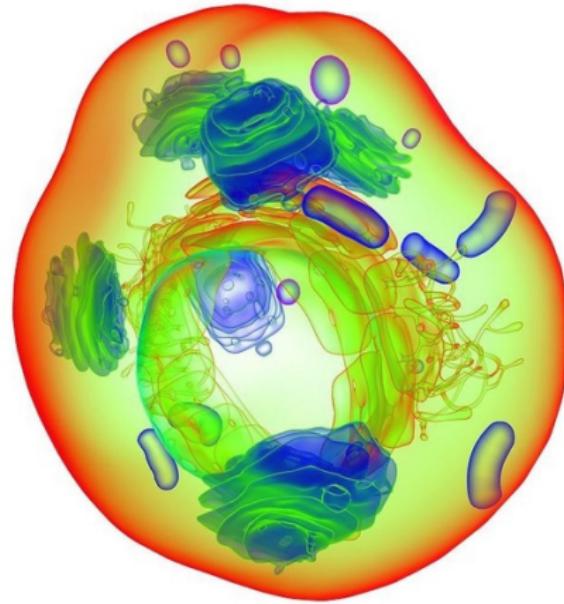


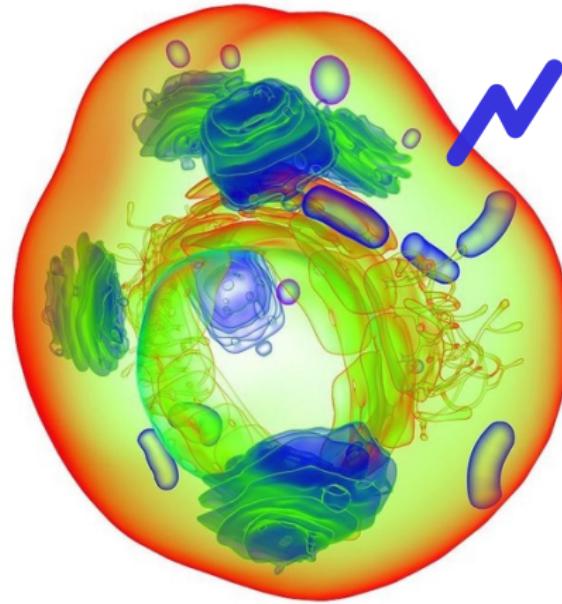
# Modelling single-cell dynamics with trajectories and gene regulatory networks

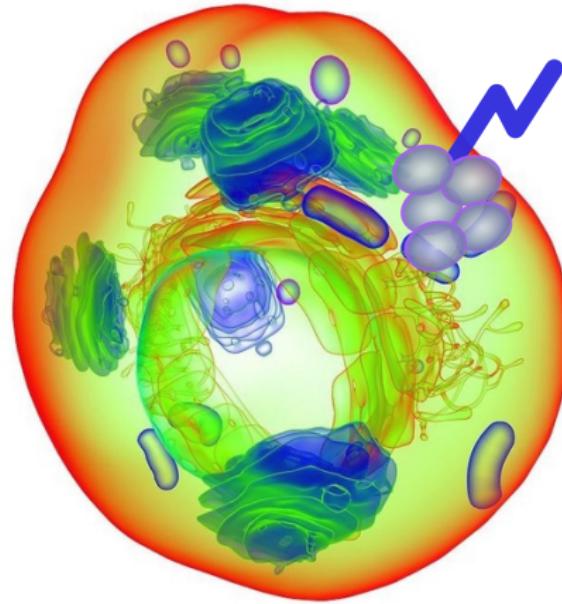
Robrecht Cannoodt

16 december 2019



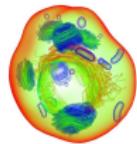






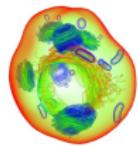
# Hoe maken cellen eiwitten aan?

Cel

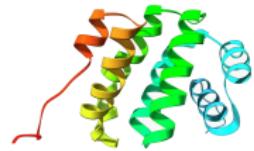


# Hoe maken cellen eiwitten aan?

Cel

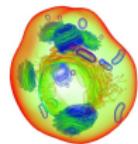


Eiwit

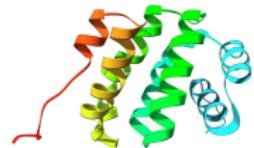


# Hoe maken cellen eiwitten aan?

Cel



Eiwit



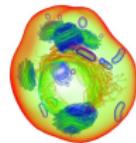
Restaurant



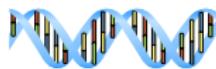
Sushi

# Hoe maken cellen eiwitten aan?

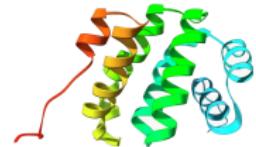
Cel



DNA



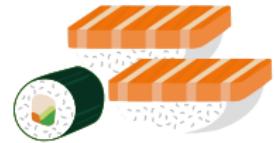
Eiwit



Restaurant



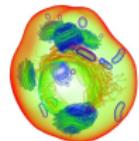
Kookboek



Sushi

# Hoe maken cellen eiwitten aan?

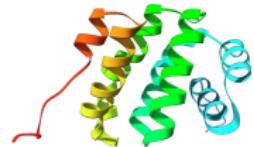
Cel



DNA



Eiwit

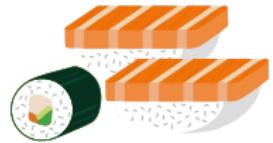


Restaurant



Kookboek

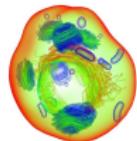
Recept



Sushi

# Hoe maken cellen eiwitten aan?

Cel



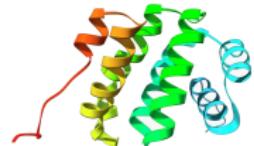
DNA



RNA



Eiwit



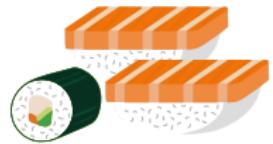
Recept



Restaurant

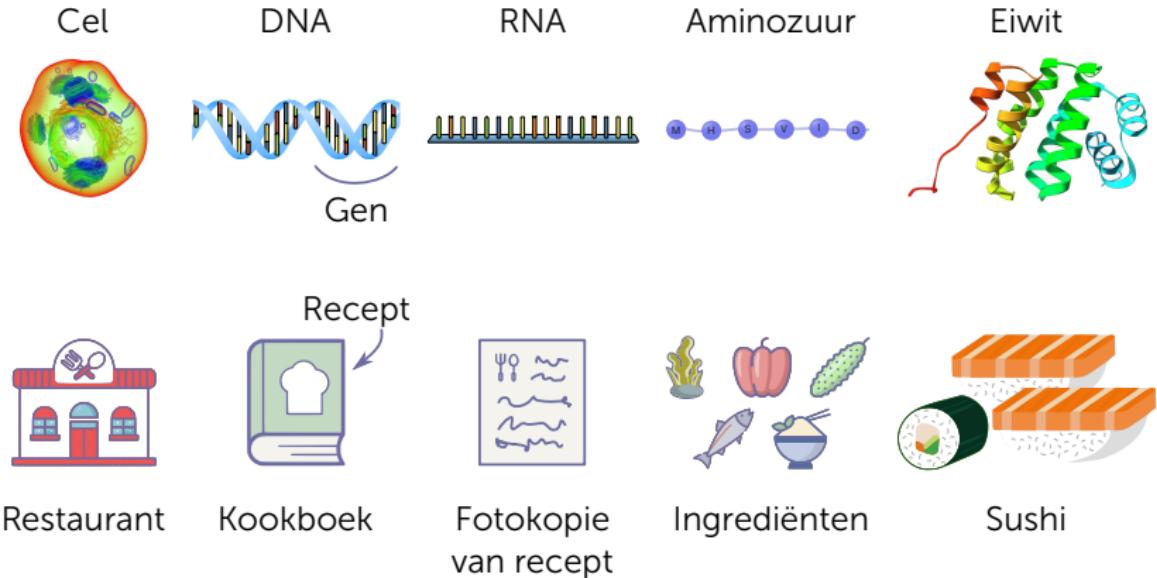
Kookboek

Fotokopie  
van recept

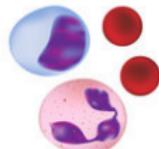


Sushi

# Hoe maken cellen eiwitten aan?



# Het menselijk lichaam bevat >210 soorten cellen



Blood cells



Surface skin cells



Bone cell



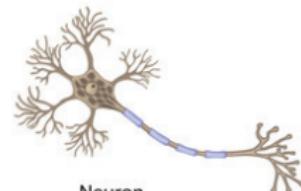
Columnar epithelial and Goblet cells



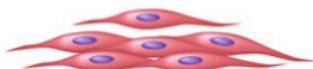
Cardiac muscle cell



Skeletal muscle cells

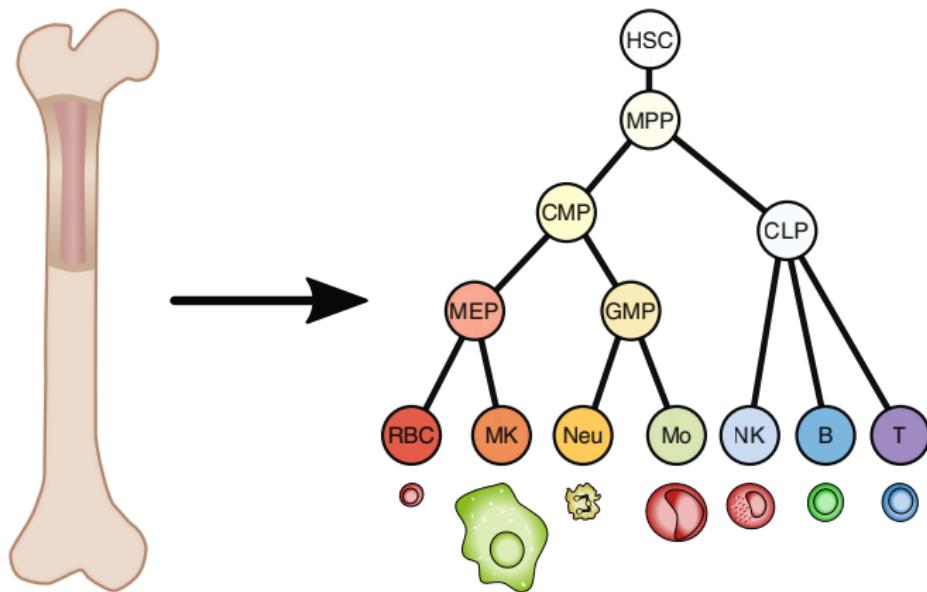


Neuron

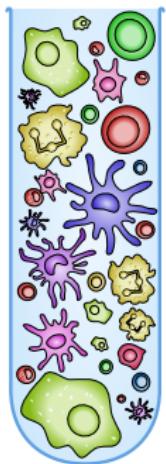


Smooth muscle cells

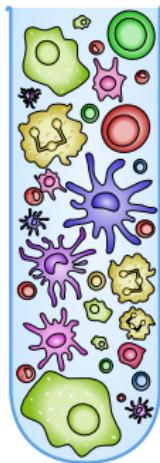
Cellen kunnen ontwikkelen van één type naar een ander



# Veel voorkomende vraag in celbiologie

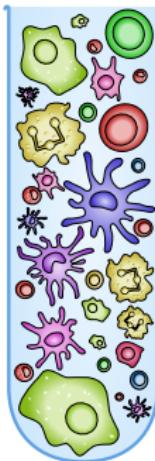


# Veel voorkomende vraag in celbiologie



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

# Veel voorkomende vraag in celbiologie

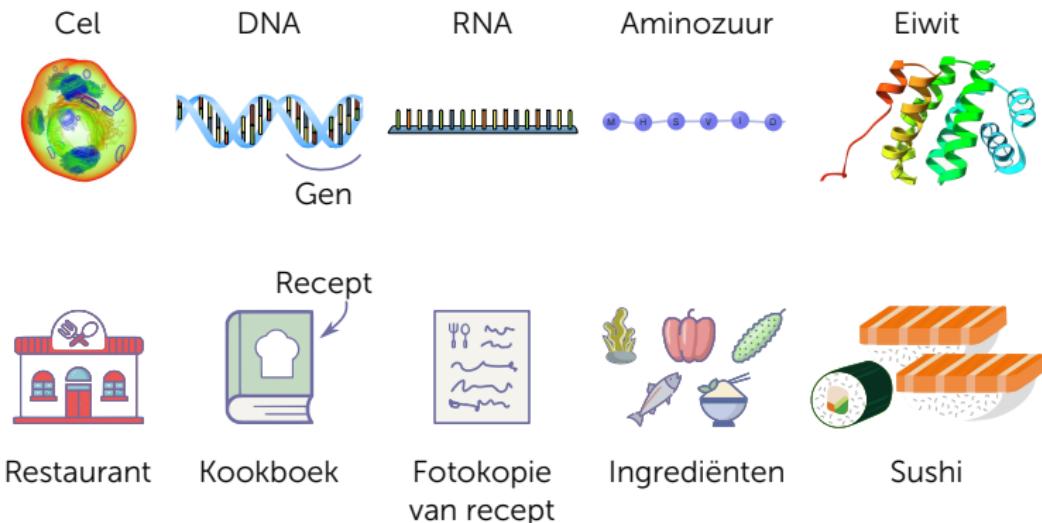


Wat voor een cel is dit?  
Wat is zijn functie?

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

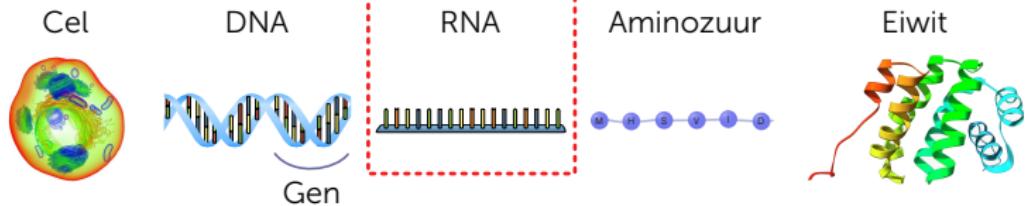


# Welke types cellen komen voor in een populatie?

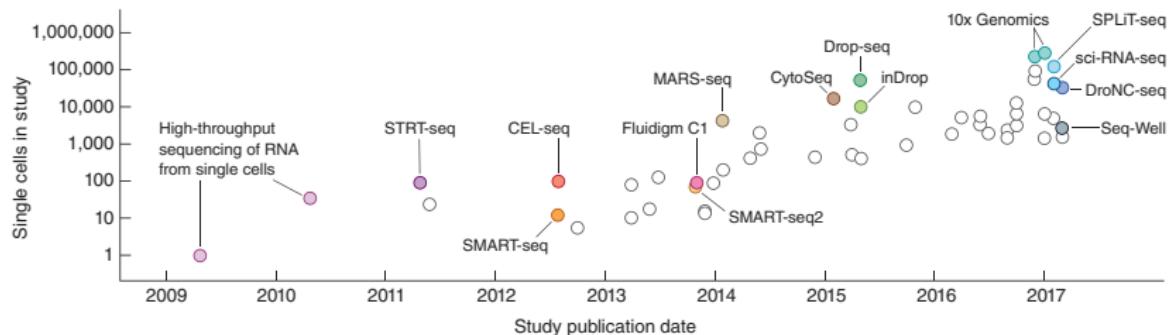
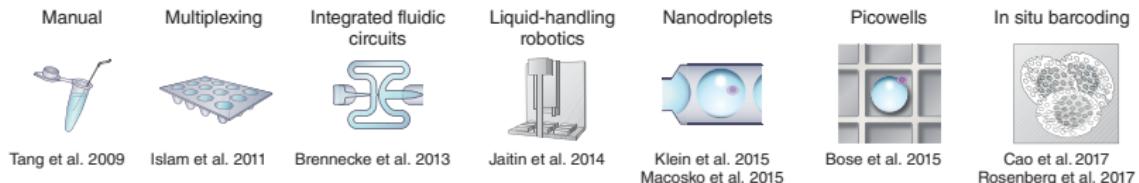


# Welke types cellen komen voor in een populatie?

Single-cell  
RNA sequencing  
(scRNA-seq)

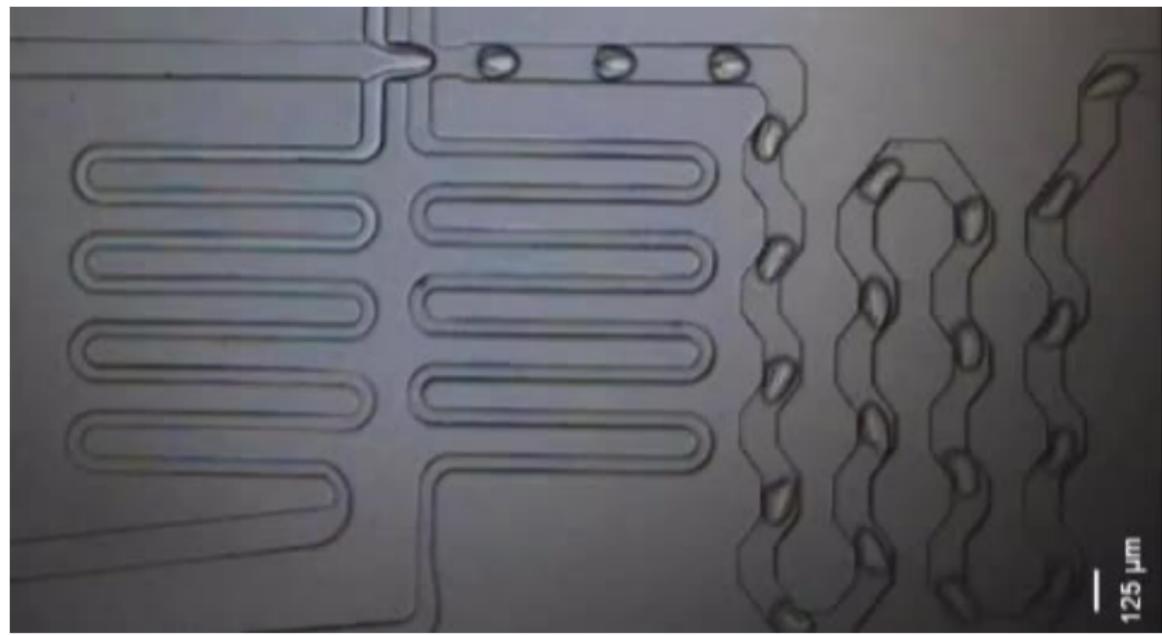


# 2014: doorbraak in schaalbaarheid van scRNA-seq

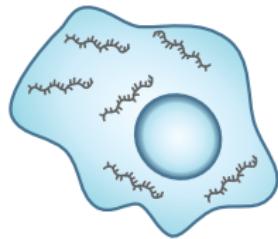


Treutlein et al. 2018

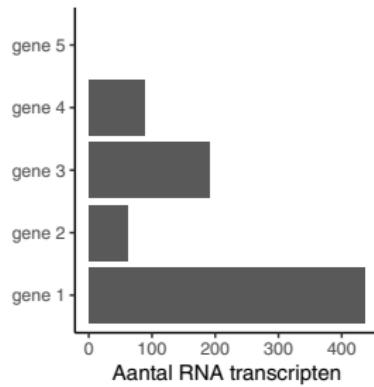
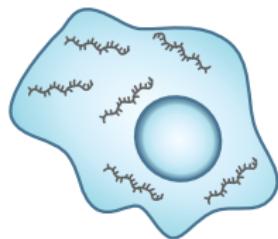
## Voorbeeld van een scRNA-seq technologie: Drop-seq



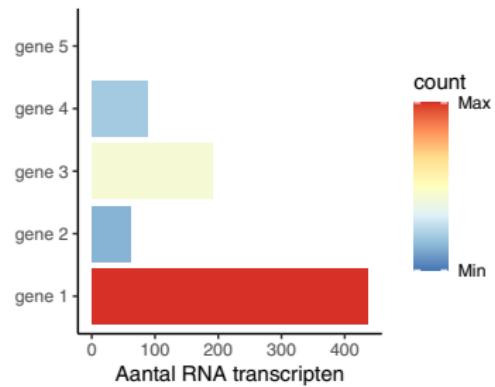
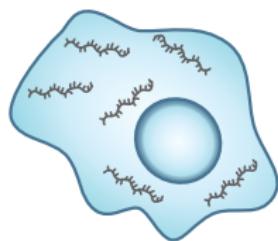
# Moleculen tellen met scRNA-seq



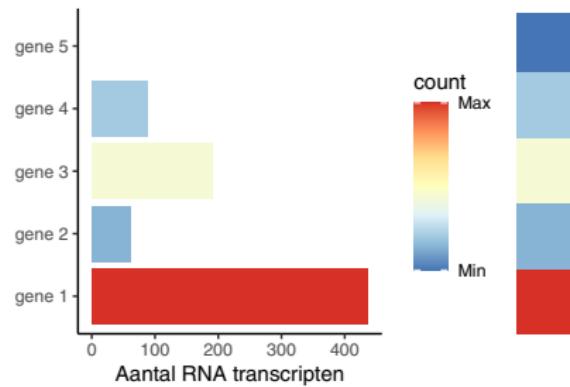
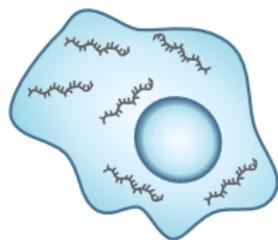
# Moleculen tellen met scRNA-seq



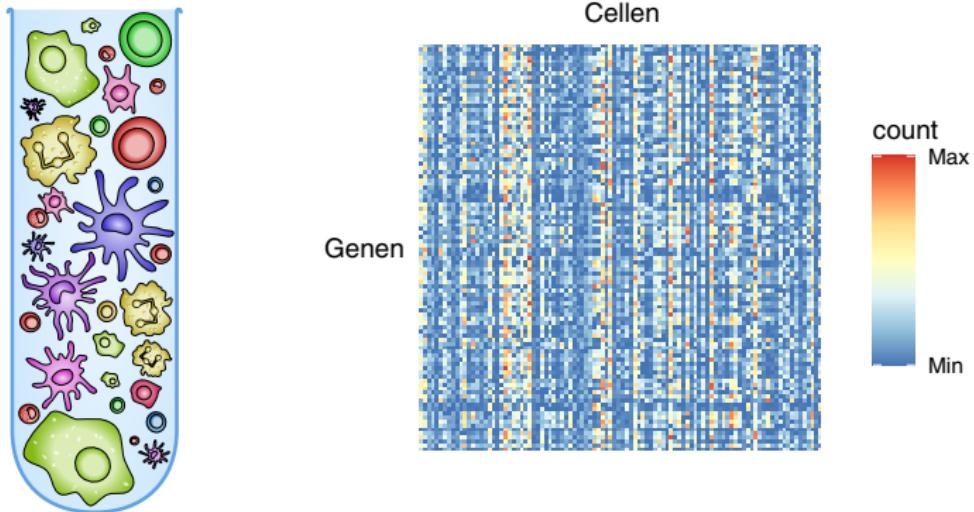
# Moleculen tellen met scRNA-seq



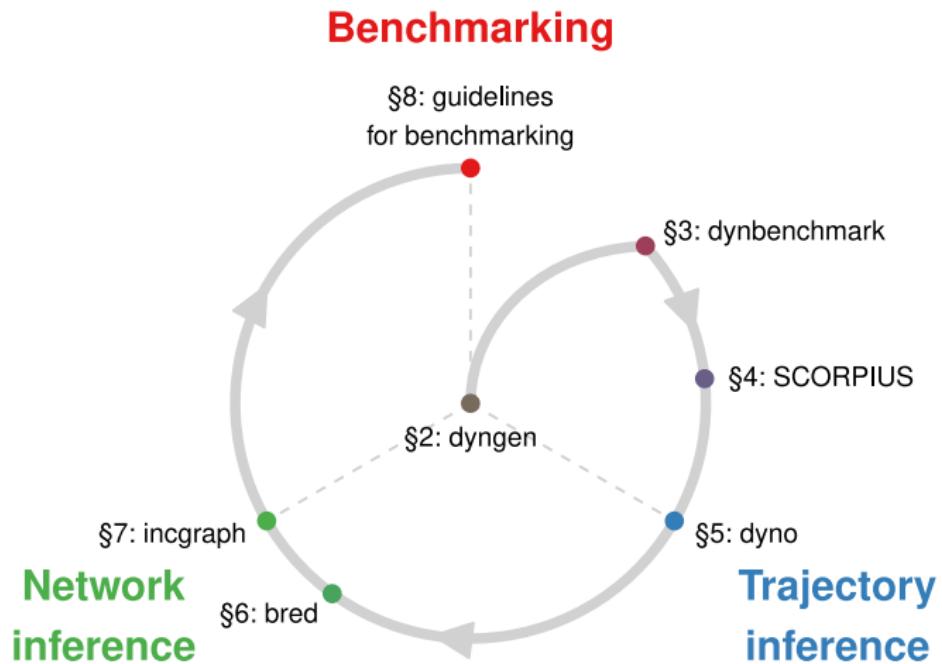
# Moleculen tellen met scRNA-seq



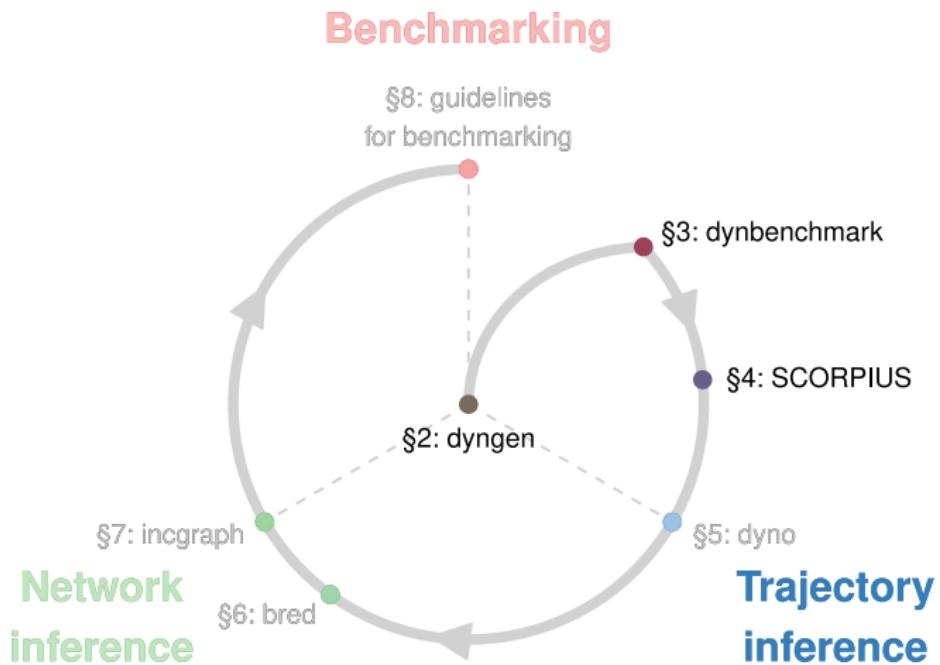
# Moleculen tellen met scRNA-seq



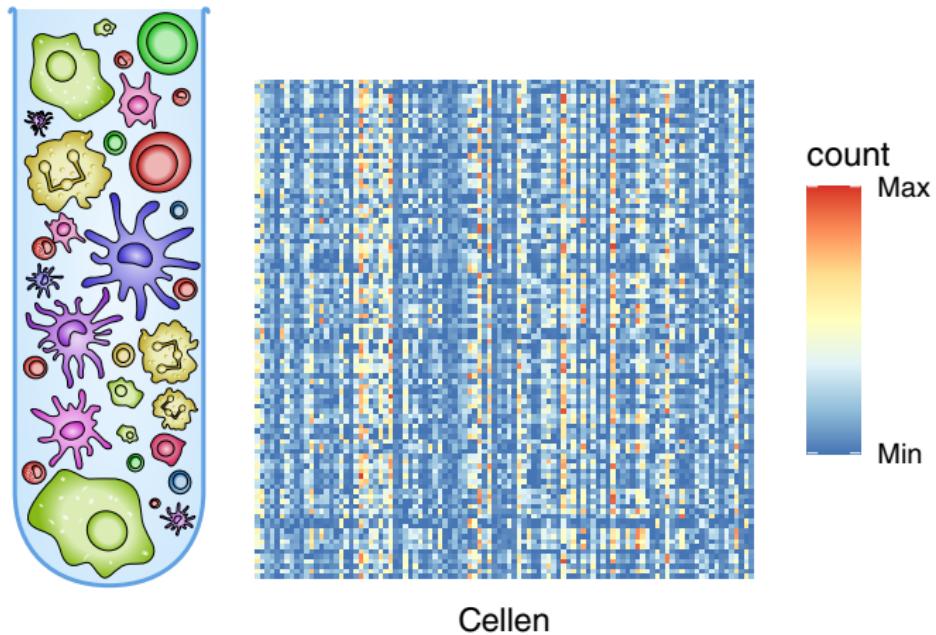
# Opbouw van de thesis



# Opbouw van de thesis

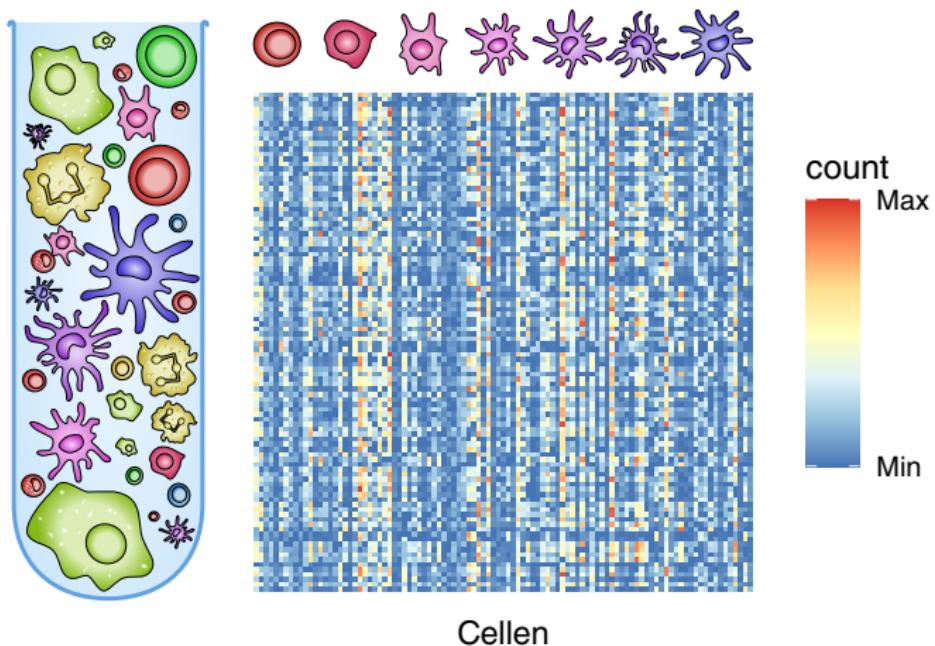


Yvan in 2015:

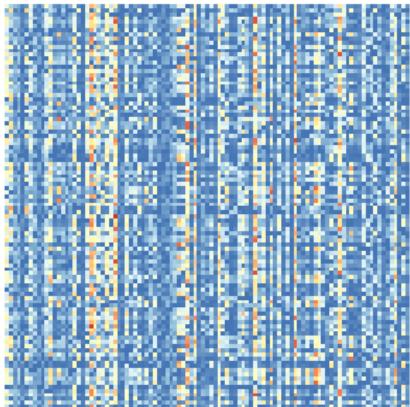


Yvan in 2015:

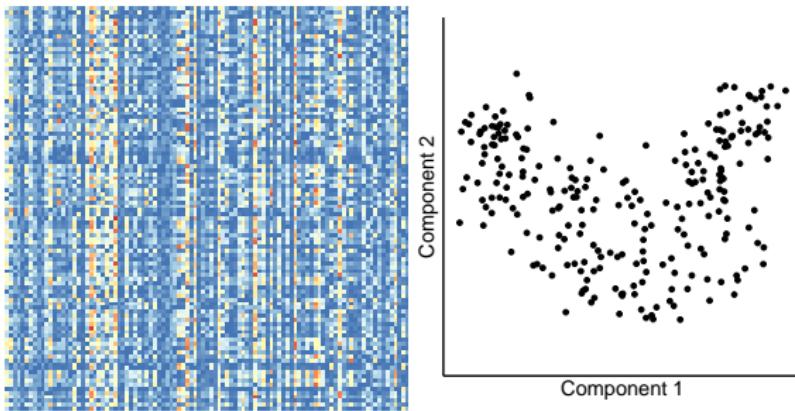
"hé Robrecht, kan je deze cellen even ordenen?"



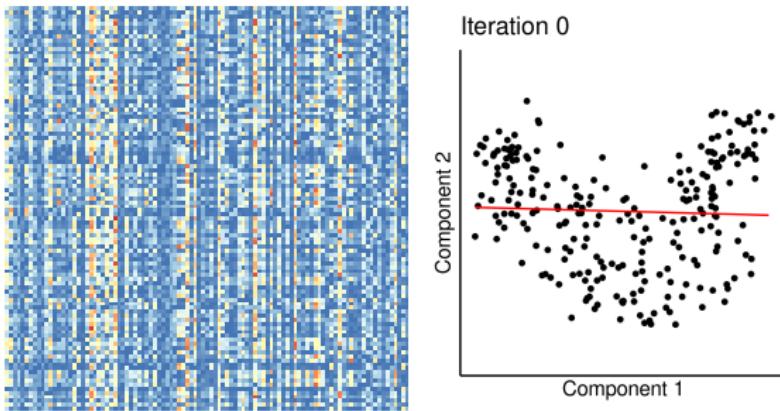
# Cellen ordenen met SCORPIUS



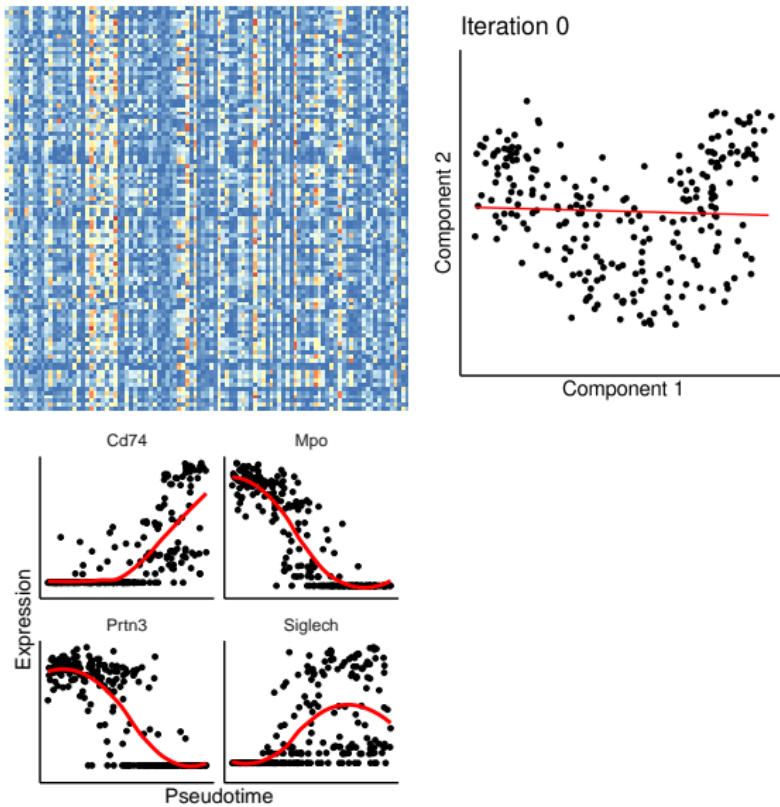
# Cellen ordenen met SCORPIUS



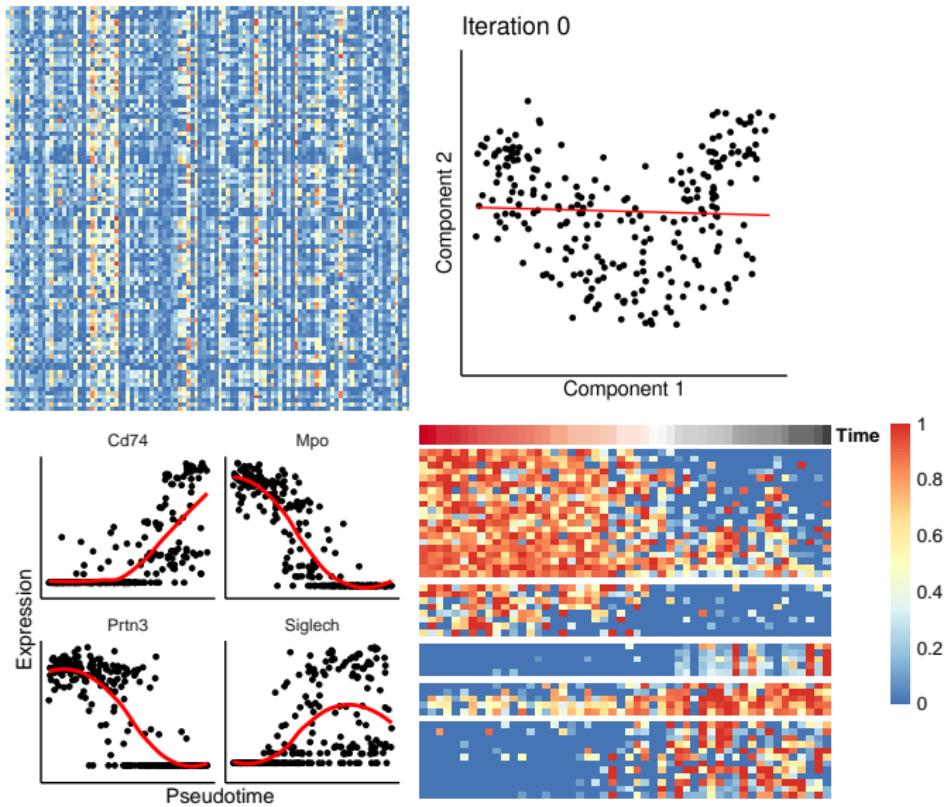
# Cellen ordenen met SCORPIUS



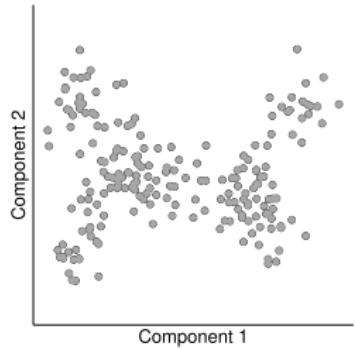
# Cellen ordenen met SCORPIUS



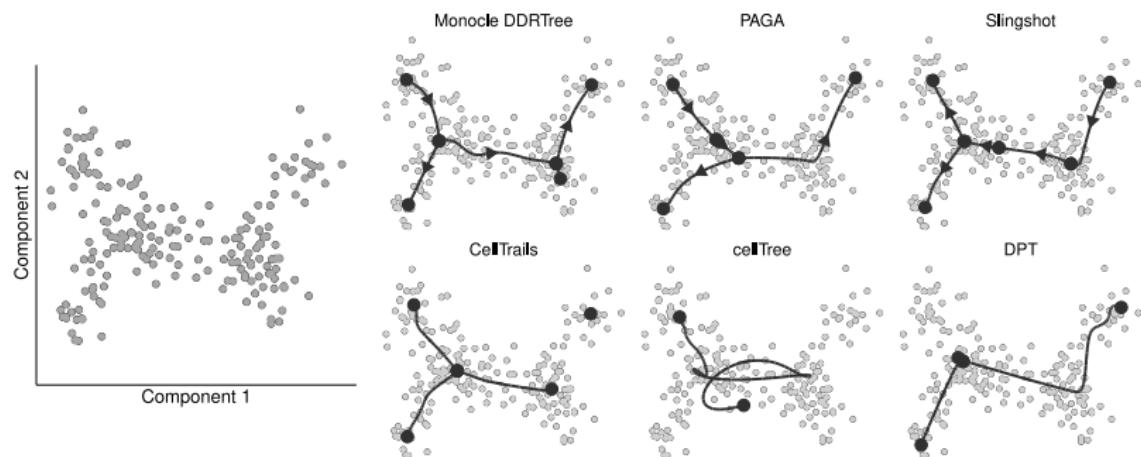
# Cellen ordenen met SCORPIUS



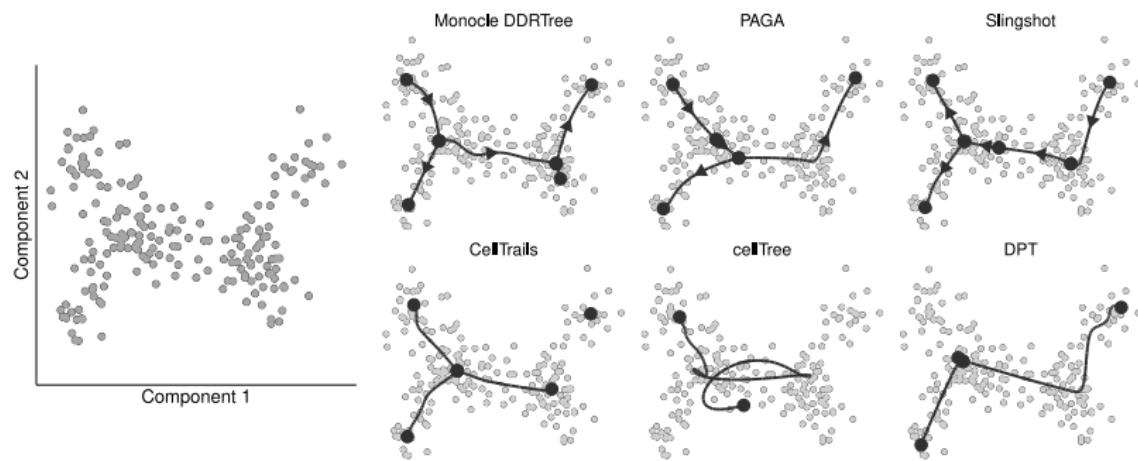
Niet alle datasets zijn even gemakkelijk



Niet alle datasets zijn even gemakkelijk  
→ Trajectory inference methoden

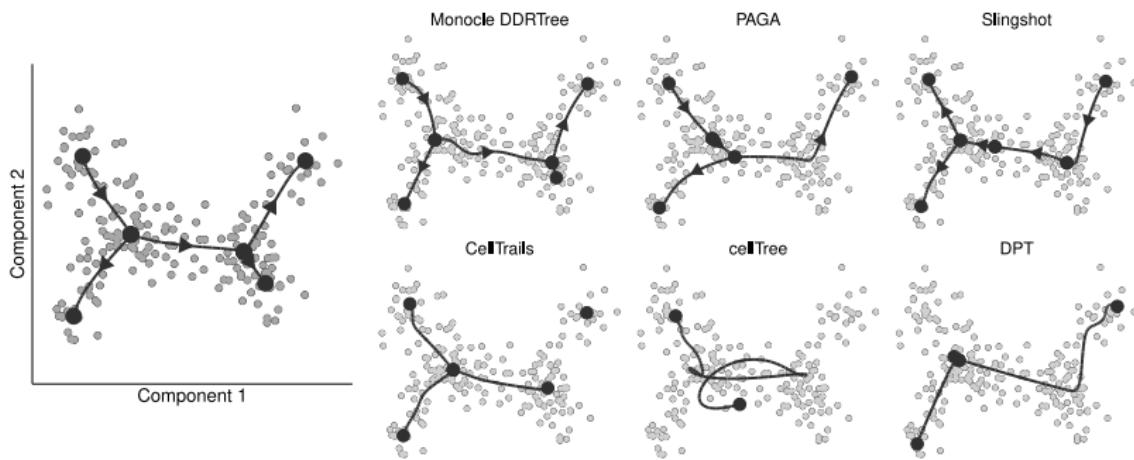


Niet alle datasets zijn even gemakkelijk  
→ Trajectory inference methoden



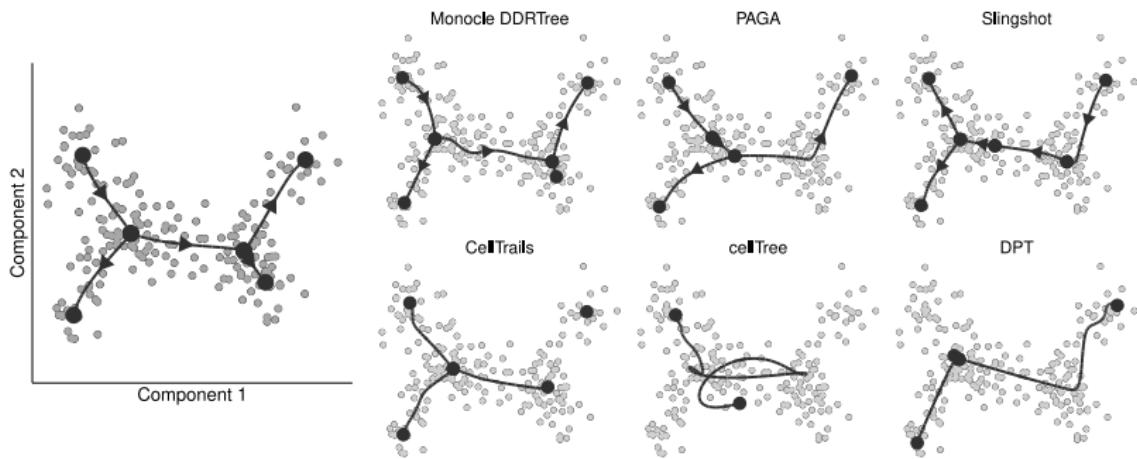
Zeer populair: >70 methoden

Niet alle datasets zijn even gemakkelijk  
→ Trajectory inference methoden



Zeer populair: >70 methoden

Niet alle datasets zijn even gemakkelijk  
→ Trajectory inference methoden



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

## Uitdagingen voor het uitvoeren van een vergelijking

## Uitdagingen voor het uitvoeren van een vergelijking

- 45 verschillende tools op meerdere computers

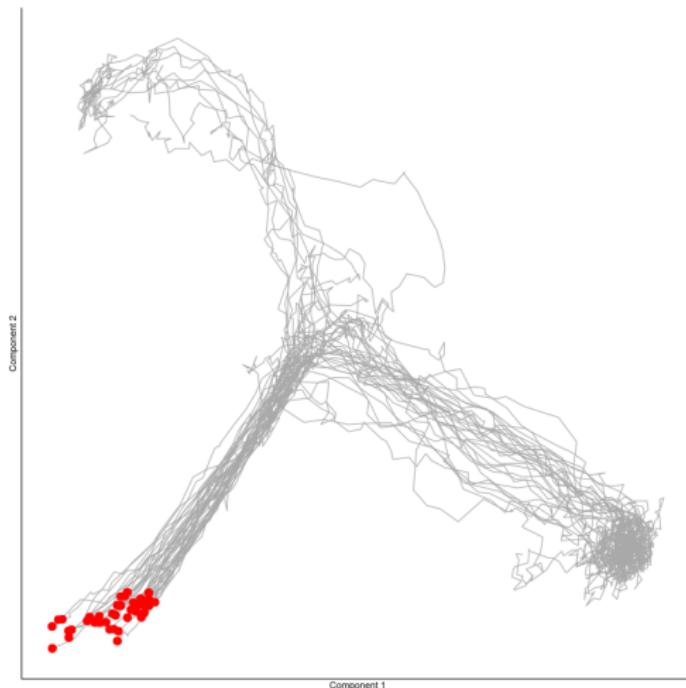
## Uitdagingen voor het uitvoeren van een vergelijking

- 45 verschillende tools op meerdere computers
- Nog niet voldoende datasets, experimenten zijn zeer duur

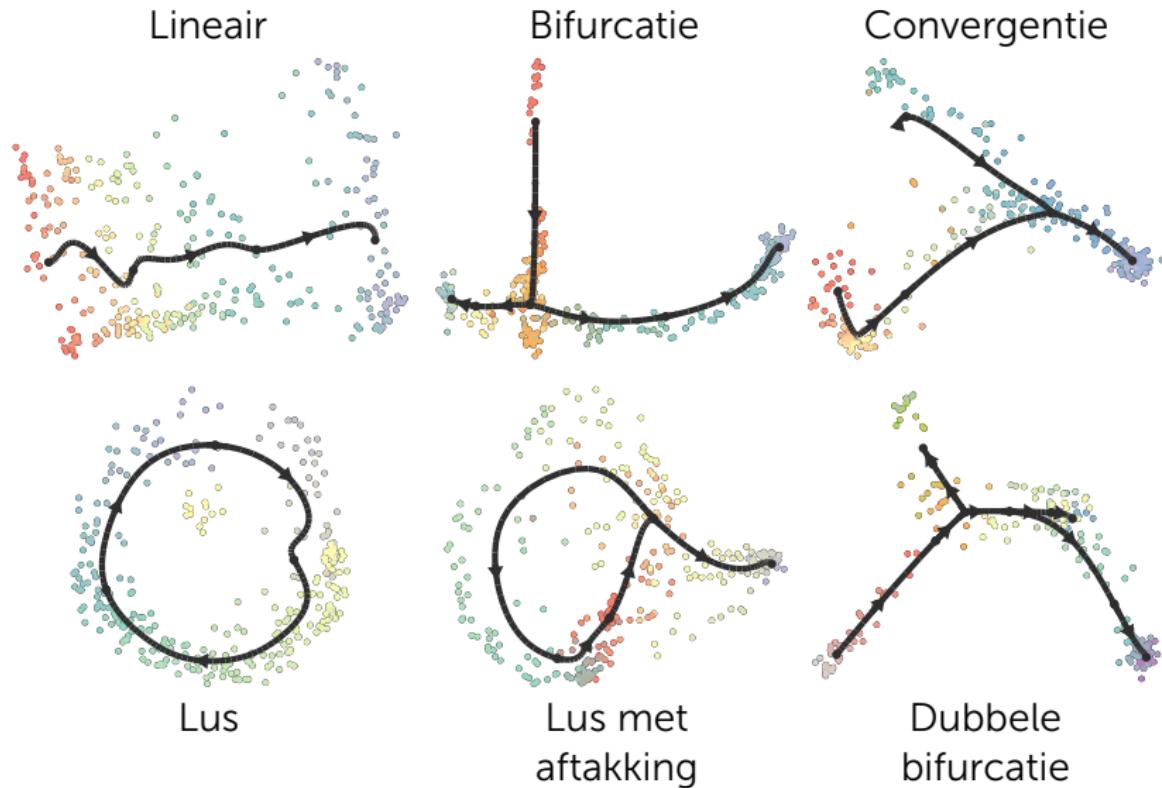
## Uitdagingen voor het uitvoeren van een vergelijking

- 45 verschillende tools op meerdere computers
- Nog niet voldoende datasets, experimenten zijn zeer duur
- Nog geen metrieken

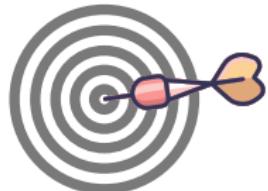
# dyngen: Simulatie van virtuele cellen



# Simulatie van virtuele cellen

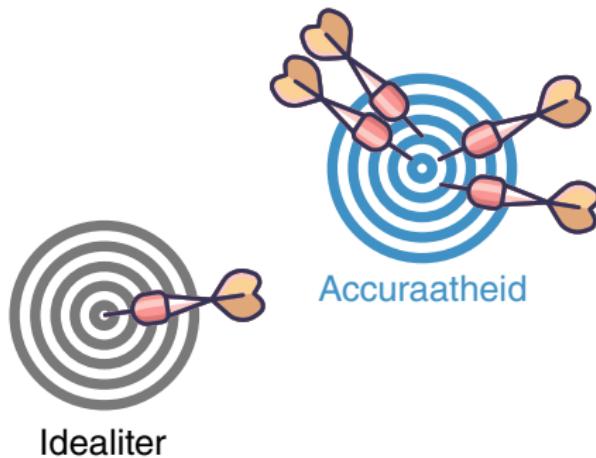


# Grootschalige evaluatie van trajectory inference methoden

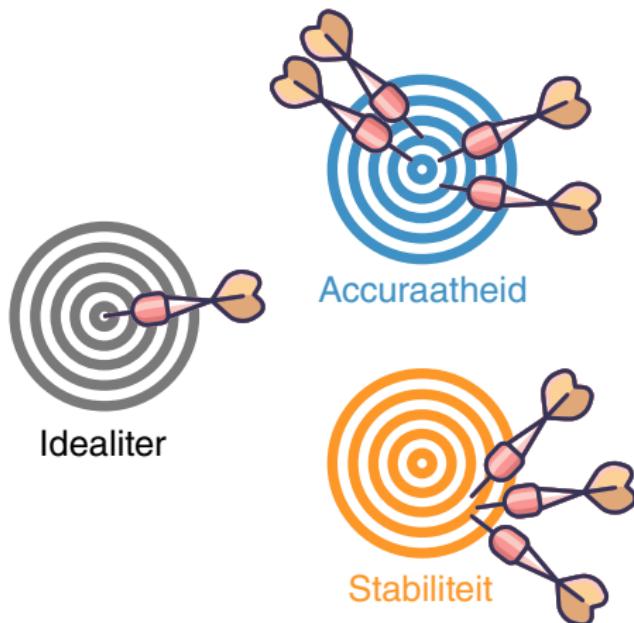


Idealiter

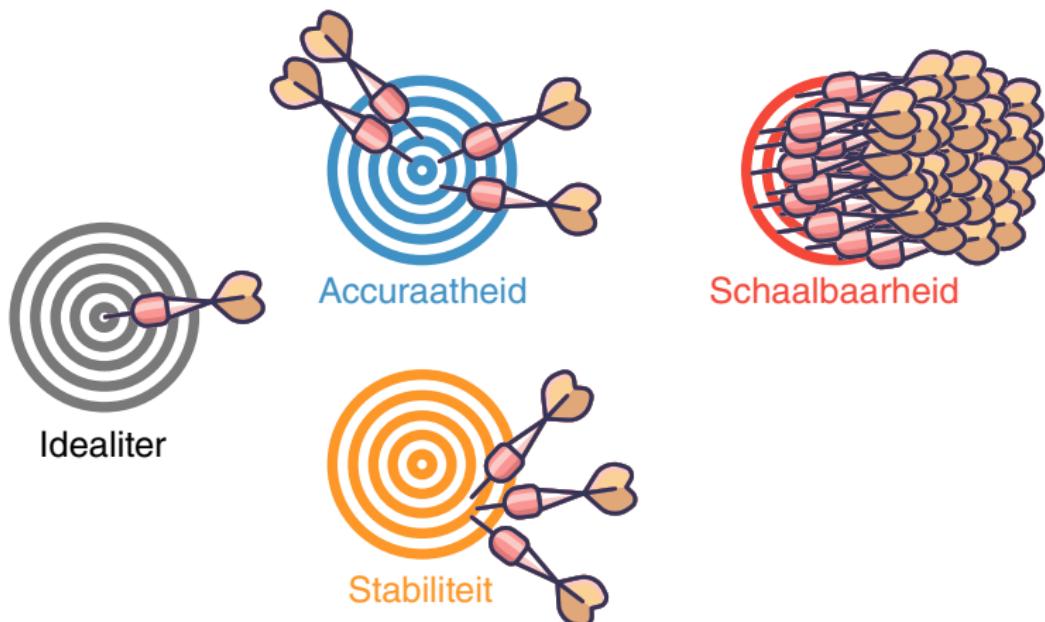
# Grootschalige evaluatie van trajectory inference methoden



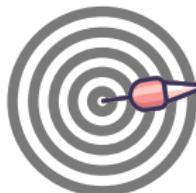
# Grootschalige evaluatie van trajectory inference methoden



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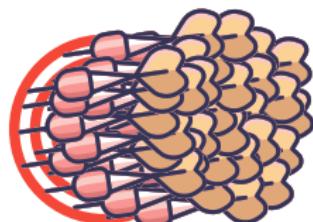
# Grootschalige evaluatie van trajectory inference methoden



Idealiter



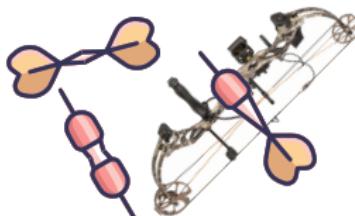
Accuraatheid



Schaalbaarheid

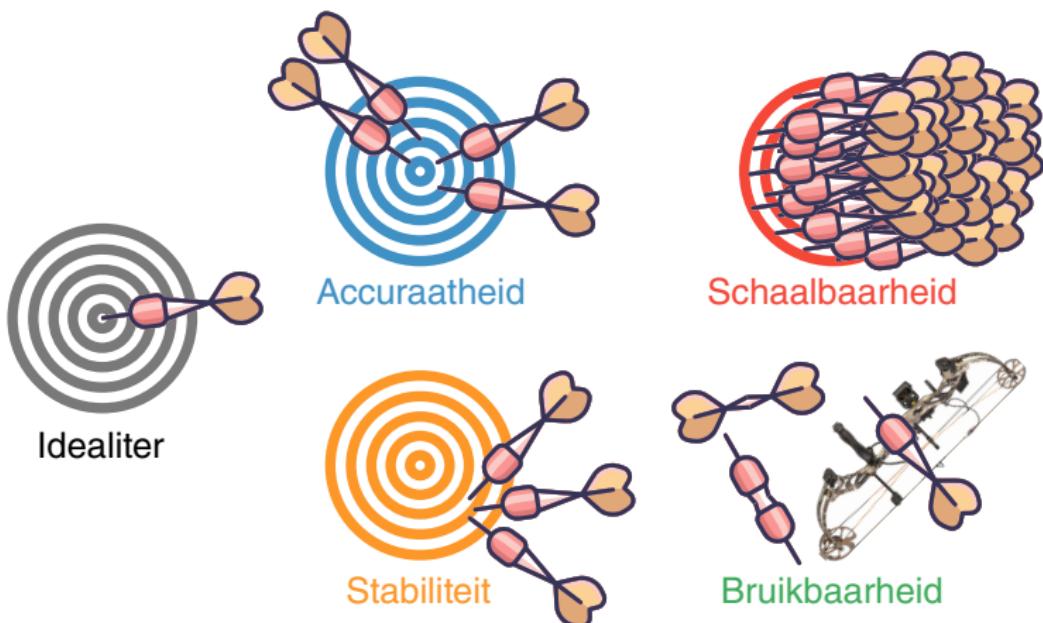


Stabiliteit

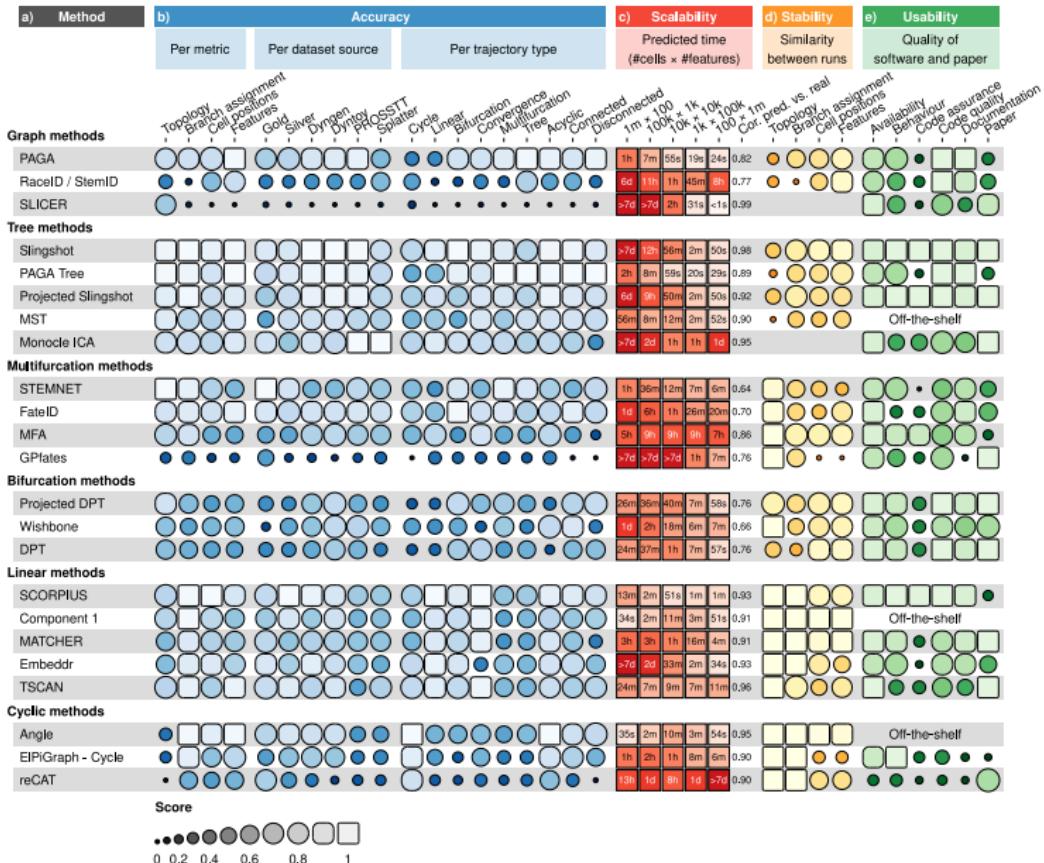


Bruikbaarheid

# Grootschalige evaluatie van trajectory inference methoden



# Resultaten van evaluatie



# Set van richtlijnen voor gebruikers

dynguidelines

Tutorial Citation

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

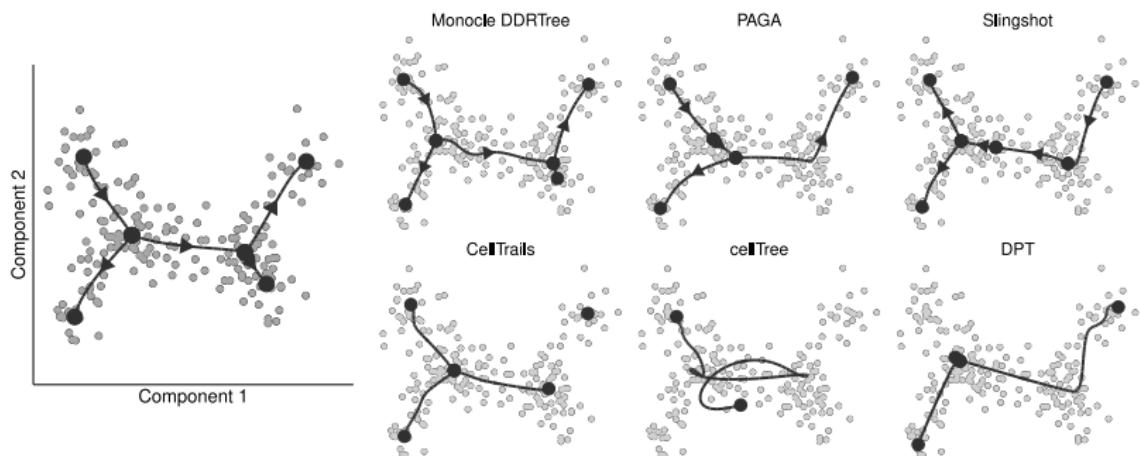
Scalability COMPUTED  
Number of cells: 1000  
Number of features (genes): 1000  
Time limit: 10s (1h)  
Memory limit: 10MB (10GB)

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

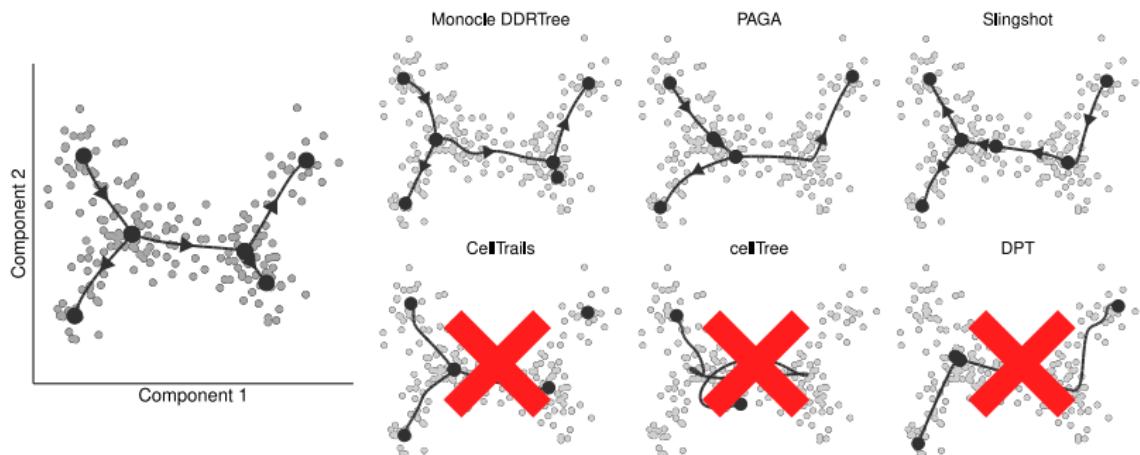
Benchmark study Evaluating methods with dynbenchmark Part of

Method	Accuracy	Scalability	Stability
Slingshot	100	8s	942MB
SCORPIUS	96	3s	507MB
Angle	92	1s	308MB
PAGA	99	15s	559MB
Embeddr	89	5s	581MB
MST	89	4s	572MB
Waterfall	89	5s	369MB
TSCAN	88	5s	476MB
Component 1	87	1s	516MB
SLICE	83	16s	713MB
Monocle DDRTree	82	41s	647MB
EPIGraph Linear	81	1m	573MB

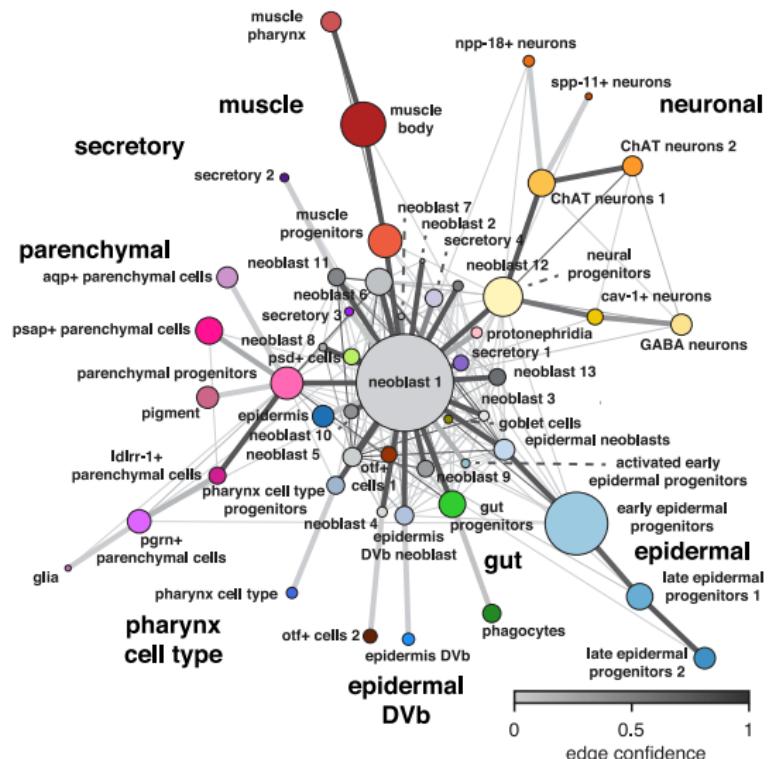
# Eliminatie van sommige methoden



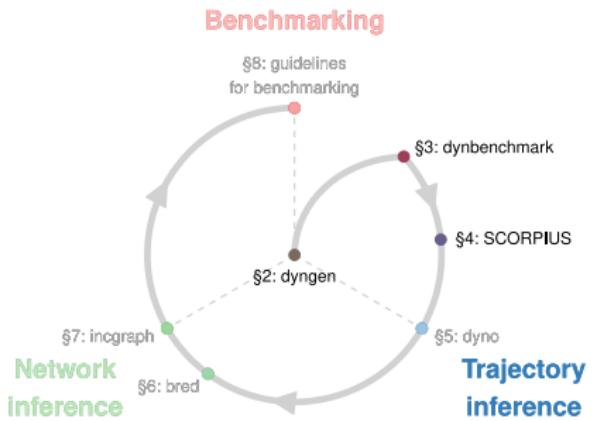
# Eliminatie van sommige methoden



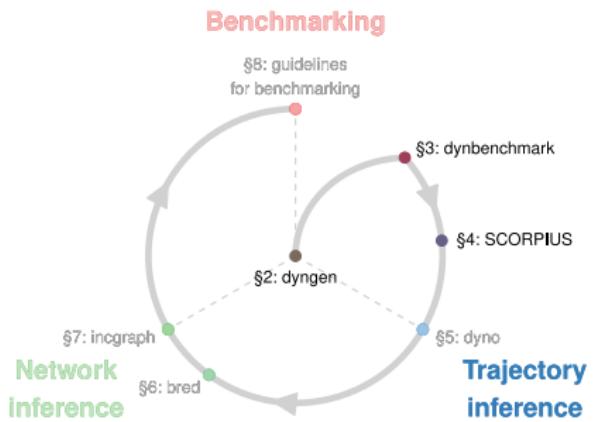
# Tot nader order: pas meerdere methoden toe en vergelijk



# Relevantie van dit werk



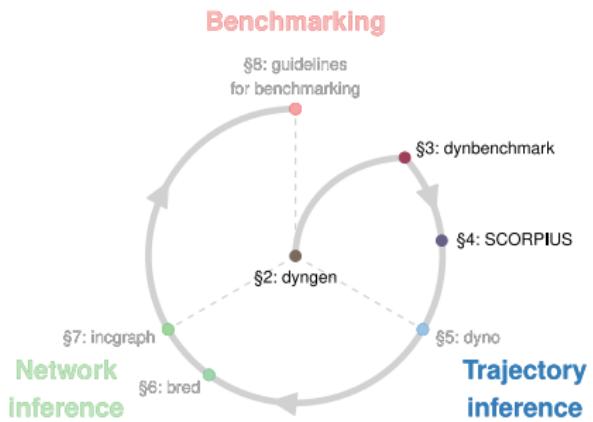
# Relevantie van dit werk



## Evaluatie:

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

# Relevantie van dit werk



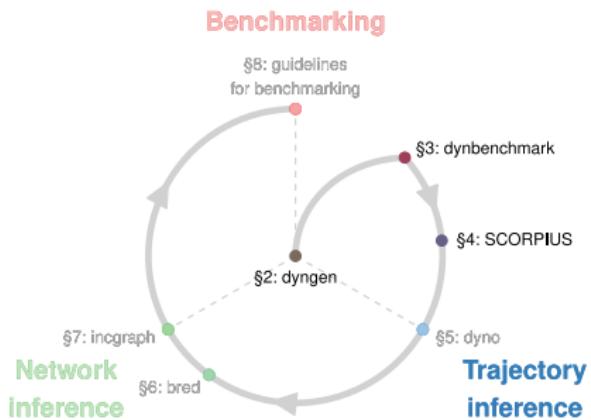
## Evaluatie:

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

## Simulator:

- Evaluatie van andere soorten analyses in single-cell data

# Relevantie van dit werk



## Evaluatie:

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

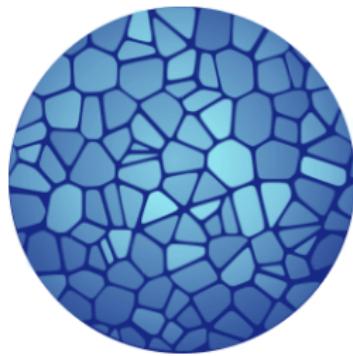
## Simulator:

- Evaluatie van andere soorten analyses in single-cell data

## SCORPIUS:

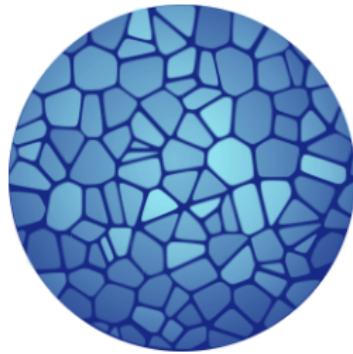
- Wordt gebruikt om veranderingen in cellen te onderzoeken en visualiseren

# Wat brengt de toekomst?



Human cell atlas

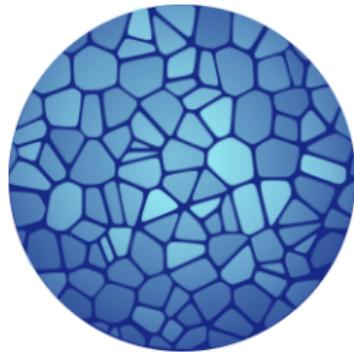
# Wat brengt de toekomst?



## Human cell atlas

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

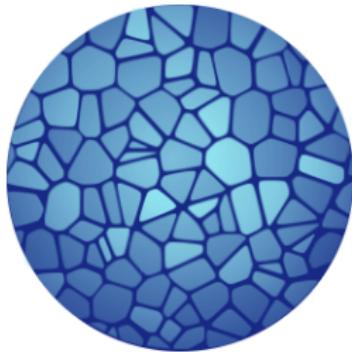
# Wat brengt de toekomst?



## Human cell atlas

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