

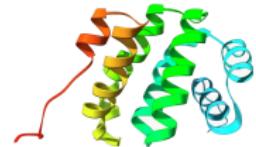
Cel



DNA



Eiwit



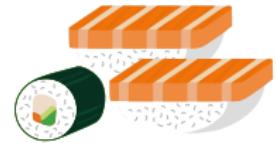
Recept



Restaurant



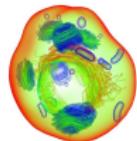
Kookboek



Sushi

# Hoe maken cellen eiwitten aan?

Cel



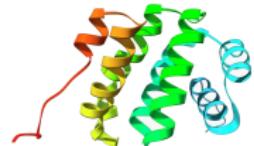
DNA



RNA



Eiwit



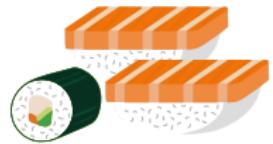
Recept



Restaurant

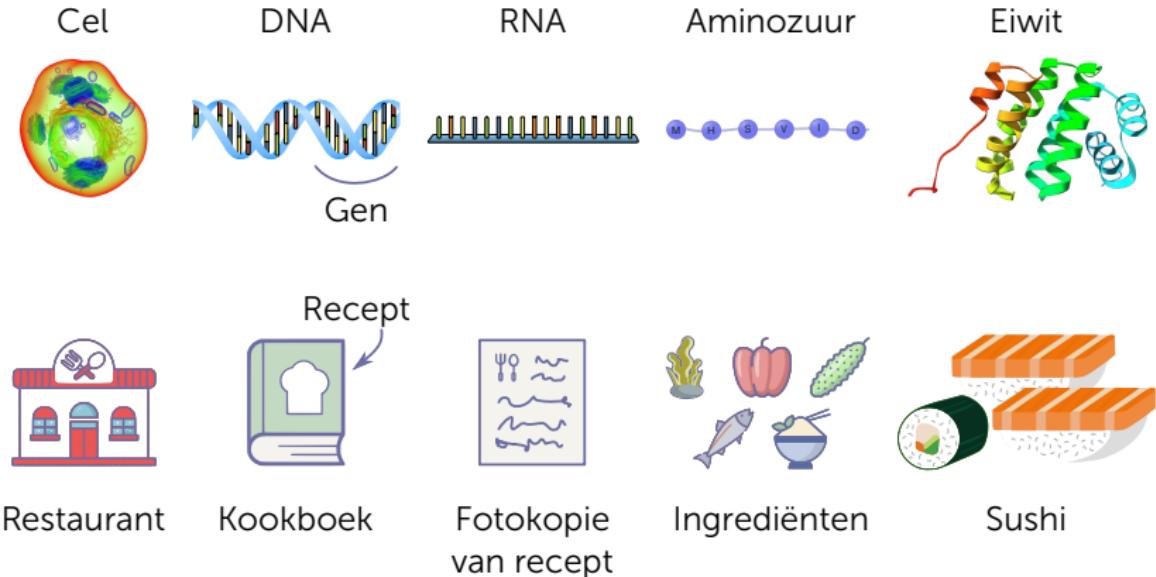
Kookboek

Fotokopie  
van recept

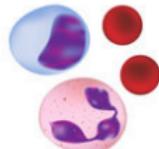


Sushi

# Hoe maken cellen eiwitten aan?



# Het menselijk lichaam bevat >210 soorten cellen



Blood cells



Surface skin cells



Bone cell



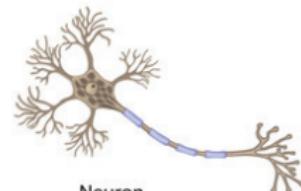
Columnar epithelial and Goblet cells



Cardiac muscle cell



Skeletal muscle cells

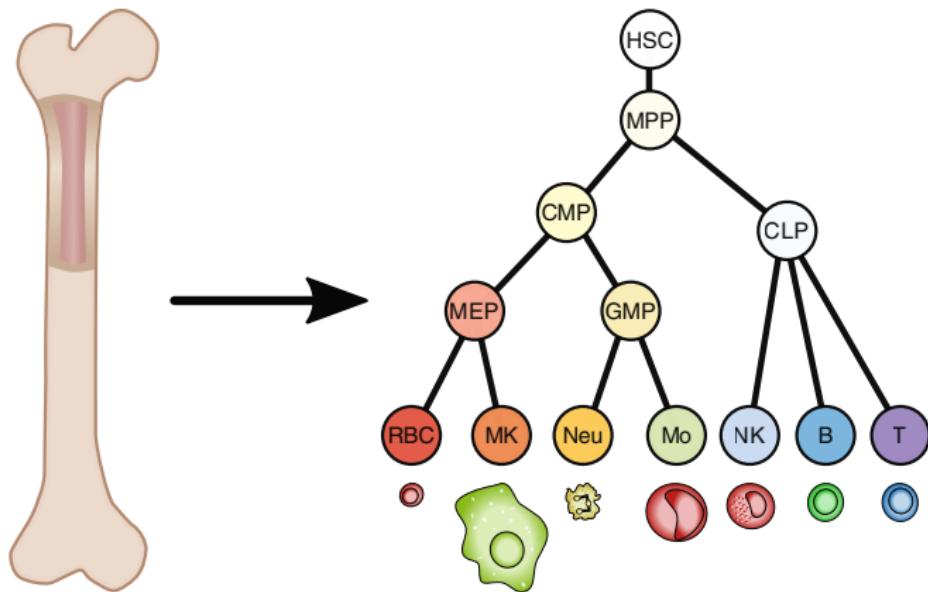


Neuron

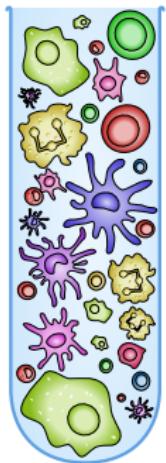


Smooth muscle cells

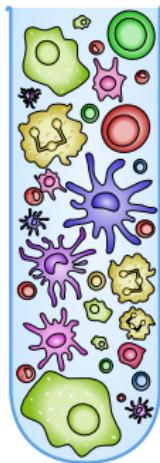
Cellen kunnen ontwikkelen van één type naar een ander



# Veel voorkomende vraag in celbiologie

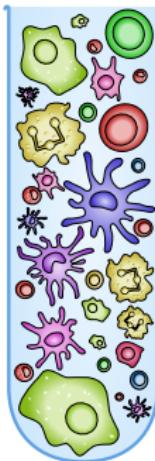


# Veel voorkomende vraag in celbiologie



Wat voor een cel is dit?  
Wat is zijn functie?

# Veel voorkomende vraag in celbiologie

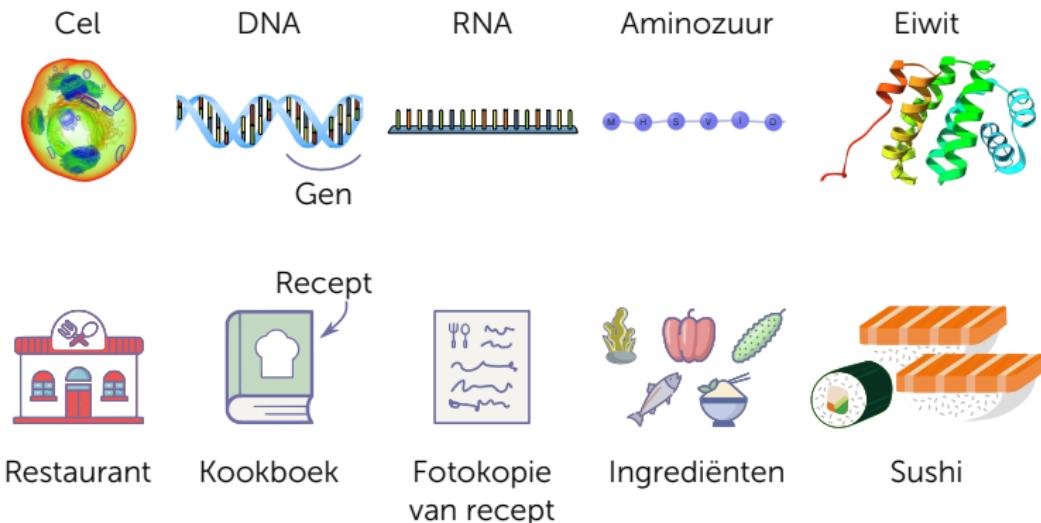


Wat voor een cel is dit?  
Wat is zijn functie?

Welk type restaurant is dit?  
• Mexikaans, chinees, italiaans, ...  
• À la carte, all you can eat, drivethrough  
• Hoeveel sterren op yelp?

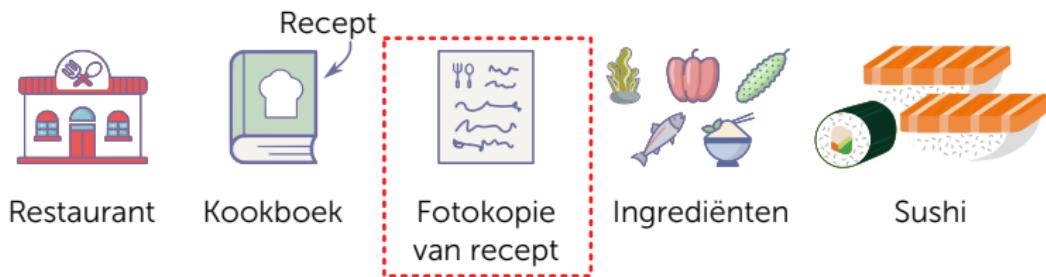
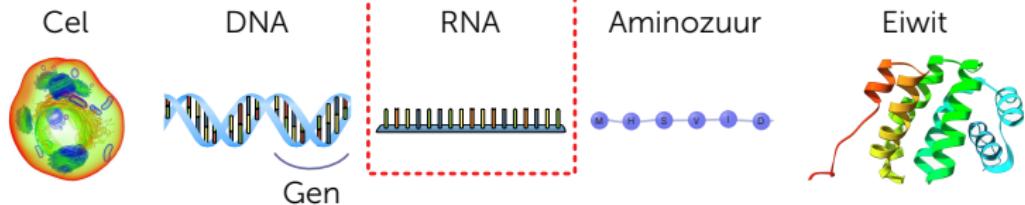


# Welke types cellen komen voor in een populatie?

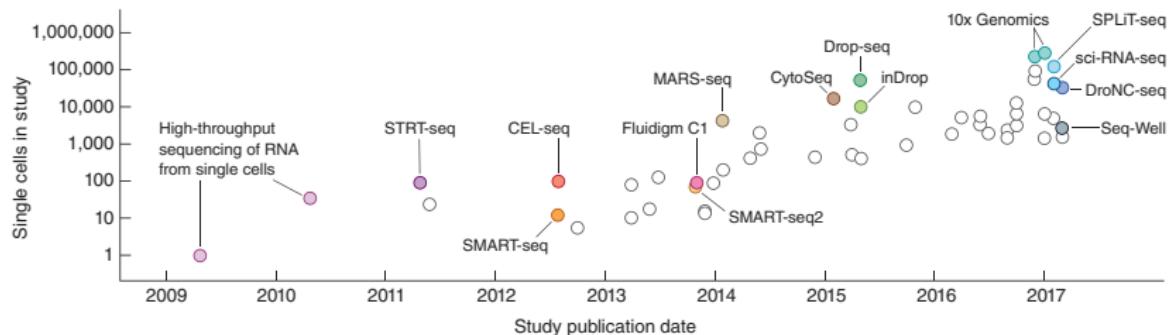
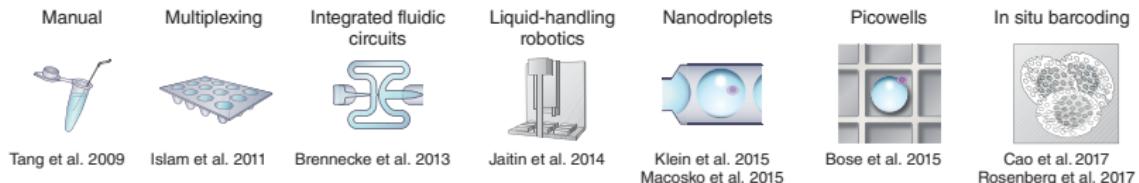


# Welke types cellen komen voor in een populatie?

Single-cell  
RNA sequencing  
(scRNA-seq)

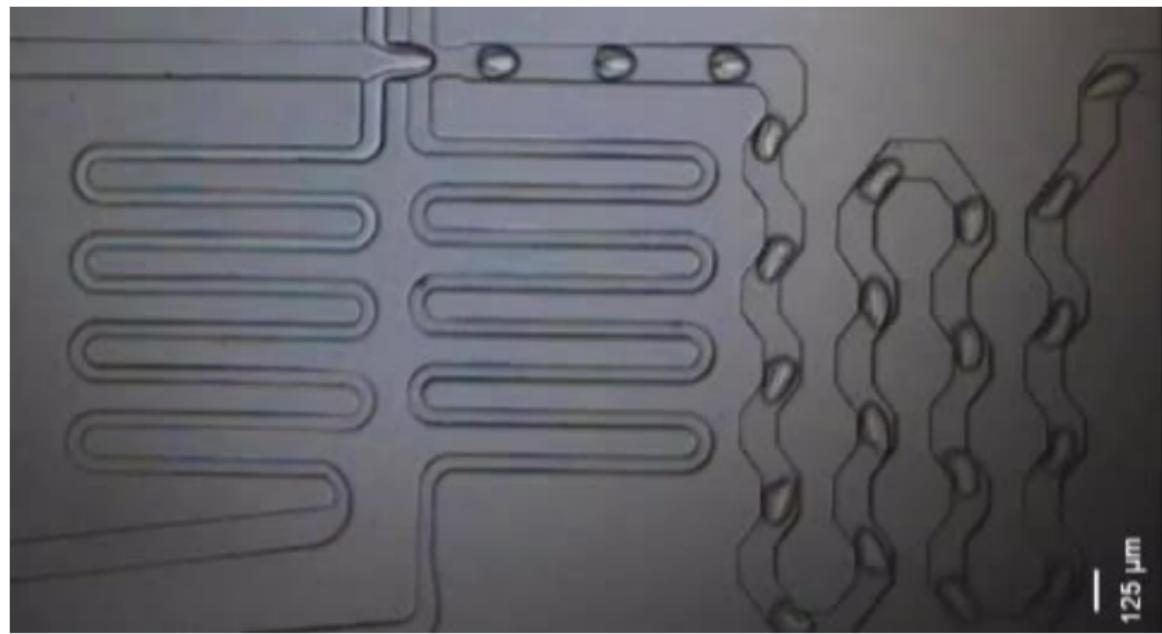


# 2014: doorbraak in schaalbaarheid van scRNA-seq

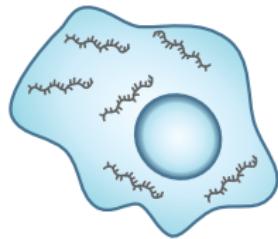


Treutlein et al. 2018

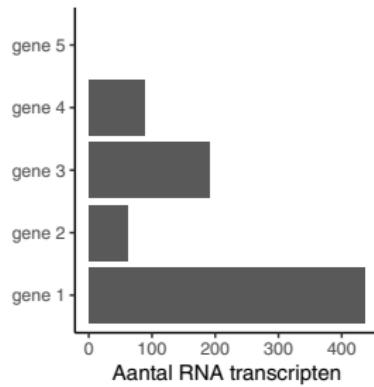
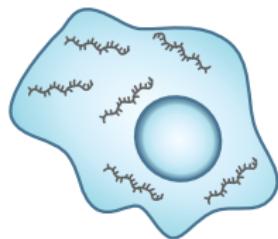
## Voorbeeld van een scRNA-seq technologie: Drop-seq



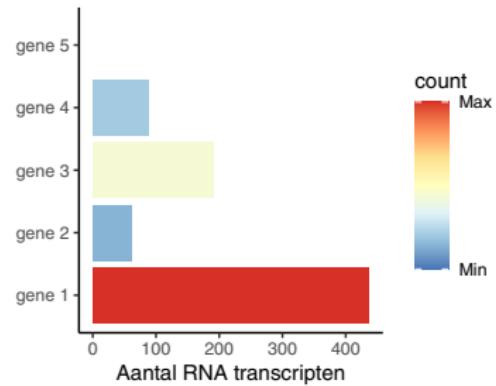
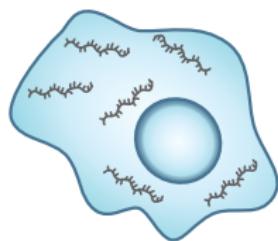
# Moleculen tellen met scRNA-seq



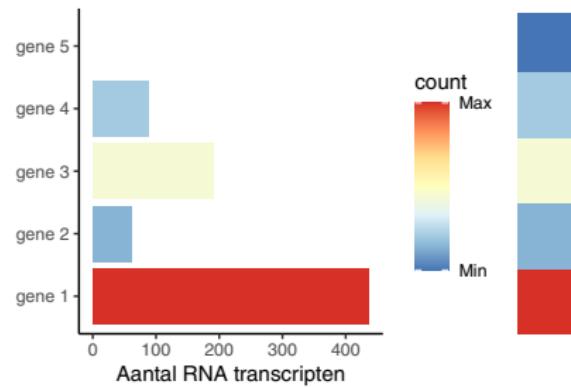
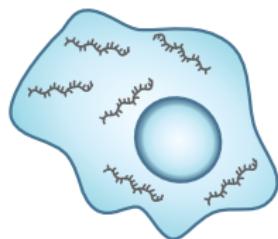
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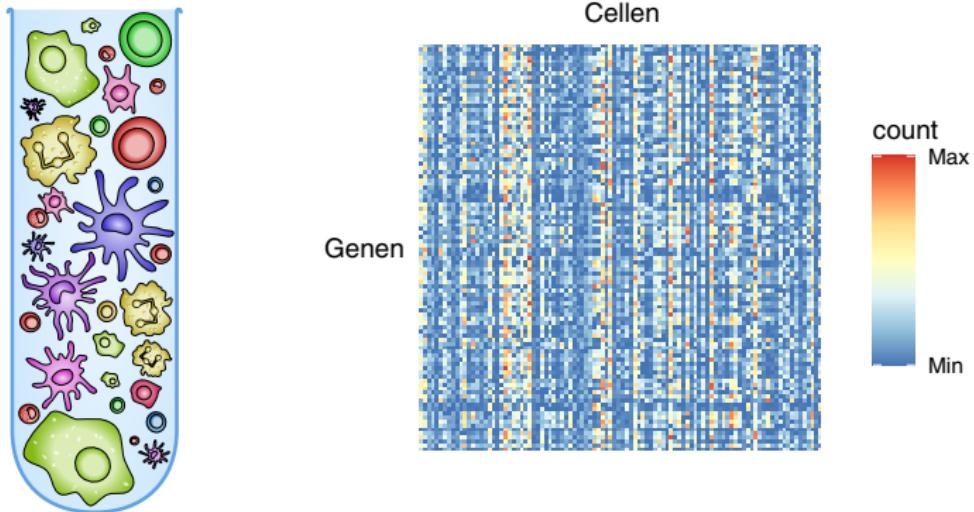
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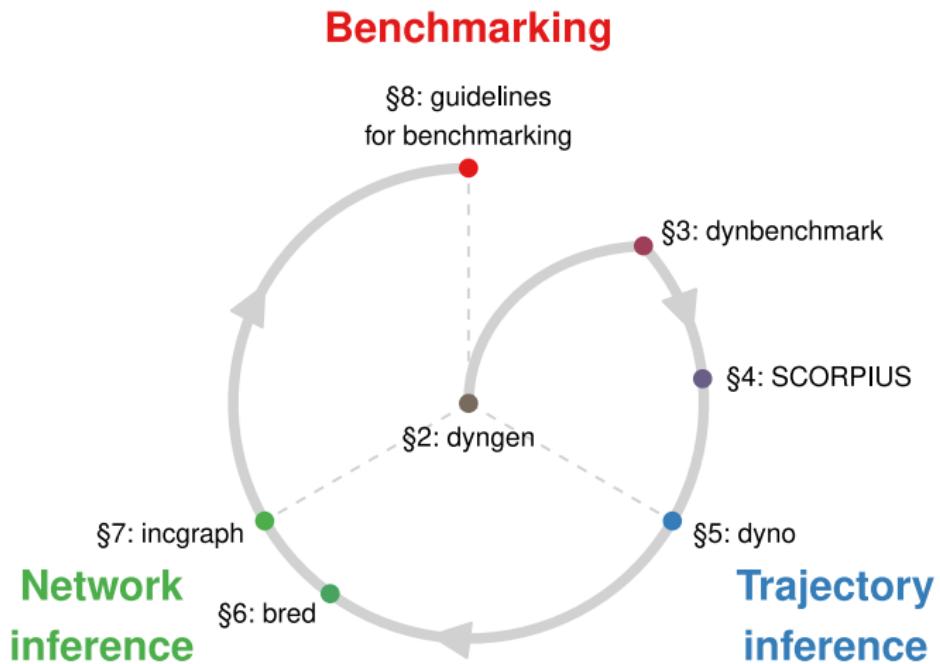
# Moleculen tellen met scRNA-seq



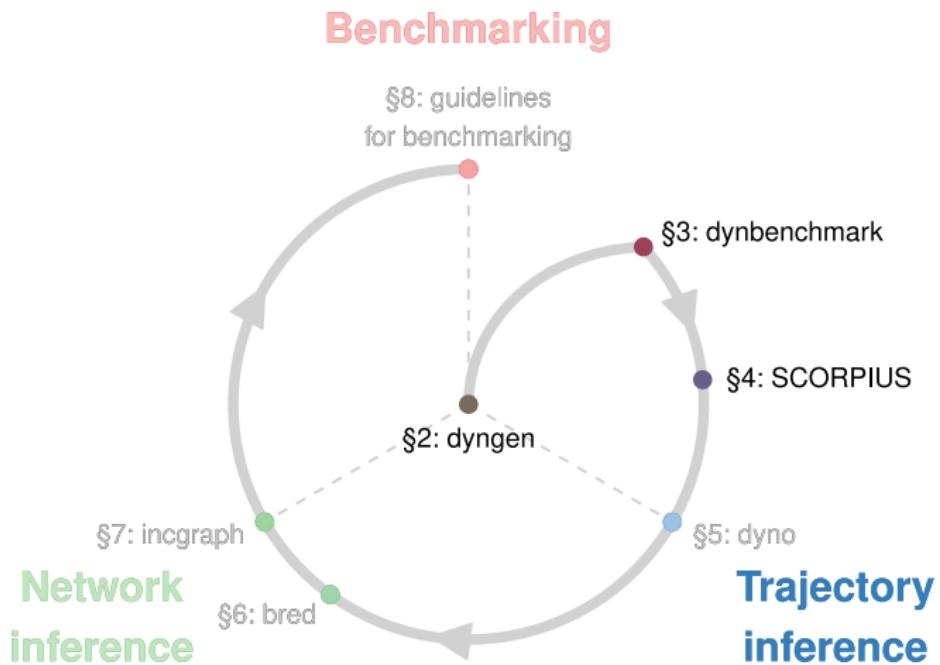
# Moleculen tellen met scRNA-seq



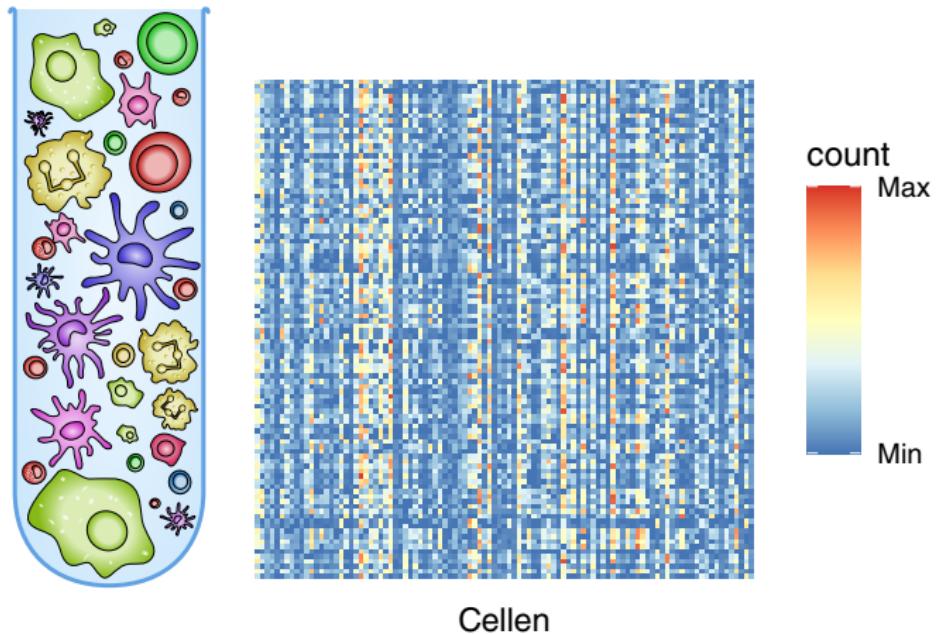
# Opbouw van de thesis



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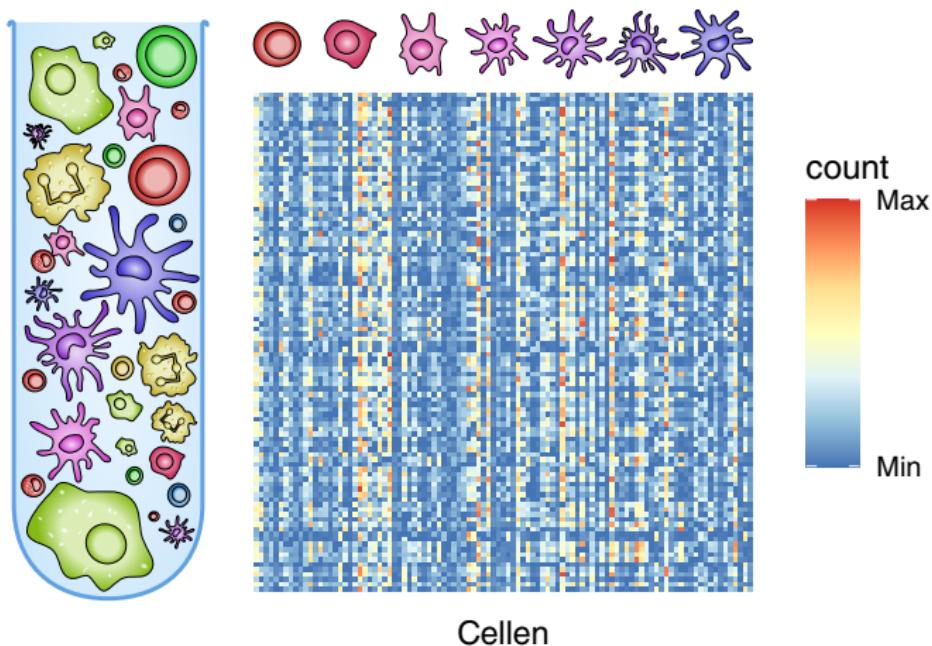


Yvan in 2015:

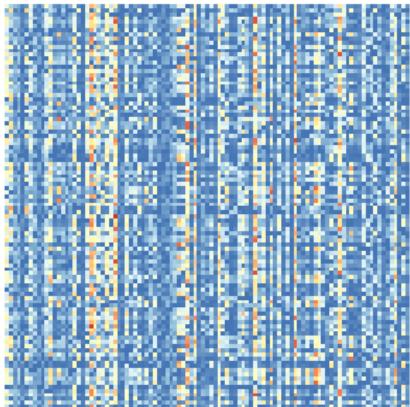


Yvan in 2015:

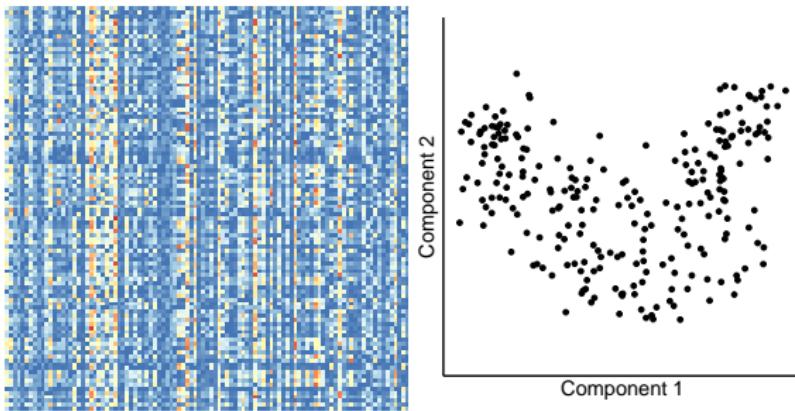
"hé Robrecht, kan je deze cellen even ordenen?"



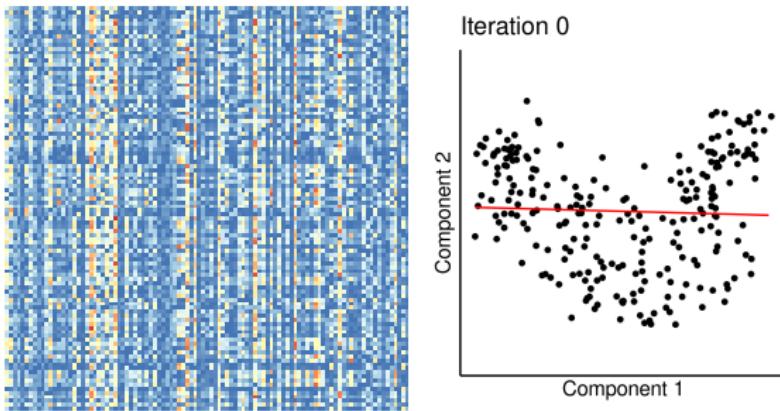
# Cellen ordenen met SCORPIUS



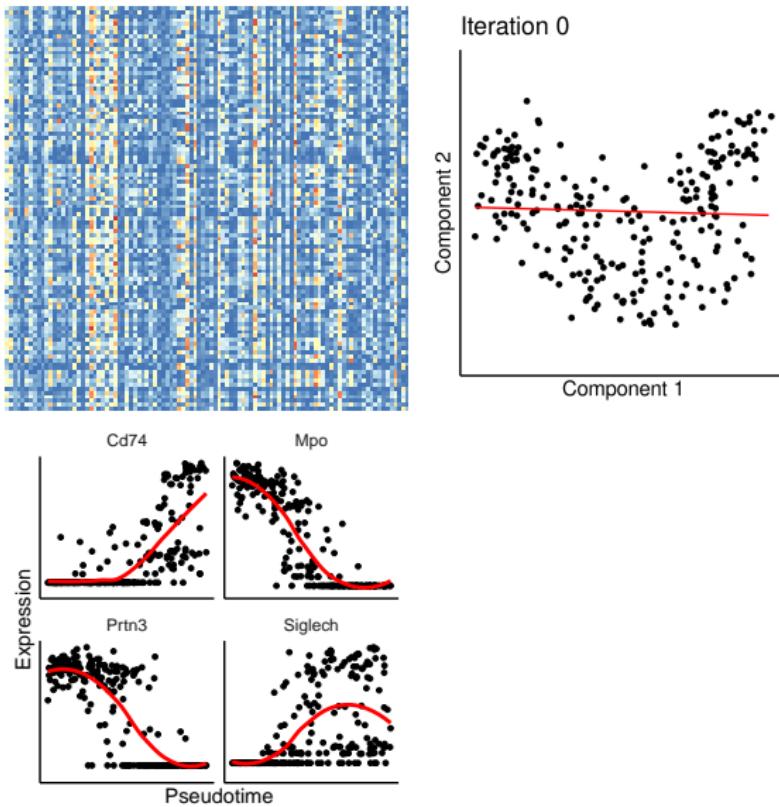
# Cellen ordenen met SCORPIUS



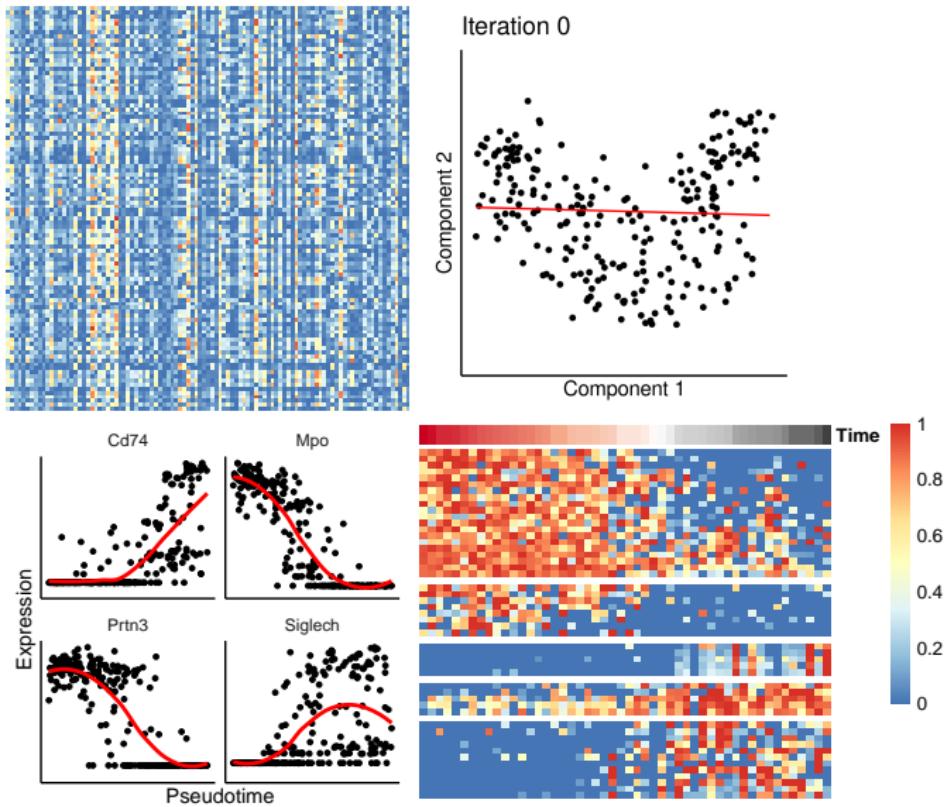
# Cellen ordenen met SCORPIUS



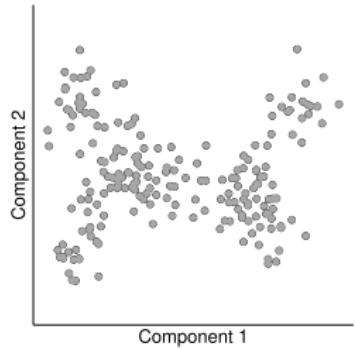
# Cellen ordenen met SCORPIUS



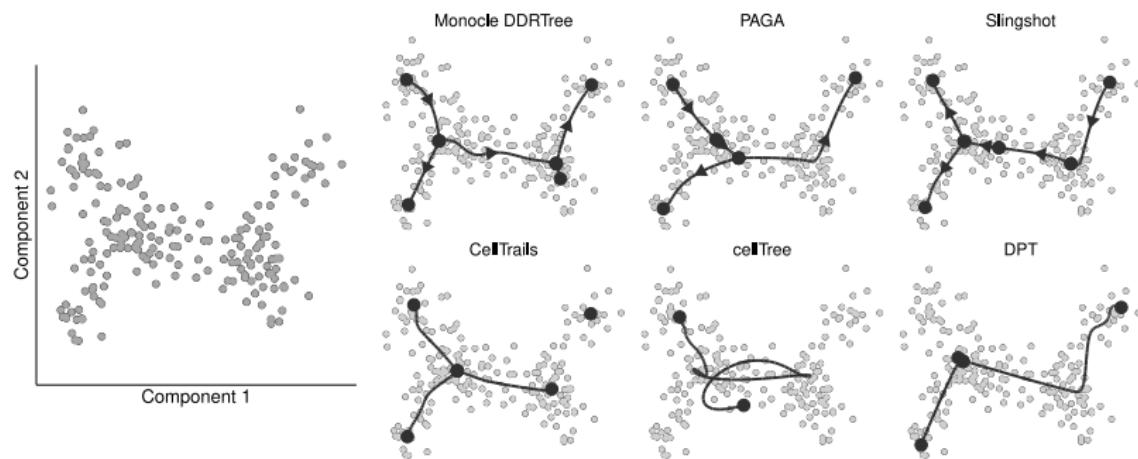
# Cellen ordenen met SCORPIUS



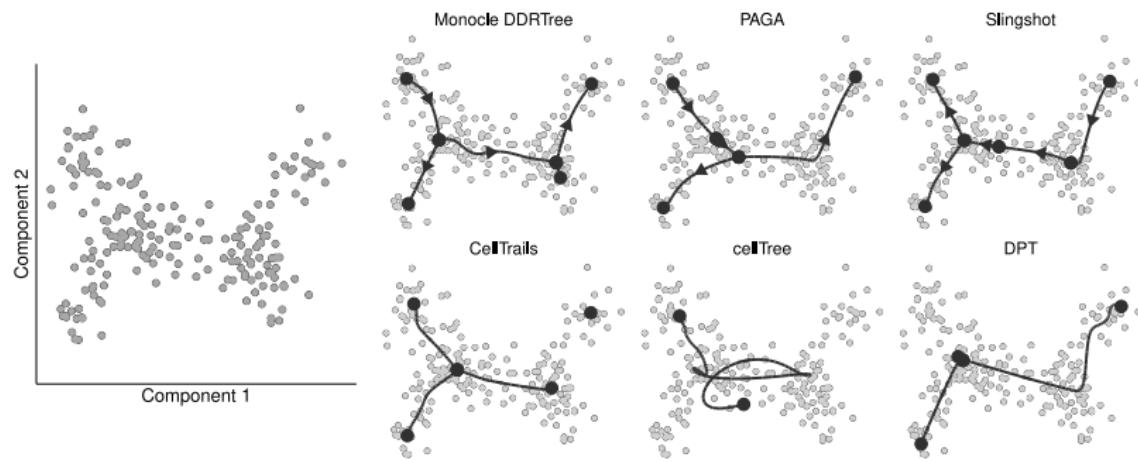
Niet alle datasets zijn even gemakkelijk



Niet alle datasets zijn even gemakkelijk  
→ Trajectory inference methoden

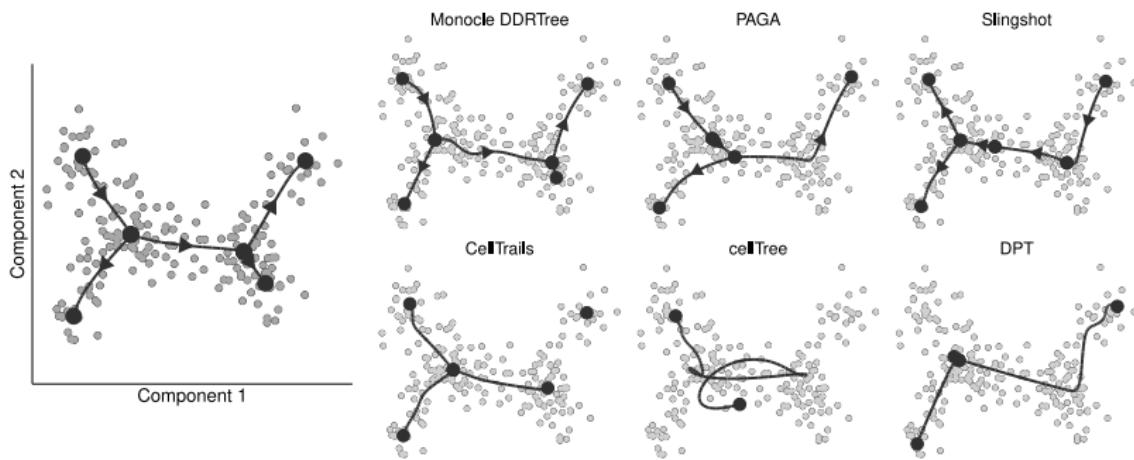


Niet alle datasets zijn even gemakkelijk  
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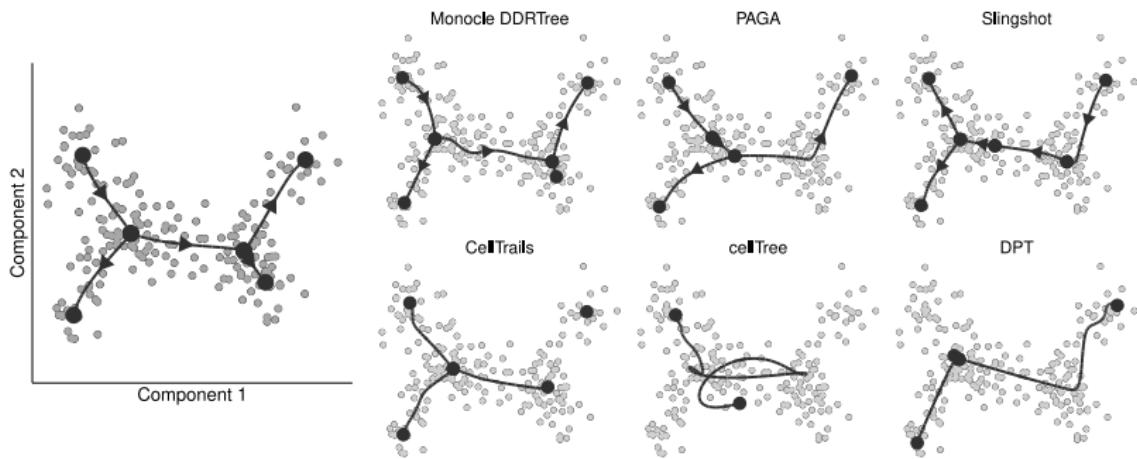
Zeer populair: >70 methoden

Niet alle datasets zijn even gemakkelijk  
→ Trajectory inference methoden



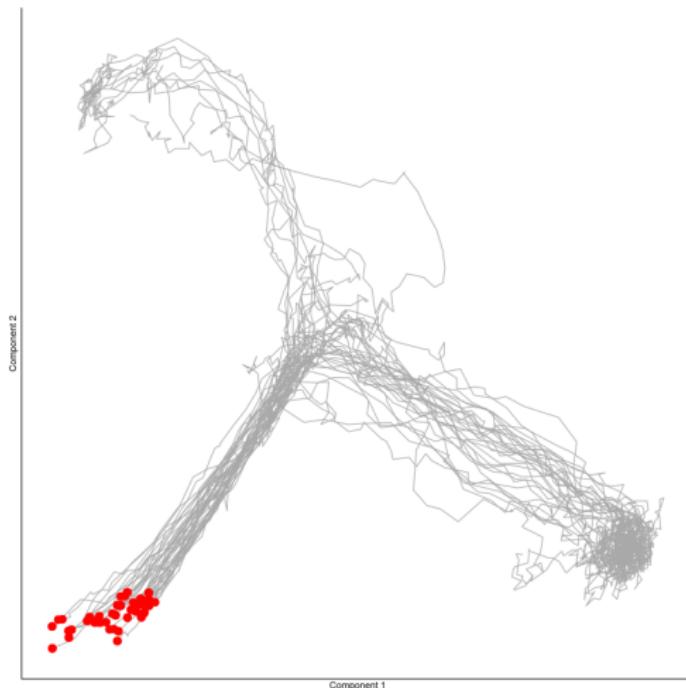
Zeer populair: >70 methoden

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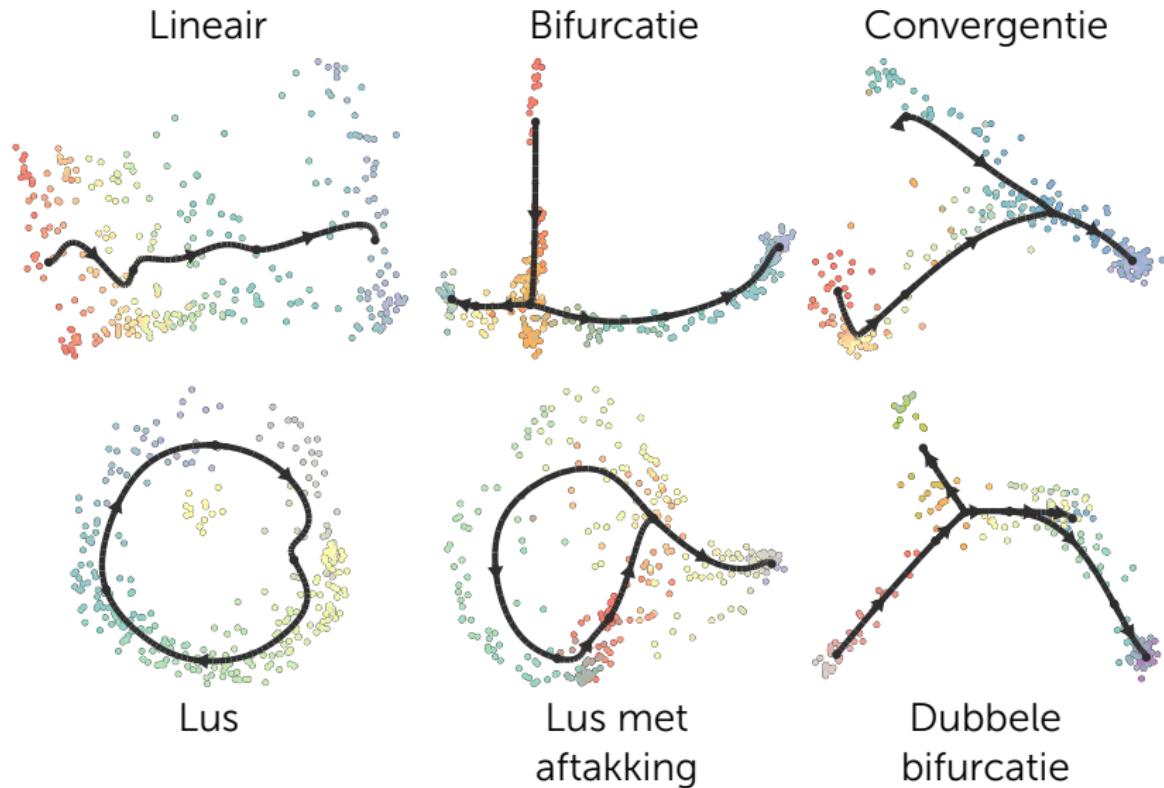


Zeer populair: >70 methoden  
Nood aan een vergelijking van methoden

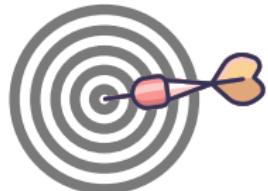
# dyngen: Simulatie van virtuele cellen



# Simulatie van virtuele cellen

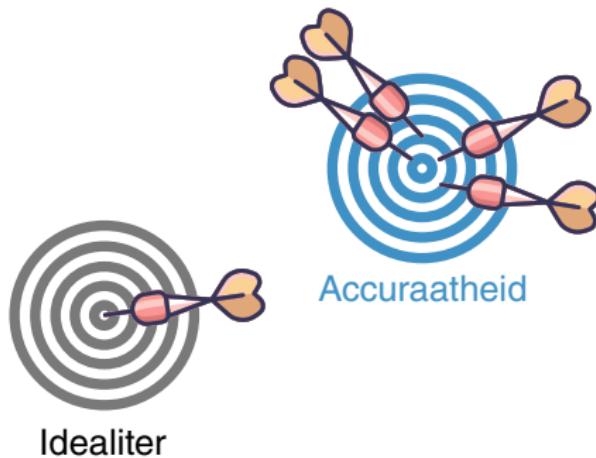


# Grootschalige evaluatie van trajectory inference methoden

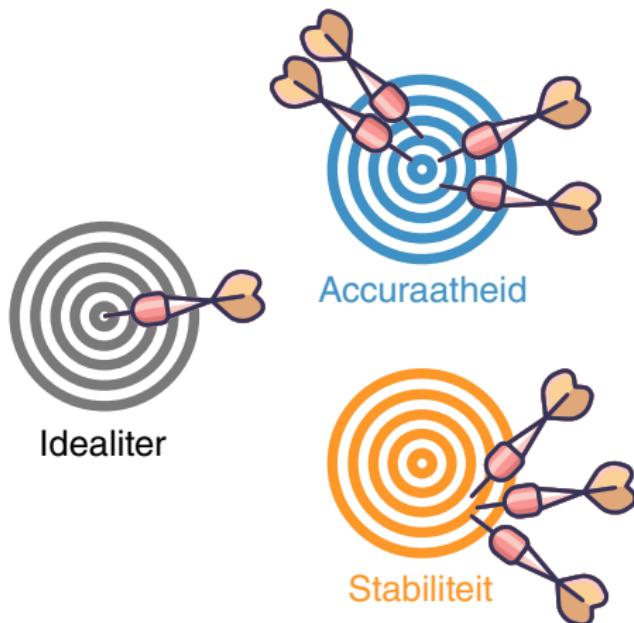


Idealiter

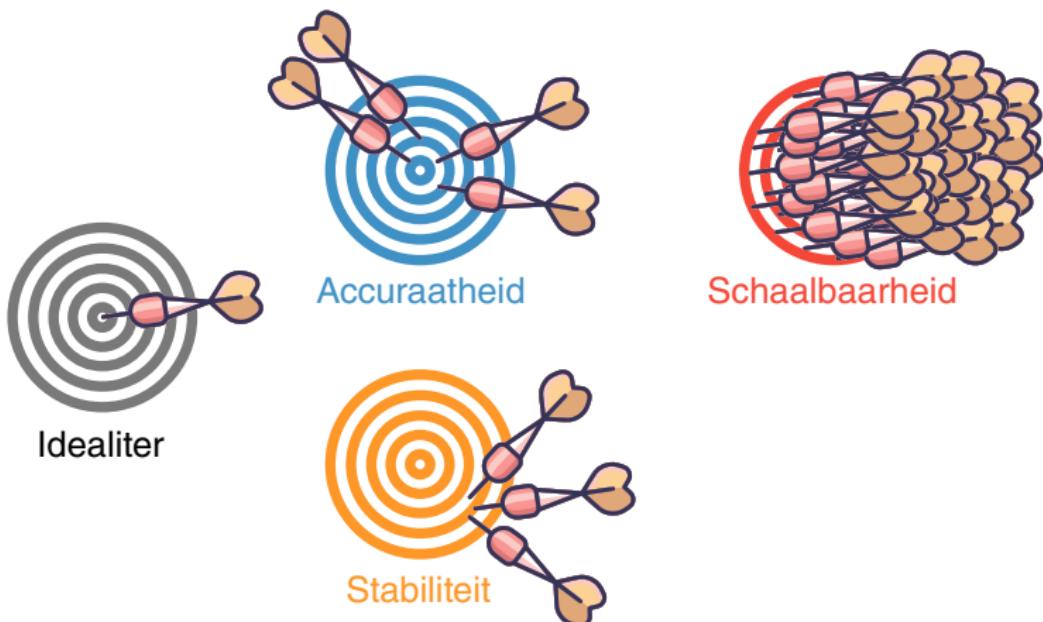
# Grootschalige evaluatie van trajectory inference methoden



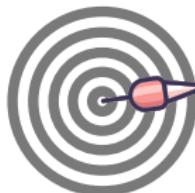
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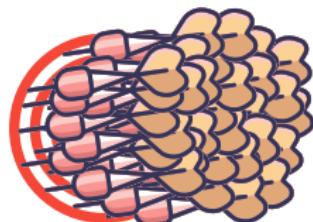
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Idealiter



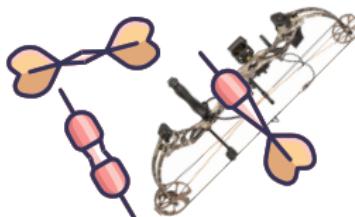
Accuraatheid



Schaalbaarheid

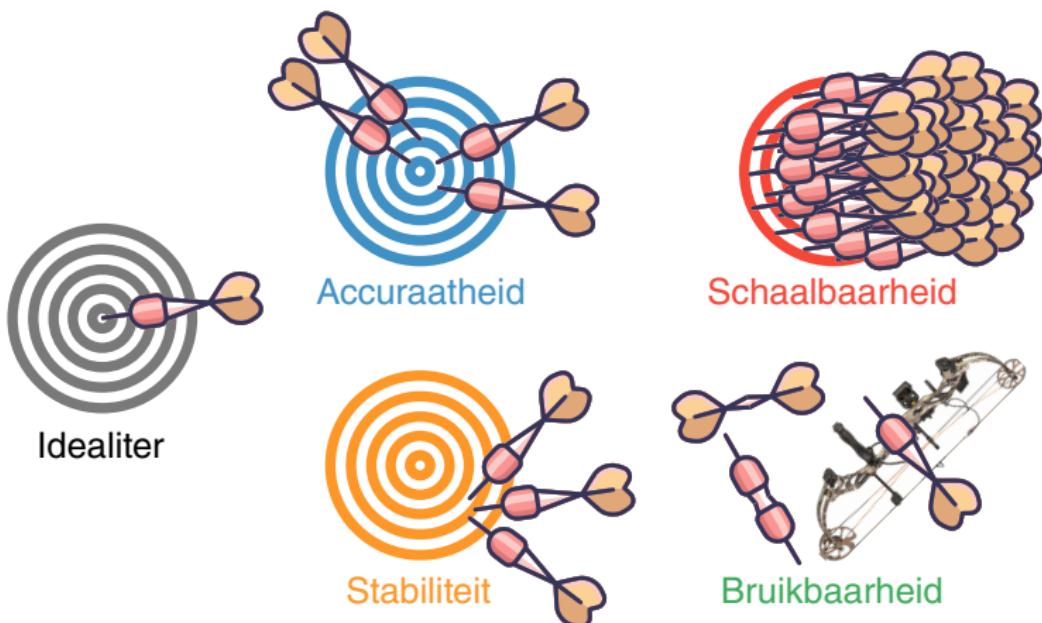


Stabiliteit



Bruikbaarheid

# Grootschalige evaluatie van trajectory inference methoden



# Uitdagingen

# Uitdagingen

- 45 verschillende tools op meerdere computers (Docker)

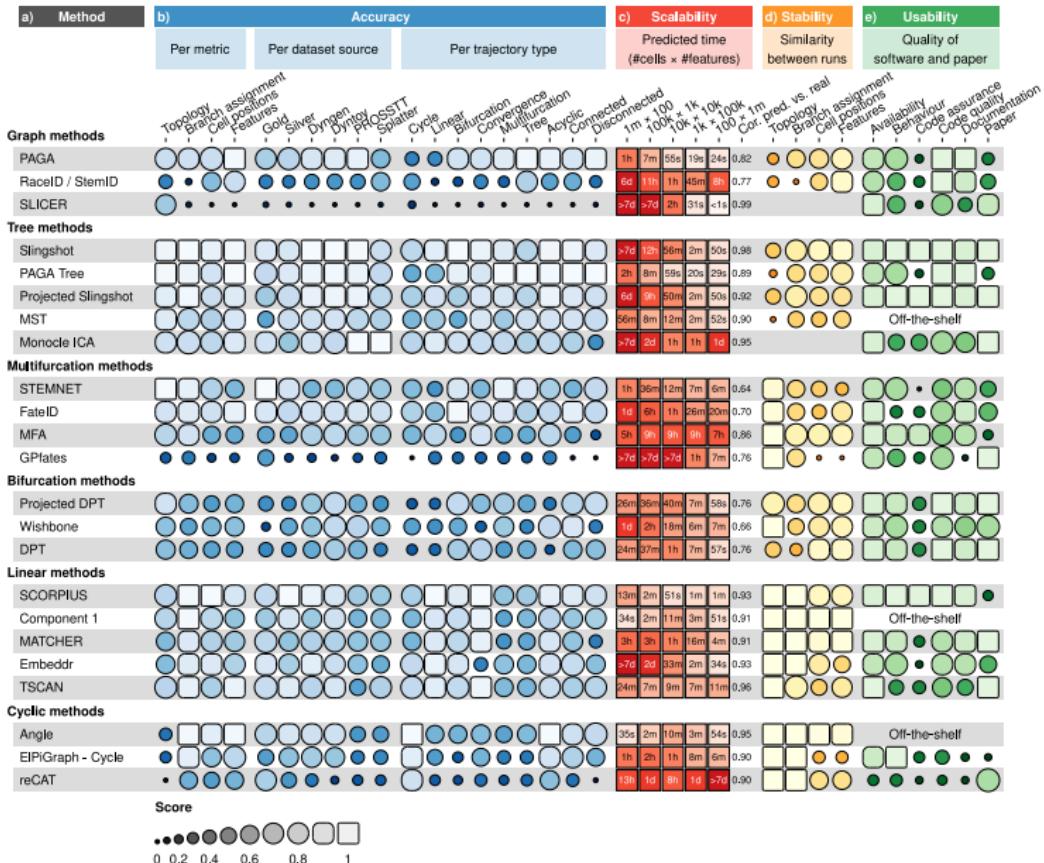
# Uitdagingen

- 45 verschillende tools op meerdere computers (Docker)
- ± 100 echte datasets, ± 100 gesimuleerde datasets

# Uitdagingen

- 45 verschillende tools op meerdere computers (Docker)
- ± 100 echte datasets, ± 100 gesimuleerde datasets
- Nog geen metrieken

# Resultaten van evaluatie



# Set van richtlijnen voor gebruikers

dynguidelines

Tutorial 7 Citation 13

Topology  
Do you expect multiple disconnected trajectories in the data?  
Yes I don't know No

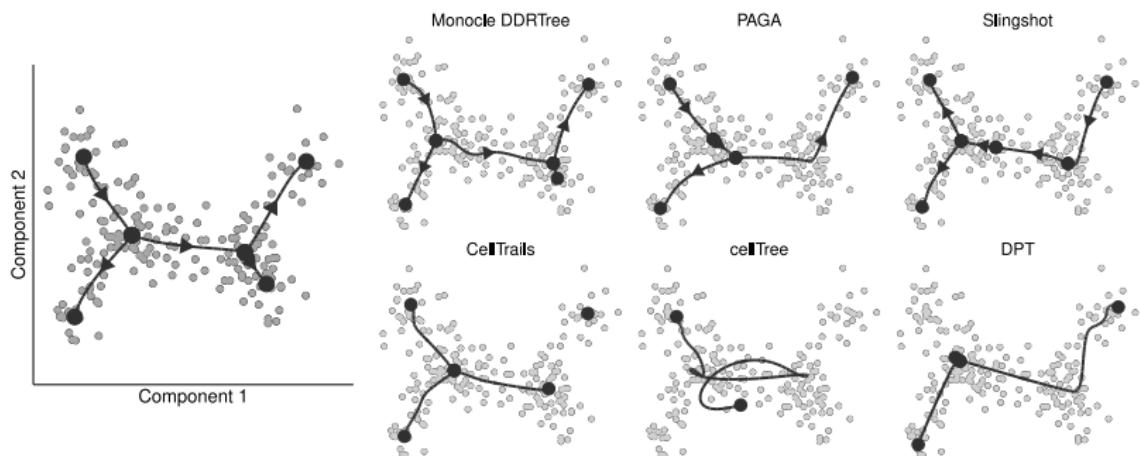
Scalability COMPUTED  
Number of cells  
1000  
Number of features (genes)  
1000  
Time limit  
10s  
Memory limit  
10MB

Show code </> Show/hide columns Options  
Lenses Default Summary (Fig. 2) Method Scalability Stability Usability Accuracy Overall Everything  
Method Accuracy Scalability Stability

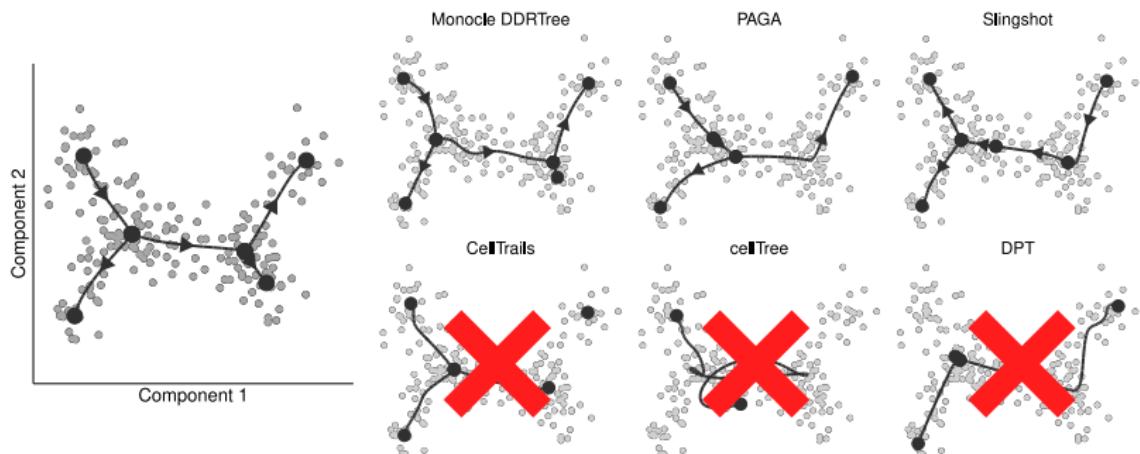
Method	Accuracy	Scalability	Stability
Singshot	100	8s	942MB
SCORPIUS	96	3s	507MB
Angle	92	1s	308MB
PAGA	59	15s	559MB
Embeddr	89	5s	581MB
MST	69	4s	572MB
Waterfall	69	5s	369MB
TSCAN	68	5s	476MB
Component 1	67	1s	516MB
SLICE	63	16s	713MB
Monocle DDRTree	62	41s	647MB
EPIGraph Linear	61	1m	573MB

Benchmark study Evaluating methods with dynbenchmark Part of dynguidelines

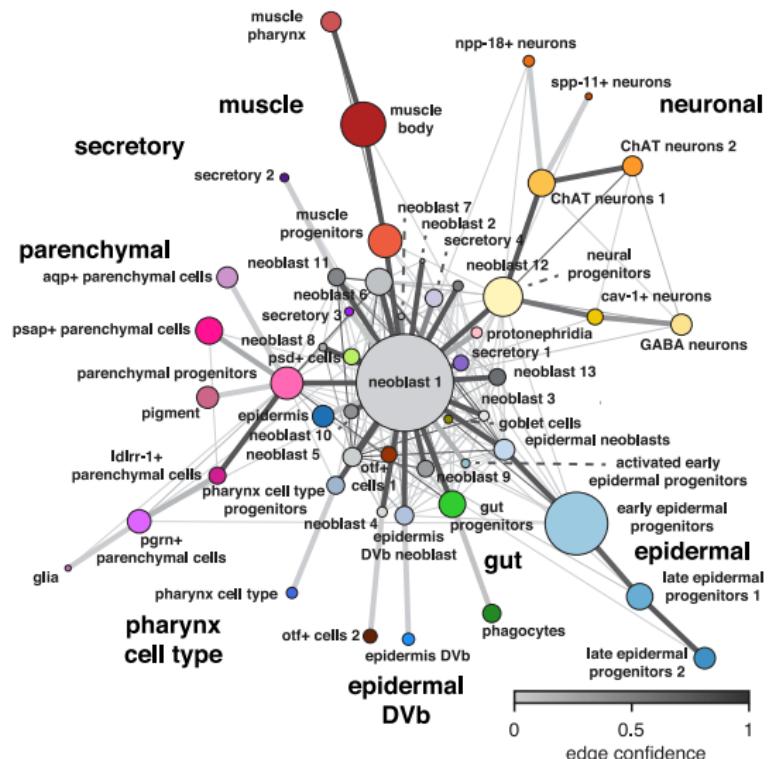
# Eliminatie van sommige methoden



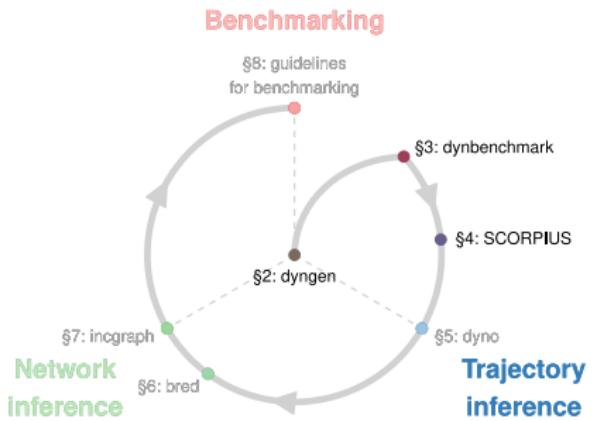
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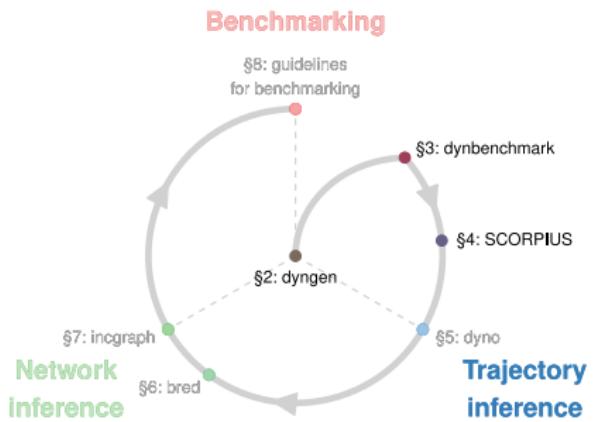
# Tot nader order: pas meerdere methoden toe en vergelijk



# Relevantie van dit werk



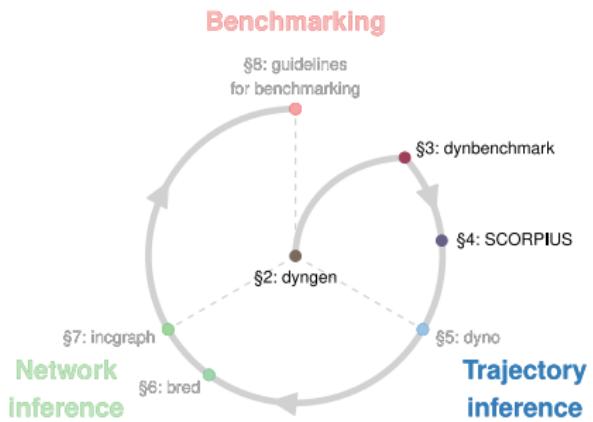
# Relevantie van dit werk



## Evaluatie:

- Wordt gebruikt in onderzoek en industrie
- Vaak vermeld in artikels en presentaties

# Relevantie van dit werk



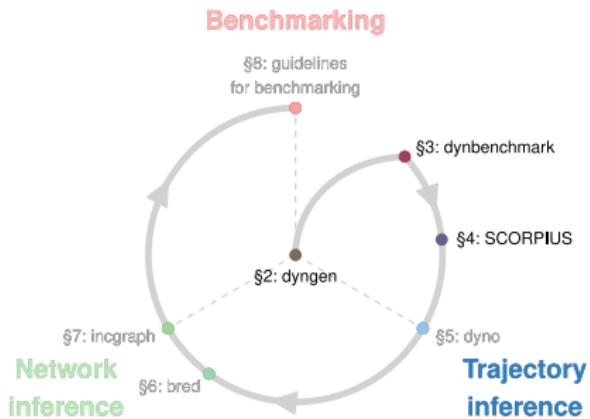
## Evaluatie:

- Wordt gebruikt in onderzoek en industrie
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## Simulator:

- Evaluatie van andere soorten analyses in single-cell data

# Relevantie van dit werk



## Evaluatie:

- Wordt gebruikt in onderzoek en industrie
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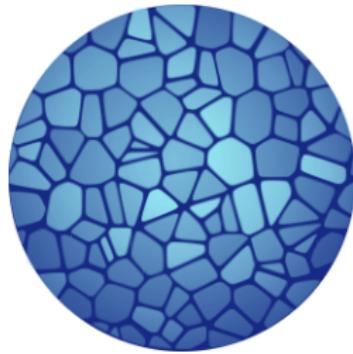
## Simulator:

- Evaluatie van andere soorten analyses in single-cell data

## SCORPIUS:

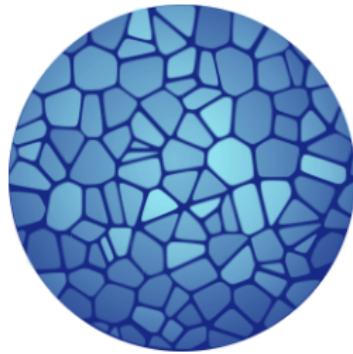
- Wordt gebruikt om veranderingen in cellen te onderzoeken en visualiseren

# Wat brengt de toekomst?



Human cell atlas

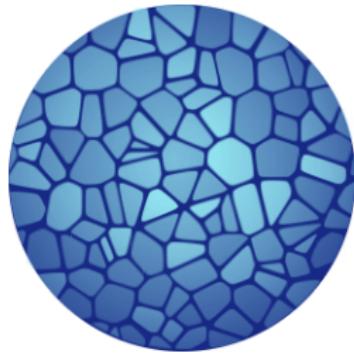
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## Human cell atlas

- 50 biljoen cellen in het lichaam, maar hoeveel verschillende soorten cellen?

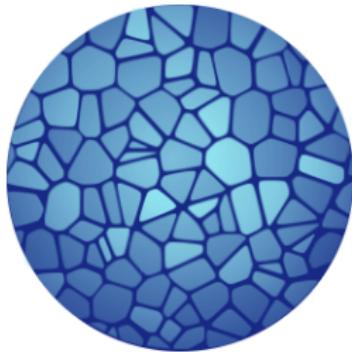
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- Doelstelling: Maak een Google Maps van cel(types)

# Wat brengt de toekomst?



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- Begrijpen van ziektes en ontwikkelen van nieuwe medicijnen

