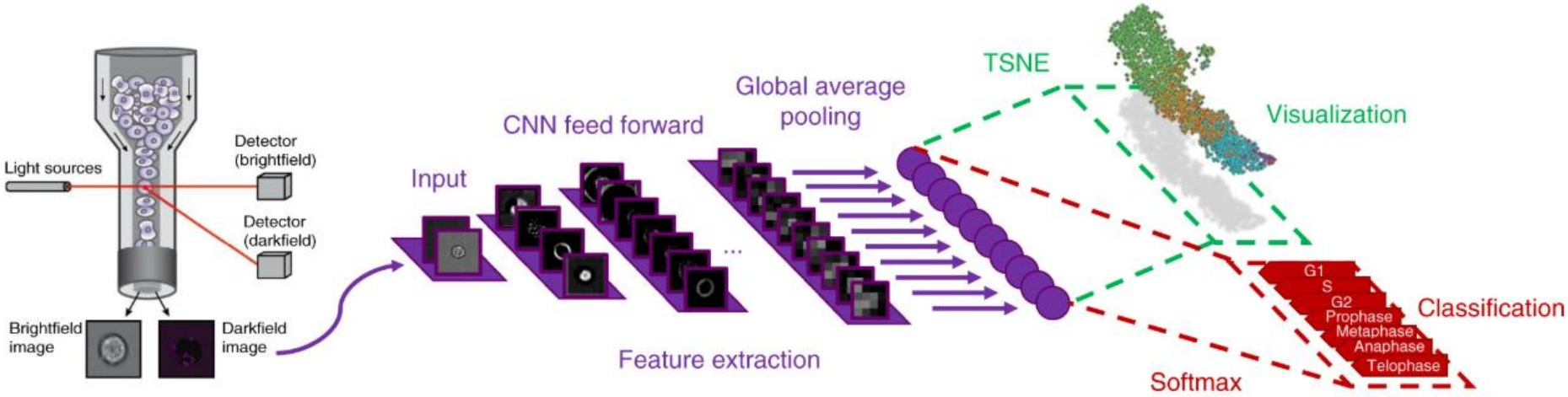
Predicting cell cycle / disease progression stage (“pseudo time”) with deep learning



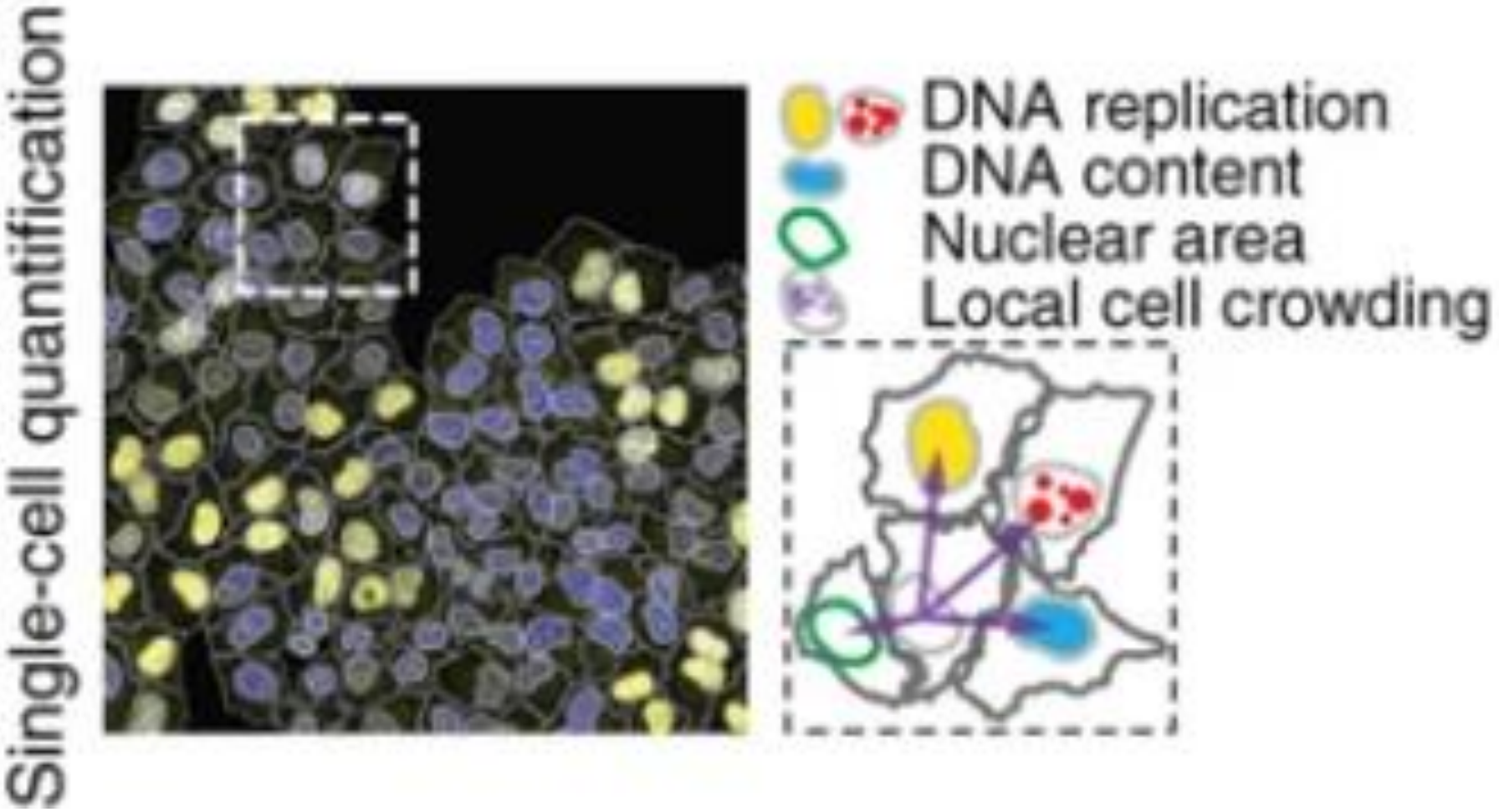
Eulenberg (2017)

Constructs of cell-cycle progression trajectories from fixed cell images in heterogeneous microenvironments

- Pseudo time: ideas from systems biology
  - Developmental path trajectory from single-cell mass cytometry data (Bendall et al., 2014)
  - Recover cell-cycle progression from features extracted from fixed microscopy images
- Role of microenvironment

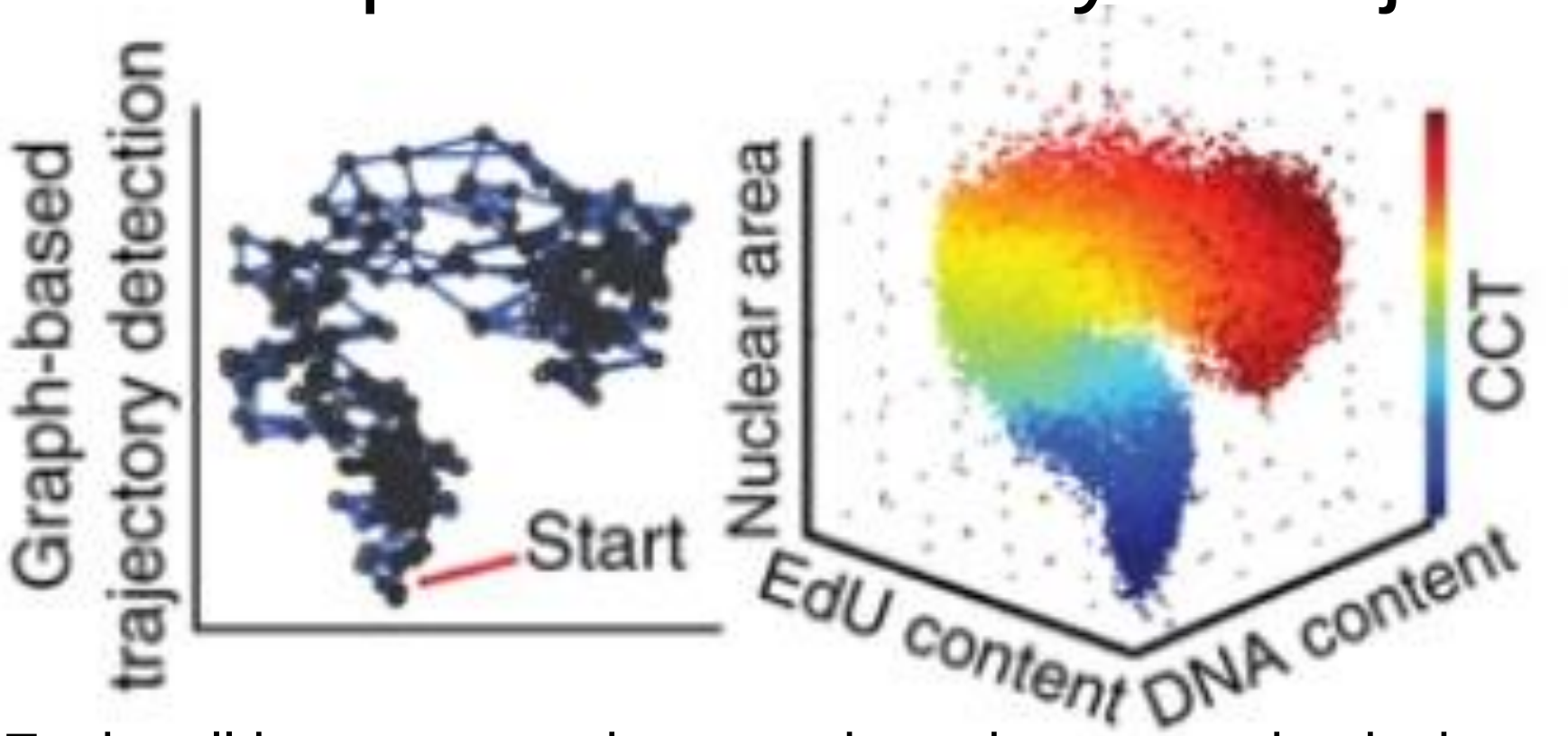
Gut, Tadmor, et al. (2014)

1. Single cell quantification



Gut, Tadmor, et al. (2014)

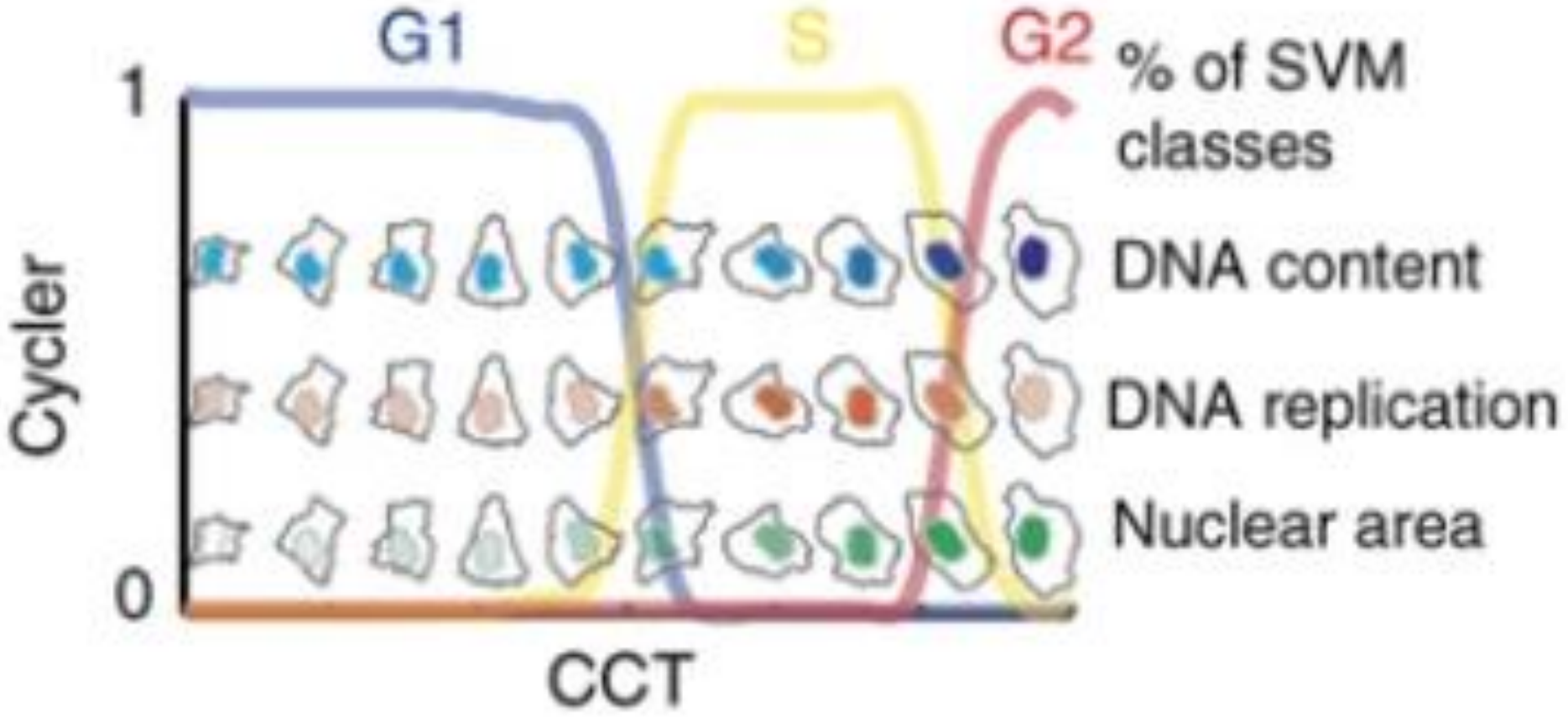
2. KNN graph-based embedding of the feature space to 1D cell cycle trajectory



Each cell is represented as a node and connected to its k nearest neighbors. A cell's distance to another cell is the shortest-path. The position is the mean distance to a user defined starting point + randomly selected “waypoints”.

Gut, Tadmor, et al. (2014)

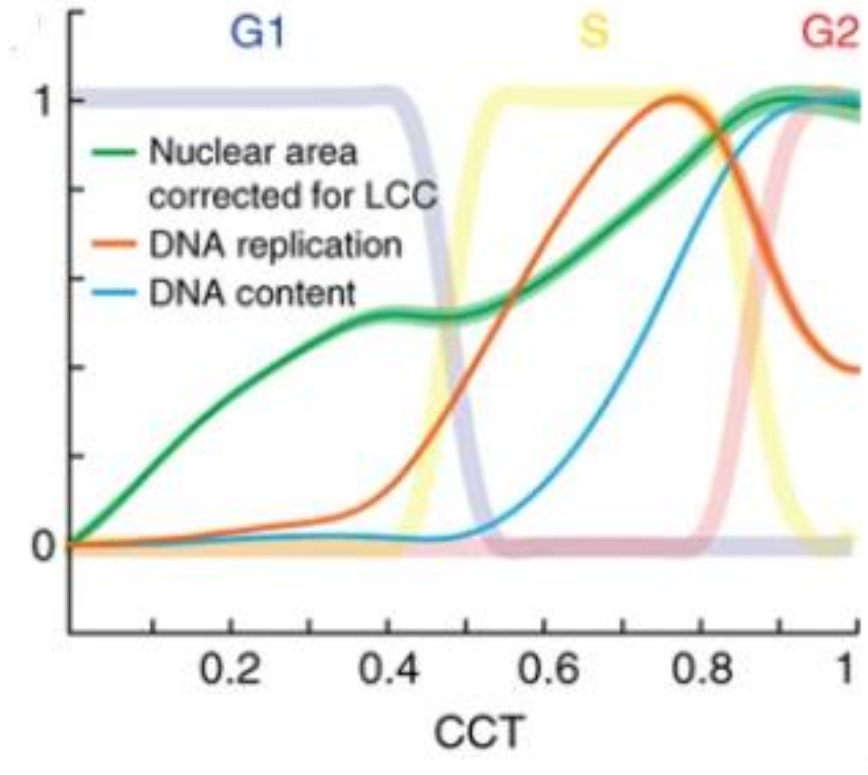
3. Cells are aligned along the cell cycle trajectory



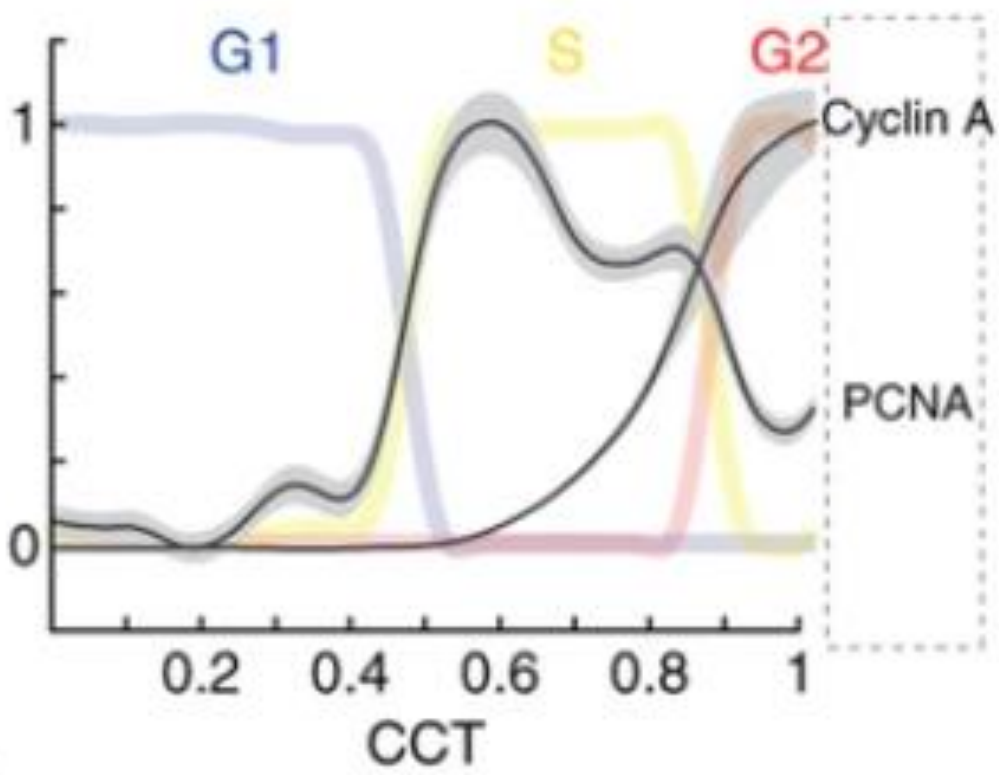
Gut, Tadmor, et al. (2014)

Validations

Single-cell features along the cell cycle trajectory



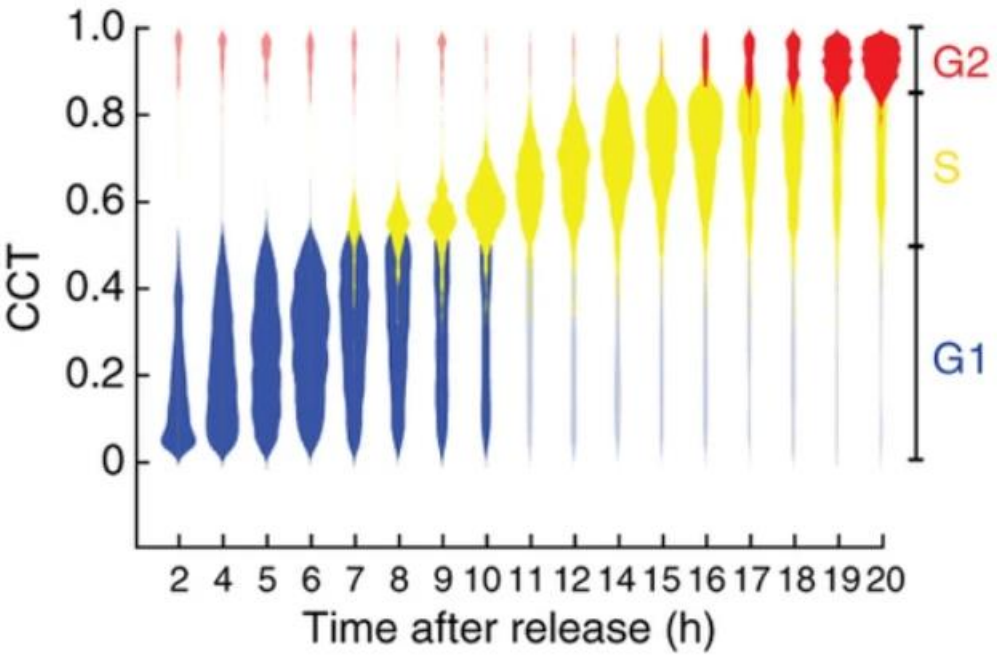
Cell cycle markers along the cell cycle trajectory



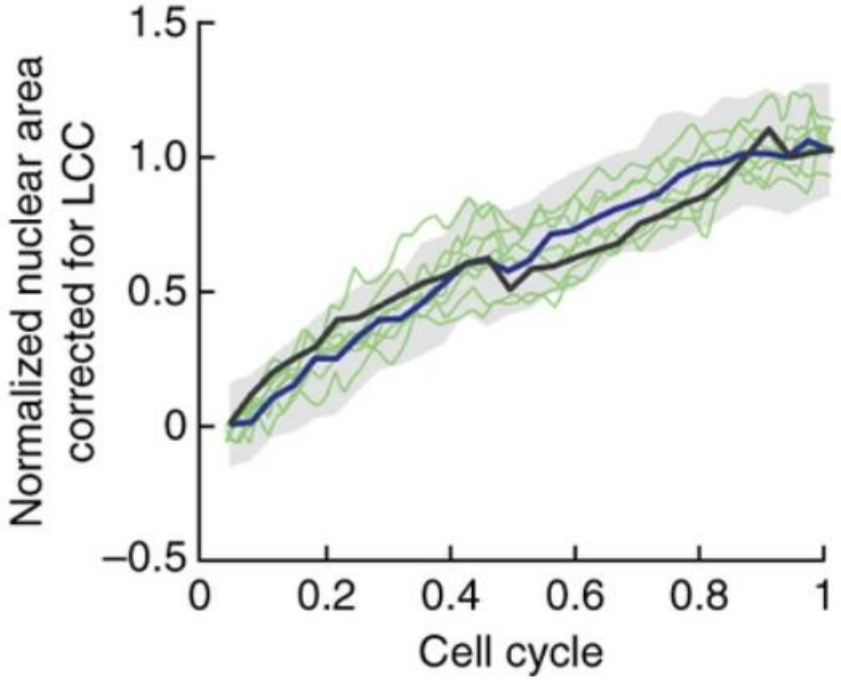
Gut, Tadmor, et al. (2014)

Validations

Cell cycle state over time
(synchronization w growth arrest)

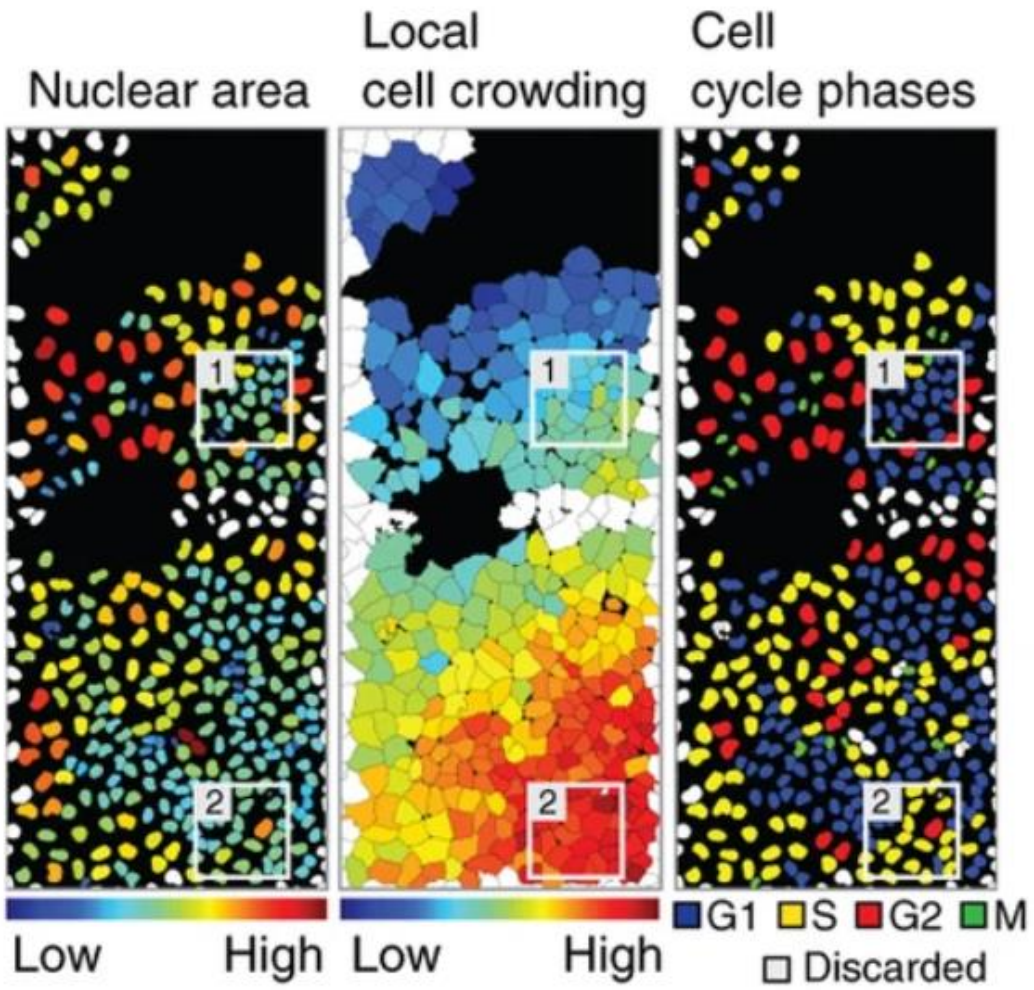


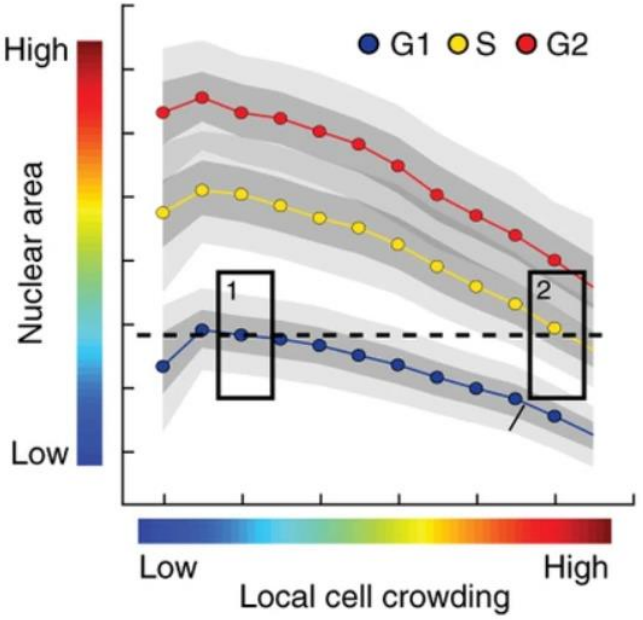
Live imaging vs. CCT

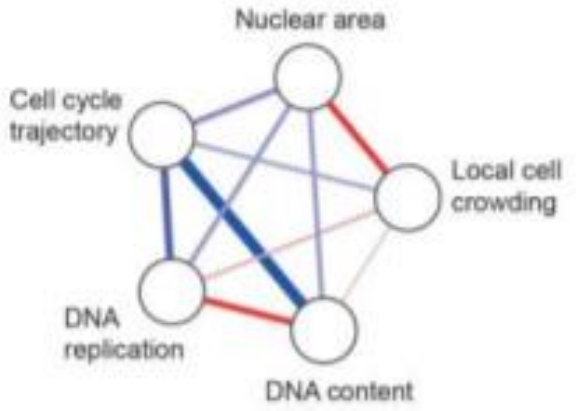


Gut, Tadmor, et al. (2014)

The microenvironment is important for accurate cell cycle trajectory

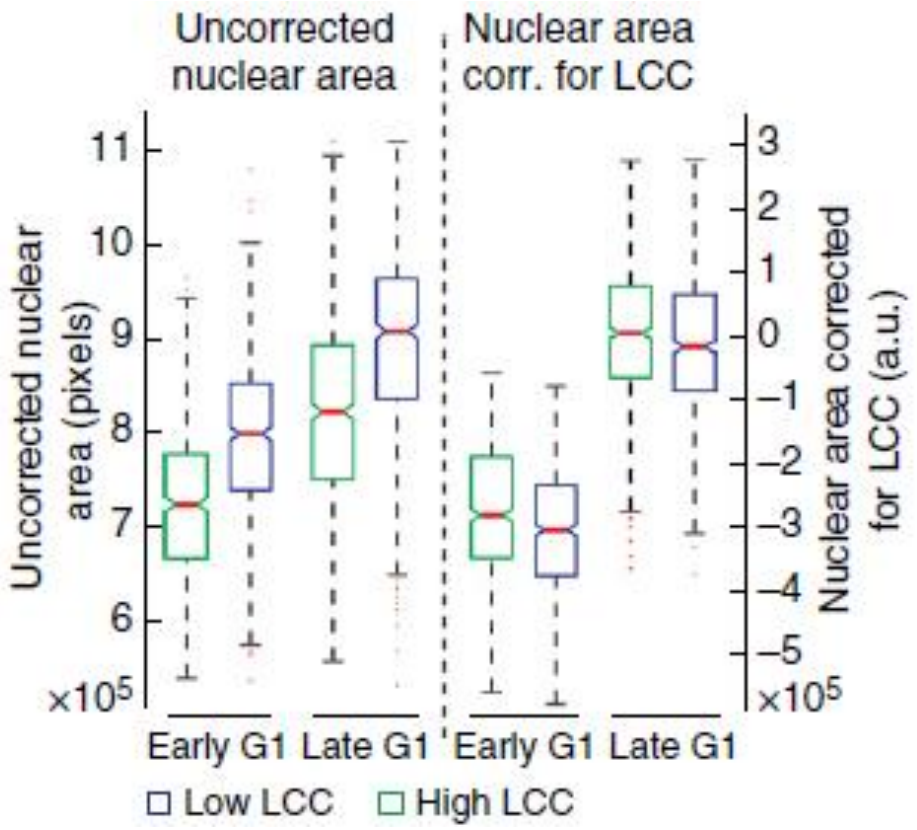




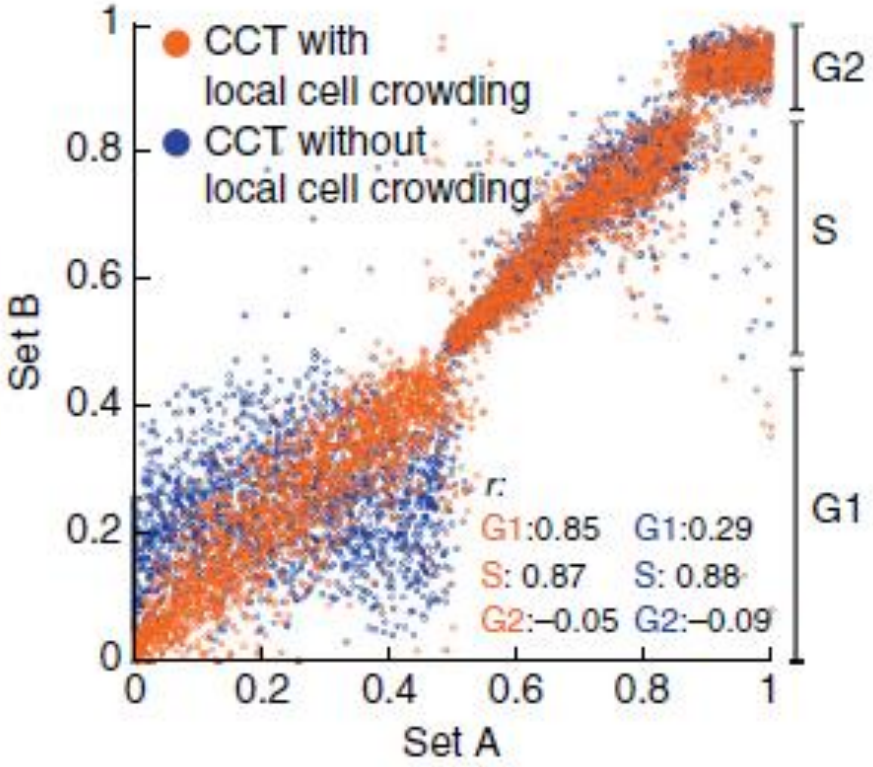


Gut, Tadmor, et al. (2014)

Correcting for local cell crowding

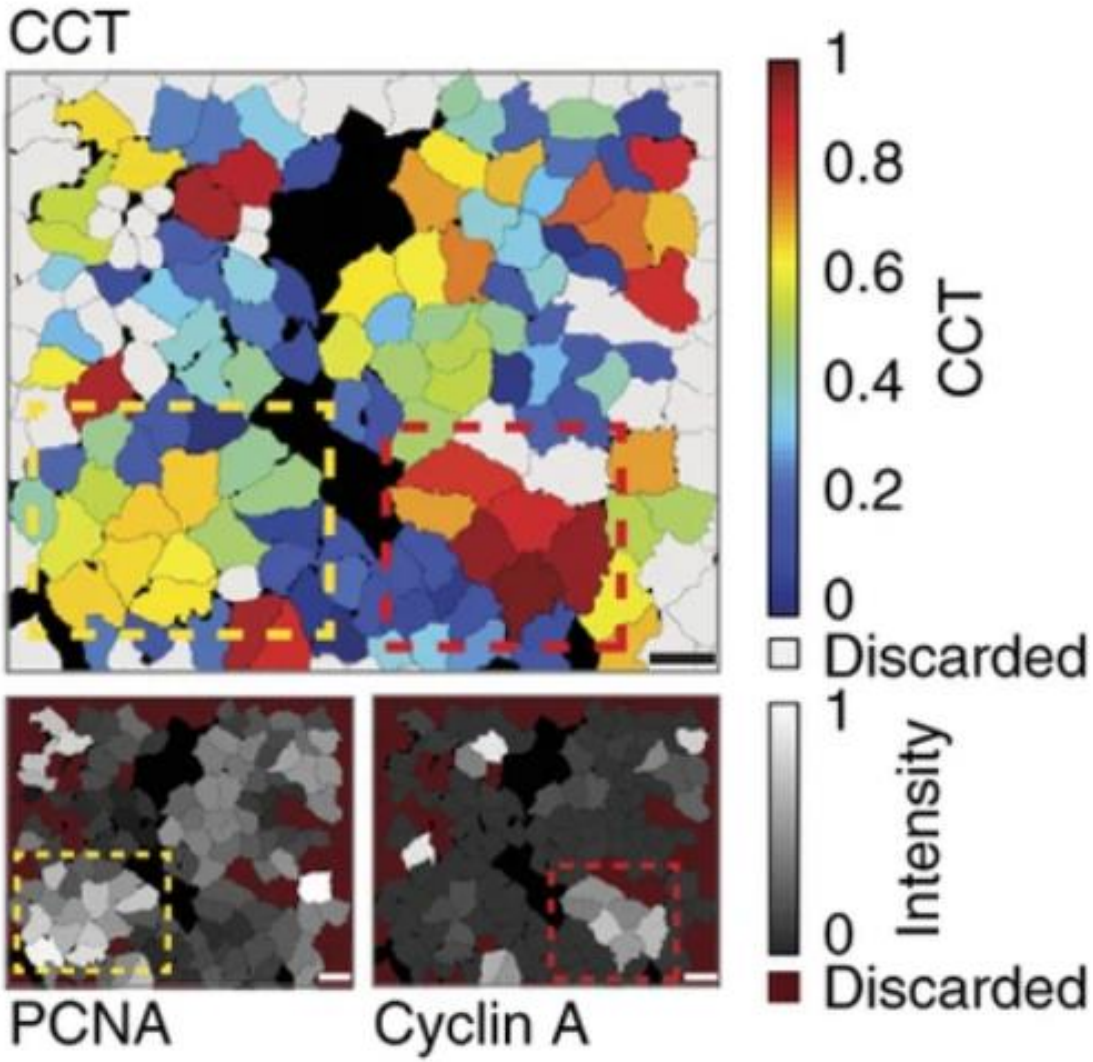


two independent cell populations



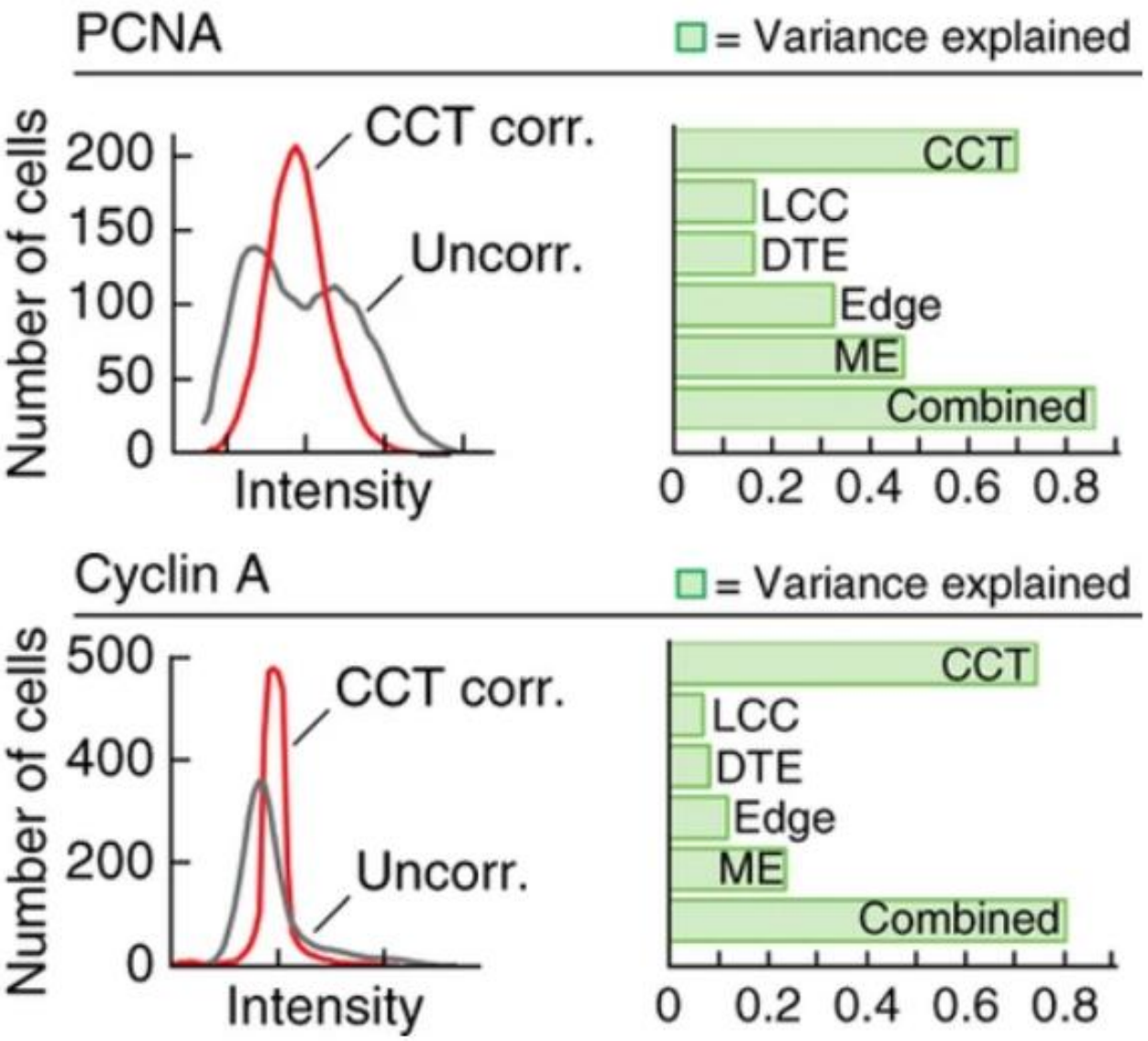
Gut, Tadmor, et al. (2014)

Variability in cell-cycle progression in unsynchronized cell cultures



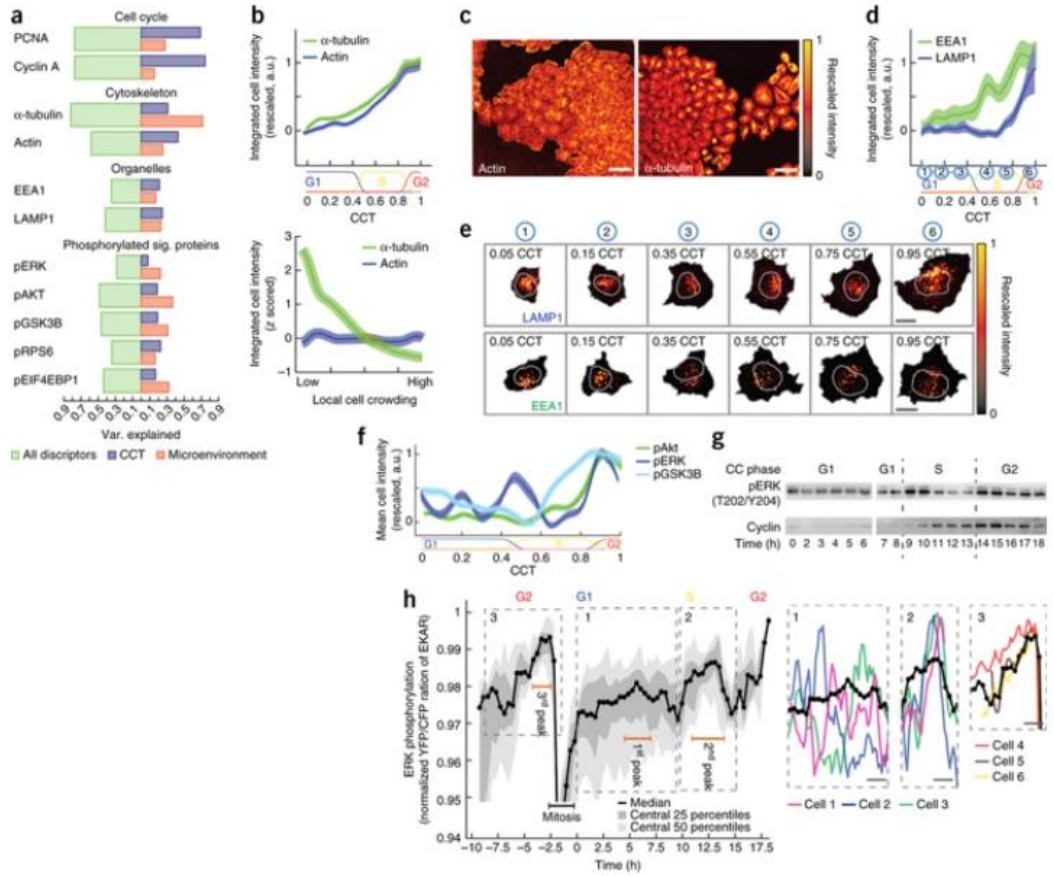
Gut, Tadmor, et al. (2014)

CCT explains most of the variability



Gut, Tadmor, et al. (2014)

Deconvolution of the dominant sources of cell-to-cell variability enables detection of novel dynamics along the cell cycle



Gut, Tadmor, et al. (2014)