

Modelling single-cell dynamics with trajectories and gene regulatory networks

Robrecht Cannoodt

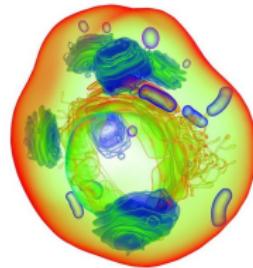


Single-cell biology

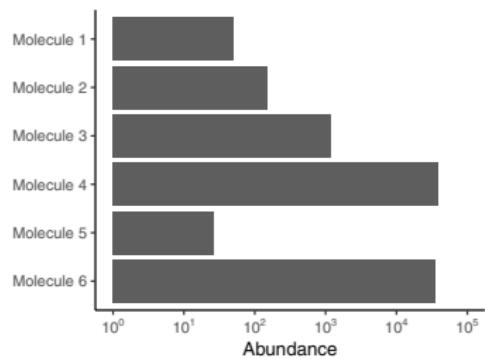
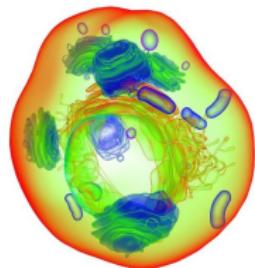
Single-cell biology is to study an organism



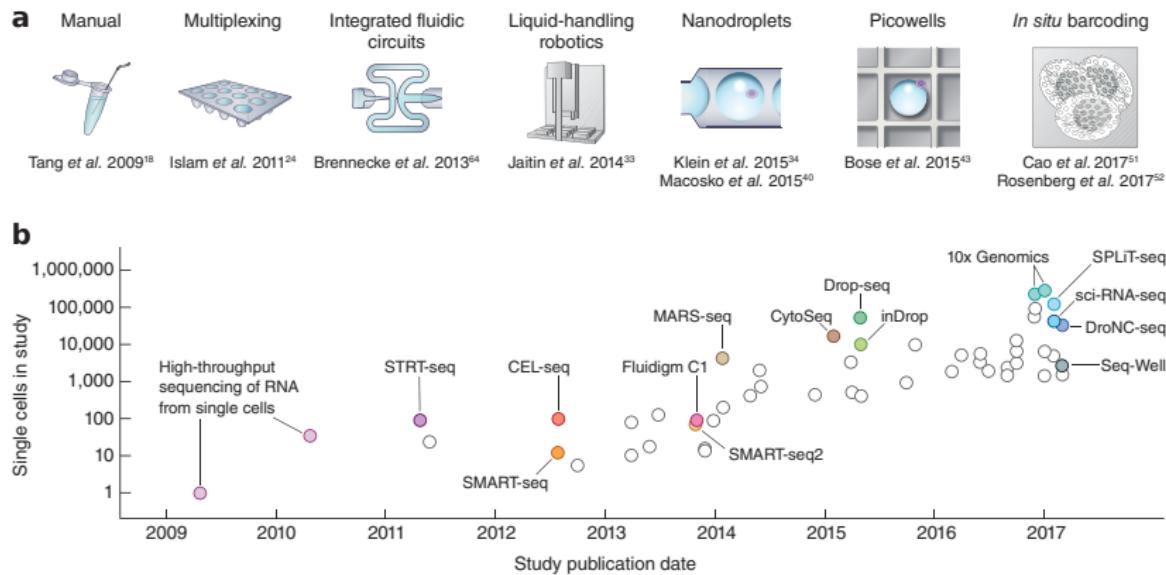
Single-cell biology is to study an organism
by studying the behaviour of its cells



Single-cell biology is to study an organism
by studying the behaviour of its cells



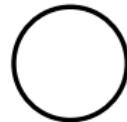
Technological advances allow high-throughput single-cell biology



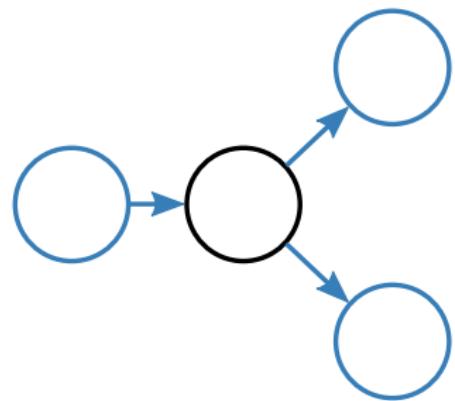
Regev *et al.* 2018

Research questions

Research questions

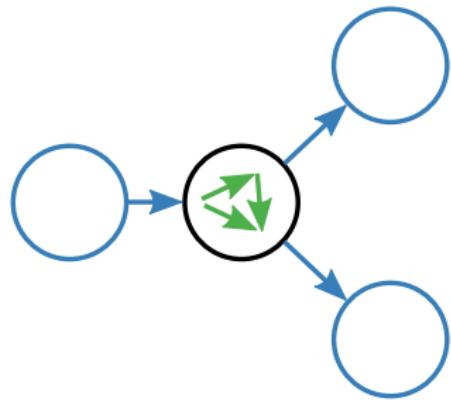


Research questions



How do cells change over time?

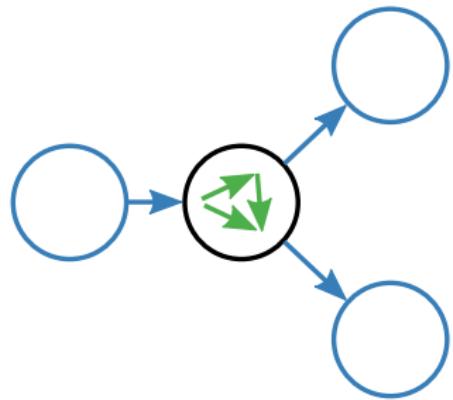
Research questions



How do cells change over time?

What drives cells to change?

Research questions



How do cells change over time?

→ Trajectory inference

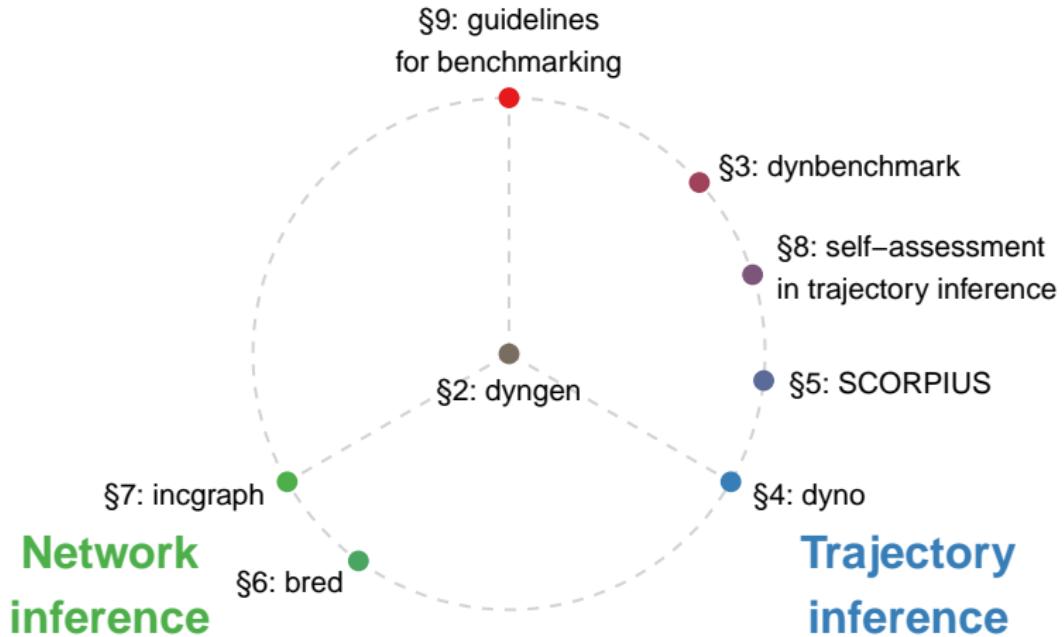
What drives cells to change?

→ Network inference

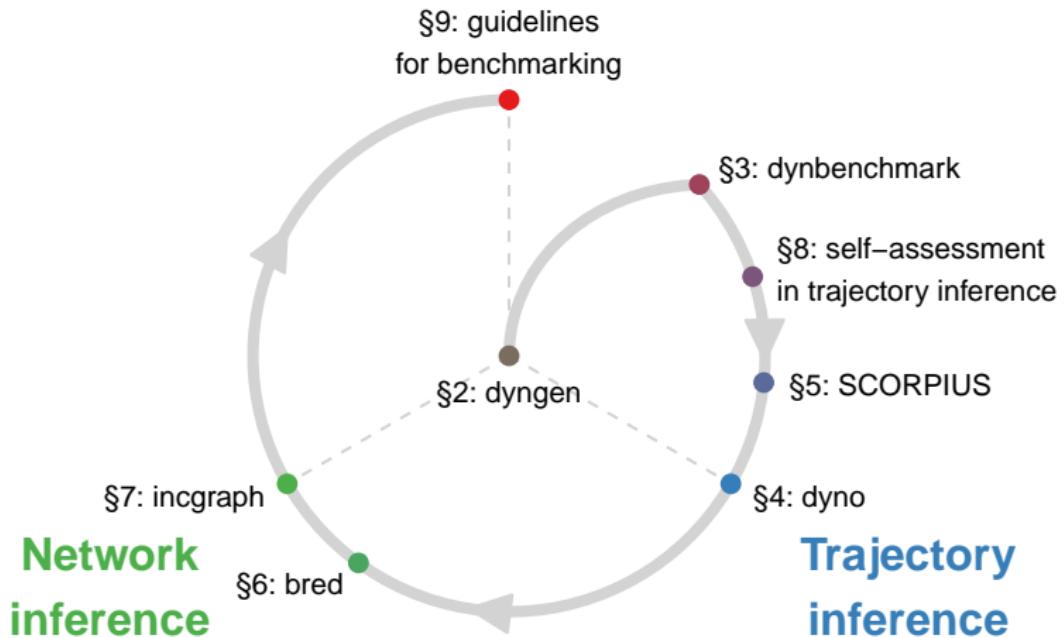
Benchmarking

Network inference Trajectory inference

Benchmarking

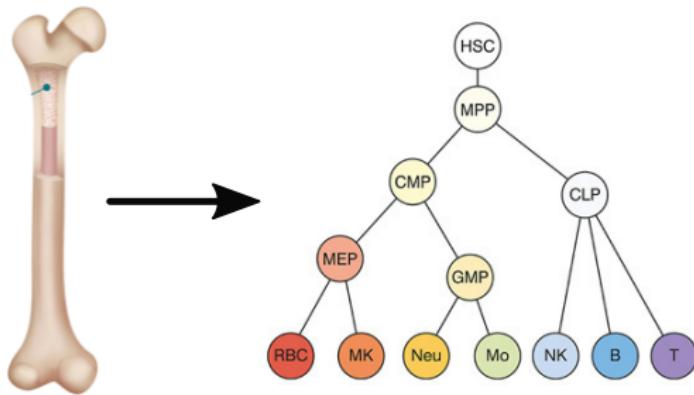


Benchmarking

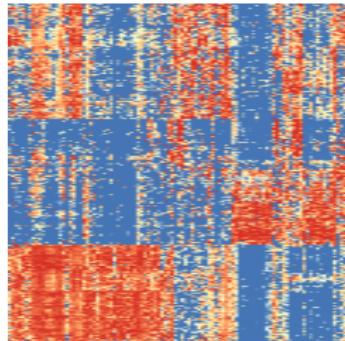


Trajectory inference

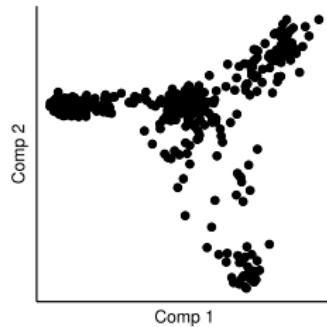
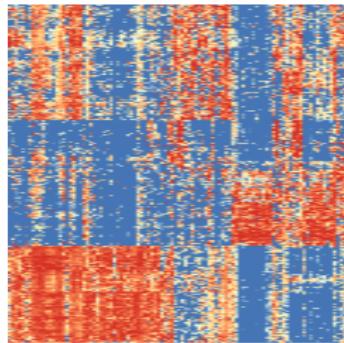
Cells are highly dynamic entities



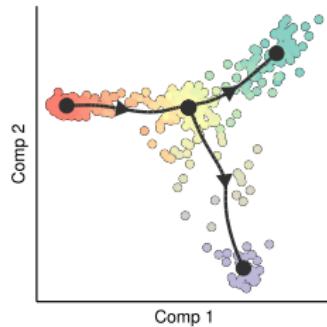
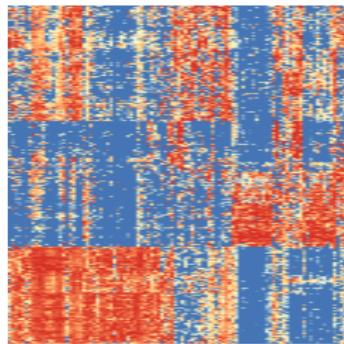
A typical trajectory inference analysis



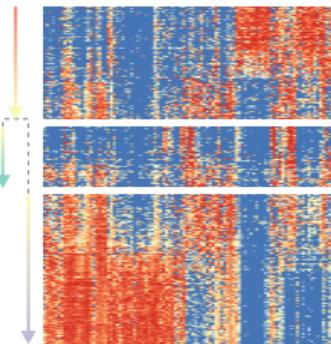
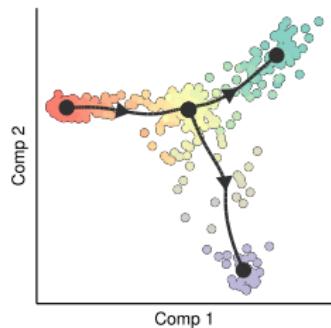
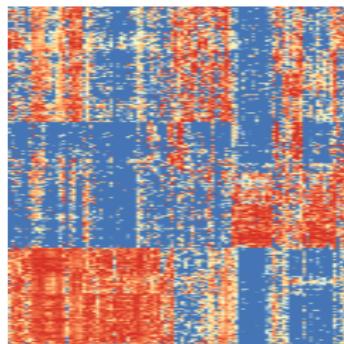
A typical trajectory inference analysis



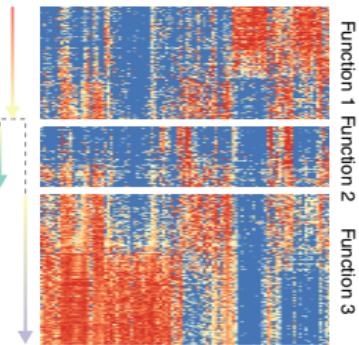
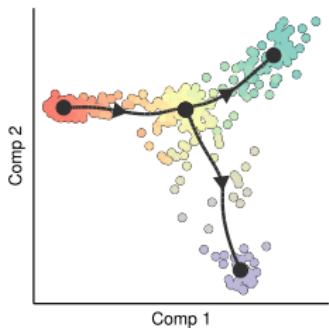
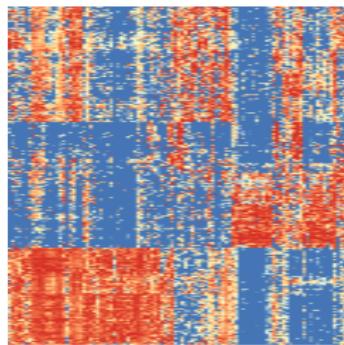
A typical trajectory inference analysis



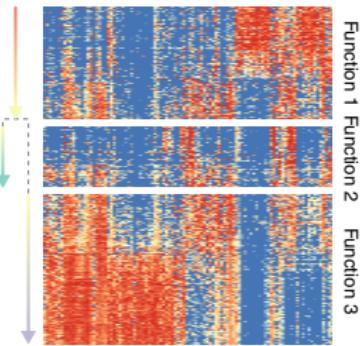
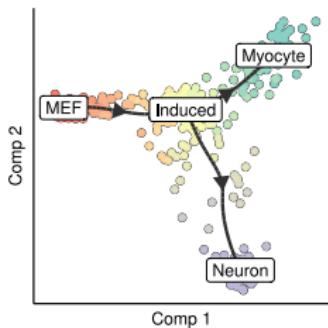
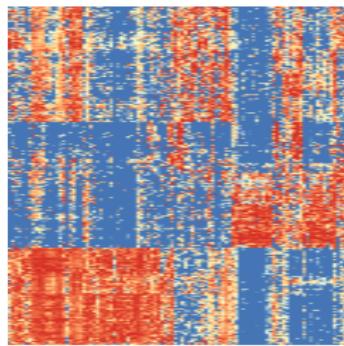
A typical trajectory inference analysis



A typical trajectory inference analysis

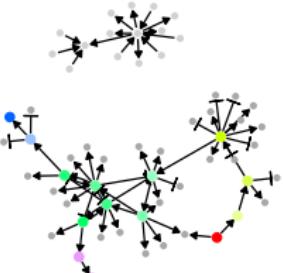


A typical trajectory inference analysis

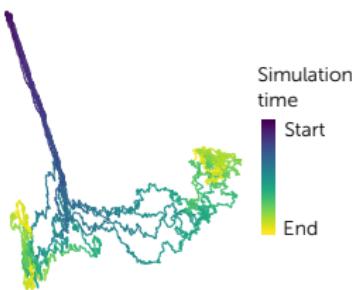


dyngen: Benchmarking with *in silico* cells

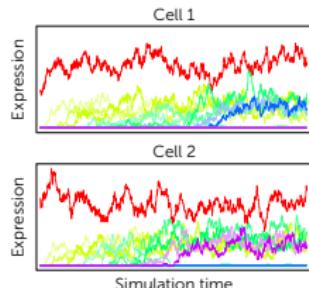
Gene regulatory network



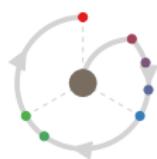
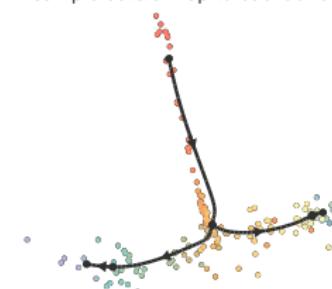
Combine simulations



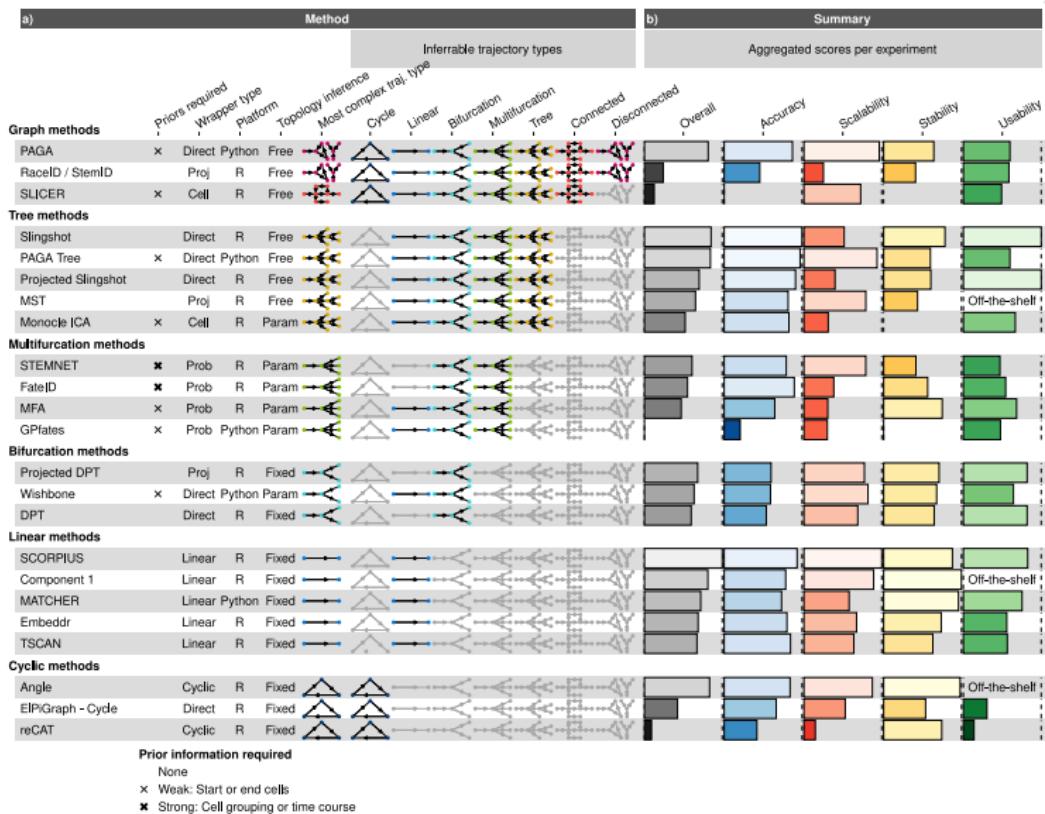
Simulate expression over time



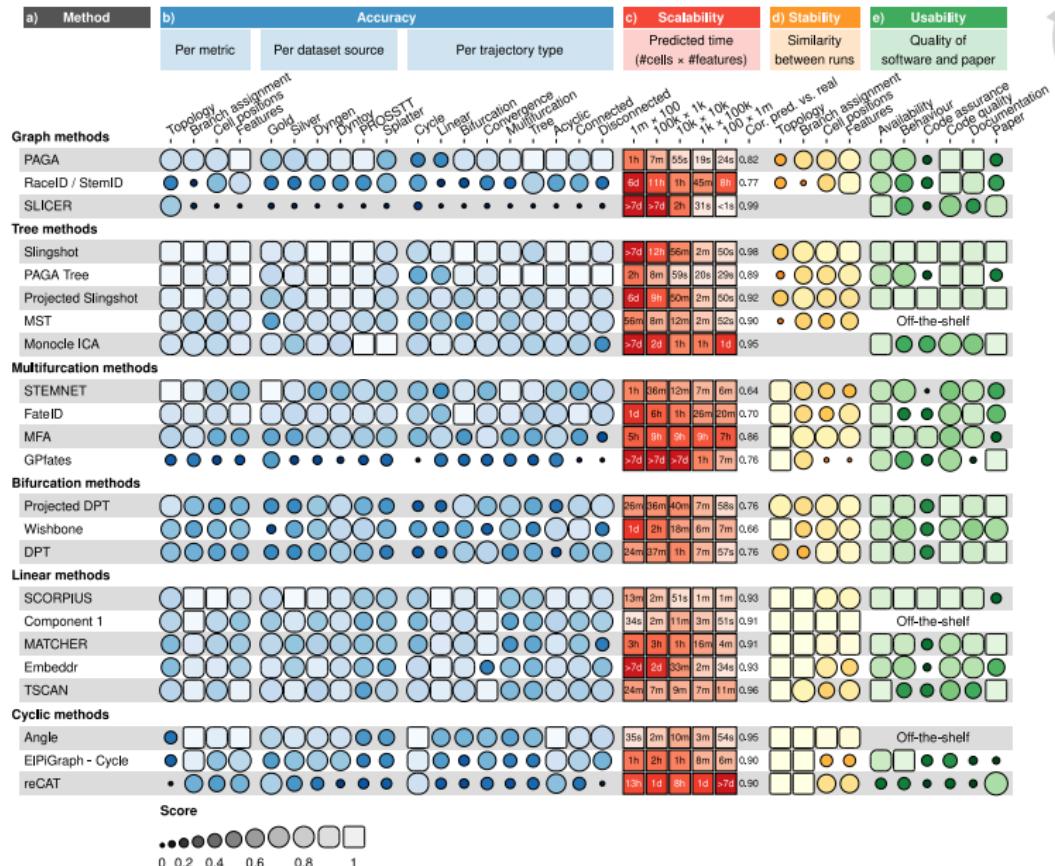
Sample cells & map to backbone



Benchmark of 45 trajectory inference methods



Benchmark of 45 trajectory inference methods



Interactive guidelines



dynguidelines

Tutorial Citation

Topology
Do you expect multiple disconnected trajectories in the data?

Scalability COMPUTED

Number of cells

Number of features (genes)

Time limit
10s

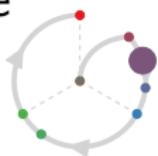
Memory limit
10MB

Show code Show/hide columns Options

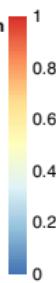
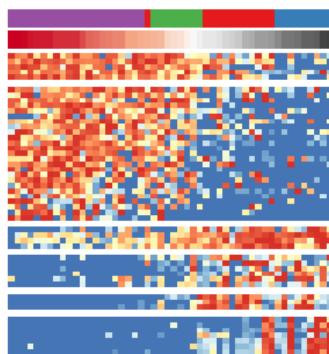
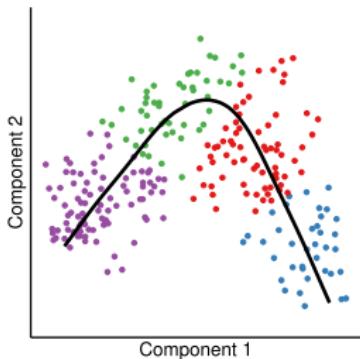
Benchmark study Evaluating methods with dyngbenchmark Part of

Lenses	Default	Summary (Fig. 2)	Method	Scalability	Stability	Usability	Accuracy	Overall	Everything
Method									
							Accuracy	Scalability	Stability
			Name	Priors			Errors	Overall #	O.T
			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

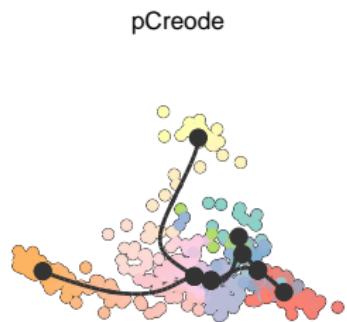
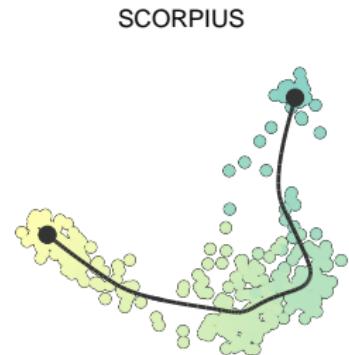
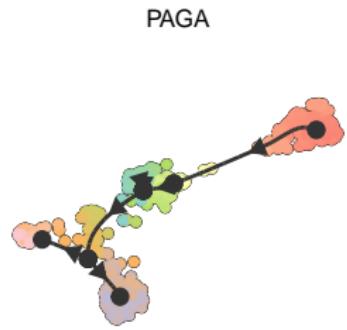
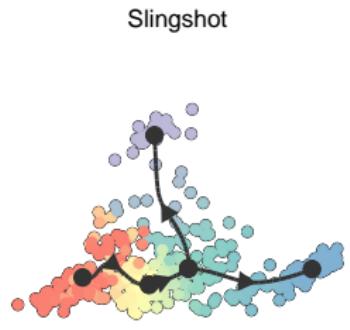
Perspective: self-assessment in trajectory inference



SCORPIUS: Linear trajectory inference



dyno: A toolkit for inferring and interpreting trajectories



Network inference

Cellular dynamics is (i.a.) driven by gene regulation



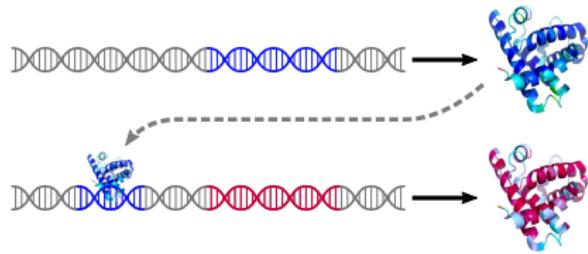
Cellular dynamics is (i.a.) driven by gene regulation



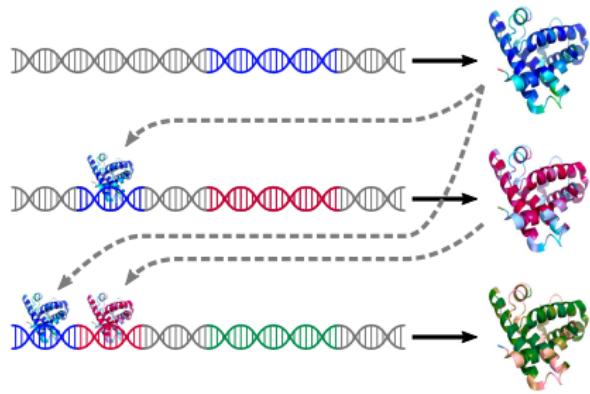
Cellular dynamics is (i.a.) driven by gene regulation



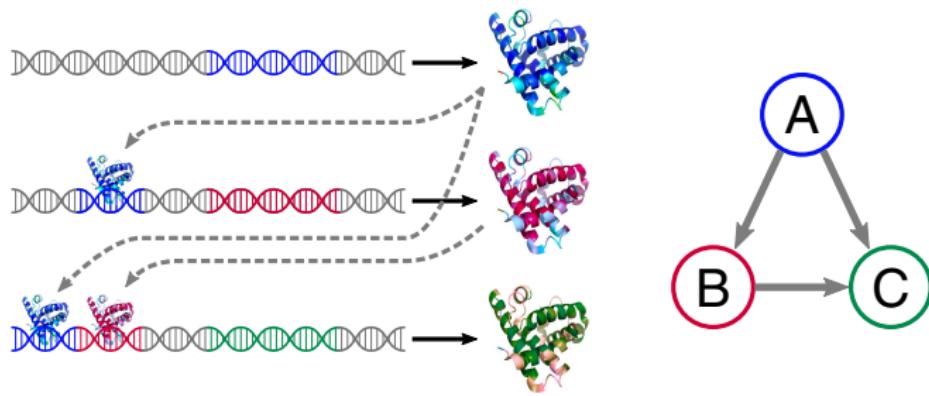
Cellular dynamics is (i.a.) driven by gene regulation



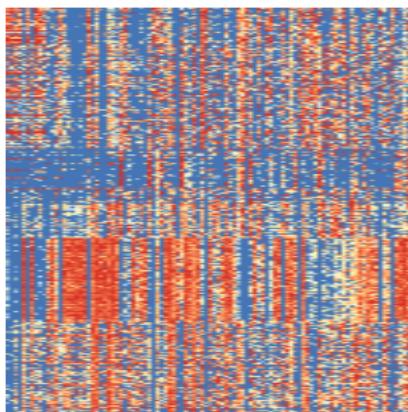
Cellular dynamics is (i.a.) driven by gene regulation



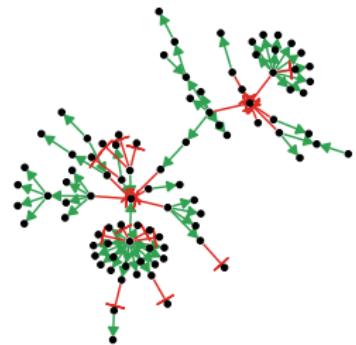
Cellular dynamics is (i.a.) driven by gene regulation



Classical network inference

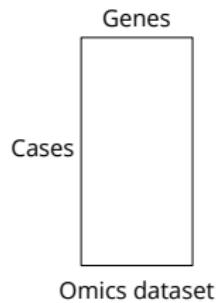


Network
inference

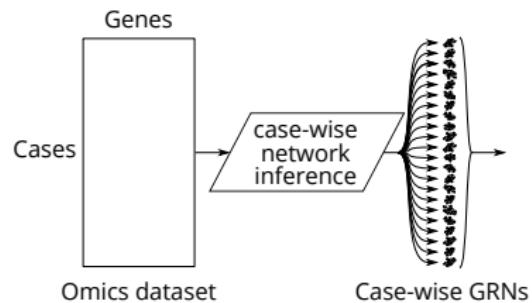


Interaction type → Promotes → Represses

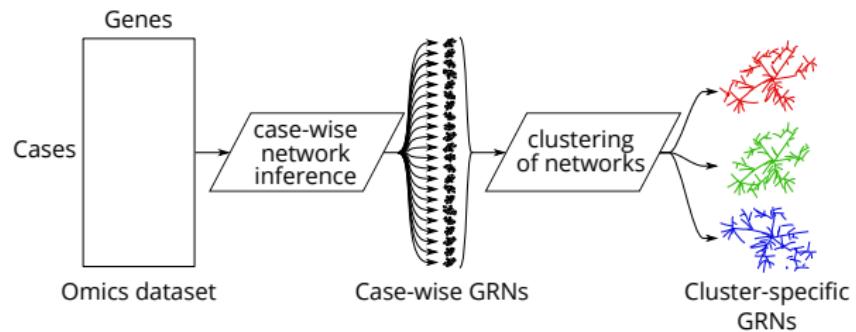
Case-specific network inference



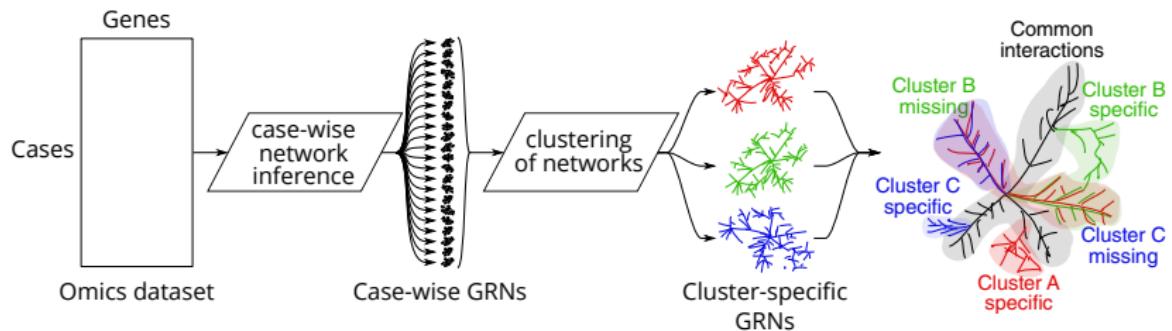
Case-specific network inference



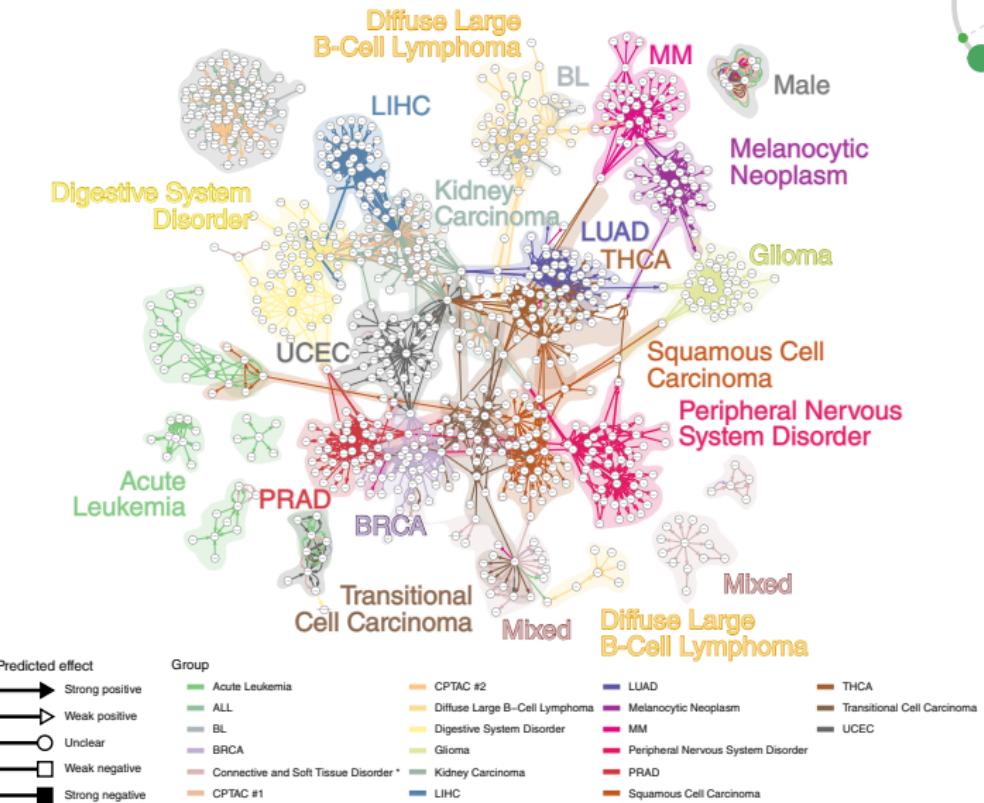
Case-specific network inference



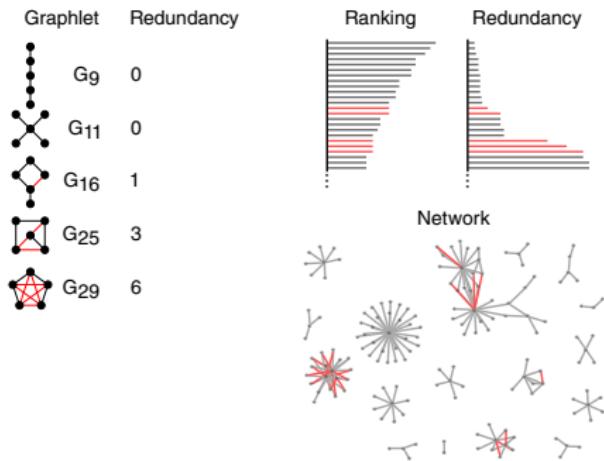
Case-specific network inference



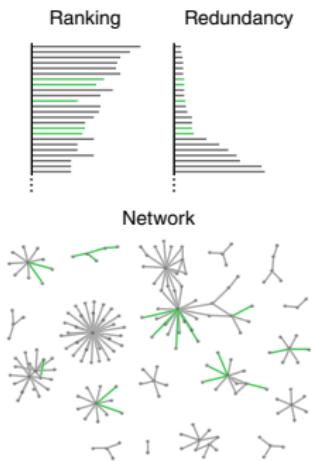
bred applied to TCGA



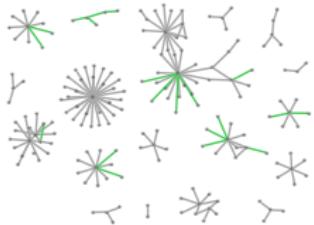
incgraph: Optimising regulatory networks



Rerank to lower redundancy

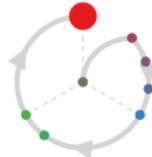


Network



Benchmarking

Essential guidelines for benchmarking computational tools



1. Define the purpose and scope of the benchmark.
2. Include all relevant methods.
3. Select (or design) representative dataset.
4. Choose appropriate parameter values and software versions.
5. Evaluate methods according to key quantitative performance metrics.
6. Evaluate secondary measures including computational requirements, user-friendliness, installation procedures, and documentation quality.
7. Interpret results and provide recommendations from both user and method developer perspectives.
8. Publish results in an accessible format
9. Design the benchmark to enable future extensions.
10. Follow reproducible research best practices, by making code and data publicly available.

Practical implications



Practical implications

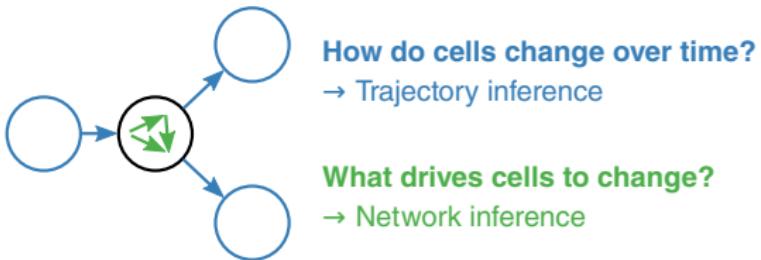


- Fundamental research in single-cell analyses

Practical implications



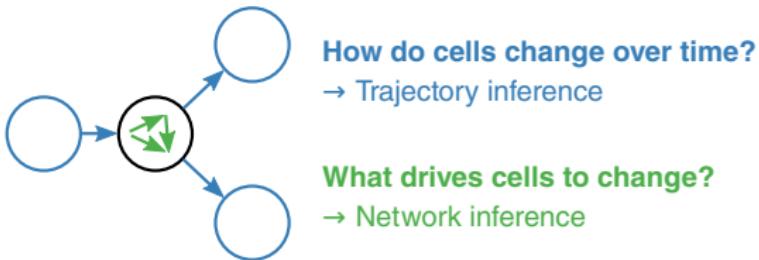
- Fundamental research in single-cell analyses



Practical implications



- Fundamental research in single-cell analyses

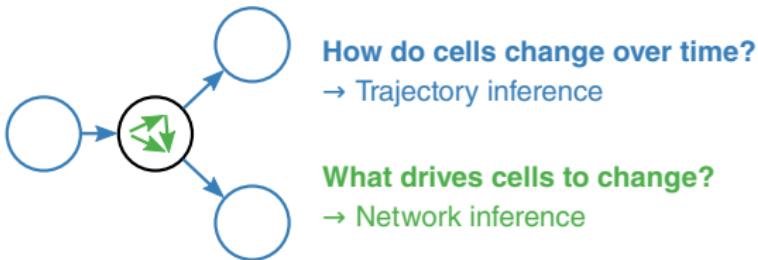


- Benchmarking

Practical implications



- Fundamental research in single-cell analyses



- Benchmarking
- R & tidyverse