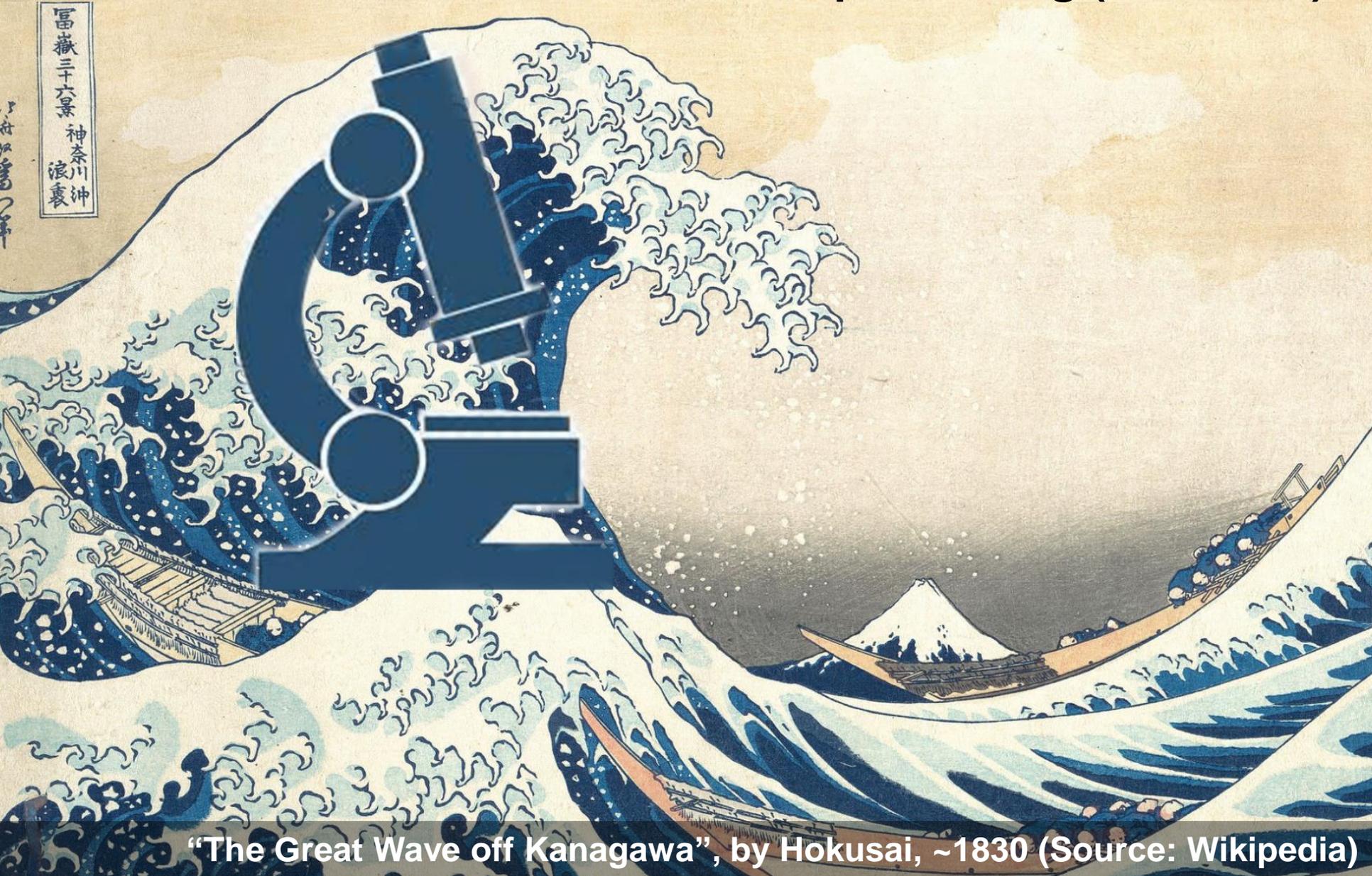


Data science in cell imaging

Lecture 10: Multicellular information processing (and more)



“The Great Wave off Kanagawa”, by Hokusai, ~1830 (Source: Wikipedia)

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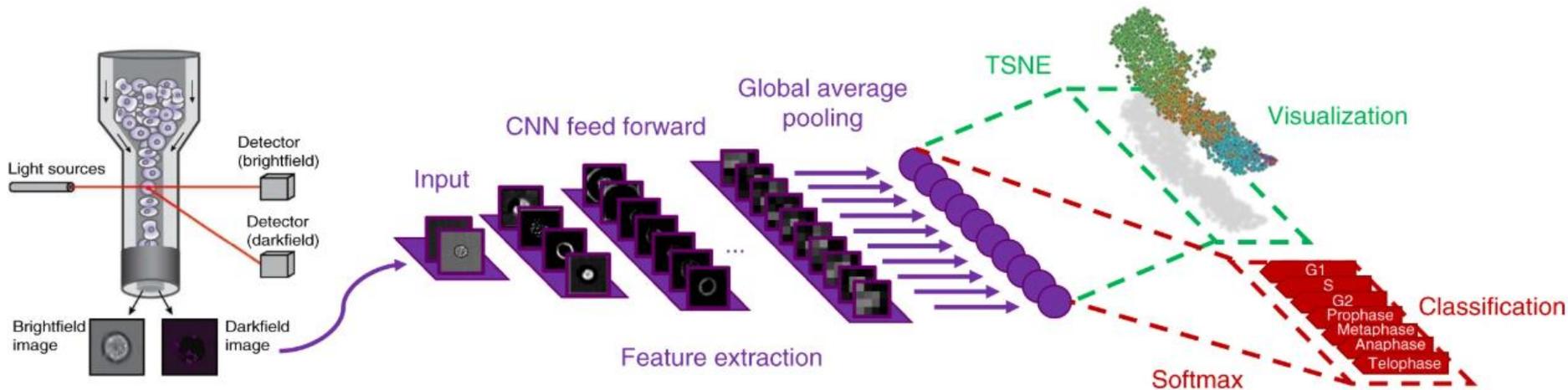
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PPTX slides available here



“Pseudo” time in microscopy

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

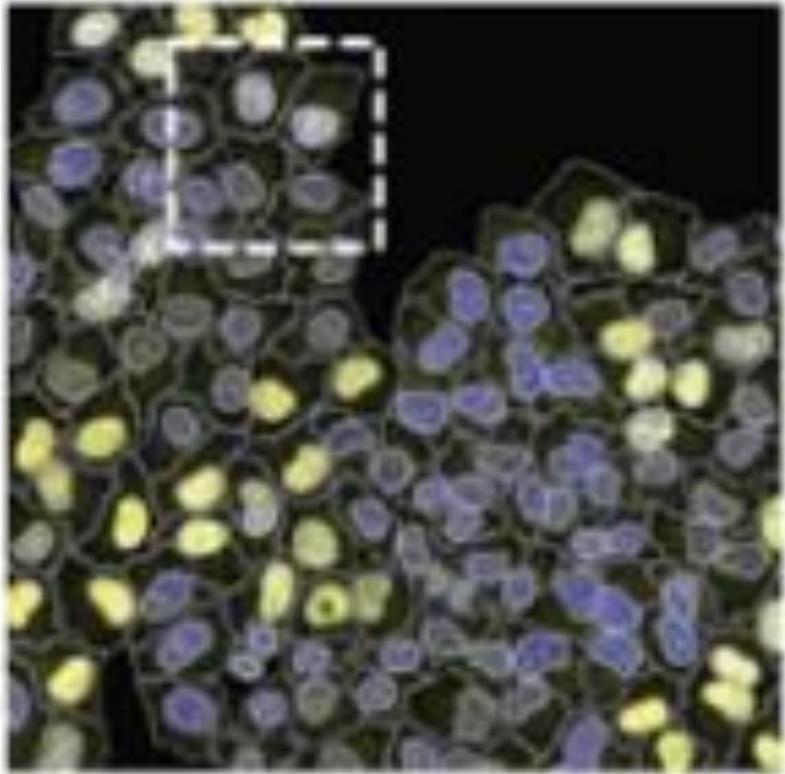


Constructs of cell-cycle progression trajectories from fixed cell images in heterogeneous microenvironments

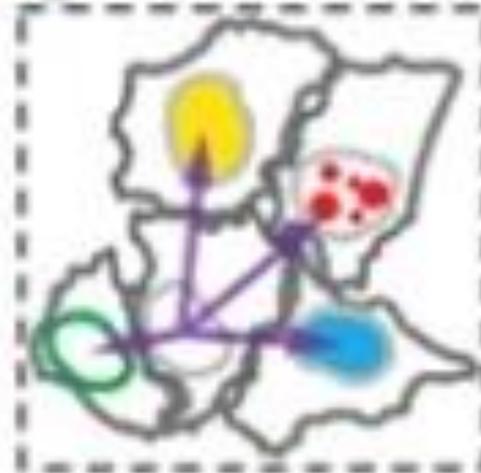
- Pseudo time: ideas from systems biology
 - Developmental path trajectory from single-cell mass cytometry data (Bendall et al., 2014)
 - Recover cell-cycle progression from features extracted from fixed microscopy images
- Role of microenvironment

1. Single cell quantification

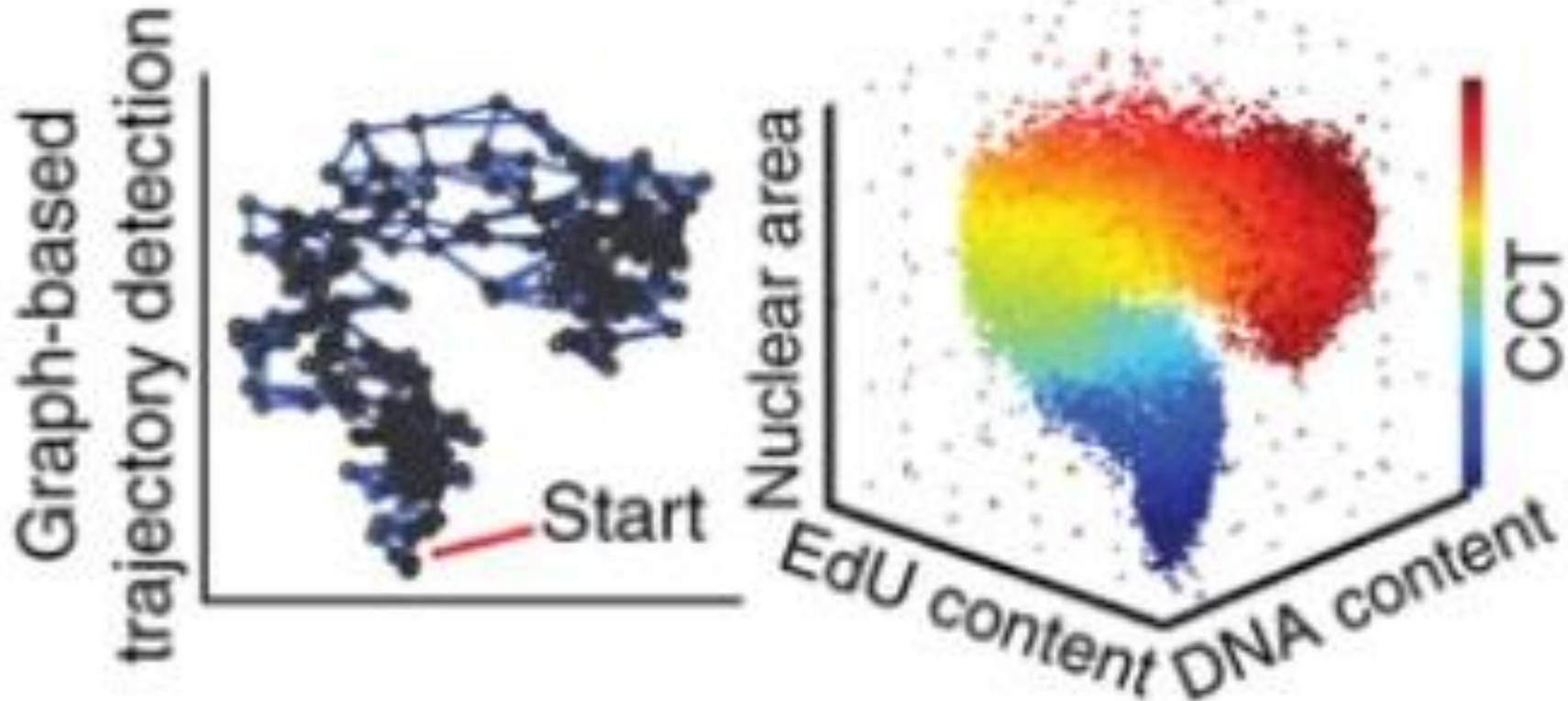
Single-cell quantification



-  DNA replication
-  DNA content
-  Nuclear area
-  Local cell crowding

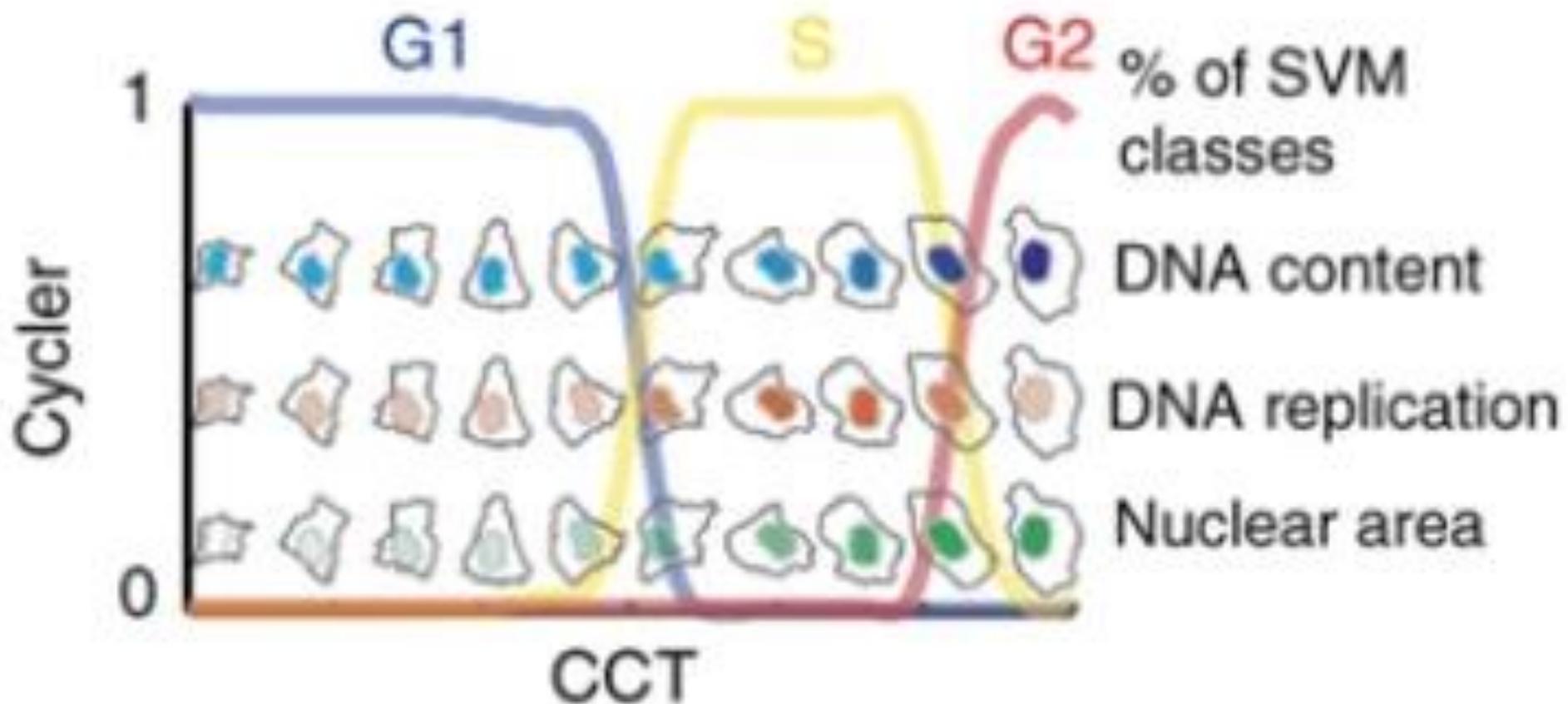


2. KNN graph-based embedding of the feature space to 1D cell cycle trajectory



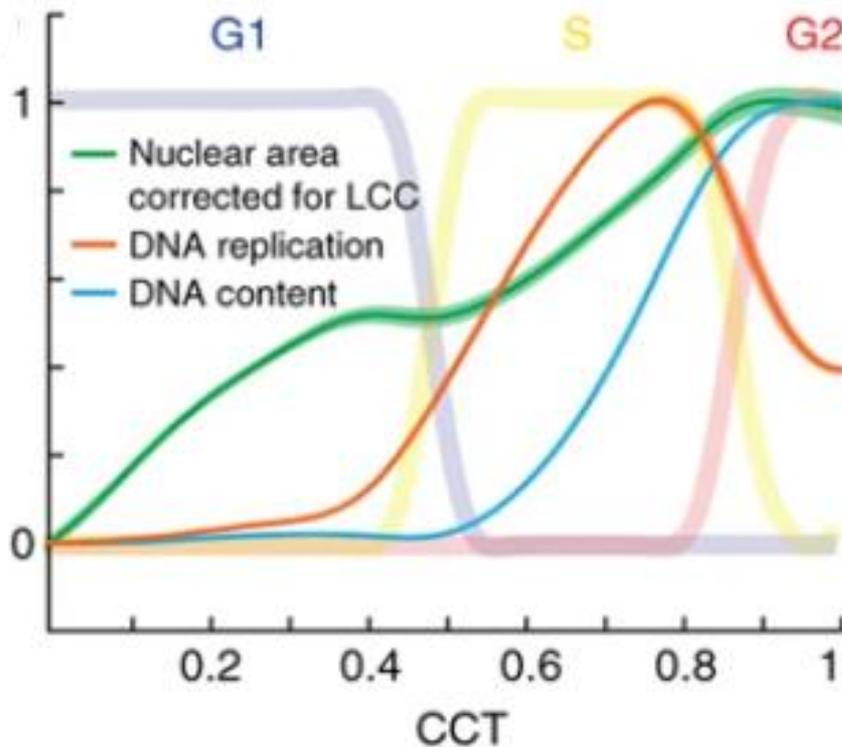
Each cell is represented as a node and connected to its k nearest neighbors. A cell's distance to another cell is the shortest-path. The position is the mean distance to a user defined starting point + randomly selected “waypoints”.

3. Cells are aligned along the cell cycle trajectory

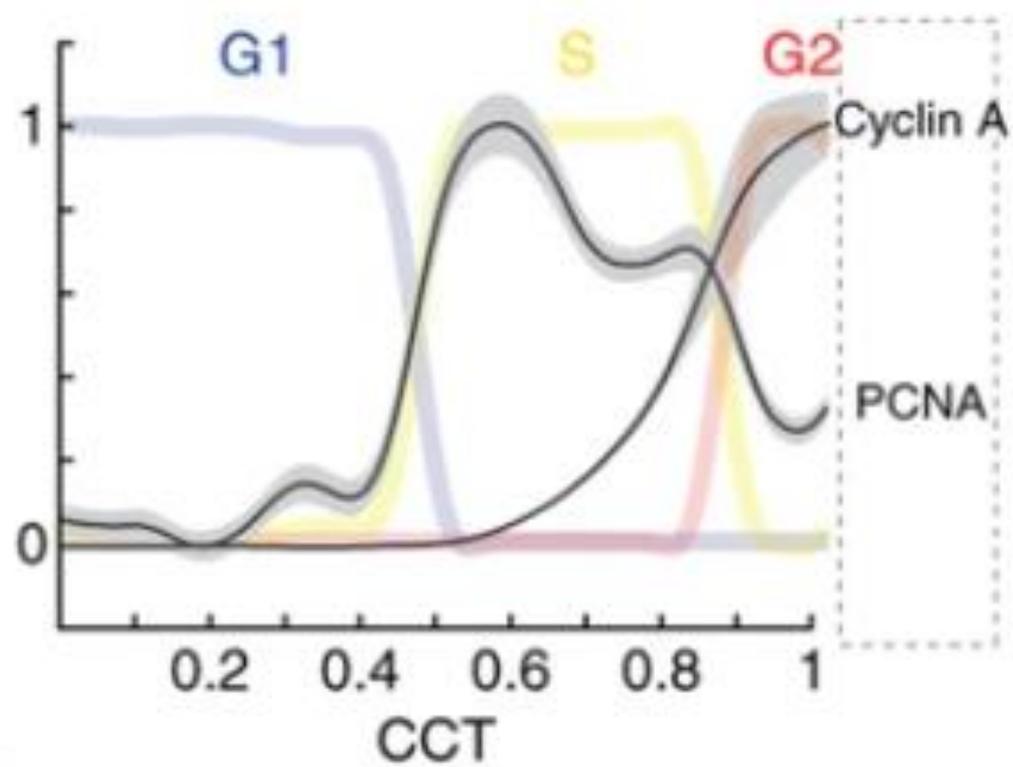


Validations

Single-cell features along the cell cycle trajectory

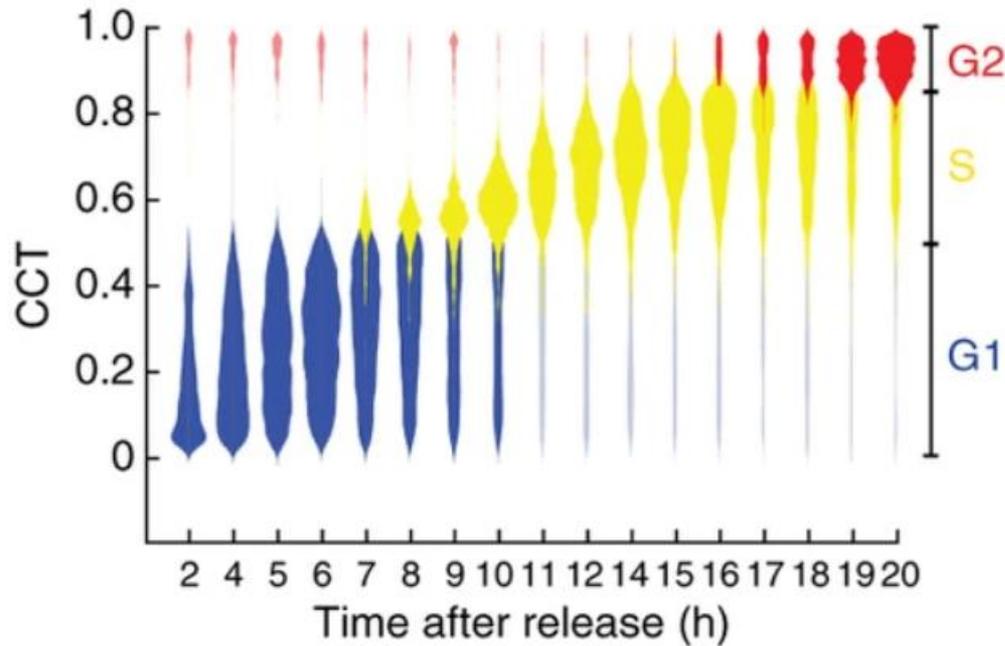


Cell cycle markers along the cell cycle trajectory

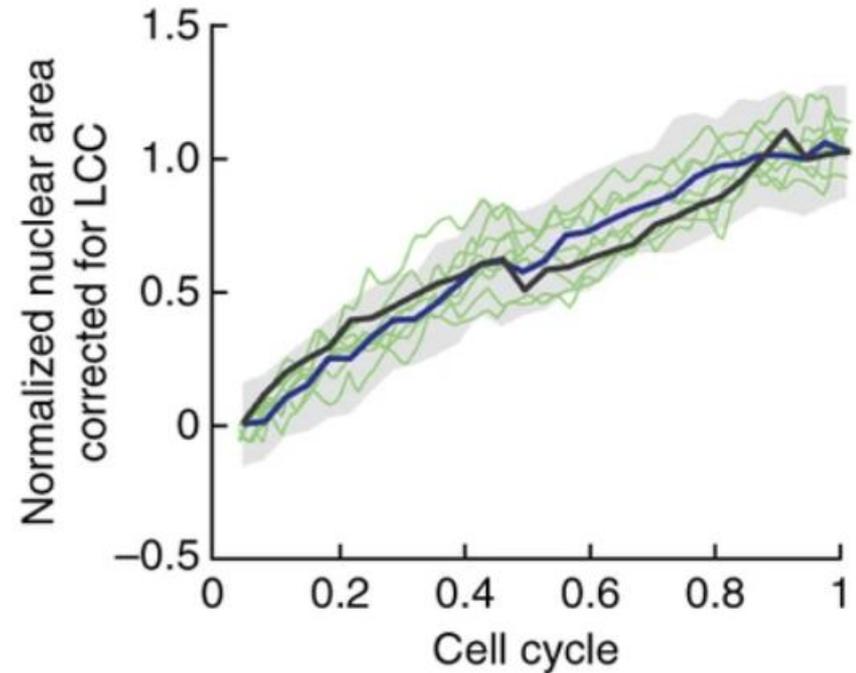


Validations

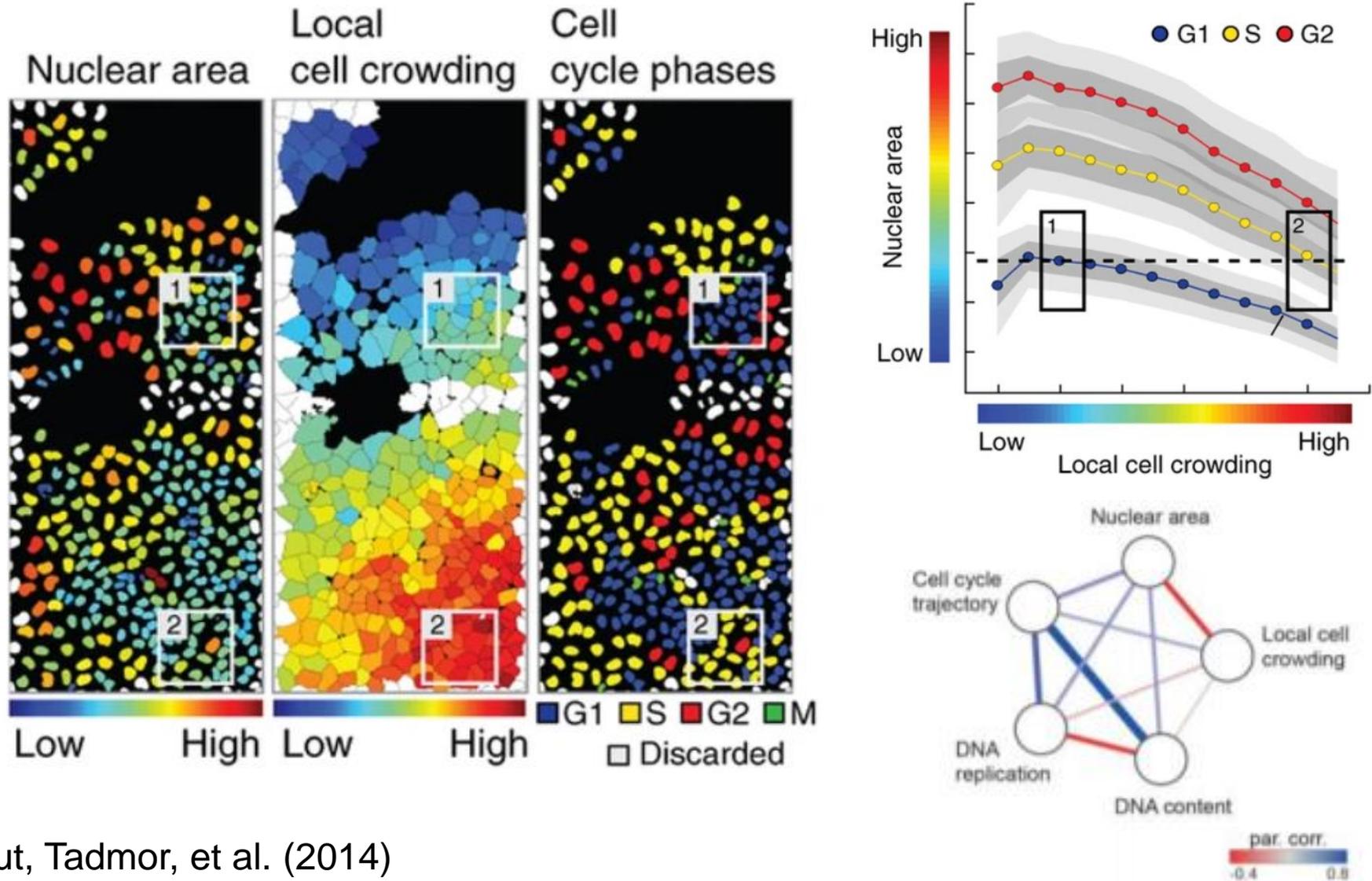
Cell cycle state over time
(synchronization w growth arrest)



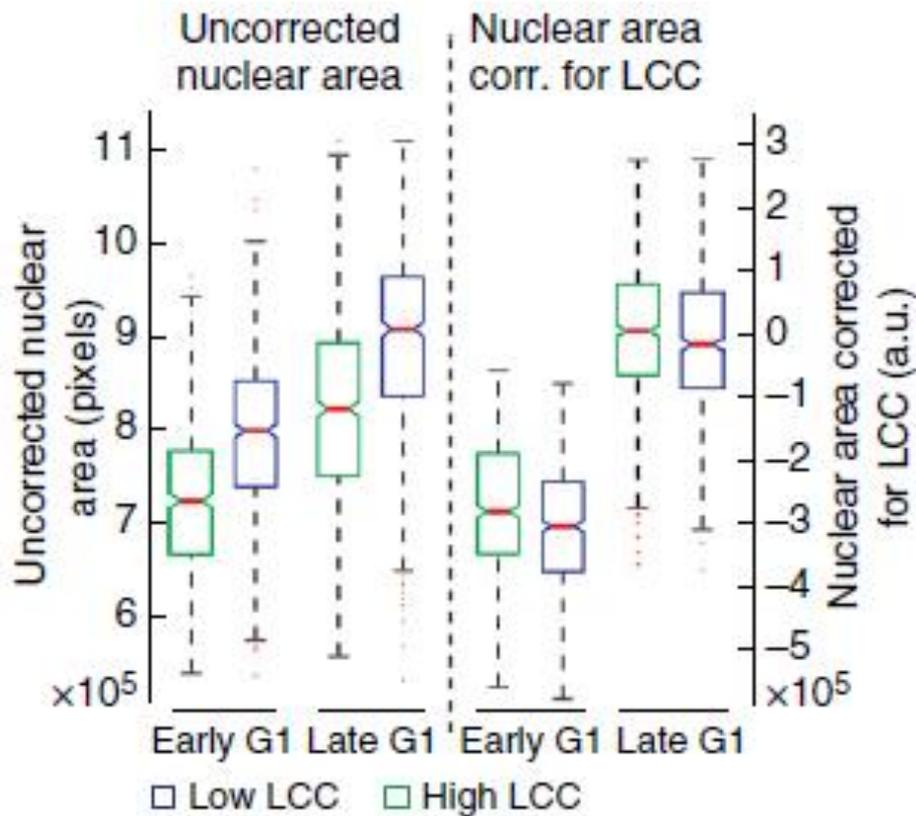
Live imaging vs. CCT



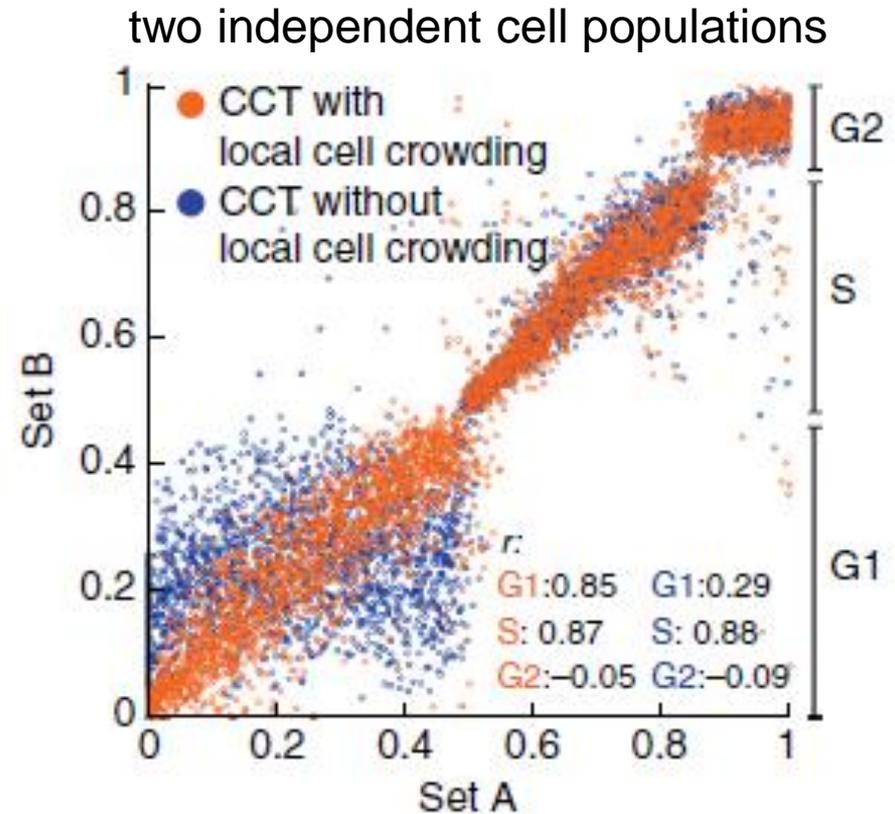
The microenvironment is important for accurate cell cycle trajectory



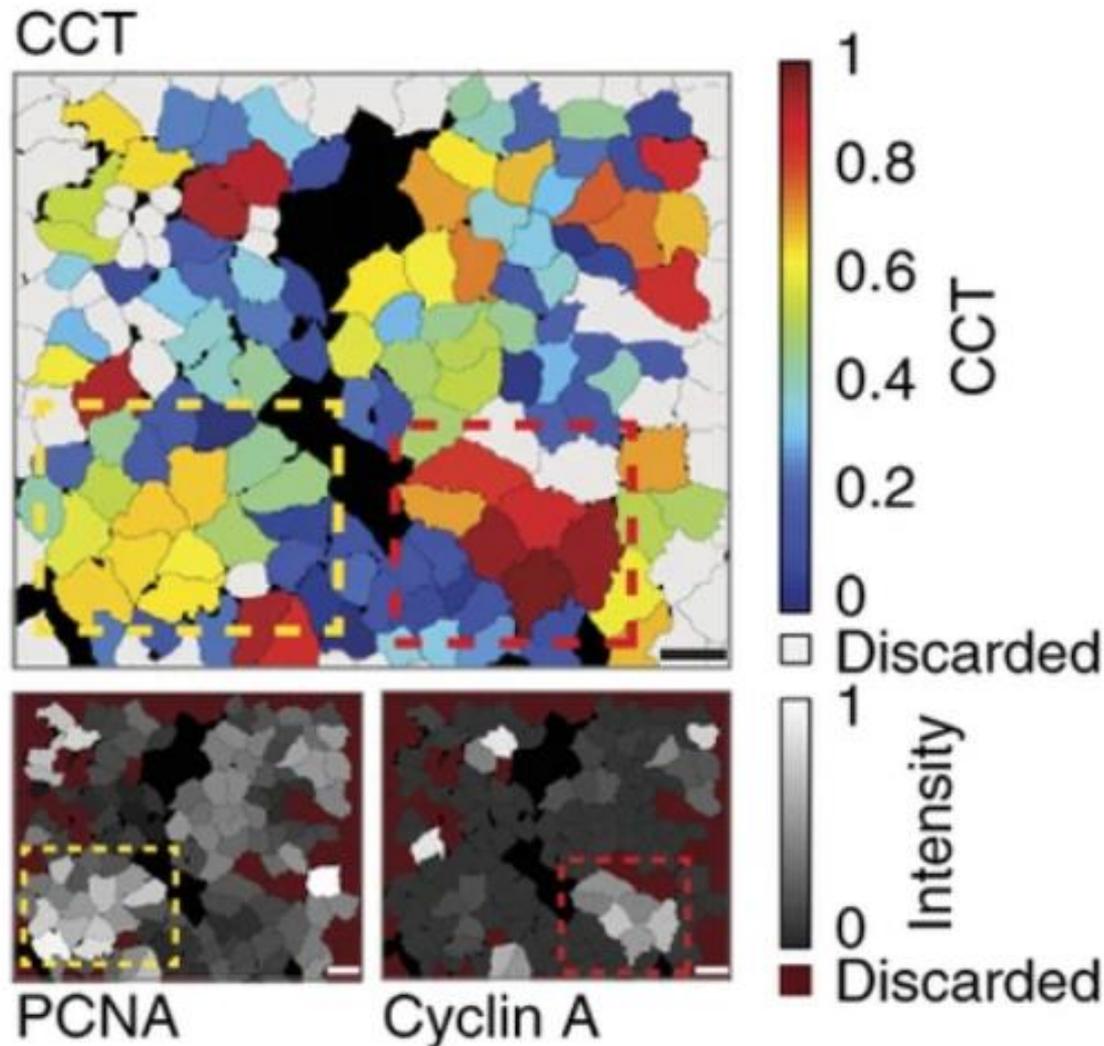
Correcting for local cell crowding



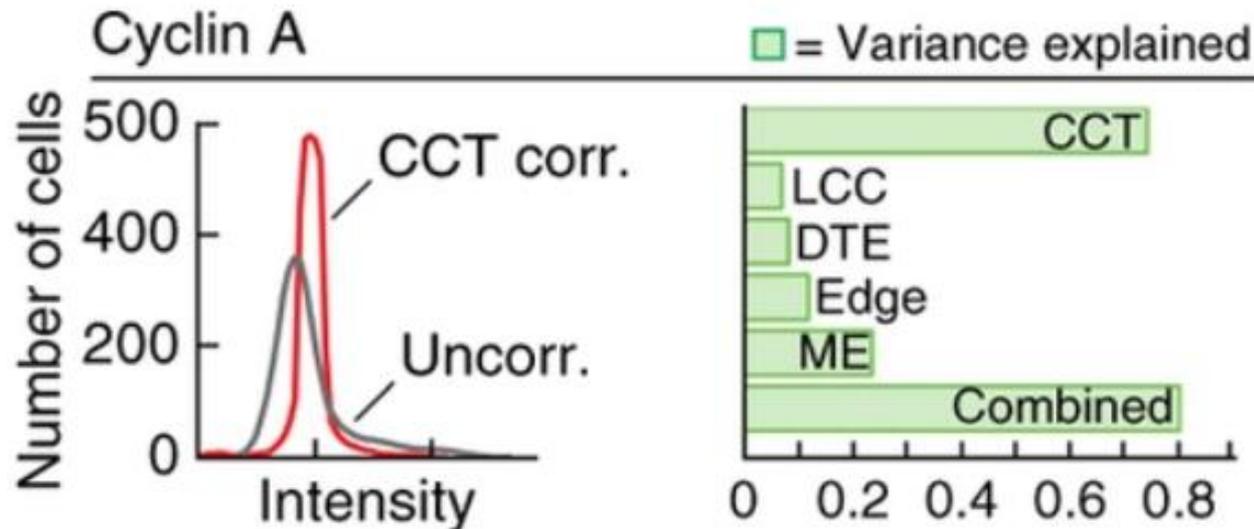
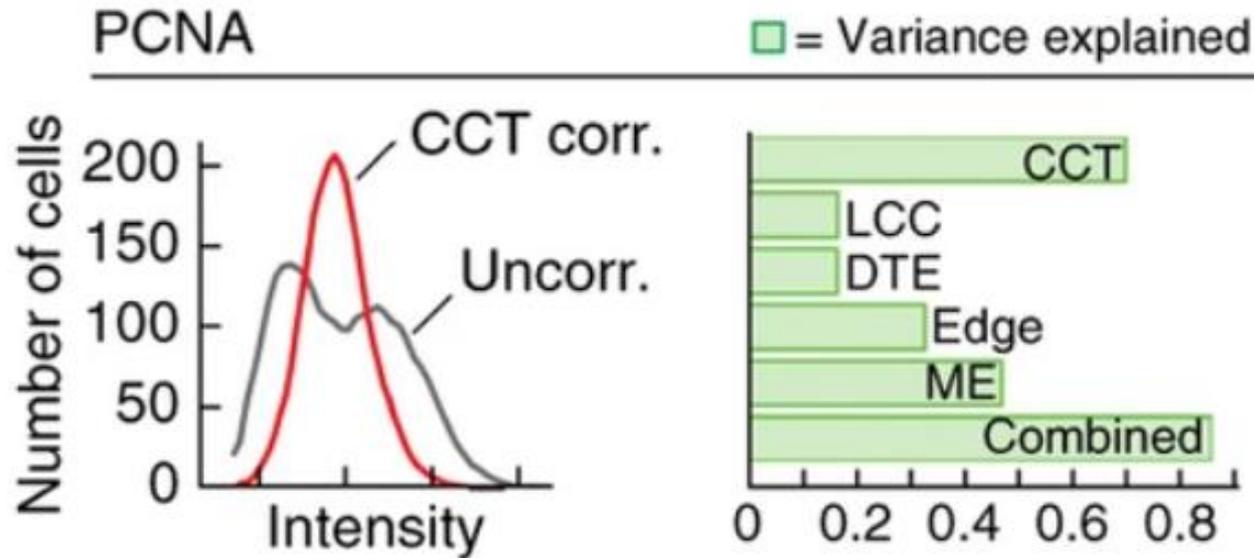
LCC – local cell crowding



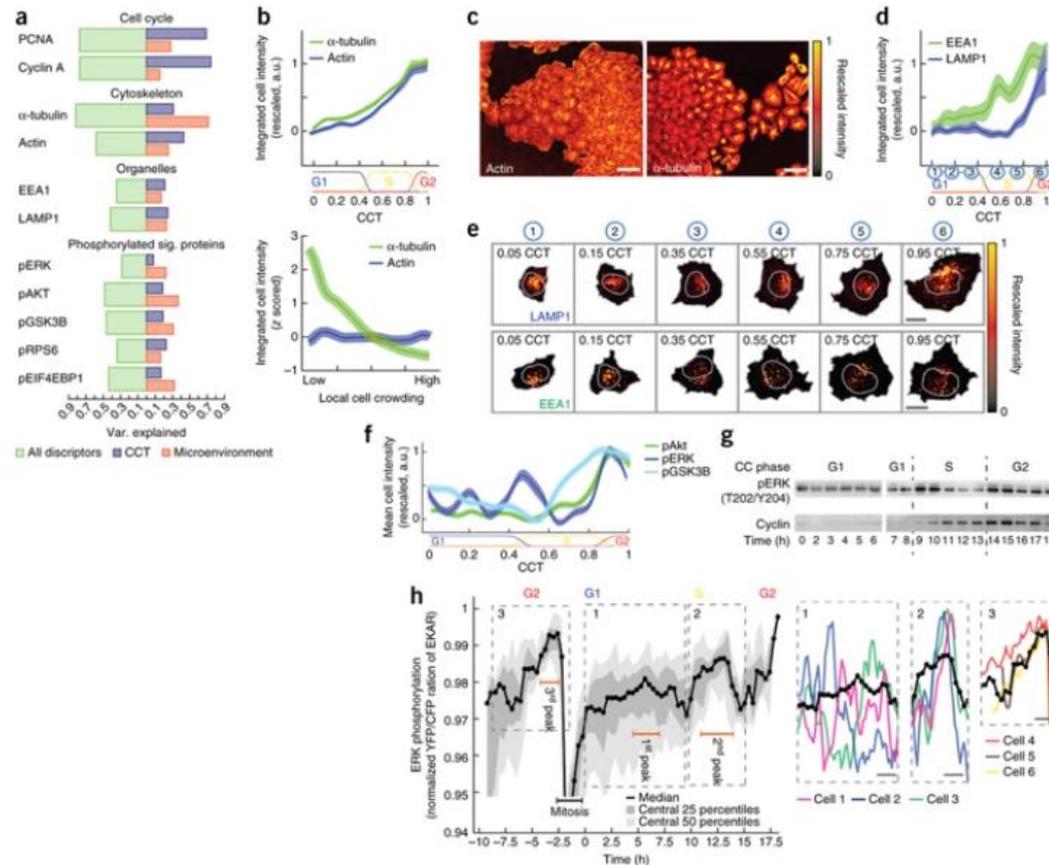
Variability in cell-cycle progression in unsynchronized cell cultures



CCT explains most of the variability



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



Student lecture by Hila Ben Ami and
Saar Ben David on “DeepCycle”,
Rappez et al. , 2020

Information processing in multicellular systems

Assaf Zaritsky

Software and Information Systems Engineering

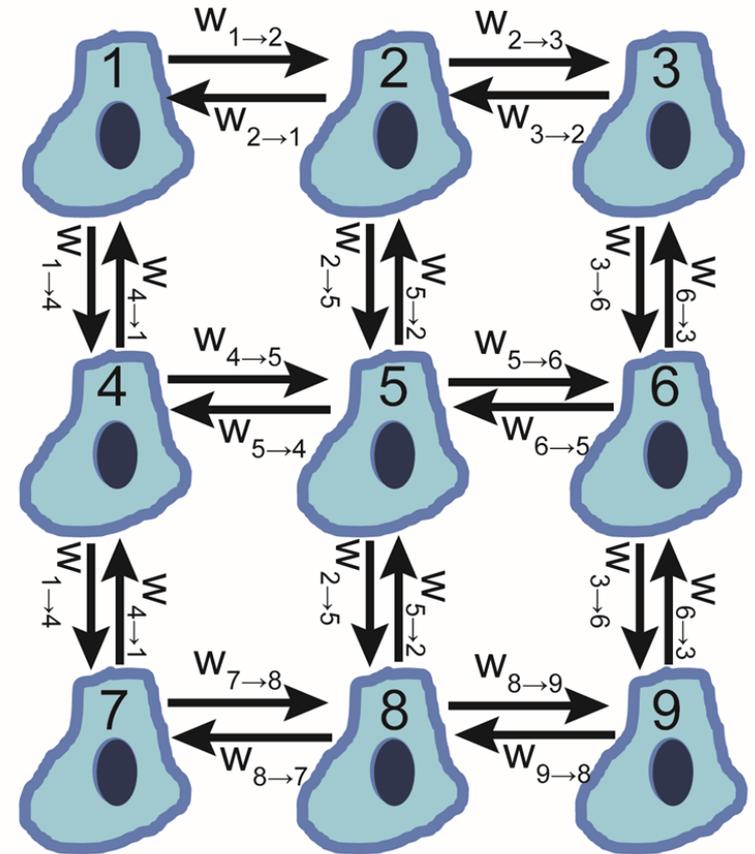
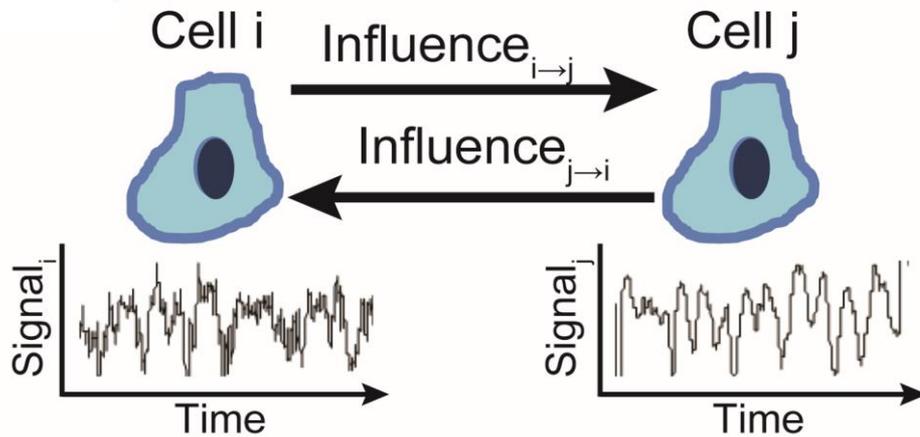
Ben-Gurion University of the Negev, Israel

Lab of computational cell dynamics

assafza@bgu.ac.il, @AssafZaritsky 

www.assafzaritsky.com

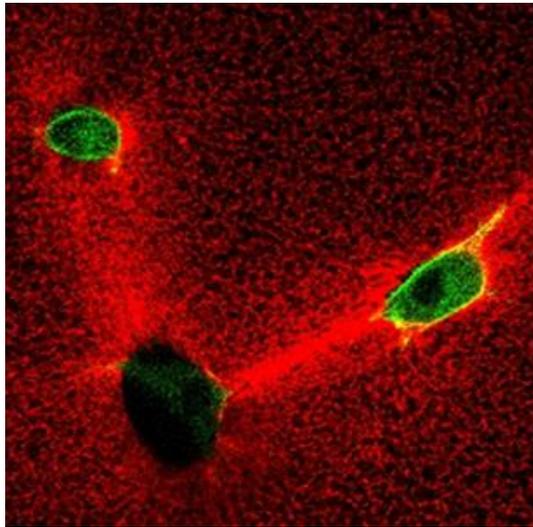
Data modeling networks of spatial influence at the single cell resolution



Multicellular information processing

Different systems to study different aspects

Cell-EMC-cell
communication

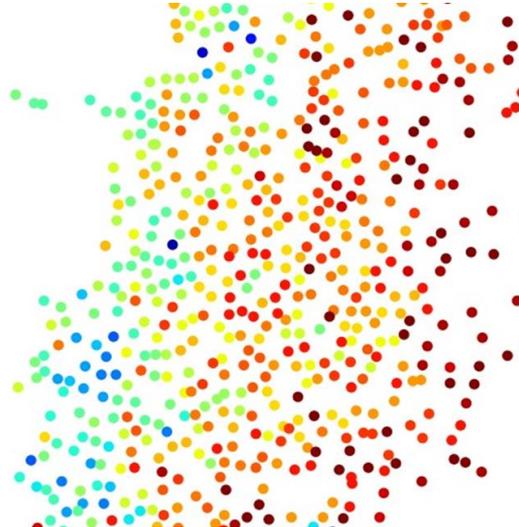


Nahum et al. (2020)

With Ayelet
Lesman, TAU



Collective cell
death



Riegman et al. (2020)

With Mike
Overholtzer,
MSKCC



Collective
synchronization



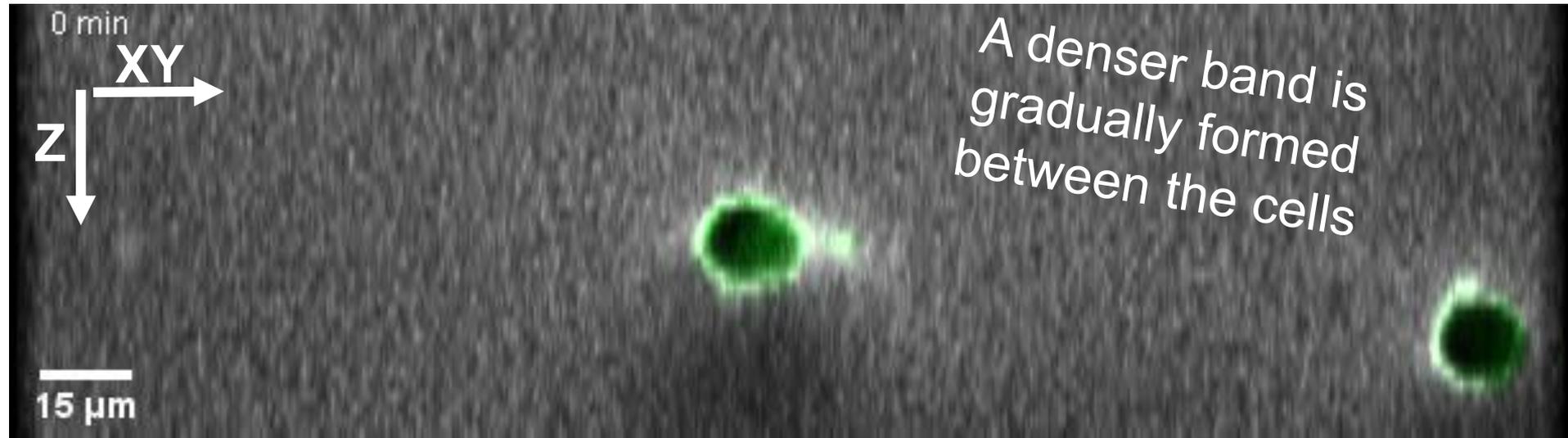
Amos Zamir

Zamir et al. (2020)

With Bo Sun,
OSU



Quantifying long-range cell-cell mechanical communication



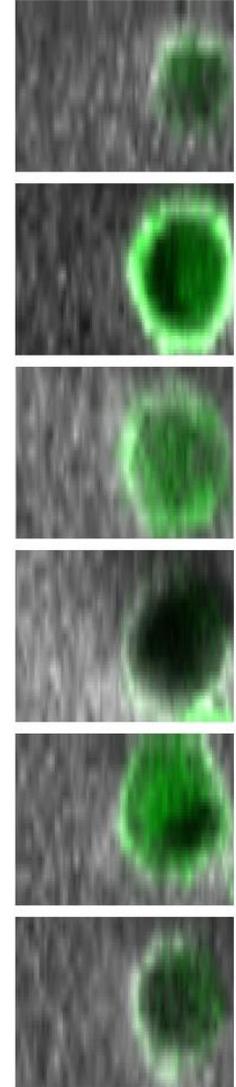
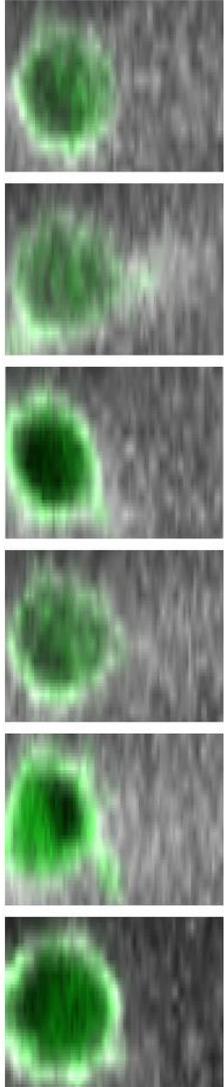
Assaf Nahum



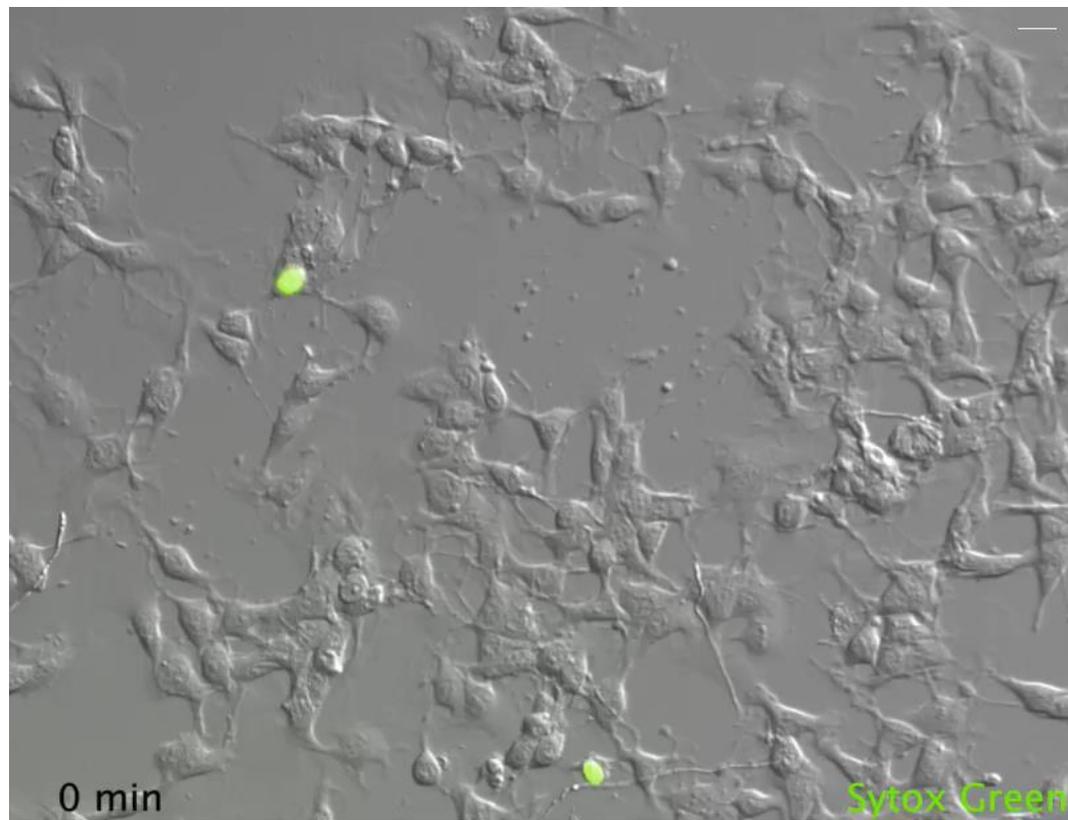
With Ayelet
Lesman, TAU



Quantifying long-range cell-cell mechanical communication



Quantitative spatiotemporal characterization of collective cell death



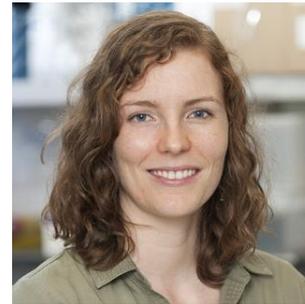
Liran
Sagie



Chen
Galed

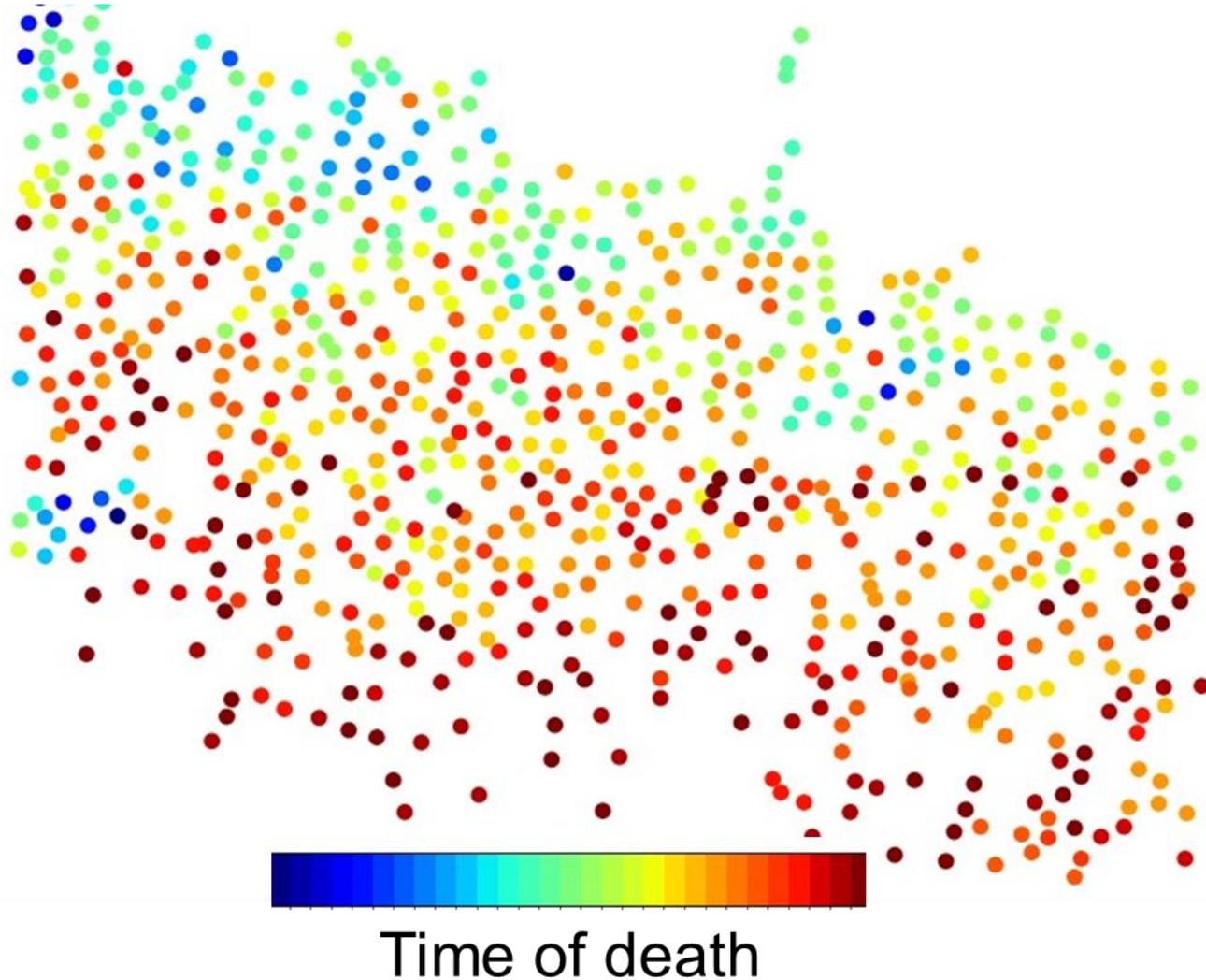


Tom
Levin



With Michelle Riegman and
Mike Overholzer, MSKCC

Cell death spreading = nucleation + propagation

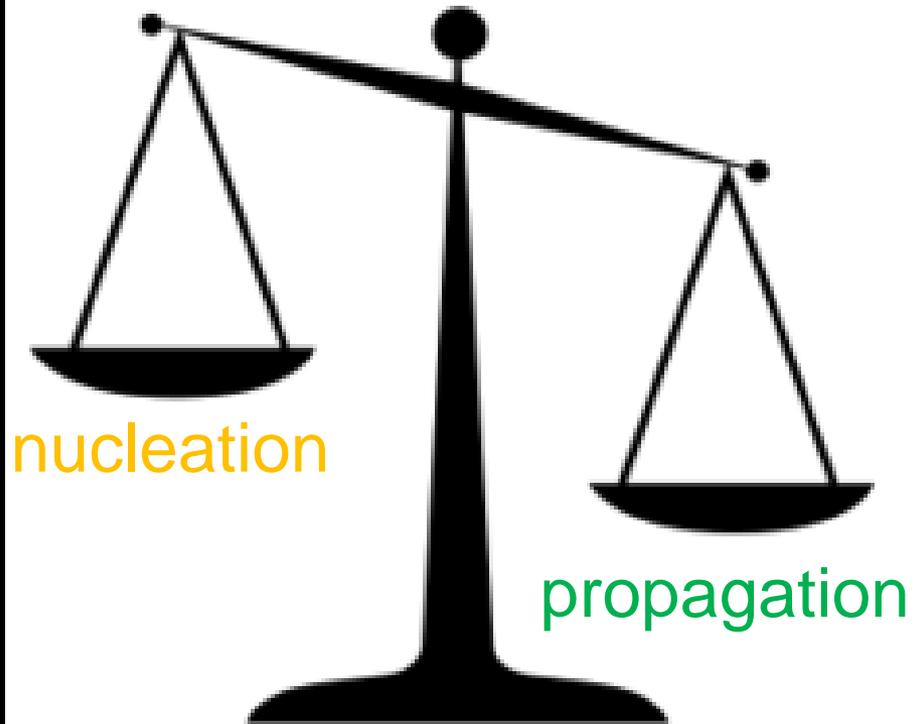


Yishaia
Zabary

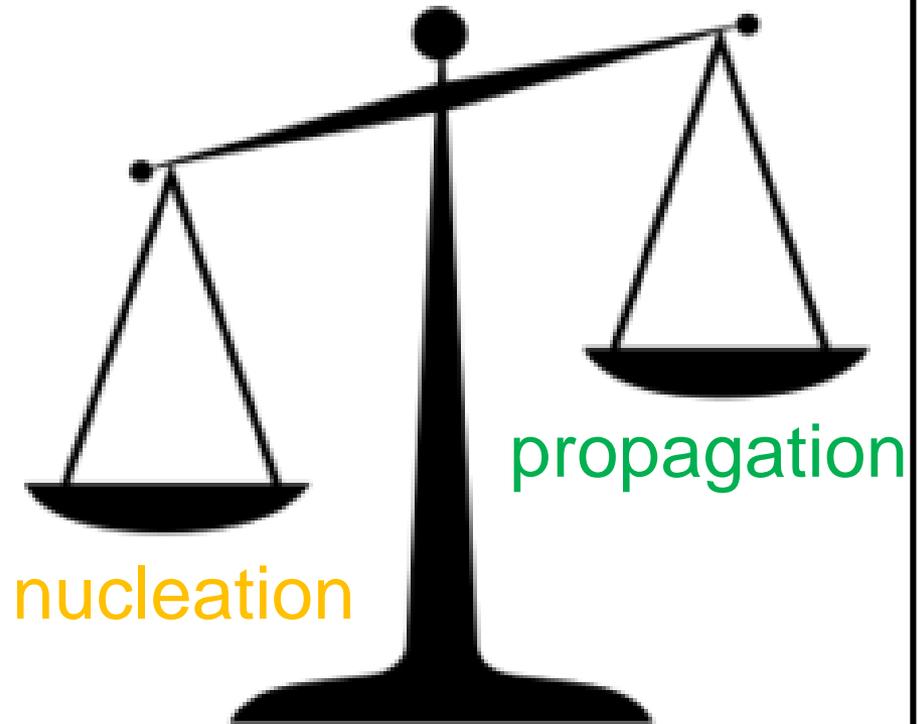


Cell death spreading =
nucleation + propagation

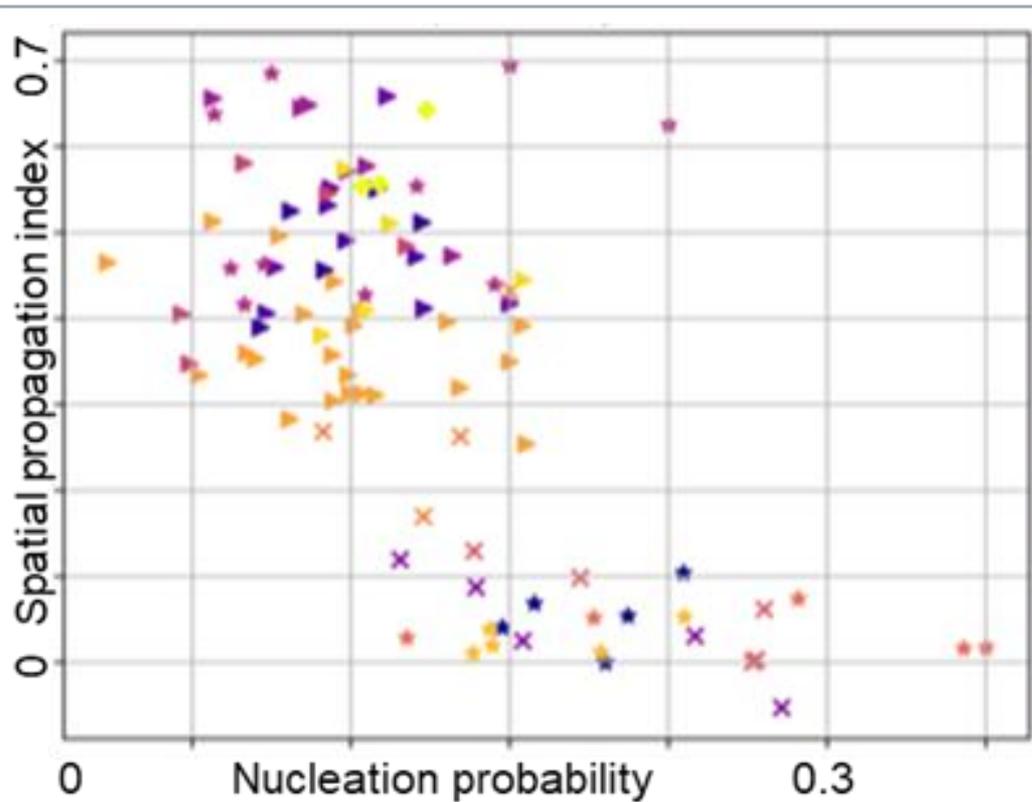
Apoptosis



Ferroptosis



Cell death spreading = nucleation + propagation



Propagative deaths

- ▲ FAC + BSO (collective ferroptosis)
- ▲ FAC + BSO (collective ferroptosis)
- ▲ FAC + BSO (collective ferroptosis)
- ▲ FAC + BSO + PEG1450
- ▲ FAC + BSO + PEG3350
- ▲ FAC + BSO - amino acids (collective ferroptosis)
- ▲ FAC + BSO - amino acids (collective ferroptosis)
- ★ erastin (collective ferroptosis)
- C' dot nanoparticles (collective ferroptosis)

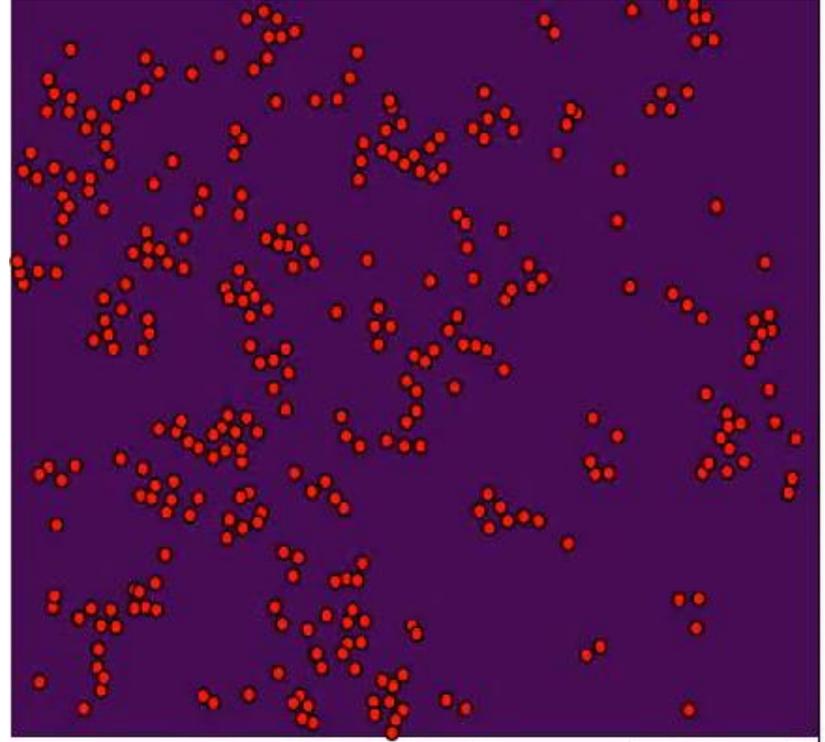
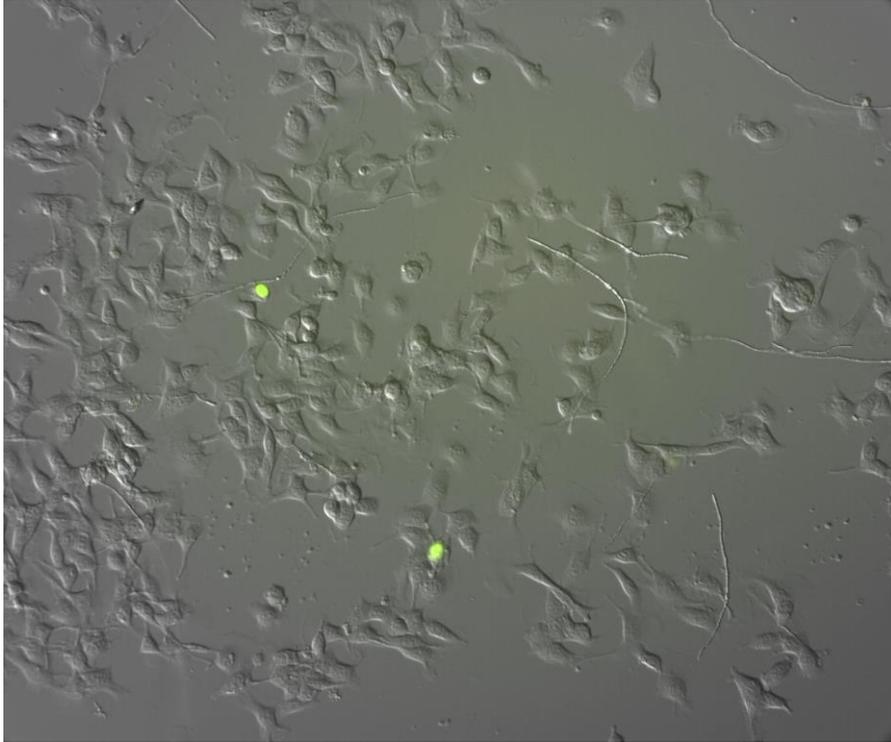
Intermediate death

- × ML162 - amino acids

Nucleative deaths

- ★ TRAIL (apoptosis)
- ★ H₂O₂ (necrosis)
- × ML162 (single cell ferroptosis)
- × ML162 (single cell ferroptosis)
- TNF α + SMAC + zVAD (necroptosis)

Combining quantitative imaging and simulations for spatiotemporal characterization of collective cell death



With Paul Macklin
and Randy Heiland
IU

Calcium dynamics in mechanically stimulated monolayers of endothelial cells



Amos Zamir

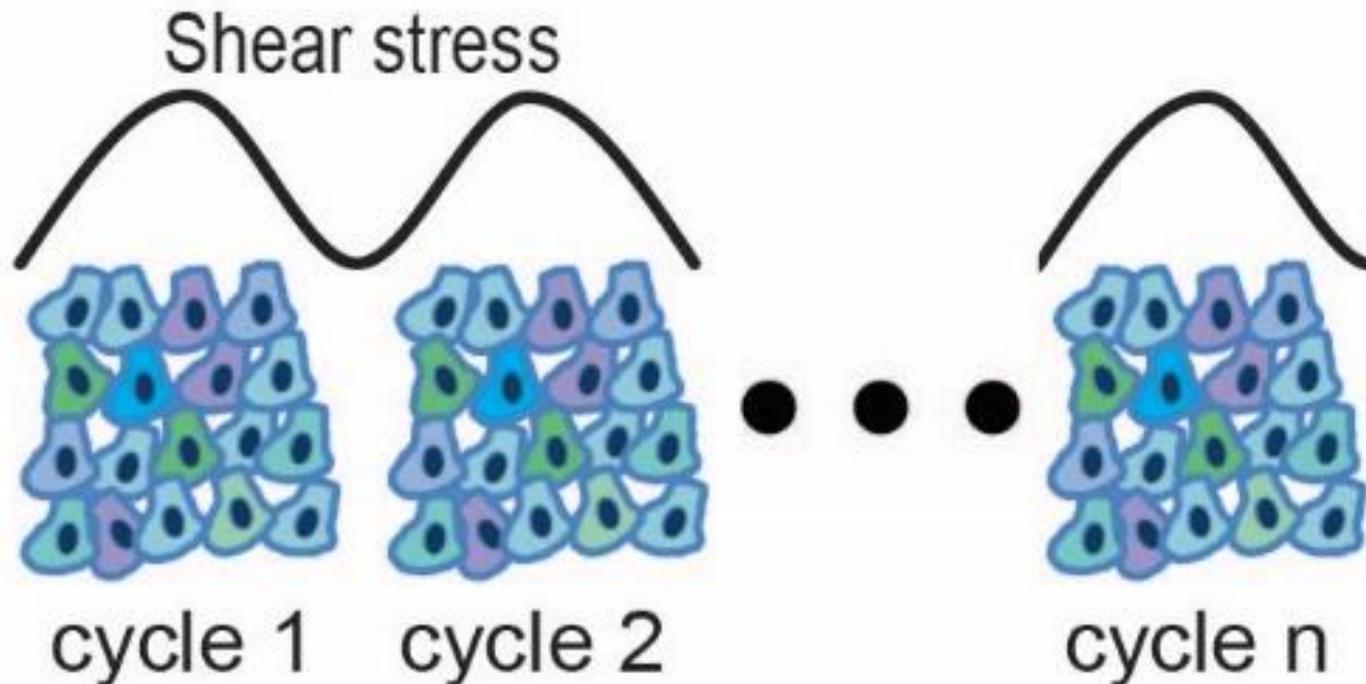


With Bo Sun,
OSU

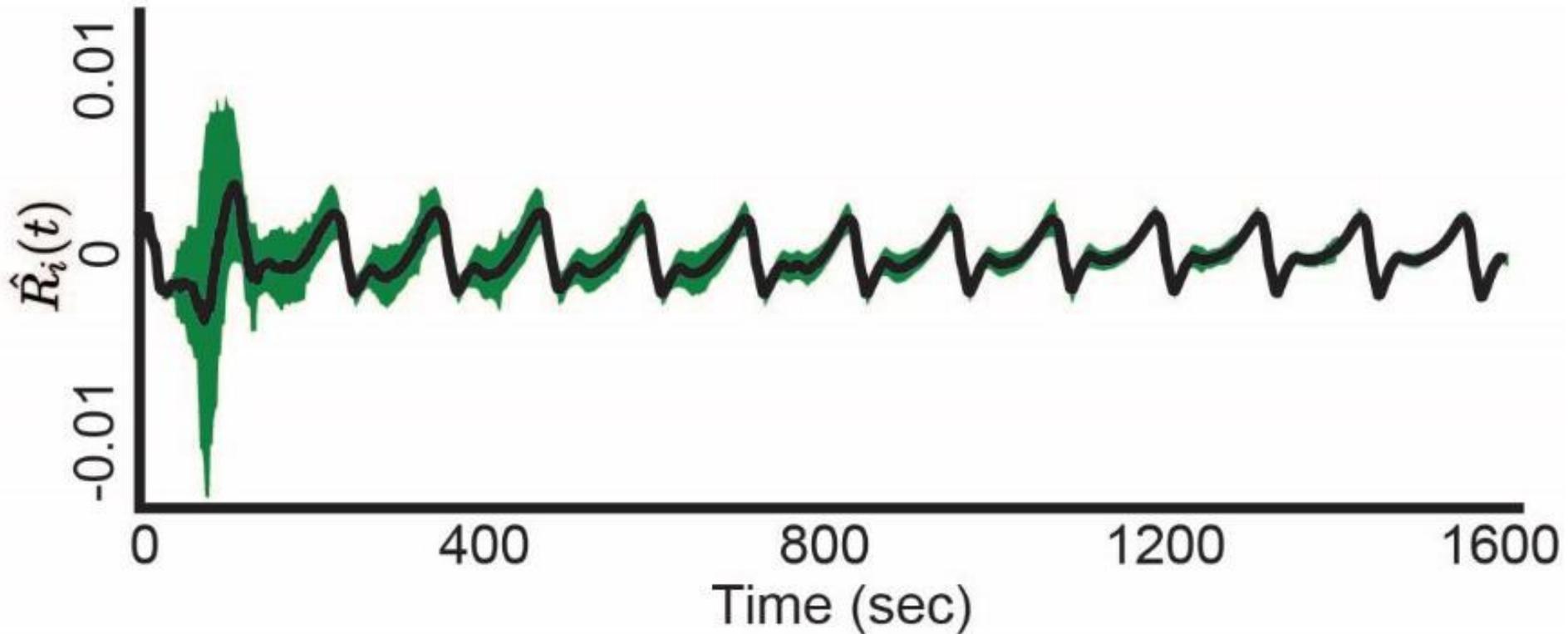


Can the multicellular network learn to adapt to changing external stimuli?

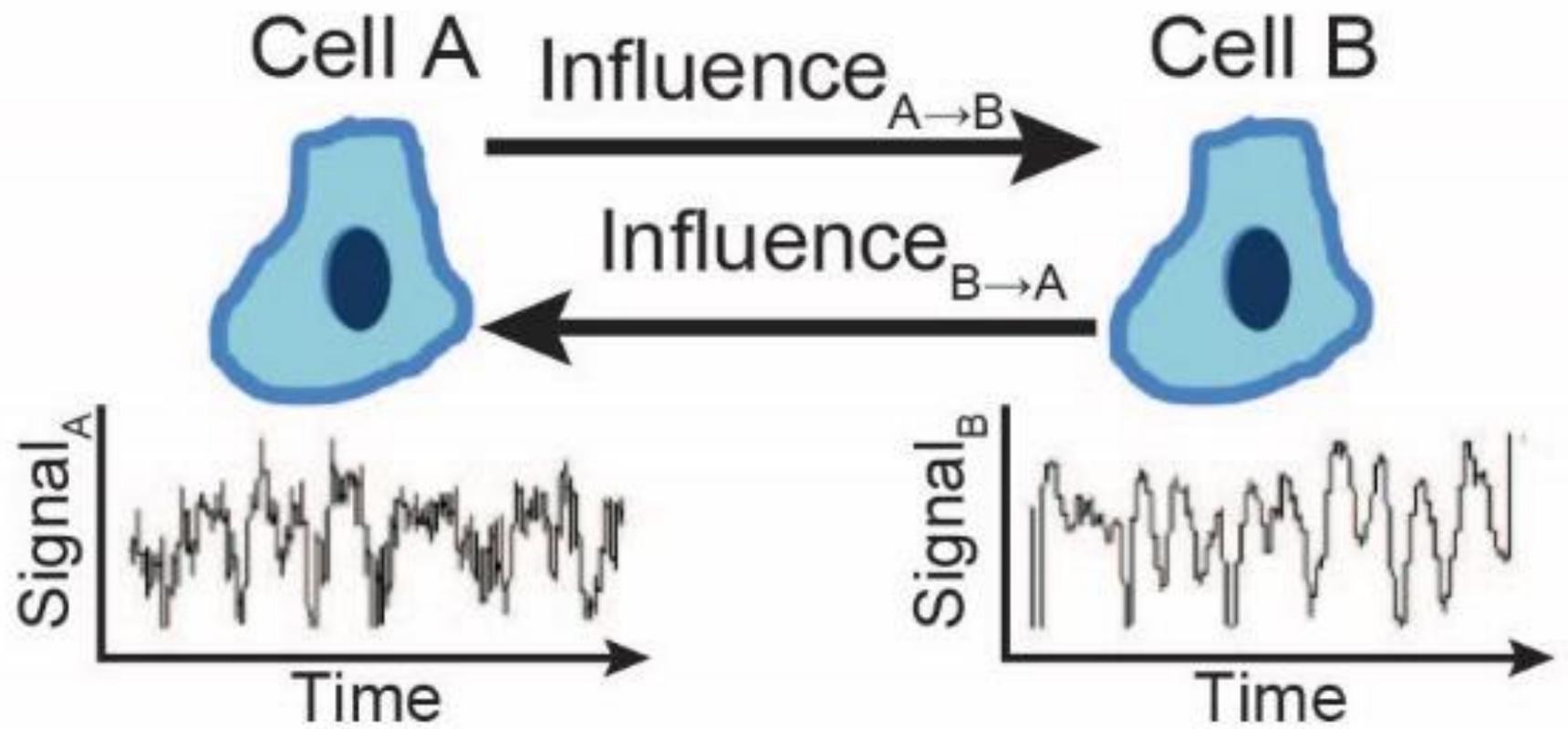
Applying global external periodic mechanical stimuli



Synchronization is gradually reinforced



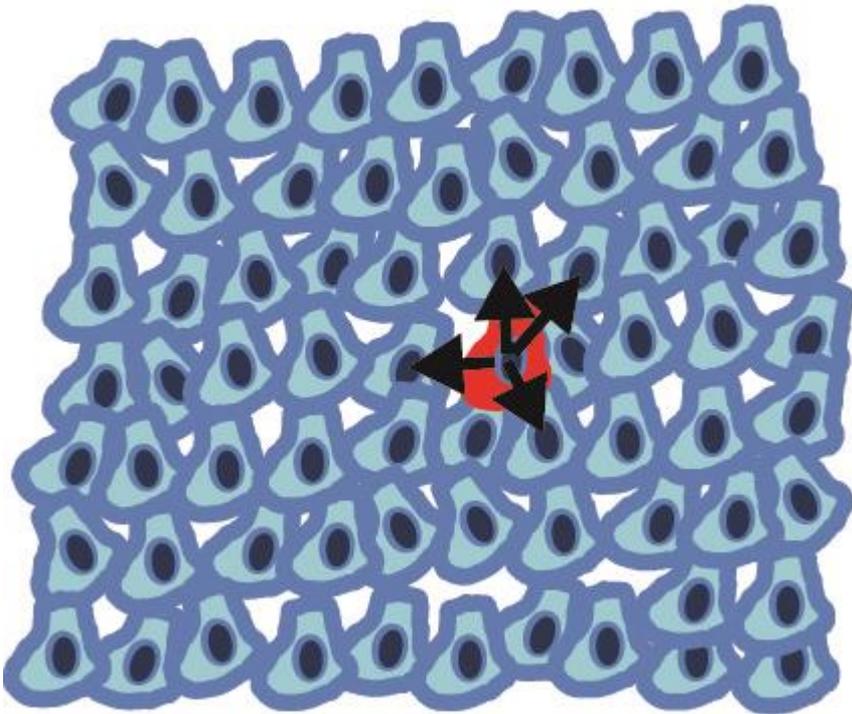
Cell-cell asymmetric information-transfer inference via information-theory



Transmission/receiver score

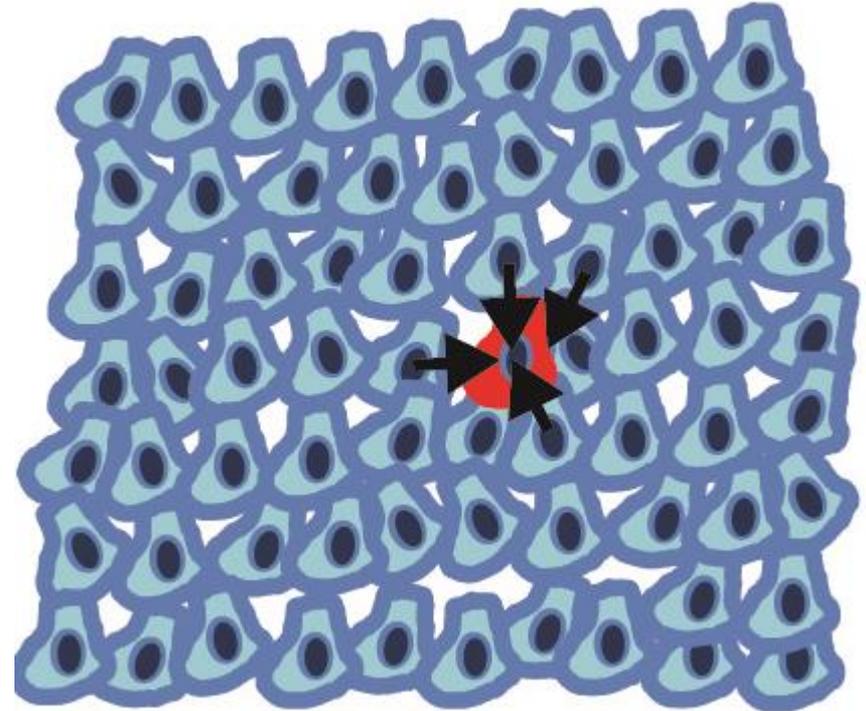
Transmission score

Probability of an outgoing edge



Receiver score

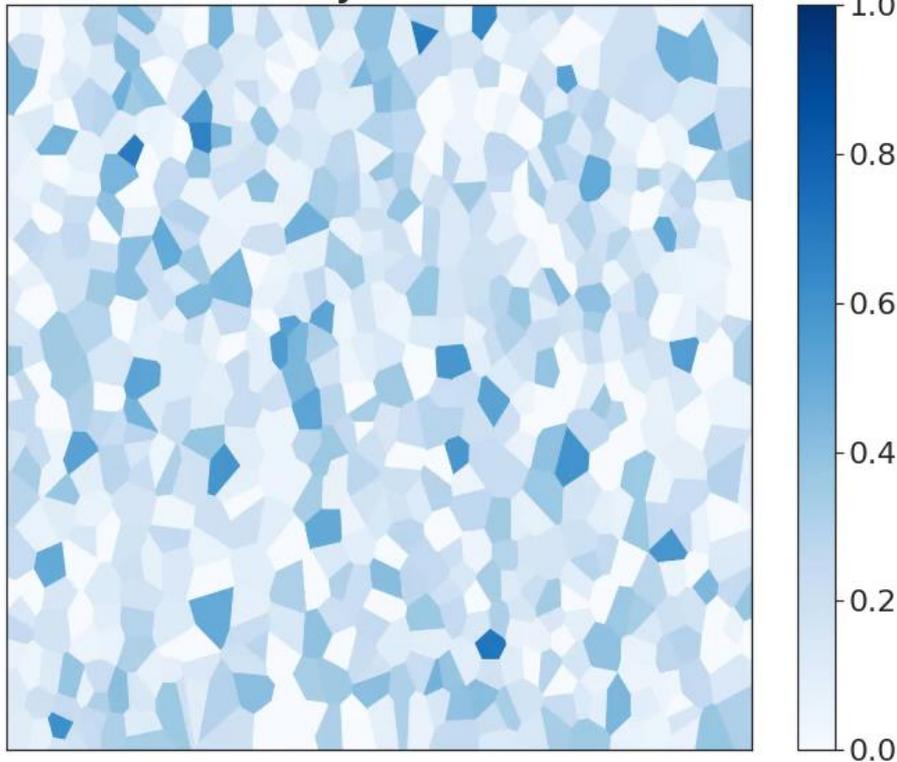
Probability of an incoming edge



Gradual increase in information flow

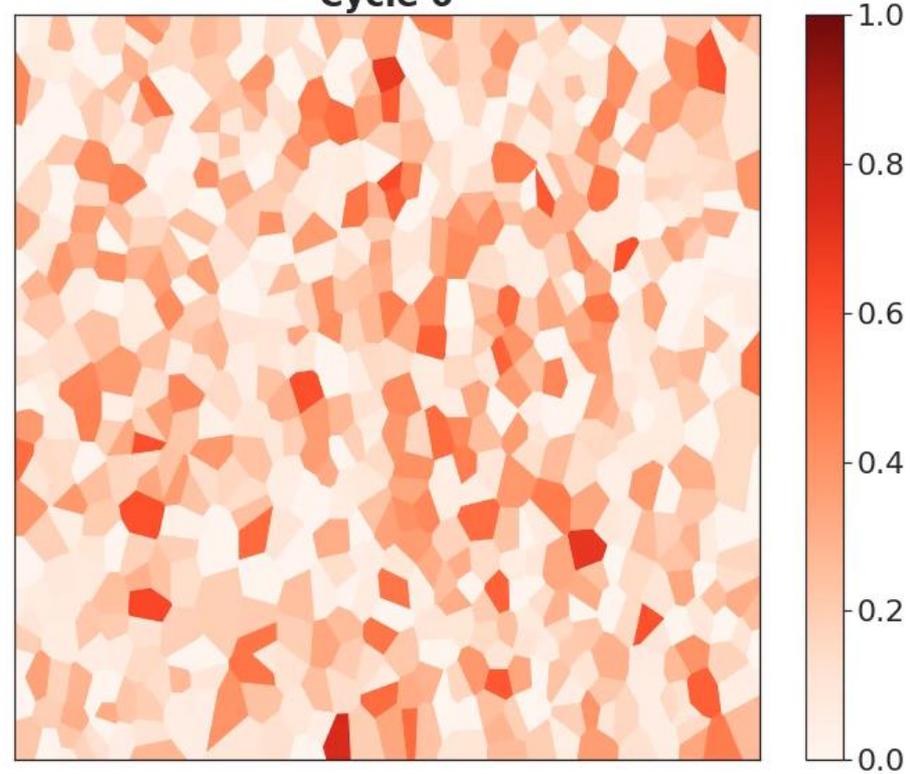
Transmission score

Cycle 0

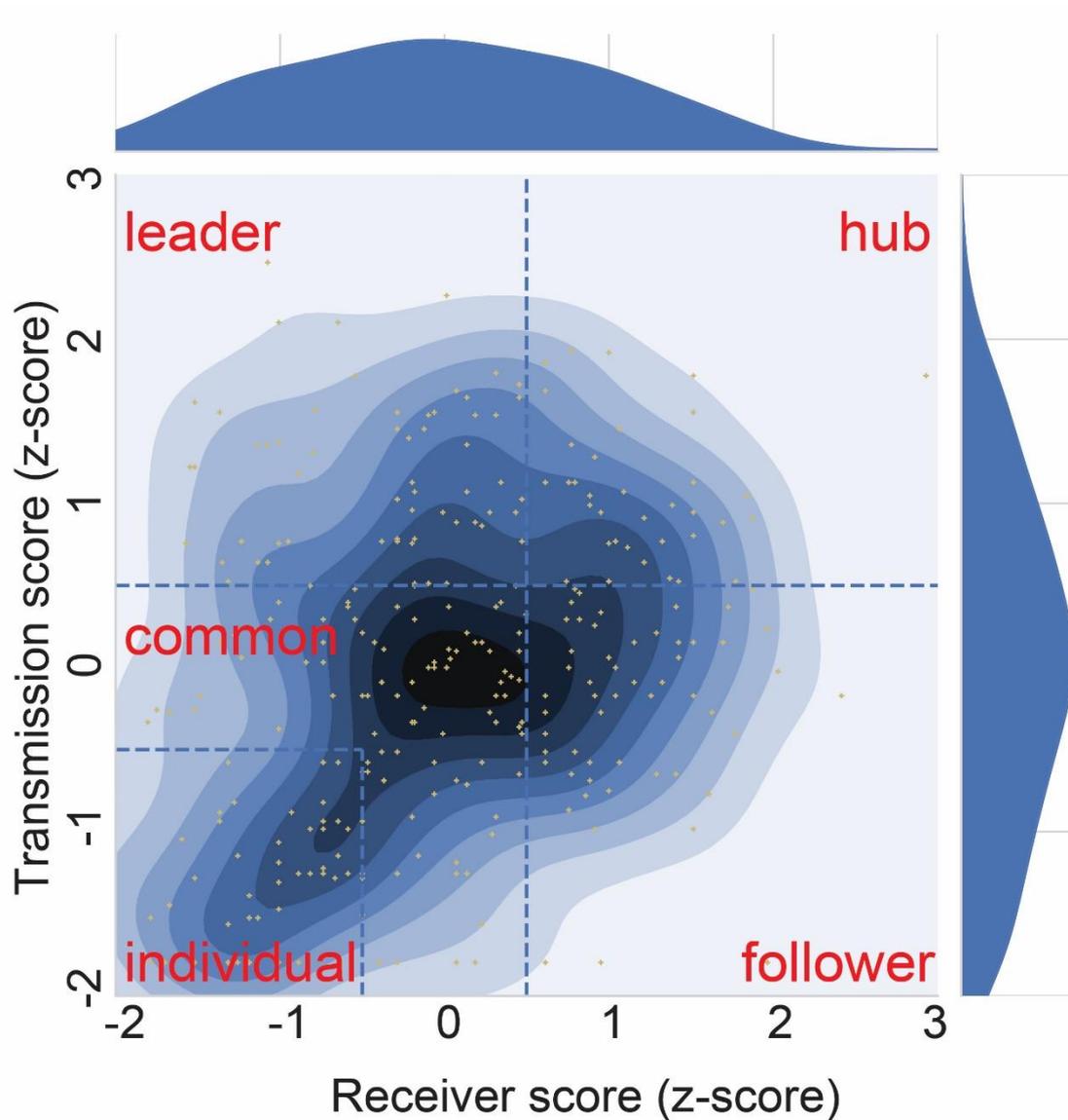


Receiver score

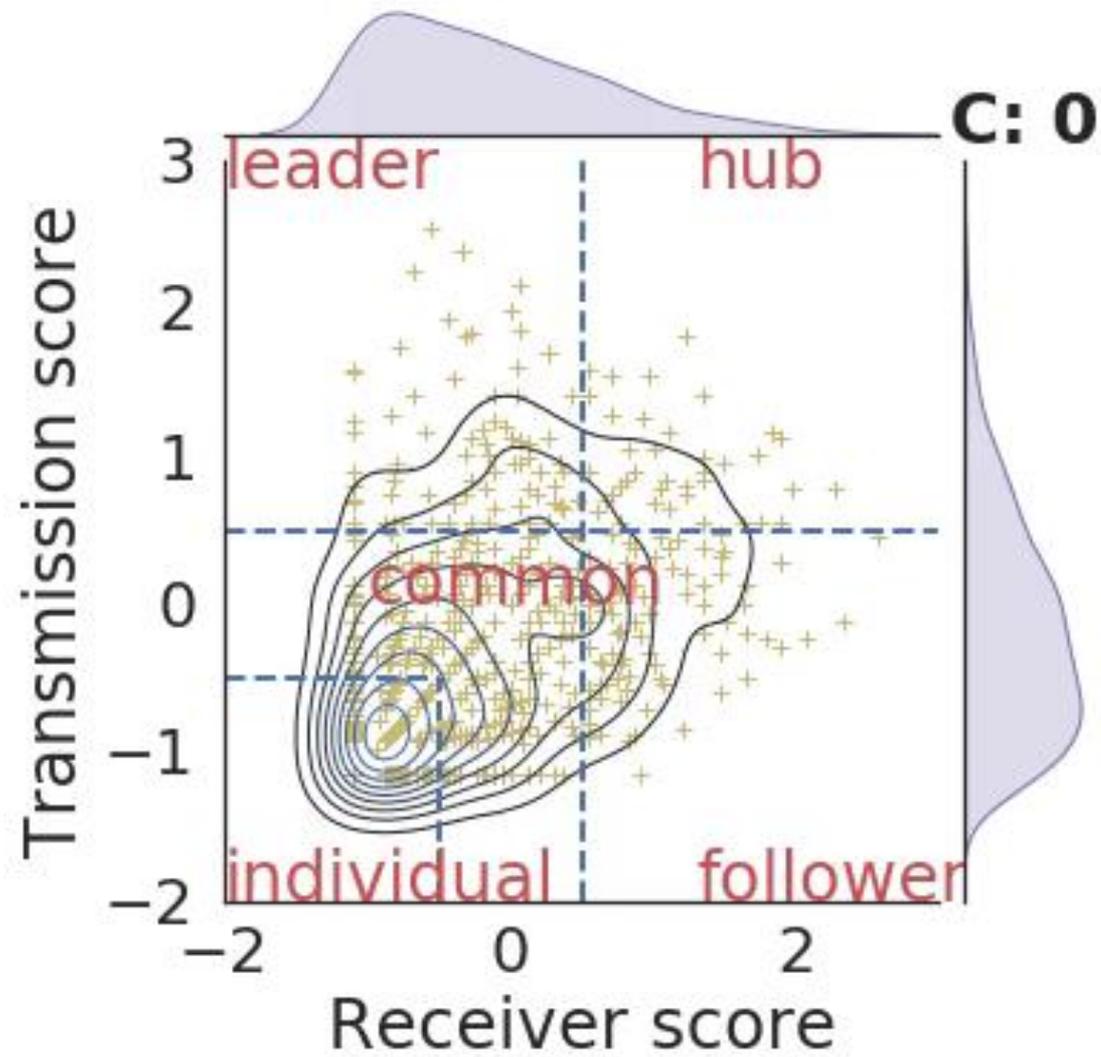
Cycle 0



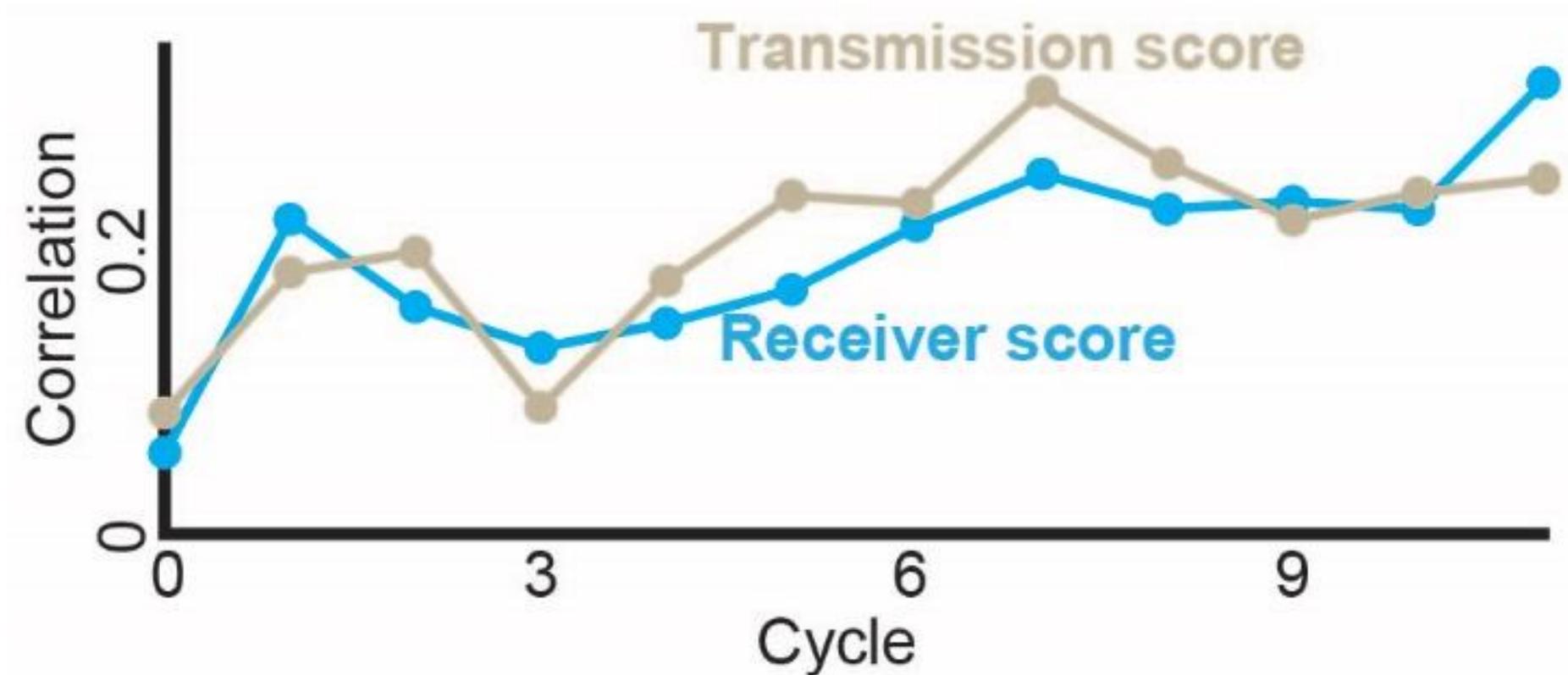
Single cell heterogeneity in intercellular communication



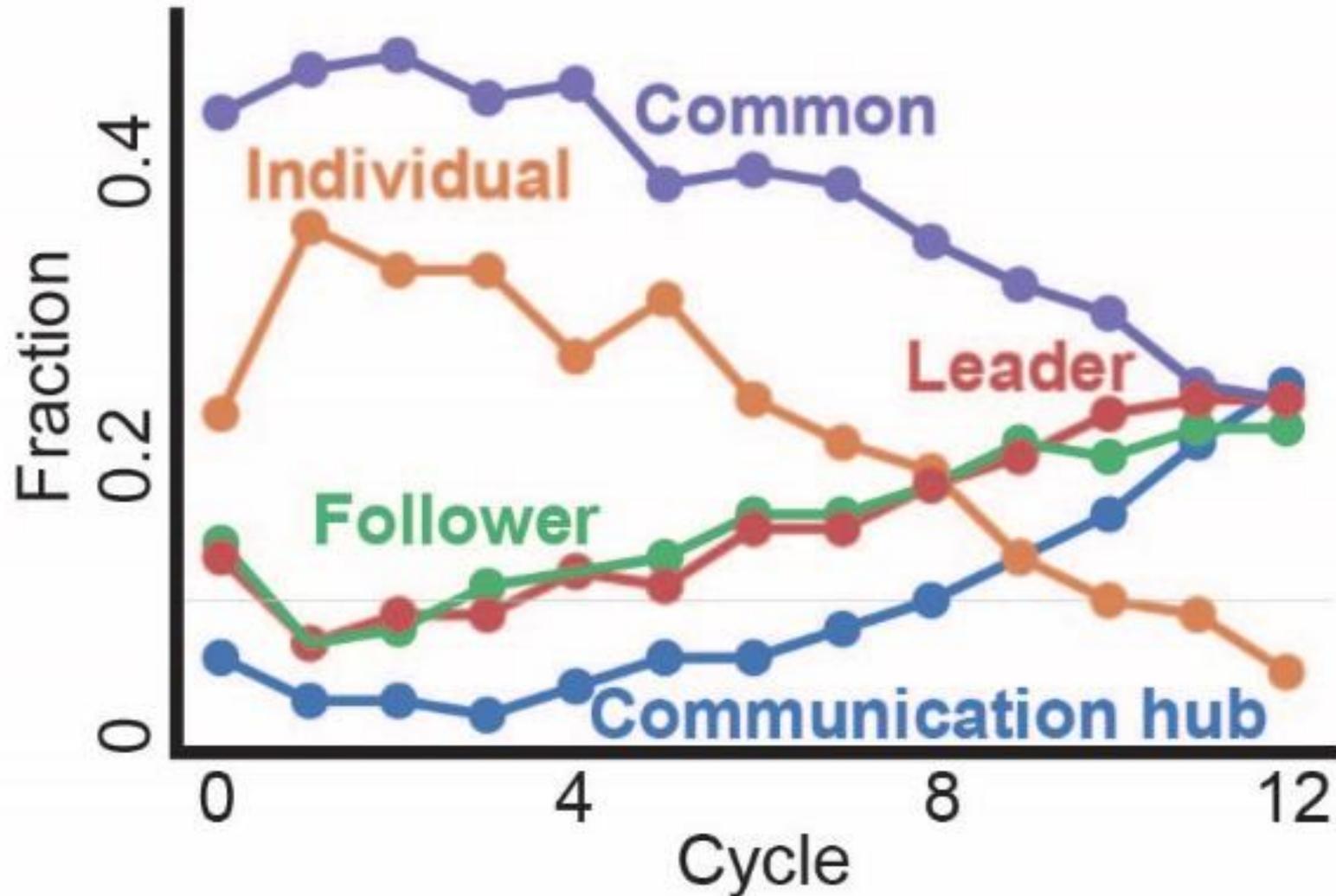
Synchronization associates with information flow within the multicellular network



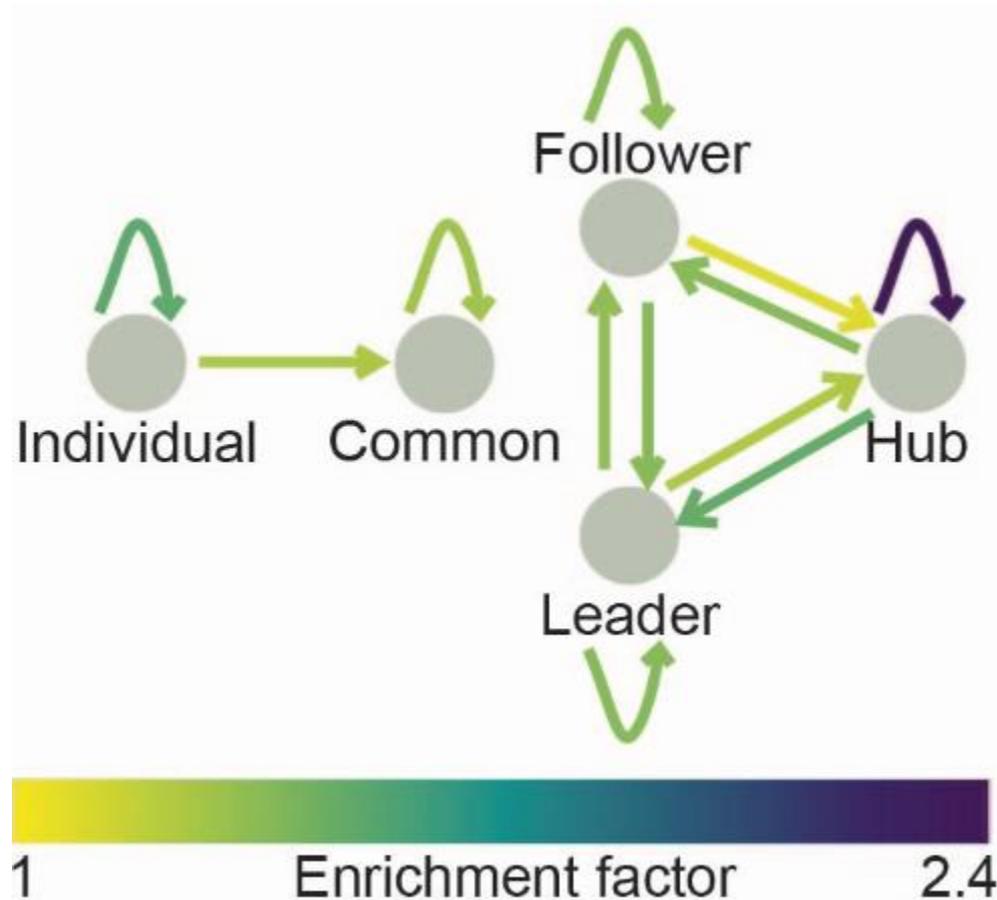
Cells maintain memory and reinforce their role in cell-cell communication



Enhanced information flow and memory lead to evolution in cell roles



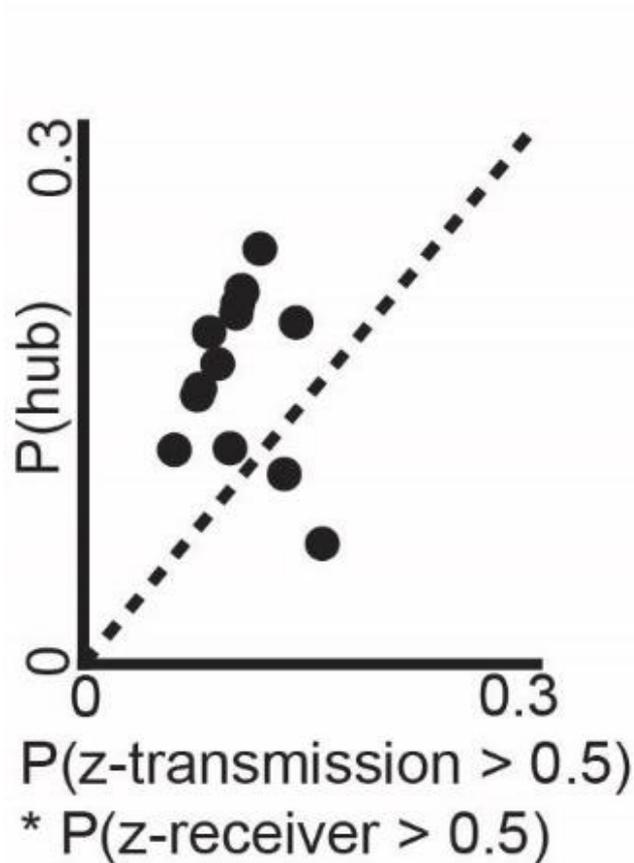
Enrichment factors of cellular state transitions



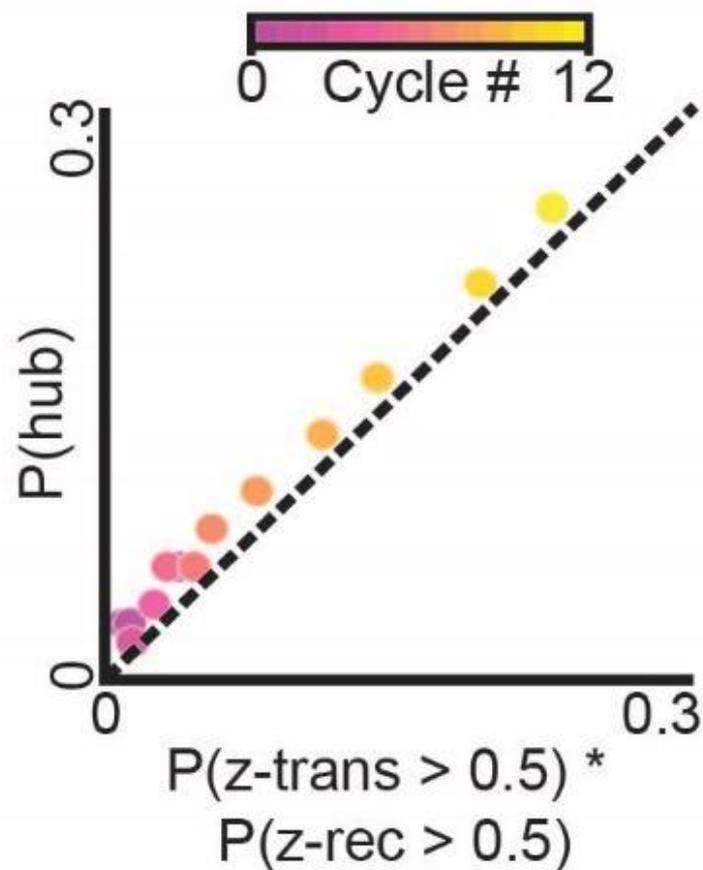
Enrichment beyond the expected values derived from a marginal distribution null model

Exceptional enrichment of communication hubs over time

“Step”

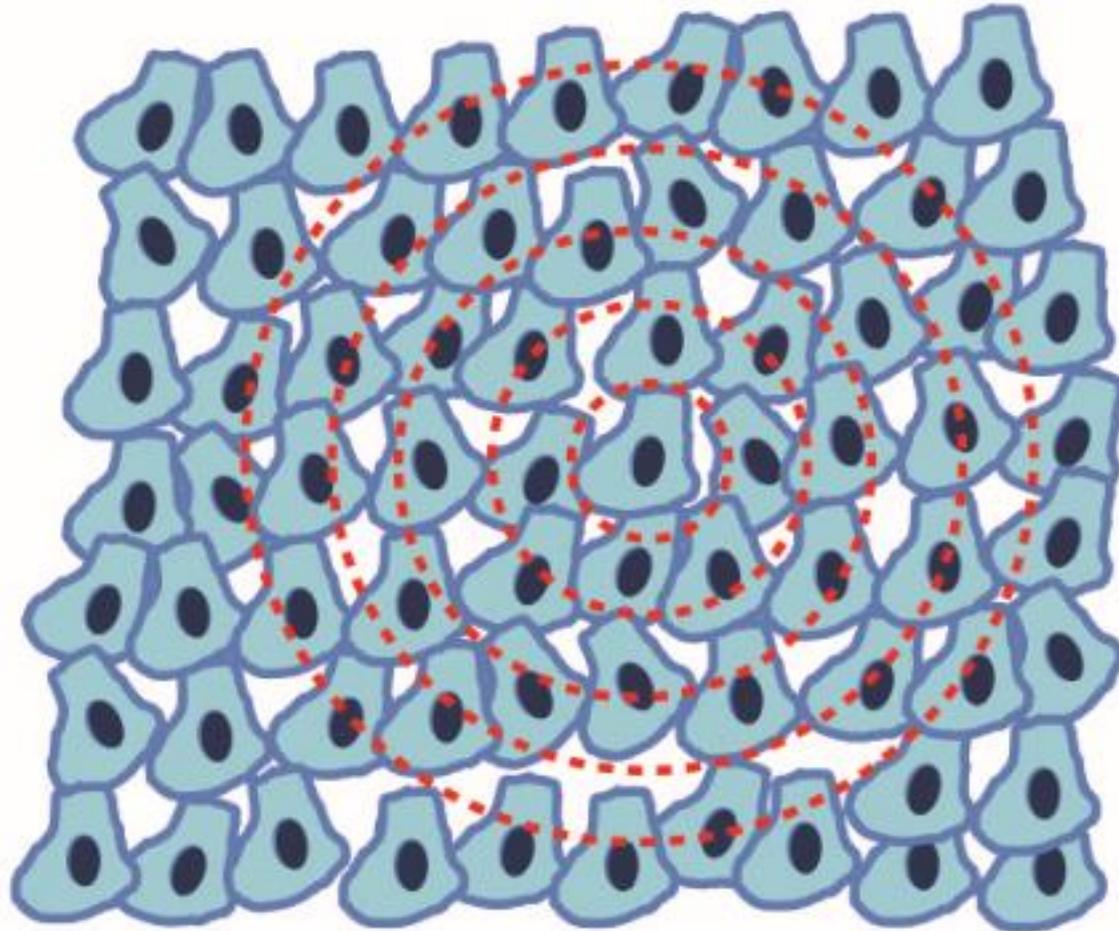


“Cycles”

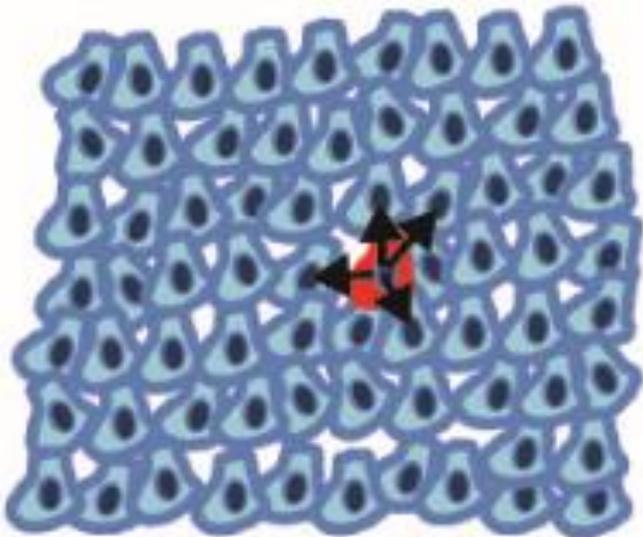


Values above the null model (dashed diagonal) indicate enrichment

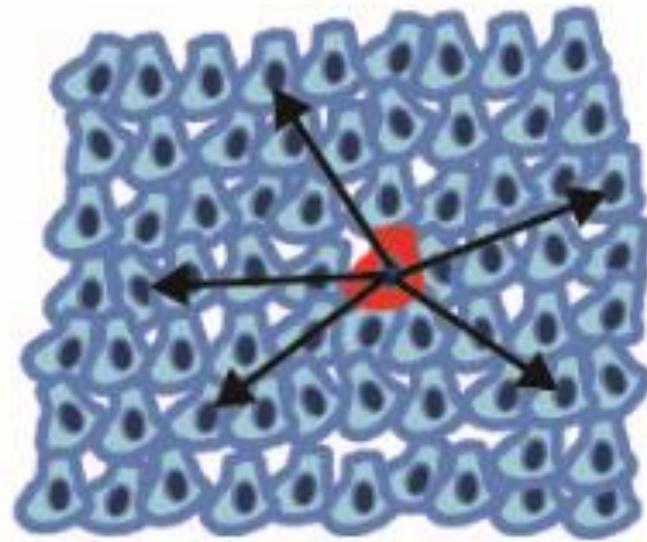
Hypothesis: information propagates from
the (local) single cell to the (global)
multicellular scale



Correlating topological distance to cell-cell influence probability



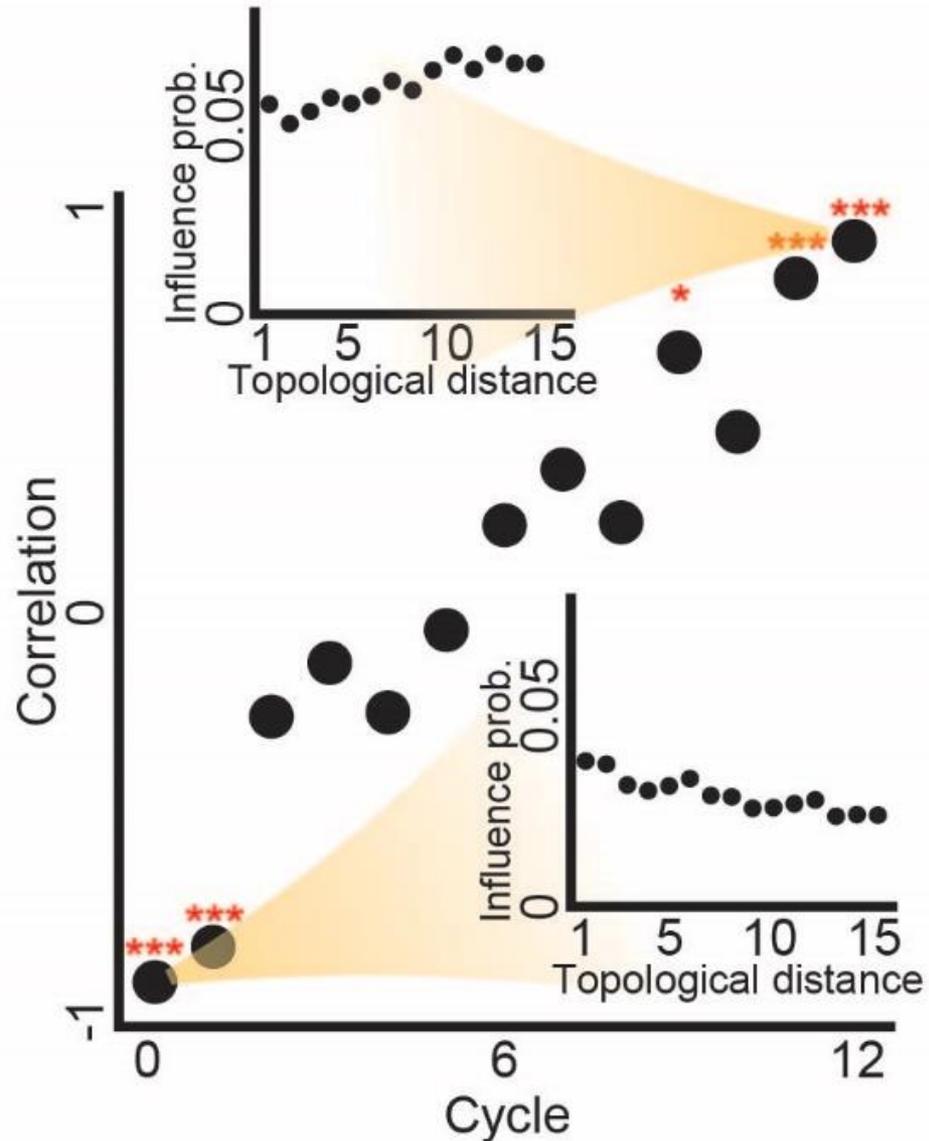
Topological distance = 1



Topological distance = 4



Gradual local to global transition in information spreading



Summary

**Heterogeneity, memory and
information flow contribute to
collective information
processing**

Amos Zamir



With Bo Sun,
OSU

