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

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Motivation

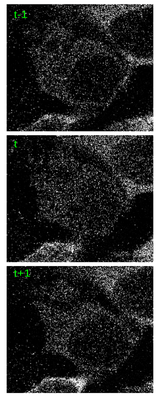
The dynamic localization patterns of proteins dictate their function.

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.

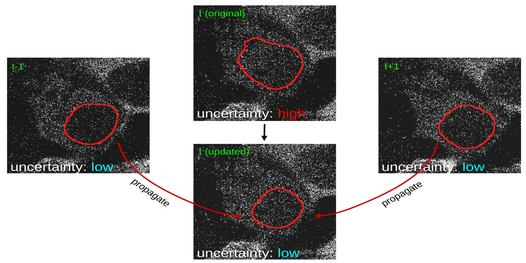


Time-lapse confocal images of HEK293T cells with fusion protein mCherry-LINuS

Our Contributions

Mask R-CNN (He et al., 2017) with uncertainty to detect erroneous predictions.

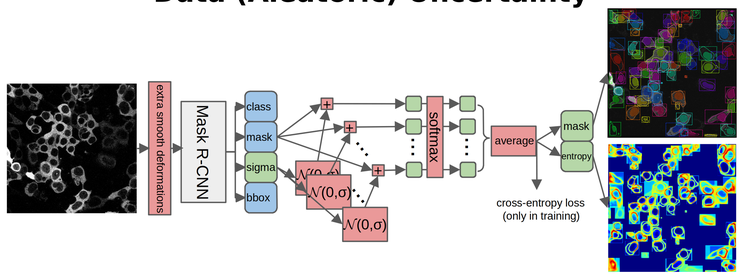
Optical flow to refine detected errors by propagating certain predictions from neighboring frames.



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

Overview of Approaches

Data (Aleatoric) Uncertainty



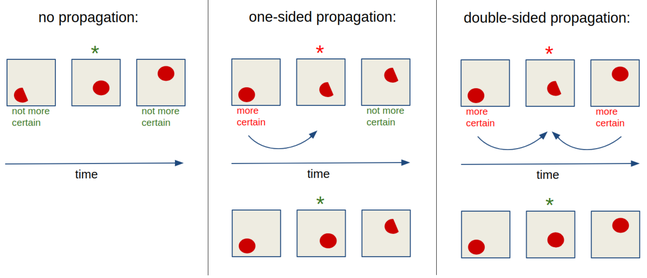
Overview of Mask R-CNN with added data uncertainty. Changes to the original architecture are shown in red (operations) and green (outputs).

Model (Epistemic) Uncertainty

We investigate existing sampling methods for neural networks to obtain model uncertainty following the work by Ilg et al. [2]: Dropout, Ensemble, SGDR Ensemble, Winner-Takes-All (WTA) and Evolving WTA [3].

Uncertainty-Based Nuclei Mask Propagation

Traverse the video in increasing average uncertainty order:



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

Results

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

WTA merged is the best at 0.5 IoU threshold and at 0.75 ensemble is the best. We use the WTA merged with data uncertainty since it is computationally more efficient than ensemble.

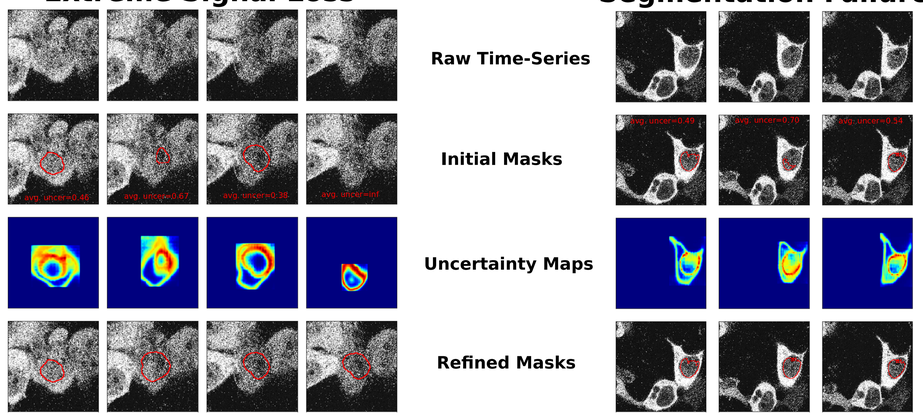
Propagation Evaluation in mean IoU

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.

Extreme Signal Loss

Segmentation Failure



Conclusions

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.

References

[1] He, K., Gkioxari, G., Dollar, P., Girshick, R.B.: Mask R-CNN. In: ICCV (2017)
[2] Ilg, E., Cicek, O., Galesso, S., Klein, A., Makansi, O., Hutter, F., Brox, T.: Uncertainty estimates and multi-hypotheses networks for optical flow. In: ECCV (2018)
[3] Makansi, O., Ilg, E., Cicek, O., Brox, T.: Overcoming limitations of mixture density networks: A sampling and fitting framework for multimodal future prediction. In:CVPR (2019)

Acknowledgements

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