Understanding Cancer Evolution Through Single Cell Expression Dynamics

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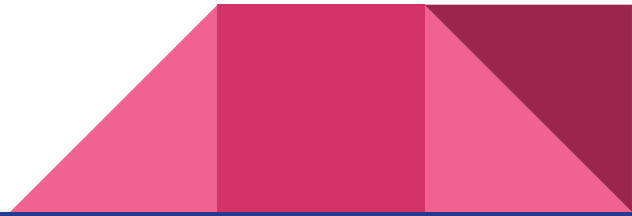
Trajectory inference (pseudotemporal ordering)

- Pseudotime is an abstract unit of progress = the distance between a cell and the start of the trajectory

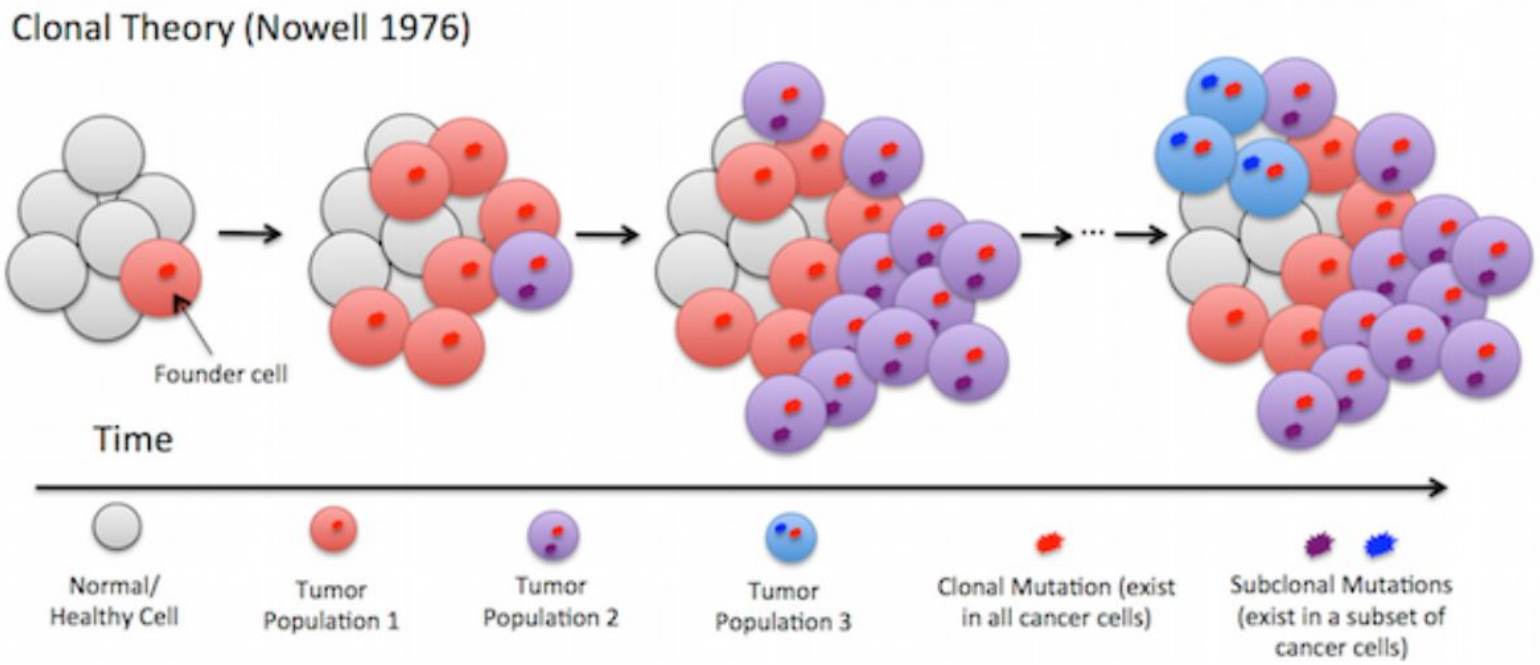
  → Pseudotime is a measure of how much progress an individual cell has made through a process ***such as cell differentiation***

- In single-cell expression studies, captured cells might be widely distributed in terms of progress (Cells don't progress in synchrony!)

  → Ordering each cell according to its progress along a learned trajectory



Cancer Heterogeneity

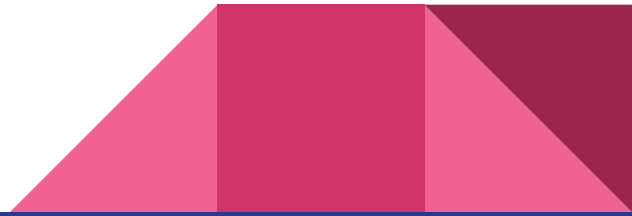


Question

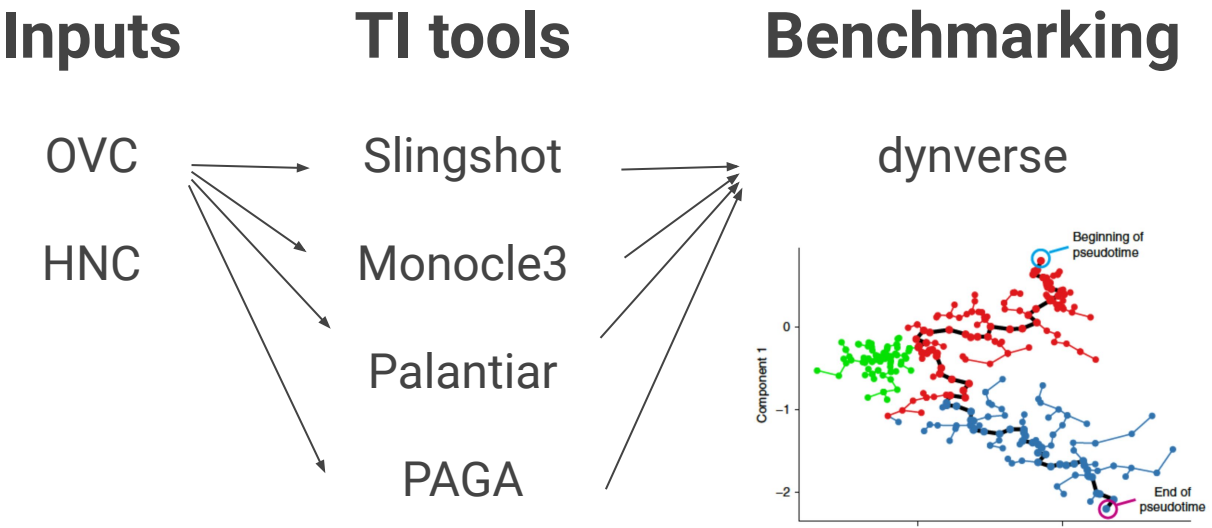
- If cancer samples are a mixture of different cells (e.g. cancer subtypes, tissues of origin), can we infer the stage and/or origin of cells from their evolutionary trajectory?

Approach

- **Datasets**
  - Ovarian cancer → subtype heterogeneity + tissue of origin
  - Head and neck cancer → primary vs metastasis
- **Tools**
  - Monocle3
  - Slingshot
  - Palantir
  - PAGA



Workflow


Inputs
TI tools
Benchmarking
OVC
HNC
Slingshot
Monocle3
Palantiar
PAGA
dynverse
Beginning of pseudotime
End of pseudotime
Component 1
0
−1
−2

Deliverables

- **Benchmark summary** ← Apply trajectory inference tools on different single-cell cancer samples
- **Analysis workflows**
- **Proposal on tool updates** *(e.g. what is the biological difference between differentiating cells and cancer cells need to be considered)*