

Image and data analytic pipeline for studying signalling dynamics in cancer

Maciej Dobrzański

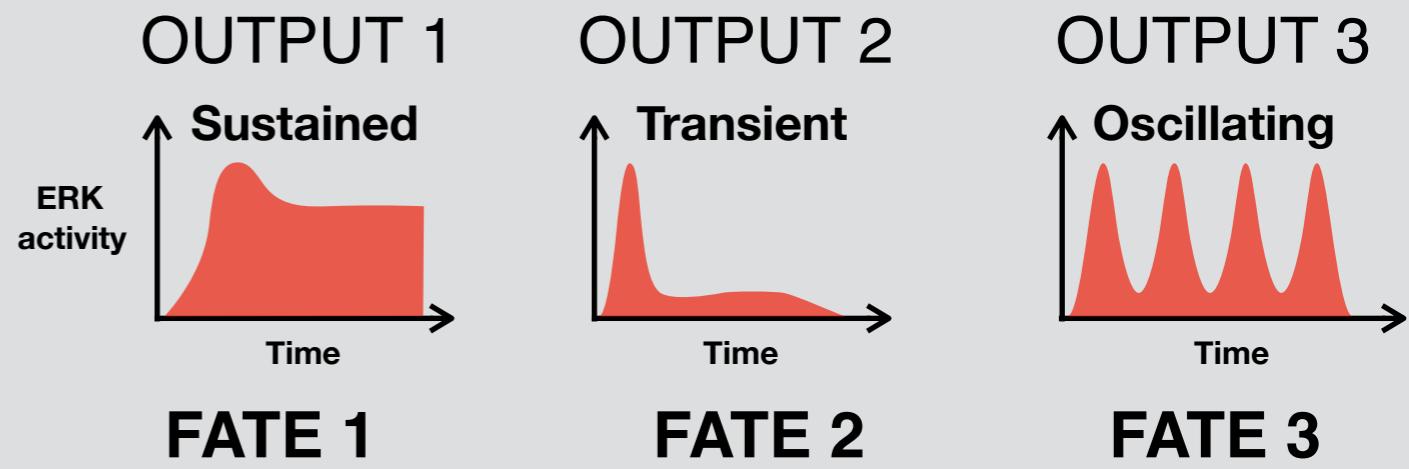
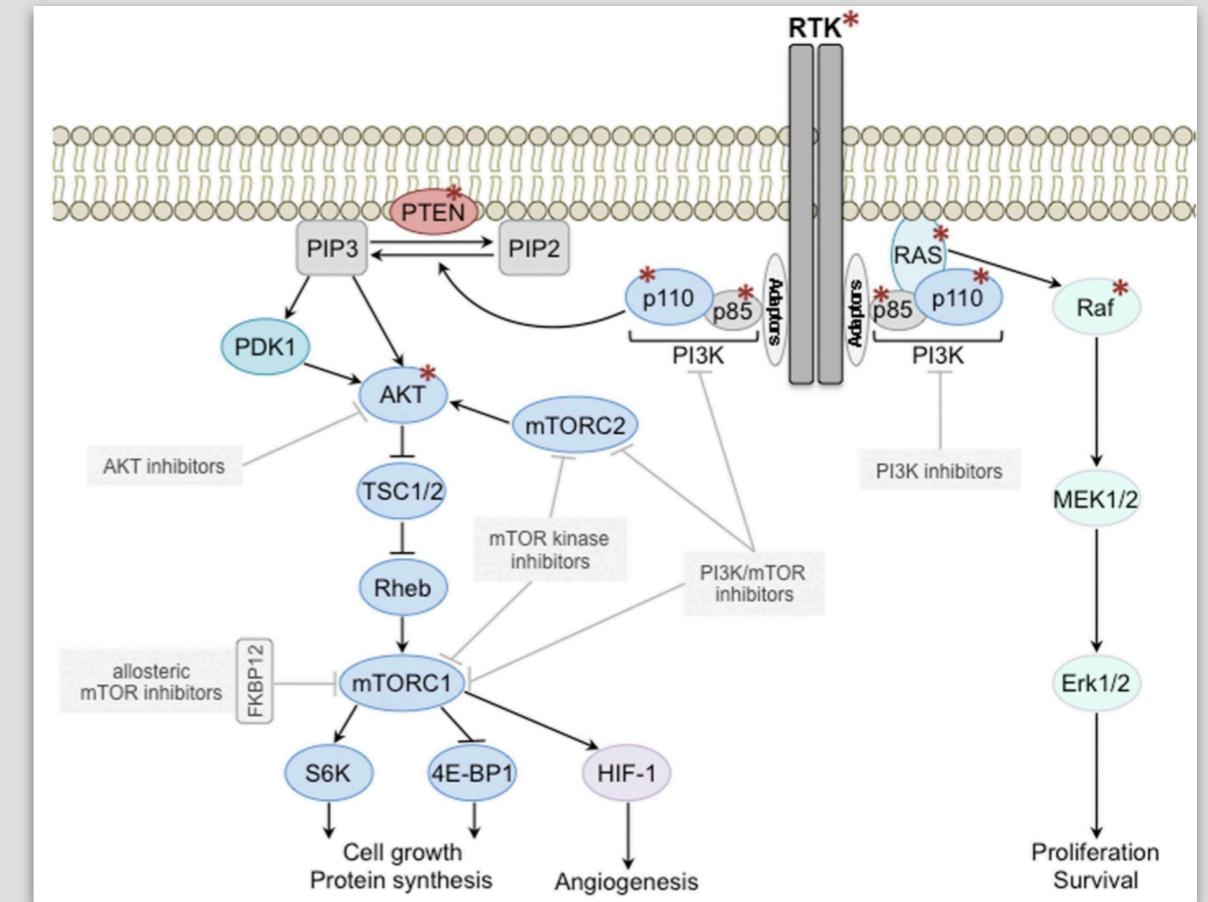
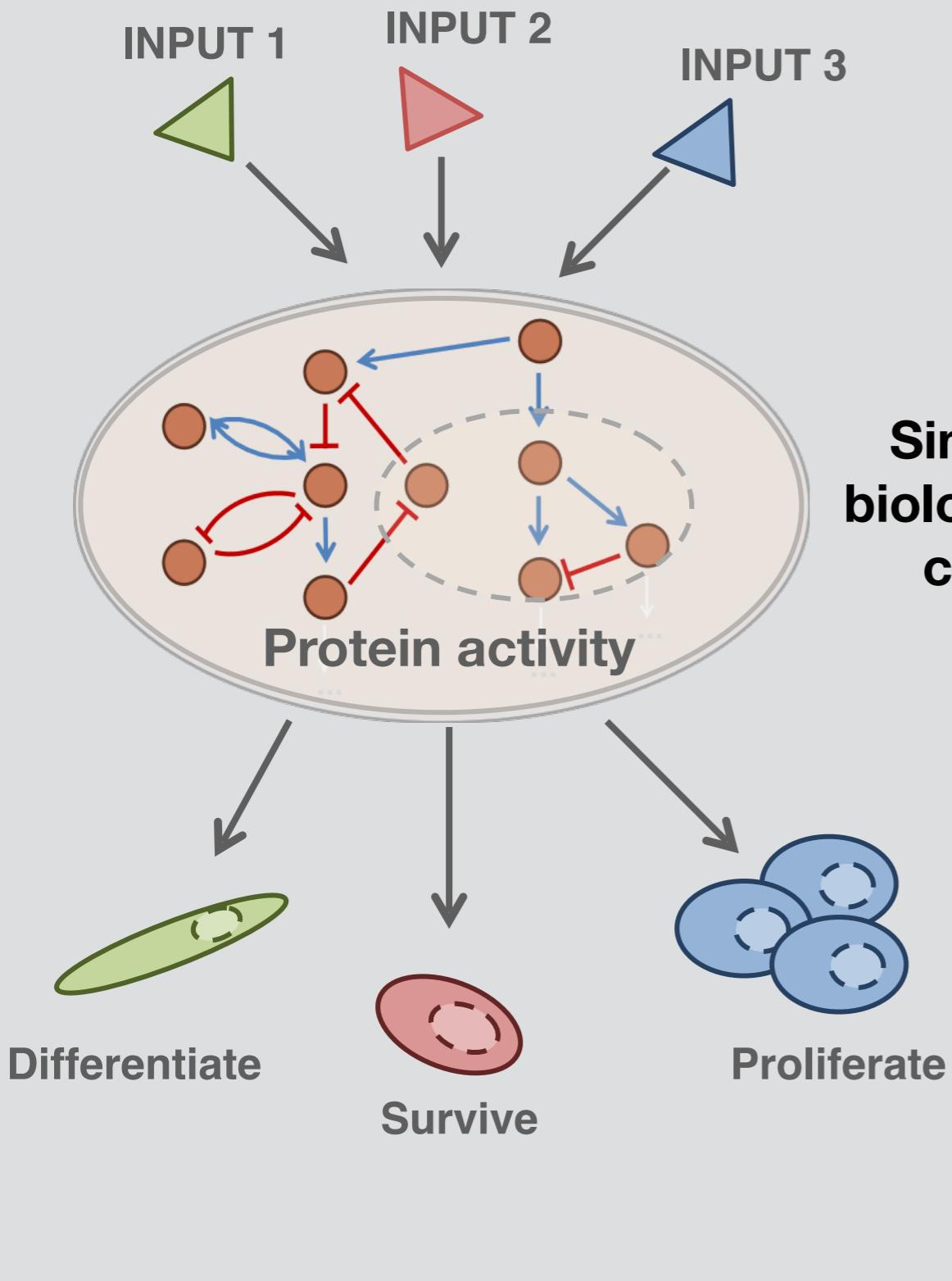
Cellular Dynamics Lab, Olivier Pertz
Institute of Cell Biology, UniBern 

QuantBio Workshop,
Fiesch 16.09.2019

Biological signalling networks determine cell fate

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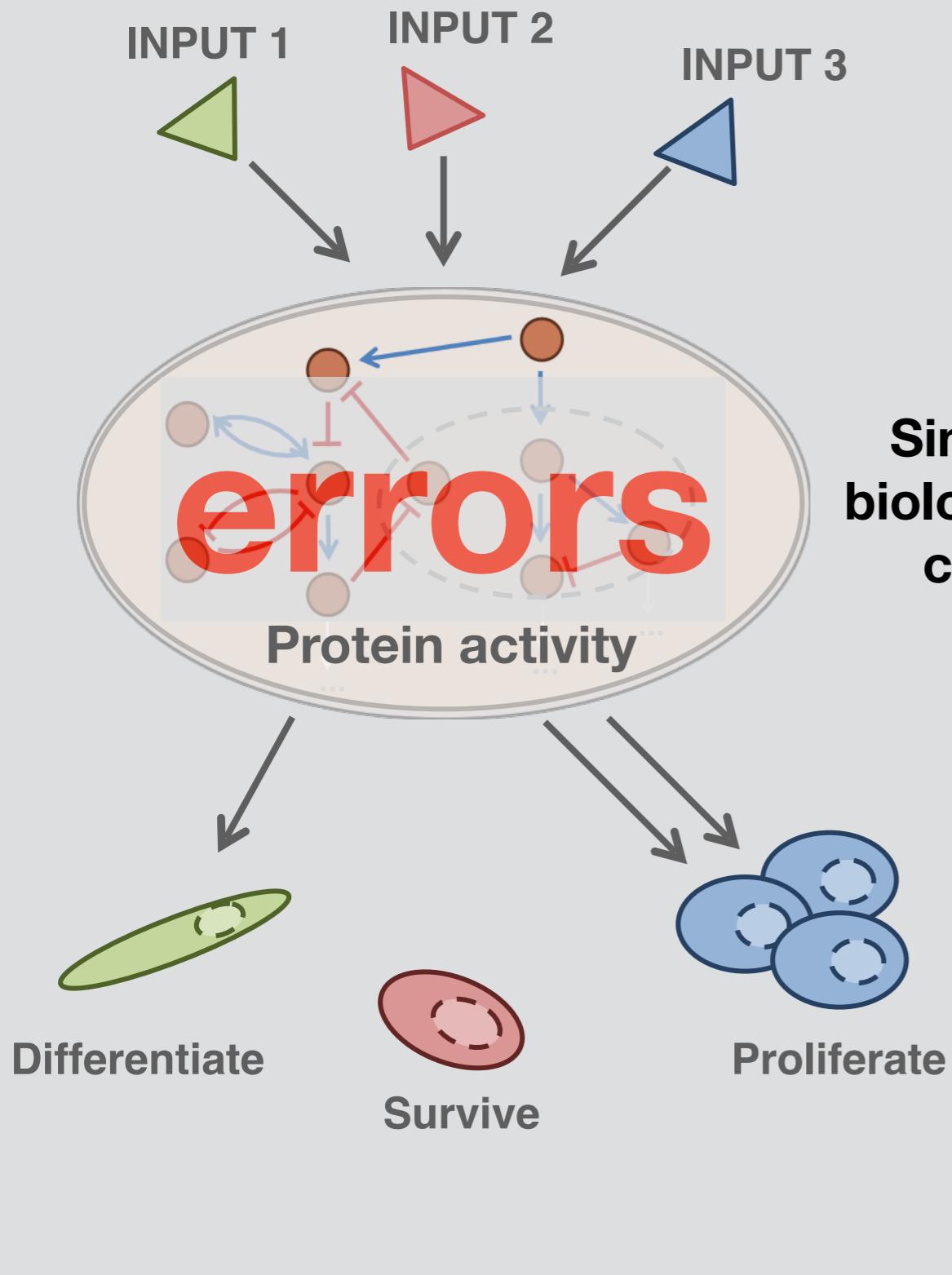
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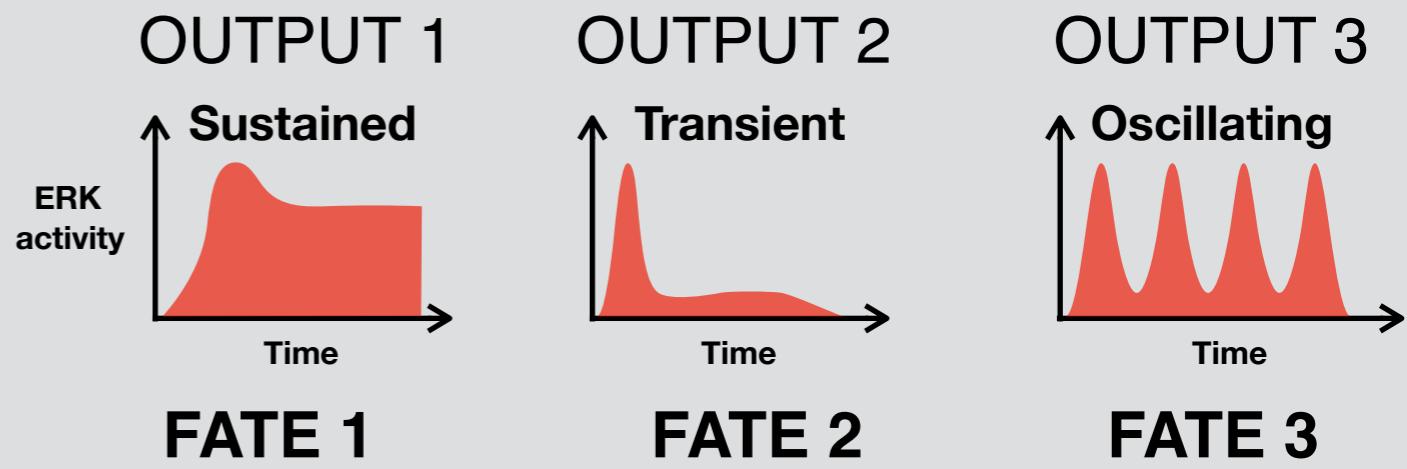
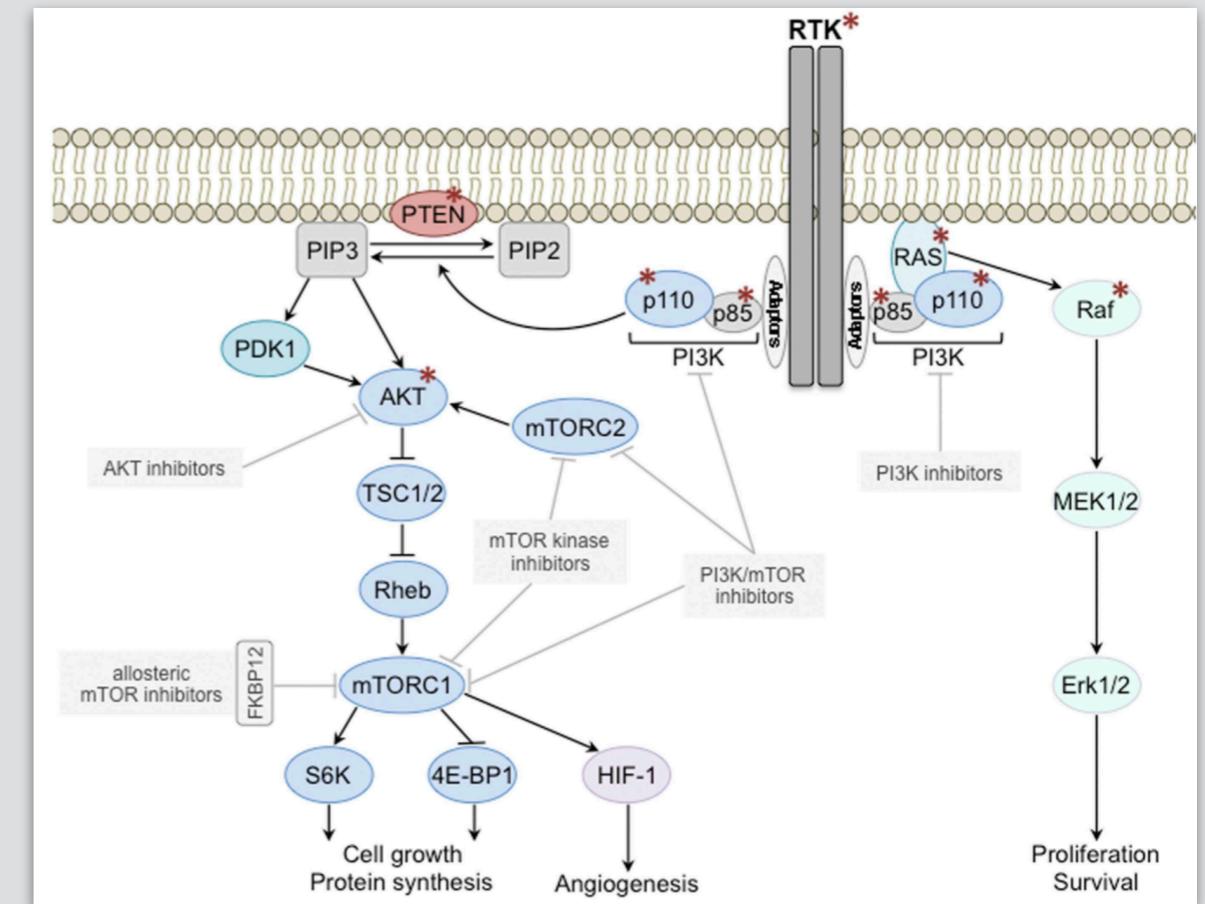
Biological signalling networks determine cell fate

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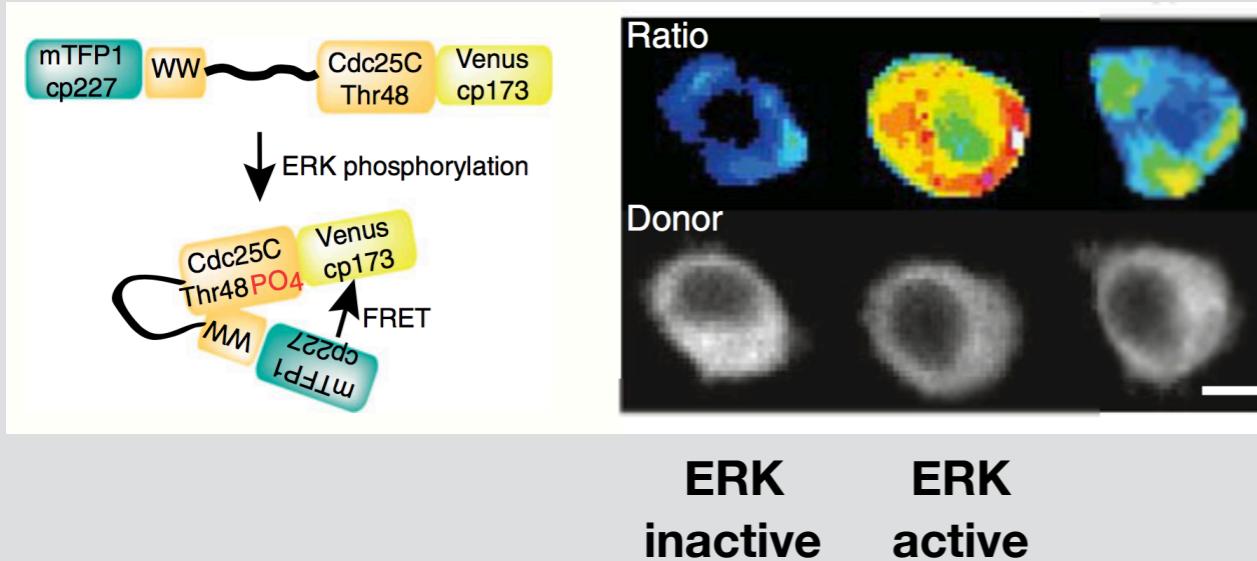
Single
biological
cell



Key experimental technologies

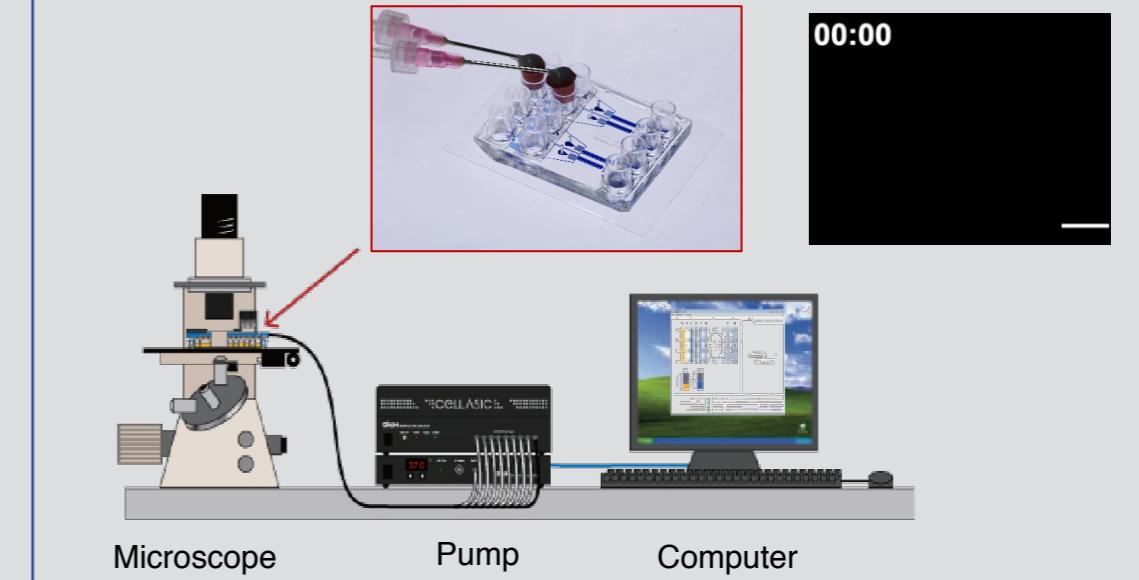
Fluorescent Biosensors

EKAR2G biosensor

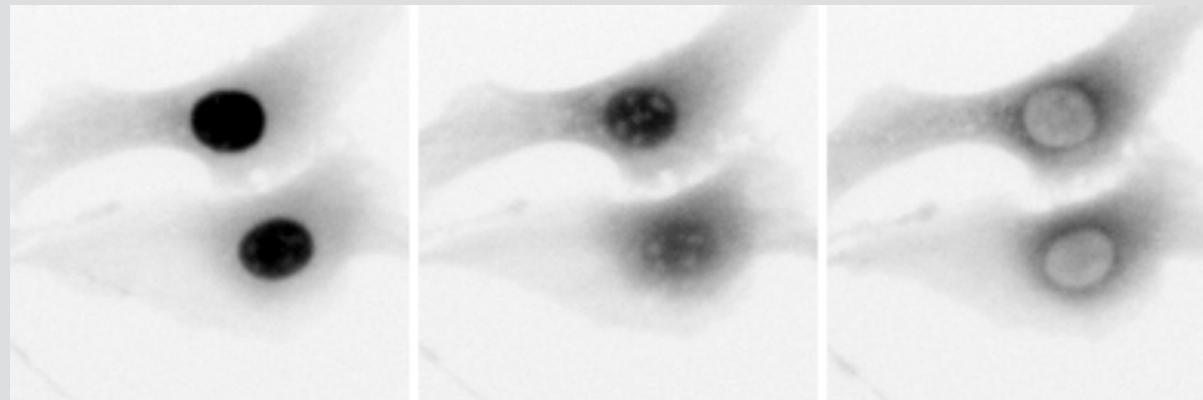


Cell Perturbations

Microfluidics



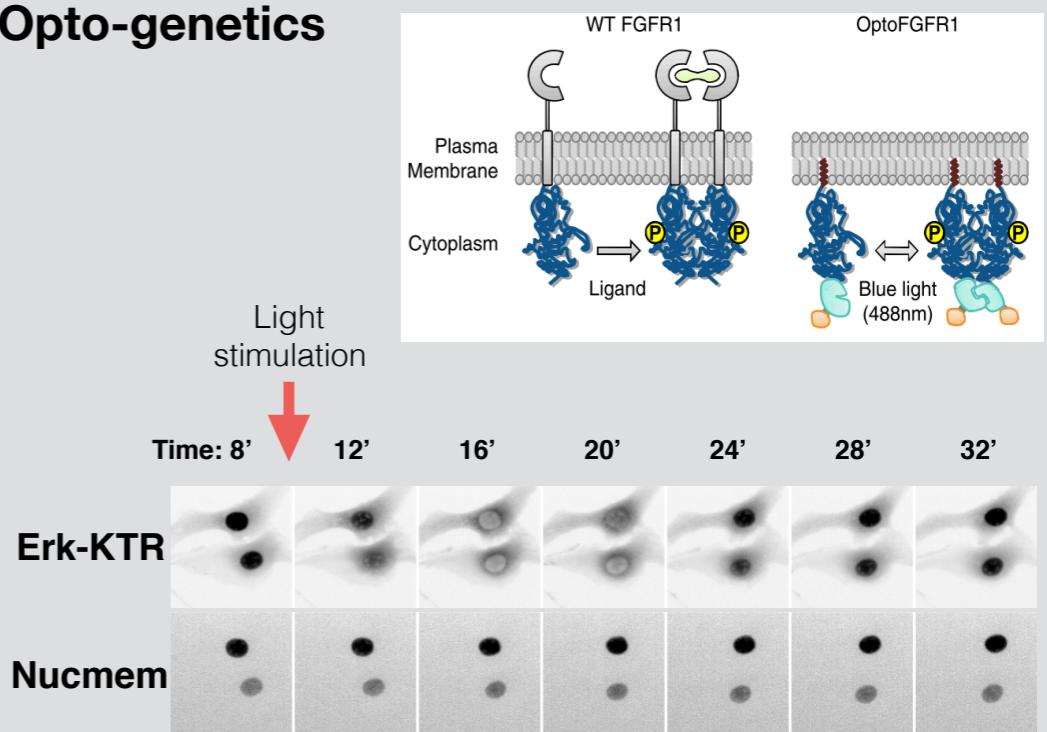
Kinase translocation reporter

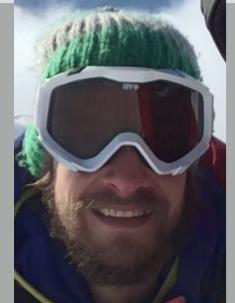


ERK inactive

ERK active

Opto-genetics



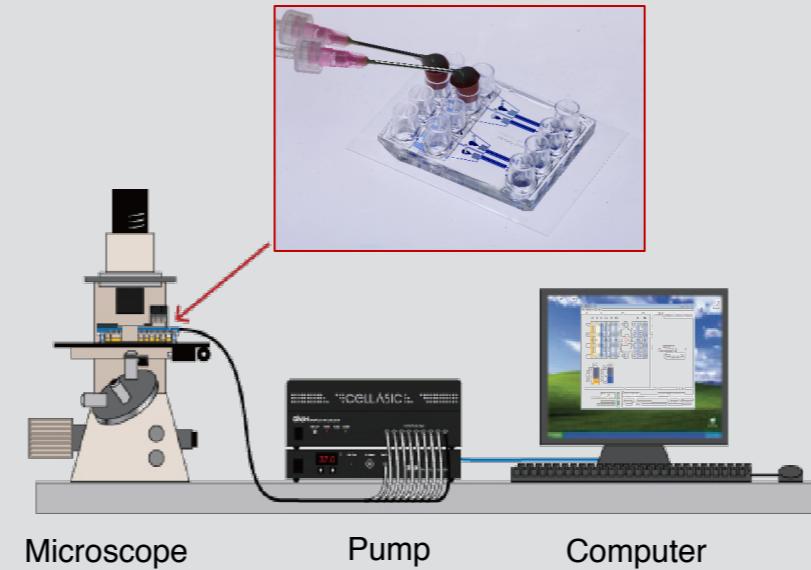


Perturbing with microfluidics

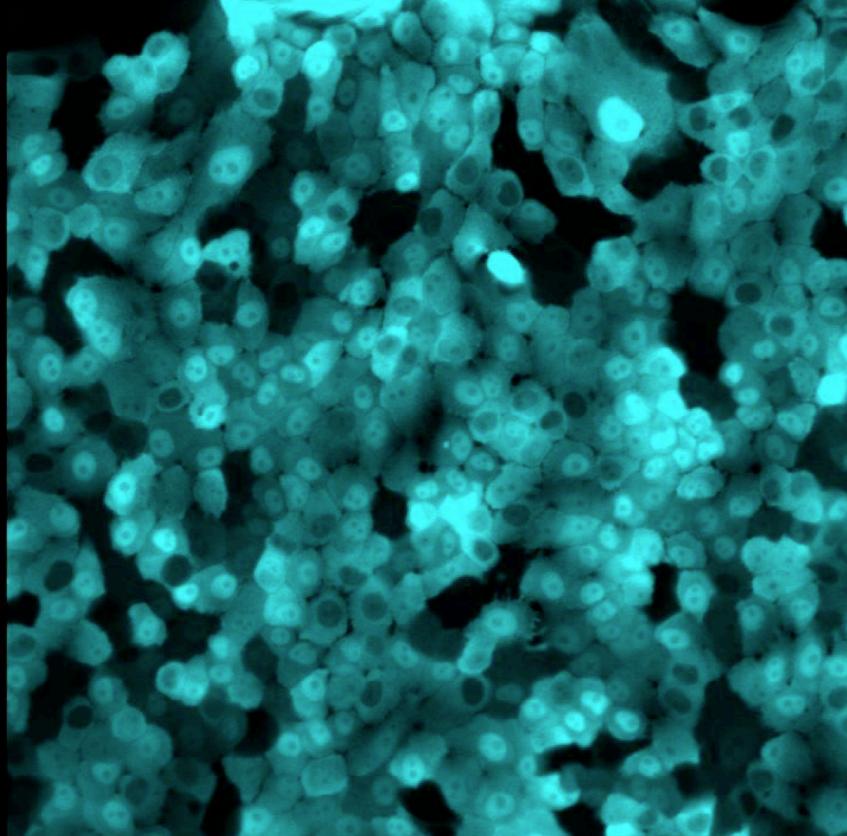
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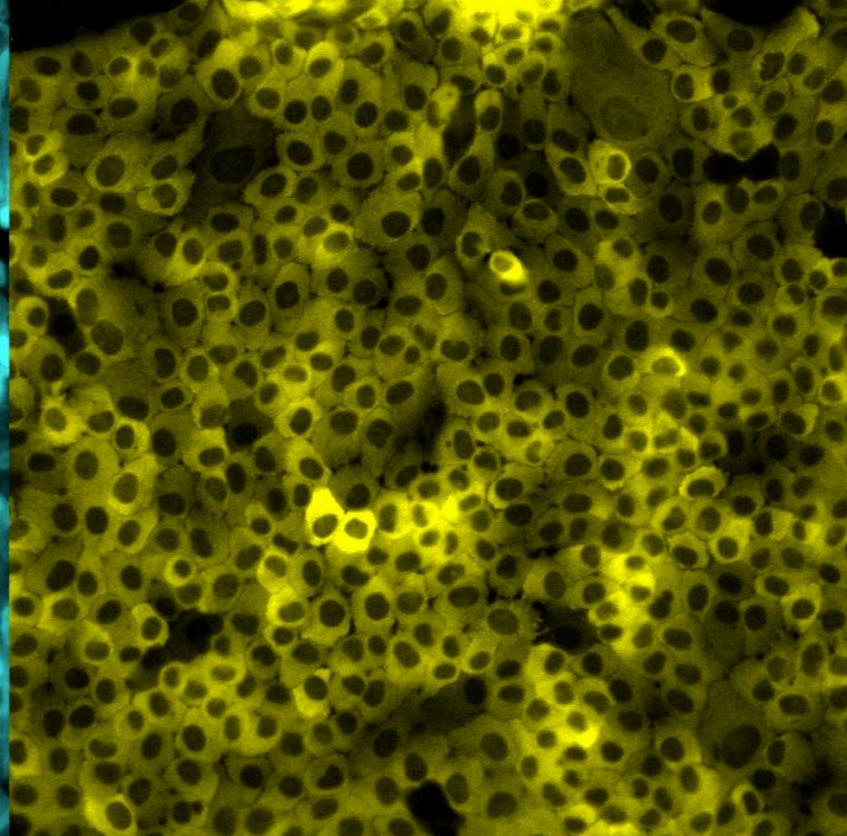
Yannick Blum
Pertz Group



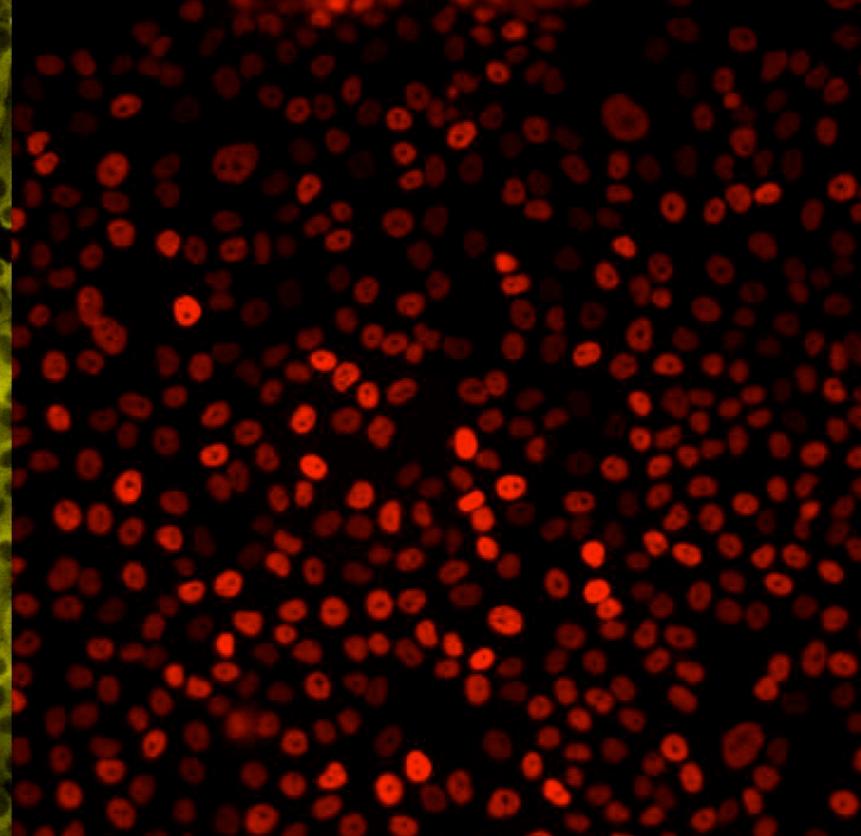
Protein 1 activity



Protein 2 activity



Cell nuclei

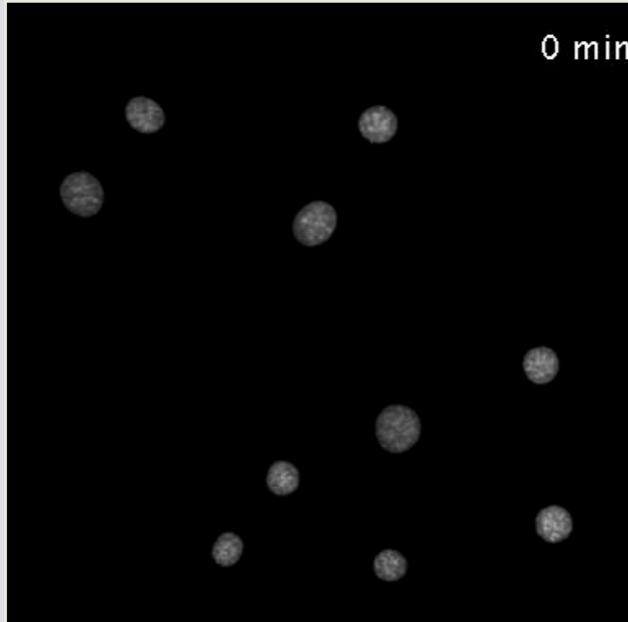




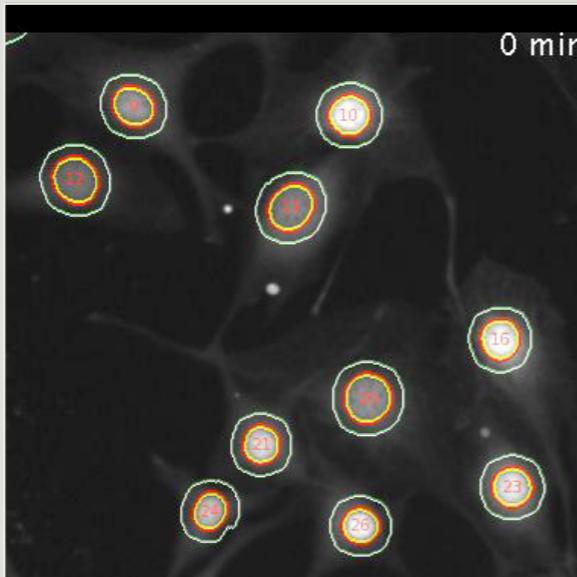
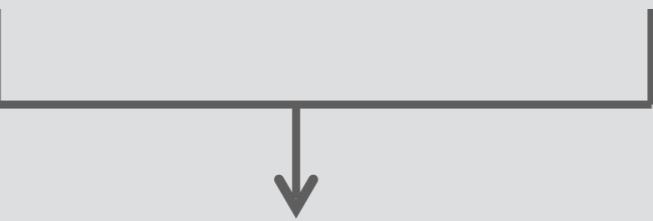
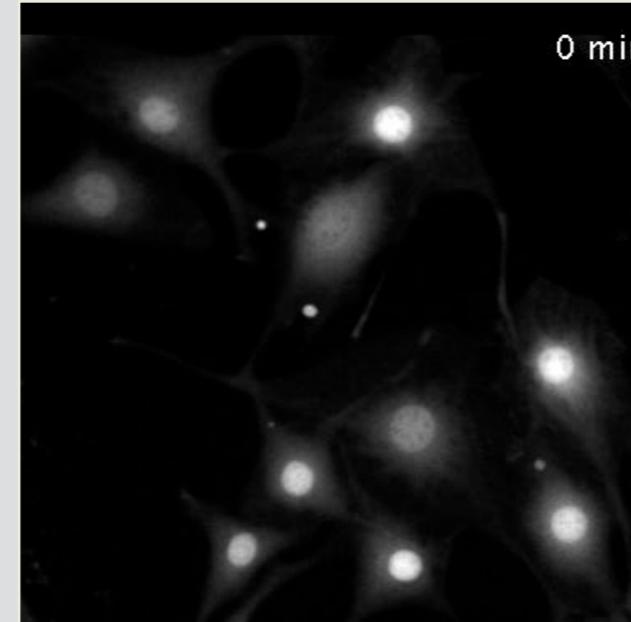
Perturbing with optogenetics

Coralie Dessauges
Pertz Group

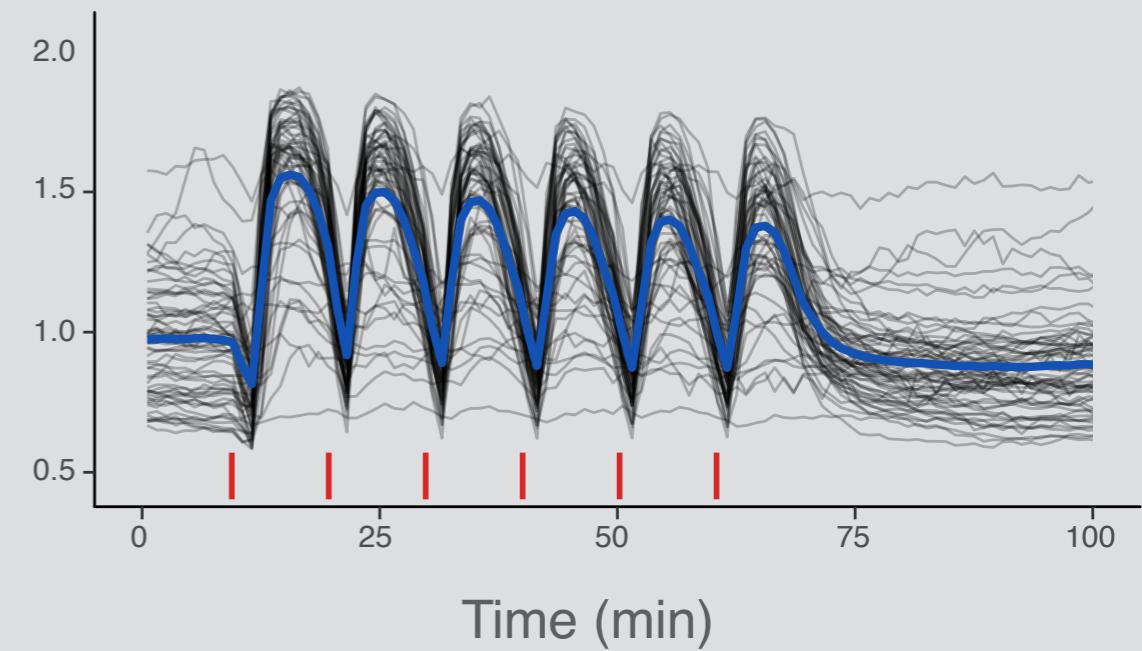
Cell nuclei



Protein activity



R Studio[®]
Shiny

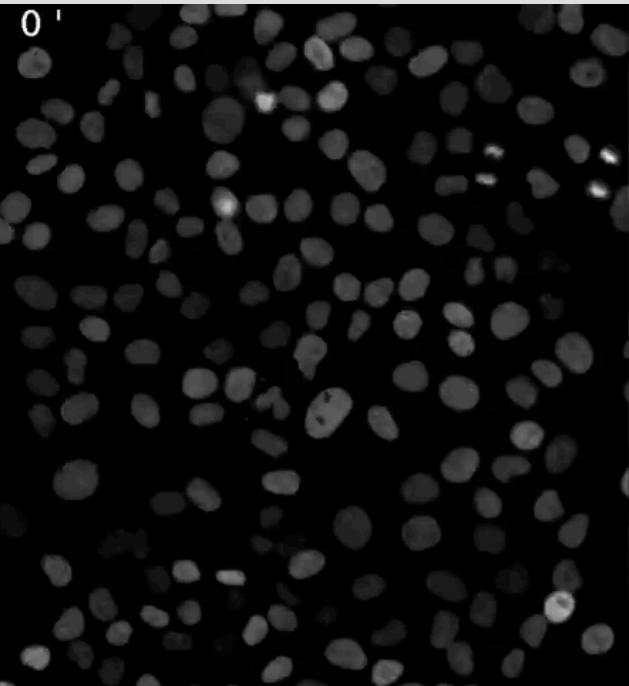


Things we actually measure

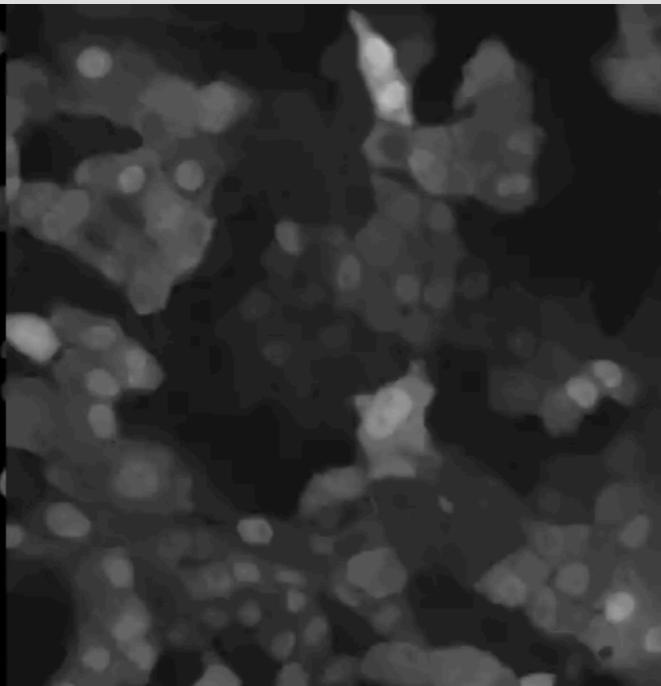
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Cell nuclei



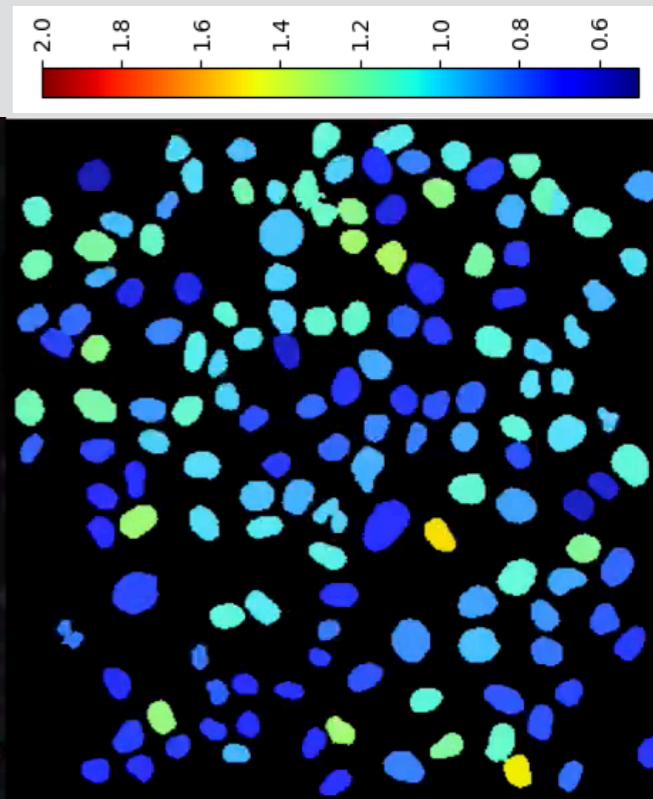
Protein activity



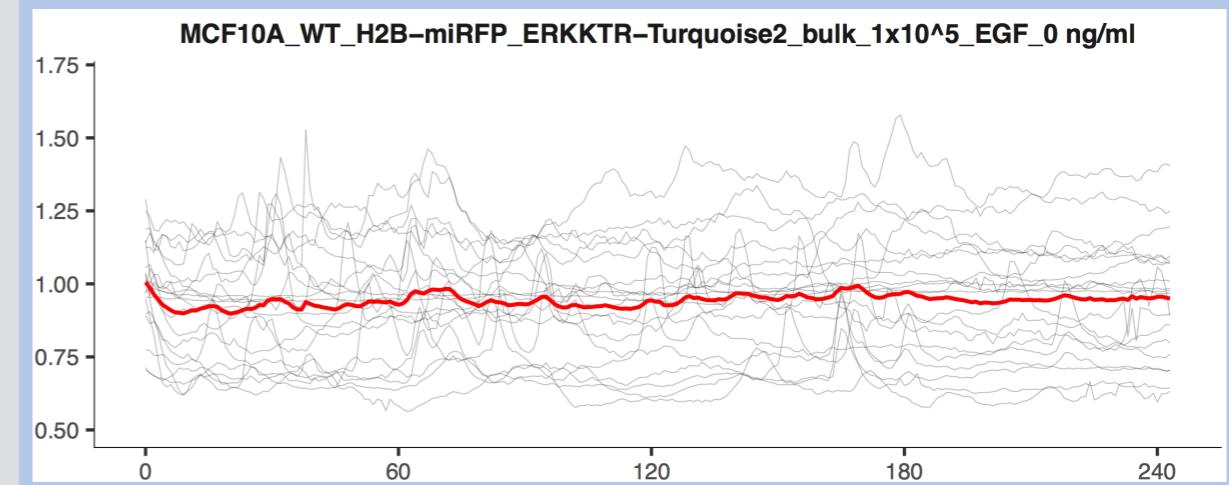
Segmentation & Tracking



Protein activity

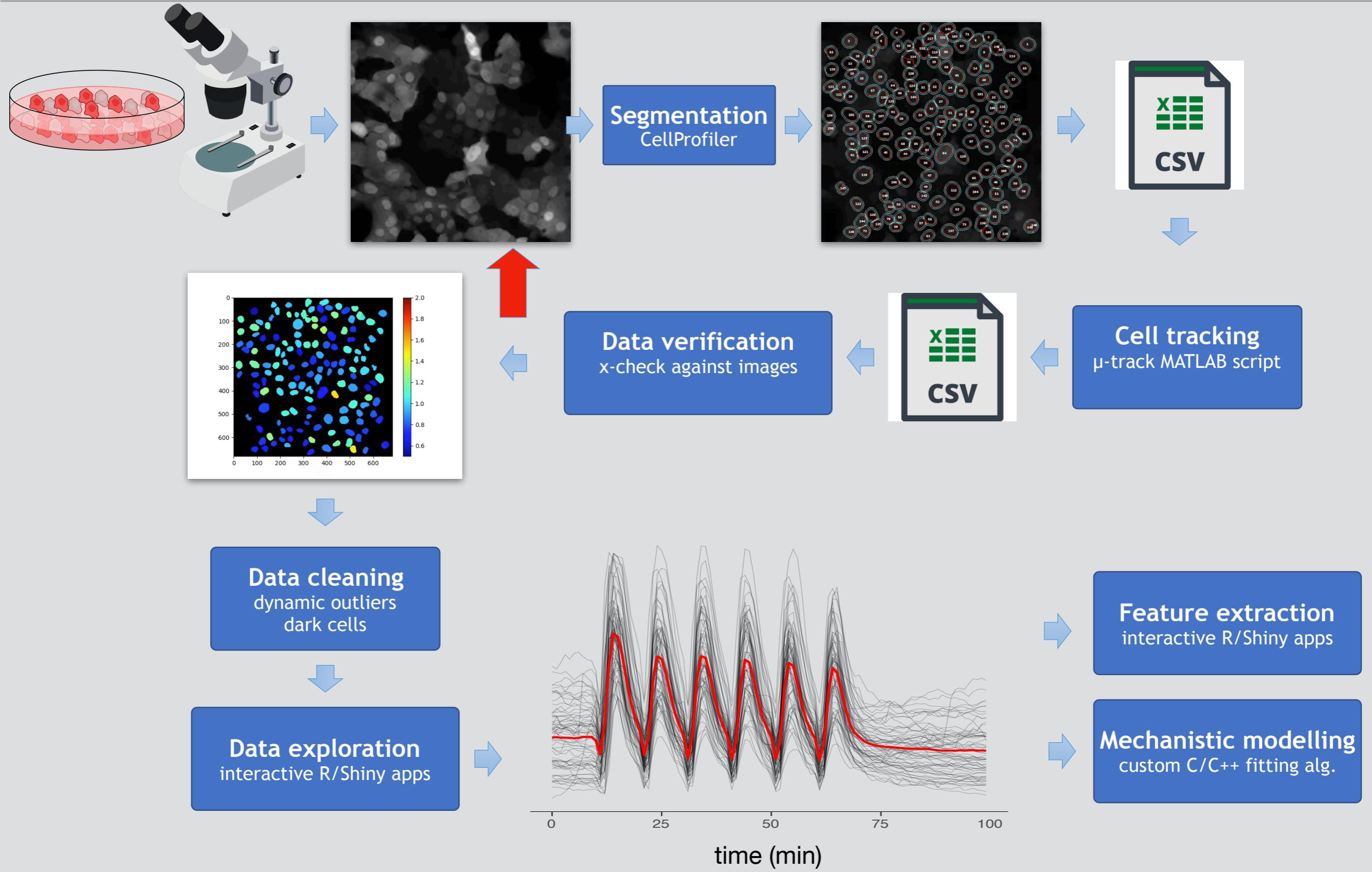


Measured

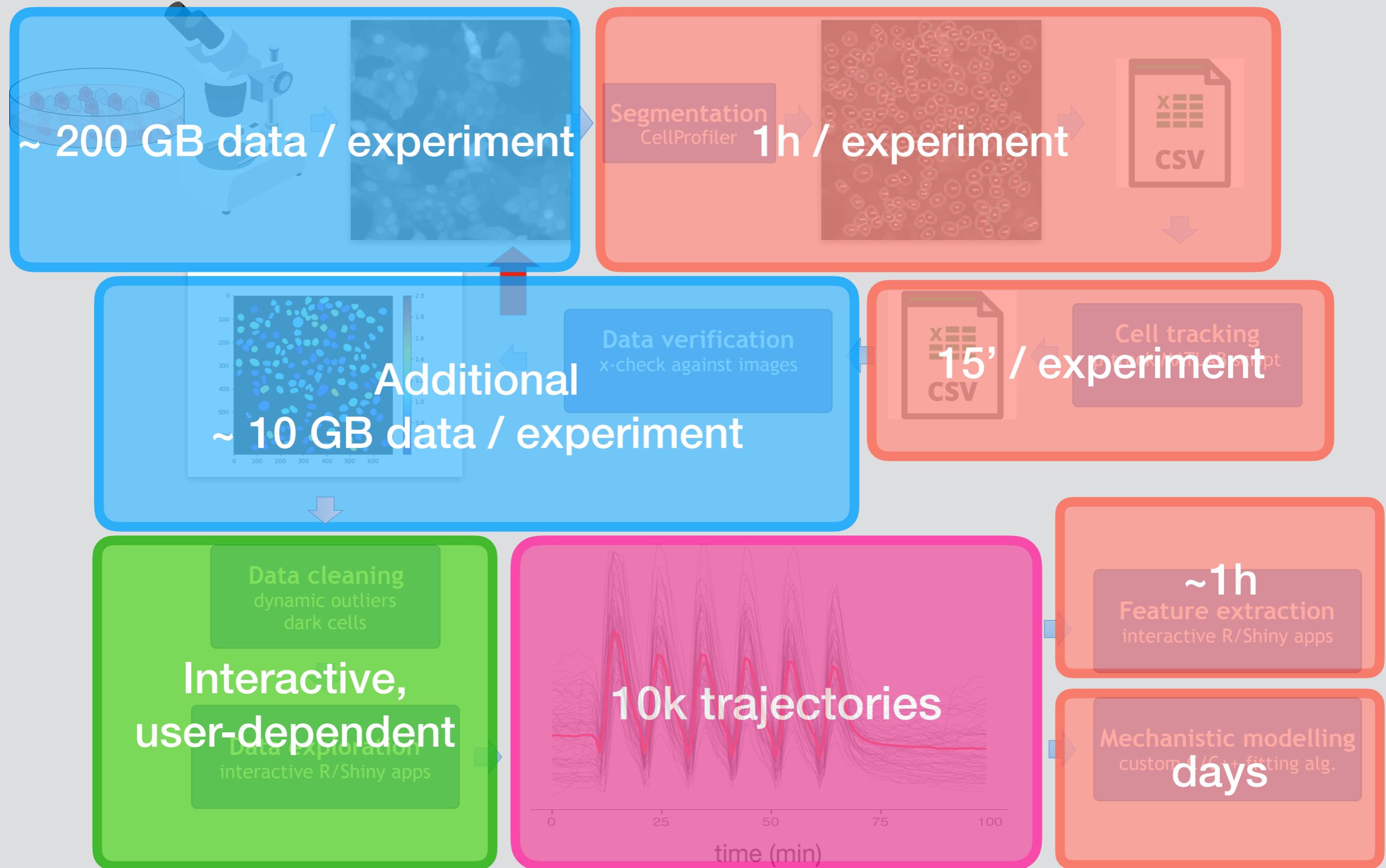


Processed

Our pipeline in practice



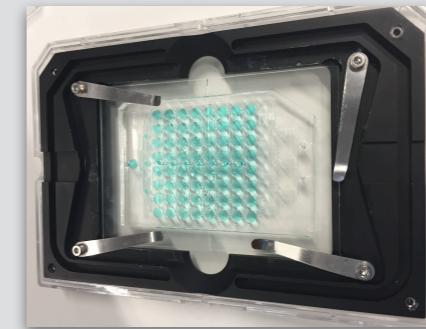
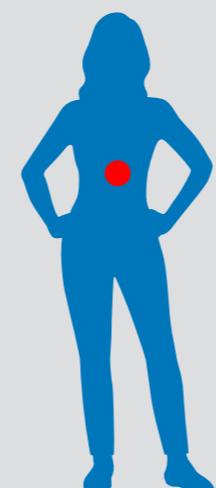
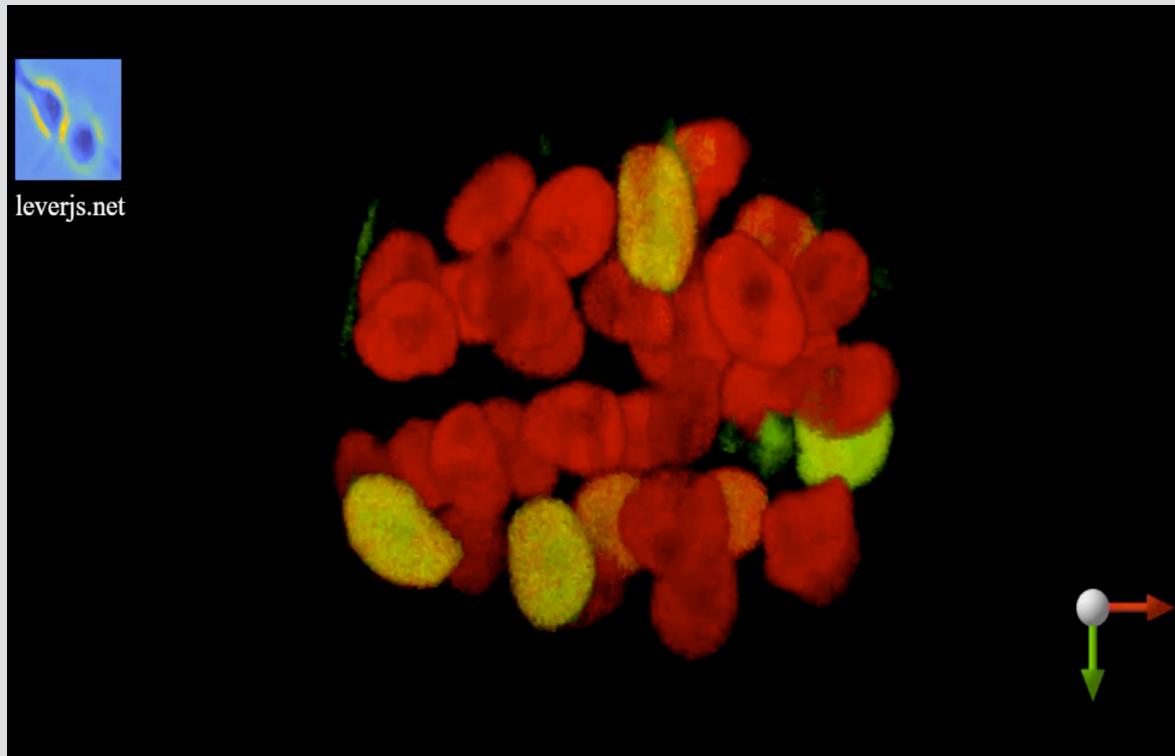
Our pipeline in practice



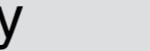


Organoids: physiologically-relevant human disease models

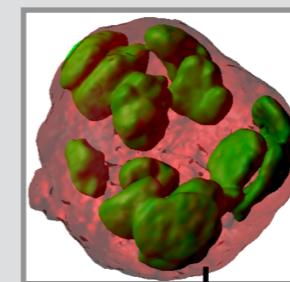
Paolo Gagliardi & Pascal Ender
Pertz Group



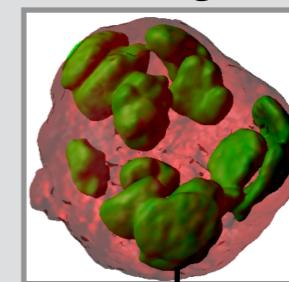
Grow biopsies as
organoids
(mini-tumors)



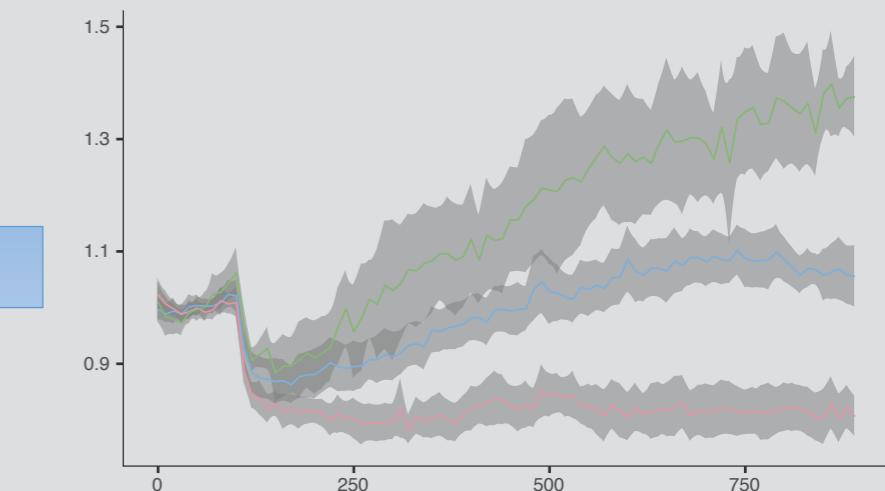
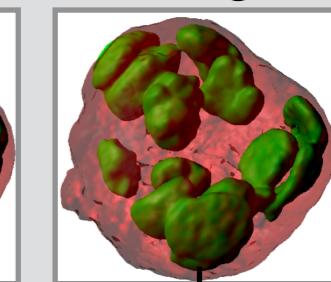
Drug 1



Drug 2



Drug 3



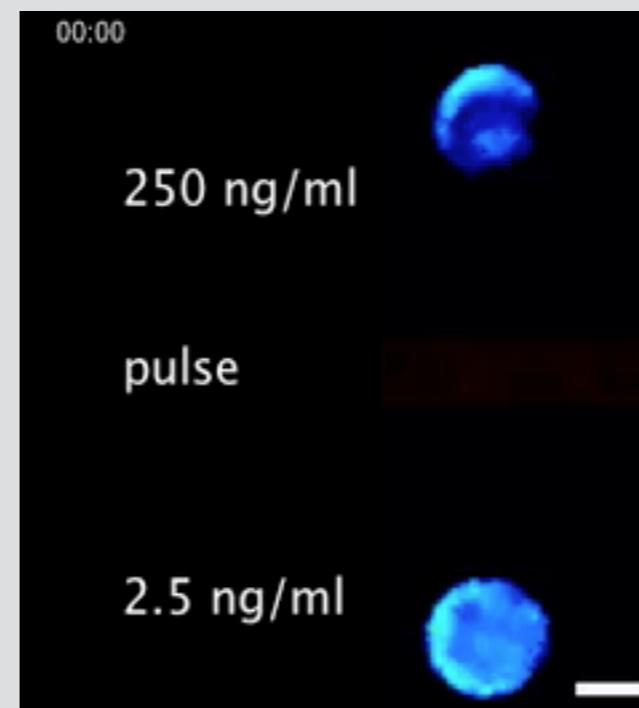
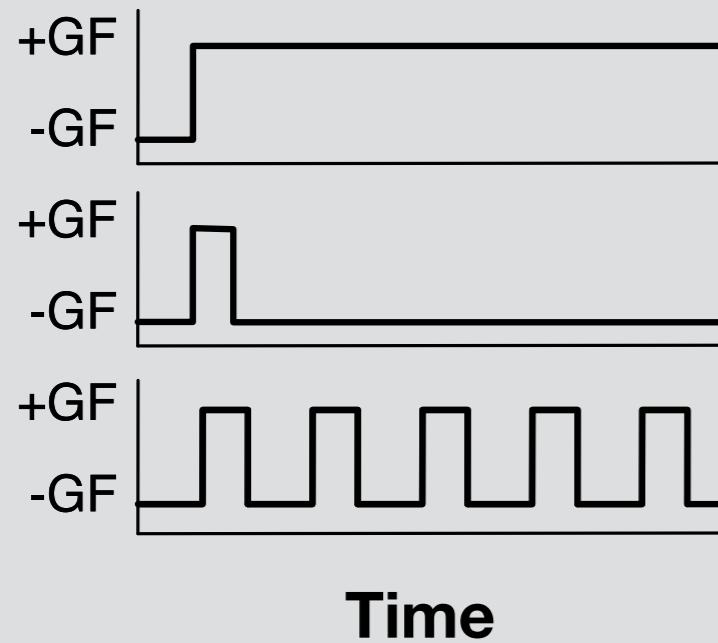
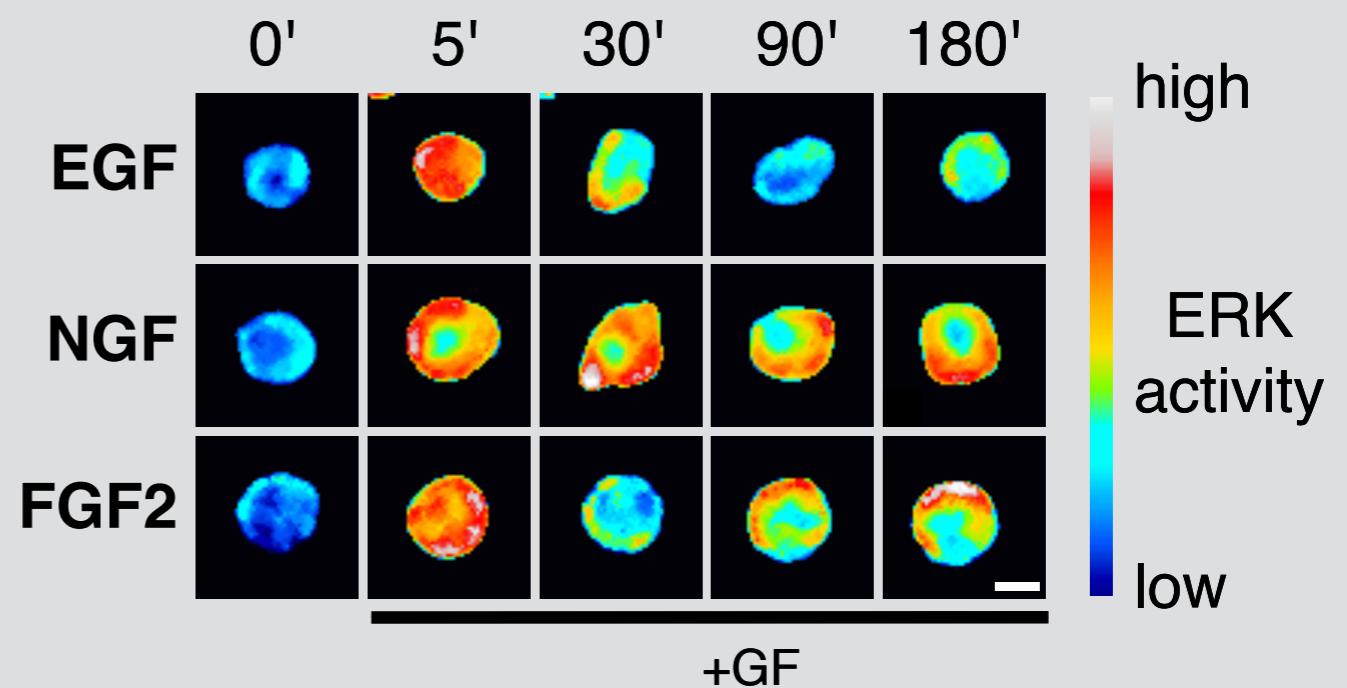
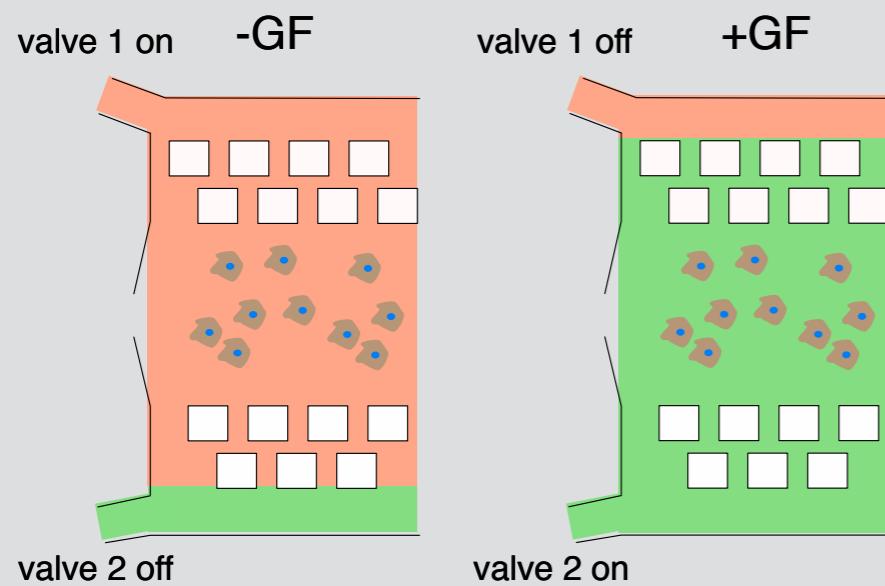
Predict drug,
drug combinations
that are effective on
patients



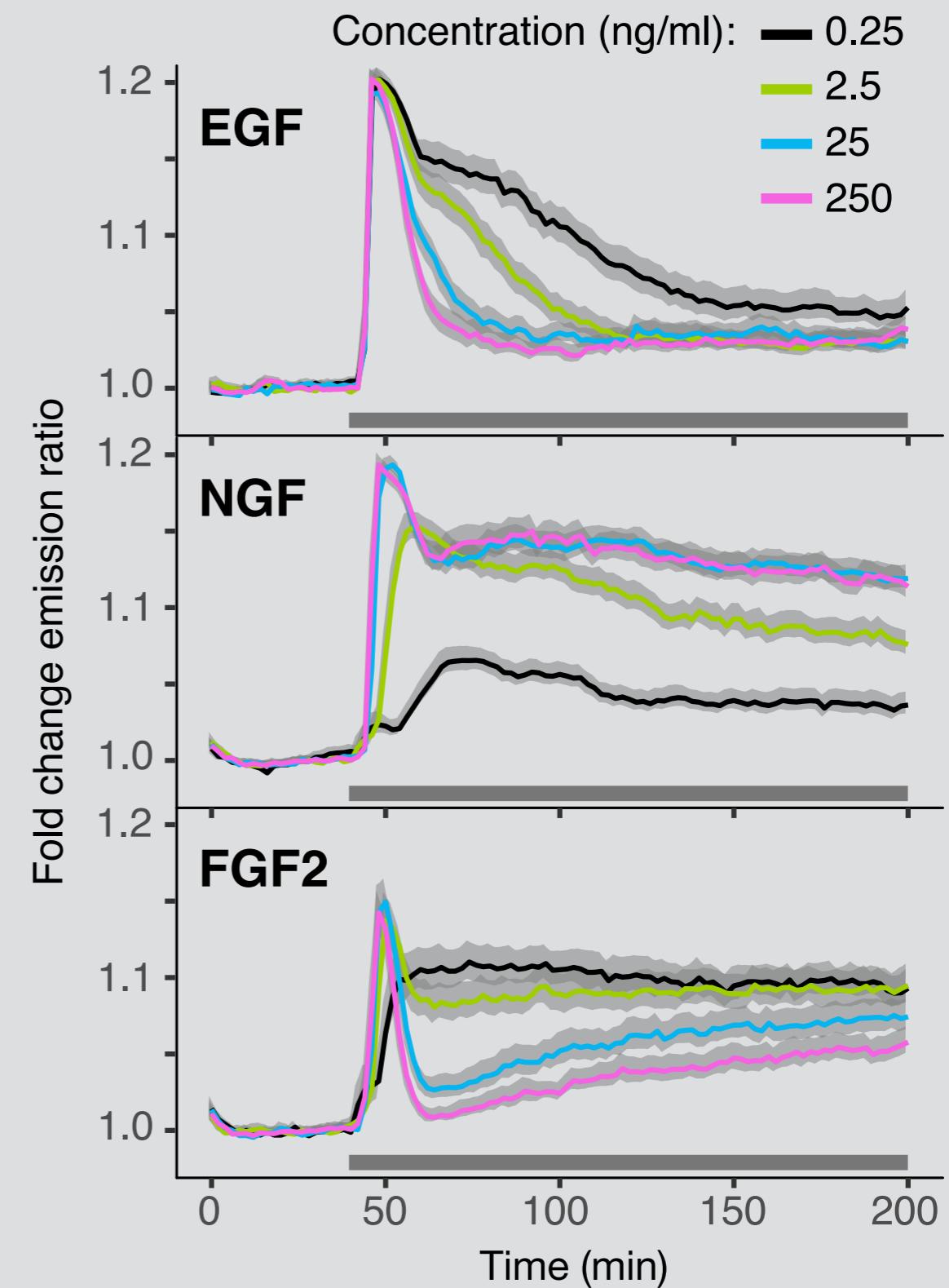
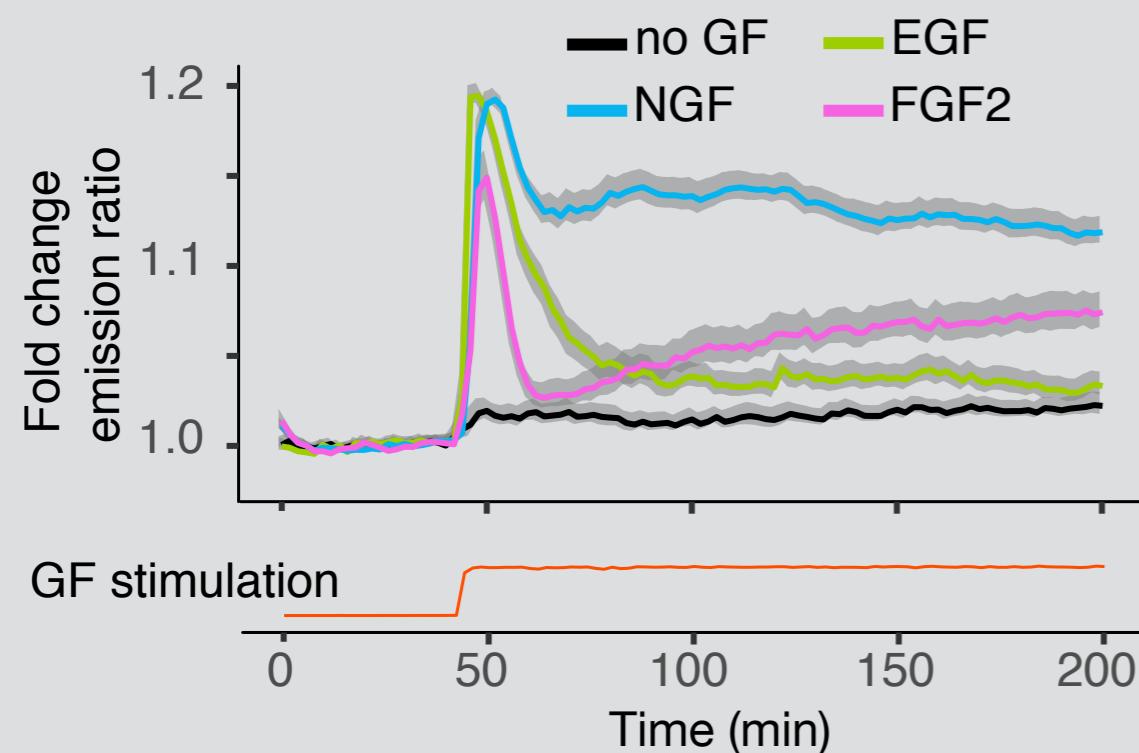
High dimensionality,
complex datasets
Statistical analysis
Mathematical modelling
Needs multidisciplinary
approaches !!!!



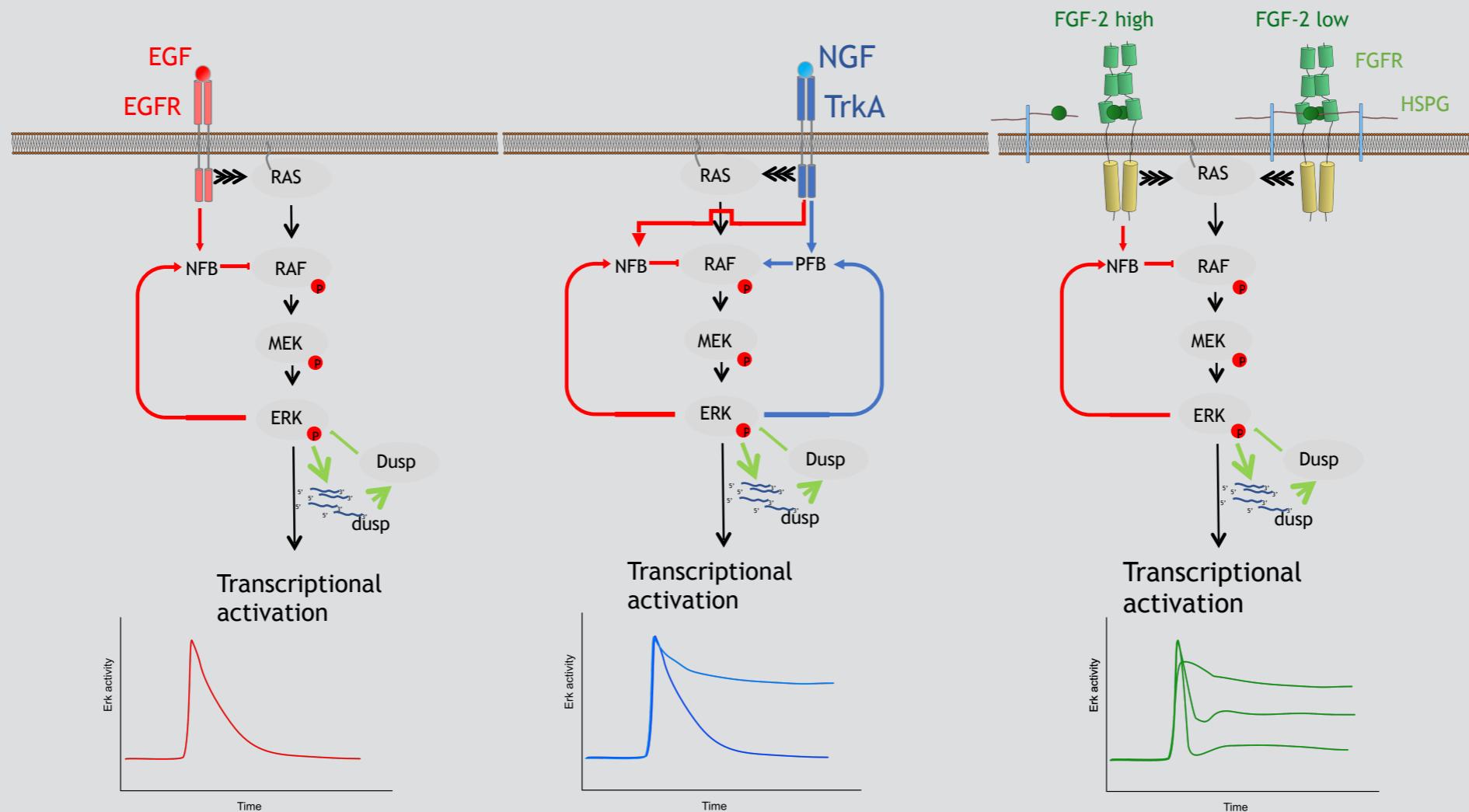
Experiment description



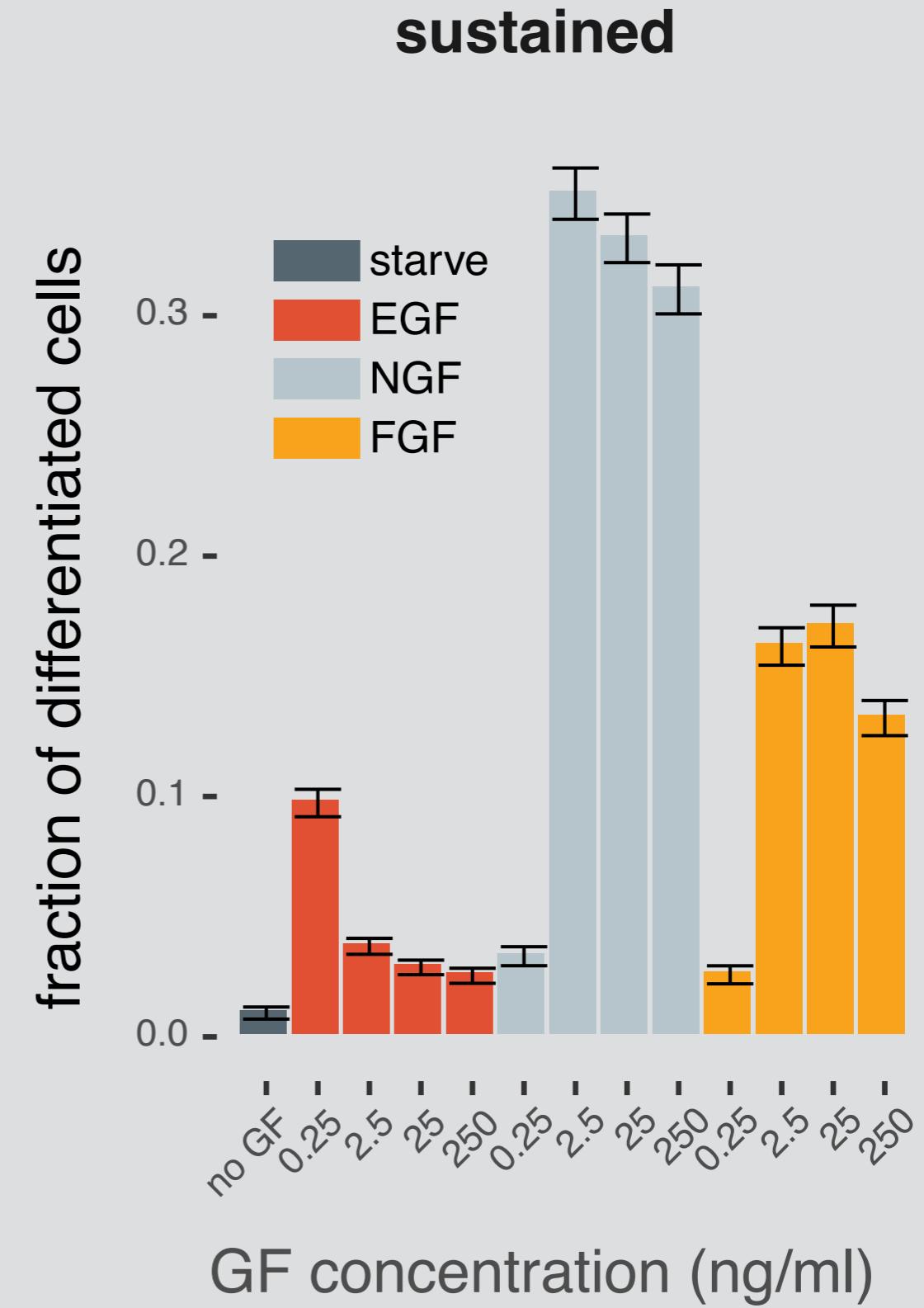
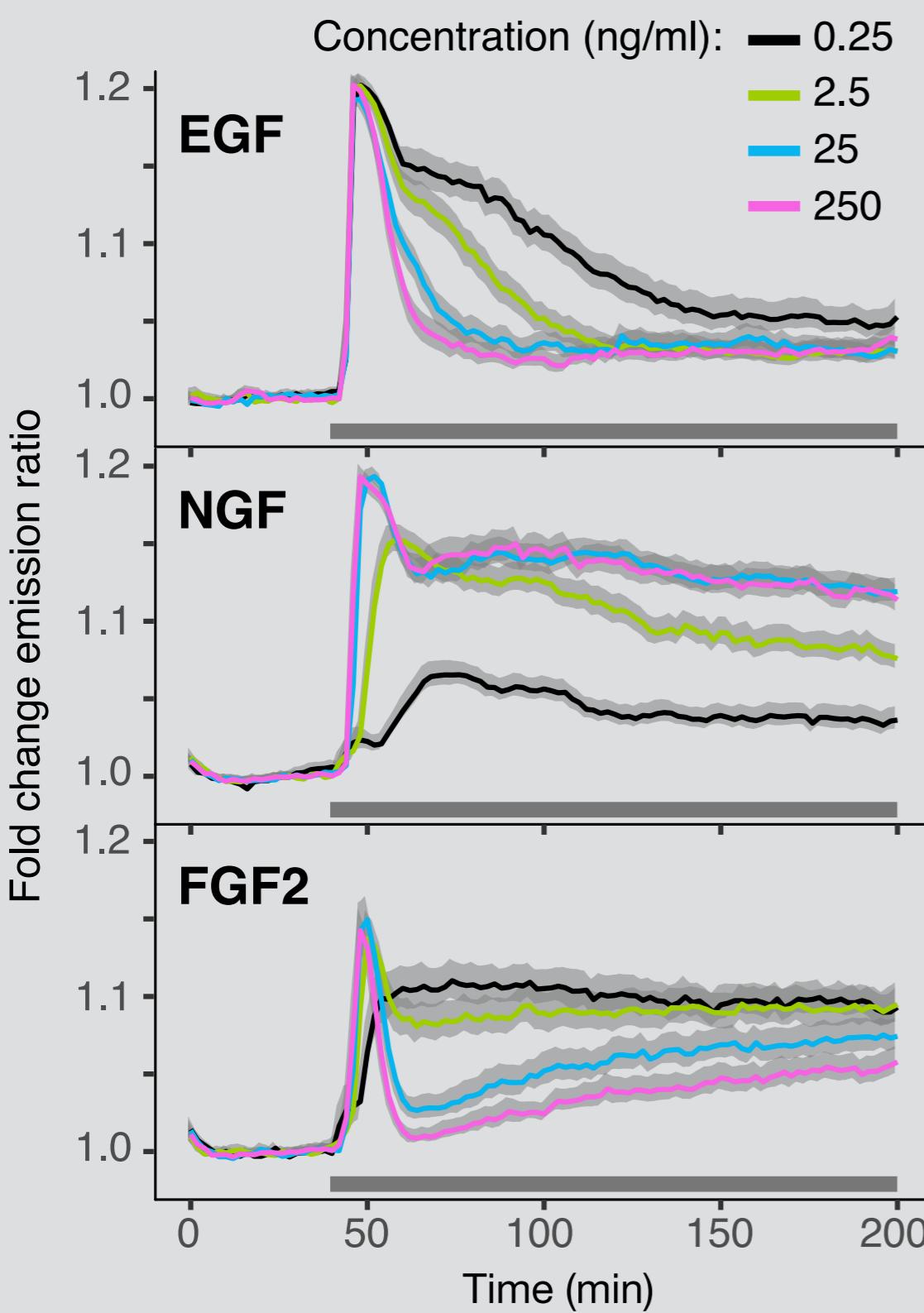
Different GF's induce different dynamics



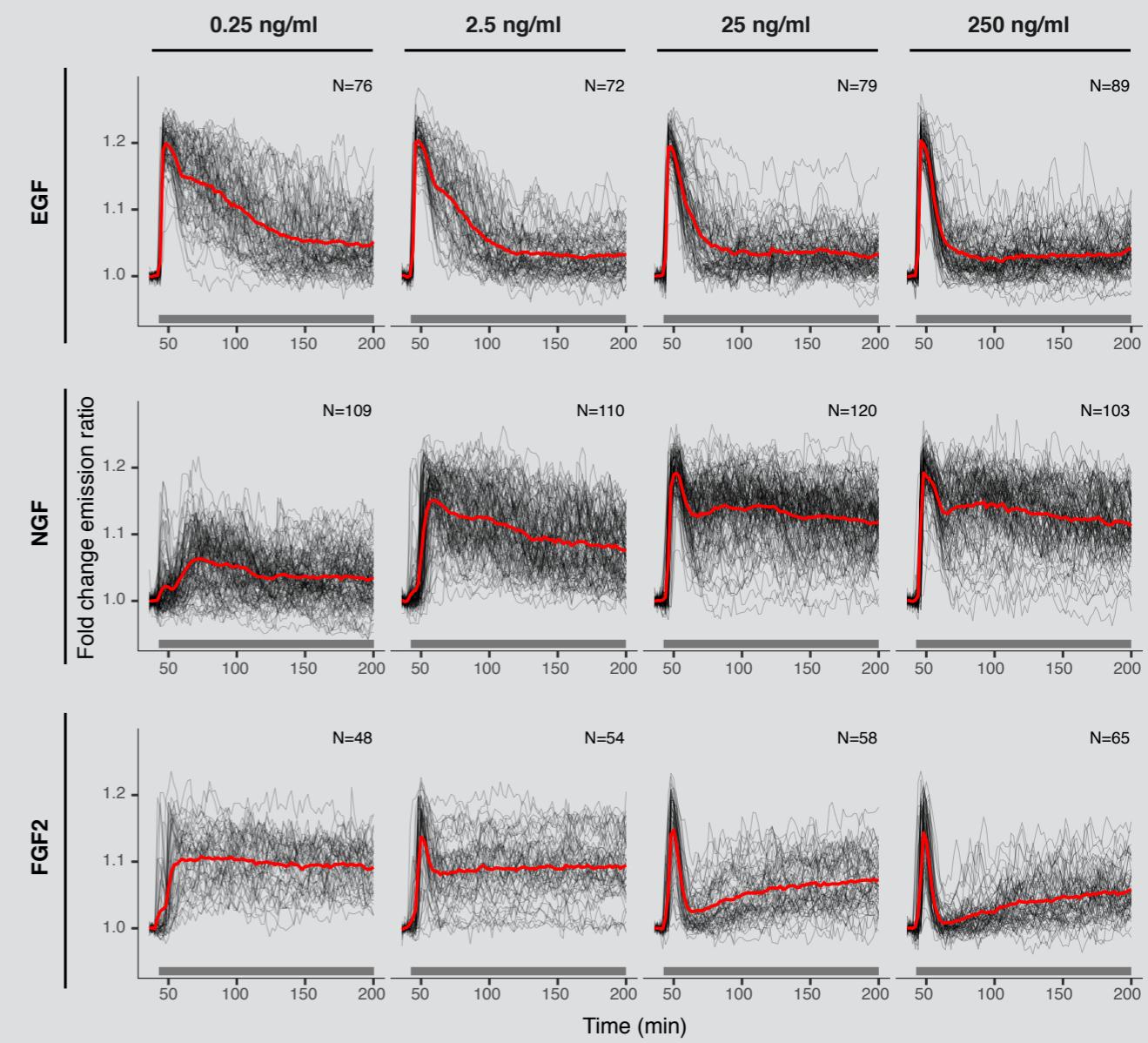
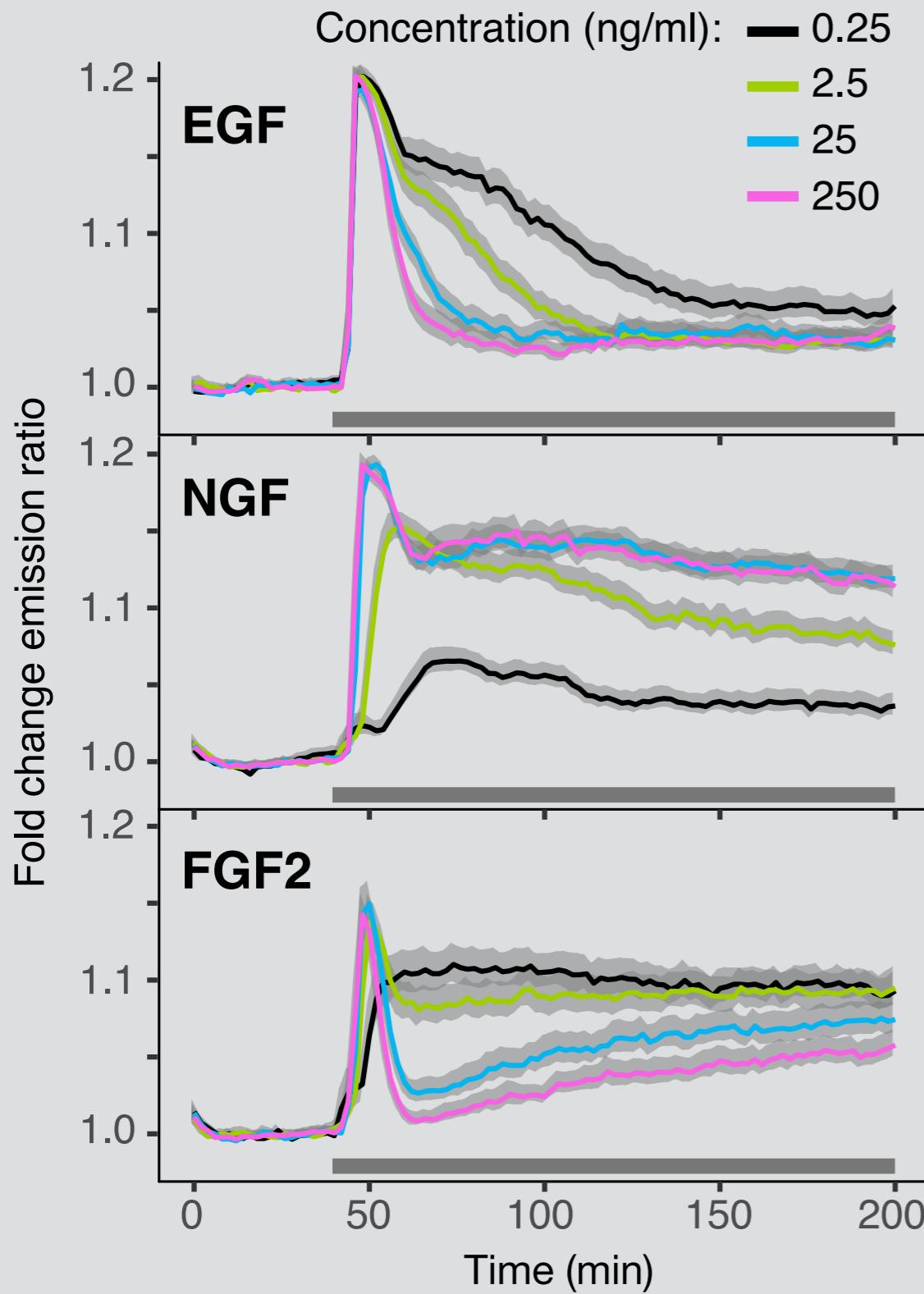
Different GF's induce different dynamics



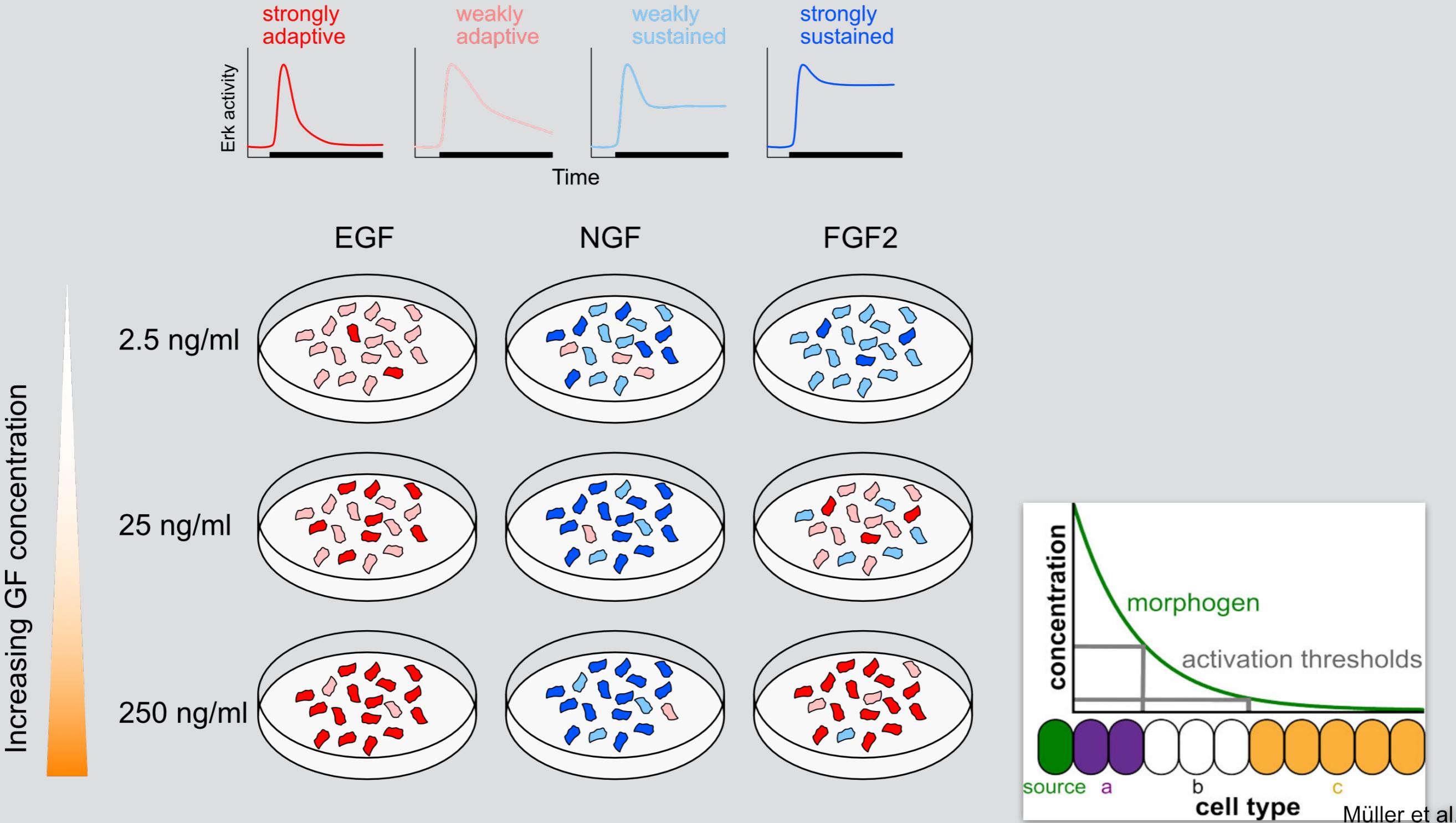
Different dynamics result in different fates



Population vs single-cell dynamics



The FGF2 dose response produces a wider variety of signalling states than EGF/NGF



Important to specify different fates in a developmental morphogen gradient?

Links and references

Temporal perturbation of Erk dynamics reveals network architecture of FGF2-MAPK signaling

Yannick Blum, Jan Mikelson, Maciej Dobrzański, Hyunryul Ryu, Marc-Antoine Jacques,
Noo Li Jeon, Mustafa Khammash, Olivier Pertz

<http://biorxiv.org/content/10.1101/629287v1>

Time Course Inspector interactive clustering R/Shiny

<https://github.com/dmattek/shiny-timecourse-inspector>

Outlier Selector interactive R/Shiny

<https://github.com/dmattek/shiny-timecourse-inspector>

Materials for QuantBio Workshop

<https://github.com/dmattek/workshop-QUANTBIO2019>