Imperial College London
Department of Computing

Automatic Cell Tracking in Noisy Images for Microscopic Image Analysis

by

Pedro Damian Kostelec

September 2014

Supervised by Ben Glocker

Submitted in part fulfilment of the requirements for the
MSc degree in Computer Science (Artificial Intelligence) of Imperial College London

Contents

1 Introduction DRAFT I **7**

1.1 Motivation DRAFT I 7

1.2 Objectives DRAFT I 8

1.3 Contributions DRAFT I 8

1.4 Report structure DRAFT I 9

2 Related work DRAFT I **10**

2.1 Cell detection DRAFT I 10

2.1.1 Cell segmentation using the Watershed technique DRAFT I 10

2.1.2 Cell segmentation using level sets DRAFT I 11

2.1.3 Cell detection by model learning DRAFT I 11

2.1.4 Cell detection by image restoration DRAFT I 12

2.2 Cell tracking DRAFT I 12

2.2.1 Tracking by model evolution DRAFT I 13

2.2.2 Tracking by frame-by-frame data association DRAFT I 13

2.2.3 Tracking with a dynamics filter DRAFT I 14

2.2.4 Cell tracking by global data association DRAFT I 14

2.3 Conclusion DRAFT I 15

3 Detection of cells DRAFT I **17**

3.1 Method overview DRAFT I 17

3.2 Detection of candidate regions DRAFT I 18

3.3 Inference under the non-overlap constraint DRAFT I 19

3.4 Learning the classifier DRAFT I 20

3.5 Feature selection DRAFT I 20

3.6 Performance improvements DRAFT I 21

4 Tracking of cells DRAFT I **24**

4.1 Method overview DRAFT I 24

4.2 Joining cell detections into robust tracklets DRAFT I 26

4.3 Global data association DRAFT I 27

4.4 Implementation using linear programming DRAFT I 29

4.5 Hypotheses likelihood definitions DRAFT I 30

4.6 Computing the likelihoods DRAFT I 31

4.7 Features for the linking classifier OUTLINE 33

4.7.1 Estimating the velocity with Kalman filters NEW 34

4.7.2 Gaussian broadening feature DRAFT I 34

4.7.3 Best feature selection NEW . . . 35

5 Data acquisition and annotation DRAFT I **36**
5.1 Data acquisition and example datasets DRAFT II . . . 36
5.1.1 Datasets DRAFT II . . . 37
5.1.2 Imaging analysis challenges DRAFT II . . . 40
5.2 The annotation tool DRAFT I . . . 42

6 Experimental results NEW **45**
6.1 Cell detector NEW . . . 45
6.1.1 Speed NEW . . . 45
6.1.2 Detection accuracy NEW . . . 47
6.2 Cell tracker NEW . . . 47
6.2.1 Performance metrics NEW . . . 47
6.2.2 Speed NEW . . . 47
6.2.3 Tracking accuracy . . . 47
6.3 Limitations and areas of improvement NEW . . . 47
6.4 Summary NEW . . . 47

7 Conclusions and future work DRAFT I **48**
7.1 Conclusion DRAFT I . . . 48
7.2 Future work DRAFT I . . . 49

Appendices **51**

A User Guide for the Annotation Tool **52**

B User Guide for the Interactive Annotation Viewer **53**

C User Guide for the Cell Detector and Tracker **54**

Bibliography **55**

6 Experimental results NEW

This feature has not yet been implemented

Explain the software used

Explain the computur used for the evaluation

Separation of experimentail method and results

in experimnental methods they explain the data and the datasets

See the cell population tracking and linear construction with spationtemporal ocntet by Kang et al for a good results section

- tracking examples

- detection and tracking accuracy

- computation time

great Metrics: Research Article, Evaluating Multiple Object Tracking Performance: The CLEAR MOT Metrics

Think about which experiments to do, analyses, comparison with other methods if possible

6.1 Cell detector NEW

Figure 6.1 displays a temporal view of the detected cells. The vertical axis represents the frame of the sequence. The figure clearly shows that "cell tracks" are clearly discernible, even if the number of outliers is significant. For the tracking module it is better to have a higher recall than precision, as outliers can be much more easily discarded than segmented tracks linked.

6.1.1 Speed NEW

Measure the speed of detection in images of different sizes, and different number of cells

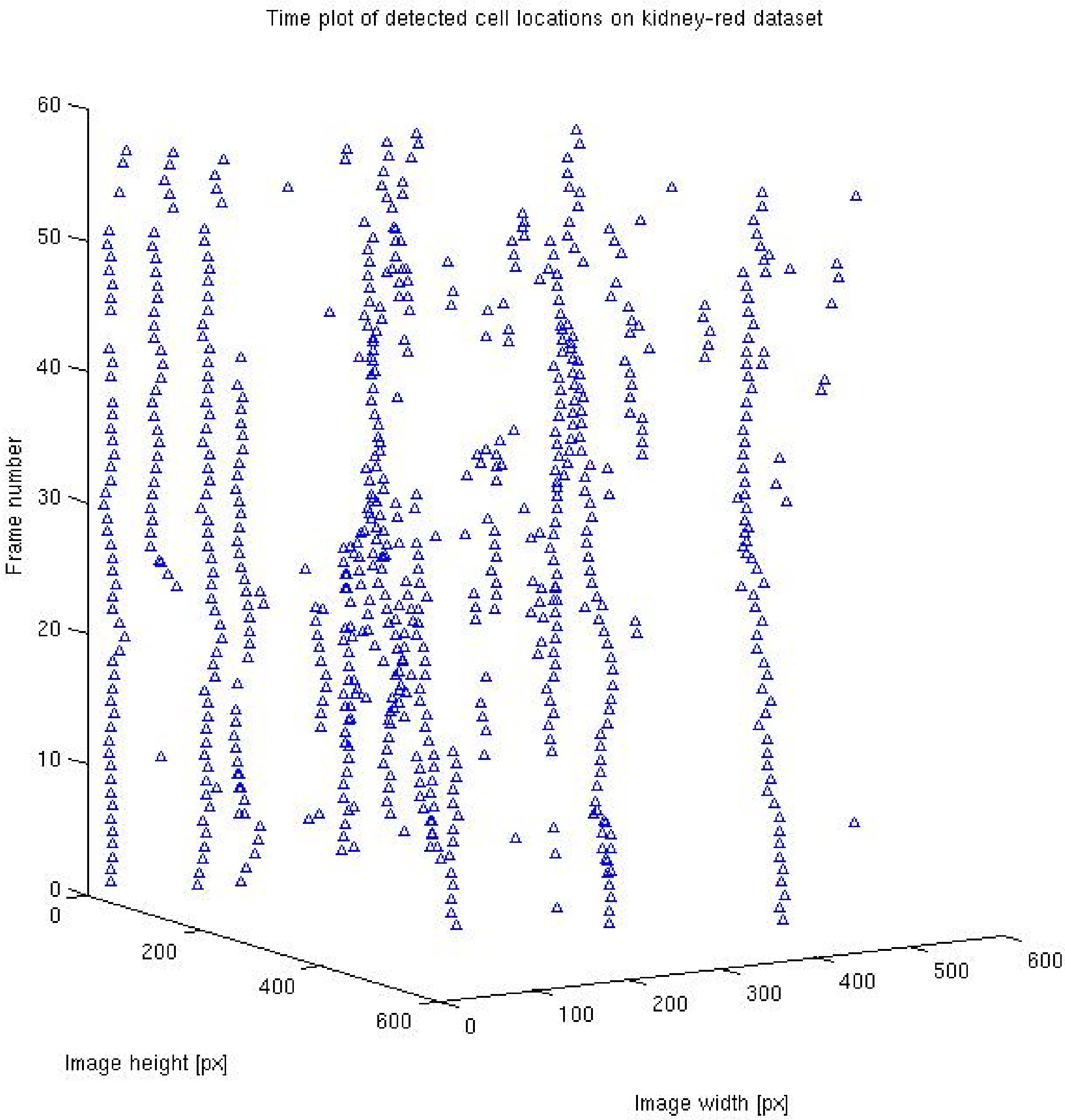

Figure 6.1: Cells detected over 60 consecutive frames are visualized as a time series. The vertical axis corresponds to the frames. Even in this raw detection data, it is possible to see the tracks of some of these cells.

6.1.2 Detection accuracy NEW

6.2 Cell tracker NEW

Define the different measures of accuracy

6.2.1 Performance metrics NEW

6.2.2 Speed NEW

Meause the speed of generating tracks, as a measure of per 1, 100, 1000 frames, depending on the number of tracks

6.2.3 Tracking accuracy

6.3 Limitations and areas of improvement NEW

Answer: what, why, how to improve in future

- detection training: only first few frames of datasets, not random – expect to detect later frames worse - testing on only long datasets: no data on short datasets. diffucult to train (what to link?), difficult to annotate - speed of detector. Reduce number of hypothesis

6.4 Summary NEW

Appendices

Bibliography

[1] P. K. Elzbieta Kolaczkowska, "Neutrophil recruitment and function in health and inflammation," 2013. 7

[2] J. Pillay, I. den Braber, N. Vrisekoop, L. M. Kwast, R. J. de Boer, J. A. M. Borghans, K. Tesselaar, and L. Koenderman, "In vivo labeling with 2h2o reveals a human neutrophil lifespan of 5.4 days," *Blood*, vol. 116, no. 4, pp. 625–627, 2010. 7

[3] P. S. Tofts, T. Chevassut, M. Cutajar, N. G. Dowell, and A. M. Peters, "Doubts concerning the recently reported human neutrophil lifespan of 5.4 days," *Blood*, vol. 117, no. 22, pp. 6050–6052, 2011. 7

[4] C. Arteta, V. Lempitsky, J. A. Noble, and A. Zisserman, "Learning to detect cells using non-extremal regions," in *Proceedings of the 15th International Conference on Medical Image Computing and Computer-Assisted Intervention - Volume Part I*, MICCAI'12, (Berlin, Heidelberg), pp. 348–356, Springer-Verlag, 2012. 8, 9, 11, 17, 18, 19, 20, 21, 22, 48

[5] Y. Chen, K. Biddell, A. Sun, P. Relue, and J. Johnson, "An automatic cell counting method for optical images," in *[Engineering in Medicine and Biology, 1999. 21st Annual Conference and the 1999 Annual Fall Meetring of the Biomedical Engineering Society] BMES/EMBS Conference, 1999. Proceedings of the First Joint*, vol. 2, pp. 819 vol.2–, Oct 1999. 10

[6] X. Chen, X. Zhou, and S.-C. Wong, "Automated segmentation, classification, and tracking of cancer cell nuclei in time-lapse microscopy," *Biomedical Engineering, IEEE Transactions on*, vol. 53, pp. 762–766, April 2006. 10, 13

[7] L. Vincent, "Morphological grayscale reconstruction in image analysis: applications and efficient algorithms," *Image Processing, IEEE Transactions on*, vol. 2, pp. 176–201, Apr 1993. 10

[8] J. Serra, *Image Analysis and Mathematical Morphology.* Orlando, FL, USA: Academic Press, Inc., 1983. 10

[9] D. Mukherjee, N. Ray, and S. Acton, "Level set analysis for leukocyte detection and tracking," *Image Processing, IEEE Transactions on*, vol. 13, pp. 562–572, April 2004. 11, 13

[10] C. Tang, Y. Wang, and Y. Cui, "Tracking of active cells based on kalman filter in time lapse of image sequences of neuron stem cells." 11, 14

[11] D. Xu and L. Ma., "Segmentation of image sequences of neuron stem cells based on level-set

algorithm combined with local gray threshold.," Master's thesis, Harbin Engineering University, 2010. 11

[12] C. Arteta, V. S. Lempitsky, J. A. Noble, and A. Zisserman, "Learning to detect partially overlapping instances.," in *CVPR*, pp. 3230–3237, IEEE, 2013. 11, 12, 19

[13] J. Matas, O. Chum, M. Urban, and T. Pajdla, "Robust wide baseline stereo from maximally stable extremal regions," in *Proceedings of the British Machine Vision Conference*, pp. 36.1–36.10, BMVA Press, 2002. doi:10.5244/C.16.36. 11

[14] T. Joachims, T. Finley, and C.-N. J. Yu, "Cutting-plane training of structural svms," *Mach. Learn.*, vol. 77, pp. 27–59, Oct. 2009. 11

[15] R. Bise, T. Kanade, Z. Yin, and S. il Huh, "Automatic cell tracking applied to analysis of cell migration in wound healing assay," in *Engineering in Medicine and Biology Society,EMBC, 2011 Annual International Conference of the IEEE*, pp. 6174–6179, Aug 2011. 12, 25

[16] S. Huh, *Toward an Automated System for the Analysis of Cell Behavior: Cellular Event Detection and Cell Tracking in Time-lapse Live Cell Microscopy.* PhD thesis, Robotics Institute, Carnegie Mellon University, Pittsburgh, PA, March 2013. 12, 13

[17] D. House, M. Walker, Z. Wu, J. Wong, and M. Betke, "Tracking of cell populations to understand their spatio-temporal behavior in response to physical stimuli," in *Computer Vision and Pattern Recognition Workshops, 2009. CVPR Workshops 2009. IEEE Computer Society Conference on*, pp. 186–193, June 2009. 13

[18] B. Xu, M. Lu, P. Zhu, Q. Chen, and X. Wang, "Multiple cell tracking using ant estimator," in *Control, Automation and Information Sciences (ICCAIS), 2012 International Conference on*, pp. 13–17, Nov 2012. 14

[19] K. Li and T. Kanade, "Cell population tracking and lineage construction using multiple-model dynamics filters and spatiotemporal optimization," in *Proceedings of the 2nd International Workshop on Microscopic Image Analysis with Applications in Biology (MIAAB)*, September 2007. 14

[20] A. Massoudi, D. Semenovich, and A. Sowmya, "Cell tracking and mitosis detection using splitting flow networks in phase-contrast imaging," in *Engineering in Medicine and Biology Society (EMBC), 2012 Annual International Conference of the IEEE*, pp. 5310–5313, Aug 2012. 14

[21] L. Zhang, Y. Li, and R. Nevatia, "Global data association for multi-object tracking using network flows," in *Computer Vision and Pattern Recognition, 2008. CVPR 2008. IEEE Conference on*, pp. 1–8, June 2008. 15, 27

[22] C. Huang, B. Wu, and R. Nevatia, "Robust object tracking by hierarchical association of detection responses," in *Computer Vision - ECCV 2008* (D. Forsyth, P. Torr, and A. Zisserman,

eds.), vol. 5303 of *Lecture Notes in Computer Science*, pp. 788–801, Springer Berlin Heidelberg, 2008. 15, 27

[23] R. Bise, Z. Yin, and T. Kanade, "Reliable cell tracking by global data association.," in *ISBI*, pp. 1004–1010, IEEE, 2011. 15, 25, 27, 30, 48

[24] H. Kuhn, "The hungarian method for the assignment problem," *Naval Research Logistics Quarterly*, vol. 2, pp. 83–97, 1955. 15

[25] J. Matas, O. Chum, M. Urban, and T. Pajdla, "Robust wide-baseline stereo from maximally stable extremal regions," *Image and Vision Computing*, vol. 22, no. 10, pp. 761 – 767, 2004. British Machine Vision Computing 2002. 18

[26] I. Tsochantaridis, T. Hofmann, T. Joachims, and Y. Altun, "Support vector machine learning for interdependent and structured output spaces," in *Proceedings of the Twenty-first International Conference on Machine Learning*, ICML '04, (New York, NY, USA), pp. 104–, ACM, 2004. 20

[27] K. Li, E. D. Miller, M. Chen, T. Kanade, L. E. Weiss, and P. G. Campbell, "Cell population tracking and lineage construction with spatiotemporal context," *Medical Image Analysis*, vol. 12, no. 5, pp. 546 – 566, 2008. Special issue on the 10th international conference on medical imaging and computer assisted intervention - {MICCAI} 2007. 25, 50

[28] M. Looney, E. Thornton, D. Sen, W. Lamm, R. Glenny, and M. Krummel, "Stabilized imaging of immune surveillance in the mouse lung.," *Nature Methods*, vol. 8, no. 5, pp. 91–6, 2011-01-01 00:00:00.0. 36