Learning to segment clustered amoeboid cells from brightfield microscopy via multi-task learning with adaptive weight selection

Rituparna Sarkar, Suvadip Mukherjee, Elisabeth Labruyère and Jean Christophe Olivo-Marin

Bioimage Analysis Unit, Institut Pasteur, Paris, France

Institut Pasteur | CELL BIOLOGY & INFECTION | Bioimage Analysis Unit

Detecting and segmenting individual cells from microscopy images is critical to various life science applications[1]. We pay attention to cells exhibiting *amoeboid* motion, a particular model of cell motility, characterized by repetitive formation of small protrusions of the cell membrane which are better visible via *brightfield* microscopy.

Challenges: Poor contrast, signal variation in *brightfield* images pose significant challenges, which are accentuated when the cells are in close proximity.

Objective:

- A novel supervised technique for cell segmentation in a multi-task learning paradigm.
- A combination of a multi-task loss, based on the region and cell boundary detection, is employed for an improved prediction efficiency of the network.
- The learning problem is posed in a novel min-max framework which enables adaptive estimation of the hyper-parameters in an automatic fashion.

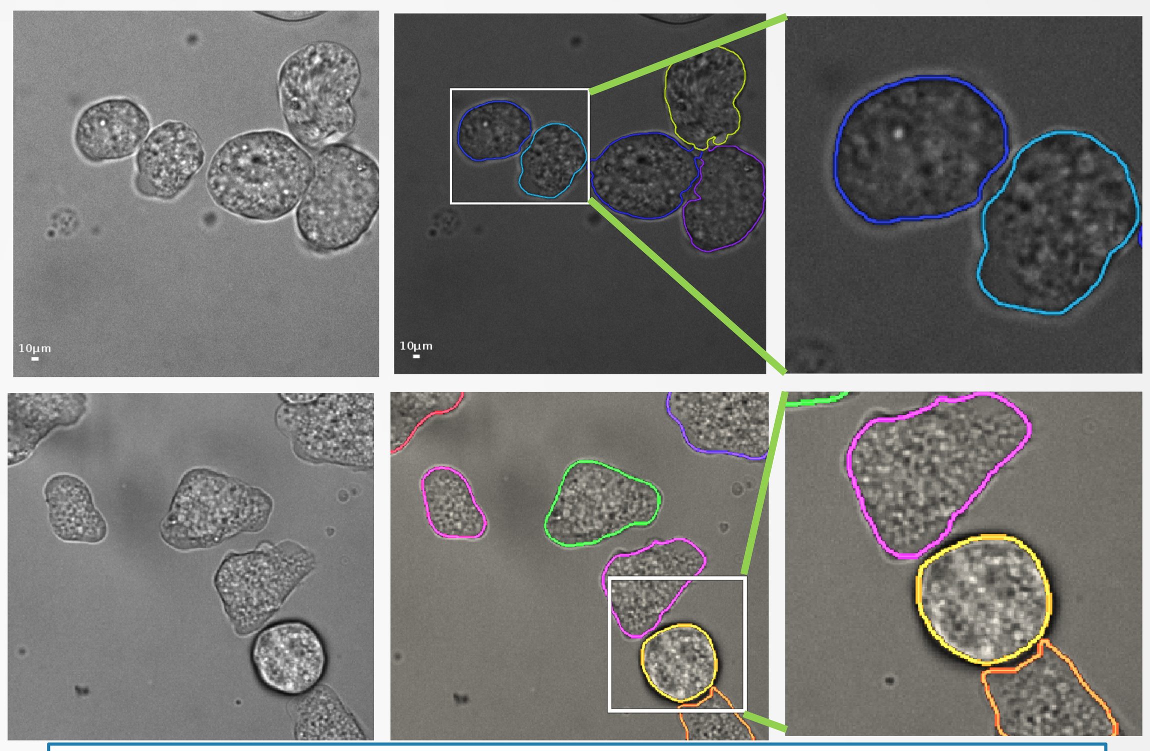


Figure: Cell Segmentation using proposed method

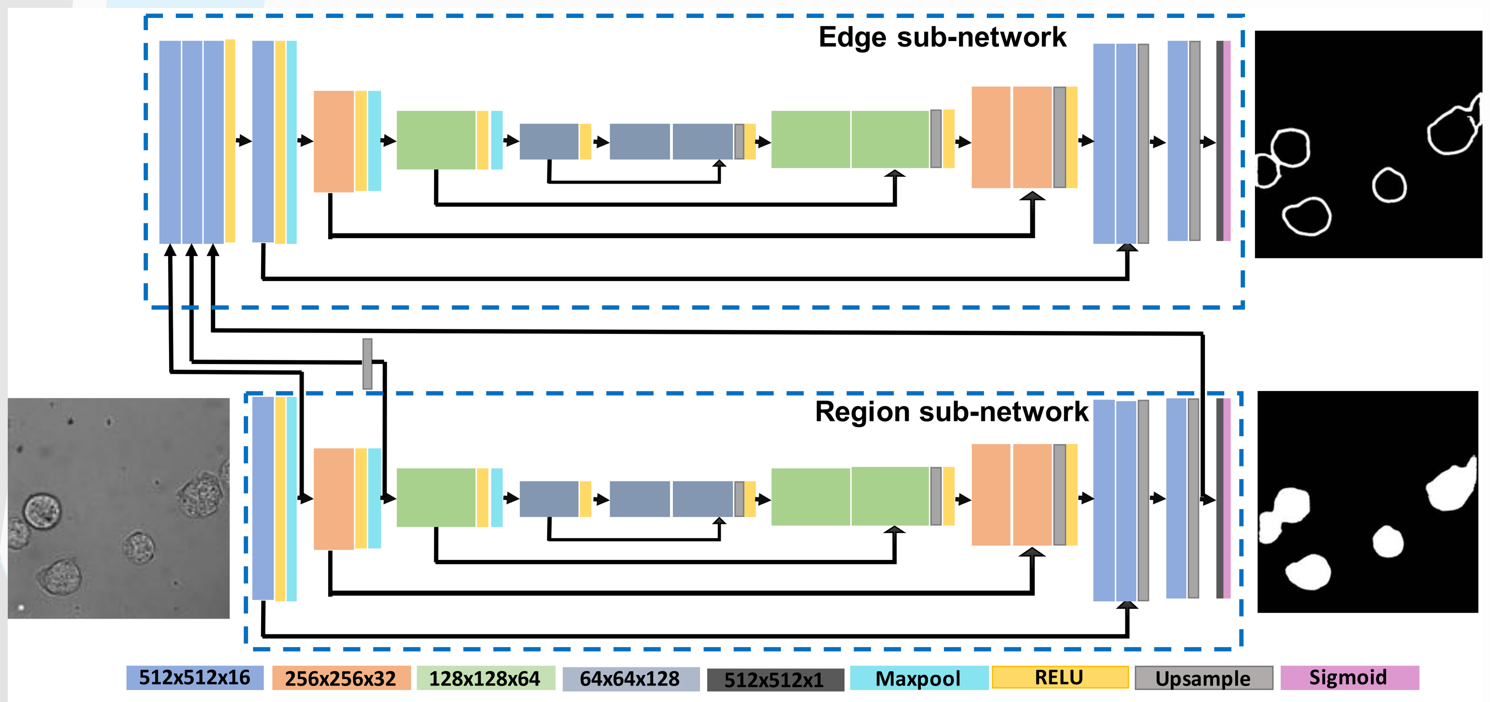
Multi-CellNet

A multi-task convolutional neural network (CNN) architecture, **Multi-CellNet**, is trained to simultaneously predict the cell foreground and the cell boundary with adaptive estimation of the task hyper-parameters.

Multi-CellNet architecture

- Neither region prediction, nor edge indicators are adequately sufficient to segment cells from brightfield imagery.
- Two sub-networks, viz. a region and an edge sub-network provide cell foreground and boundary predictions, respectively and coupled via network weight sharing
- Trained with multi-task los s: $\mathcal{E} = \boldsymbol{\alpha}\, \boldsymbol{E_1(\theta_1)} + \boldsymbol{\beta}\, \boldsymbol{E_2(\theta_2)}$

$$E_2(\theta_2) = 1 - \mathcal{D}(|\nabla g(f)|, f_e); \quad E_1(\theta_1) = 1 - \mathcal{D}(g(f), f_r)$$



Hyperparameter estimation by min-max optimization

- A typical practice is to assign them equal values or select them arbitrarily. This could lead to imbalance in the contribution of the associated loss functions.
- The training loss is written as: $\mathcal{E}(\boldsymbol{\lambda}, \boldsymbol{\theta_1}, \boldsymbol{\theta_2}) = \boldsymbol{\lambda}\, \boldsymbol{E_1(\theta_1)} + \sqrt{\{\mathbf{1} - \boldsymbol{\lambda}^2\}}\boldsymbol{E_2(\theta_2)}$
- The partial derivatives reveal that $\mathcal{E}$ is concave in λ :

$$\frac{\partial}{\partial\lambda}\mathcal{E}(\lambda, \theta_1, \theta_2) = E_1 - \lambda(1-\lambda^2)^{-\frac{1}{2}}E_2 \;\; ; \;\; \frac{\partial^2}{\partial\lambda^2}\mathcal{E}(\lambda, \theta_1, \theta_2) = -E_2(1-\lambda^2)^{-\frac{3}{2}}$$

- This non-linear concave combination leads to a min-max optimization problem

$$\boldsymbol{min}_{\{\theta_1, \theta_2\}}\, \boldsymbol{max}_{\lambda}\mathcal{E}(\boldsymbol{\lambda}, \boldsymbol{\theta_1}, \boldsymbol{\theta_2})$$

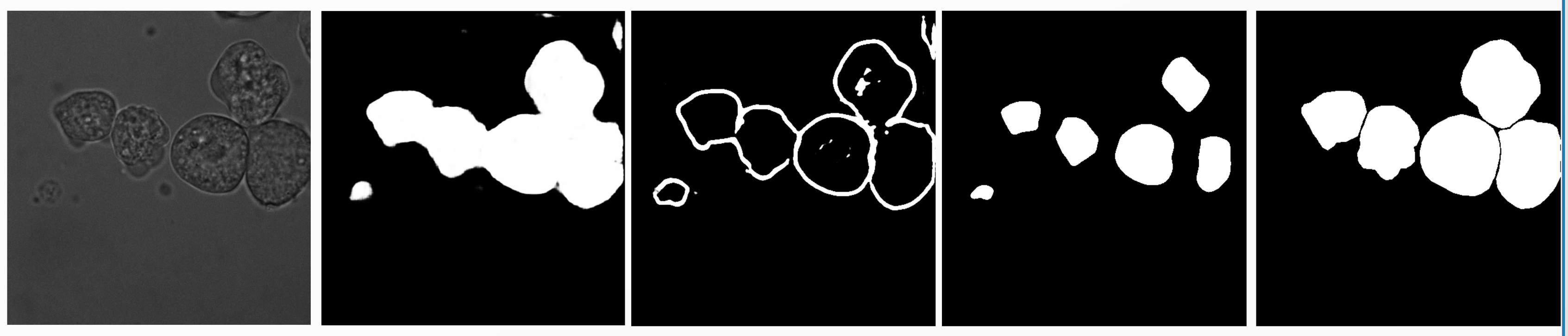
- The relative weights are obtained adaptively using alternating minimization[2].

$$\lambda^* = \frac{E_1(\widehat{\theta_1})}{\sqrt{\left\{E_1(\widehat{\theta_1})^2 + E_2(\widehat{\theta_2})^2\right\}}} \;\; ; \;\; \widehat{\theta_1}, \widehat{\theta_2} = \operatorname{argmin}_{\{\theta_1, \theta_2\}}\mathcal{E}(\lambda^*, \theta_1, \theta_2)$$

- $\widehat{\theta_1}, \widehat{\theta_2}$ are network parameters optimized using stochastic gradient.
- This formulation could be interpreted as an optimization problem which seeks to minimize the worst-case performance of the system

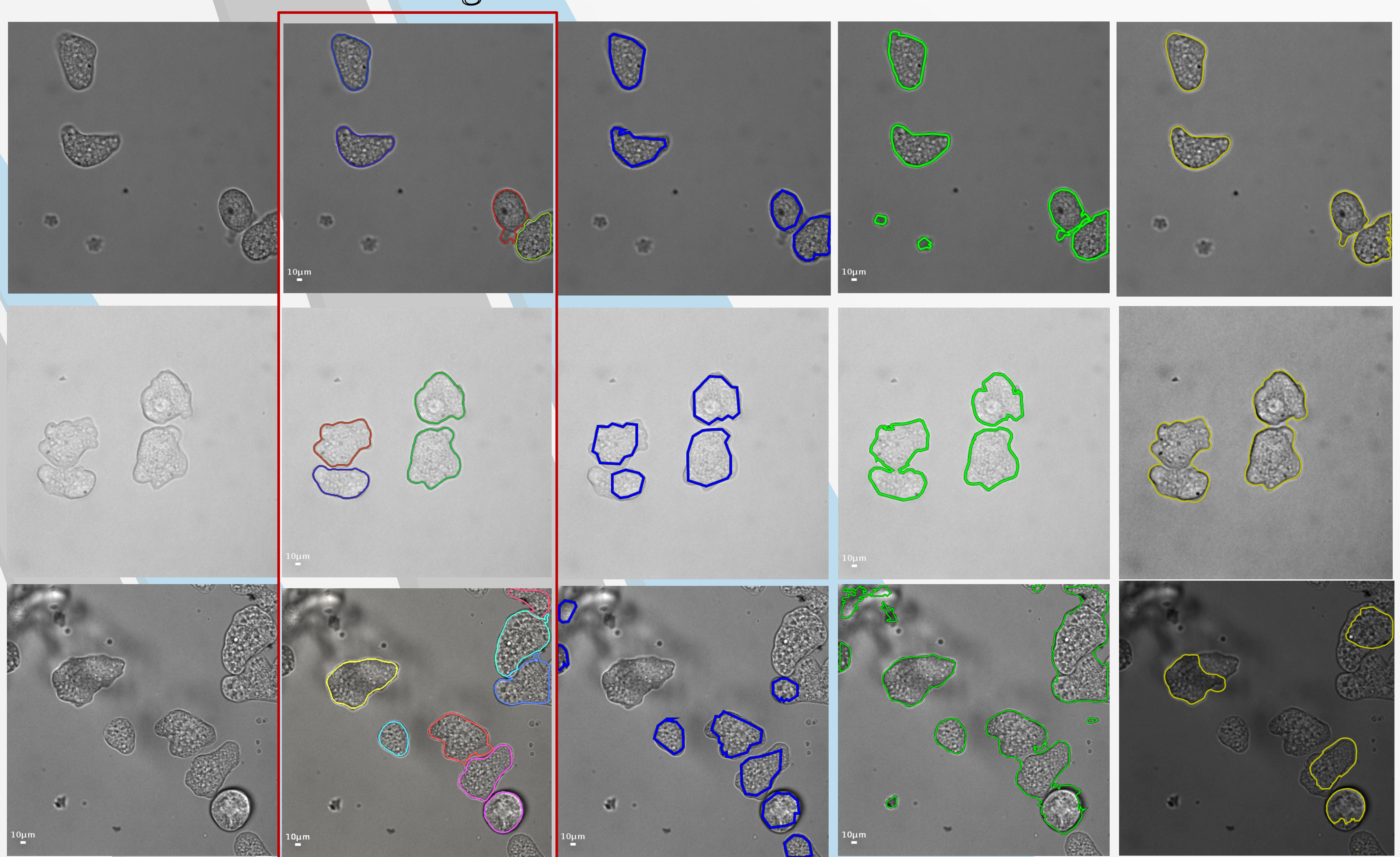
Segmentation Experiments and Results

- Neither region prediction, nor edge indicators are adequately sufficient to segment cells from brightfield imagery.
- Automatic contour initialization is performed by estimating initial cell localization using the variational, hierarchical clustering scheme [5].
- Initialized curves are then evolved outwards with the balloon force function, which encourages curve motion for pixels with high region and low edge prediction value



Original | Reg Sub-net | Edge Sub-net | Initialization | Final

Segmentation results visualization



Original | Multi Cell-Net | ANCIS [4] | U-net [3] | L2S [2]

Multi Cell-Net	L2S [2]	U-net [3]	ANCIS [4]	Multi Cell-Net $\lambda = 0.5$	Multi Cell-Net $\lambda = 0.3$
Average Dice for the dataset					
0.94 ± 0.02	0.78 ± 0.23	0.88 ± 0.14	0.66± 0.26	**0.94 ±0.02**	0.93 ±0.02
Average error for individual cells					
0.83 ± 0.27	0.62 ± 0.35	0.79 ± 0.30	0.66 ± 0.32	0.78 ± 0.16	0.78 ± 0.16

Conclusion

The proposed method is suited to automatically segment touching cells from brightfield microscopy images. Quantitatively, we observe an overall Dice score of 0.93 on test dataset, an improvement of at least 15.9% over an unsupervised method and 5.8% on average over U-net.

References

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