

CellTrails: Reconstruction, visualization, and analysis of branching trajectories from single-cell expression data

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Abstract

High-throughput single-cell technologies facilitate the generation of -omic readouts from thousands of cells captured at different cellular maturation stages during development, or other normal or pathological processes with unprecedented resolution. A single snapshot of an asynchronously developing specimen, for example, constitutes a time series in which individual cells represent distinct time points along a continuum. However, recoding of valuable cell-specific information, such as a cell's developmental age, its location in a tissue, or its functional phenotype is limited during sample preparation, and remains hidden in high dimensional cellular expression profiles. This formulates the computational challenge to infer the latent internal time axis of the biological process from the obtained expression matrix alone, while considering common parameters of single-cell measurements, such as noise, dropouts and redundancy. In other words, biological samples need to be placed by means of hidden information onto a non-linear trajectory, which might constitute of branching processes towards distinct functional cell types.

CellTrails is an R package for the *de novo* chronological ordering, visualization and analysis of single-cell expression data. *CellTrails* makes use of a geometrically motivated concept of lower-dimensional manifold learning, which exhibits a multitude of virtues that counteract intrinsic noise of single cell data caused by drop-outs, technical variance, and redundancy of predictive variables. *CellTrails* enables the reconstruction of branching trajectories and provides an intuitive graphical representation of expression patterns along all branches simultaneously. It allows the user to define and infer the expression dynamics of individual and multiple pathways towards distinct phenotypes.

Before ready to use, the **CellTrails** libraries must be loaded into the *R* environment:

```
library(CellTrails)
```

Please refer to <https://dcellwanger.github.io/CellTrails-handbook/> for detailed information on **CellTrails's** features and how to utilize them.