



Universiteit  
Leiden  
The Netherlands

## Image Analysis and Platform Development for Automated Phenotyping in Cytomics

Yan, K.

### Citation

Yan, K. (2013, November 27). *Image Analysis and Platform Development for Automated Phenotyping in Cytomics*. Retrieved from <https://hdl.handle.net/1887/22550>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/22550>

**Note:** To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/22550> holds various files of this Leiden University dissertation.

**Author:** Yan, Kuan

**Title:** Image analysis and platform development for automated phenotyping in cytomics

**Issue Date:** 2013-11-27

# **Image Analysis and Platform Development for Automated Phenotyping in Cytomics**

K. Yan

严 宽

## Colophon

The studies described in this thesis were performed at the Leiden Institute of Advanced Computer Science in the Imaging & BioInformatics group, Leiden University, Leiden, The Netherlands.

The research was financially supported by the BioRange Project of the Netherlands Bioinformatics Centre (NBIC).

**Printed by** Proefschriftmaken.nl || Uitgeverij BOXPress

**Published by** Uitgeverij BOXPress, 's-Hertogenbosch

**ISBN** 978-90-8891-762-2

# Image Analysis and Platform Development for Automated Phenotyping in Cytomics

## **Proefschrift**

ter verkrijging van

de graad van Doctor aan de Universiteit Leiden,

op gezag van Rector Magnificus Prof. Mr. C.J.J.M. Stolker,

volgens besluit van het College voor Promoties

te verdedigen op woensdag 27 November 2013

klokke 10:00 uur

door

Kuan Yan

geboren te Shanghai, China, in 1982

## **Promotiecommissie**

### *Promotores:*

Prof. Dr. J. N. Kok

Prof. Dr. B. Van de Water

### *Co-promotor:*

Dr. Ir. F.J. Verbeek

### *Overige Leden:*

Prof. Dr. X. Liu

Prof. Dr. H. Tanke

Prof. Dr. P. Lucas

---

The studies described in this thesis were performed at the Leiden Institute of Advanced Computer Science in the Imaging & BioInformatics group, Leiden University, Leiden, The Netherlands.

The research was financially supported by the BioRange Project of the Netherlands Bioinformatics Centre (NBIC).

## Table of Contents

|                                                                    |    |
|--------------------------------------------------------------------|----|
| Chapter 1 Introduction to High-throughput Cytomics.....            | 3  |
| 1.1.    Bioinformatics and Cell Biology .....                      | 4  |
| 1.2.    Image Analysis in High-throughput/High-Content Screen..... | 5  |
| 1.3.    Thesis Scope and Structure .....                           | 10 |
| Chapter 2 Robust Image Segmentation for Cytomics.....              | 13 |
| Chapter Summary .....                                              | 14 |
| 2.1    Introduction .....                                          | 15 |
| 2.2    Existing Segmentation Algorithms .....                      | 16 |
| 2.2.1    Otsu’s Method.....                                        | 16 |
| 2.2.2    Bernsen’s Threshold.....                                  | 16 |
| 2.2.3    Level-set Segmentation.....                               | 16 |
| 2.2.4    Hysteresis Thresholding .....                             | 18 |
| 2.2.5    Watershed Masked Clustering Algorithm .....               | 18 |
| 2.3    Performance Evaluation.....                                 | 25 |
| 2.3.1    Assessment Metrics and Methodology.....                   | 27 |
| 2.3.2    Artificial Objects and Test Images .....                  | 29 |
| 2.3.3    HT29 Phalloidin Images.....                               | 29 |
| 2.3.4    MTLn3 GFP Images.....                                     | 30 |
| 2.3.5    MA Images.....                                            | 30 |
| 2.3.6    Result of Benchmark Study .....                           | 31 |
| 2.4    Computation Complexity .....                                | 35 |
| 2.5    Conclusion and Discussion .....                             | 36 |
| Chapter 3 Robust Object Tracking for Cytomics .....                | 39 |
| Chapter Summary .....                                              | 40 |
| 3.1.    Introduction .....                                         | 41 |
| 3.2.    Performance Study.....                                     | 48 |
| 3.2.1.    Tracking Efficiency Metrics .....                        | 50 |
| 3.2.2.    Results of Efficiency Estimation .....                   | 53 |
| 3.2.3.    Temporal Resolution Variance .....                       | 57 |
| 3.3.    Conclusions and Discussion.....                            | 59 |
| Acknowledgement .....                                              | 60 |
| Chapter 4 A Study to Cell Migration Analysis .....                 | 61 |
| Chapter Summary .....                                              | 62 |
| 4.1.    Workflow of Growth Factor Analysis .....                   | 63 |
| 4.1.1.    Experiment Design .....                                  | 63 |
| 4.1.2.    Image Analysis.....                                      | 64 |

|                                |                                                                                                   |     |
|--------------------------------|---------------------------------------------------------------------------------------------------|-----|
| 4.1.3.                         | Data Analysis .....                                                                               | 67  |
| 4.2.                           | Analysis of GF Regulation .....                                                                   | 69  |
| 4.2.1.                         | Differential effect of individual and combined GF stimulation .....                               | 69  |
| 4.2.2.                         | HGF stimulation increases speed while EGF increases the migration persistence of MTLn3 cells..... | 70  |
| 4.2.3.                         | Temporal-Order Statistics .....                                                                   | 71  |
| 4.3.                           | Conclusions and Discussion .....                                                                  | 72  |
| Chapter 5                      | A Study to the Dynamics of Matrix Adhesion.....                                                   | 75  |
| Chapter Summary.....           |                                                                                                   | 76  |
| 5.1.                           | Workflow of Matrix Adhesion dynamics Analysis.....                                                | 77  |
| 5.1.1.                         | Experiment Preparation and Image Acquisition .....                                                | 77  |
| 5.1.2.                         | Image Analysis .....                                                                              | 79  |
| 5.1.3.                         | Data Analysis .....                                                                               | 87  |
| 5.2.                           | Phenotypical Correlation Study of the Live Cell .....                                             | 88  |
| 5.3.                           | Conclusion and Discussion .....                                                                   | 91  |
| Chapter 6                      | Reasoning over Data in HT/HC Management.....                                                      | 93  |
| Chapter Summary.....           |                                                                                                   | 94  |
| 6.1.                           | Principle Design of HT/HC Management System .....                                                 | 95  |
| 6.2.                           | Implementation of Layers .....                                                                    | 97  |
| 6.2.1.                         | End-user GUI Layer.....                                                                           | 97  |
| 6.2.2.                         | WS-API Layer .....                                                                                | 101 |
| 6.3.                           | Conclusion and Discussion .....                                                                   | 104 |
| Acknowledgement.....           |                                                                                                   | 106 |
| Chapter 7                      | Conclusion and Discussion.....                                                                    | 107 |
| 7.1.                           | Conclusions.....                                                                                  | 108 |
| 7.2.                           | Discussion .....                                                                                  | 109 |
| References.....                |                                                                                                   | 112 |
| Nederlandse Samenvatting ..... |                                                                                                   | 121 |
| English Summary .....          |                                                                                                   | 123 |
| List of Publications.....      |                                                                                                   | 125 |
| Curriculum Vitae.....          |                                                                                                   | 126 |
| Acknowledgements .....         |                                                                                                   | 127 |