

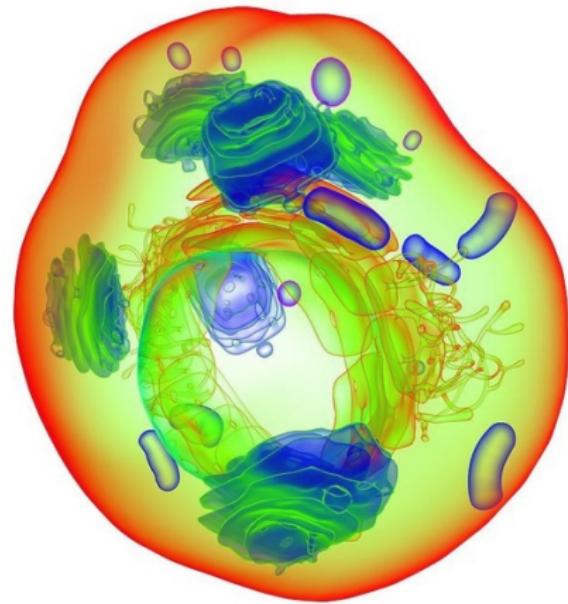
Modelling single-cell dynamics with trajectories and gene regulatory networks

Robrecht Cannoodt

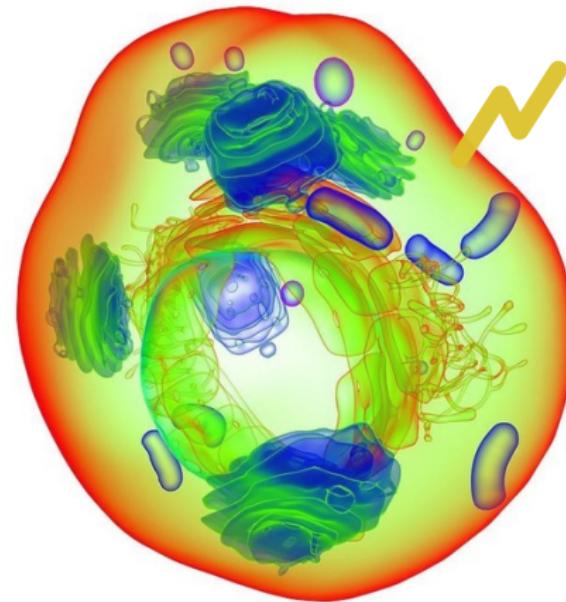
16 december 2019



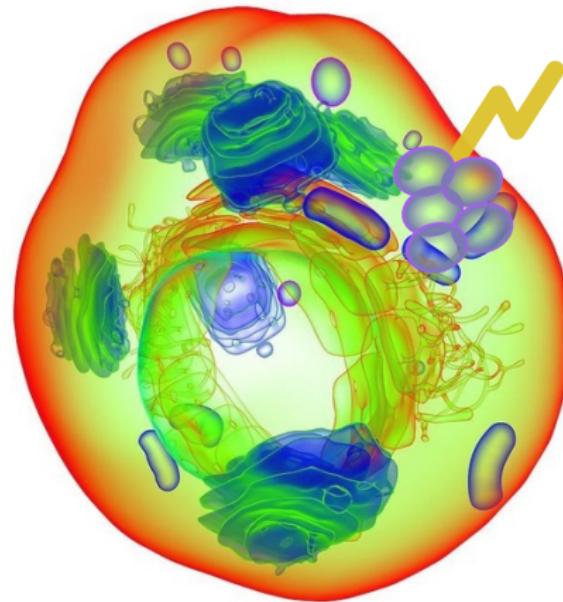
Cellen zijn dynamisch



Cellen zijn dynamisch

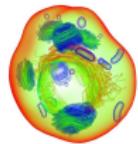


Cellen zijn dynamisch



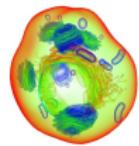
Hoe maken cellen eiwitten aan?

Cel

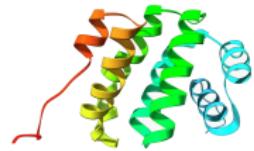


Hoe maken cellen eiwitten aan?

Cel

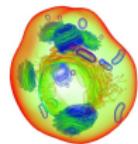


Eiwit

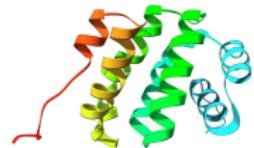


Hoe maken cellen eiwitten aan?

Cel



Eiwit



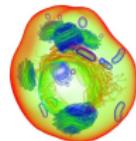
Restaurant



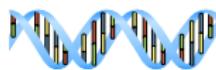
Sushi

Hoe maken cellen eiwitten aan?

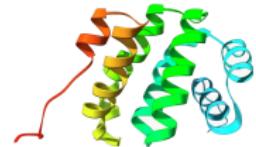
Cel



DNA



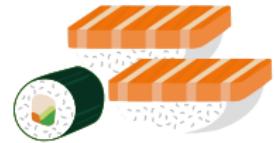
Eiwit



Restaurant



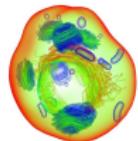
Kookboek



Sushi

Hoe maken cellen eiwitten aan?

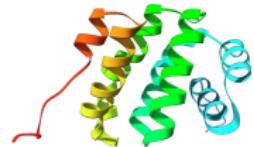
Cel



DNA



Eiwit

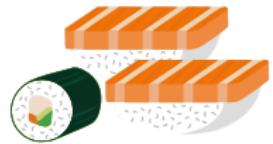


Restaurant



Kookboek

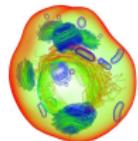
Recept



Sushi

Hoe maken cellen eiwitten aan?

Cel



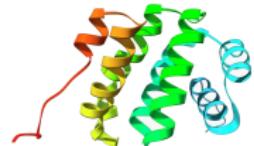
DNA



RNA



Eiwit



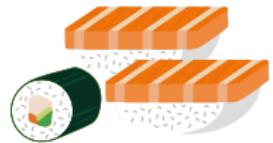
Recept



Restaurant

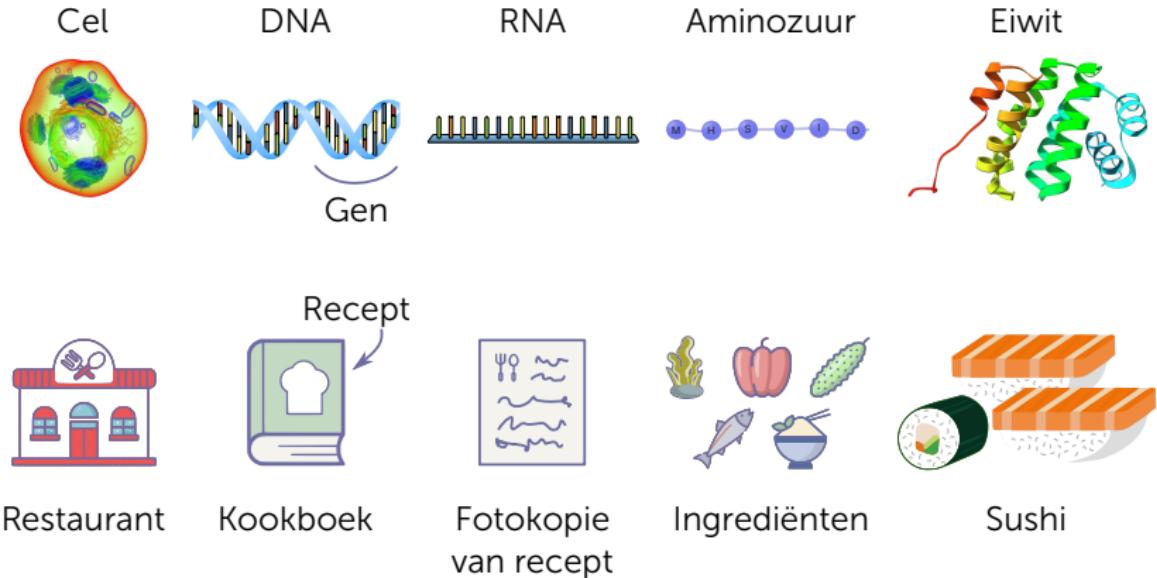
Kookboek

Fotokopie
van recept

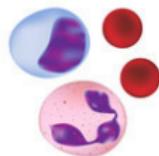


Sushi

Hoe maken cellen eiwitten aan?



Het menselijk lichaam bevat >210 soorten cellen



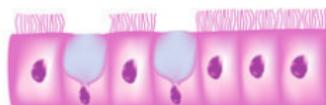
Blood cells



Surface skin cells



Bone cell



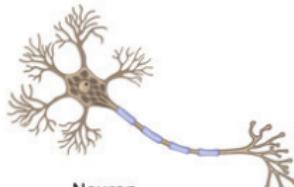
Columnar epithelial and Goblet cells



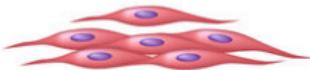
Cardiac muscle cell



Skeletal muscle cells



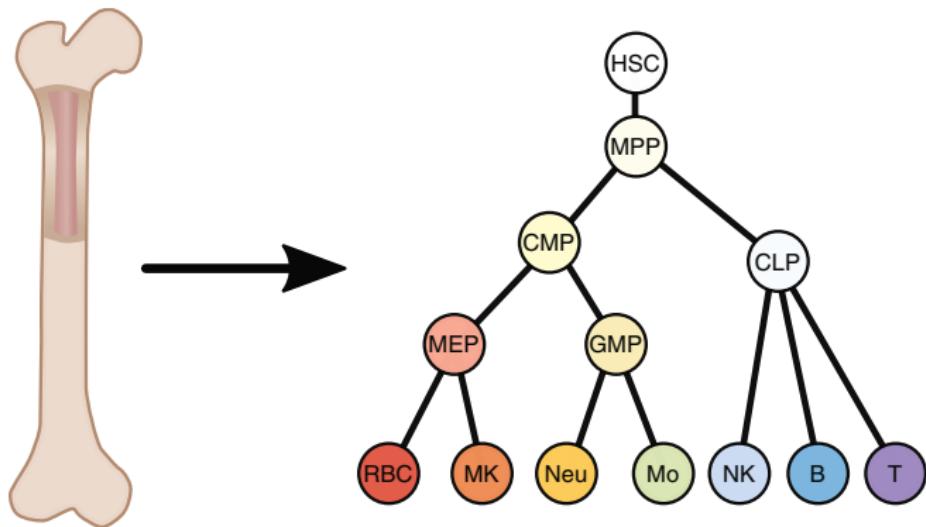
Neuron



Smooth muscle cells

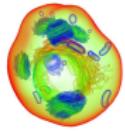
(placeholder figuur)

Cellen kunnen ontwikkelen van één type naar een ander

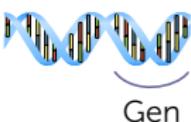


Welke types cellen komen voor in een populatie?

Cel



DNA



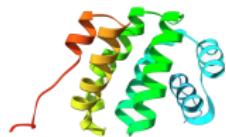
RNA



Aminozuur



Eiwit



Restaurant



Kookboek

Recept



Fotokopie
van recept

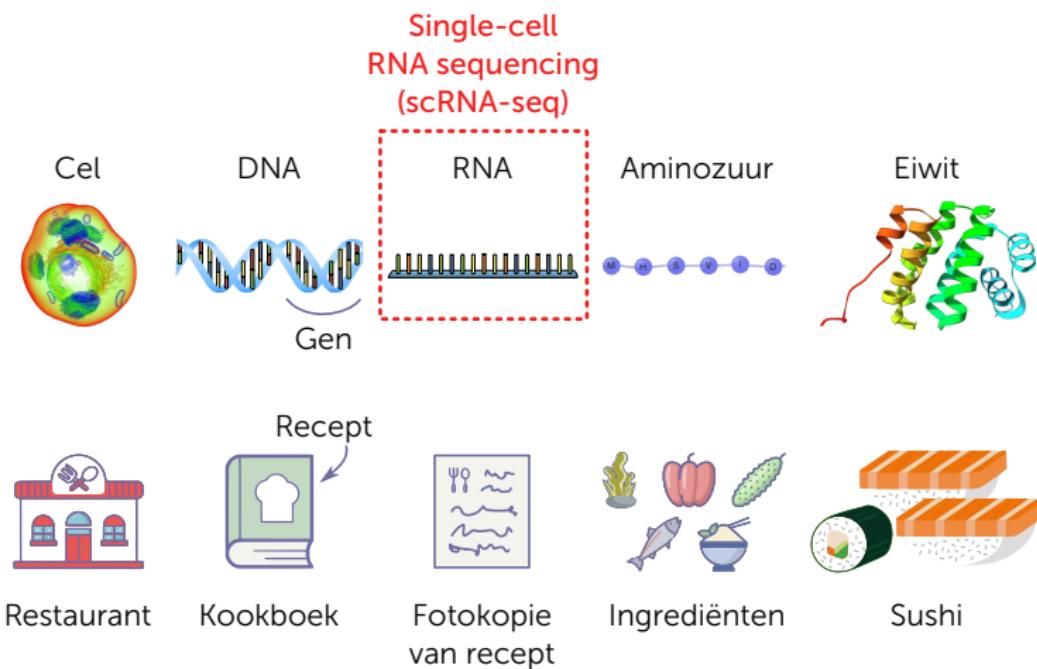


Ingrediënten



Sushi

Welke types cellen komen voor in een populatie?

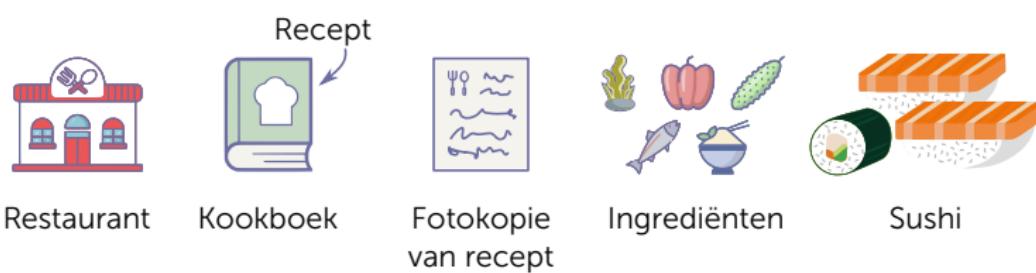
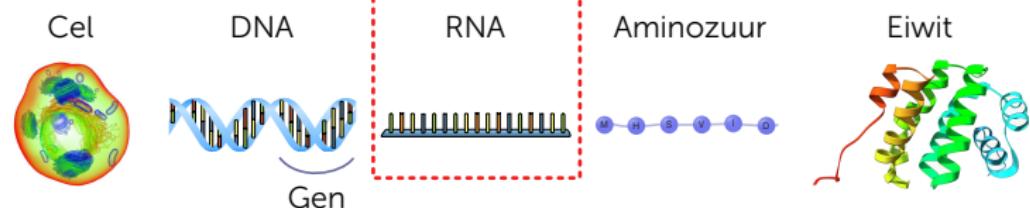


Welke types cellen komen voor in een populatie?

Wat voor een cel is dit?

Wat is zijn functie?

Single-cell
RNA sequencing
(scRNA-seq)



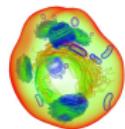
Welke types cellen komen voor in een populatie?

Wat voor een cel is dit?

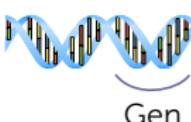
Wat is zijn functie?

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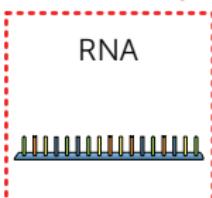
Cel



DNA



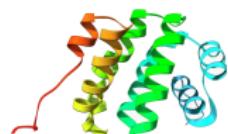
RNA



Aminozuur



Eiwit



Recept



Restaurant



Kookboek



Fotokopie
van recept



Ingrediënten

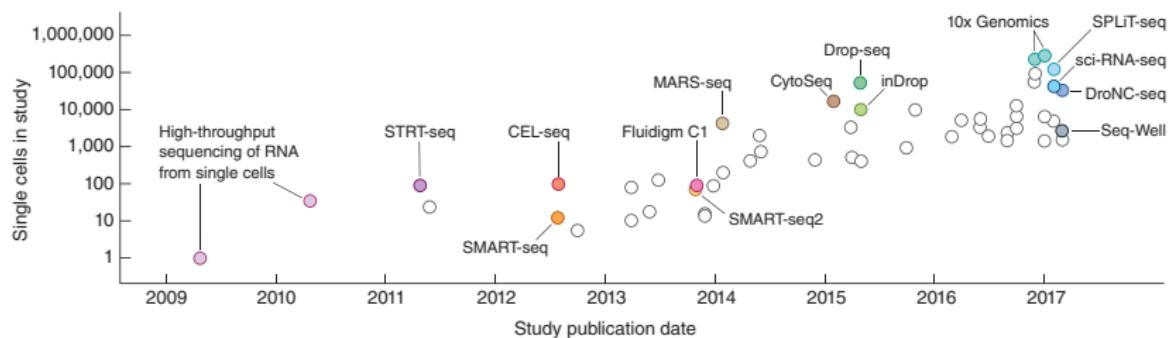
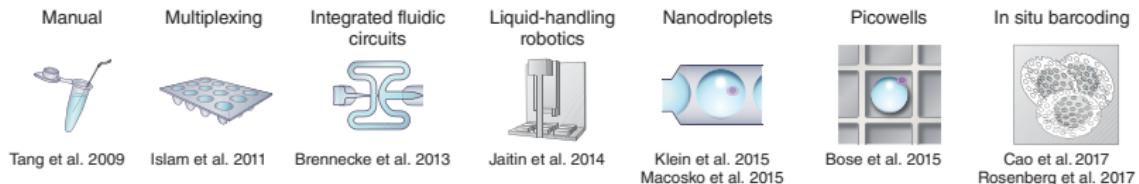


Sushi

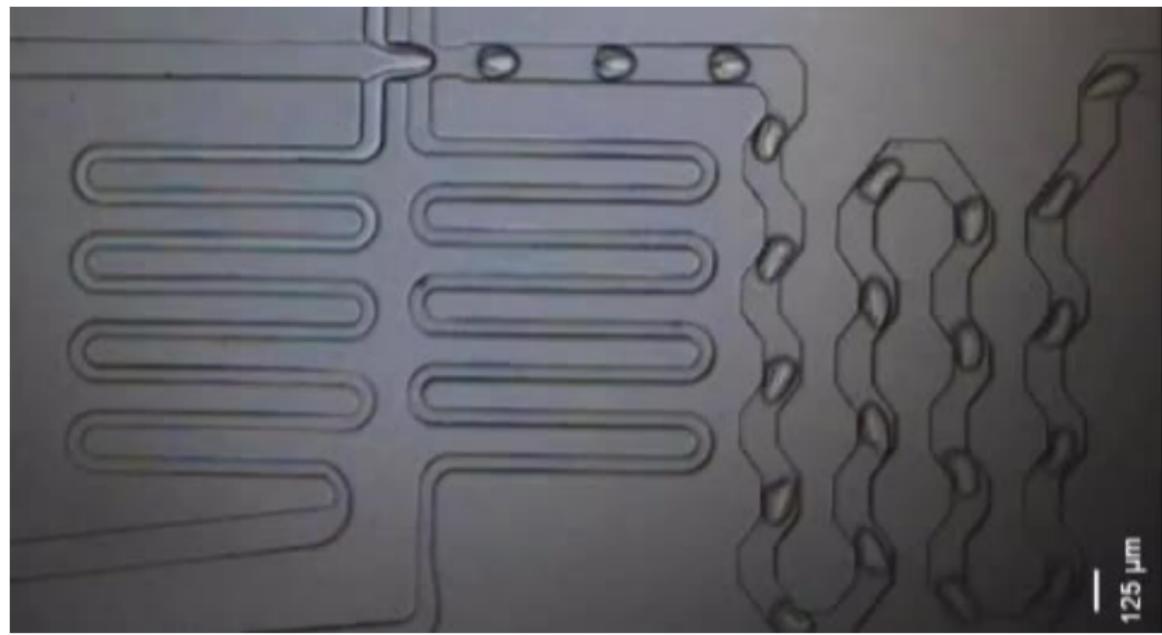
Welk type restaurant is dit?

- Mexikaans, chinees, italiaans, ...
- À la carte, all you can eat, drivethrough
- Hoeveel sterren op yelp?

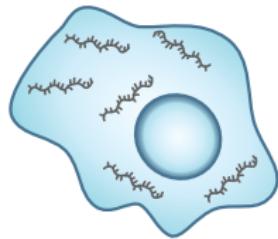
2014: doorbraak in schaalbaarheid van scRNA-seq



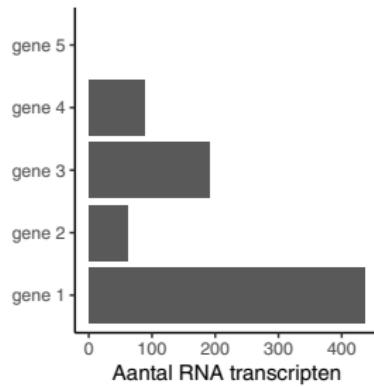
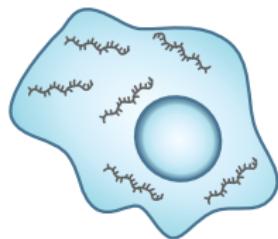
Voorbeeld van een scRNA-seq technologie: Drop-seq



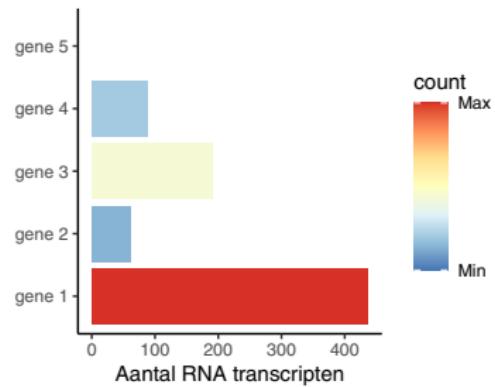
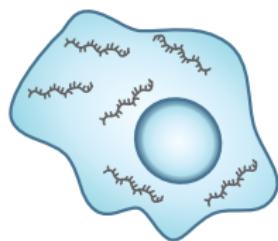
Moleculen tellen met scRNA-seq



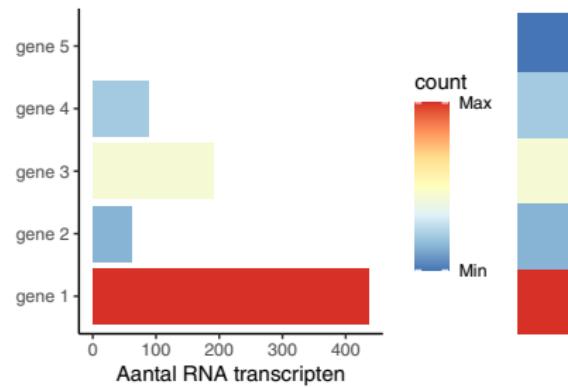
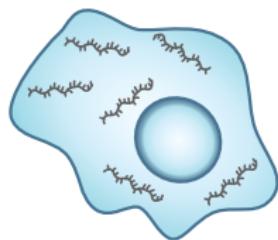
Moleculen tellen met scRNA-seq



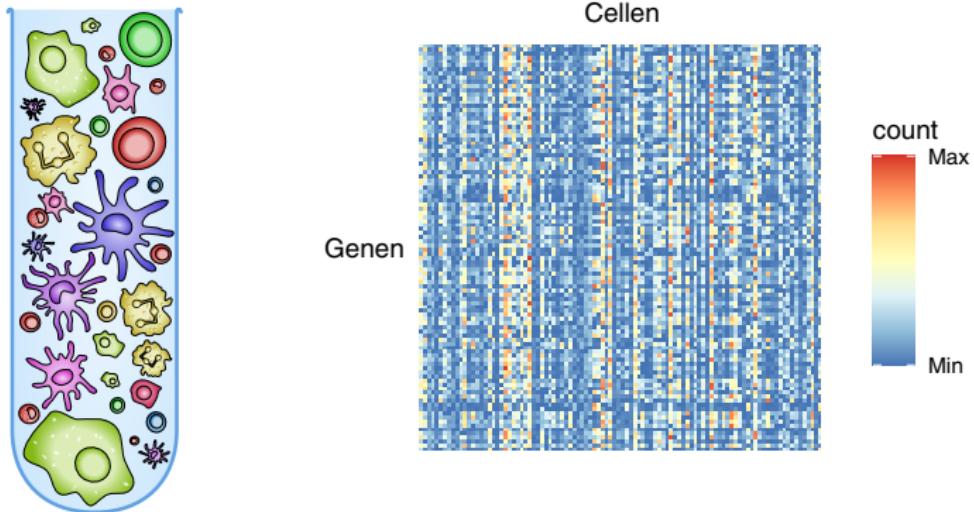
Moleculen tellen met scRNA-seq



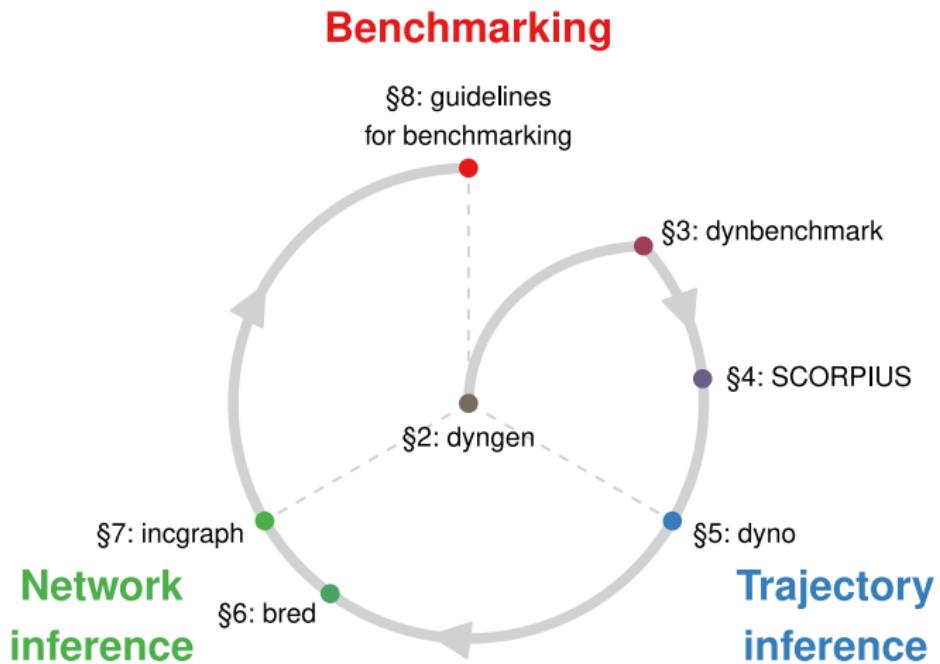
Moleculen tellen met scRNA-seq



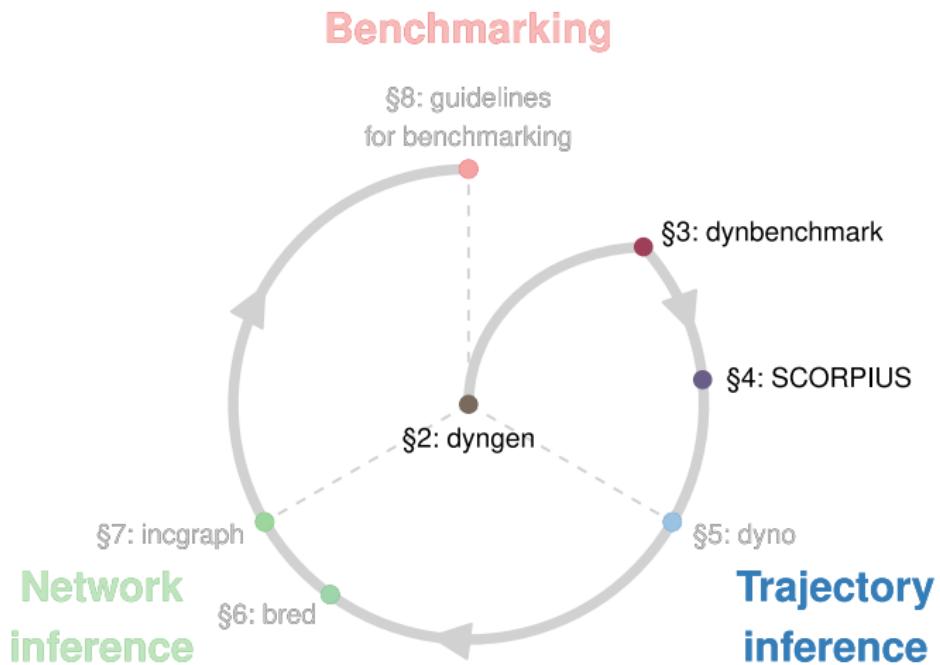
Moleculen tellen met scRNA-seq



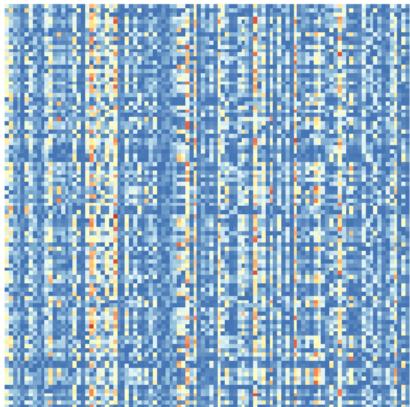
Overzicht van wetenschappelijke contributies in thesis



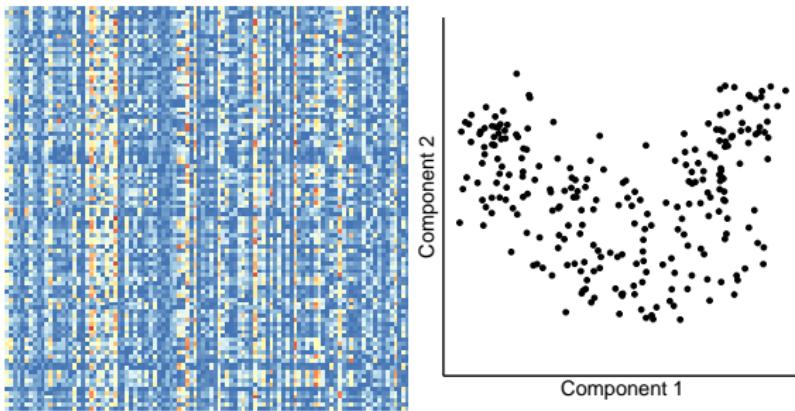
Overzicht van wetenschappelijke contributies in thesis



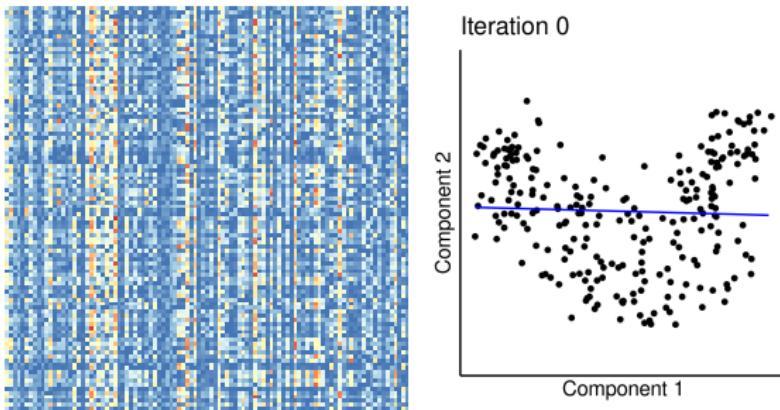
Cellen ordenen met SCORPIUS



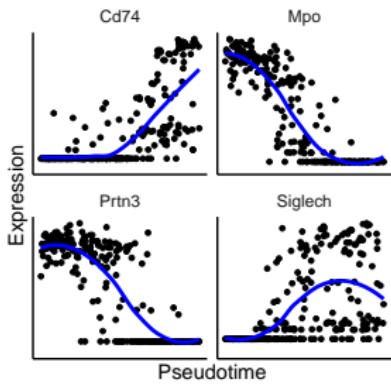
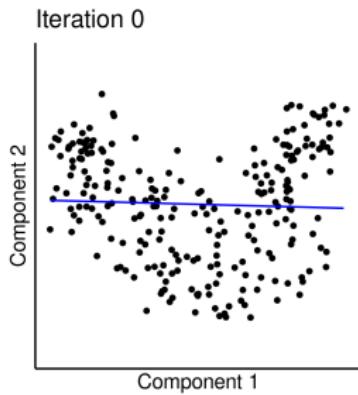
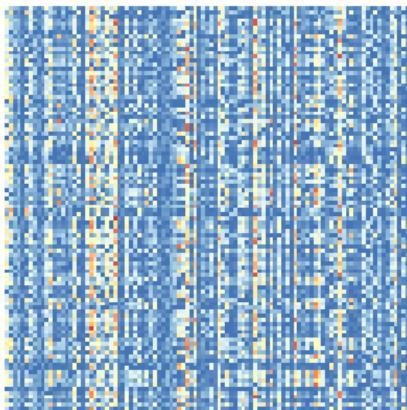
Cellen ordenen met SCORPIUS



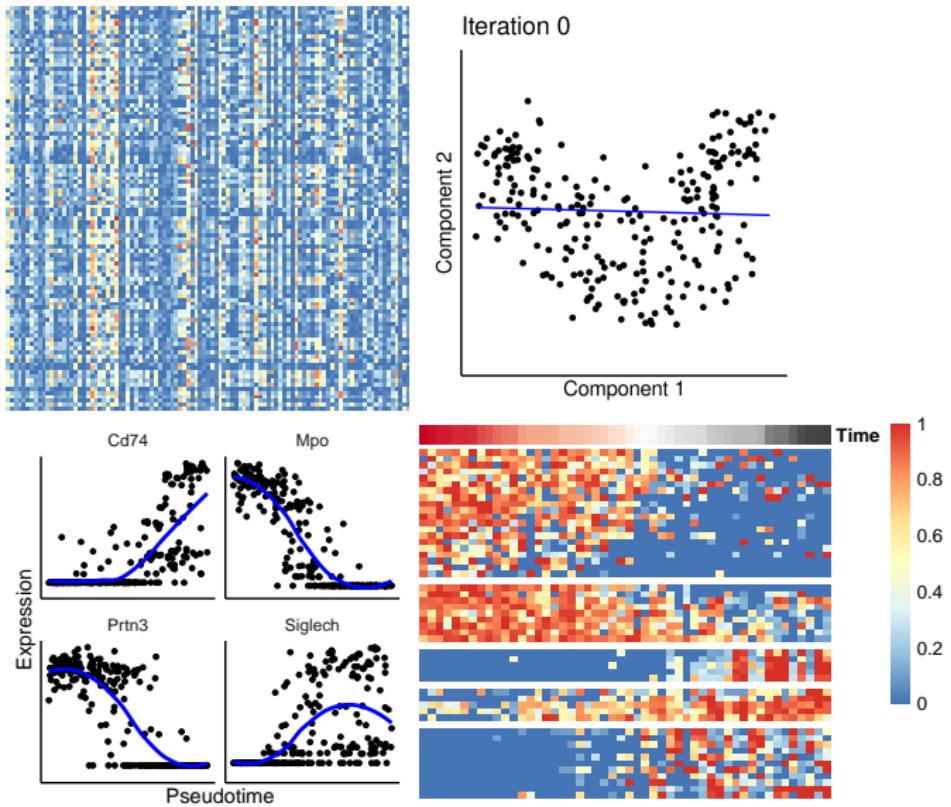
Cellen ordenen met SCORPIUS



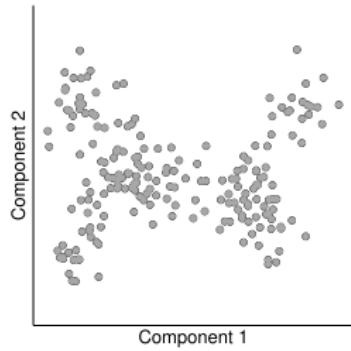
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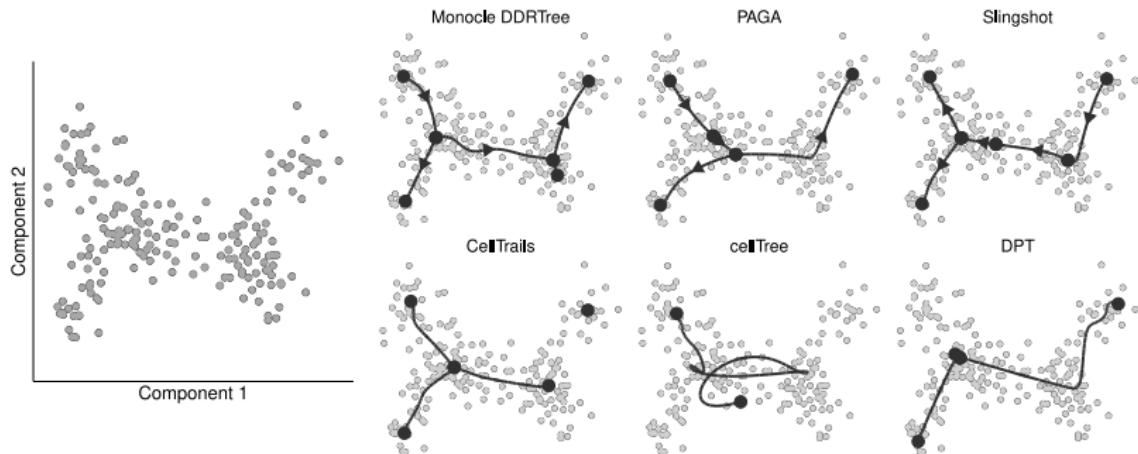
Cellen ordenen met SCORPIUS



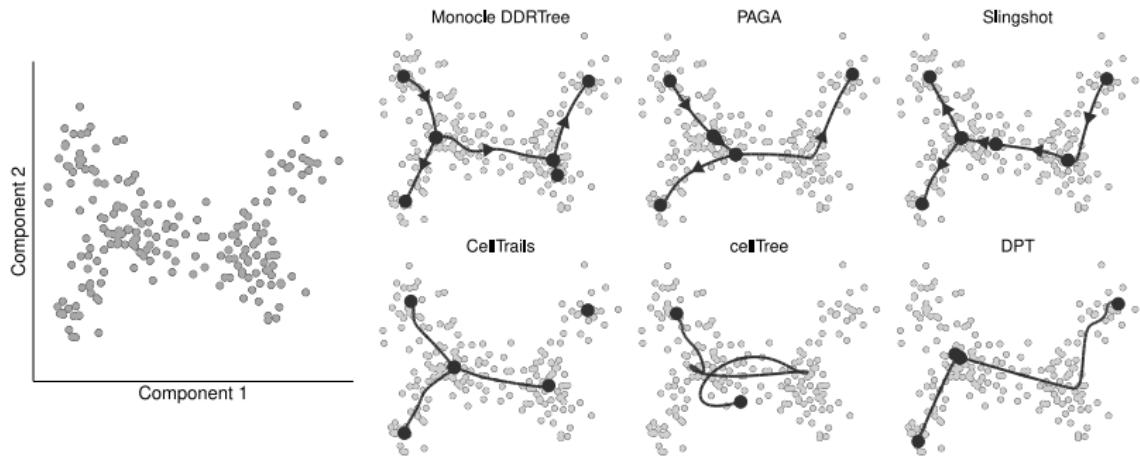
Niet alle datasets zijn even gemakkelijk



Niet alle datasets zijn even gemakkelijk

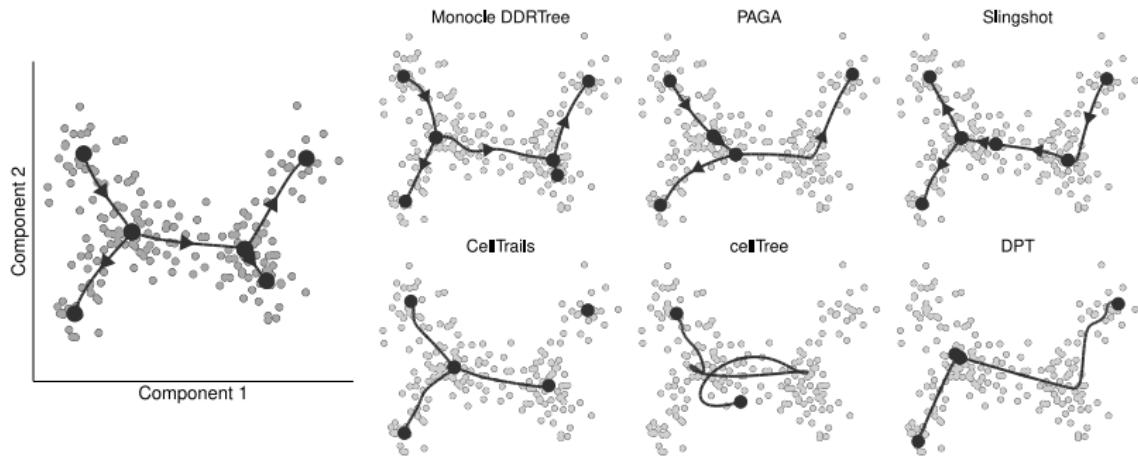


Niet alle datasets zijn even gemakkelijk



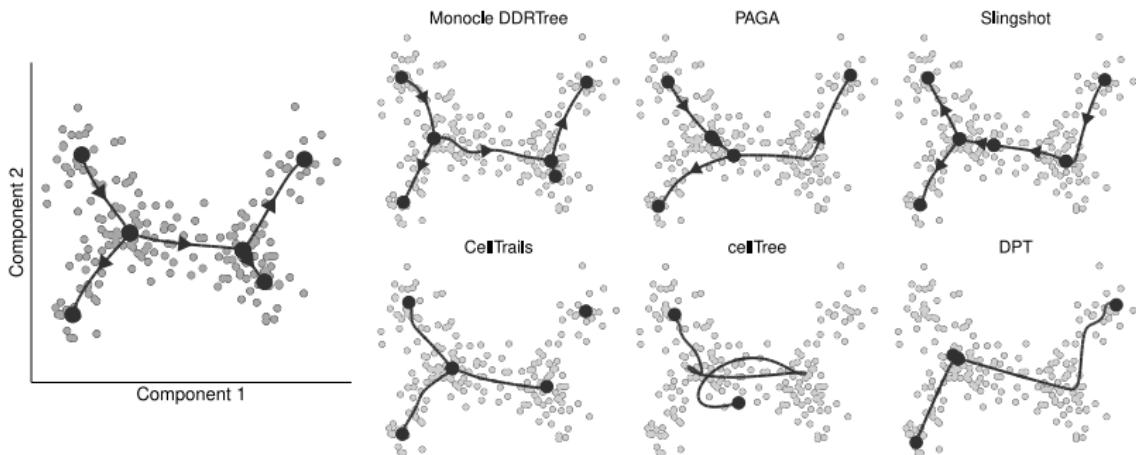
Trajectory inference; >70 methoden

Niet alle datasets zijn even gemakkelijk



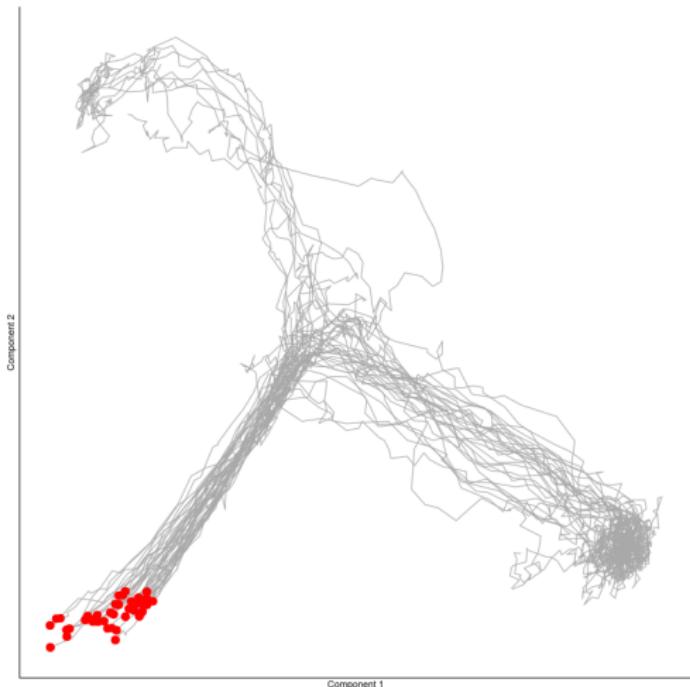
Trajectory inference; >70 methoden

Niet alle datasets zijn even gemakkelijk

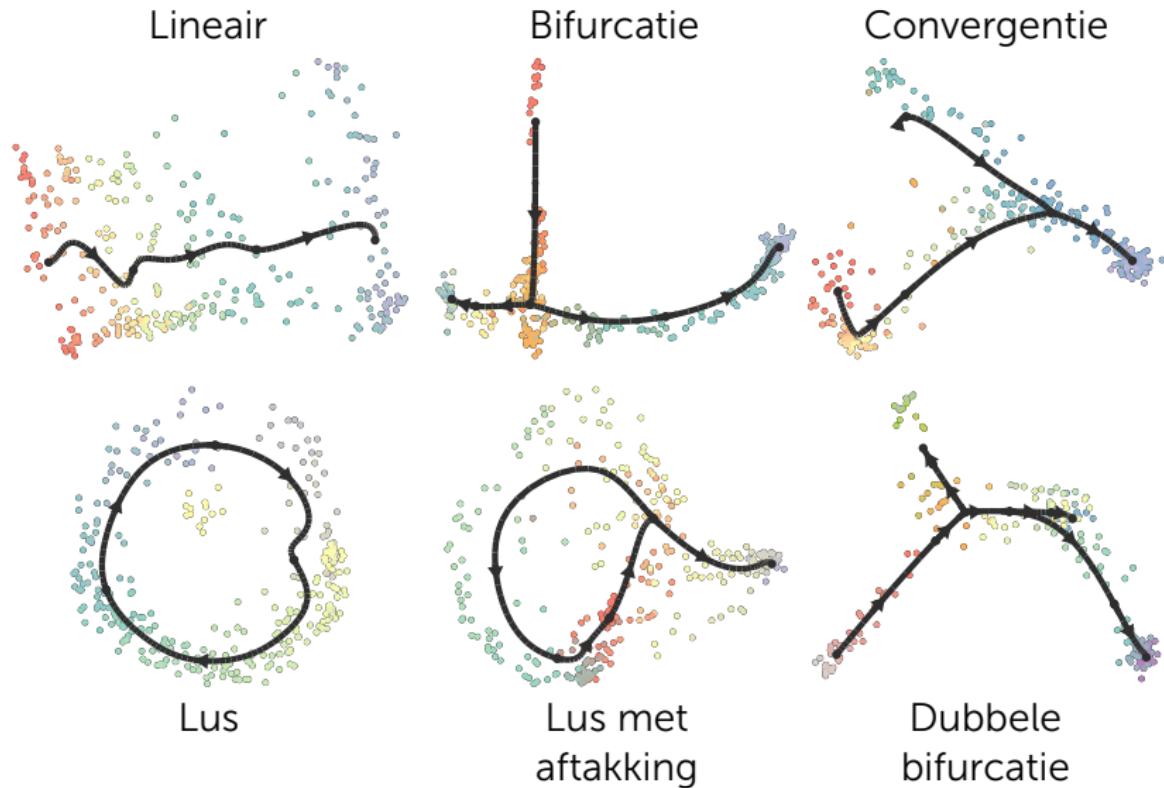


Trajectory inference; >70 methoden
Nood aan een vergelijking van methoden

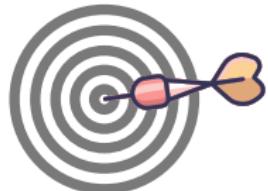
Simulatie van virtuele cellen



Simulatie van virtuele cellen

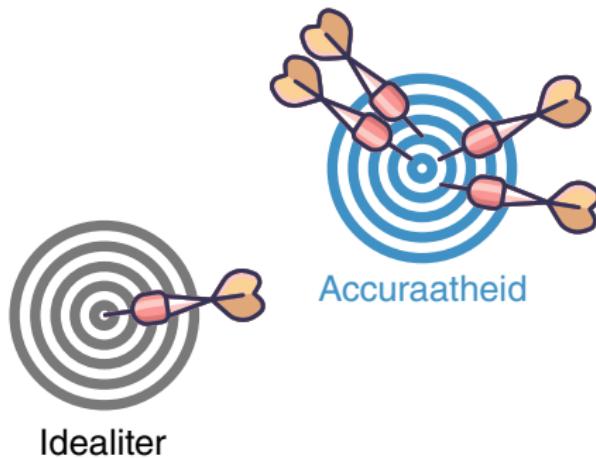


Grootschalige evaluatie van trajectory inference methoden

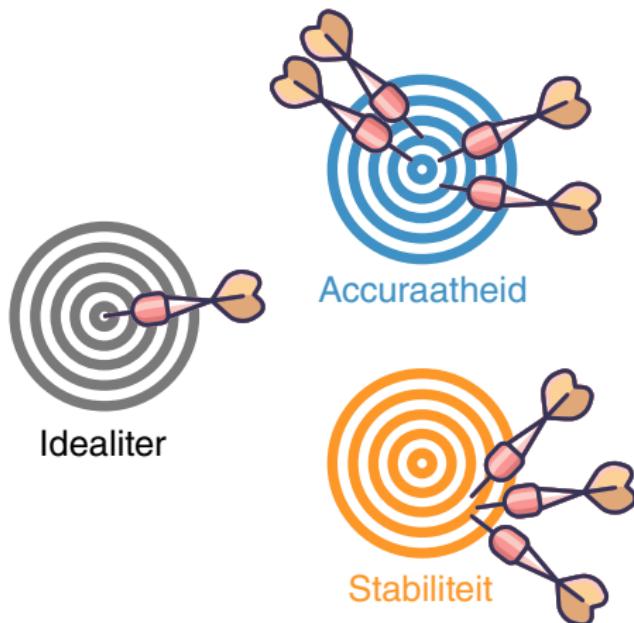


Idealiter

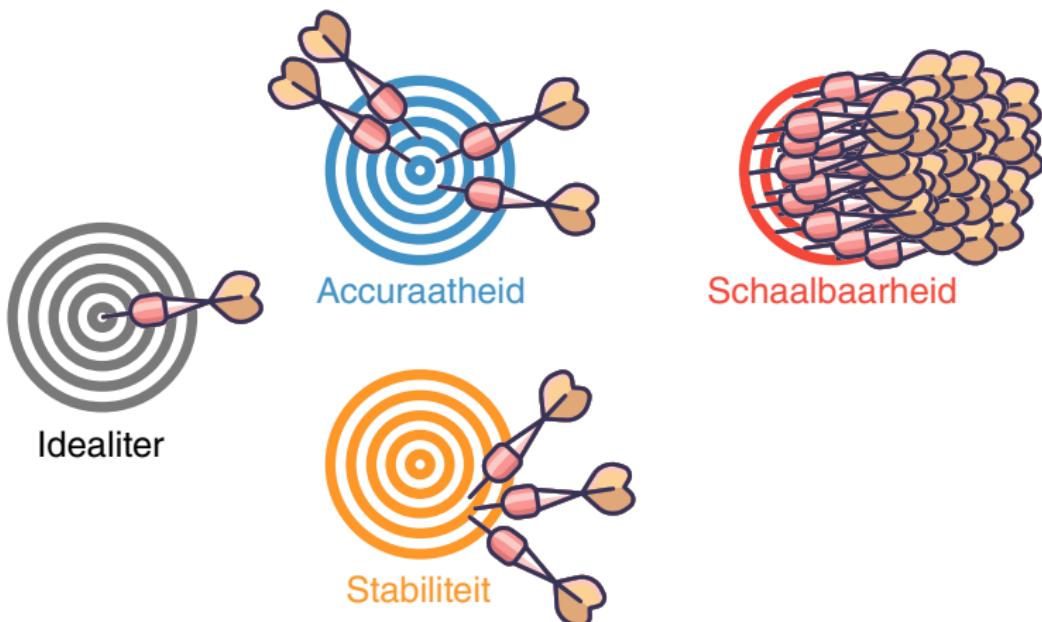
Grootschalige evaluatie van trajectory inference methoden



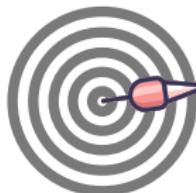
Grootschalige evaluatie van trajectory inference methoden



Grootschalige evaluatie van trajectory inference methoden



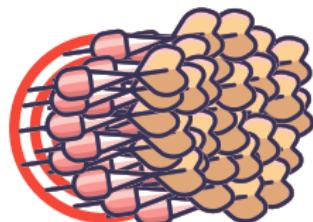
Grootschalige evaluatie van trajectory inference methoden



Idealiter



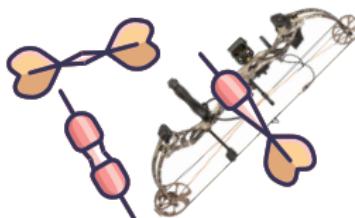
Accuraatheid



Schaalbaarheid

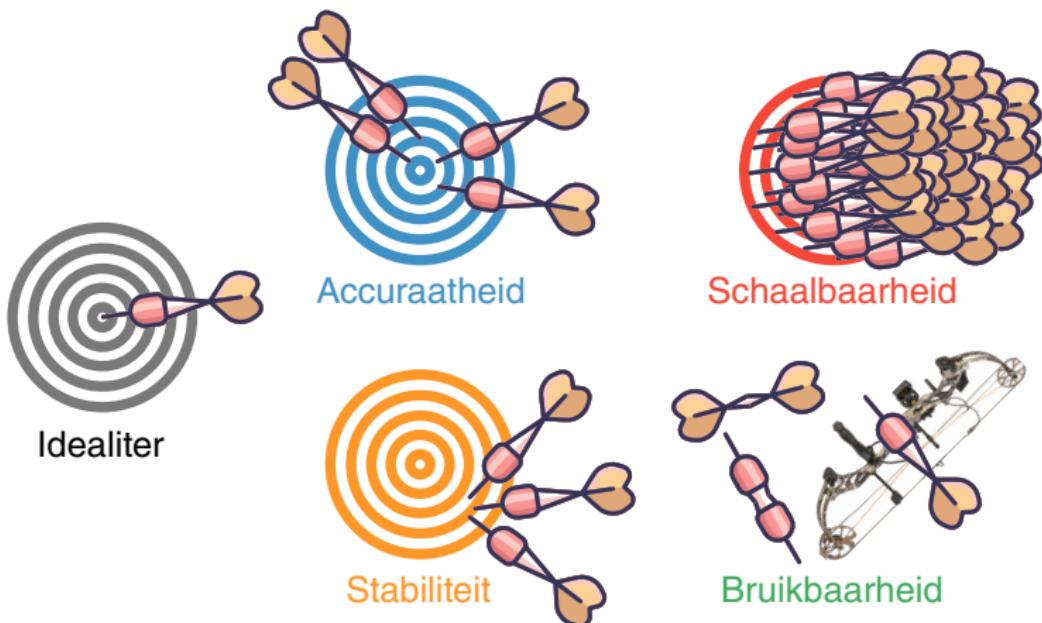


Stabiliteit

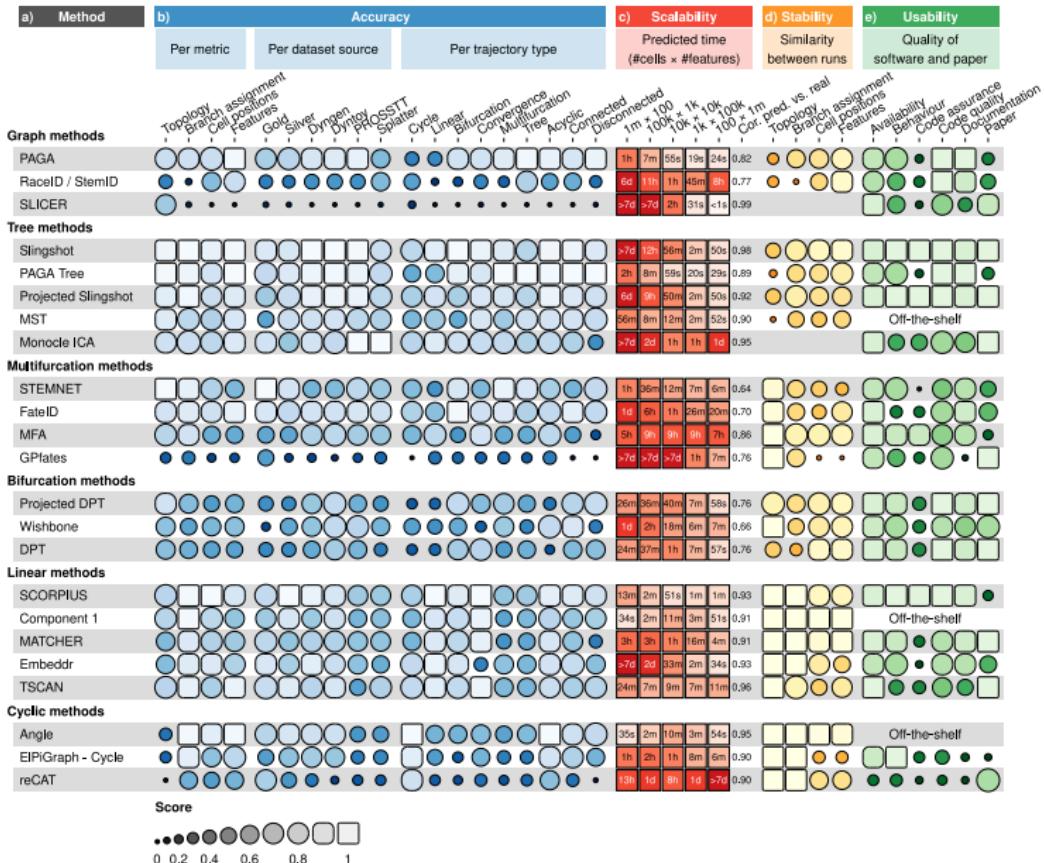


Bruikbaarheid

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

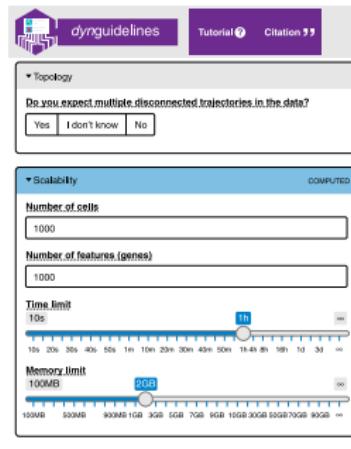
Number of cells: 1000

Number of features (genes): 1000

Time limit: 10s (1h)

Memory limit: 10MB (10GB)

COMPUTED



Benchmark study Evaluating methods with dynbenchmark Part of

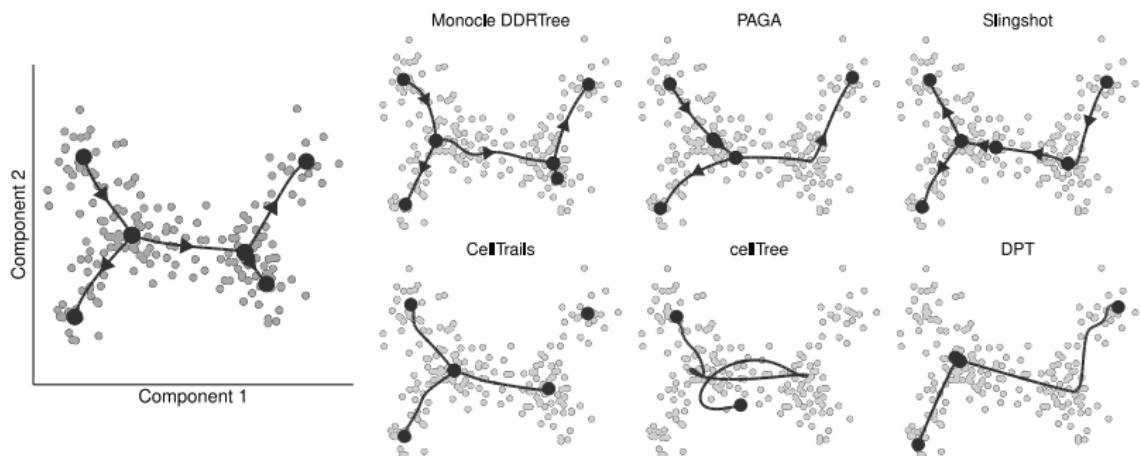
Show code Show/hide columns Options

Lenses: Default | Summary (Fig. 2) | Method | Scalability | Stability | Usability | Accuracy | Overall | Everything

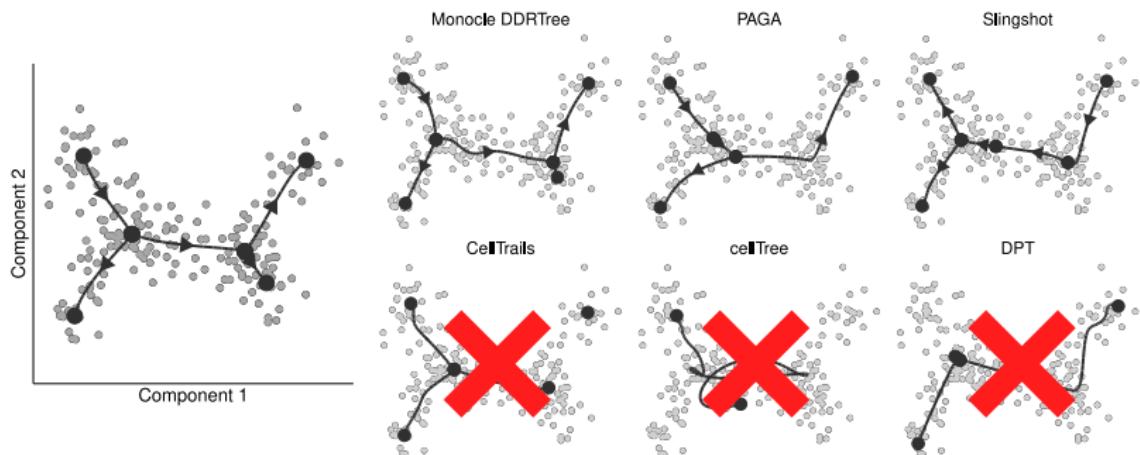
Method Accuracy Scalability Stability

Method	Priors	Errors	Overall #	O.T	S.T	Stability
✓ Screenshot		100	8s	942MB		
✓ SCORPIUS		96	3s	507MB		
✓ Angle		92	1s	308MB		
✓ PAGA		59	15s	559MB		▲ Unstable
✗ Embeddr		89	5s	581MB		
MST		69	4s	572MB		▲ Unstable
✗ Waterfall		69	5s	369MB		
✗ TSCAN		68	5s	476MB		▲ Unstable
Component 1		67	1s	516MB		
✗ SLICE		63	16s	713MB		
✗ Monocle DDRTree		62	41s	647MB		▲ Unstable
EPIGraph Linear		61	1m	573MB		

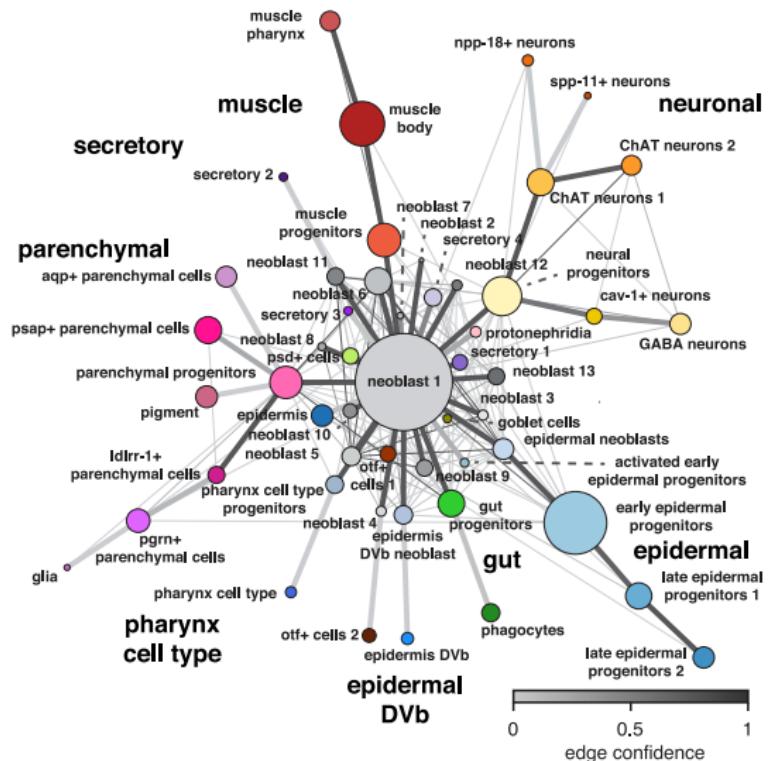
Eliminatie van sommige methoden



Eliminatie van sommige methoden



Gevolgen benchmark paper



Toekomstvisie

- Werk Helena rond GNG (toon filmpje)
- Trajectory alignment
- Combinatie met spatial omics
- Human Cell Atlas (vergelijk met de human genome project)