universität freiburg

Cell-TADA 🎉

Cell Tracking and Analysis with Domain Adaptation

Presented by:

Florian Vogt
Sejal Jadhav

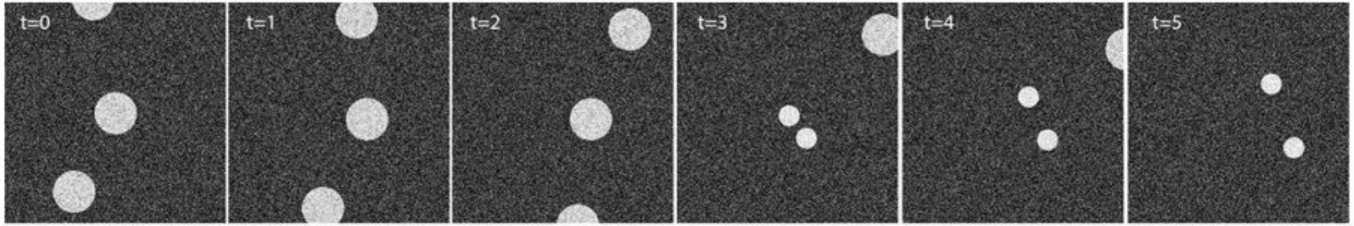
Shi Bin Hoo (Liam)
Yumna Ali

ellis | UNIT FREIBURG

Introduction to Cell Tracking

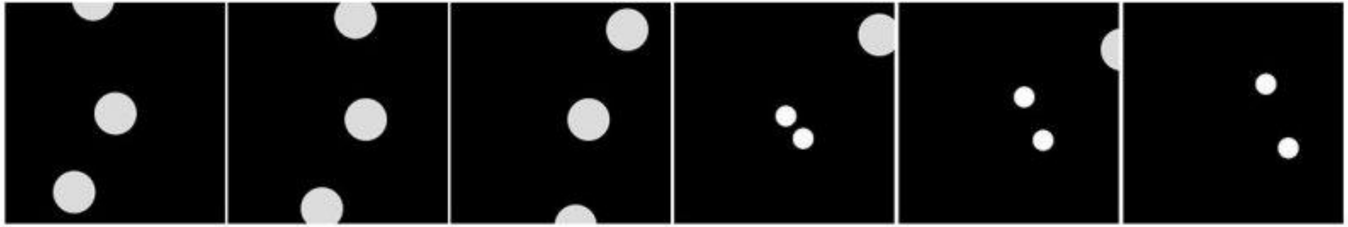
What is Cell-Tracking?

- **Monitoring the Localization, Survival, Migration, Invasion and Growth** of cells



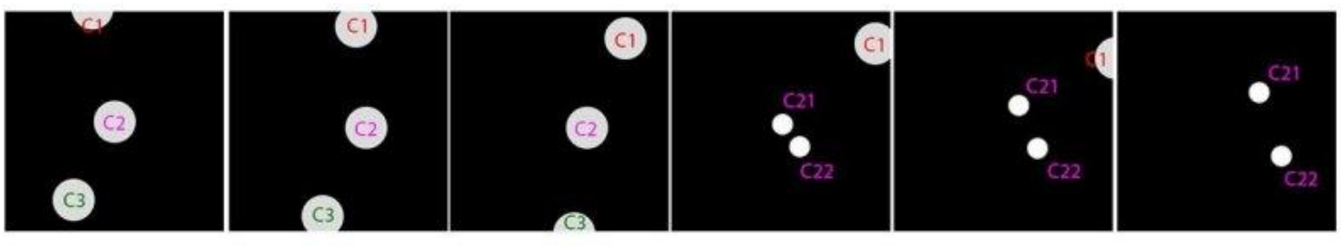
What is Cell-Tracking?

- **Monitoring the Localization, Survival, Migration, Invasion and Growth** of cells
  - **Identify Cells**



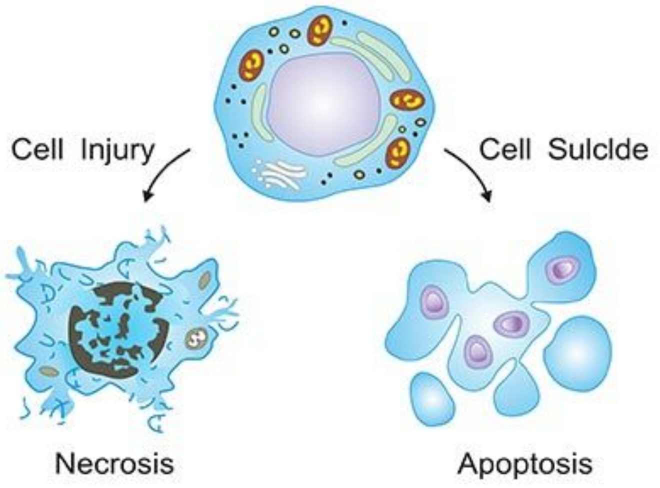
What is Cell-Tracking?

- Monitoring the **Localization, Survival, Migration, Invasion and Growth** of cells
  - Identify Cells
  - **Track Cells**



Why do we perform Cell-Tracking?

- **Introduction to Apoptosis**
  - Programmed death of a cell

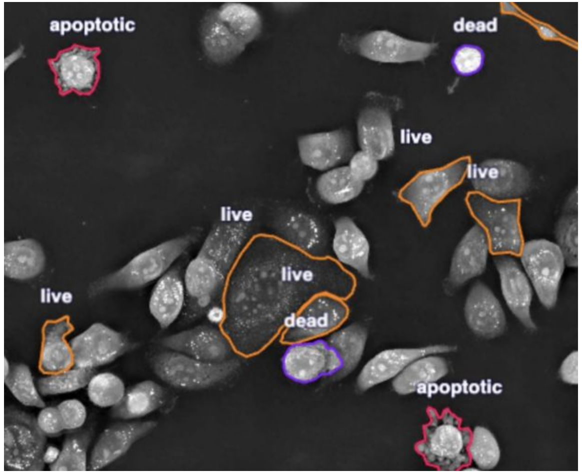


Why do we perform Cell-Tracking?

- **Introduction to Apoptosis**
  - Programmed death of a cell
  - Increased Apoptosis may be an indicator for diseases

Why do we perform Cell-Tracking?

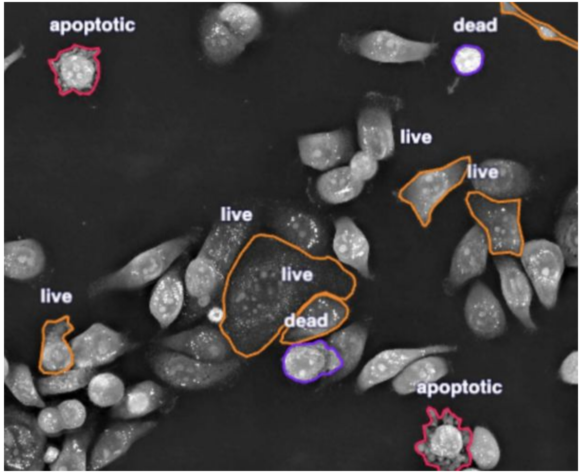
- **Introduction to Apoptosis**
  - Programmed death of a cell
  - Increased Apoptosis may be an indicator for diseases
  - Morphological assessment to identify Apoptosis



Why do we perform Cell-Tracking?

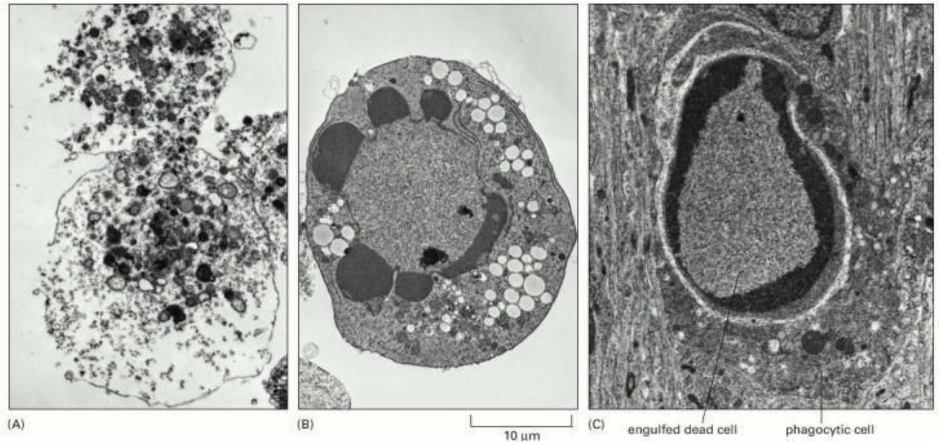
- **Introduction to Apoptosis**
  - Programmed death of a cell
  - Increased Apoptosis may be an indicator for diseases
  - Morphological assessment to identify Apoptosis

➡ **No Insights about cell survival**



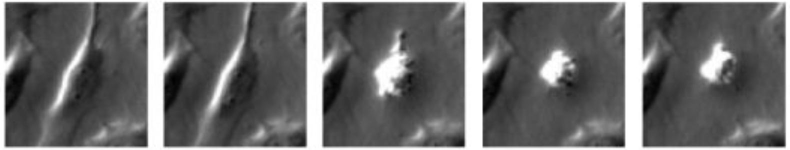
Why do we perform Cell-Tracking?

- **Apoptosis and Cell Tracking**
  - Single frames provide some information about the cell state

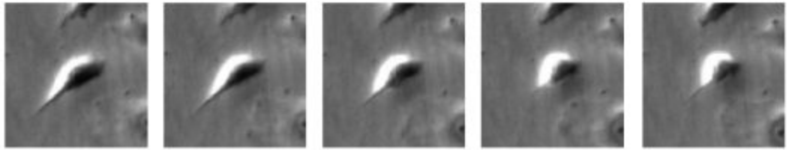


Why do we perform Cell-Tracking?

- **Apoptosis and Cell Tracking**
  - Single frames provide some information about the cell state
  - Consecutive frames allow to gain insights about cell survival



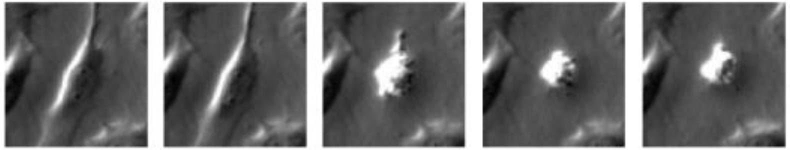
An apoptotic cell observed over a **short** time period **(less than 5 minutes)**



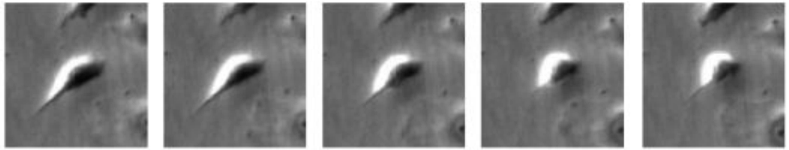
An apoptotic cell observed over a **long** time period **(up to a few hours)**

Why do we perform Cell-Tracking?

- **Apoptosis and Cell Tracking**
  - Single frames provide some information about the cell state
  - Consecutive frames allow to gain insights about cell survival



An apoptotic cell observed over a **short** time period **(less than 5 minutes)**

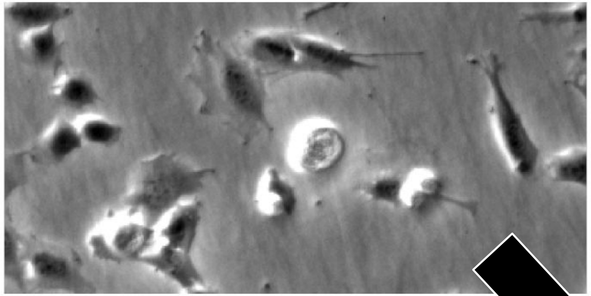


An apoptotic cell observed over a **long** time period **(up to a few hours)**

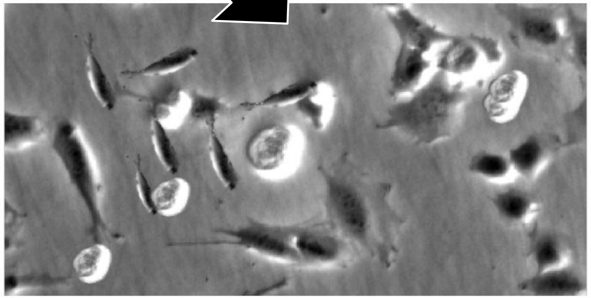
→ **Insights about cell survival**

Why do we perform Cell-Tracking?

- **Apoptosis and Cell Tracking**
  - Cells move unpredictable
  - Cells change their appearance
  - Cells can divide
  - Cells can move out of the image / appear in the image



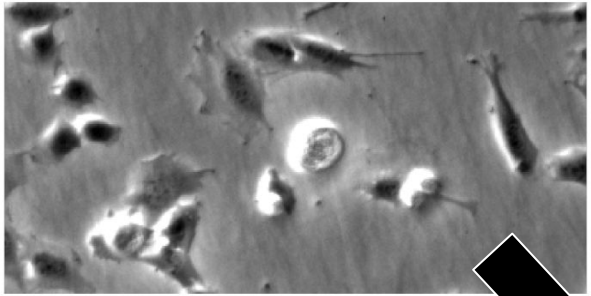
10 frames apart



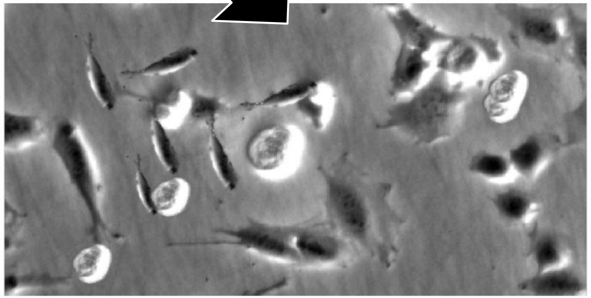
Why do we perform Cell-Tracking?

- **Apoptosis and Cell Tracking**
  - Cells move unpredictable
  - Cells change their appearance
  - Cells can divide
  - Cells can move out of the image / appear in the image

➡ **Tracking is required to predict cell survival**



10 frames apart



Prior Work

An Overview

Conventional Method

- Leverage ***classical Computer Vision (CV)*** and ***Optimization*** *technique* to compute segmentation and tracking.
- *For instance:*
  - ***Optimization*** *– Energy Functional Minimization*
  - ***Classical CV*** *– Hand-crafted features, Contour Optimization*

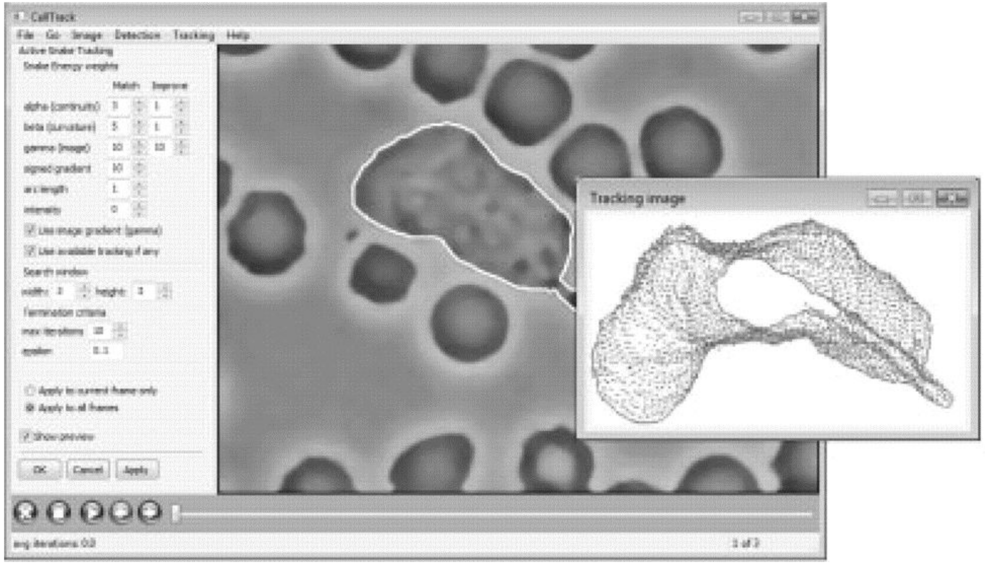
ML-based methods

- Leverage ***deep-learning*** to directly learn the task (segmentation and tracking) from the **available data**

Prior Work

Conventional Method Example – CellTrack

- Uses active contour model for tracking
- Implements an energy functional to match cell configuration across frames
- Both automated and manual editing capabilities



Snapshot of CellTrack GUI

ML-based Methods

Tracking-by-detection

1. Segment the cells in **all** frames
2. Establish temporal associations between the segmented cells.

Top-3 state-of-the-arts methods.

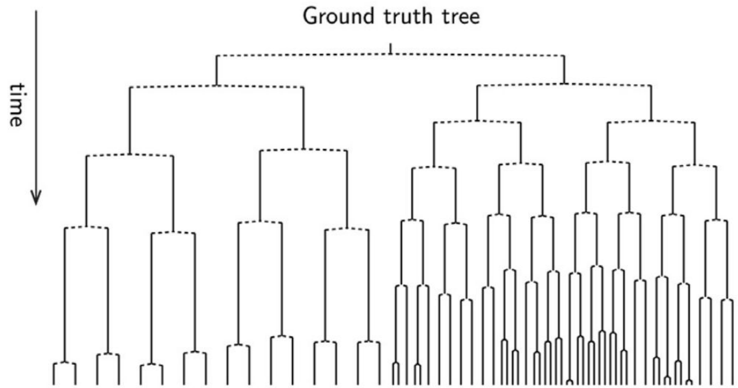
Tracking-by-contour-evolution

1. Segment the cells in the **first** frame
2. Evolve their contours in consecutive frames (solving segmentation and tracking simultaneously)

Rely on **substantial cell-to-cell overlaps** between successive frames.

The Limitations

- Tracking (multi-generational lineage)
- Doesn't adapt well to unseen cell type
- Domain-shift in test data
  - Spatial resolution
  - Temporal resolution

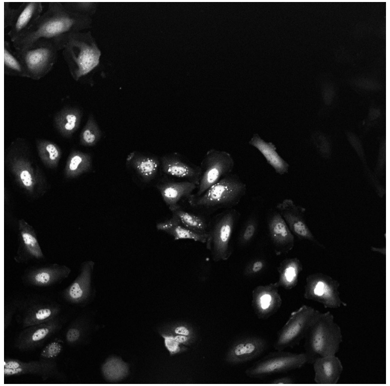


Data Exploration

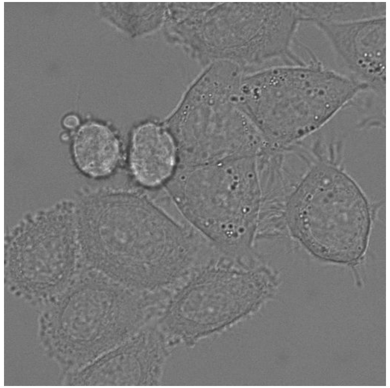
volume, variety, and veracity

Cell Tracking Challenge (CTC)

- **Size**: 20 datasets (2D & 3D videos)
- **Cell Types:** Diverse, including human liver cancer cells, mouse blood stem cells.
- **Annotations:** Segmentation and tracking included
- **Purpose:** Improve cell tracking and segmentation algorithms.

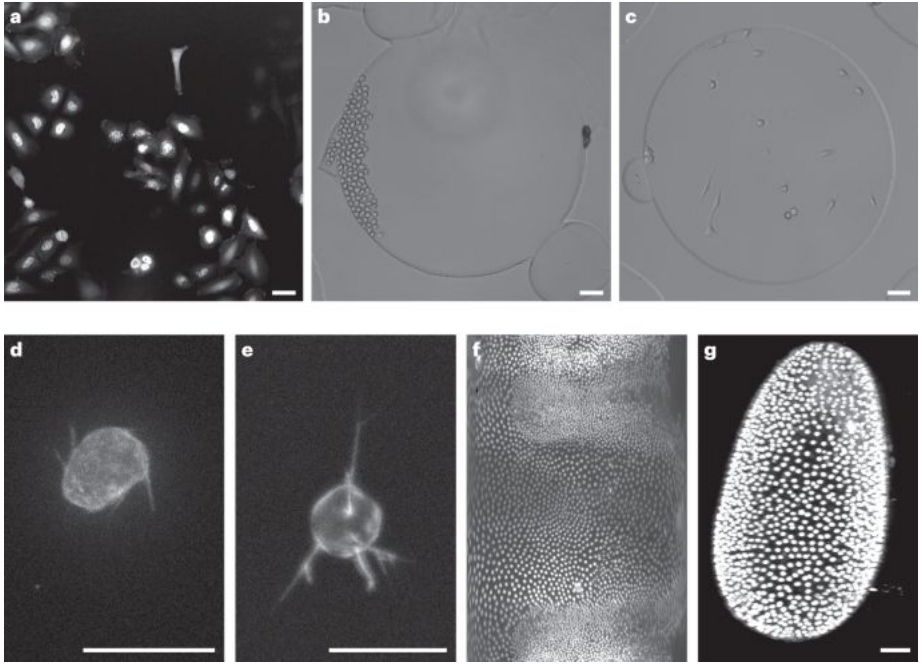


Human hepatocarcinoma-derived cells



HeLa cells on a flat glass

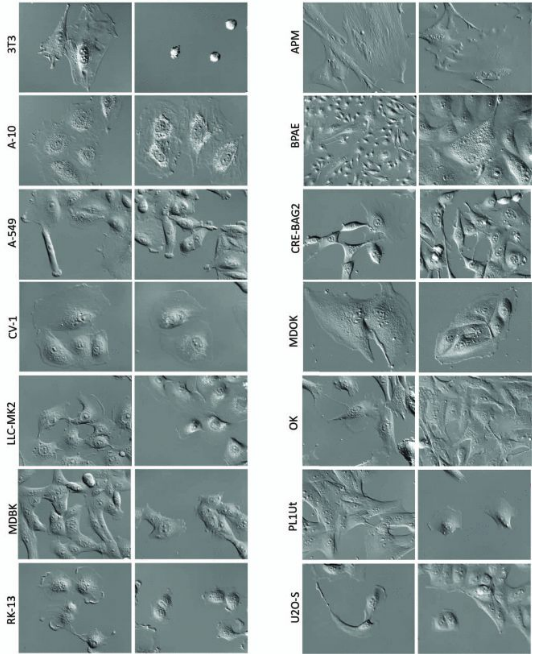
Cell Tracking Challenge (CTC)



a, human hepatocarcinoma-derived cells b, mouse hematopoietic stem cells. c, mouse muscle stem cells d, human lung adenocarcinoma cell. e, simulated cells of d. f, g 3D cells

Cell Tracking with Mitosis Detection Dataset Challenge (CTMC)

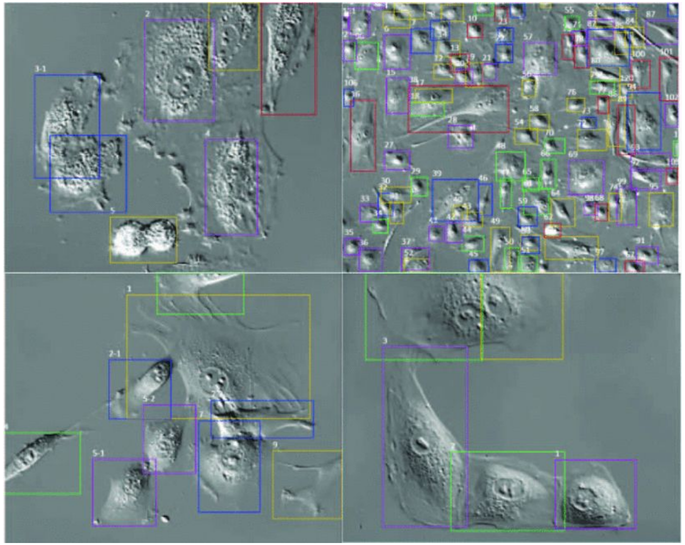
- **Size**: 86 videos of live cells
- **Cell Types:**14 different cell lines
- **Annotations**: Manual detection and tracking of cells and mitosis events.
- **Purpose:** Improve cell tracking algorithms, especially for deep learning models



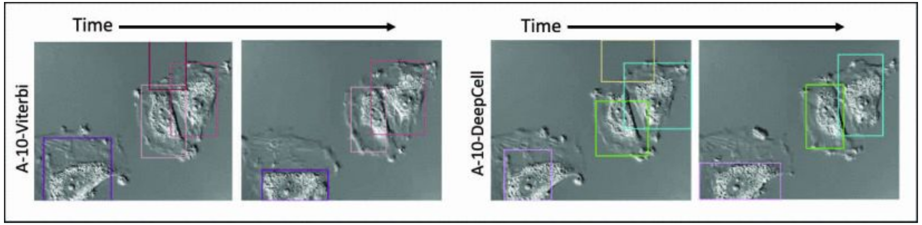
Examples of frames for each of the 14 cell lines that show that depicts the diversity in cell morphology and frame density.

Dataset Exploration

Cell Tracking with Mitosis Detection Dataset Challenge (CTMC)



Examples of the human annotations for video frames in the CTMC dataset.

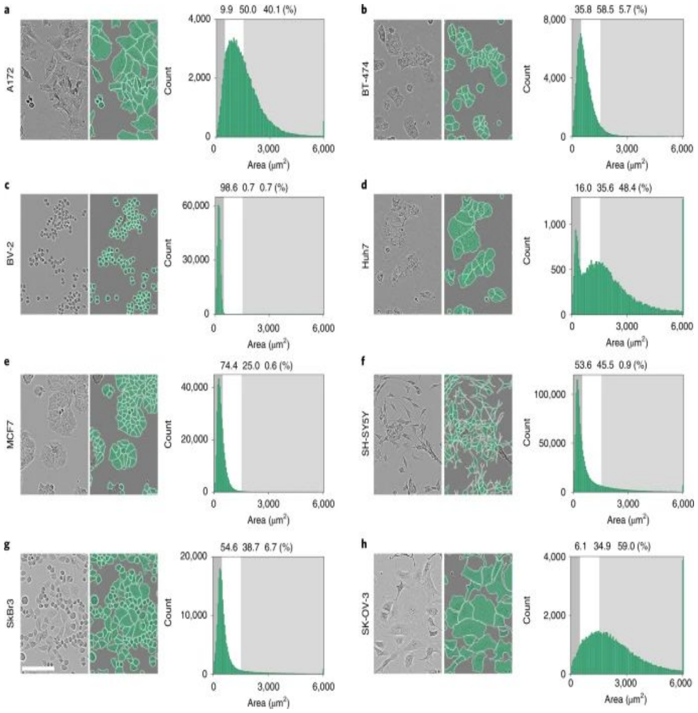


Example showing two frames of a video (A-10) where both Viterbi (left) and DeepCell (right) perform well (TRA score > 0.80).

Dataset Exploration

LIVECell

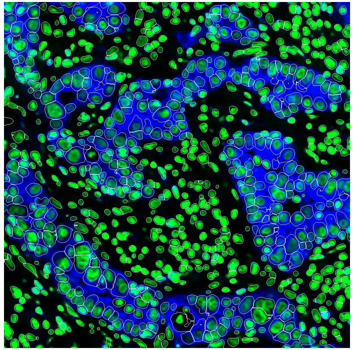
- **Size**: 5,239 annotated Incucyte HD phase-contrast microscopy images
- **Cell Types:**8 different cell types
- **Annotations**: Over 1.6 million individual cells manually annotated
- **Purpose**: For training segmentation models



Examples of annotated phase-contrast microscopy images and histograms showing cell size distributions of all cell types in LIVECell

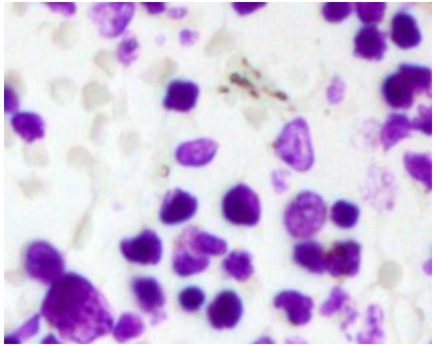
More Datasets for Cell Segmentation

TissueNet



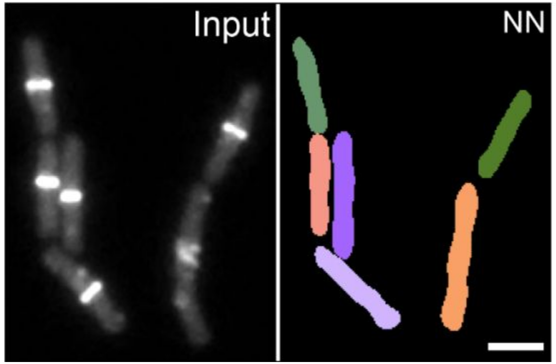
Focuses on
mammalian cells in tissues

2018 Kaggle Data Science Bowl



Focuses on nucleus
segmentation

DeepBacs



Focuses on
bacterial cell images

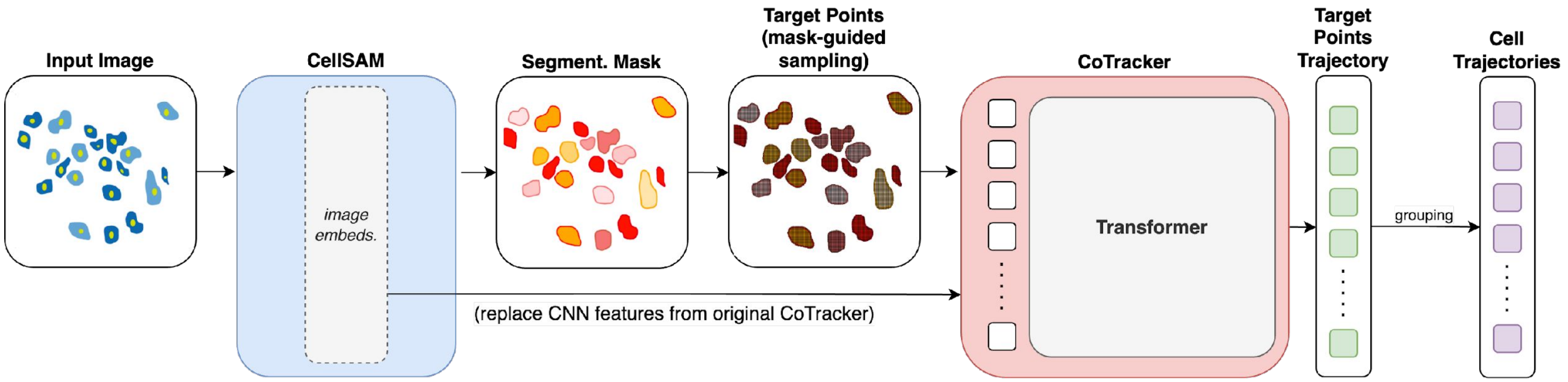
Innovative Solution

Cell-TADA 🎉

Cell Tracking and Analysis with Domain Adaptation

Innovative Solution - Cell TADA 🎉

An Overview



From the ground up

Segment Anything

CoTracker

It is Better to Track Together

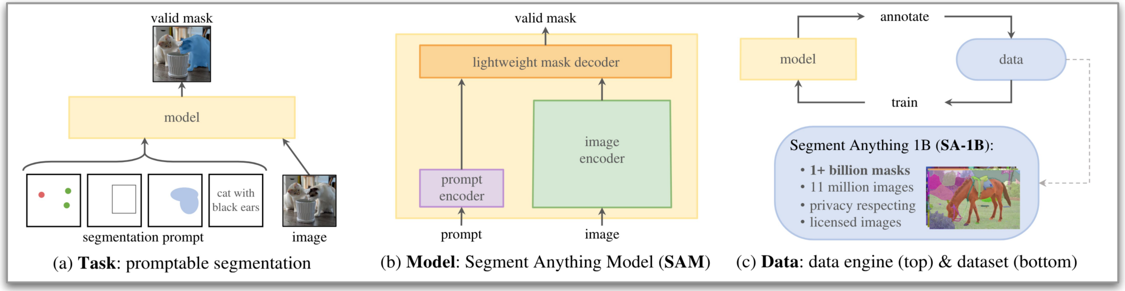
Learning to Estimate Shapley Values with Vision Transformers

Deployment of Image Analysis Algorithms under Prevalence Shifts

From the ground up

Segment Anything

Output (segmentation mask) of Segment Anything Model (SAM)



Overview of Segment Anything

Kirillov, A., et al. (2023). *Segment Anything* (arXiv:2304.02643). arXiv. https://doi.org/10.48550/arXiv.2304.02643

From the ground up

Segment Anything

Bottleneck:

- Domain Gap (natural vs medical)
- Prompting

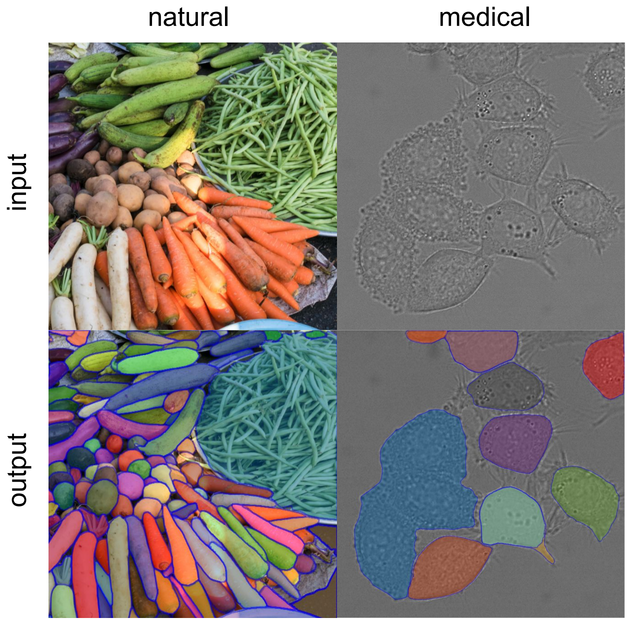


Illustration of Domain Gap

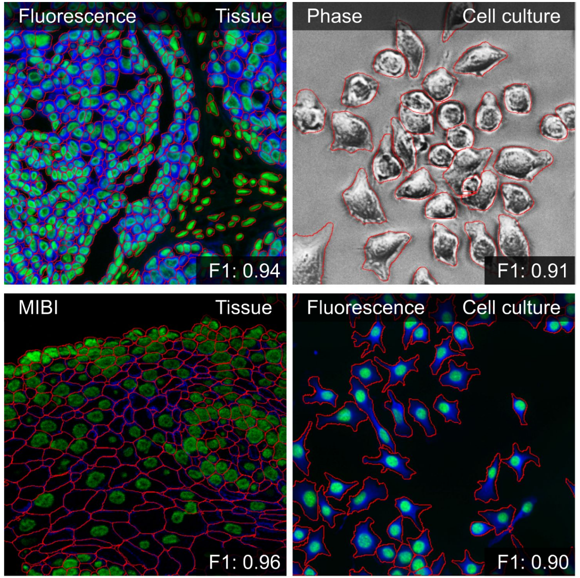
Innovative Solution - Cell TADA 🎉

From the ground up

Segment Anything

Bottleneck:

- Domain Gap (natural vs medical)
- Prompting



Images of various cell types obtained through different imaging methods.

From the ground up

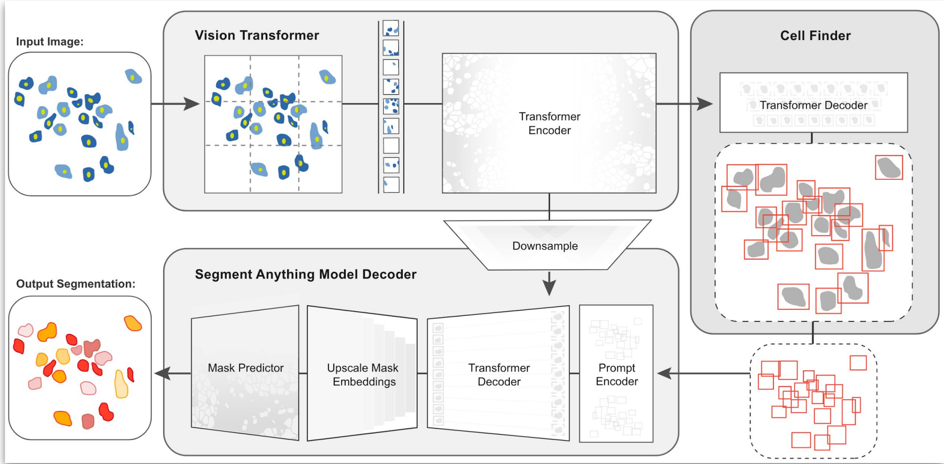
Segment Anything

Bottleneck:

- Domain Gap (natural vs medical)
- Prompting

SAM to CellSAM[5]

- Domain Adaptation
- Detection Boxes as prompt



Overview of CellSAM

Israel, U., et al. (2023). *A Foundation Model for Cell Segmentation* (arXiv:2311.11004). arXiv. https://doi.org/10.48550/arXiv.2311.11004

From the ground up

Segment Anything

CoTracker

It is Better to Track Together

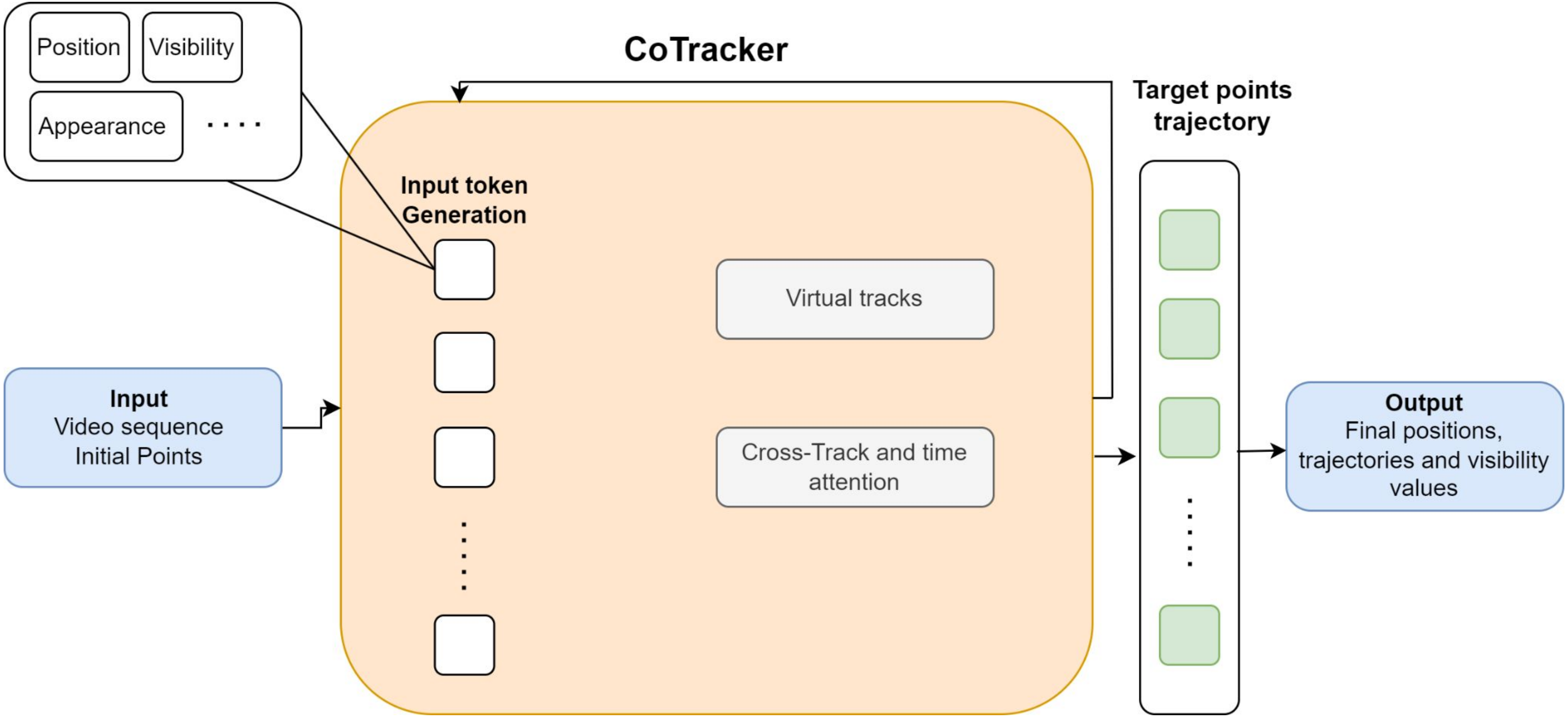
Learning to Estimate Shapley Values with Vision Transformers

Deployment of Image Analysis Algorithms under Prevalence Shifts

Innovative Solution - Cell TADA 🎉

From the ground up

CoTracker



Innovative Solution - Cell TADA 🎉

From the ground up

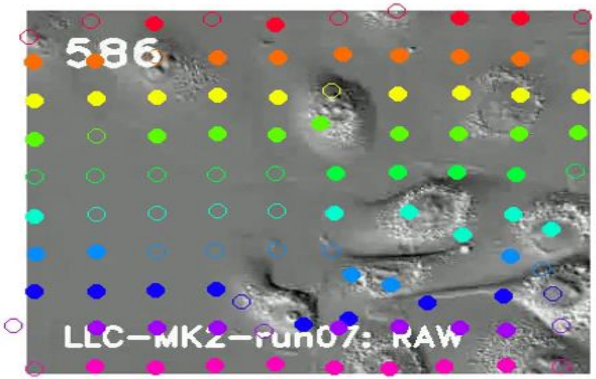
CoTracker

Innovative Solution - Cell TADA 🎉

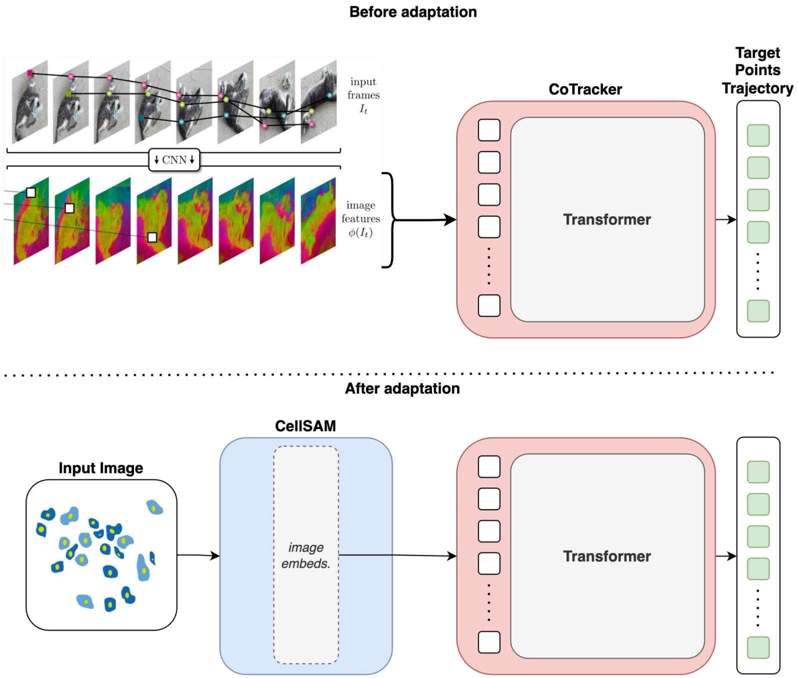
From the ground up

Bottleneck:

- Domain Gap (natural vs medical)



CoTracker



From the ground up

Segment Anything

CoTracker

It is Better to Track Together

Learning to Estimate Shapley Values with Vision Transformers

Deployment of Image Analysis Algorithms under Prevalence Shifts

From the ground up

Estimate Shapley Values

What image features were most important for the *(correct)* prediction?

Class Label: Abnormal

ML Model

Class Prediction

Abnormal

(a) Solving a classification problem

Explainer Model

Why Abnormal?

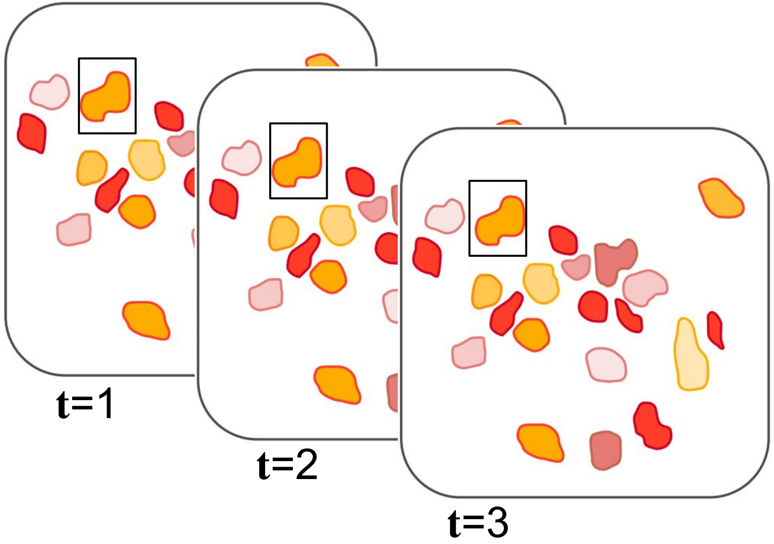
(b) Understanding the solution of the classification problem

Innovative Solution - Cell TADA 🎉

From the ground up

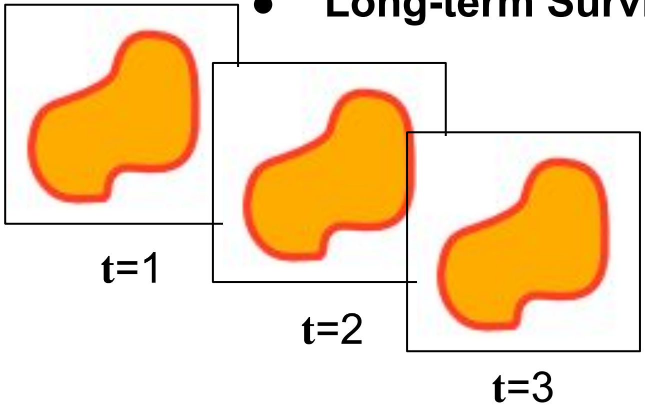
Estimate Shapley Values

Cell Tracking



Classification

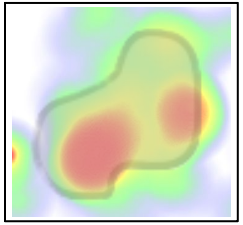
- Short-term Survival
- Long-term Survival

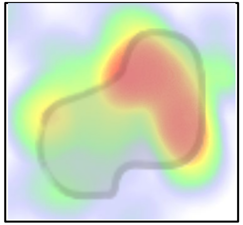


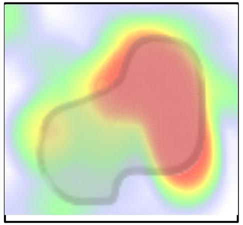
From the ground up

Estimate Shapley Values

Shapley Values to detect features responsible for the prediction *(here: Short-term Survival)*


t=1


t=2


t=3

→ **Early changes at the cell membrane seem to be an indicator for short cell survival**

From the ground up

Segment Anything

CoTracker

It is Better to Track Together

Learning to Estimate Shapley Values with Vision Transformers

Deployment of Image Analysis Algorithms under Prevalence Shifts

Innovative Solution - Cell TADA 🎉

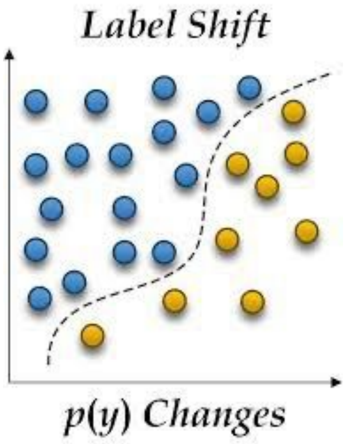
From the ground up

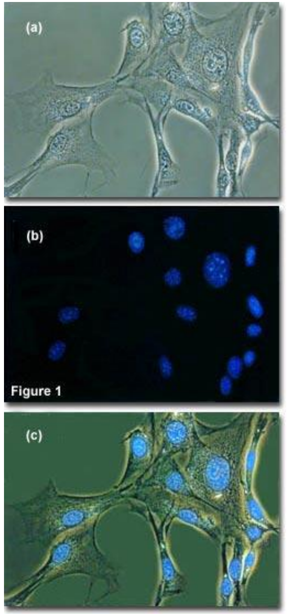
Deployment under Prevalence Shifts

Cell Types

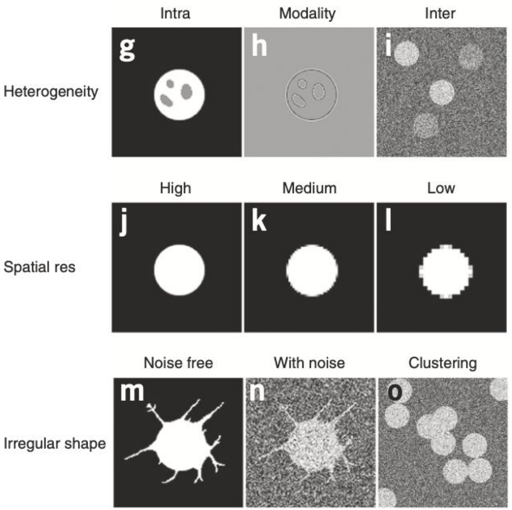
Imaging Techniques

Experimental Conditions





Different imaging techniques



Main factors that determine the quality of cell images and videos.

From the ground up

Deployment under Prevalence Shifts

- All these variations lead to prevalence shifts between development and deployment datasets
- **How could we address the prevalences shifts without retraining our model? 💸⏳**

Prevalence-aware for Cell tracking

Godau, Patrick, et al. "Deployment of image analysis algorithms under prevalence shifts." *International Conference on Medical Image Computing and Computer-Assisted Intervention.*

Innovative Solution - Cell TADA 🎉

From the ground up

Deployment under Prevalence Shifts

Black Box Shift Estimation
(for test distribution estimation)

Affine transformation with a prevalence-driven weight adjustment

$$f_{\text{aff}}(\phi(x)) = \frac{\phi(x)}{t} + b$$

Affine scaling re-calibration approach

Configure **validation metric** with deployment prevalences

Set **prevalence-aware decision rule**

External Validation

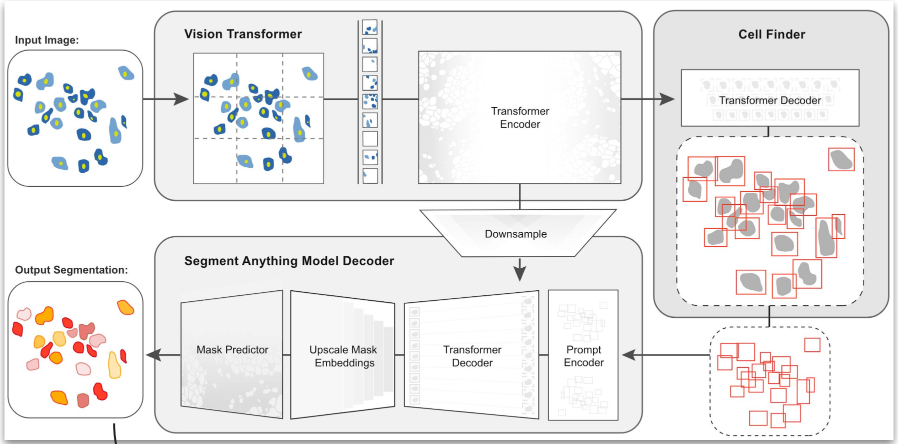
Godau, Patrick, et al. "Deployment of image analysis algorithms under prevalence shifts." International Conference on Medical Image Computing and Computer-Assisted Intervention.

Innovative Solution - Cell TADA 🎉

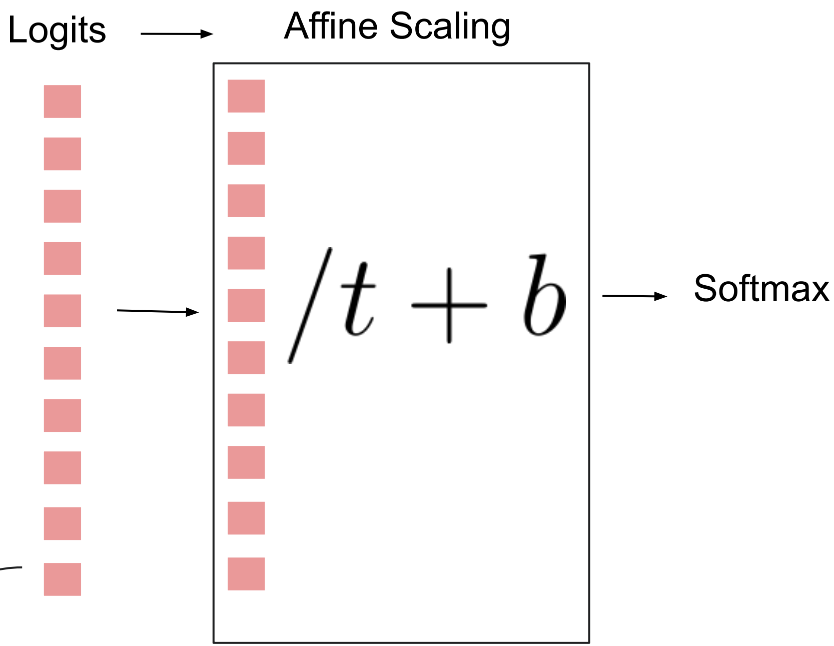
From the ground up

Deployment under Prevalence Shifts

Prevalence aware recalibration for cell Types



Overview of CellSAM



Godau, Patrick, et al. "Deployment of image analysis algorithms under prevalence shifts." International Conference on Medical Image Computing and Computer-Assisted Intervention.

Further Analysis and Evaluation

The Four Pillars

Efficiency	***Interpretability***	***Robustness***	***Accessibility***

The Four Pillars

Efficiency | *Interpretability* | *Robustness* | *Accessibility*

Foundation model **for Cell Tracking**

Strong ***zero-shot*** **segmentation performance**

tracking performance

The Four Pillars

Efficiency | **Interpretability** | Robustness | Accessibility

Cell-TADA 🎉 as a part of cell state classification pipeline

Estimated Shapley Values detect important features.

The Four Pillars

Efficiency | Interpretability | **Robustness** | Accessibility

Perform minor weight adjustment to adapt prevalence shift

Robust segmentation perf. → Robust Cell-TADA 🎉 perf.

The Four Pillars

Efficiency | *Interpretability* | *Robustness* | ***Accessibility***

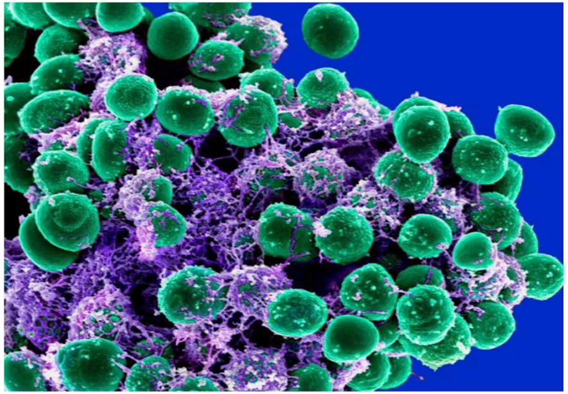
Central hosting of Cell-TADA 🎉 (on-site / remotely)

Deploy user interface as Web Application

Segment Anything
Research by Meta AI

Home Demo Dataset Blog Paper

↓ Find a photo in the gallery, or Upload an image






The Four Pillars

Efficiency | *Interpretability* | *Robustness* | ***Accessibility***

Central hosting of Cell-TADA 🎉 (on-site / remotely)

Deploy user interface as Web Application

Conclusion

Conclusion

Our Main Contribution