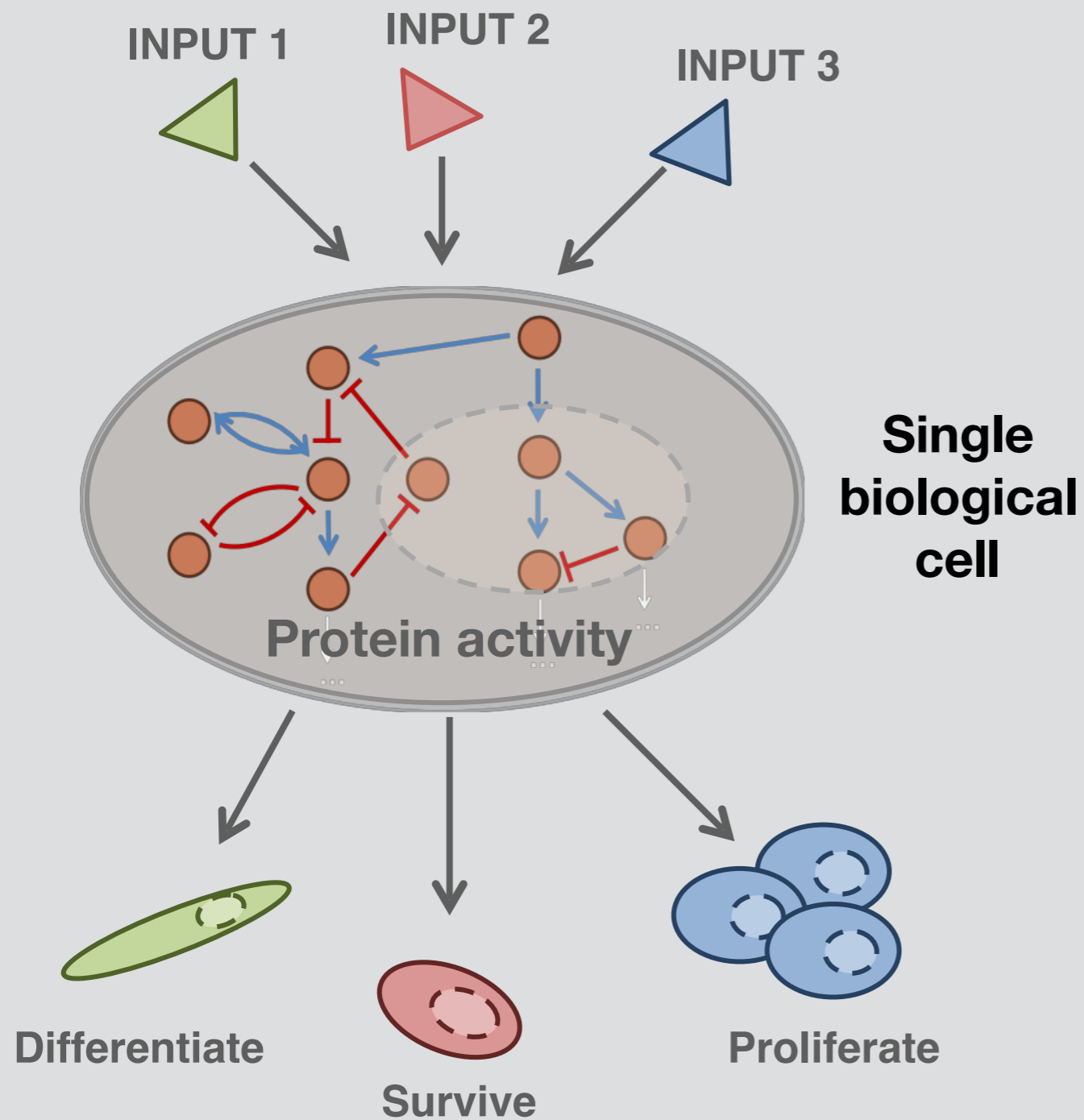


Image and data analytic pipeline for studying signaling dynamics in cancer

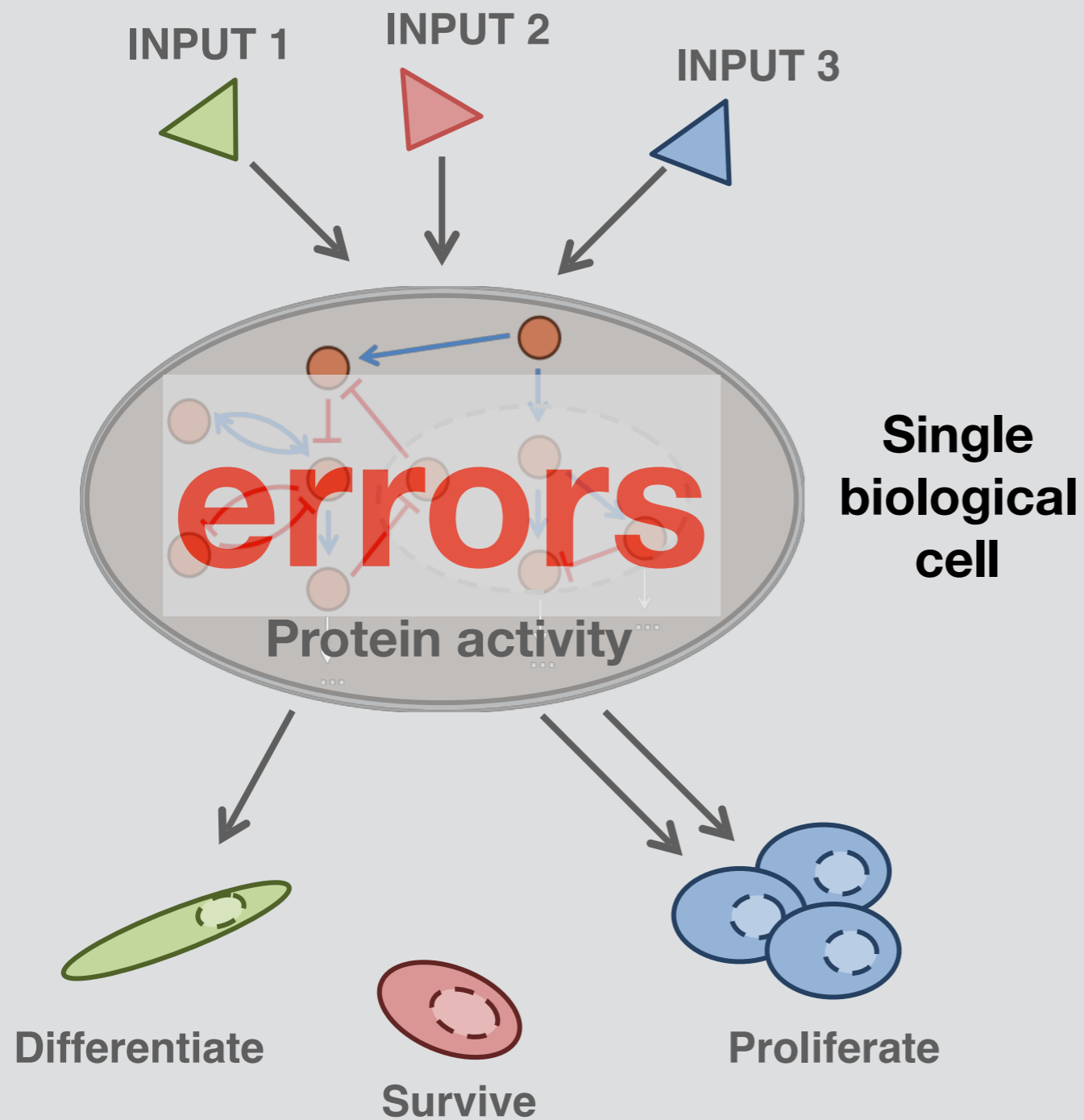
Maciej Dobrzyński

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

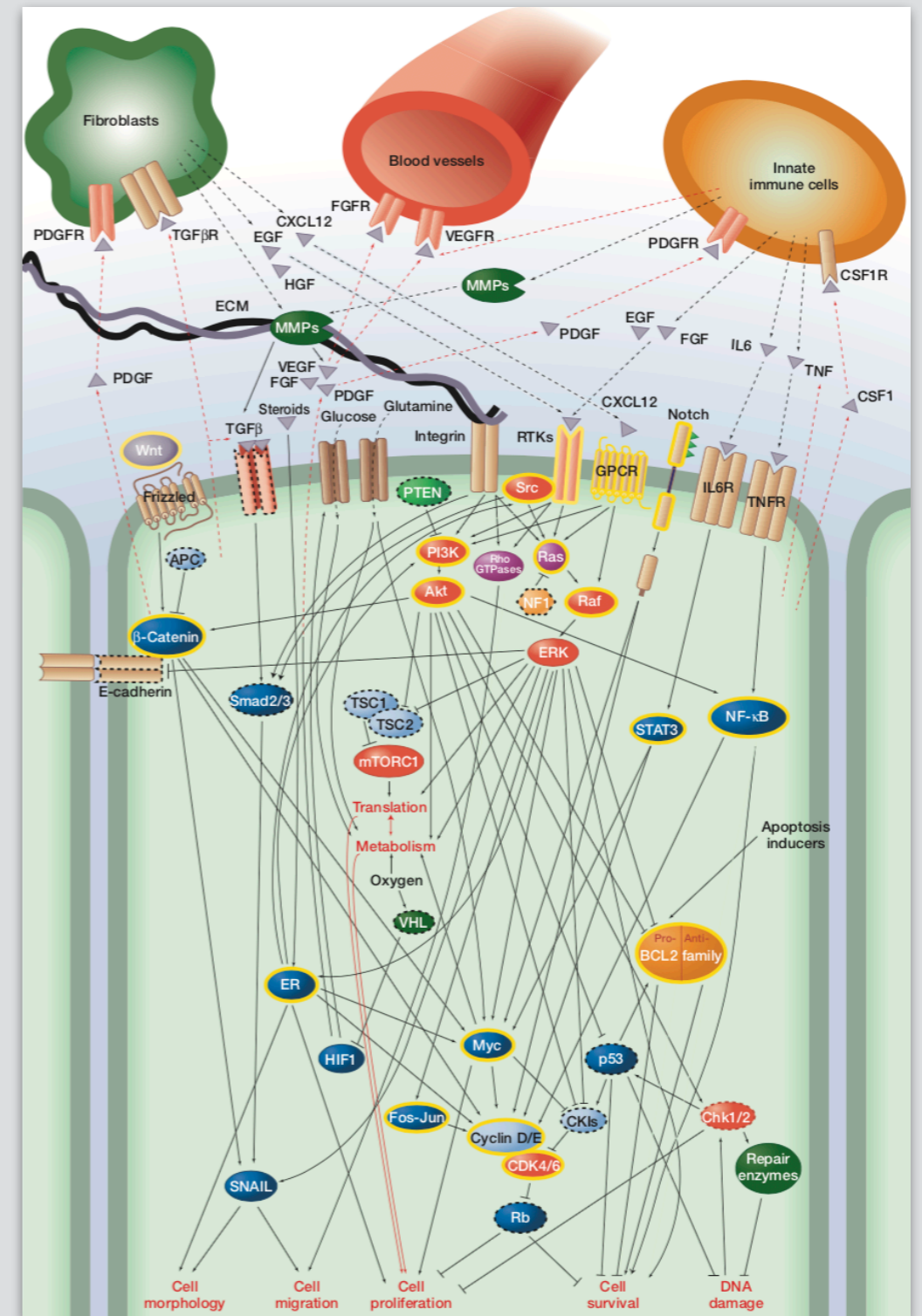
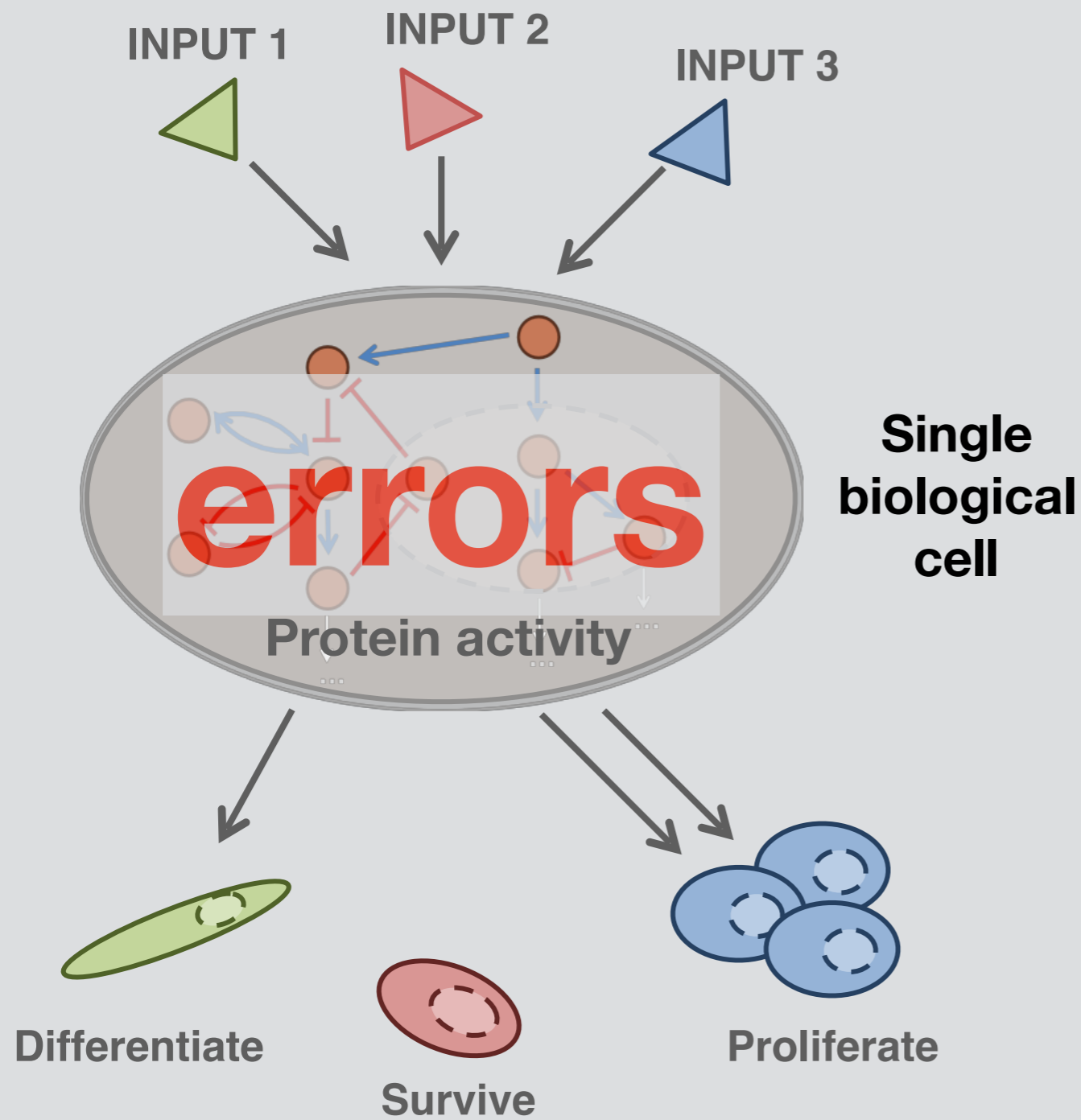
Cancer – a complex disease involving increased cell growth



Cancer – a complex disease involving increased cell growth



Cancer – a complex disease involving increased cell growth



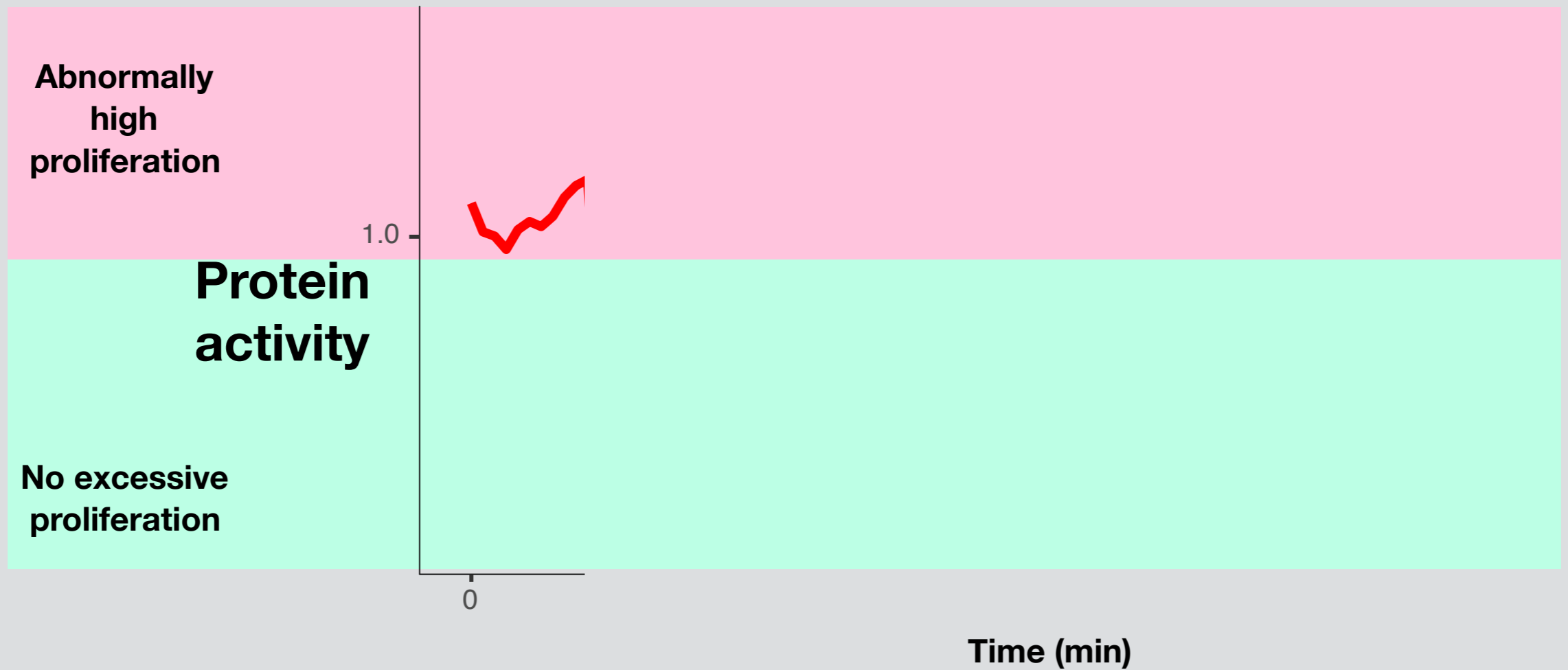


The emergence of drug resistance

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Alberto Mattei
Pertz Group



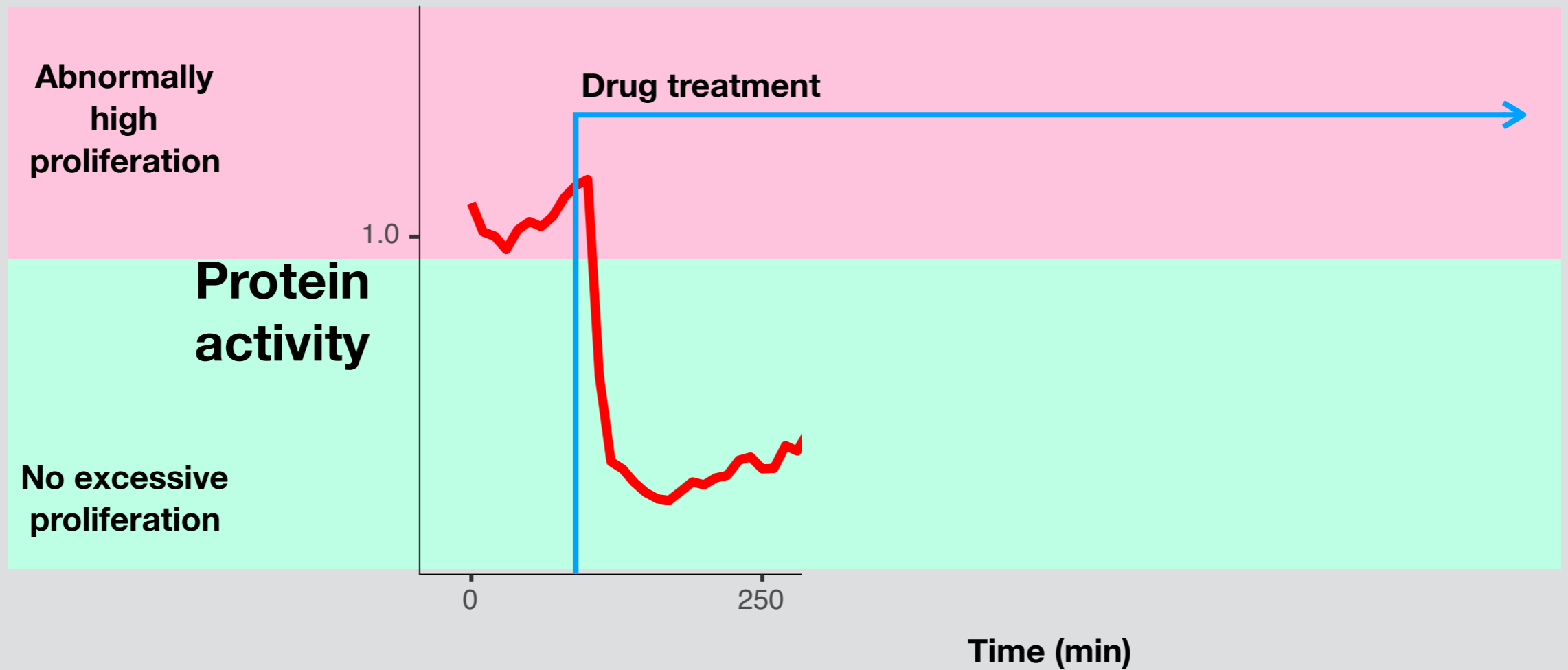


The emergence of drug resistance

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Alberto Mattei
Pertz Group



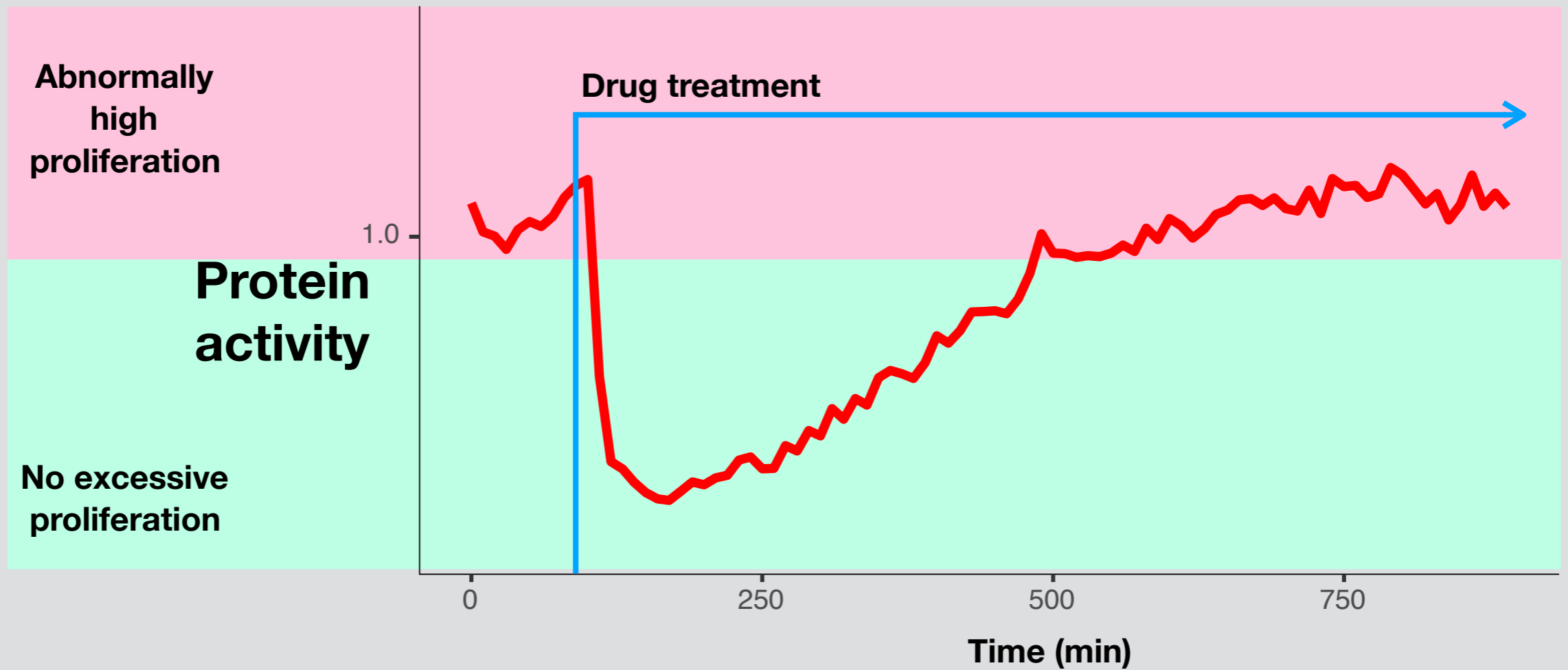


The emergence of drug resistance

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Pertz Group



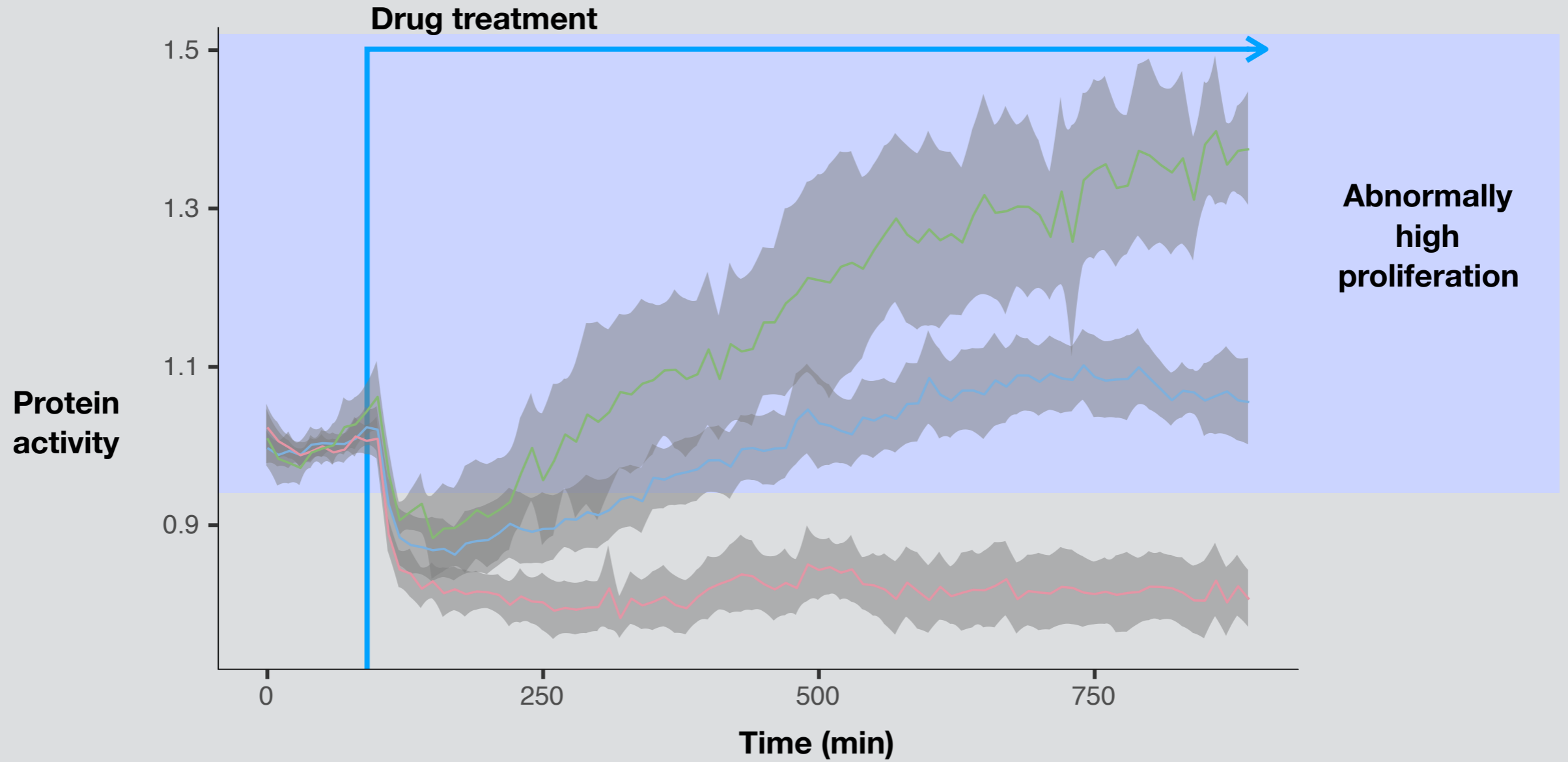


Alberto Mattei
(Pertz Group)

Cells respond differently to drugs

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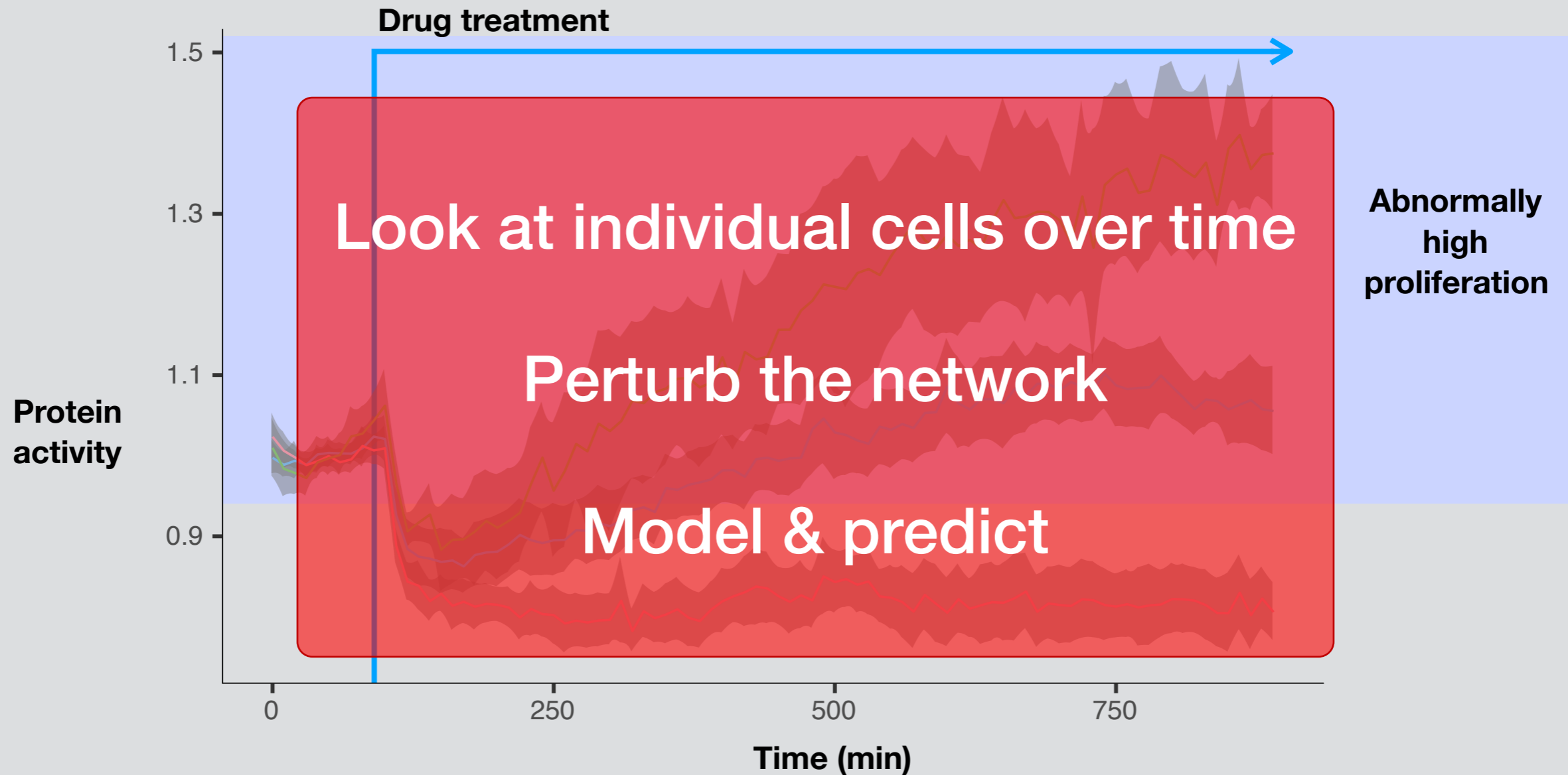


Alberto Mattei
(Pertz Group)

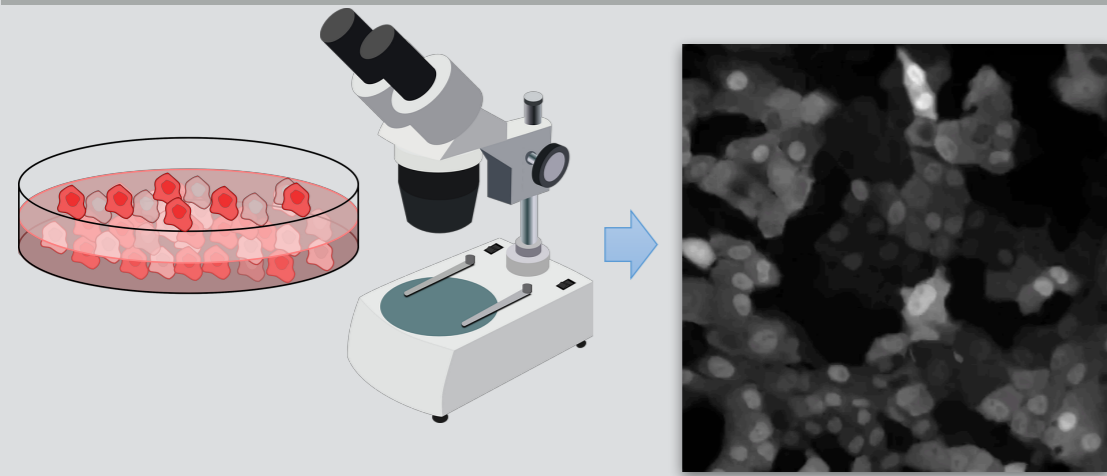
Cells respond differently to drugs

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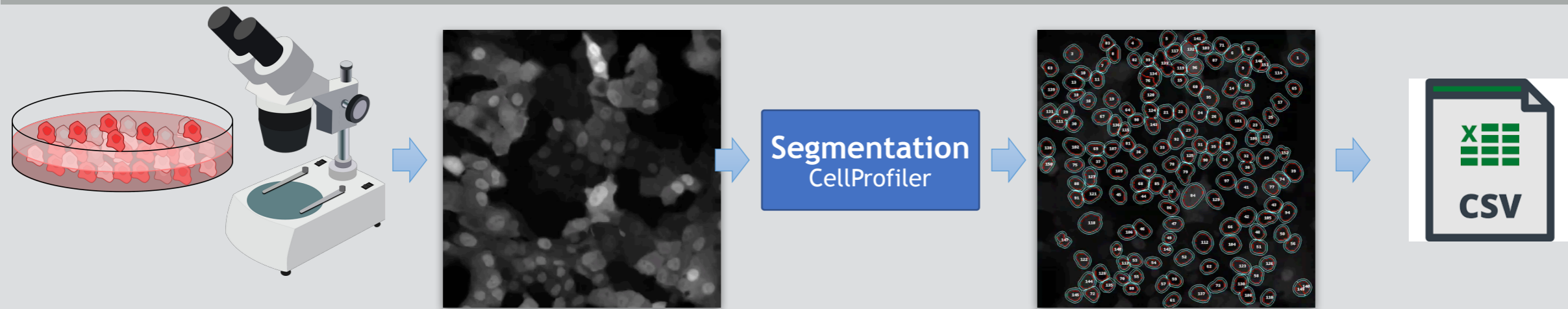
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Our pipeline in practice



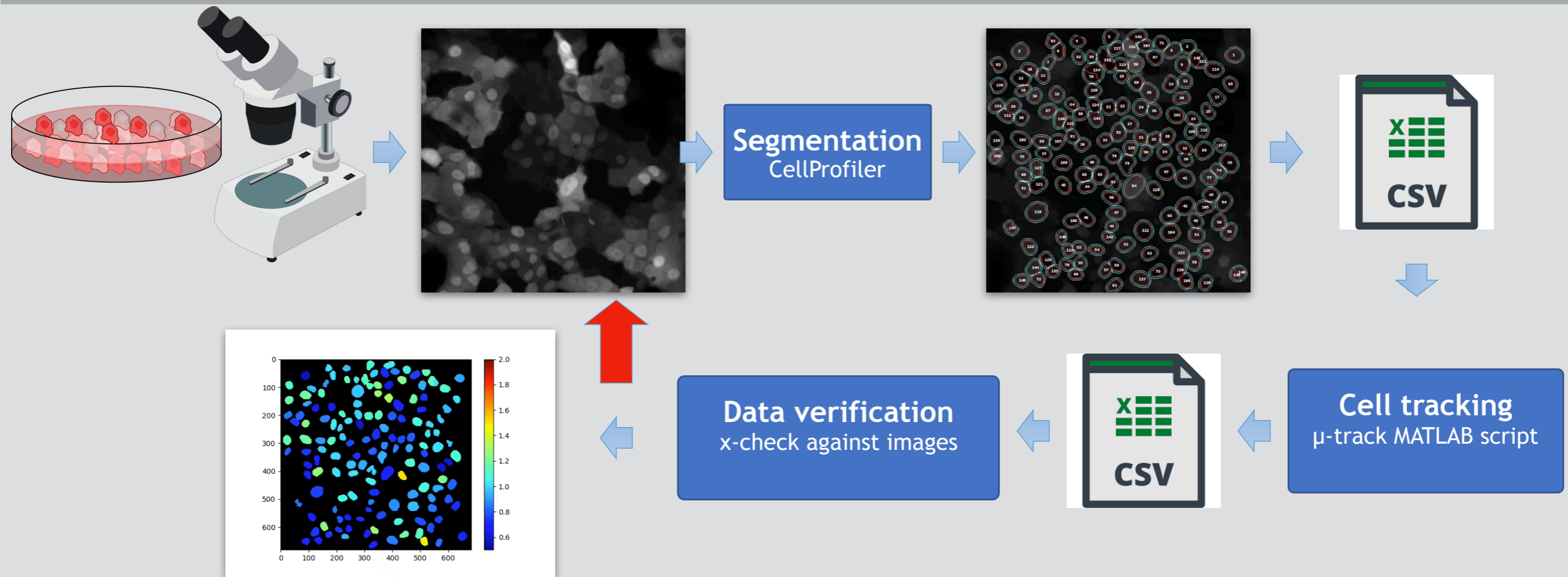
Our pipeline in practice



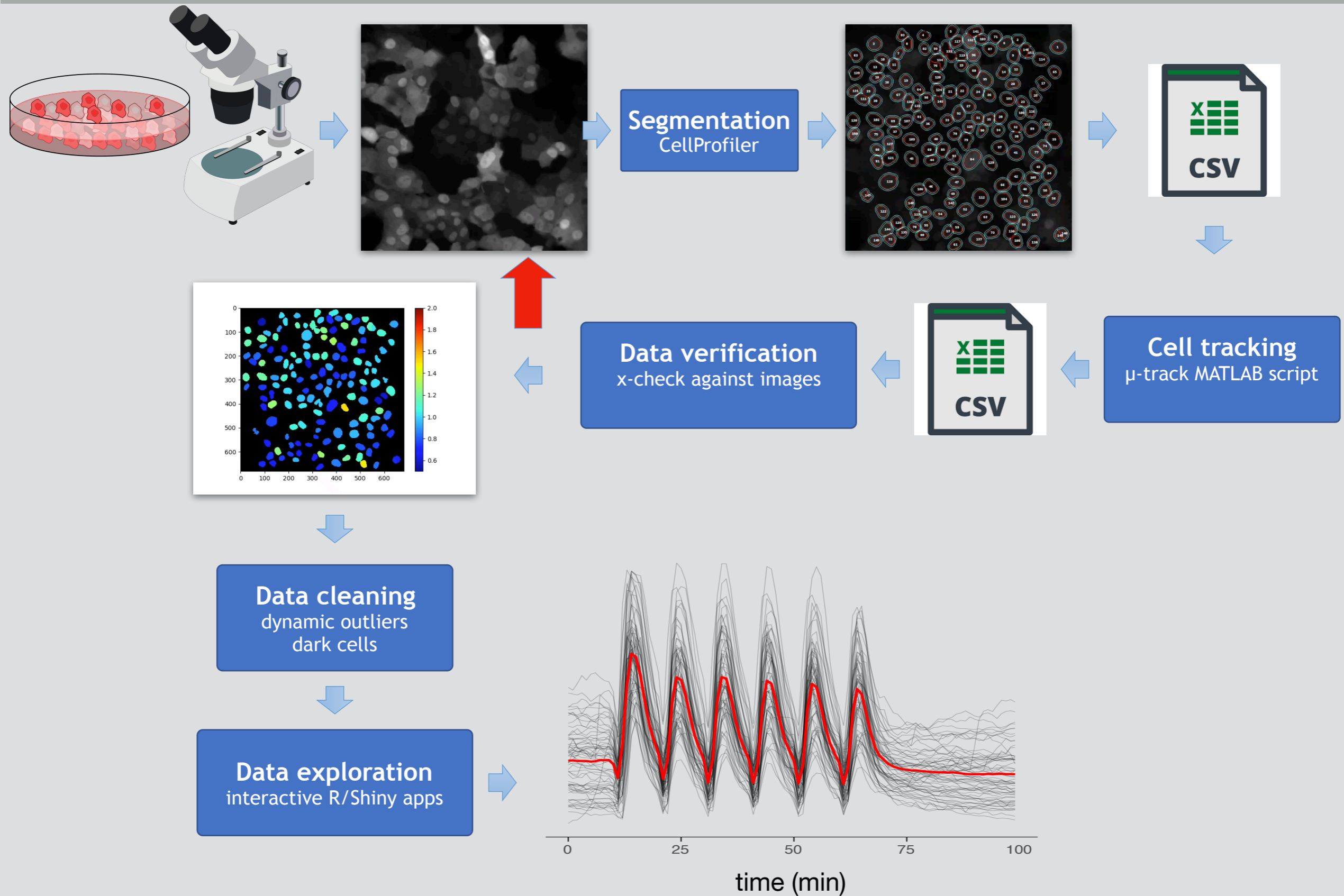
Our pipeline in practice



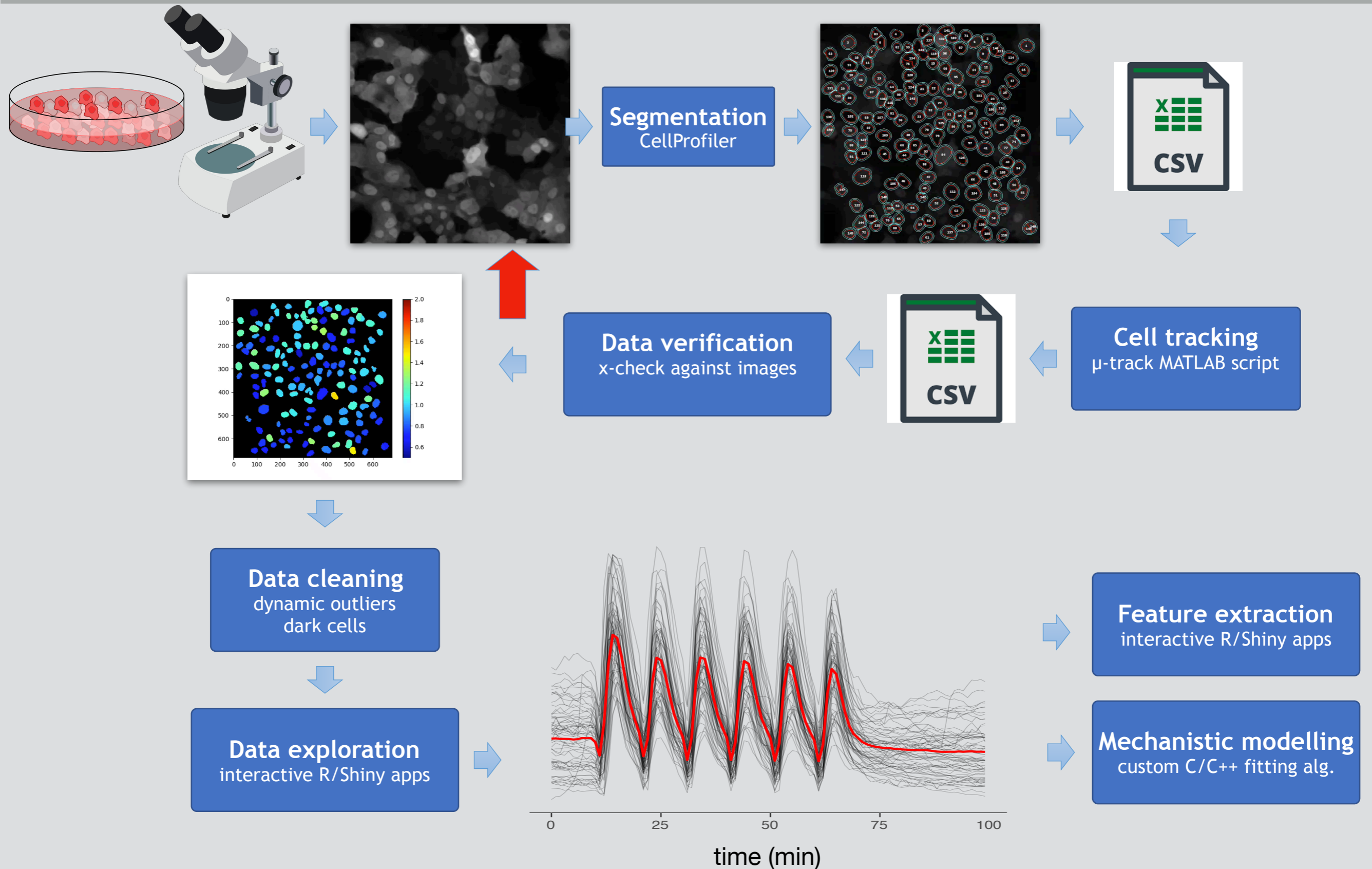
Our pipeline in practice



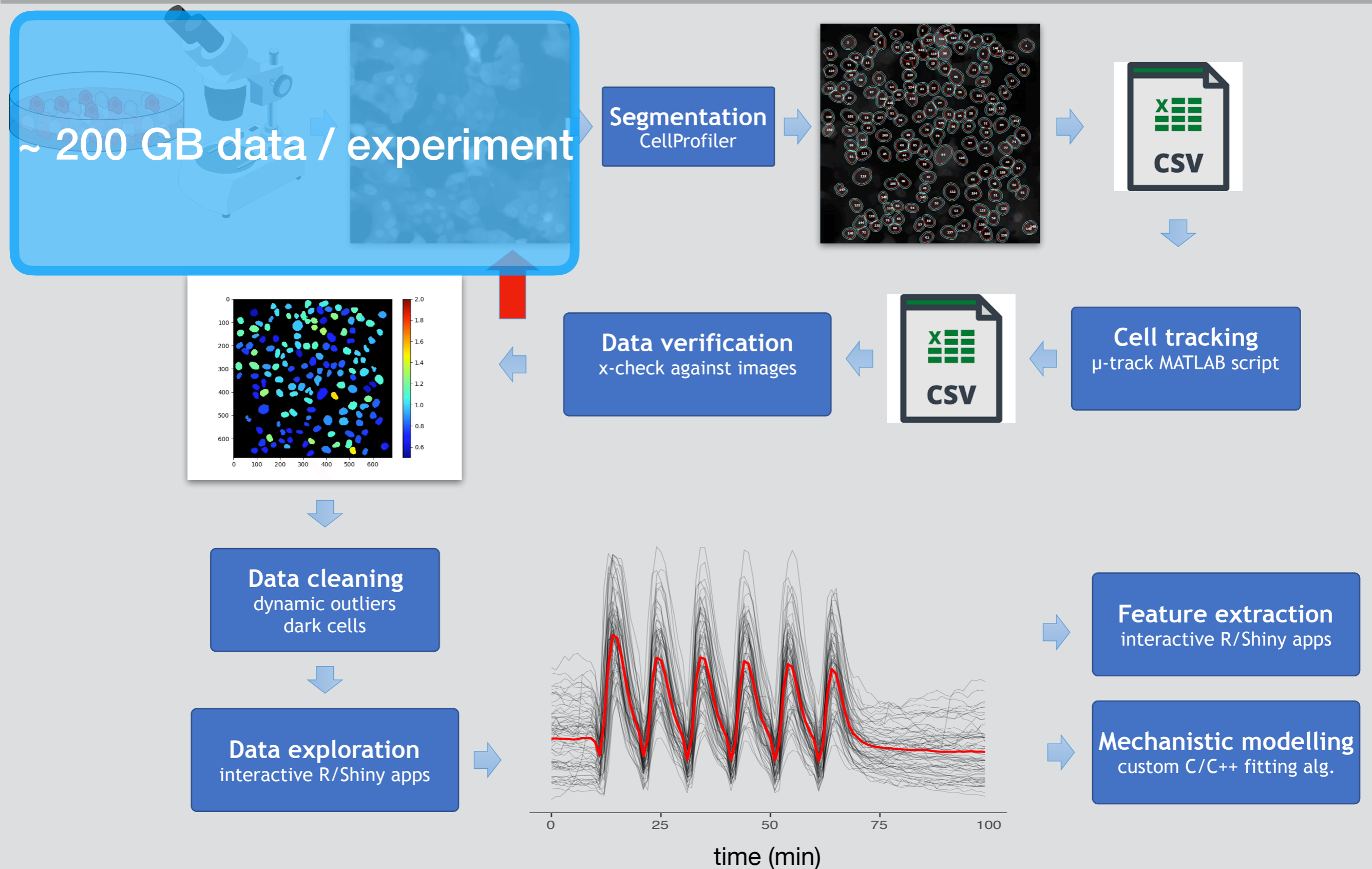
Our pipeline in practice



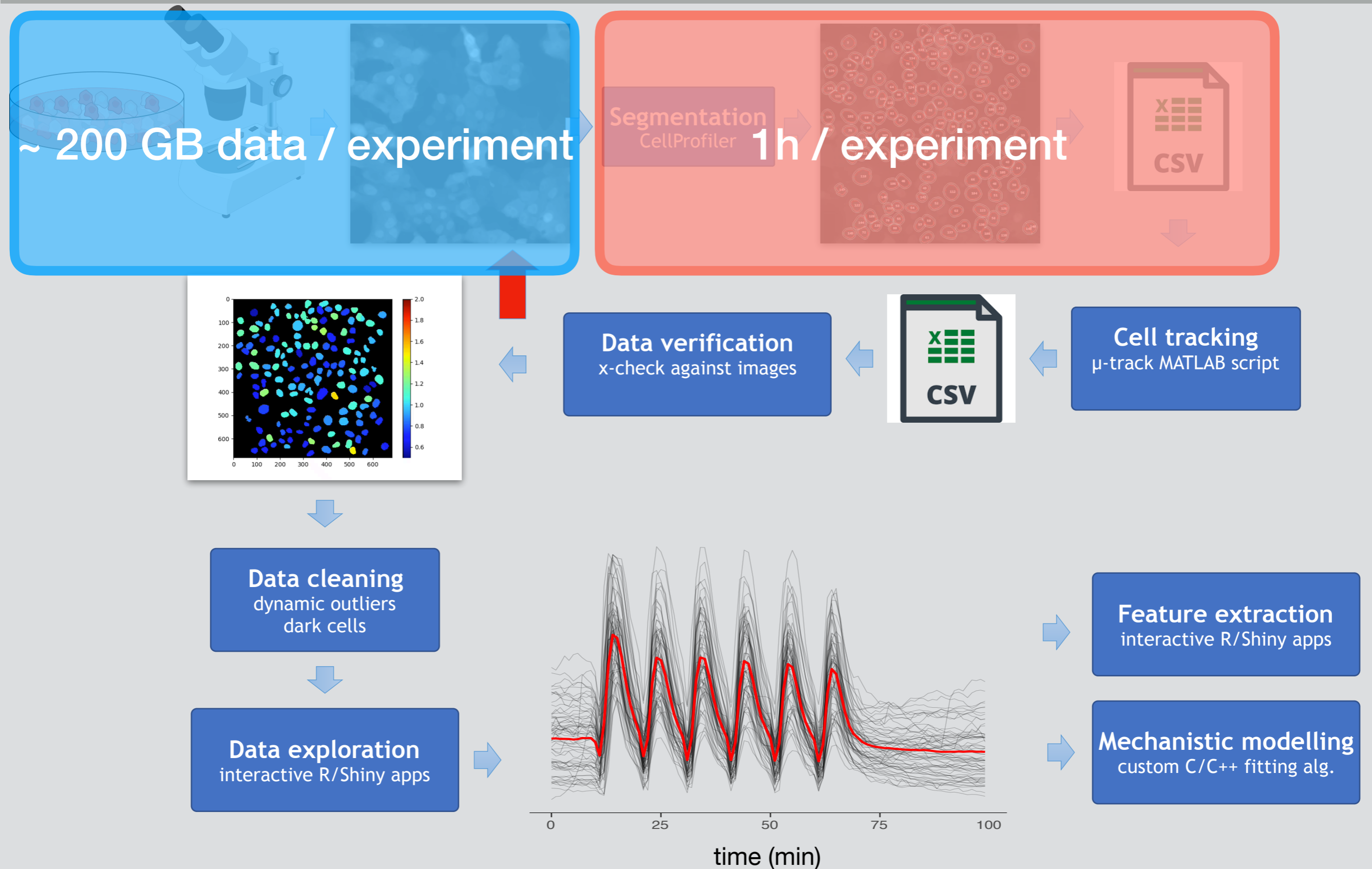
Our pipeline in practice



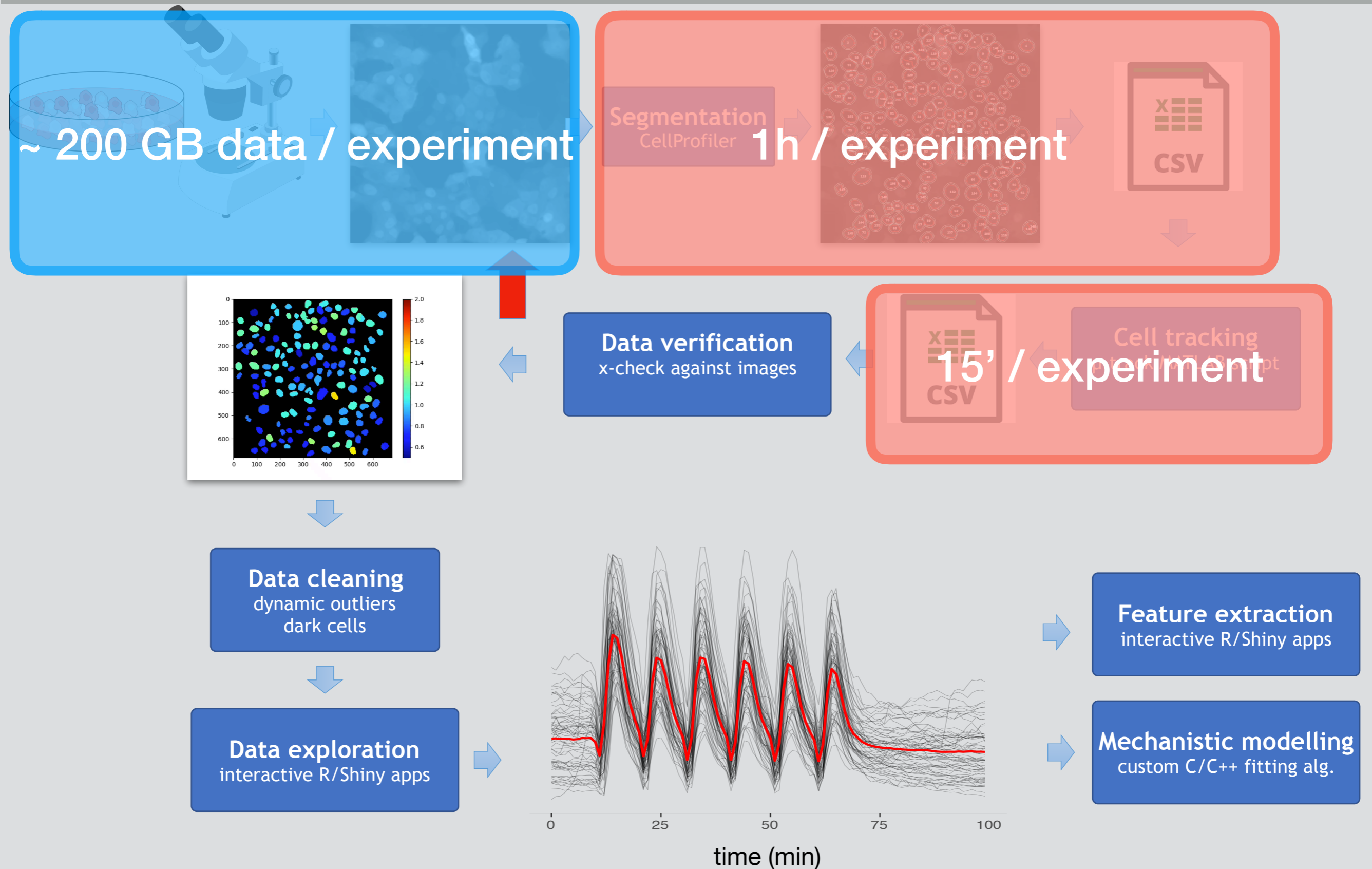
Our pipeline in practice



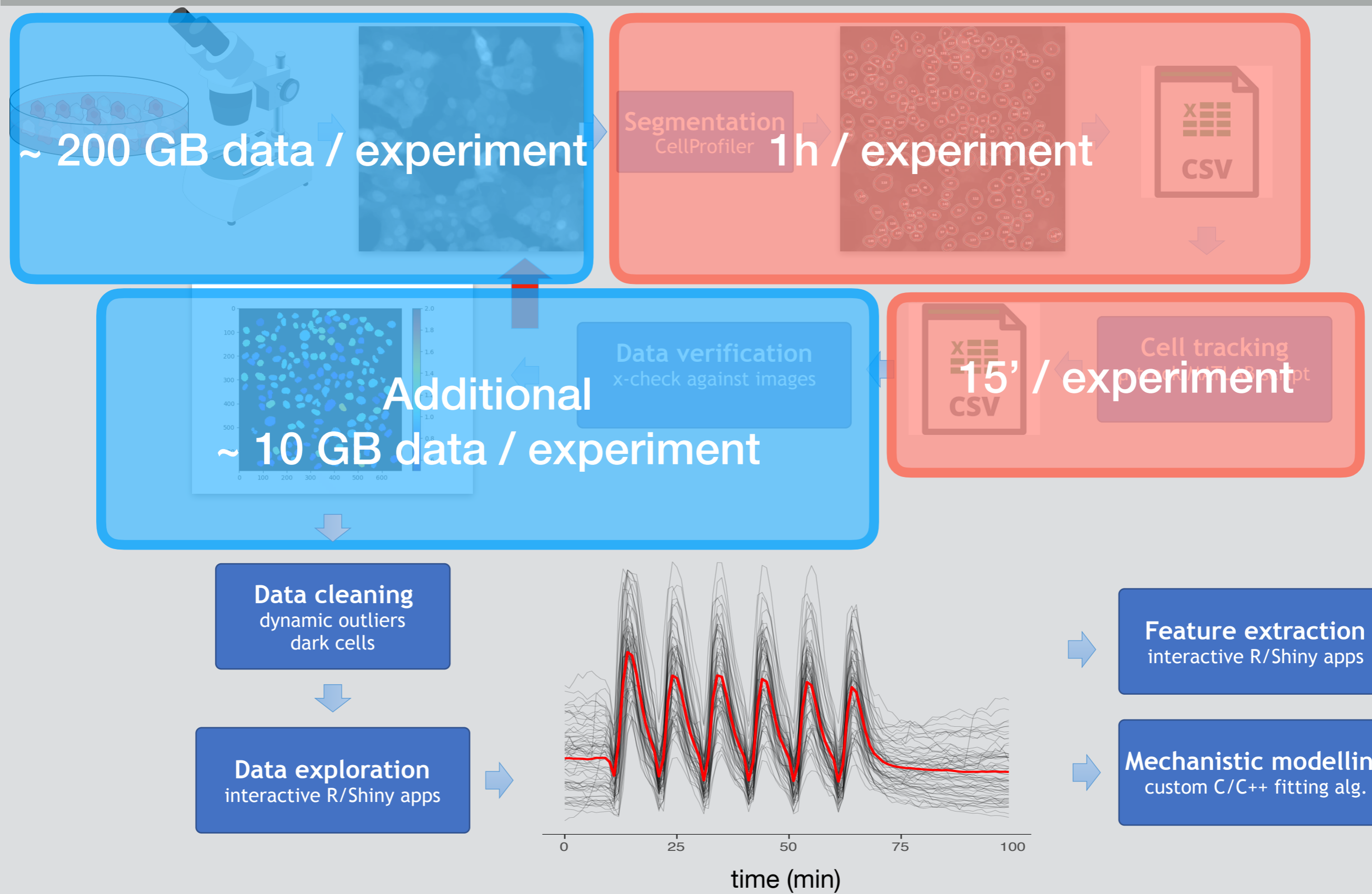
Our pipeline in practice



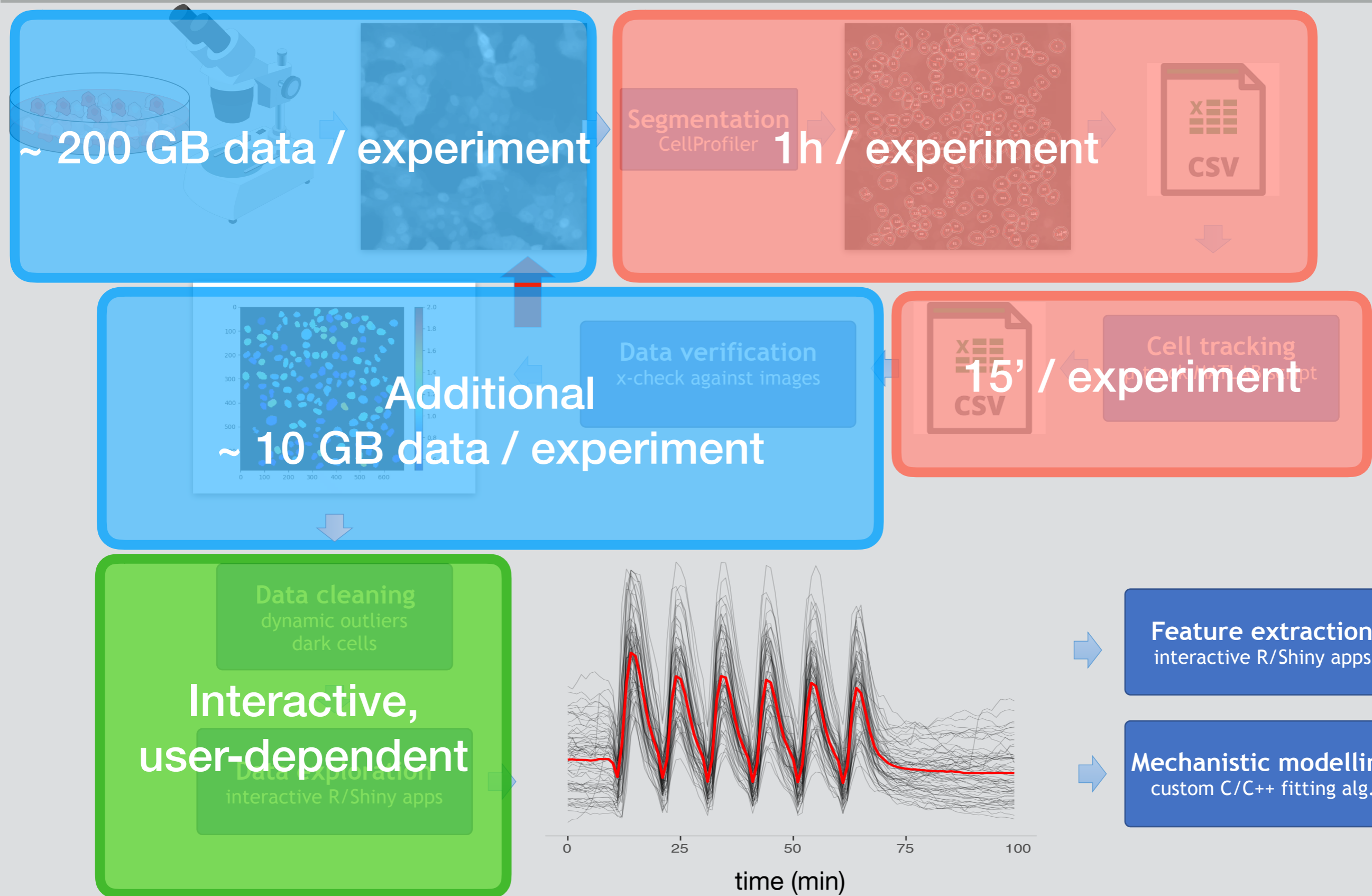
Our pipeline in practice



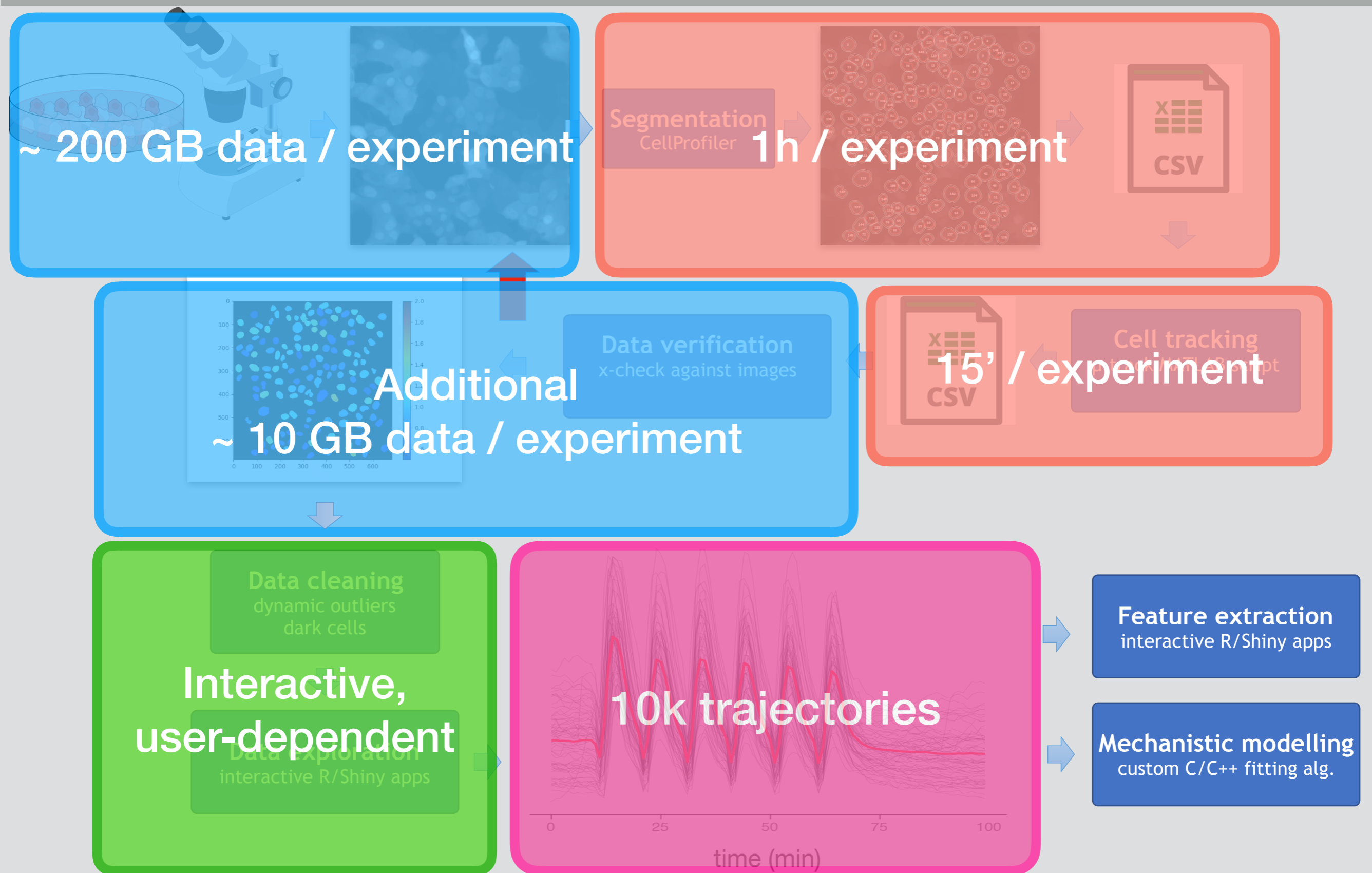
Our pipeline in practice



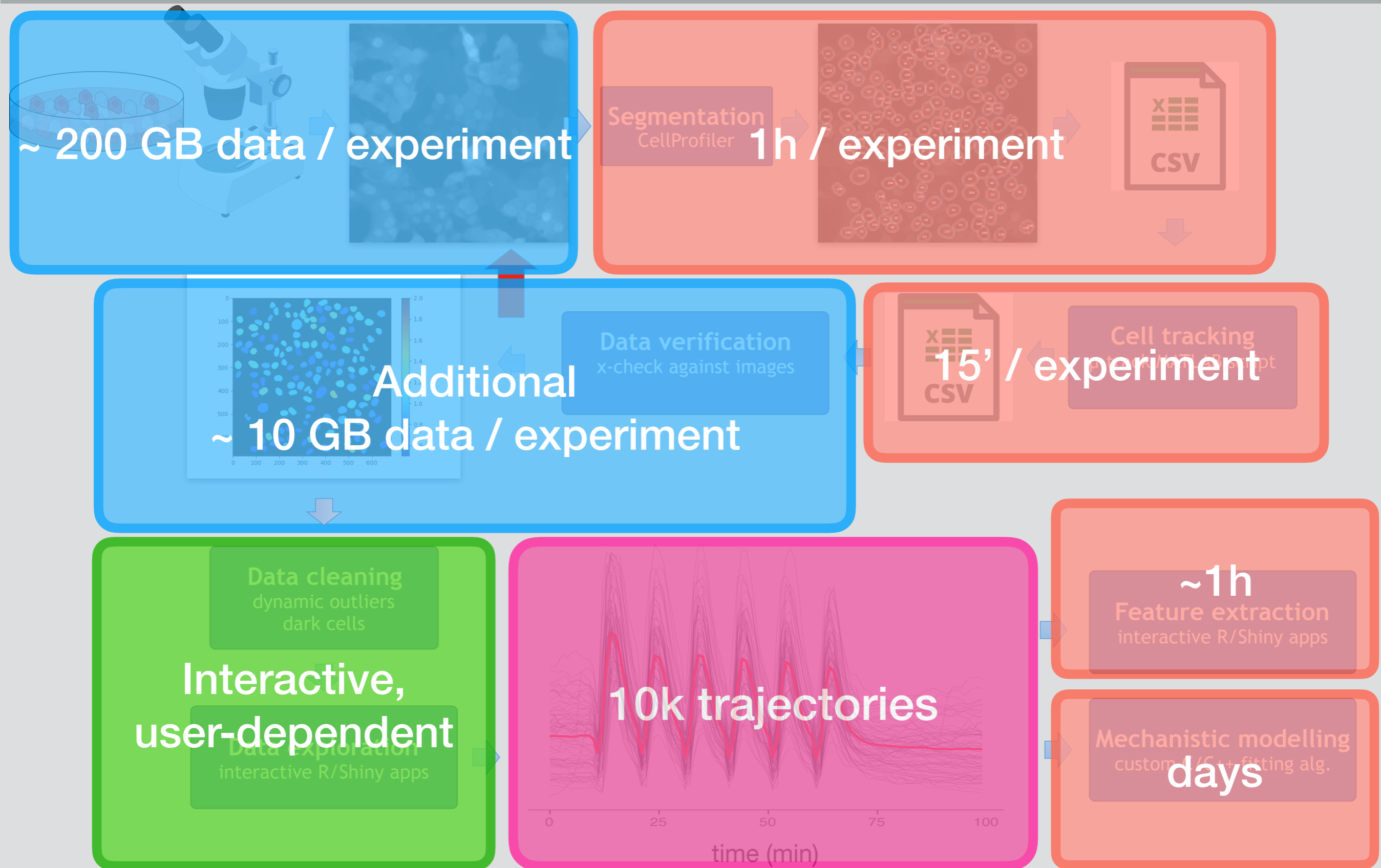
Our pipeline in practice



Our pipeline in practice



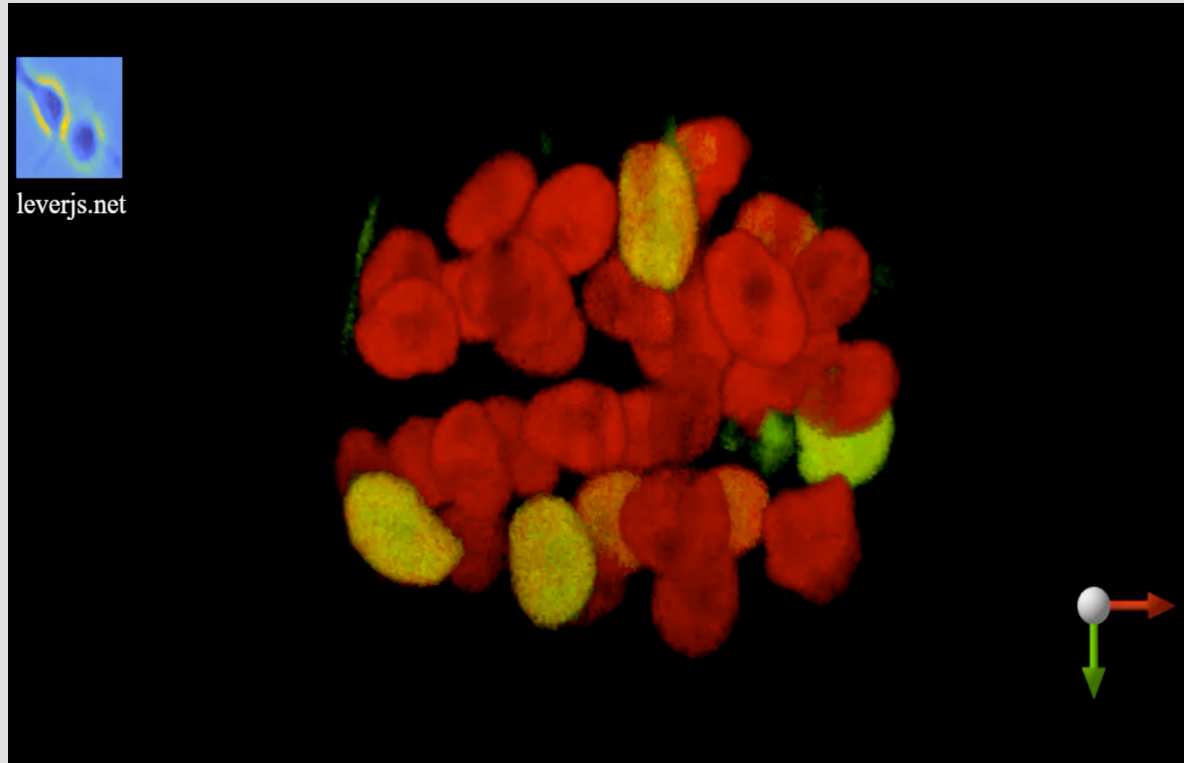
Our pipeline in practice





Organoids: physiologically-relevant human disease models

Paolo Gagliardi & Pascal Ender
Pertz Group

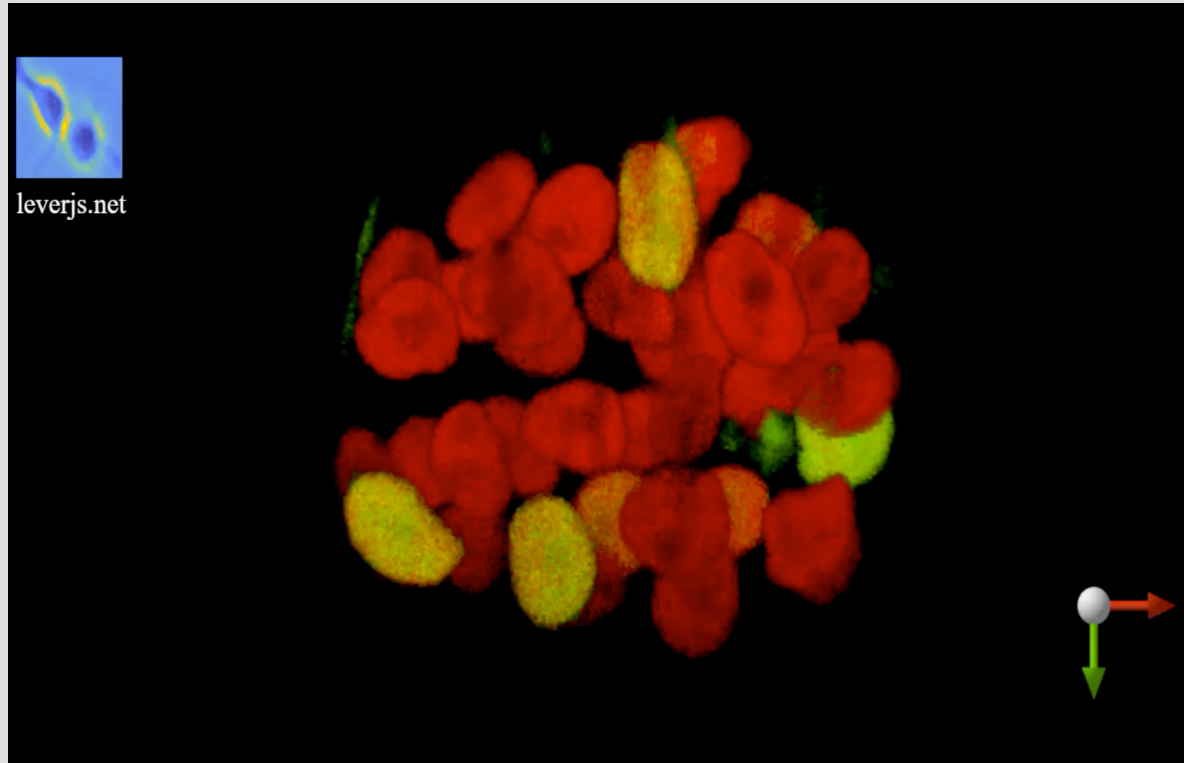


Tumor
biopsy

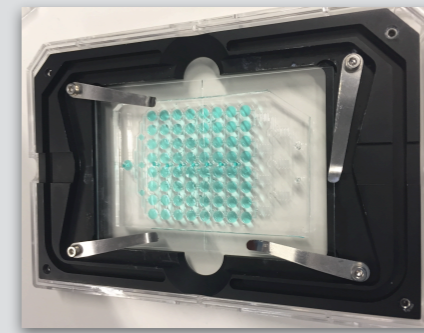


Organoids: physiologically-relevant human disease models

Paolo Gagliardi & Pascal Ender
Pertz Group



Tumor
biopsy



Grow biopsies as
organoids
(mini-tumors)

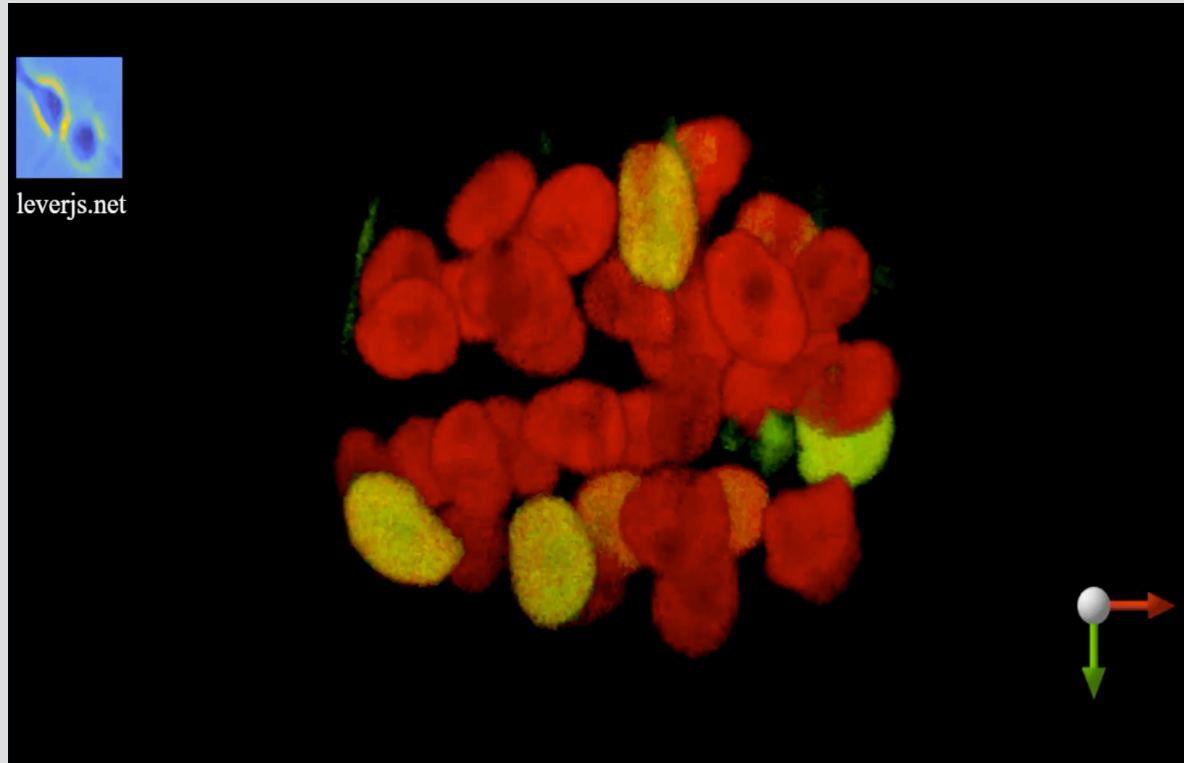


Organoids: physiologically-relevant human disease models

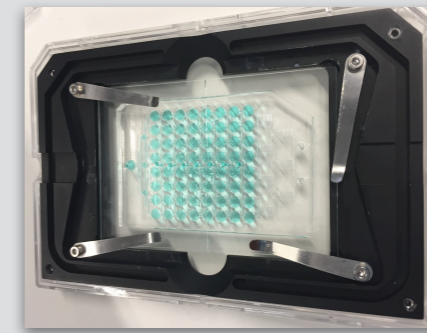
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Paolo Gagliardi & Pascal Ender
Pertz Group



Tumor biopsy

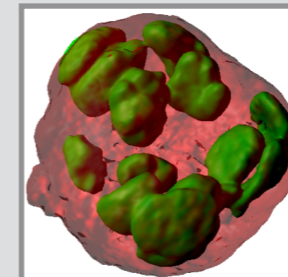


Grow biopsies as organoids (mini-tumors)

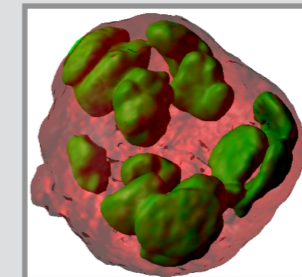


Test drug responses in live organoids

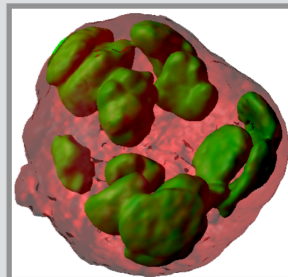
Drug 1



Drug 2



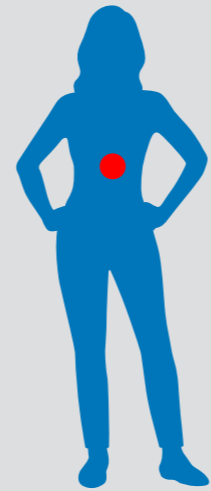
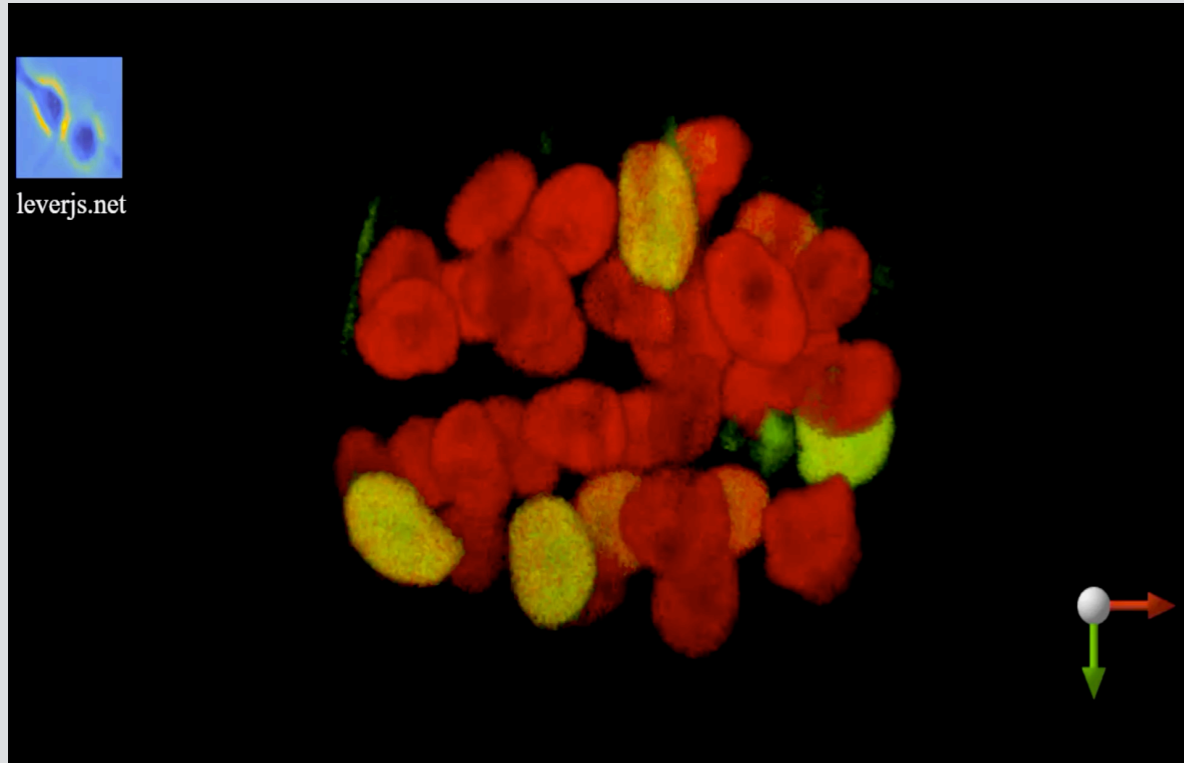
Drug 3



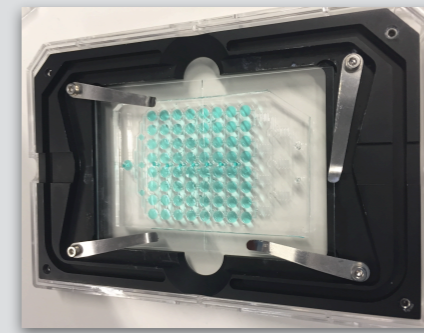


Organoids: physiologically-relevant human disease models

Paolo Gagliardi & Pascal Ender
Pertz Group



Tumor biopsy

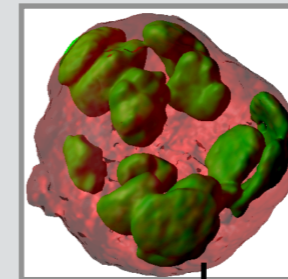


Grow biopsies as organoids (mini-tumors)

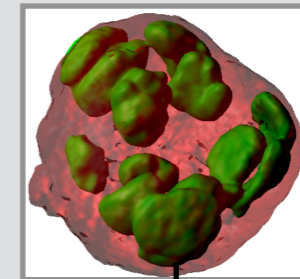


Test drug responses in live organoids

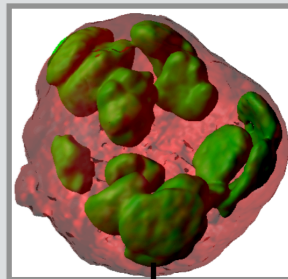
Drug 1



Drug 2



Drug 3

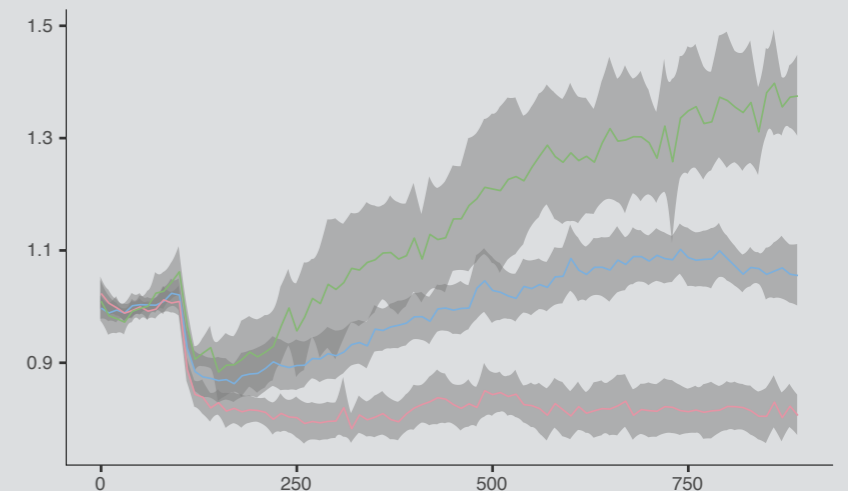


High dimensionality, complex datasets

Statistical analysis

Mathematical modelling

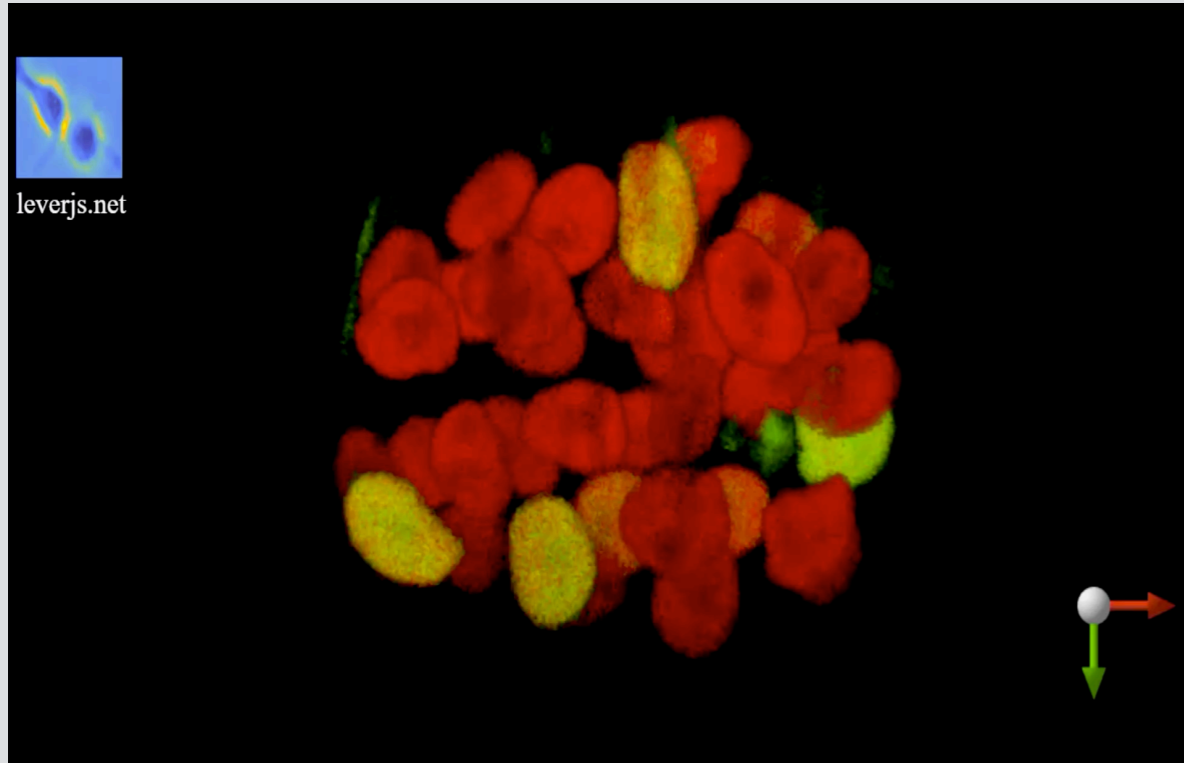
Needs multidisciplinary approaches !!!!



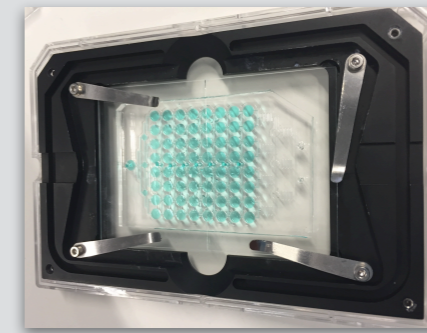


Organoids: physiologically-relevant human disease models

Paolo Gagliardi & Pascal Ender
Pertz Group



Tumor biopsy

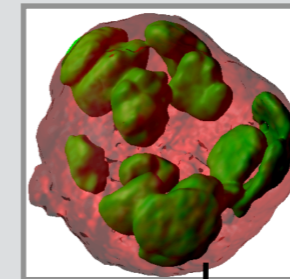


Grow biopsies as organoids (mini-tumors)

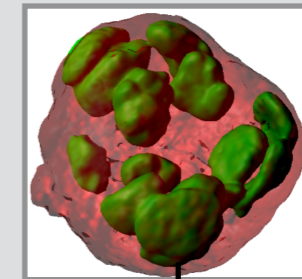


Test drug responses in live organoids

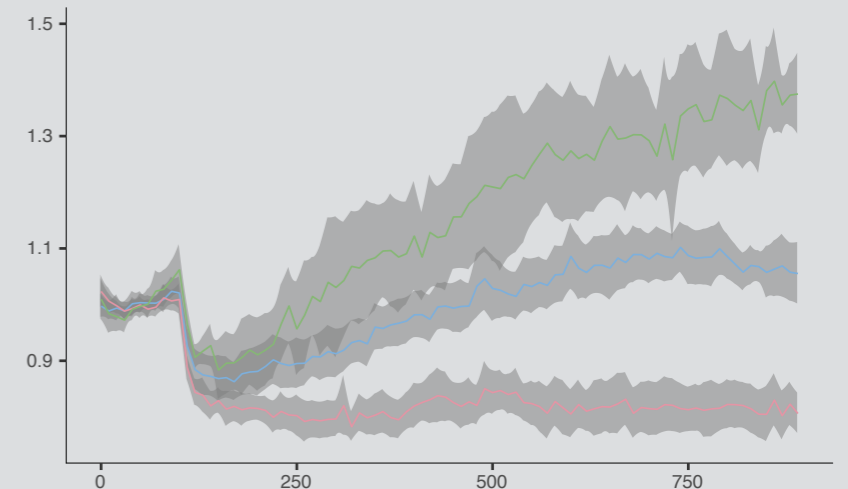
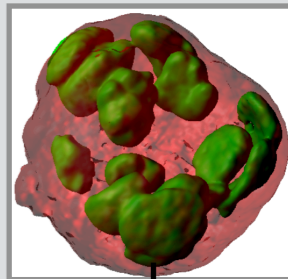
Drug 1



Drug 2



Drug 3



High dimensionality, complex datasets

Statistical analysis

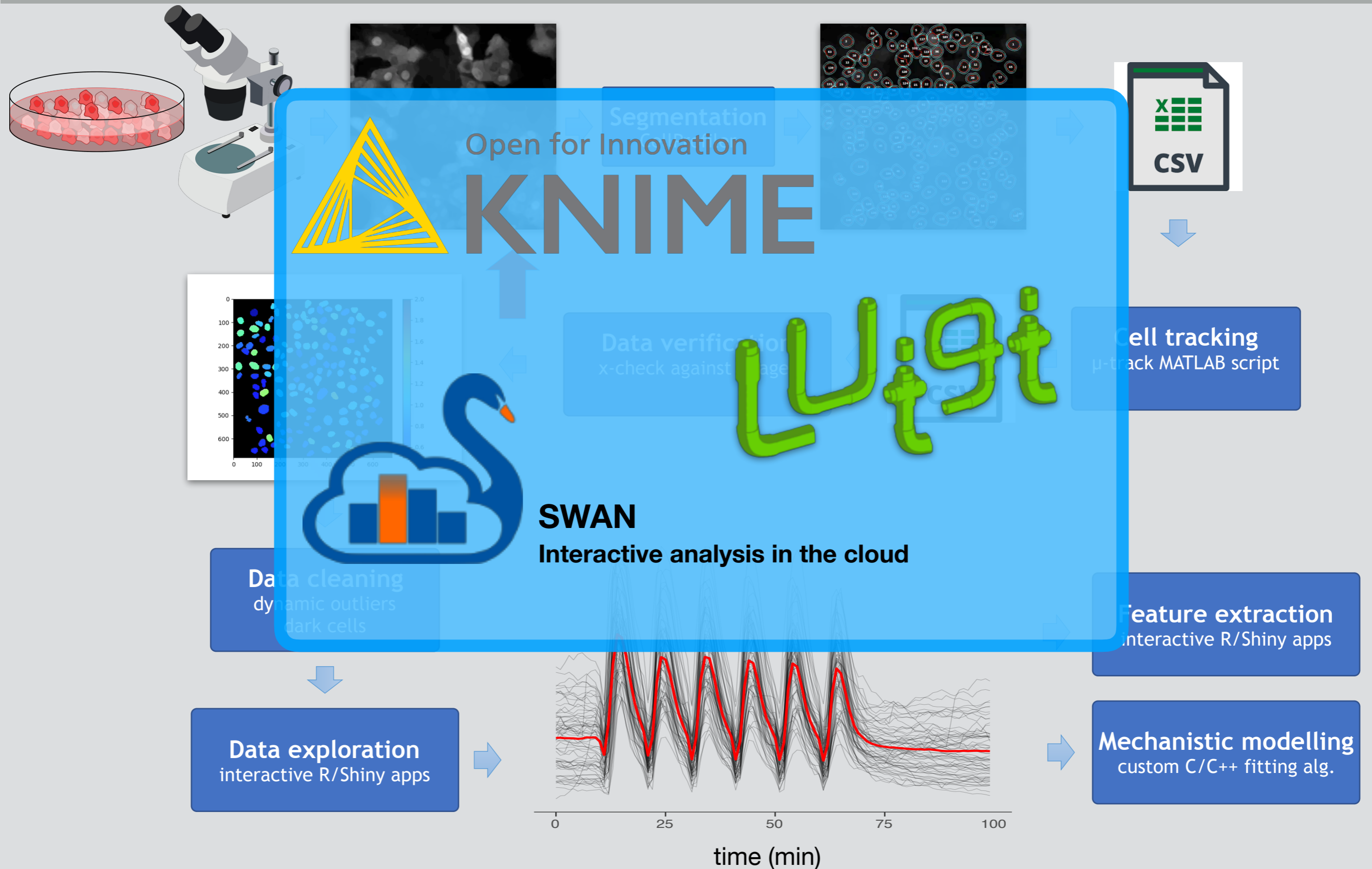
Mathematical modelling

Needs multidisciplinary approaches !!!!



Predict drug, drug combinations that are effective on patients

Challenge 1: heterogeneous pipeline





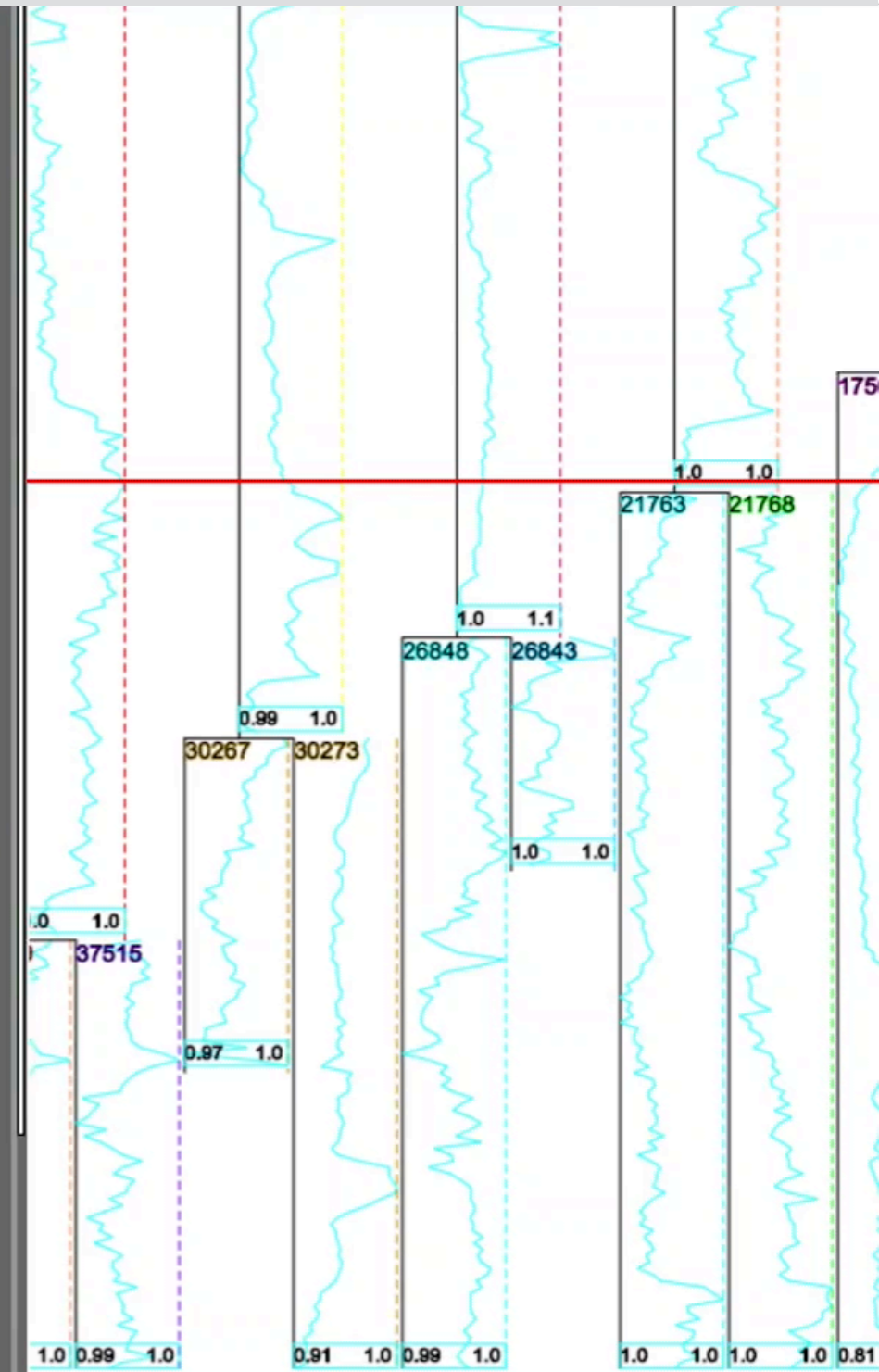
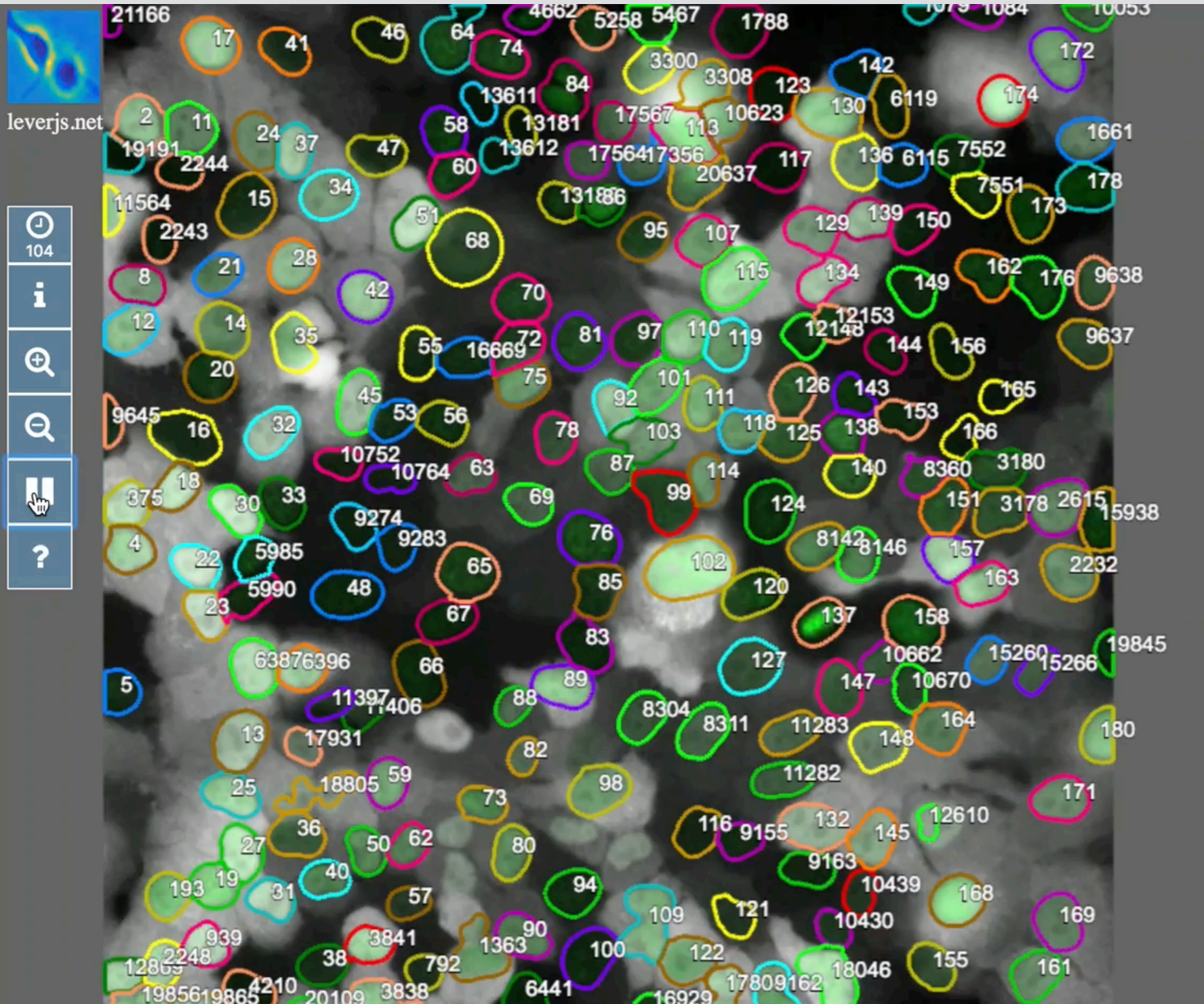
Challenge 2:

raw images \Leftrightarrow processed data

Andrew Cohen
Drexel U.

leverjs

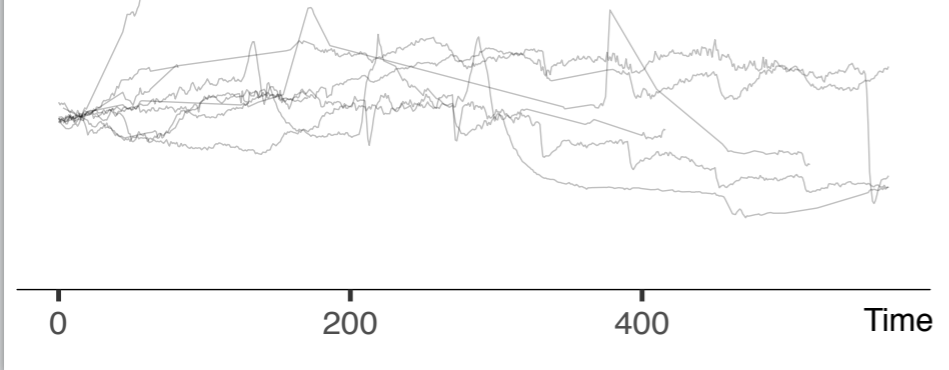
software tools for live-cell & organelle microscopy



Challenge 3: data analysis

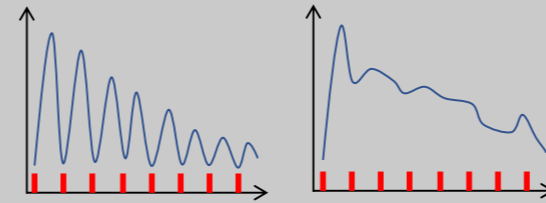
extract features from time series data

Identify “dynamic” outliers

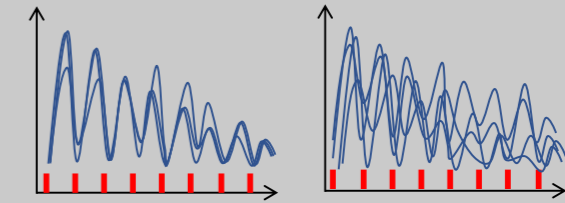


Characterise single-cell dynamics

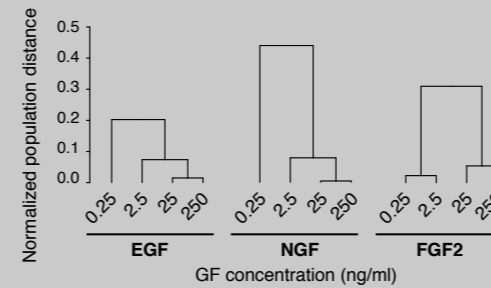
Causality



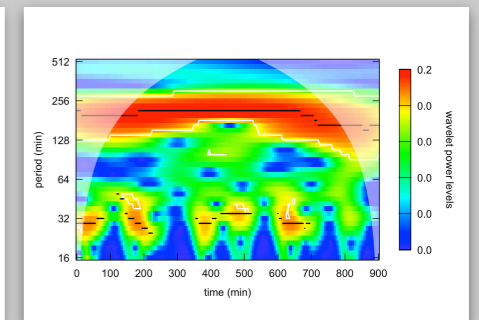
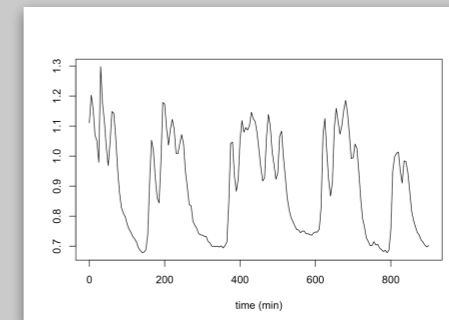
Synchronisation



Separability



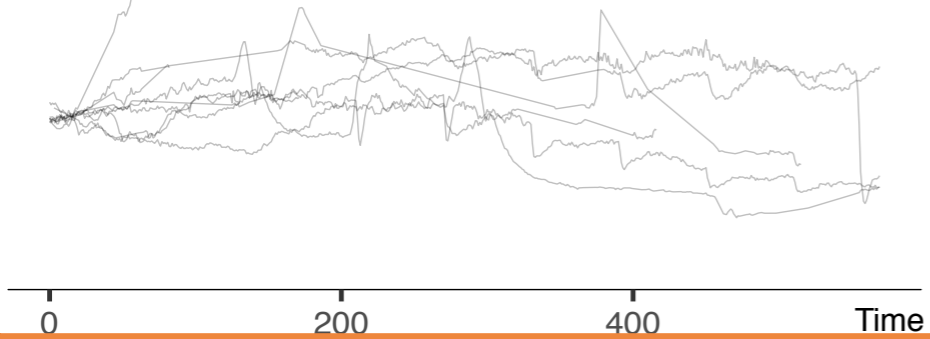
Spectral analysis



Challenge 3: data analysis

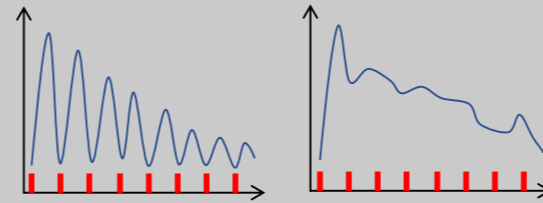
extract features from time series data

Identify “dynamic” outliers

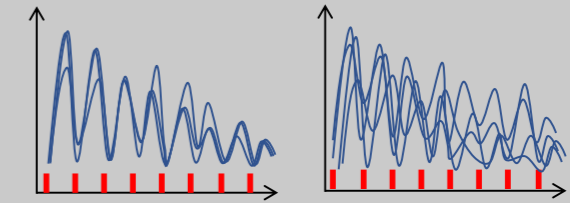


Characterise single-cell dynamics

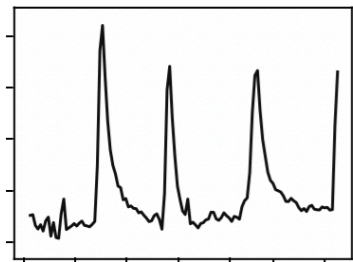
Causality



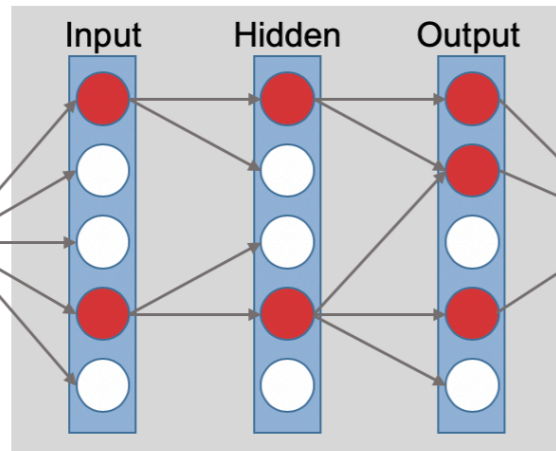
Synchronisation



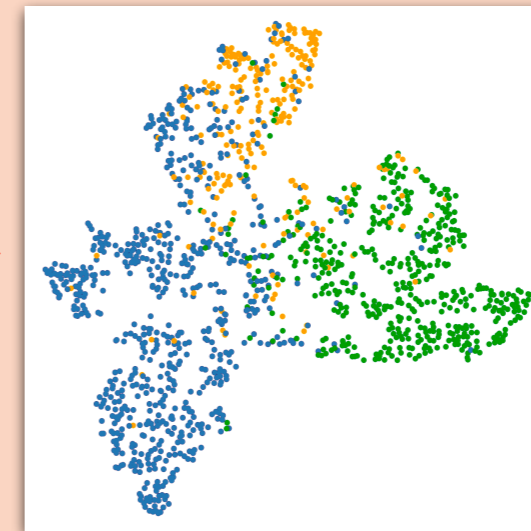
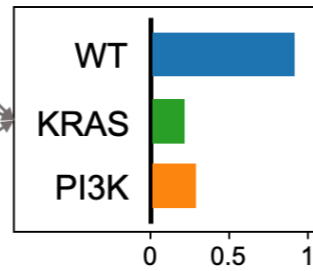
Input: ERK time-series



Convolutional Neural Network

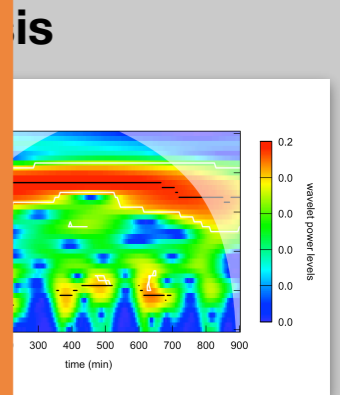


Output: Probability for each class



tSNE-1

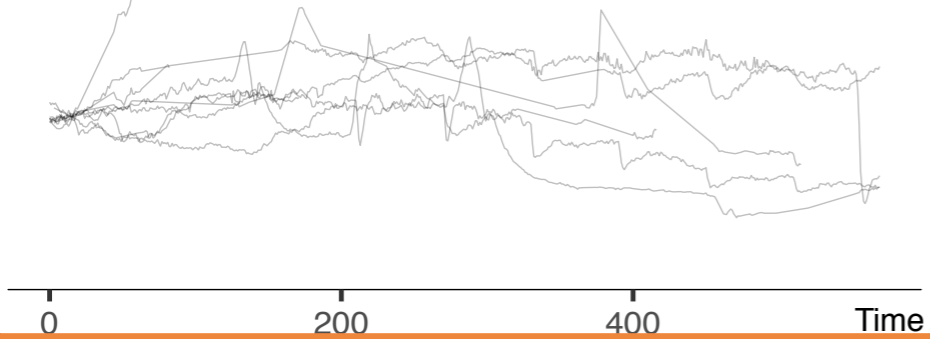
tSNE-2



Challenge 3: data analysis

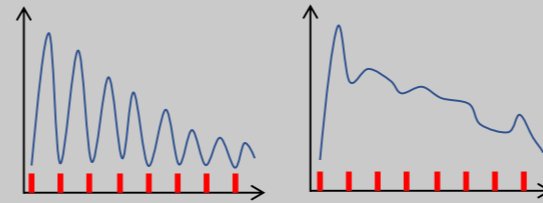
extract features from time series data

Identify "dynamic" outliers

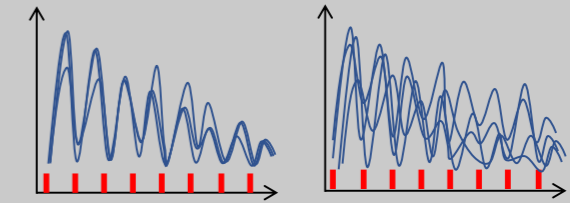


Characterise single-cell dynamics

Causality

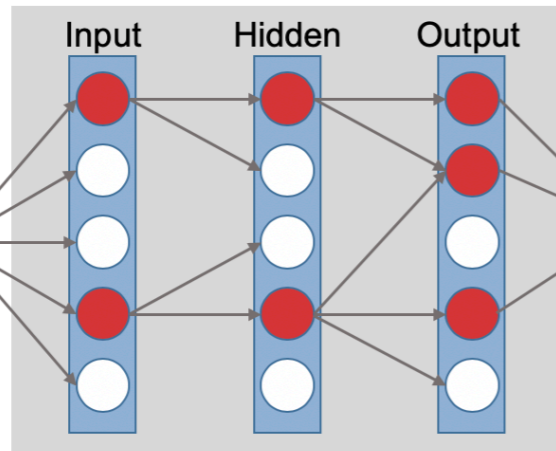
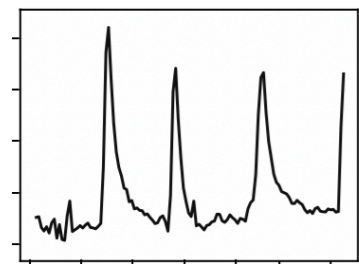


Synchronisation

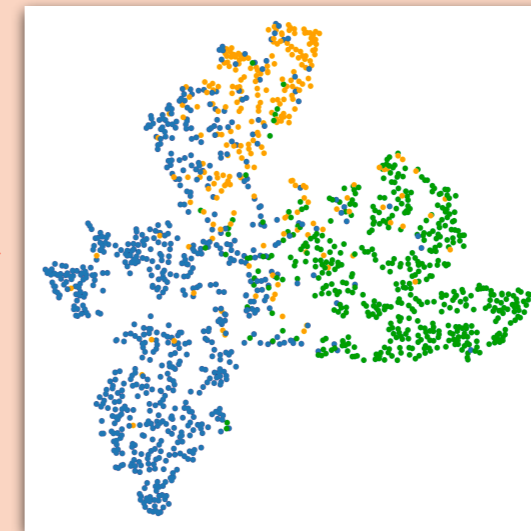
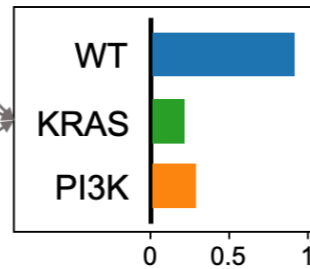


Convolutional Neural Network

Input: ERK time-series



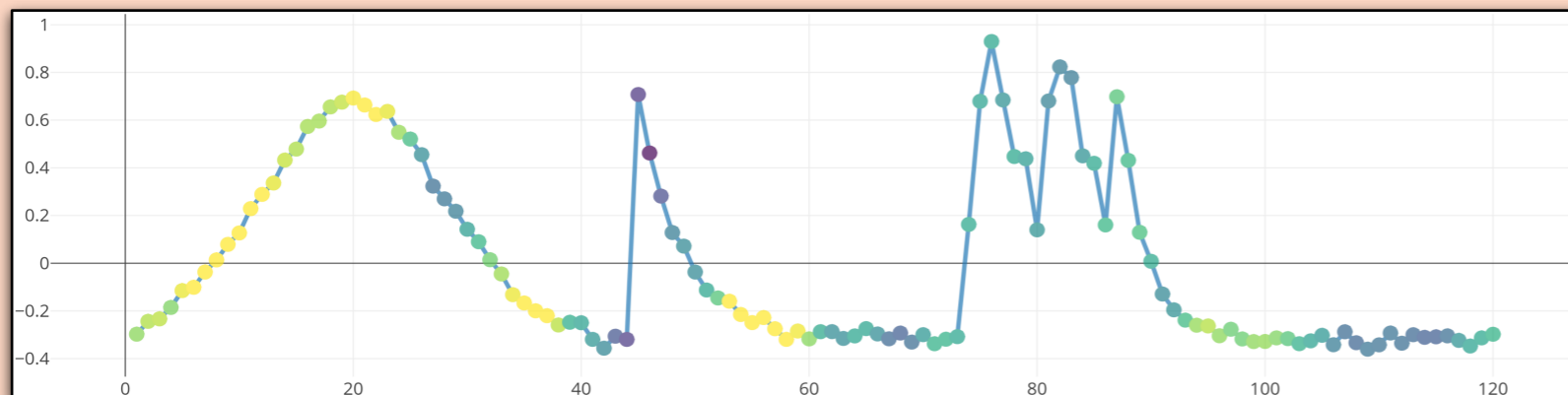
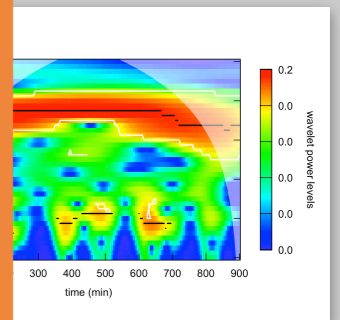
Output: Probability for each class



tSNE-1

tSNE-2

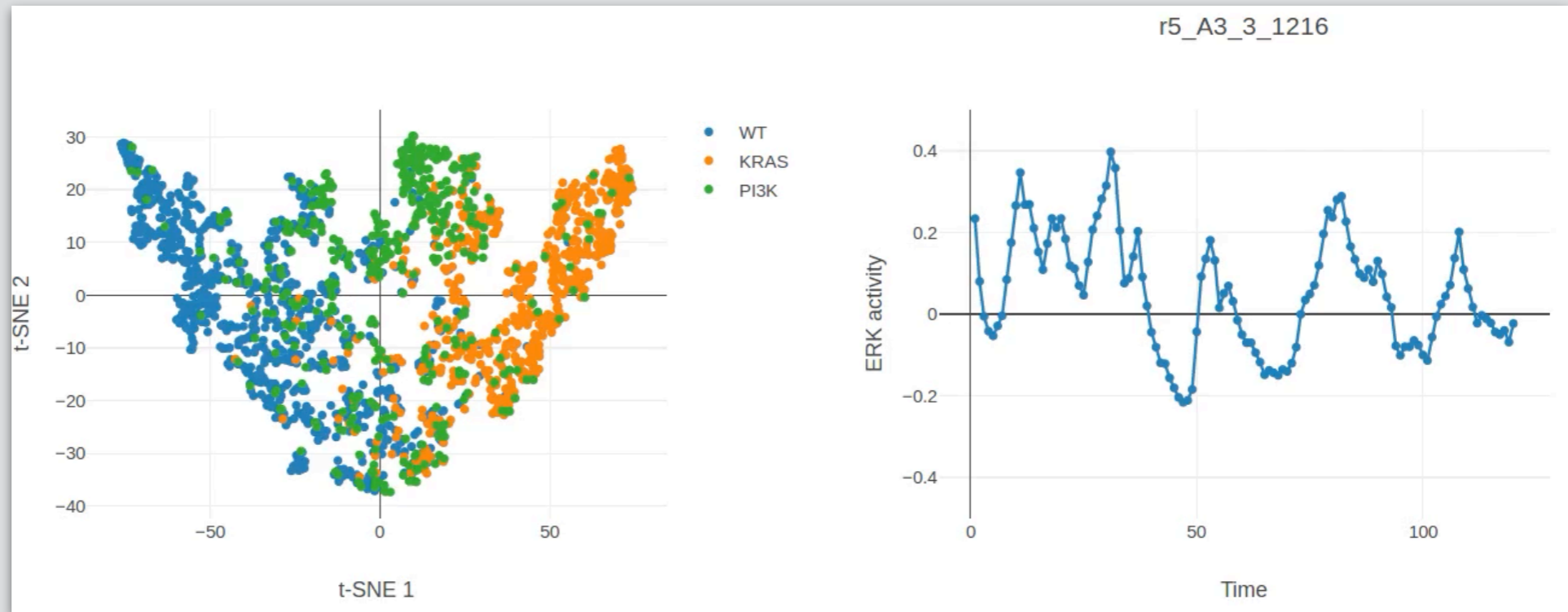
is



Challenge 4: interactive data mining

Marc-Antoine Jacques
Pertz Group

Exploration of features in t-SNE space:



Local patterns in CAMs:



Challenge 4: interactive data mining

Select data file (e.g. tCoursesSelected.csv) and press "Load Data"

Browse... sust_E_F_N.csv
Upload complete

Load Data Reset file input Generate artificial dataset

Track Label unique across entire dataset

Select FOV (e.g. Metadata_Site or Metadata_Series):
Metadata_Series

Select Track Label (e.g. objNuc_Track_ObjectsLabel):
TrackObjects_Label

Select one or more facet groupings (e.g. Site, Well, Channel):
Stim_All_Ch

Select time column (e.g. RealTime):
RealTime

Select 1st measurement:
Intensity_MeanIntensity_Ratio

Math operation 1st and 2nd meas.:
 None
 Divide
 Sum
 Multiply
 Subtract
 1 / X

Trim x-axis

Time range to include
0 200 360

Normalization

Select method
 fold-change
 z-score

Time range norm.
0 36 360

Robust stats

Normalisation grouping
 Entire dataset
 Per facet
 Per trajectory (Korean way)

Time courses Box-plots Scatter Hierarchical Hier. Sparse

Select linkage method:
Ward D2

Select type of dissimilarity measure:
Euclidean

#dendrogram branches to colour
1 5 20

Manually select clusters to display

Download CSV with cell IDs and cluster no.

Heat-map Time-courses Cluster dist.

Plot dendrogram and re-order samples

Select colour palette:
Spectral

Reverse colour palette
 Plot colour key

Margin below x-axis: 5

Margin right of y-axis: 20

Font size row labels: 1

Font size column labels: 1

Shade of grey for NA values (0 - black, 1 - white)
0 0.8 1

Display plot height [px]: 600

Classic hierarchical clustering

Download PDF

Width: 17

Height: 10

Plot!

Color Key and Density Plot

Distance measure: euclidean
Linkage method: ward.D2

CLUSTER TIME SERIES

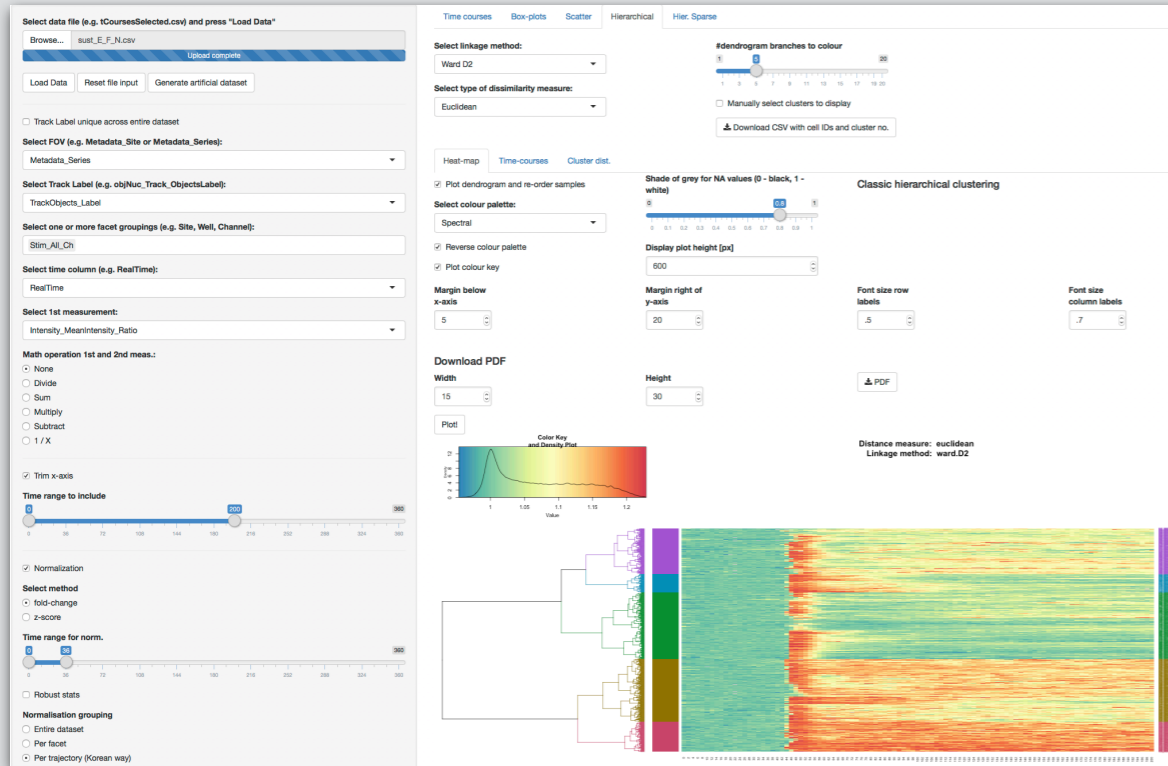
Tools for data browsing & visualisation

<http://pertzlab.unibe.ch:3838>

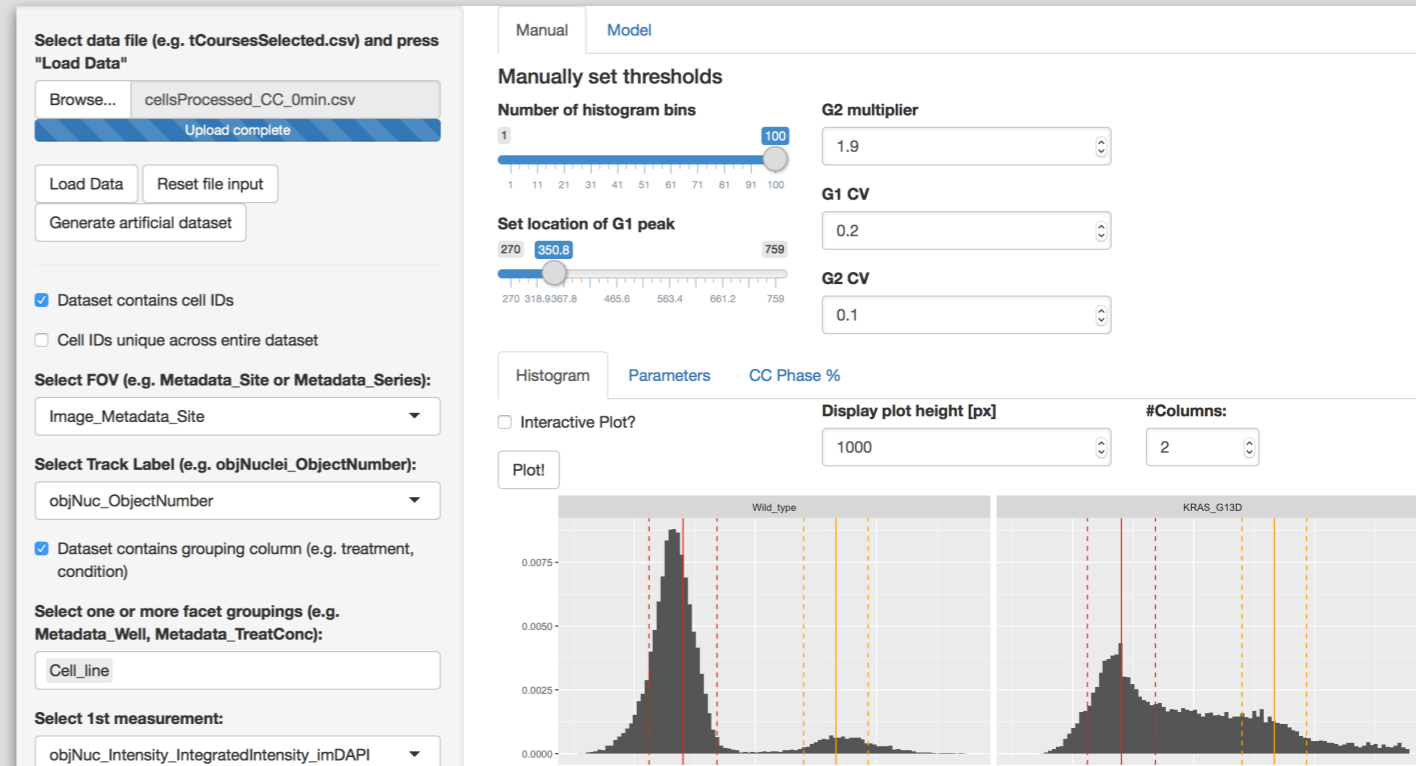
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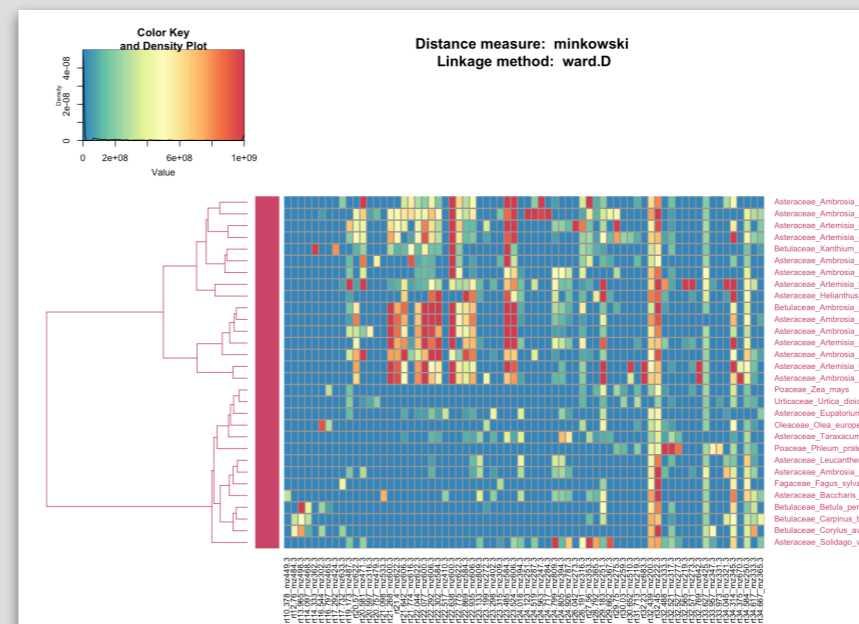
Time series analysis and clustering



1D cell cycle analysis



FreeClust

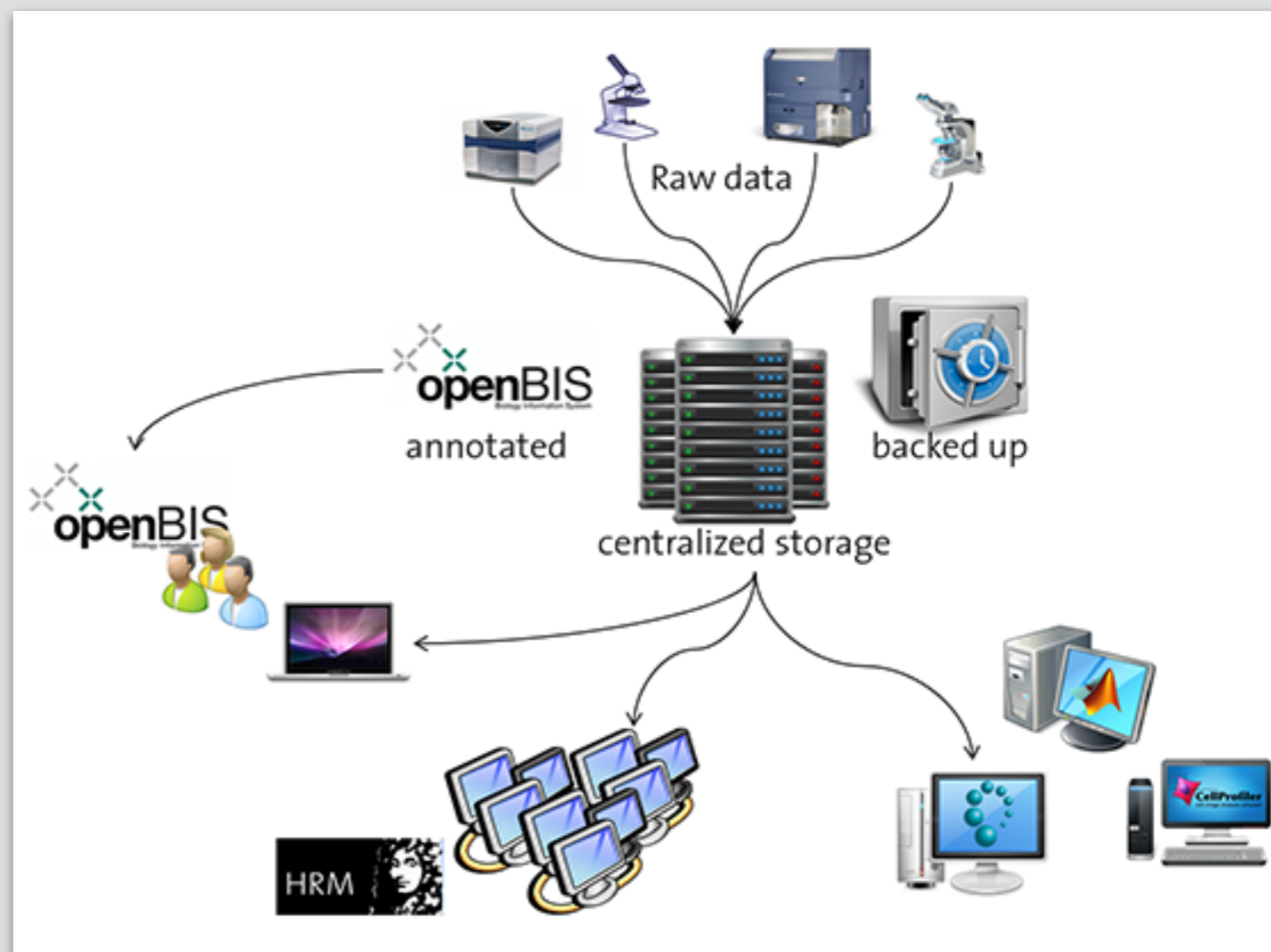
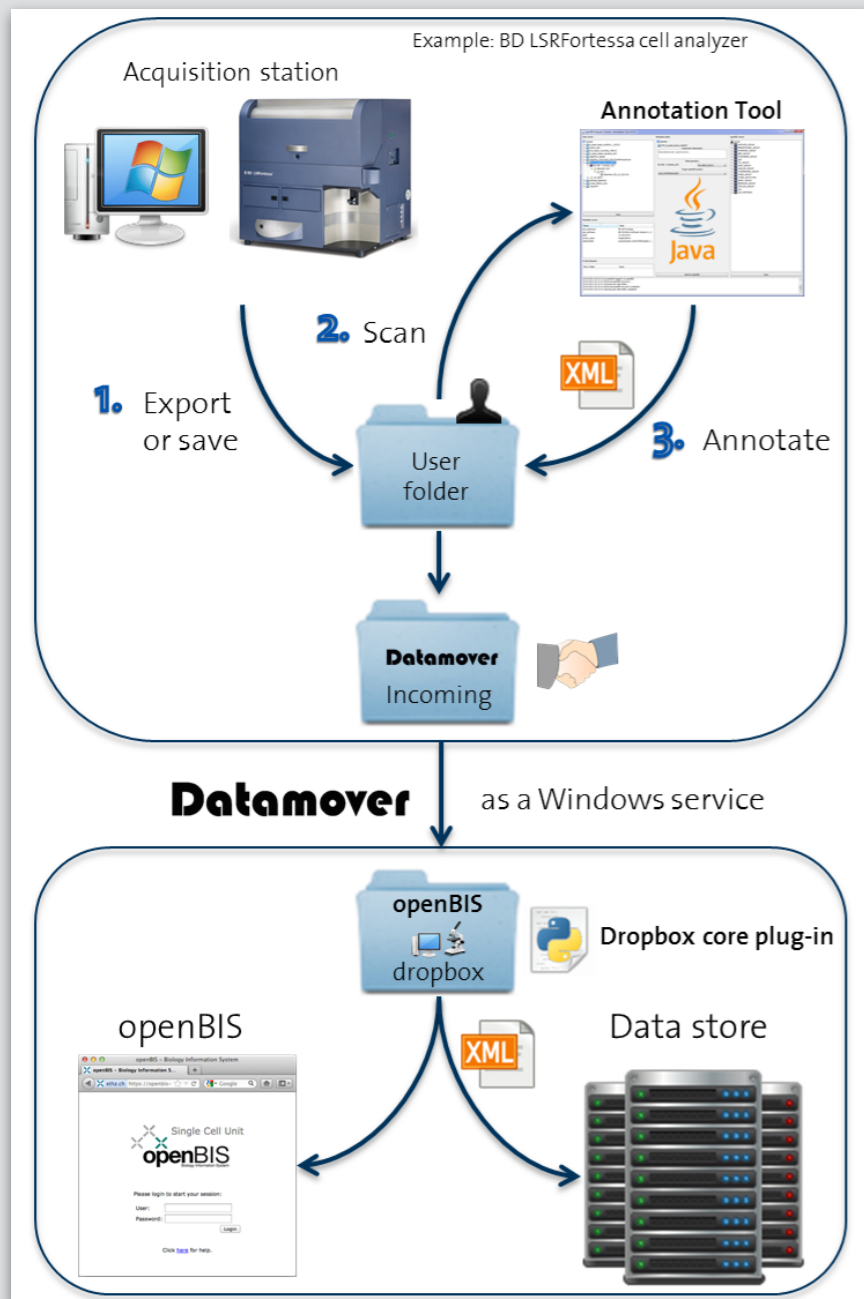




Challenge 5: data storage, annotation, backup

Aron Ponti
BSSE-ETH

OpenBIS = Open Biology Information System + oBIT = OpenBIS Importer Tool





Challenge 5: data storage, annotation, backup

Aron Ponti
BSSE-ETH

OpenBIS = Open Biology Information System + oBIT = OpenBIS Importer Tool



Challenge 6: data reproducibility

All tools on GitHub

The screenshot shows a GitHub profile page for a user named 'yannick-pc12'. At the top, there are navigation tabs: Overview (selected), Repositories (20), Stars (0), Followers (5), and Following (4). Below the navigation is a 'Popular repositories' section with six items, each with a language indicator (R or Shell):

- yannick-pc12 (R)
- zeropad (Shell)
- shiny-plot-two-sources (R)
- shiny-timecourse-inspector (R)
- coralie-nih3t3 (R)
- shiny-timecourse-cleaner (R)

At the bottom, there is a '141 contributions in the last year' section with a heatmap showing activity from September to September. A legend indicates 'Less' (light green) and 'More' (dark green) contributions.

Pipelines & system documentation on internal Wiki

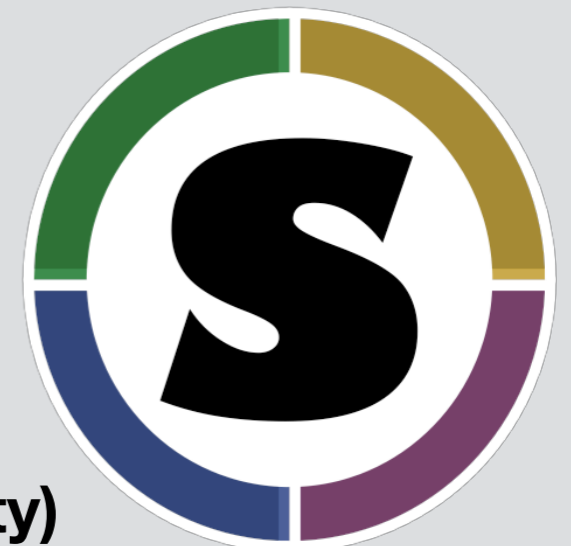
The screenshot shows an internal Wiki page titled 'PertzLab-Image-Data-Analysis'. The page is titled 'Data organisation' and contains a 'Naming convention' section. The text in the 'Naming convention' section reads: 'As a general rule, when naming folders or files avoid spaces, commas, brackets, diacritics, special characters (~, !, @, #, \$, %, ^, &, *, =, +, ?). Even though modern operating systems let users to include such characters, they may cause trouble in batch processing, or when extracting metadata from file names. The following naming convention is **strongly** advised: separate metadata with underscore, separate fields *within* metadata with a hyphen. For example, 2018-01-14_MCF10Amutants_H2B-miRFP_ERKKTR-mTurquoise_40xAir_T5min_Stim50min-IngmLEGF_30h-starving. The underscore separates the date 2018-01-01 from the cell line MCF10Amutants. This convention makes it easy to extract metadata in CellProfiler.' Below this is an 'Image format' section with the text: 'Avoid storing your images in a single nd2 file. This is a proprietary NIKON format that sometimes causes trouble when reading it with Bio-formats.'



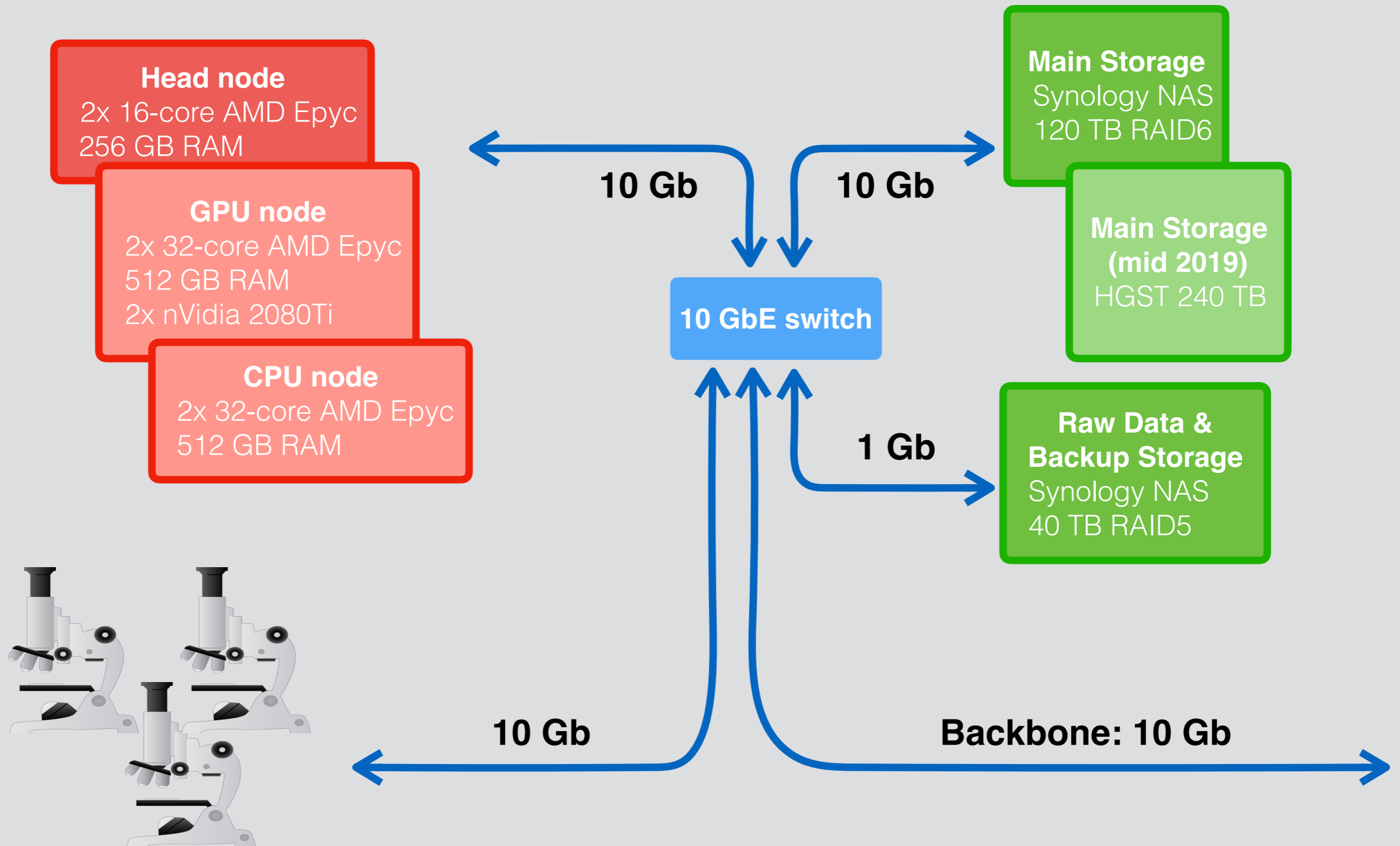
GitLab

<https://gitlab.switch.ch/pertz-lab>

Application and pipeline containerisation (**Singularity**)



Challenge 7: hardware choice cloud / local?





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