Recovering the Imperfect:
Cell Segmentation in the Presence of Dynamically Localized Proteins

Second Workshop on Medical Image Learning with Less Labels and Imperfect Data (MIL3ID)

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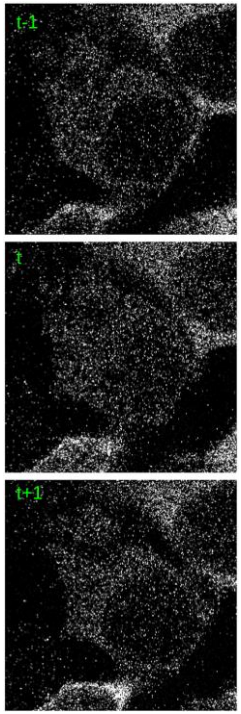
Özgün Çiçek*, Yassine Marrakchi*, Enoch B. Antwi, Barbara DiVentura and Thomas Brox

*equal contribution

University of Freiburg, Germany
Signalling Research Centres BIOSS and CIBSS, Freiburg, Germany

Motivation



Time-lapse confocal images of HEK293T cells with fusion protein mCherry-LINuS

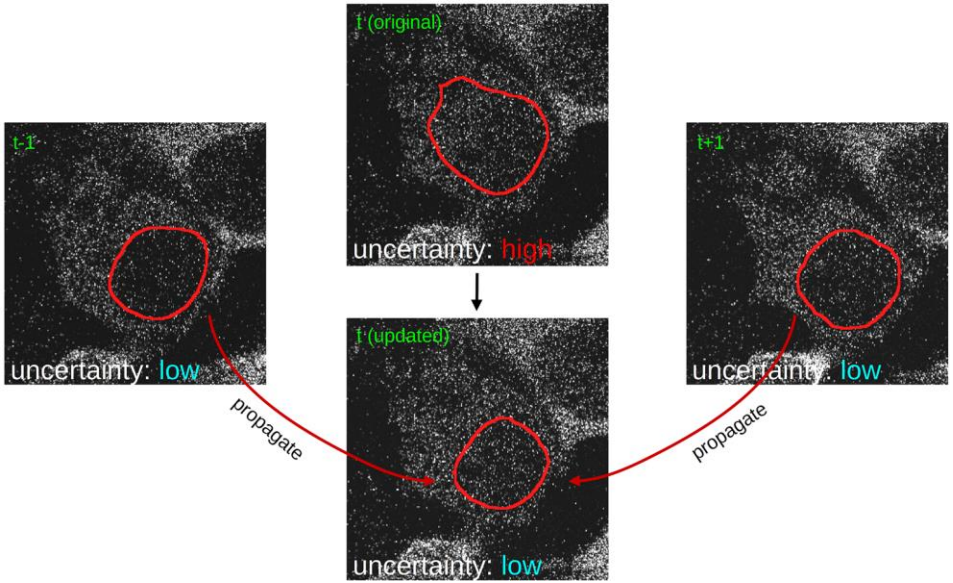
- The dynamic localization patterns of proteins dictate their function.
- Biologists use optogenetics to control protein localization via light exposure.
- Repeatedly giving light creates oscillations of the protein in and out of the nucleus.
- These oscillations cause regular and temporary deterioration in visibility.
- Deep learning methods become unreliable when the visibility is drastically deteriorated.

Related Work

- We are first to address segmentation of oscillatory fluorescent signal in videos.
- Video segmentation methods explore temporal propagation of features in their design.
- Our task is different:
  - Dense annotation in time for imperfect data is tedious.
  - We are solely interested in structures with limited visibility.

Our Contribution

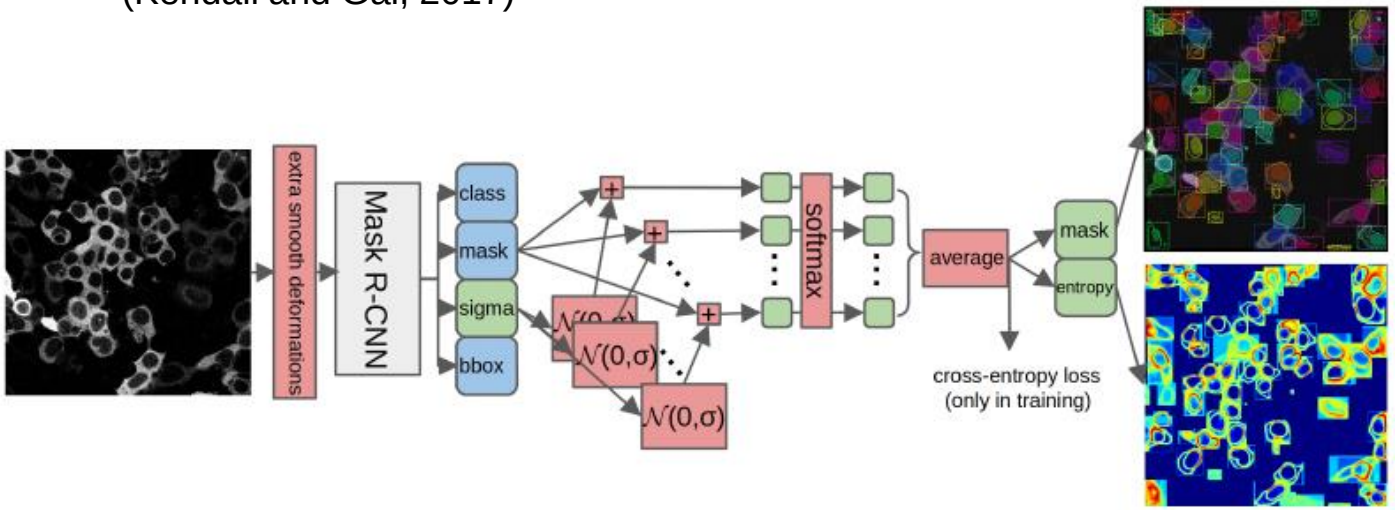
- Mask R-CNN (He et al., 2017) with uncertainty to detect erroneous predictions.
- Optical flow to refine detected errors by propagating certain predictions from neighboring frames.



Oscillation at time *t* causing bad nuclei segmentation (up) and the corrected segmentation of it using our propagation method (down).

Our Approach - Mask R-CNN with Uncertainty Estimation

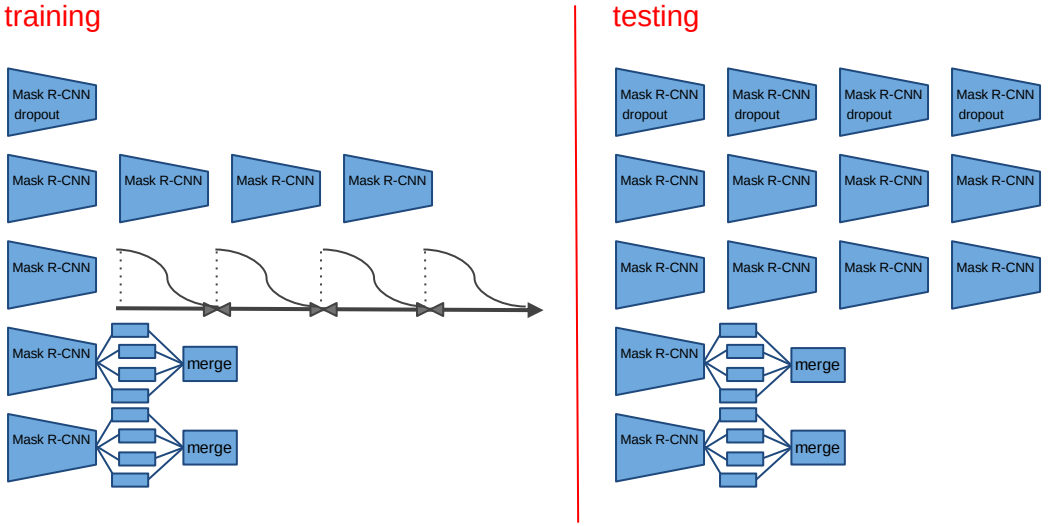
- Data uncertainty
  - Combining Mask R-CNN (He et al., 2017) with data uncertainty estimation (Kendall and Gal, 2017)



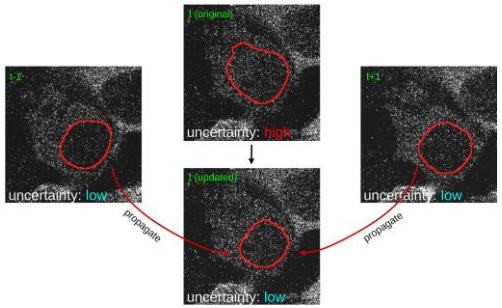
Overview of Mask R-CNN with added data uncertainty. Changes to the original architecture are shown in red (operations) and green (outputs).

Our Approach - Mask R-CNN with Uncertainty Estimation

- Model uncertainty
  - Combining Mask R-CNN with model uncertainty estimation (following Ilg et al., 2018)
    - Dropout:
    - Ensemble:
    - SGDR Ensemble:
    - Winner-Takes-All:
    - Evolving WTA: (Makansi et al., 2019)



Our Approach - Uncertainty-Based Nuclei Mask Propagation



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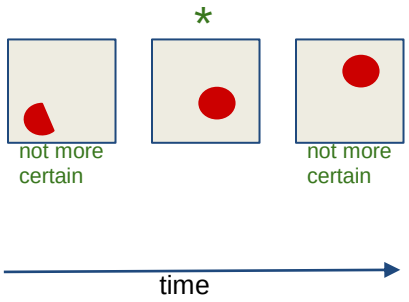
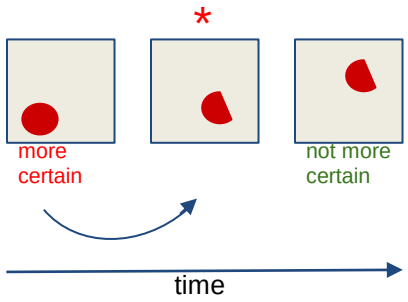
Traverse the video in increasing average uncertainty order:

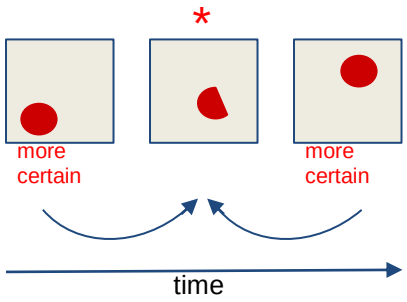
no propagation:



one-sided propagation:



double-sided propagation:



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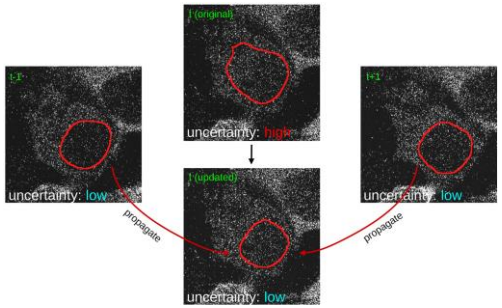

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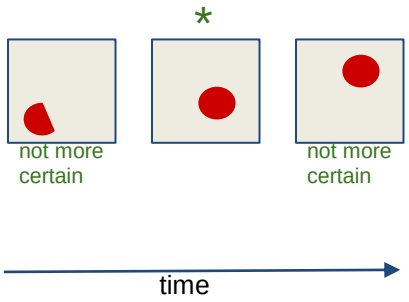

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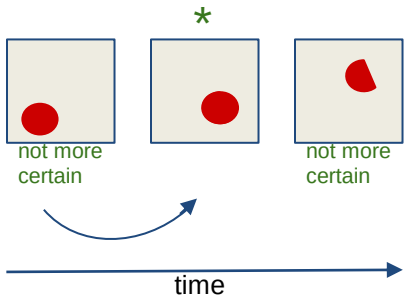

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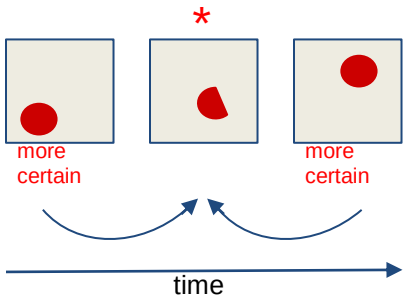

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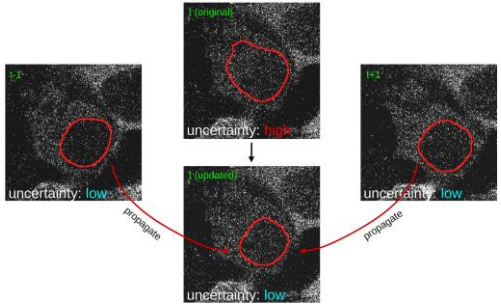

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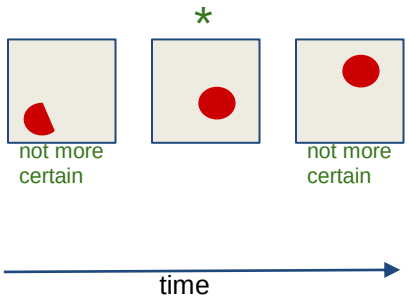

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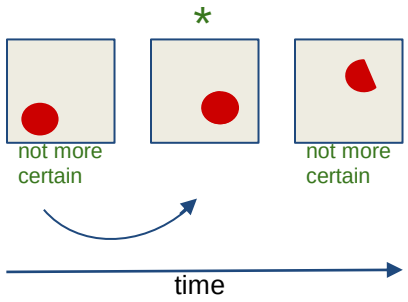

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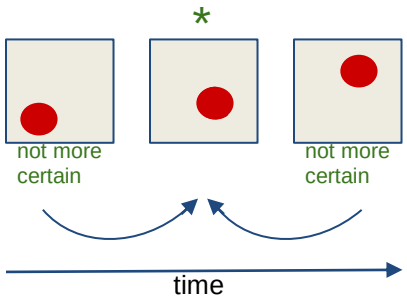

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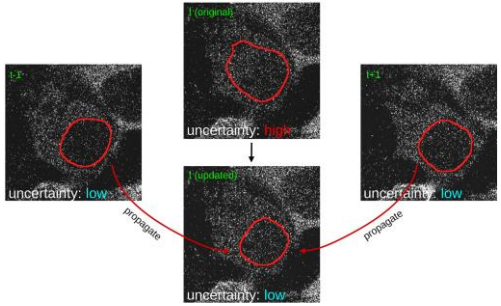

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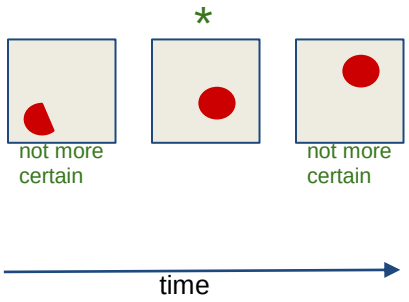

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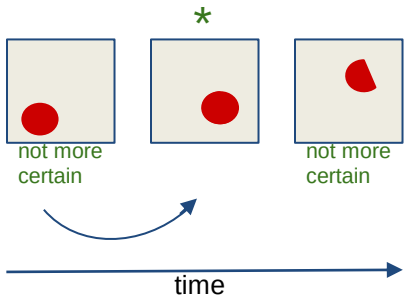

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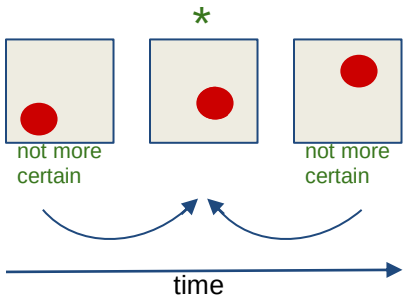

*Traversing continues with the updated masks and uncertainties to facilitate long propagation horizon.

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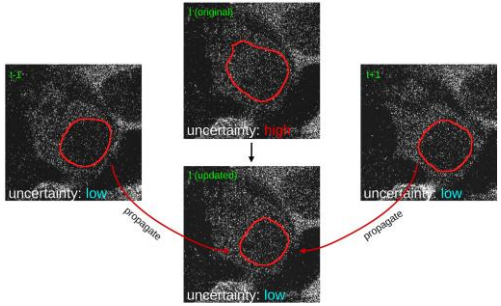

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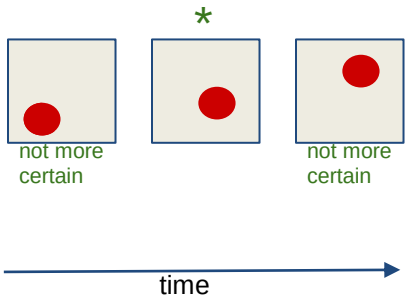

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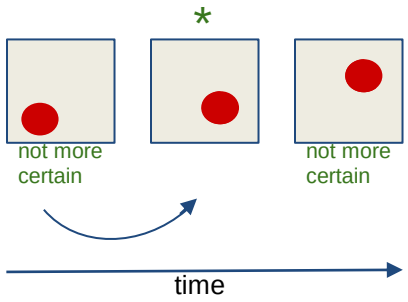

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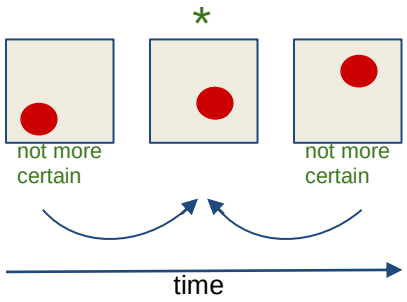

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Results - Uncertainty Estimation

Uncertainty Evaluation in mAP (@0.5/@0.75 IoU):

	model uncertainty		combined uncertainty	
	mAP (sm)	mAP (ent)	mAP (sm)	mAP (ent)
Single	0.77/0.48	0.80/0.49	0.74/0.60	0.83/0.69
Dropout	0.74/0.61	0.78/0.65	0.77/0.61	0.83/0.67
Ensemble	0.82/**0.64**	0.78/0.61	0.78/0.63	0.83/**0.70**
SGDR Ensemble	0.75/0.54	0.72/0.51	0.71/0.49	0.63/0.44
WTA Merged	0.74/0.47	0.82/0.49	**0.83**/0.56	**0.85**/0.64
EWTA Merged	0.64/0.51	0.73/0.58	0.80/**0.64**	0.77/0.59

Results - Propagation Algorithm

Propagation Evaluation in mean IoU:

update	warp with	mask fusion	all(117)	updated(51)	extrapolated(11)	non-updated(55)
none	none	no	0.62	0.55	0.00	**0.80**
uncertain	shift+scale	no	0.71	0.68	0.39	**0.80**
uncertain	mean nuclei flow	no	**0.73**	0.71	**0.45**	**0.80**
all	mean nuclei flow	no	0.69	0.70	0.40	0.74
uncertain	pixel-wise flow	no	**0.73**	**0.72**	0.44	**0.80**
uncertain	pixel-wise flow	yes	0.72	0.70	0.40	**0.80**

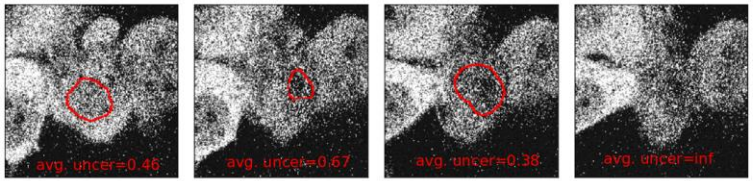
Our method can effectively improve erroneous nuclei predictions.

Results - Qualitative Examples

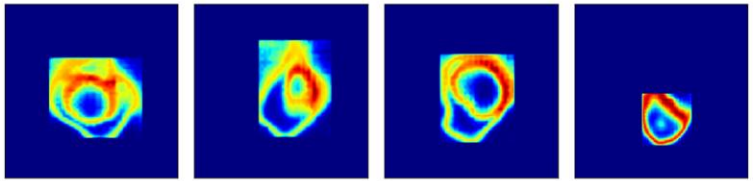
Extreme Signal Loss:

Raw Time-Series:

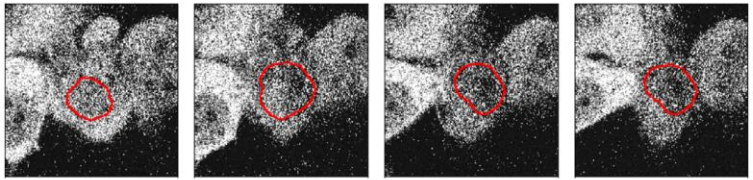
Initial Masks:



Uncertainty Maps:



Refined Masks:



time

Conclusions

- We introduce the recent uncertainty estimation methods to cell instance segmentation.
- We solve a real task commonly experienced in signalling studies which is not yet addressed.
- Our method improves nuclei segmentation over several baselines.
- Our method can facilitate automated analysis of dynamically localized proteins without additional markers.

Thank you! & Questions?

Poster and Code:

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