Particle Filtering Methods for Subcellular Motion Analysis
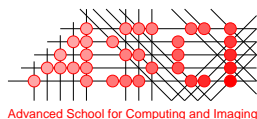
Ihor Smal

Colophon

This book was typeset by the author using LaTeX2$_\varepsilon$. The main body of the text was set using a 10-points Computer Modern Roman font. All graphics and images were included formatted as Encapsulated PostScript (^{TM}Adobe Systems Incorporated). The final PostScript output was converted to Portable Document Format (PDF) and transferred to film for printing.

Cover design by the author using the Persistence of Vision Raytracer (POV-Ray 3.6), a high-quality, totally free tool for creating three-dimensional graphics. The graphics on the cover symbolically represents some of the constituents of the Bayesian estimation framework: measurements (fluorescence microscopy images), a posterior probability density function approximated by a set of "particles", estimated tracks and randomness (symbolized by dices).

Particle Filtering Methods for Subcellular Motion Analysis

Probabilistische methoden voor subcellulaire bewegingsanalyse

Proefschrift

ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de
rector magnificus

Prof.dr. S.W.J. Lamberts

en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op
woensdag 10 juni 2009 om 9:45 uur

door

Ihor Smal

geboren te Lviv, Oekraïne

ERASMUS UNIVERSITEIT ROTTERDAM

Promotiecommissie

Promotor:	**Prof.dr. W.J. Niessen**
Overige leden:	**Prof.dr.ir. H.H. Weinans**
	Dr.ir. N.J. Galjart
	Dr. J.-C. Olivo-Marin
Copromotor:	**Dr.ir. H.W. Meijering**

Preface

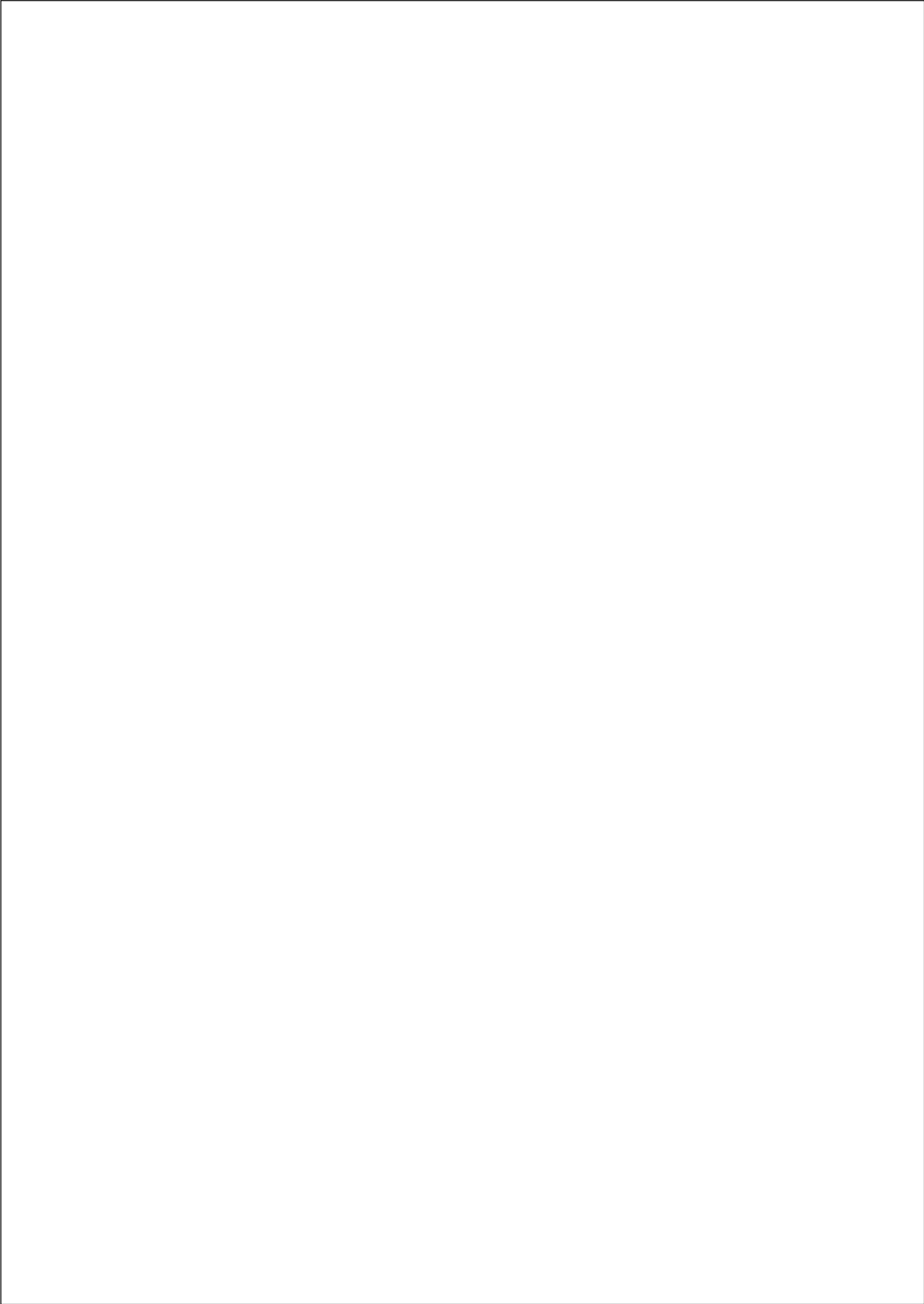*Do not be desirous of having things done quickly. Do not look at small advantages. Desire to have things done quickly prevents their being done thoroughly. Looking at small advantages prevents great affairs from being accomplished.*
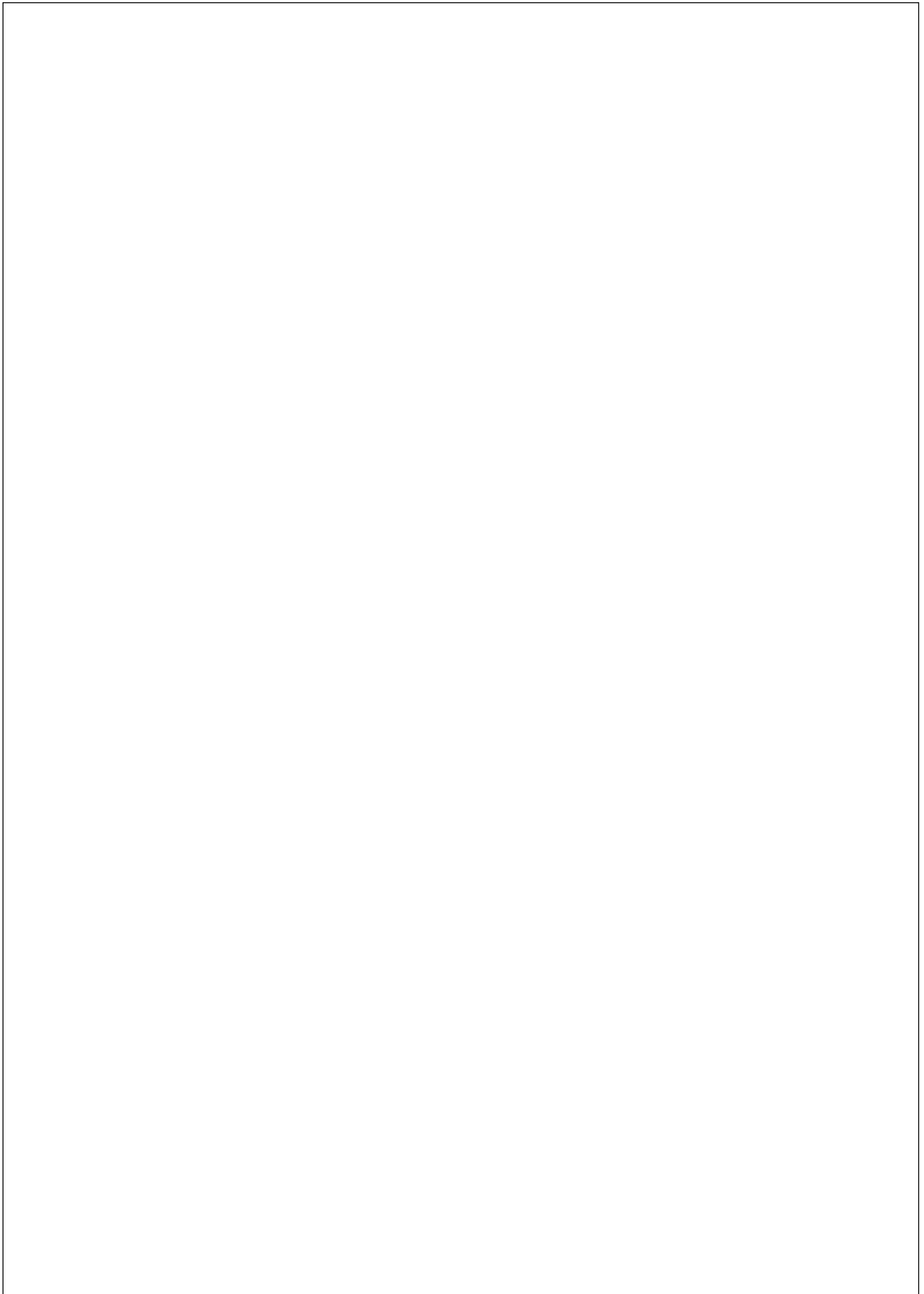
— CONFUCIUS (551–479 B.C.)

T his thesis describes the research I carried out as part of my Ph.D. study at the Erasmus University Rotterdam.

Ihor Smal
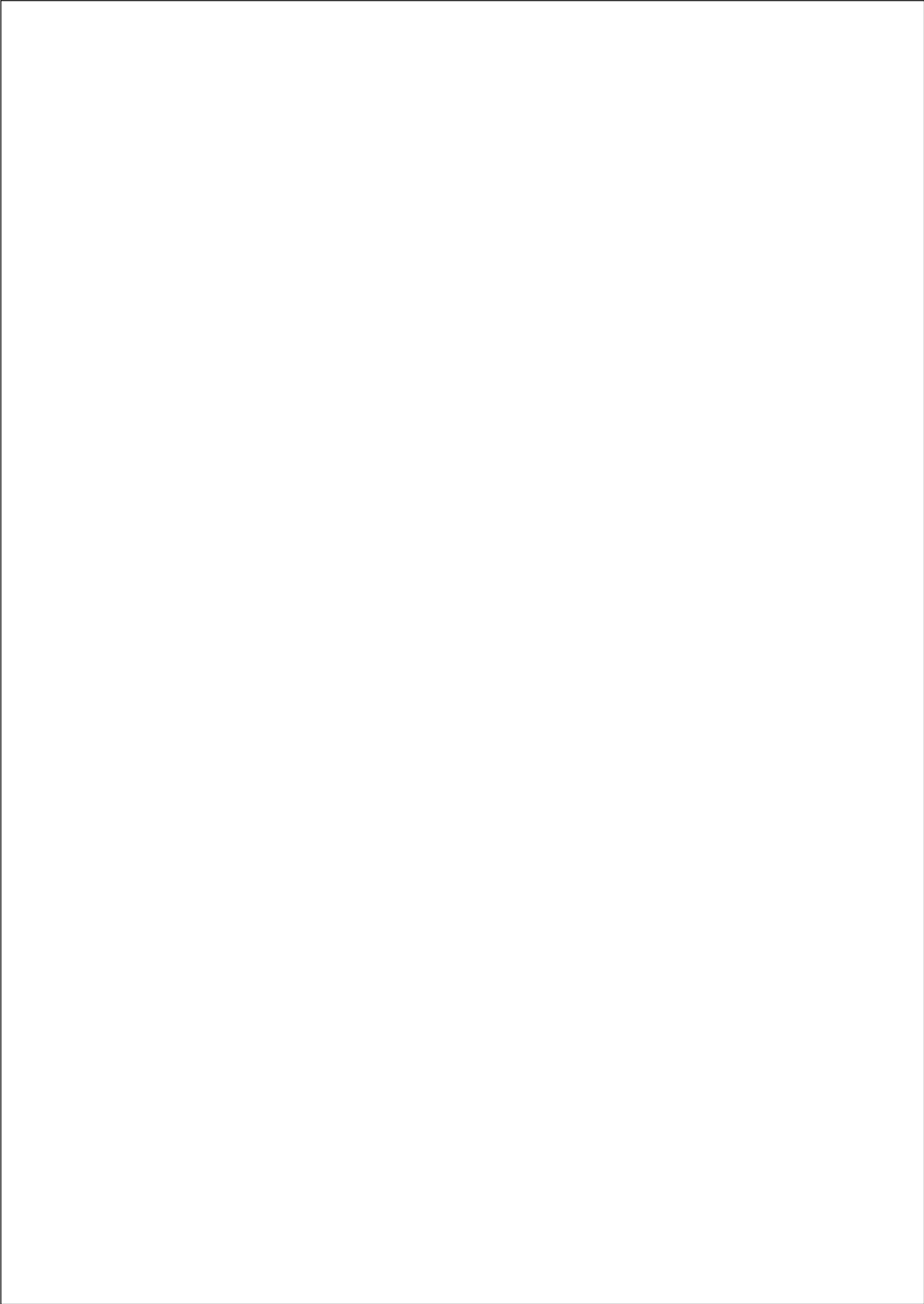Rotterdam, February 2009

Contents

Introduction

There are two possible outcomes: If the result confirms the hypothesis, then you've made a measurement. If the result is contrary to the hypothesis, then you've made a discovery.

— ENRICO FERMI (1901–1954)

1.1 Studying Intracellular Dynamics

The past decades have witnessed development of groundbreaking tools and techniques for imaging and studying cellular and intracellular structures and processes. The advent of confocal microscopy in the early sixties accompanied by discovery of fluorescent proteins has triggered the development of new imaging techniques and revolutionized the way biologists study cells and the way they function. Currently, fluorescence microscopy imaging is still the most important and frequently used tool for studying intracellular dynamics with a high spatial and temporal resolution. Proper understanding of cellular and molecular processes is of great interest to academic researches as well as pharmaceutical industries. The possibility to influence those processes in a controlled way is a prerequisite to combat diseases and improve human health care, which will have profound social and economic impact.

Quantitative Comparison of Spot Detection Methods in Fluorescence Microscopy

Not everything that can be counted counts, and not everything that counts can be counted.

— ALBERT EINSTEIN (1879-1955)

Abstract — Quantitative analysis of biological image data generally involves the detection of many subresolution spots. Especially in live cell imaging, for which fluorescence microscopy is often used, the signal-to-noise ratio (SNR) can be extremely low, making automated spot detection a very challenging task. In the past, many methods have been proposed to perform this task, but a thorough quantitative evaluation and comparison of these methods is lacking in the literature. In this chapter, we evaluate the performance of the most frequently used detection methods for this purpose. These include six unsupervised and two supervised methods. We perform experiments on synthetic images of three different types, for which the ground truth was available, as well as on real image data sets acquired for two different biological studies, for which we obtained expert manual annotations to compare with. The results from both types of experiments suggest that for very low SNRs ($\approx$2), the supervised (machine learning) methods perform best overall. Of the unsupervised methods, the detector based on the so-called h-dome transform from mathematical morphology performs comparably, and has the advantage that it does not require a cumbersome learning stage. At high SNRs (>5), the difference in performance of all considered detectors becomes negligible.

2.1   Introduction

The very first stage in the analysis of biological image data generally deals with the detection of objects of interest. In fluorescence microscopy, which is one of the most basic tools used in biology for the visualization of subcellular components and their dynamics, the objects are labeled with fluorescent proteins and appear in the images as bright spots, each occupying only a few pixels for sample images).

Summary

If people do not believe that mathematics is simple, it is only because they do not realize how complicated life is.

— JOHN LOUIS VON NEUMANN (1903–1957)

A dvances in fluorescent probing and microscopic imaging technology have revolutionized biology in the past decade and have opened the door for studying subcellular dynamical processes.

Bibliography

One's work may be finished someday, but one's education, never.

— Alexandre Dumas, père (1802 - 1870)
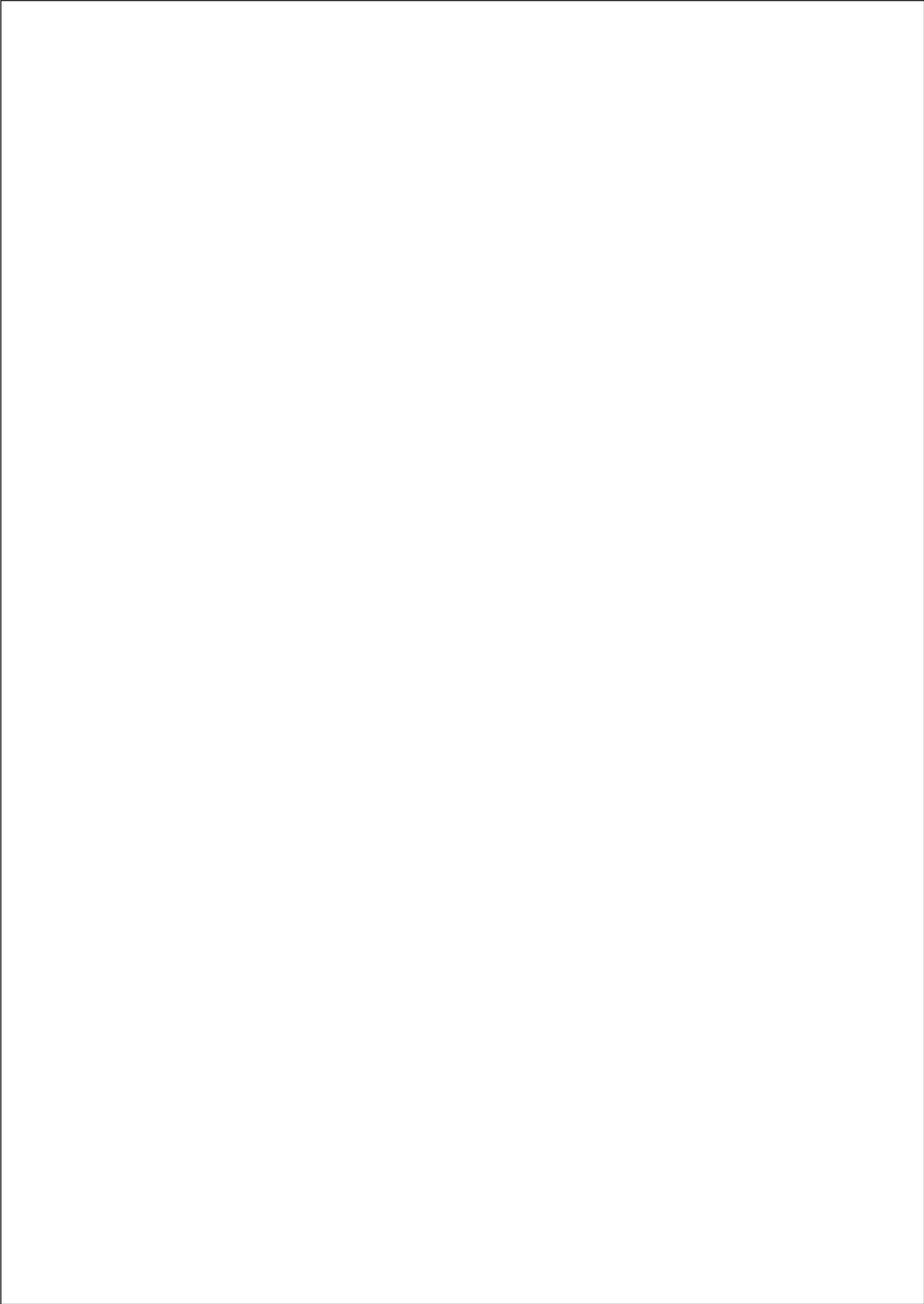
Samenvatting

D e ontwikkeling van fluorescentie microscopie heeft in de afgelopen tien jaar bijgedragen aan revolutionaire vooruitgangen in de biologie en heeft nieuwe wegen geopend voor het bestuderen van intracellulaire dynamische processen.

PhD Portfolio

Research Skills:

- M.Sc. degree in Electrical Engineering, Ivan Franko National University of Lviv, Ukraine, 1999

- Professional Doctorate in Engineering (PDEng) degree, Technical University of Eindhoven, the Netherlands, 2005

In-Depth Courses:

- Knowledge driven Image Segmentation, ASCI, 2005

- Measuring Features, ASCI, 2006

- Front-End Vision and Multiscale Image Analysis, ASCI, 2007
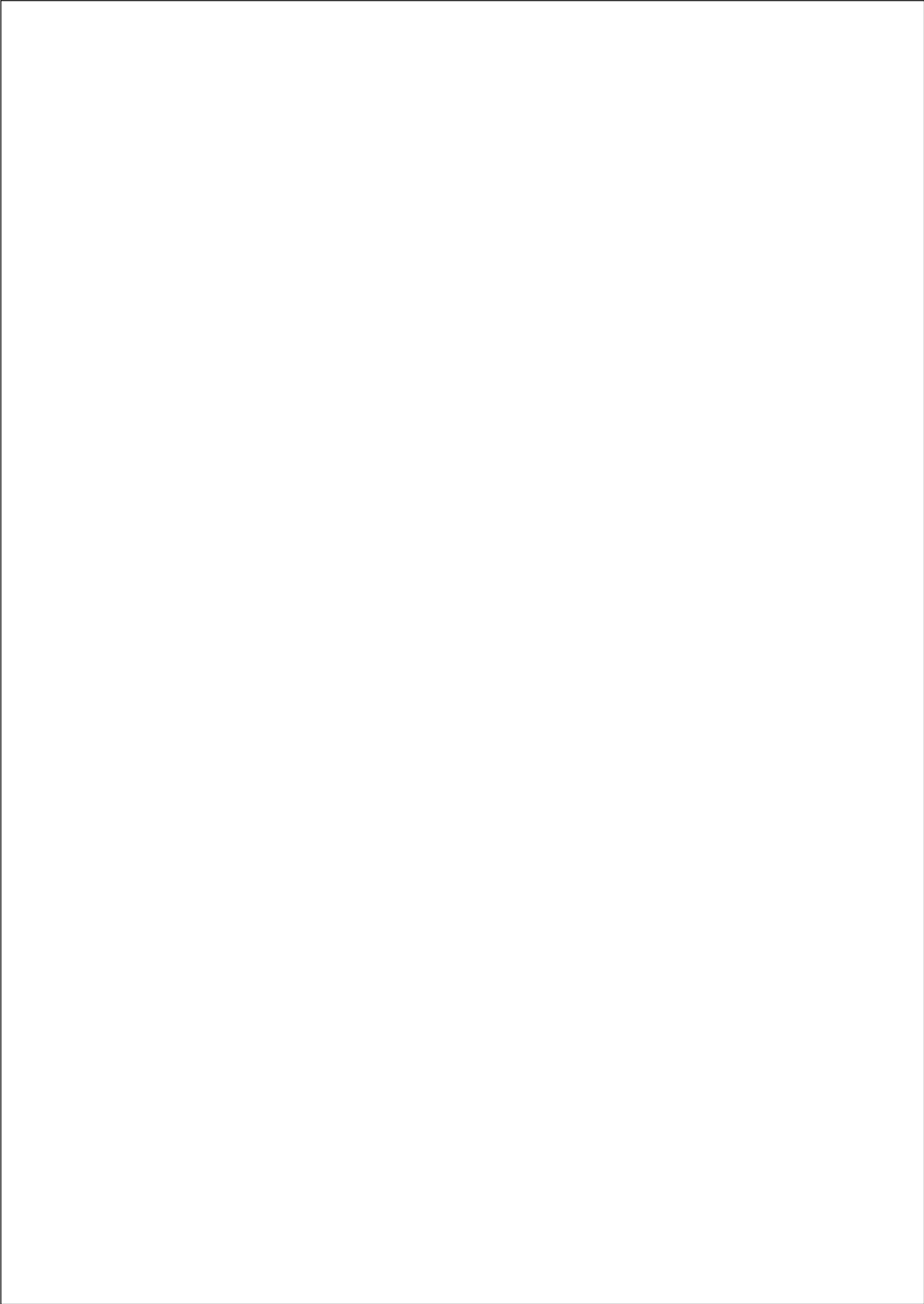
- BioInformatics, ASCI, 2007

International Conference Presentations:

- IEEE International Symposium on Biomedical Imaging: From Nano to Macro — ISBI 2006, Arlington, VA, USA, April 6–9, 2006

- IEEE Nonlinear Statistical Signal Processing Workshop: Classical, Unscented and Particle Filtering Methods — NSSPW 2006, Cambridge, UK, September 13-15, 2006

- IEEE International Symposium on Biomedical Imaging: From Nano to Macro — ISBI 2007, Arlington, VA, USA, April, 12–15, 2007

- Information Processing in Medical Imaging — IPMI 2007, Kerkrade, the Netherlands, July 2-6, 2007

- IEEE International Symposium on Biomedical Imaging: From Nano to Macro — ISBI 2008, Paris, France, May 14–17, 2008

Invited Lectures and Seminars:

- Promovendidagen 2006, Maastricht, January 26-27, 2006
- Medical Imaging Symposium for PhD-Students, University Medical Center Utrecht, January 11, 2007

Travel Grants:

- Student travel grant, IEEE International Symposium on Biomedical Imaging: From Nano to Macro — ISBI 2007, Arlington, VA, USA, April, 12–15, 2007

Other:

- Referee activities for various international scientific journals (IEEE Transactions on Medical Imaging, IEEE Transactions on Image Processing, IEEE Transactions on Biomedical Engineering, Image and Vision Computing, Sensors) and international conferences (IEEE International Conference on Image Processing (ICIP) and International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI))

Publications

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- E. Meijering, **I. Smal**, G. Danuser, "Tracking in Molecular Bioimaging", *IEEE Signal Processing Magazine*, vol. 23, no. 3, pp, 46–53, May 2006

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Curriculum Vitae

Ihor Smal was born in Lviv, Ukraine, on April 7, 1977. He received a M.Sc. degree (cum laude) in Electrical Engineering from Ivan Franko National University of Lviv, Ukraine, in 1999. From 1999 to 2002, he was a Research Scientist at the Electrical Engineering department of the same university. During that period he carried out research in the field of nonlinear and chaotic dynamical systems.

From 2003 to 2005, he was a Research Assistant (postmaster program "Mathematics for Industry") at the department of Mathematics and Computer Science of Technical University of Eindhoven, the Netherlands. In 2005 he graduated on the project "Design and implementation of a six camera scanning unit" and was awarded a Professional Doctorate in Engineering degree (PDEng).

From Feb. 2005 to Feb. 2009 he was a Ph.D. student at the Departments of Medical Informatics and Radiology of the Erasmus University Rotterdam, the Netherlands. His research topic was tracking and motion analysis in cellular and molecular bioimaging. The project was carried out in collaboration with the Department of Cell Biology and Department of Pathology at Erasmus MC Rotterdam. The results are described in this thesis.