Machine learning-based image detection for lensless microscopy in life science

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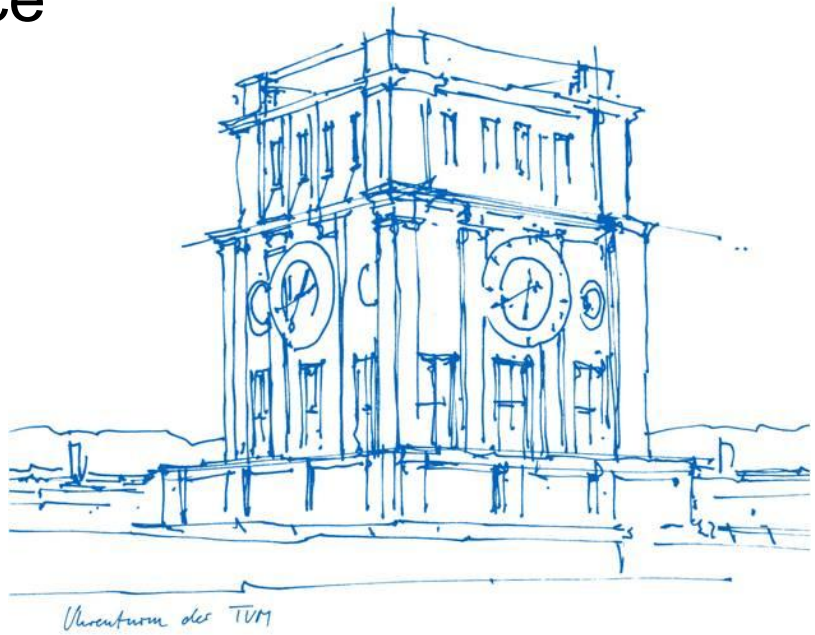
Munich, 6th August 2019



Overview

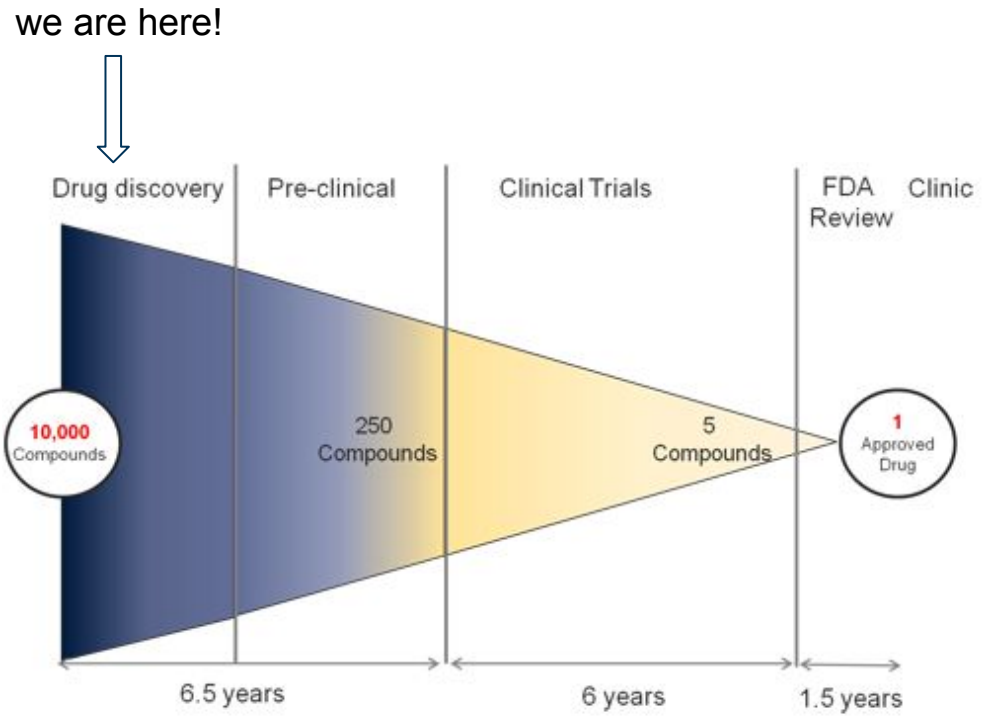
1. Introduction
2. Neural Network Architectures
3. Cell Counting
4. Cell Covered Area Detection
5. Conclusion

Introduction

Motivation

Cultivating cells is an essential task in life science:

- Drug development
- Cancer research
- Medical diagnosis
- etc.

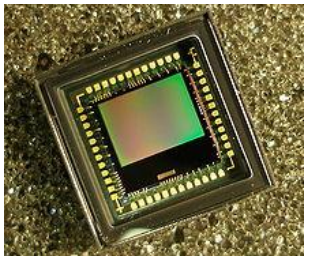


https://www.nimh.nih.gov/about/directors/thomas-insel/blog/2012/experimental-medicine.shtml

Motivation

Lensfree microscopy (LFM) is an alternative to more common microscopes:

- Less bulky
- Easier deployment in larger numbers
- Cells can stay in their preferred environment



https://commons.wikimedia.org/wiki/File:Olympus-BX61-fluorescence_microscope.jpg
https://commons.wikimedia.org/wiki/File:Matrixw.jpg

Motivation

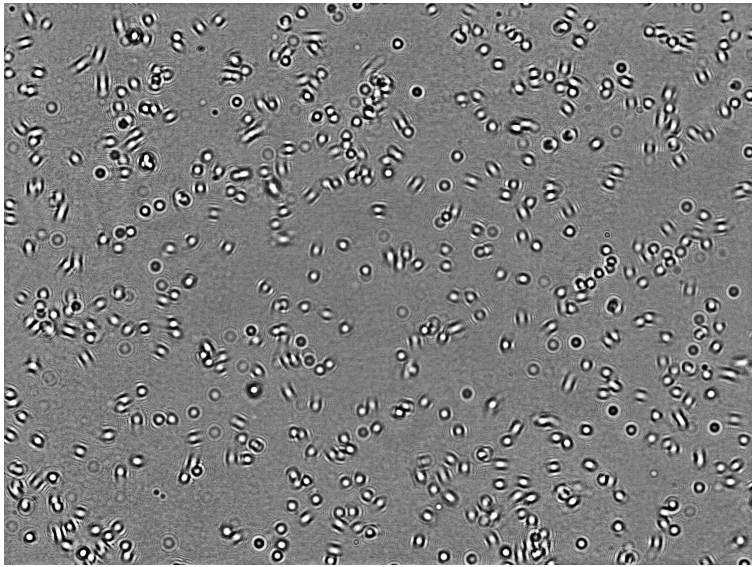
Monitoring cell behavior is part of many experiments:

- **Count** - how concentrated are cells in a unit of medium?
- **Growth** - how do cells grow over time?
- **Motility** - how do cells move?
- **Morphology** - what is the shape of cells?
- etc.

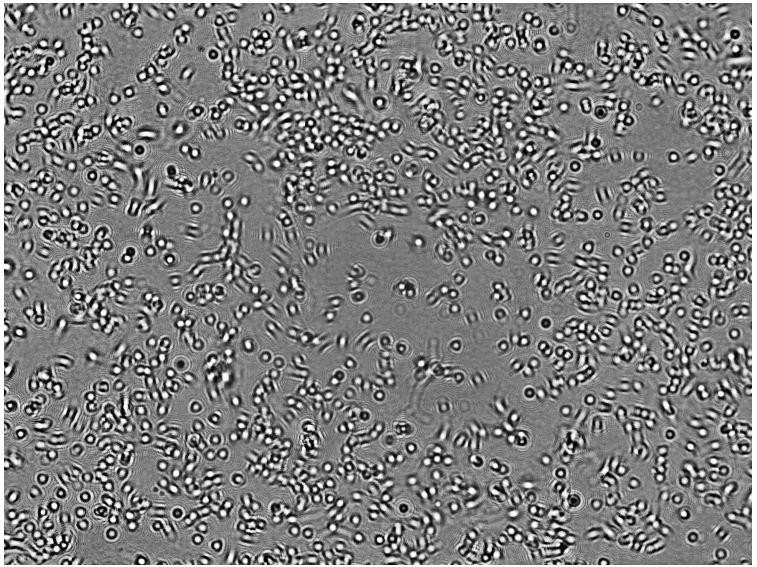
⟹ focus of this project

From Cell Counting to Cell-Covered Area

Cells are **sparse** -> counting is feasible!



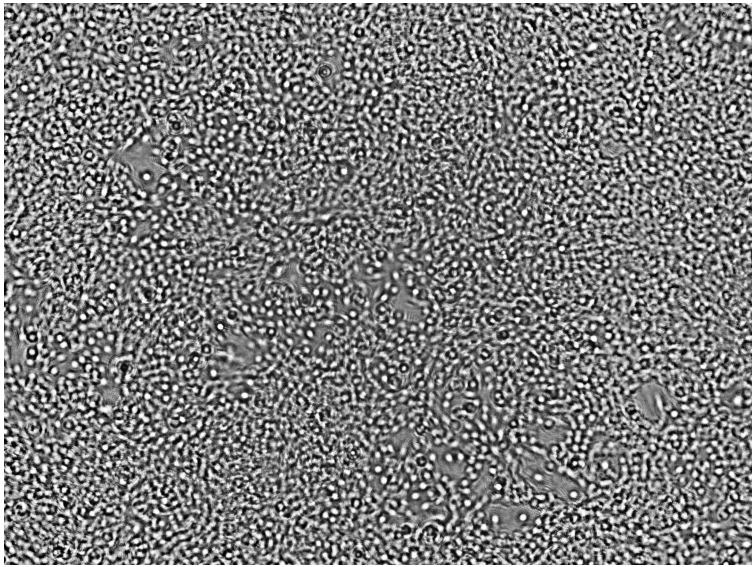
Number of cells **increases** -> counting becomes harder!



https://www.biocompare.com/Editorial-Articles/189708-Automated-Cell-Counting-Selecting-the-Appropriate-System/

From Cell Counting to Cell-Covered Area

Cells are **dense** -> counting is not feasible!



Metric for sparse cells:
Cell count

Metric for growth monitoring:
Cell-covered area

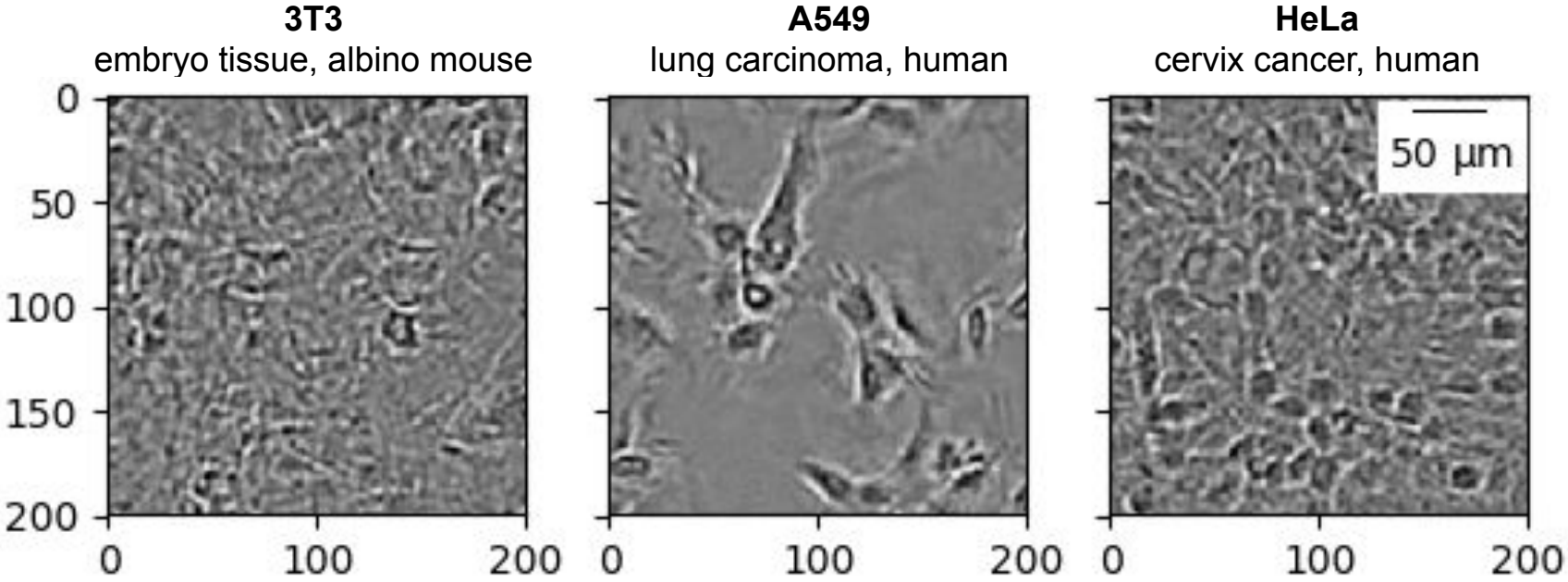
Goal of the Project

We want to provide automated tools for

1. **Cell counting**
2. **Cell-covered area detection**

for lensfree microscopes!

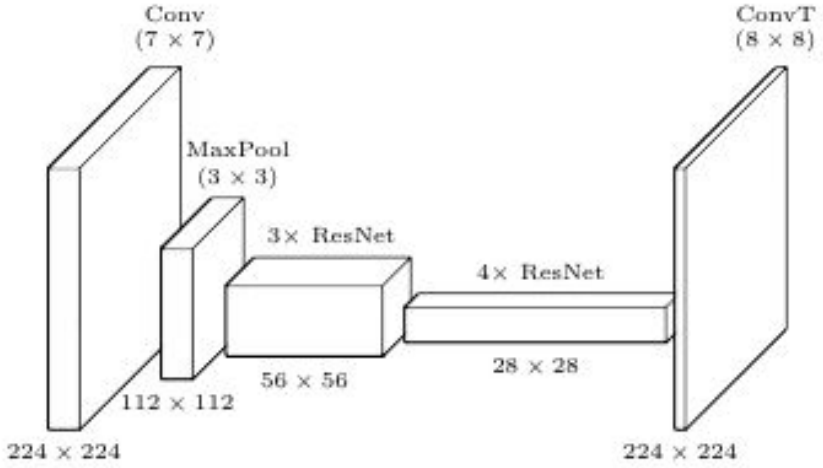
Cell Lines


3T3
embryo tissue, albino mouse
A549
lung carcinoma, human
HeLa
cervix cancer, human
0
50
100
150
200
0
100
200
50 µm

Neural Network Architectures

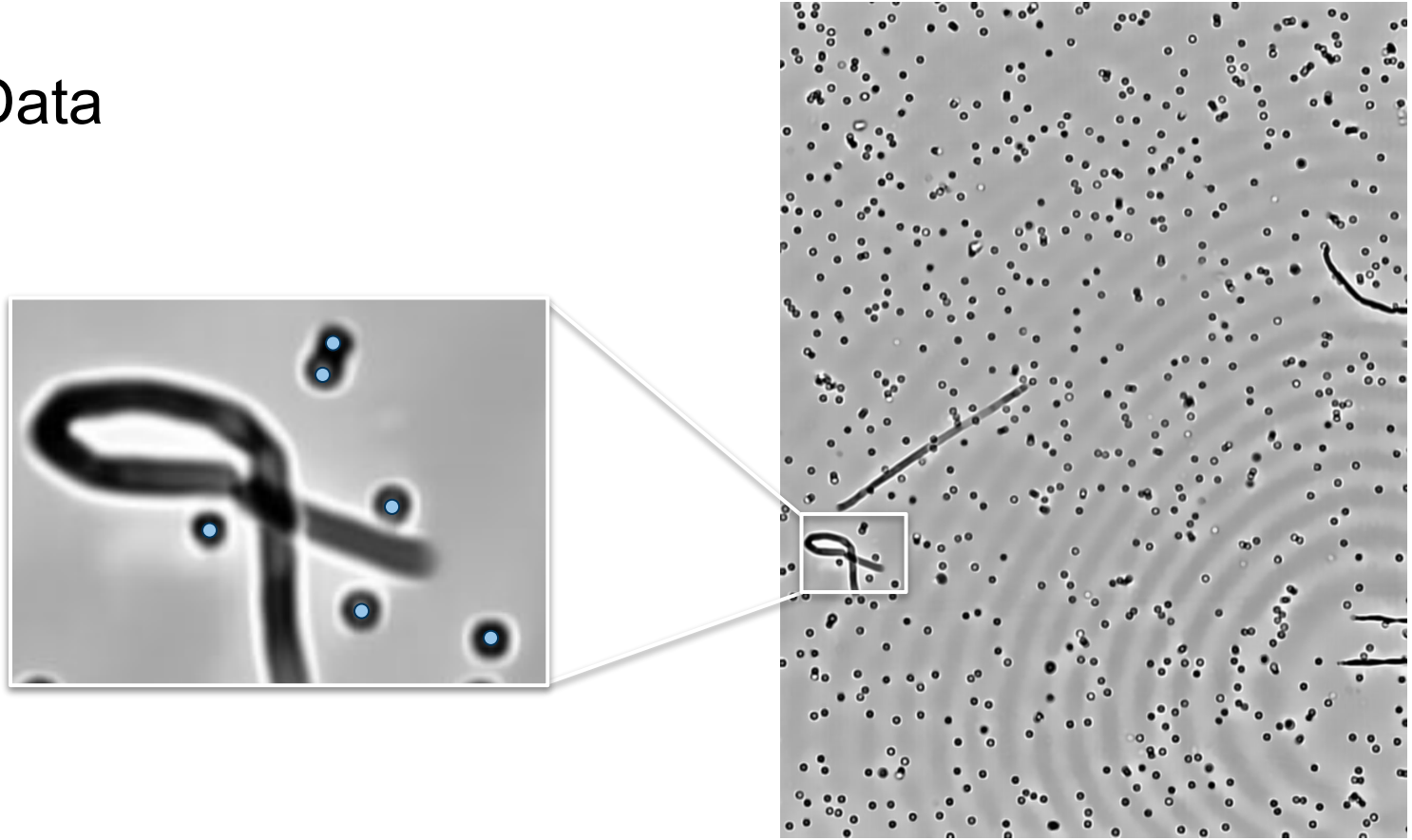
Models

- ResNet-23 (Rempfler et al., 2018) ~ 1.7 mio param.
- U-Net (Ronneberger et al., 2015) ~ 7.7 mio param.
- LinkNet (Chaurasia et al., 2017) ~ 2.9 mio param.

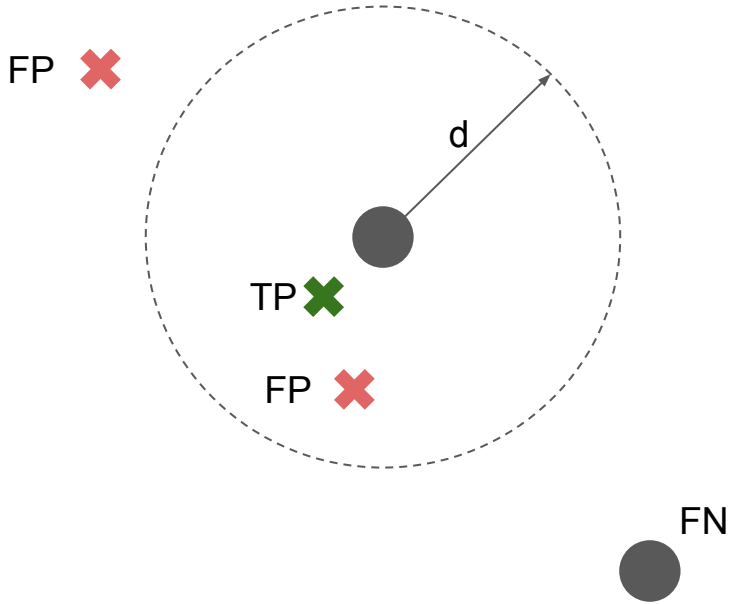


Cell Counting

The Data



Reliable Counting Requires Cell Detection

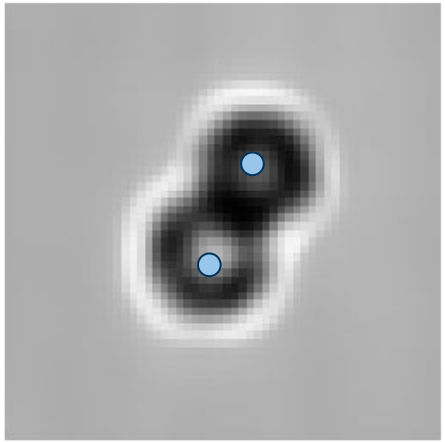


$$Precision = \frac{TP}{TP + FP} \qquad Recall = \frac{TP}{TP + FN}$$

$$F1 = 2 \cdot \frac{Precision \cdot Recall}{Precision + Recall}$$

Representing Annotations as Distances

Lens-free Image

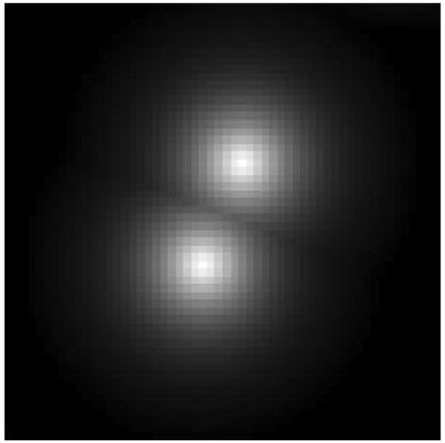


$$\begin{cases} e^{\alpha(1-\frac{D_C(x)}{d_{max}})} - 1 & D_C(x) < d_{max} \\ 0 & otherwise \end{cases}$$

α : *decay parameter*

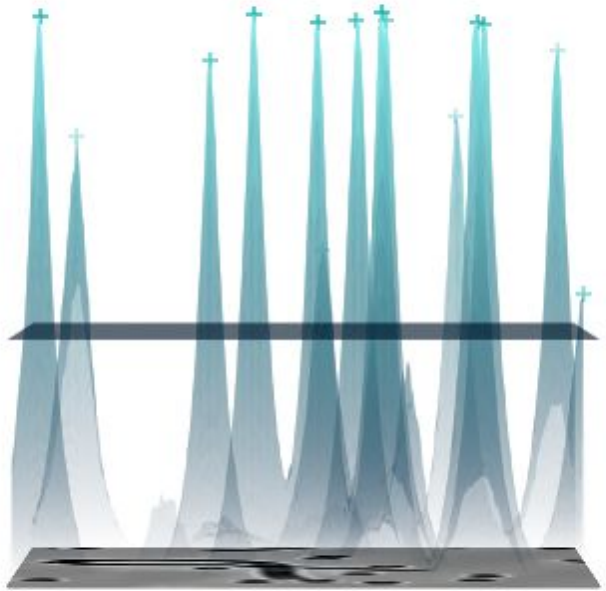
d_{max} : *maximum distance*

Distance Mapping

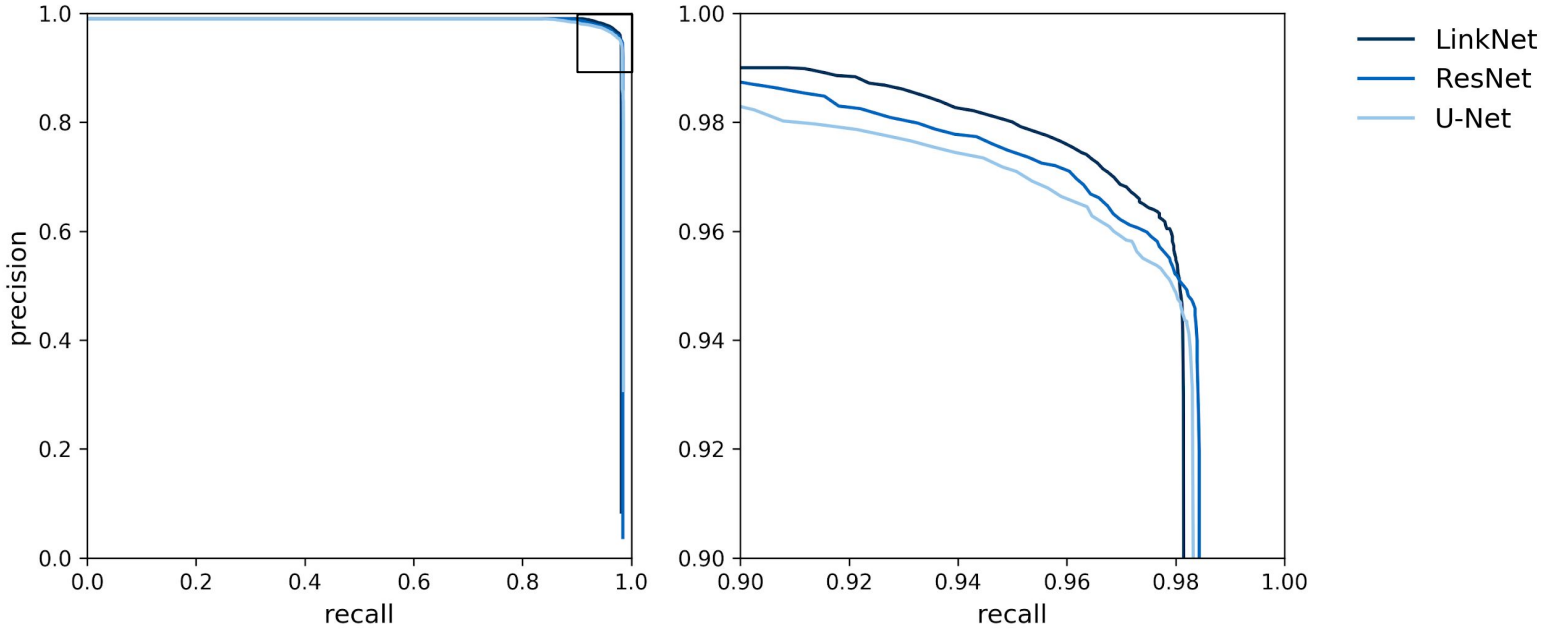


Locating Cells - Pipeline

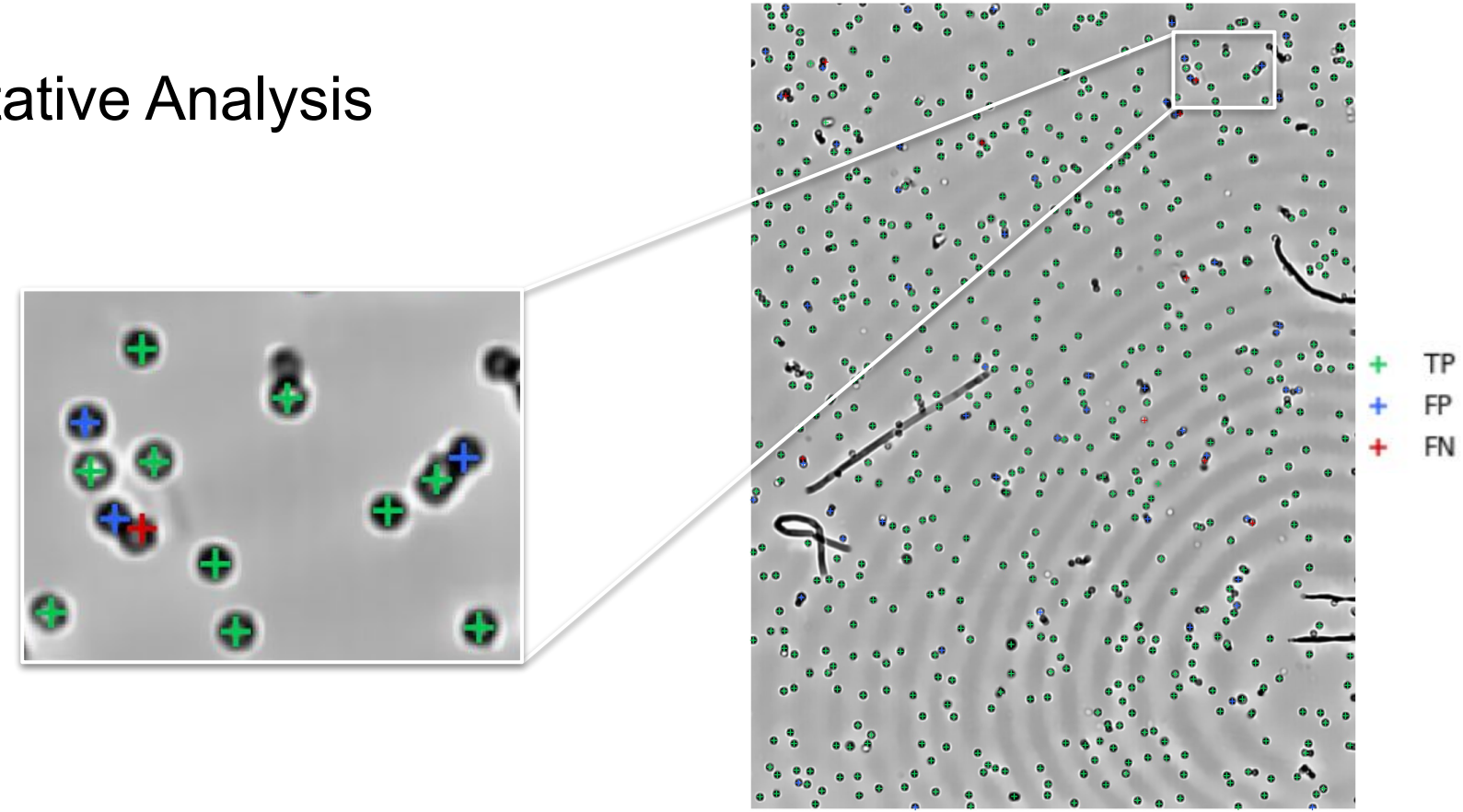
1. Feed image to a fully convolutional network
2. Local maxima indicate potential cell centers
3. Remove low density peaks
4. Remaining maxima correspond to cells



Precision/Recall Trade-Off



Qualitative Analysis



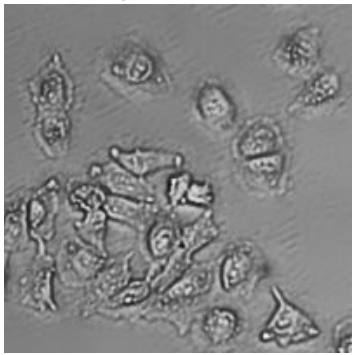
Model Comparison

	F1 score	Precision	Recall	Counting error
ResNet	96.74	96.65	96.84	2.34%
U-Net	96.44	95.50	97.40	2.86%
LinkNet	**96.95**	**96.81**	**97.09**	**2.13%**

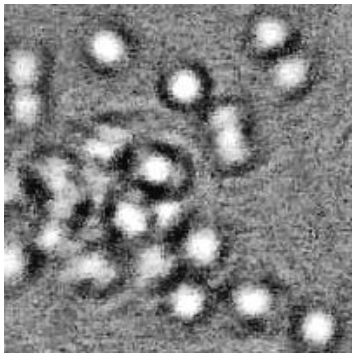
Cell Covered Area Detection

Dataset - Bright-Field and Lensfree images

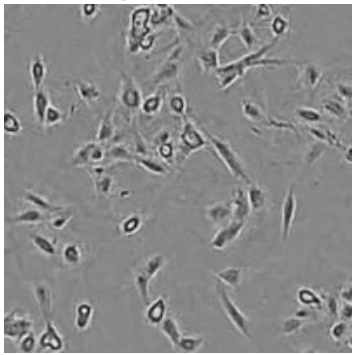
Bright-Field



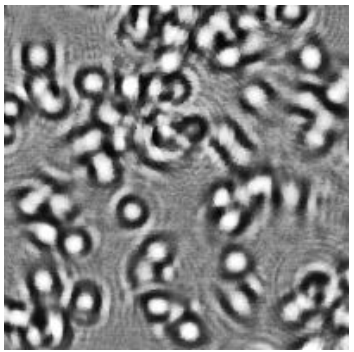
Lensfree



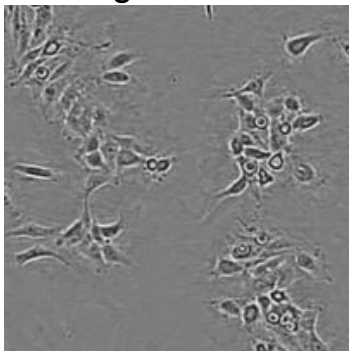
Bright-Field



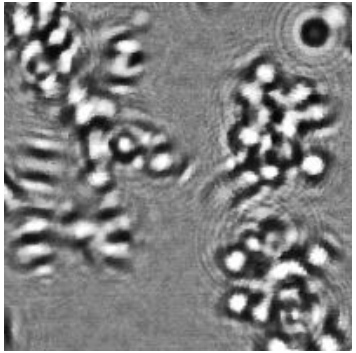
Lensfree



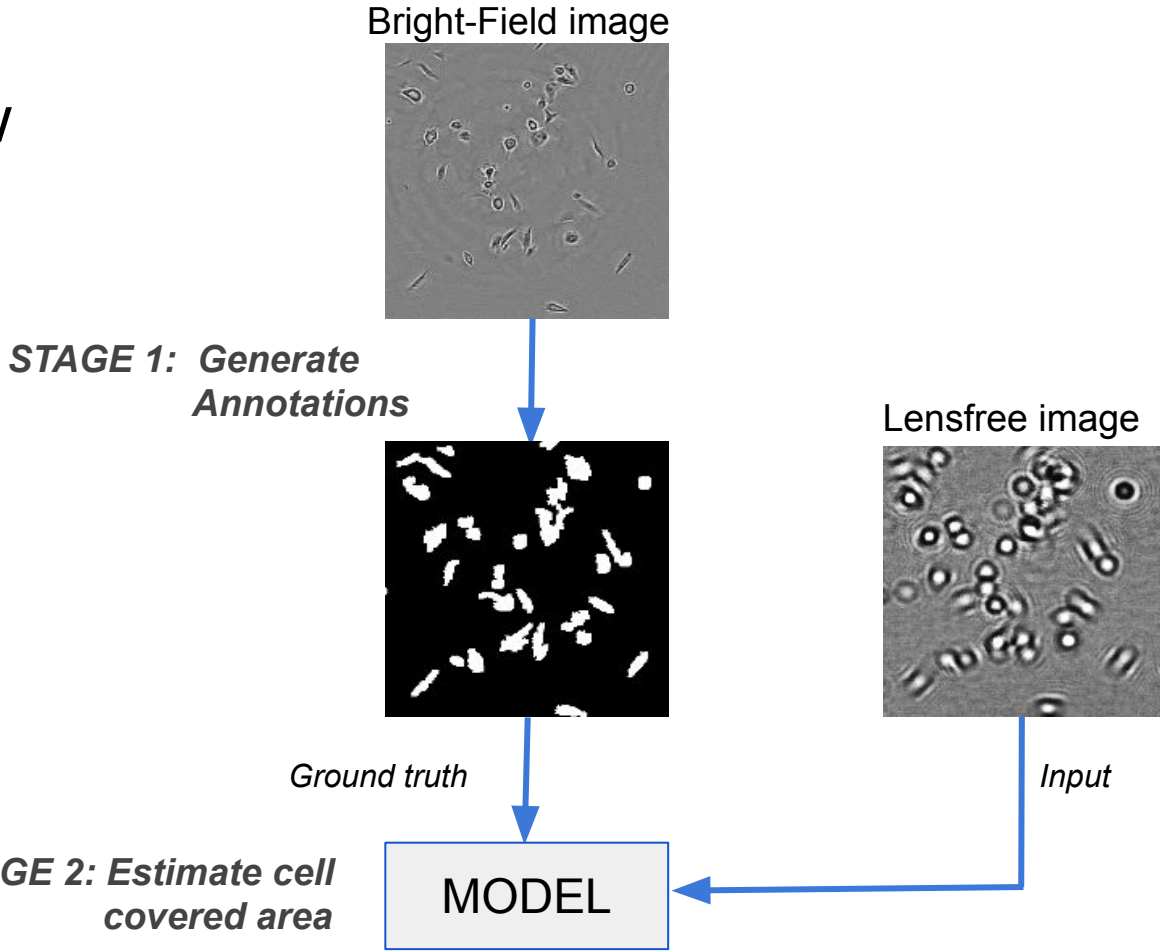
Bright-Field



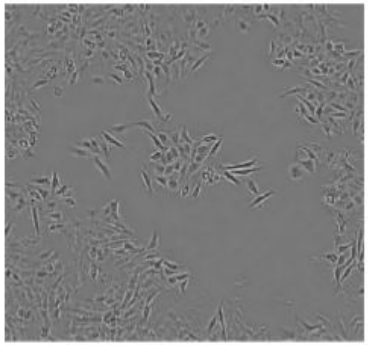
Lensfree



Overview


Bright-Field image
STAGE 1: Generate Annotations
Lensfree image
Ground truth
Input
STAGE 2: Estimate cell covered area
MODEL

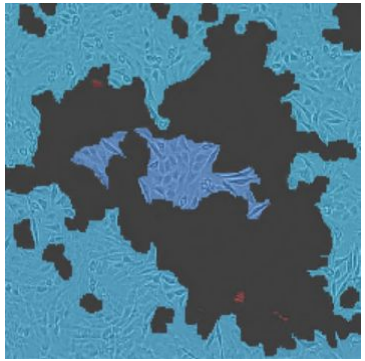
Stage 1 - Generate Annotations



Bright-Field image

Post-processed foreground mask

Final mask



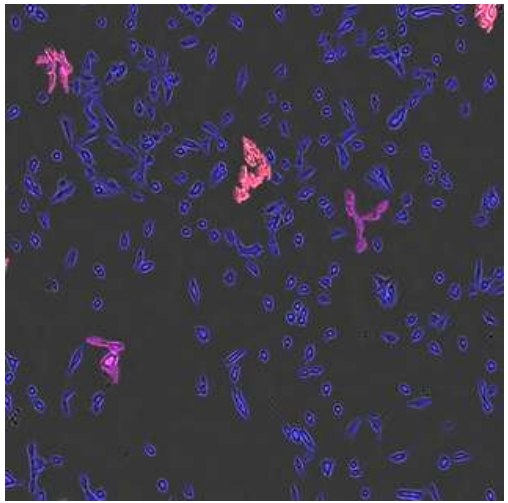
Overlay of mask on bright-field image

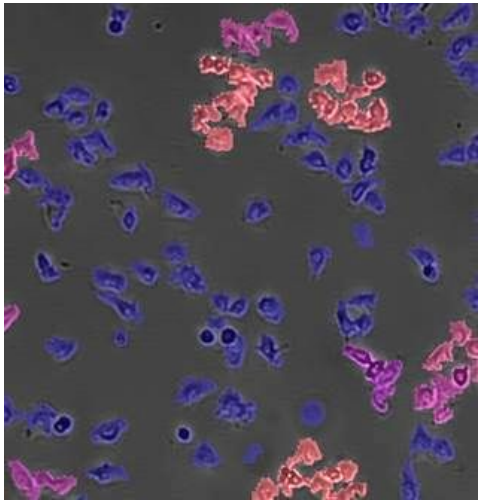
Cell clusters are obtained in the Post-processed foreground mask.

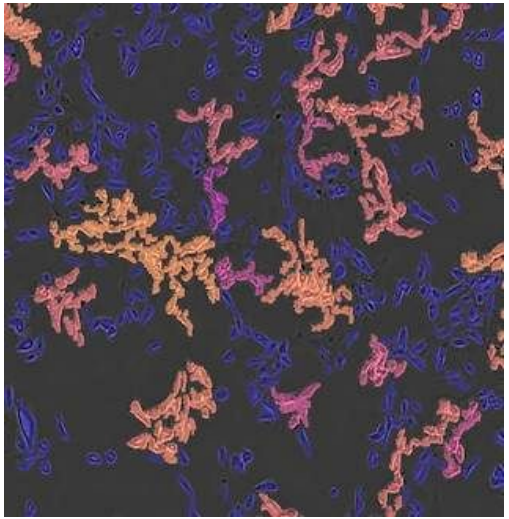
Contrast patterns are captured in the Final mask.

Visualization of Generated Annotations

Generated annotations overlayed on bright-field images.

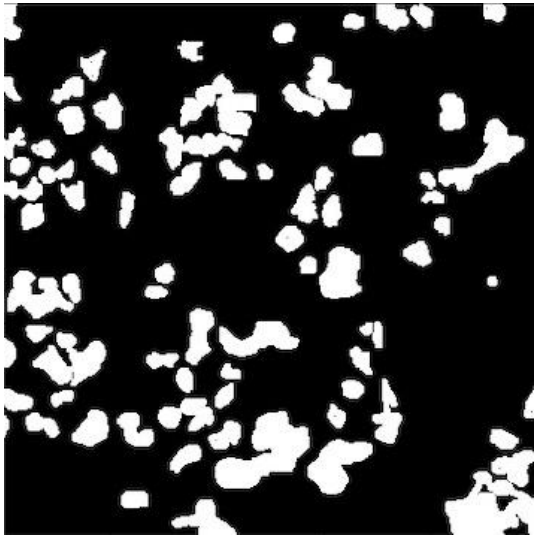






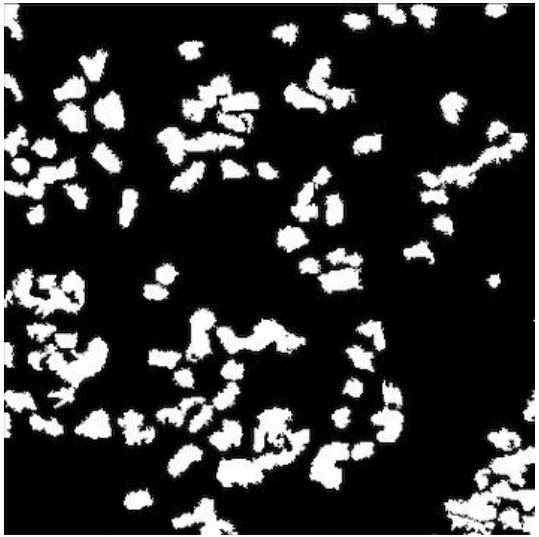
Quality Check of Generated Annotations

Manual Segmentation



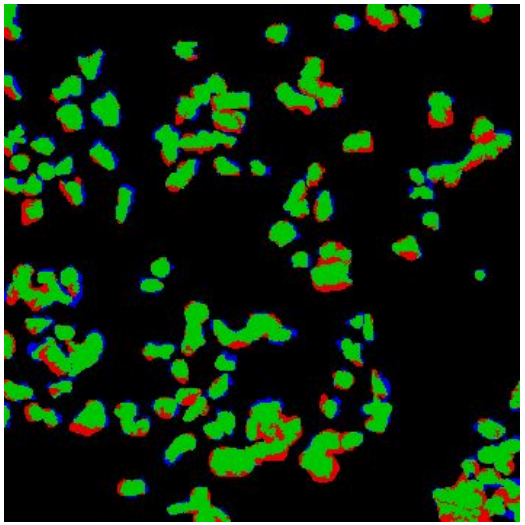
Area = 0.188

Automated Segmentation

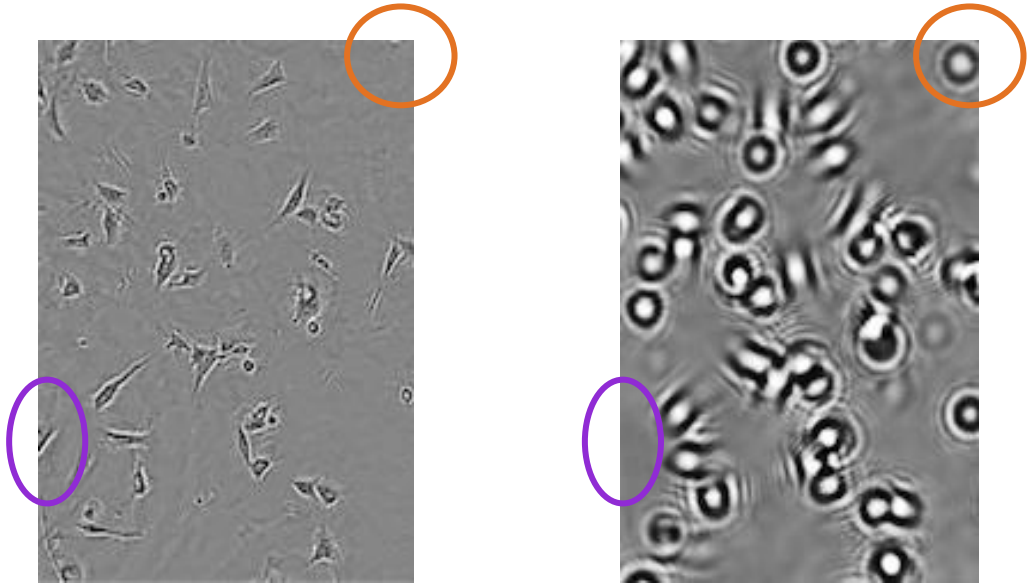


Area = 0.173

TP TN FP FN



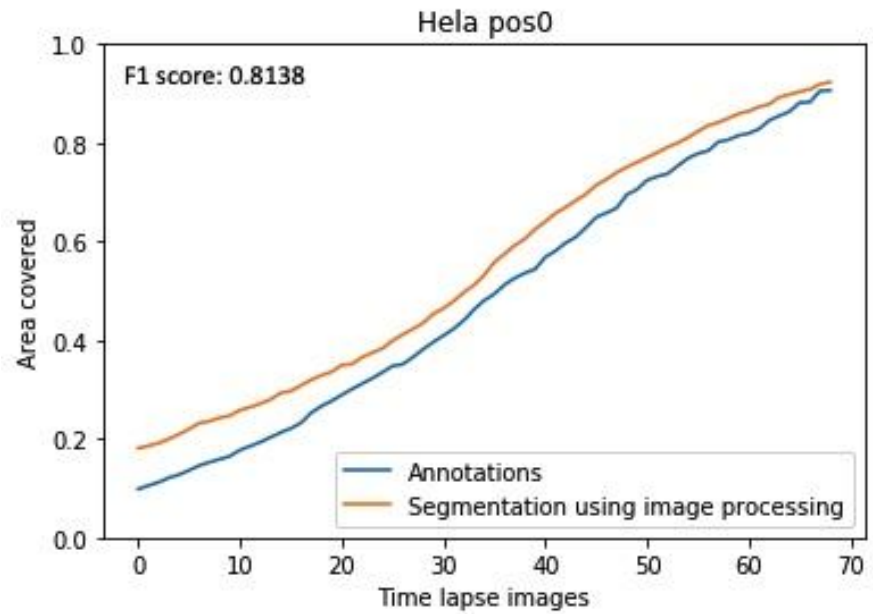
Observations on some of Bright-field and Lensfree images

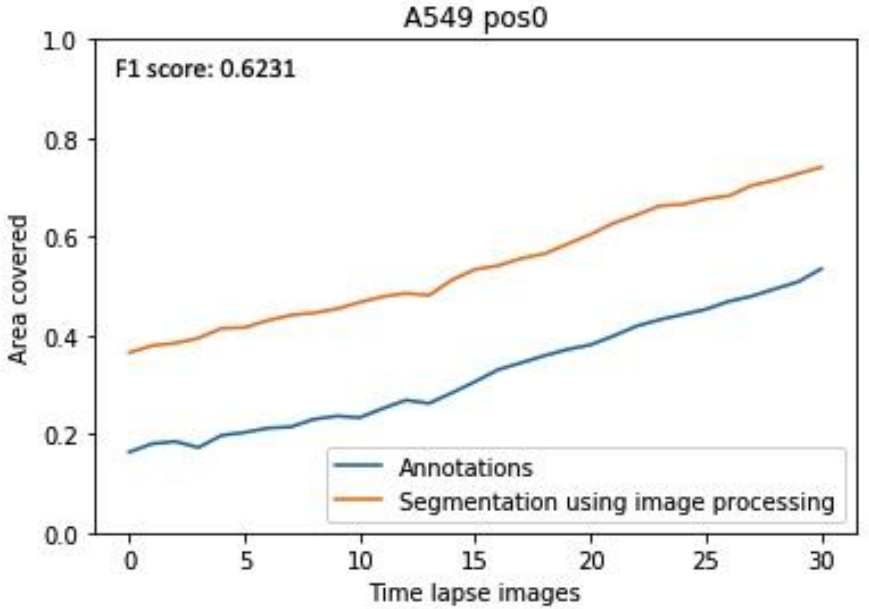


Stage 2 - Estimation of Cell Covered Area

Standard Image processing on lensfree images

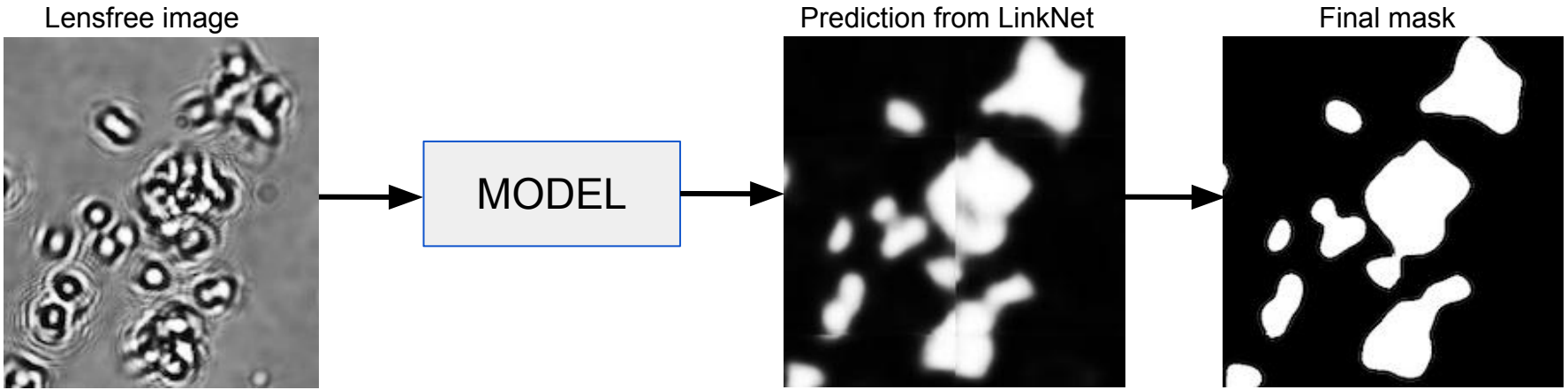
Annotations from bright-field images for comparison.





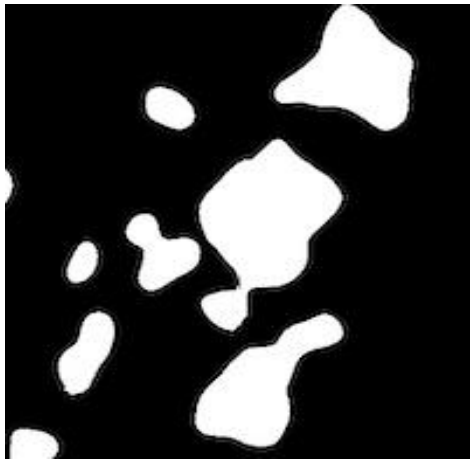
Models and Prediction

Architectures: LinkNet and UNet
Loss functions: Binary cross entropy (bce), dice loss, bce+dice
Output: Probabilistic map

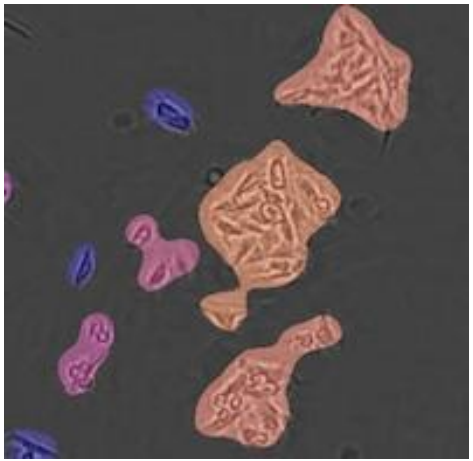


Visualize Final Masks from the model

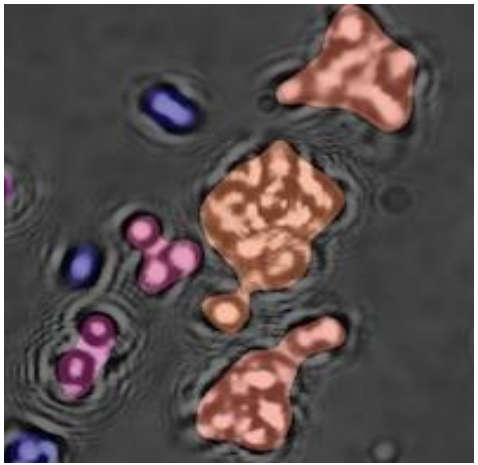
Final mask



Overlay on bright-field



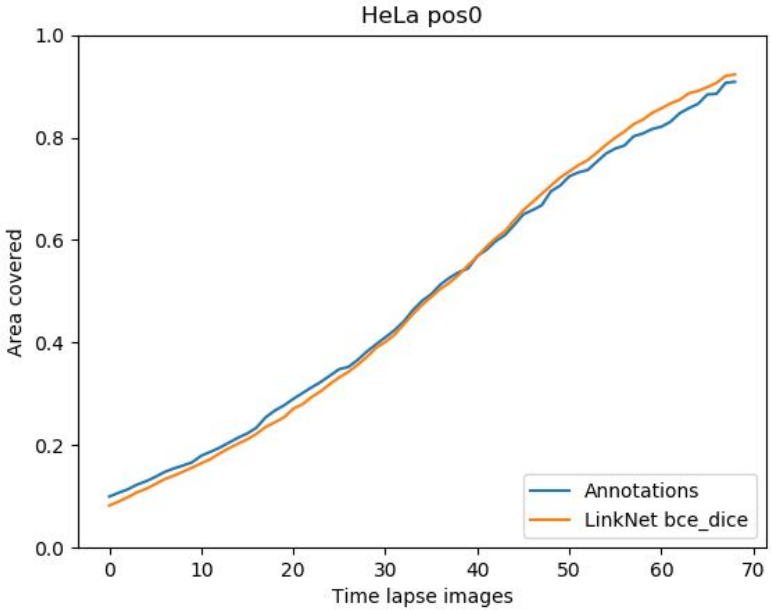
Overlay on lensfree

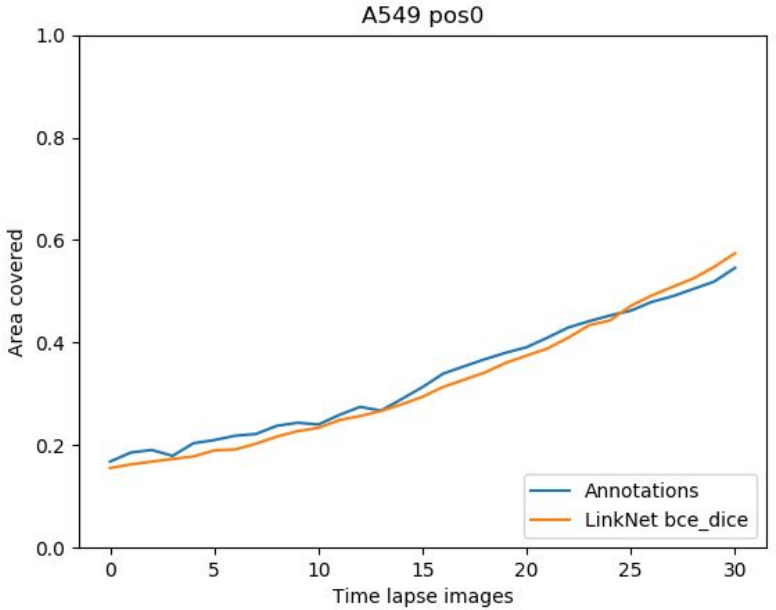


Model Comparison on Test Set

	BCE	BCE+DICE	DICE
LinkNet	F1: 0.8247 MSE: 0.001434	***F1: 0.8363*** ***MSE: 0.001566***	F1: 0.8270 MSE: 0.001594
UNet	F1: 0.7042 MSE: 0.051104	F1: 0.6988 MSE: 0.054393	F1: 0.8129 MSE: 0.001222

Growth Curve from the best model





Conclusions and Future Work

- Automated counting of cells and achieved a high F1 score close to 97%
- Automated generating annotations and estimating cell covered region
- LinkNet performs the best for both Cell Counting and Cell Covered tasks
- The main limitation for the tasks were the annotations

The results can be improved further by:

- Enhancing the annotations
- Experimenting with other networks like LSTM UNet or LSTM LinkNet

Thank you!