CENTRE FOR **STOCHASTIC GEOMETRY** AND ADVANCED **BIOIMAGING**

Annual Report 2015

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AND ADVANCED **BIOIMAGING**

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Group photo from the *Eleventh Internal CSGB Workshop,* 26 – 27 November 2015, Moesgaard Museum.

INTRODUCTION

CSGB was established 1 April 2010 with a grant from the Villum Foundation of DKK 25 million. A second funding period started April 2015, based on an additional grant from the Villum Foundation of DKK 30 million.

The background for establishing CSGB is the increasing demand for developing **stochastic analysis of advanced bioimaging data**. The data may arise from electron microscopy, giving access down to the molecular level. Bioimaging data are extremely challenging to analyze, because of their complexity and huge size.

CSGB joins four Danish research groups: the *stochastic geometry group* at Department of Mathematics, Aarhus University (AU), the *stereology and EM research laboratory*, AU, the *spatial statistics group* at Department of Mathematical Sciences, Aalborg University (AAU), and the *image section*, Department of Computer Science, University of Copenhagen (KU). Such short geographical distance facilitates the exchange of competences in the key disciplines of CSGB. These include **stereology**, **spatial statistics** and **statistical image analysis**. Denmark is the world-leading country for stereology of microscopy images.

2015 has been a year of changes for CSGB. Four PhD students have successfully defended their thesis. We expect the same number in 2016. It is always a bit sad to say goodbye to the young researchers, but at the same time it is, of course, a positive event, because they have finished an important task and are now moving on to new challenges.

Based on the new grant of the second funding period of CSGB, we started in 2015 to hire new staff. When CSGB II is up running, we expect that we will have 10-12 new PhD students and 4 new postdocs.

Since primo April 2016, an updated version of the **homepages of CSGB** (csgb.dk), describing the new research plan for the second funding period, has been available. We have tried to make the homepages informative both for research administrators, for researchers from related fields and for our own research community. We hope that we have succeeded, at least to a modest degree.

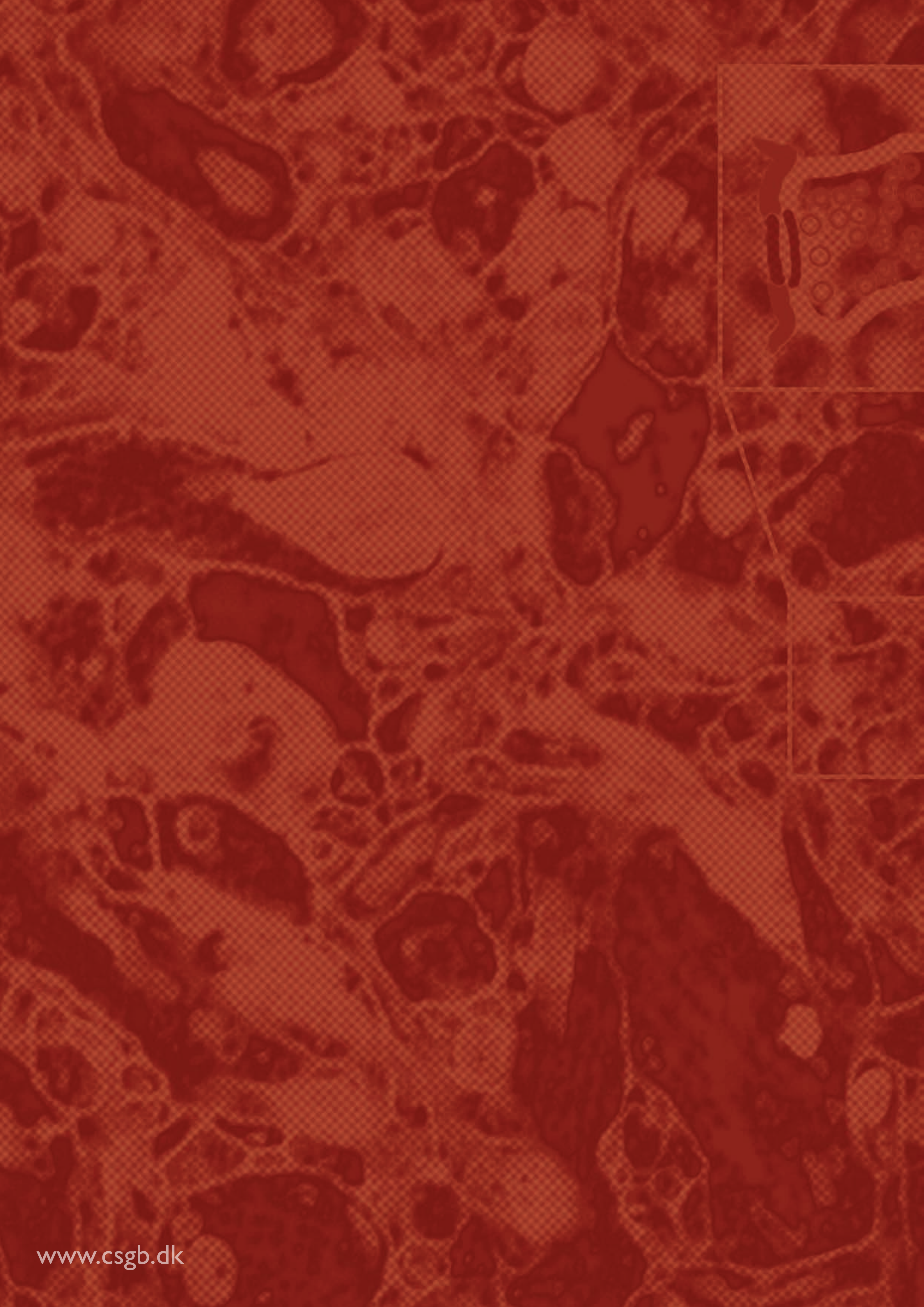
In 2015, we have initiated a number of the projects in the new research plan for CSGB II. This research plan involves **six work packages** dealing with basic research questions in stochastic geometry as well as concrete applications in bioimaging. On the experimental side, we have focused on automatic serial sampling, using Focused Ion Beam Scanning Electron Microscopy (FIB-SEM). Currently, ways of optimizing tissue preparation and image acquisition are under development.

One of the absolute highlights of 2015 was the publication of the **monograph** entitled *Spatial Point Processes: Methodology and Applications with R* by Adrian Baddeley, Rolf Turner and Ege Rubak. Also, it is worth mentioning that the list of CSGB publications for 2015 shows that CSGB researchers publish in the absolute **top international journals**. For instance, two statistical papers have in 2015 appeared in *Journal of the Royal Statistical Society, Series B*.

An important ambition for CSGB is to develop the new methods to a stage where they can be applied by the relevant users. CSGB was particularly active in this respect in 2015 where eights stereology courses were held all over the world.

In 2016, we look forward to the upcoming *Workshop on Geometry and Stochastics of Nonlinear, Functional and Graph Data*, 15 – 19 August 2016, Rønne. This workshop is arranged jointly by the stochastic geometry group, AU, and the image section, KU.

April 2016
Eva B. Vedel Jensen



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ORGANIZATION AND STAFF

ORGANIZATION AND STAFF

The research group leaders:
Markus Kiderlen, Jens R. Nyengaard, Jesper Møller and Mads Nielsen.

THE FOUR RESEARCH GROUPS

CSGB joins the following four internationally recognized Danish research groups:

AU-math: stochastic geometry group
Department of Mathematics, Aarhus University

AU-bio: stereology and EM research laboratory
Aarhus University

AAU: spatial statistics group
Department of Mathematical Sciences, Aalborg University

KU: image section
Department of Computer Science, Copenhagen University

The four research groups possess complementary competences, needed for the interdisciplinary research projects running at CSGB. It is noteworthy that within the short geographical distances in Denmark, competences in the key disciplines of CSGB are available.

Collaboration between groups

During the first funding period, CSGB has become a fruitful environment for mutual interaction between the four research groups.

Especially, the projects involving analysis of concrete bioimaging data require the involvement of two or more groups. Examples from the first funding period are projects dealing with

- the **minicolumn hypothesis** in the cerebral cortex of the brain
- **protein interactions** inferred from FRET data
- the density and level of repulsion of **vesicles** in the presynaptic area

The second funding period, that started 1 April 2015, involves an intensified collaboration between the four research groups, drawing on the experience from the first funding period.

Research group leaders

In the second funding period, **Markus Kiderlen** has taken over the direction of the stochastic geometry group (AU-math) in Aarhus. The directors of the other research groups are **Jens R. Nyengaard** (AU-bio), **Jesper Møller** (AAU) and **Mads Nielsen** (KU), as in the first funding period.

DIRECTOR AND PRINCIPAL INVESTIGATORS

Director of CSGB

The director of CSGB in the first funding period, **Eva B. Vedel Jensen**, continues in this position in the second funding period.

Principal investigators

The research in the second funding period is organized in six work packages, see the research diagram below that also shows the many interconnections between the projects.
The principal investigators of the work packages are also shown in the diagram, just below the title of the work packages.
Junior researchers have been given increased responsibility in the second funding period.

WP1

VALUATION THEORY
Eva B. Vedel Jensen and **Markus Kiderlen**

- Tensor valuations and integral geometry
- Isoperimetric inequalities with tensor constraints
- Uniqueness of measurement functions in integral formulae
- Stereology of tensors

WP2

RANDOM SHAPES
Aasa Feragen and **Stefan Sommer**

- Deformation modelling and statistics of deformations
- Modelling and inference in non-linear spaces
- Applications in diffusion weighted imaging

WP3

SPATIAL AND SPATIO-TEMPORAL POINT PROCESSES
Jesper Møller and **Rasmus P. Waagepetersen**

- Point processes on linear networks
- Point process models and inference for attributed directed graphs
- Determinantal point process modelling
- Sparse models for multivariate spatial point processes
- Inference from quadrat count data

WP4

POINT PROCESSES IN BIOIMAGING
Jens R. Nyengaard and **Ute Hahn**

- Nodule identification and classification from confocal microscopy
- Characterization of moving protein clusters using TIRF imaging
- Synaptic vesicle sampling, distribution and shape from electron microscopy
- Improved variance prediction for stereological estimators of total number

WP5

STATISTICS FOR STOCHASTIC GEOMETRY MODELS
Ute Hahn and **Kristjana Ýr Jónsdóttir**

- Asymptotics for excursion sets – extremal properties
- Monte Carlo envelope tests for random closed sets
- Estimation of sample spacing for stochastic processes

WP6

ALGORITHMS
Markus Kiderlen and **François Lauze**

- Digital grey-value stereology
- Shape reconstruction from tensors
- Reconstruction and segmentation of 3D images
- Algorithms for single particle cryo-electron microscopy

ORGANIZATION AND STAFF

AU-MATH Competences

- stereology
- stochastic geometry
- topology
- statistics for functional data
- brain imaging

AU-BIO Competences

- light microscopy
- fluorescence microscopy
- electron microscopy

AU-MATH

Within CSGB, the AU-math group is engaged in advanced mathematical research as well as in practical applications.

A key research topic for AU-math is **tensor valuations in stochastic geometry**, including their integral geometry, their role in stochastic modelling and their estimation from digital grey-value images. Tensor valuations may be used as shape descriptors. Methods for estimating shape and orientation of particles from tensor valuations are studied in close collaboration with AU-bio.

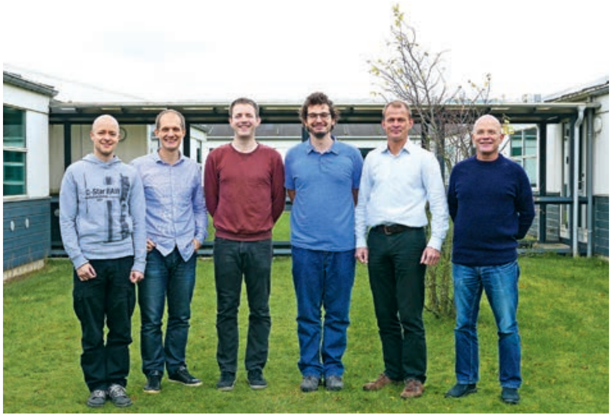
Another important research topic for AU-math concerns **statistics for stochastic geometry models**. In particular, the statistical properties of Monte Carlo envelope tests for functional data are studied.

AU-BIO

The AU-bio group plays a key role in CSGB as a forum for testing and validating methods developed in collaboration with the three other participating research groups.

The research plan for the second funding period of CSGB involves a new imaging modality, focused ion beam scanning electron microscopy **(FIB-SEM)**. By means of FIB-SEM biological objects with a resolution of 5 nm or less can be visualized. The aim is to study synaptic vesicles, using this imaging technique.

The AU-bio group follows closely the development of two novel microscopy techniques, **Clarity** and **Cubic**, and study their implementation. These tissue clearing techniques, that have appeared during the last years, are compatible with various microscopy platforms and open up new opportunities for studying subcellular structures and molecules.



AAU Competences

- spatial point processes
- spatio-temporal point processes
- computational statistics

KU Competences

- stochastic shape modelling
- Bayesian inference
- partial differential equations for imaging

AAU

Within CSGB, the AAU group contributes with basic research in spatio-temporal point processes. A focus point is modelling and statistical inference for **point processes in non-Euclidean spaces** such as linear networks and directed graphs.

In the case of linear networks, a main problem in transferring the well-established theory of point processes in Euclidean spaces is the geometry of the network itself. It is important to take the network geometry into account such that the interpretation of functions defined on the network does not depend on the geometry and data on different networks can be compared directly.

In the first funding period of CSGB, the AAU and the AU-bio group have been involved in important applications of point processes in bioimaging. The applications concern

- the **minicolumn hypothesis** in the cerebral cortex of the brain
- **protein interactions** inferred from FRET data

Both projects continue in the second funding period of CSGB.

KU

Within CSGB, the research focus of the KU group is on statistical modelling of **random shapes**. Such modelling is extremely challenging because shapes reside in non-linear spaces. Examples are manifolds, stratified spaces and general metric spaces. Applications may involve tree-like shape spaces.

In the first funding period of CSGB, the KU and the AU-bio group have collaborated in two projects on

- tomographical reconstruction of **protein structures** from cryo-electron microscopy images
- the density and level of repulsion of **vesicles** in the presynaptic area

Both projects will continue in the second funding period of CSGB. A third application area, taken up in the second funding period, is diffusion weighted imaging.

ORGANIZATION AND STAFF

NEWS ABOUT STAFF/ EVENTS 2015

PHD DEFENSES

The following PhD students at CSGB defended their thesis in 2015:

May 2015 | Mahdieh Khanmohammadi (KU)
Statistical modelling of synaptic vesicles distribution and analysing their physical characteristics

August 2015 | Farzaneh Safavimanesh (AAU)
Spatial point processes for linear structures, especially in the three-dimensional space

October 2015 | Jan-Otto Hooghoudt (AAU)
Bayesian inference of the spatial distribution of proteins from Förster resonance energy transfer data

October 2015 | Jay Rai (AU-bio)
Molecular studies of tagged wild-type and mutated pyruvate dehydrogenase complex under native and crosslinking conditions

NEW APPOINTMENTS

PhD students: Jibrin Danladi (AU-bio, July 2015), Line Kühnel (KU, January 2016), Franscisco Cuevas (AAU, February 2016).

Postdocs: Christophe Bisco (AAU, October 2015)

Ute Hahn (AU-math) and Ege Rubak (AAU) have been promoted to associate professorships in 2015 (Ute from a four-year research associate professorship).

HONOURS/AWARDS

Jesper Møller (AAU) became Knight of the Order of Dannebrog in April 2015.

In July 2015, **Stefan Sommer** (KU) was awarded an Honourable Mention at the Information Processing in Medical Imaging (IPMI) 2015 Conference for his paper entitled *Anisotropic distributions on manifolds: template estimation and most probable paths.*

HOMEPAGE.

An updated version of the homepages of CSGB (csgb.dk), describing the new research plan for the second funding period, has been available since primo April 2016.

HIGHLIGHTS

Monograph
Baddeley, A., Turner, R. & Rubak, E. (2015): *Spatial Point Patterns: Methodology and Applications with R.* Chapman & Hall/CRC, Boca Raton.

The publication of the **monograph** represents one of the absolute highlights of 2015. The monograph describes modern statistical methodology and software for analyzing spatial point patterns. It covers a wider range of advanced techniques than other books on spatial point pattern analysis which focus on a particular domain (ecology, geography, biology, etc.) and it explains the core principles of statistical methodology for spatial point patterns, yet it is focused on applications.

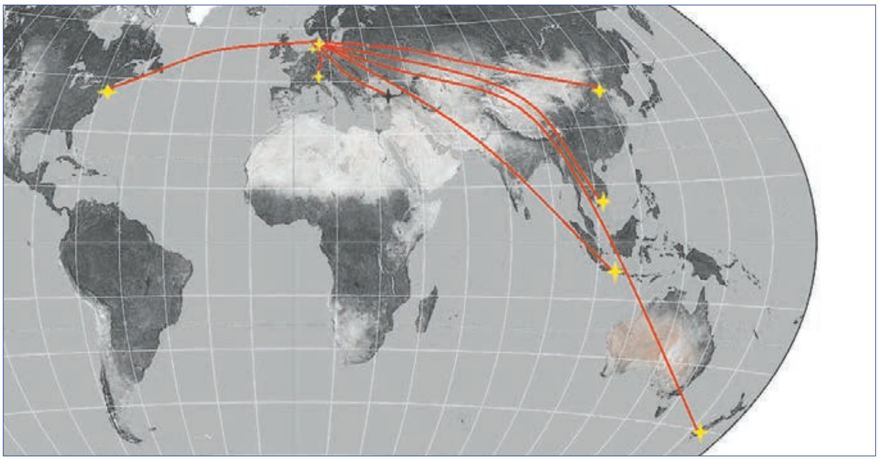
Jens R. Nyengaard (AU-bio) was in 2015 appointed as scientific editor of *Journal of Microscopy*.

The Faculty of Engineering and Science, Aalborg University, has awarded **Adrian Baddeley** a Doctor philosophiae honoris causa at a graduation ceremony on 17 April 2015.

NATIONAL DISSEMINATION

Talks for high-school audiences and UNF

Jon Sporring (KU) gave in 2015 the talk "Statistik på de små grå - om nerveceller" for high-school audiences at several occasions. He also gave the talk "Hvoraf opstår tanker? Kan de beskrives ved en computer model?" in the forum of Ungdommens Naturvidenskabelige Forening (UNF).



Stereology courses/workshops were held in 2015 by CSGB researchers at the following locations: Dunedin, New Zealand; Samsun, Turkey; Boston, USA; Beijing, China; Bern, Switzerland; Sandbjerg, Denmark; Can Tho, Vietnam; Yogyakarta, Indonesia. The map is modified from wikipedia.org/wiki/World_map.

INTERNATIONAL DISSEMINATION

Stereology courses

An important ambition for CSGB is to develop the new methods to a stage where they can be applied by the relevant users. New stereological methods are taught at a variety of international courses for researchers interested in sampling and measurement of 3D structures.

Three type of courses are organized, 1-day crash courses in stereology, 3-4-day PhD courses and more extensive 1-week courses featuring lectures, classroom exercises with real biomedical images, laboratory practicals, demonstrating the implementation of proper sampling and processing techniques on real biological organs, as well as introduction to stereological software. Topics covered include

- design of efficient, design-unbiased sampling strategies in combination with appropriate probes
- estimation of volume, surface area, length, number and connectivity, spatial distribution, shape and directions of cells and tissues in 3D
- application of statistical methods appropriate for stereology including estimation of the optimal number of animals per group and measurements per animal.

Applications involve different types of microscopy (e.g. light microscopy, confocal laser scanning microscopy, multi-photon microscopy, electron microscopy) as well as non-invasive scanning techniques like MRI and CT.

During 2015, eight stereology courses with **Jens R. Nyengaard** (AU-bio) as one of the main organizers were held all over the world.

Participants from the stereology courses (top to bottom) at Can Tho (Vietnam), Yogyakarta (Indonesia), Sandbjerg (Denmark) and Bern (Switzerland).

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RESEARCH

RESEARCH

RESEARCH PLAN 2015 - 2020

In the second funding period of CSGB, the research is organized in six work packages

WP1: Valuation theory
WP2: Random shapes
WP3: Spatial and spatio-temporal point processes
WP4: Point processes in bioimaging
WP5: Statistics for stochastic geometry models
WP6: Algorithms

Below, we summarize the focus points within each work package. The research, that has taken place during 2015, is described on the following pages.

In the work package **Valuation theory**, the main focus is on tensor valuations which are tensor-valued additive functionals. Special cases are the classical intrinsic volumes (volume, surface area, length, Euler number) which are Minkowski tensors of rank zero. We study Minkowski tensors of rank one or higher which provide information about position, orientation and shape of spatial structures. Integral geometry of Minkowski tensors is of particular interest. Minkowski tensors have been used extensively as shape descriptors in physical applications. The potential of Minkowski tensors in biological applications is currently under investigation.

The aim of the work package **Random shapes** is to advance the theory of statistical modelling of random shapes which reside in non-linear spaces such as manifolds and stratified spaces. Important topics are deformation modelling and mixture models for multi-tensors. Modelling in non-linear spaces are used extensively in the analysis of geometric trees, using a skeletal or a hierarchical representation. A large class of examples is anatomical networks such as blood vessels, dendrite trees and airway trees in lungs. This work package also involves development of non-linear statistics in diffusion weighted imaging (DWI).

In the work package **Spatial and spatio-temporal point processes**, the study objects are the fundamental building blocks of stochastic geometry: point processes. An important example is particle models that can be represented as marked point processes. Modelling and statistical analysis of point processes in Euclidean spaces is very well developed. One of the aims of this work package is to transfer this methodology to non-Euclidean spaces such as linear networks and directed graphs. The challenge of modelling multivariate point processes is also taken up. Point processes are used as modelling tool in a variety of fields.

During the first funding period of CSGB, a number of important applications of point processes have been studied, involving (a) the minicolumn hypothesis in the cerebral cortex in the brain, (b) protein interactions inferred from FRET data and (c) the density and level of repulsion of vesicles in the presynaptic area. New challenges in these projects are taken up in the second funding period under the work package **Point processes in bioimaging**. New bioimaging applications of point processes are also studied in the second funding period. The applications relate to nodule identification and particle tracking. Imaging modalities are confocal microscopy, super-resolution fluorescence imaging and transmission electron microscopy.

Within the work package **Statistics for stochastic geometry models**, the focus is on new statistical inference issues, directly related to the analysis of bioimaging data. The model classes considered are spatial point processes and random fields. Typically, it is not possible to use classical statistical methods, based e.g. on likelihood functions, for the analysis of such stochastic geometry models. One of the important (and difficult) topics is asymptotic results for excursion sets of random fields. Equally challenging is the development of Monte Carlo envelope tests for random closed sets.

The work package **Algorithms** involves the development of computer-intensive algorithms, including a study of their mathematical and statistical properties. In the second funding period of CSGB, we study as new projects (a) estimation of Minkowski tensors from grey-value images and (b) shape reconstruction from finitely many tensors. We also want to develop new algorithms for tomographic reconstruction and segmentation of 3D data with complex content. The development of algorithms for single-particle cryo-electron microscopy, started in the first funding period, is continued.

For more information about the work packages, see http://csgb.dk/research-topics/.

FOCUSED ION BEAM SCANNING ELECTRON MICROSCOPY

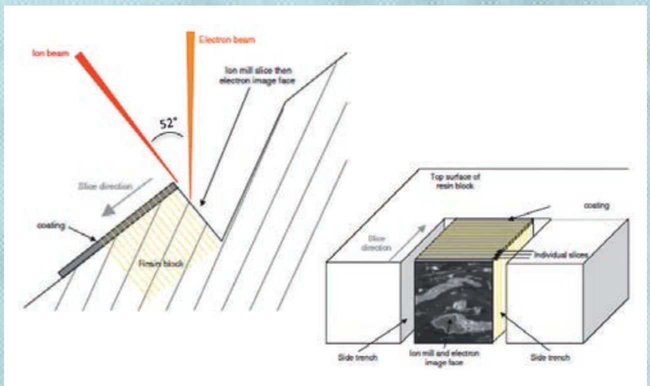

Figure 1: Principle of Focused Ion Beam Scanning Electron Microscopy
In Focused Ion Beam Scanning Electron Microscopy, a focused gallium ion beam (left, red) moves across the surface of a sample block in a raster pattern and mills off the outermost layer of the block. An electron beam (left, dark yellow) then scans across the newly exposed surface, resulting in detachment of secondary electrons from molecules at the sample surface. Detected secondary electrons are used to image the block surface (right). Repeated alternating removal of a specified thickness of the block surface by the ion beam and electron scanning will give rise to a complete series of equally spaced images from the block surface (illustrated by light yellow lines). Adapted by permission from Macmillan Publishers Ltd: Bushby *et al.* (2011, *Nature Protocols*). Copyright 2011.

Communication in the brain takes place at contact points between nerve cells – synapses. Here, signalling molecules are released from synaptic vesicles in one cell and taken up by the other. The number of synapses and vesicles provide an indication of brain activity. However, as nerve cells contain reserve pools of vesicles not directly involved in signalling it is also essential to gain information about vesicle localization and movement. This requires three dimensional (3D) reconstructions of synapses.

Focused Ion Beam Scanning Electron Microscopy (FIB-SEM) allows for automated acquisition of large, complete image series for synapse reconstruction, see Figure 1. In 2015, we have been involved in automated serial sampling with the FIB-SEM setup (Figure 2). Currently, we are optimizing tissue preparation for and image acquisition with FIB-SEM. The aim is to produce high quality images for clear identification of individual vesicles and automatic segmentation to be used in 3D modelling. The outer diameter of mammalian synaptic vesicles varies between individual synapses but is generally 35-45 nm (Qu *et al.*, 2009). The *z*-axis resolution of FIB-SEM images is superior to that of traditional transmission electron microscopy images, because of reduced overprojection, but resolution still needs to be increased if edges of vesicles and other organelles are to be unambiguously identified. An example of the present image quality is shown in Figure 3.

Figure 2: The FIB-SEM setup
The versa 3D DualBeam system from FEI at iNANO, Aarhus University, operated by lab technician Lone Lysgaard.

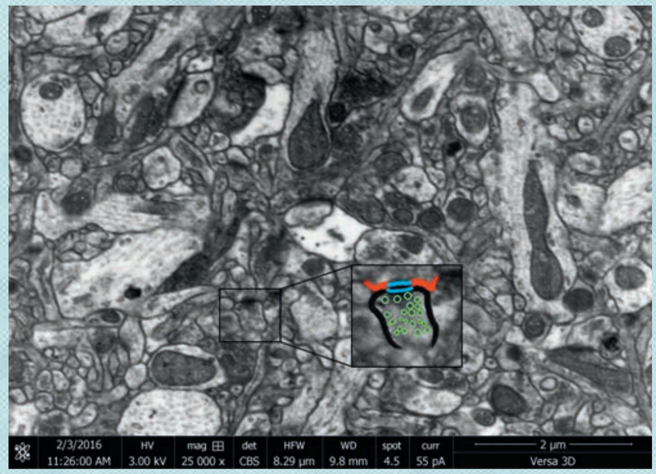

Figure 3: Ultrastructure in the brain region medial prefrontal cortex of a mouse
Individual nerve cells and their organelles are seen. The highlighted area contains a connection between two nerve cells – a synapse (blue). From vesicles (green) in the sender nerve cell (black), signalling molecules are released to the cleft between the two cells and are taken up by the nerve cell receiving the signal (red). Hereby, the two nerve cells can communicate. The image was acquired using Focused Ion Beam Scanning Electron Microscopy. Resolution 3072x2048. The image was brightness corrected, using Adobe Photoshop CS6.

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WP1

Researchers
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Jens R. Nyengaard
Andrew du Plessis
Ali Hoseinpoor Rafati
Anne Marie Svane
Johanna F. Ziegel

Valuation theory

This project is an extended and further developed version of the project **rotational integral geometry** that was part of the research plan for CSGB I. We take into account and build on the progress that has been made in CSGB I. The focus is on tensor valuations of rank one or higher. These valuations contain important information about position, shape and orientation of spatial structures.

Integral geometry of tensor valuations has been studied intensively during 2015. A number of new results is collected in a CSGB research report that appeared early this year (Jensen & Kiderlen, 2016). A characterization result for rotation invariant polynomial valuations, published in Alesker (1999), is formulated for tensor valuations and rotational integral geometry is developed for some of the valuations appearing in the characterization theorem. Using the recently established kinematic formula in Bernig & Hug (2016) for **trace-free tensors**, it is shown how any translation invariant Minkowski tensor of order at least 2 can be expressed as a non-trivial rotational Crofton integral. Finally, a new result due to Anne Marie Svane on rotational averages of Minkowski tensors is shortly mentioned in Jensen & Kiderlen (2016, Theorem 13). A separate paper about this new result is planned for 2016.

In Jensen & Kiderlen (2016), the new locally defined Minkowski tensors (Hug & Schneider, 2014) are used to establish **principal rotational formulae**. This class of formulae deal with the case where an unknown spatial structure K is studied via the intersection with a randomly rotated set M. In microscopy, M is typically a sampling window constructed by the observer. Such principal rotational formulae play an important role in applications since they can give a certain class of existing measurement techniques in optical microscopy a common formulation. Furthermore, because of the unification approach, the formulae are expected to lead to new measurement techniques on microscopy images. Right now, the existing formulae require, however, certain analytic knowledge of M.

When studying cell populations by microscopy, an extra challenge is that cells might not be observable directly, but only via sections. An important contribution in Ziegel *et al.* (2015) is the development of estimators of volume tensors that combine **observations in several optical planes** through sampled cells, but avoid observations in the peripheral parts of the cells. This type of geometric sampling, called the optical rotator, was already described in Tandrup *et al.* (1997) for estimation of cell volume and surface area. The estimators developed in Ziegel *et al.* (2015) are local estimators, since measurements on a sampled cell are relative to a reference point of the cell, typically the nucleus of the cell.

In Rafati *et al.* (2015), this type of robust estimation of volume tensors from optical microscopy images is described with the purpose of making this method available to scientists working in microscopy. Different aspects of the method are illustrated in Figure 1 and 2. For cell populations, the 3D shape and orientation of the typical cell can be represented by the so-called **Miles ellipsoid** which can be estimated from the volume tensors of a sample of cells. (The Miles ellipsoid is named after Roger Miles who was amongst the first to introduce geometric sampling theory in stereology.) The statistical behaviour of the estimator of the Miles ellipsoid is studied in Rafati *et al.* (2015) under a flexible model for 3D cell shape and orientation. The particle model is illustrated in Figure 3. The simulation study shows that the lengths of the axes of the Miles ellipsoid can be estimated with CVs of about 2% if 100 cells are sampled.

During 2015, the research on **surface tensor estimation** from linear sections has been published in Kousholt *et al.* (2015). A general structural theory of operators between functions has been developed in Gardner & Kiderlen (2015).

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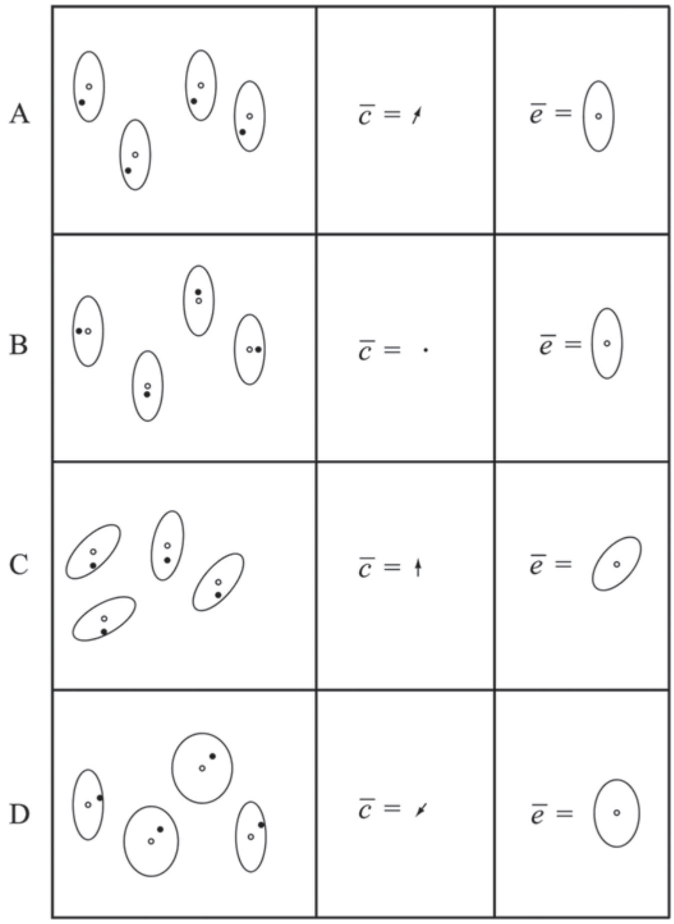
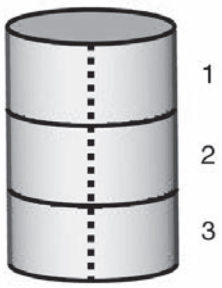


Figure 1:
Interpretation of the displacement vector $\bar{c}$ and the Miles ellipsoid $\bar{e}$. The left column shows elliptic particles with their centre of gravity indicated by an open circle and their reference point by a closed circle. The middle column shows the displacement vector $\bar{c}$, i.e. the average vector pointing from the reference point to the centre of gravity. The right column shows the Miles ellipsoid $\bar{e}$, representing the average shape and orientation of the particles shown to the left. From Rafati *et al.* (2015).



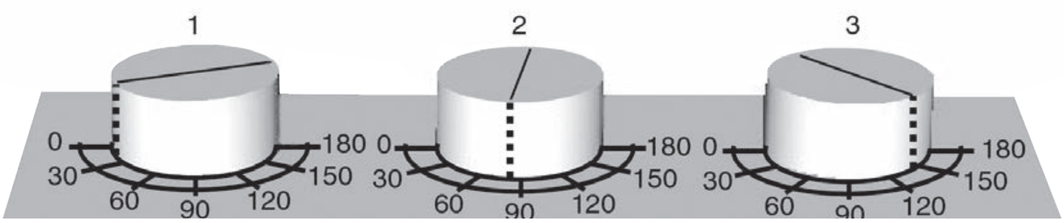


Figure 2:
(Upper) The cylinder containing the particles are cut into three blocks (1, 2, 3). Their relative position is indicated by the stippled vertical line. (Lower) A systematic stack of parallel vertical uniform random thick sections is cut within each block. The sections are all parallel to a vertical plane rotated by an angle θ where $\theta = 20^o, 80^o, 140^o$ for blocks 1, 2, 3, respectively. The first angle has been chosen uniform randomly in the interval $[0^o, 60^o)$ and the subsequent angles were then chosen systematically. From Rafati *et al.* (2015).

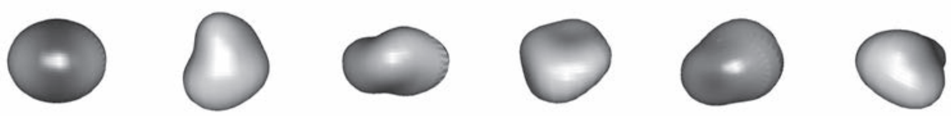


Figure 3:
Particles simulated under the stochastic particle model. Five random deformations are shown of the ellipsoidal particle to the left. From Rafati *et al.* (2015).

WP2

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Jens R. Nyengaard
Andrew du Plessis
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Anne Marie Svane

Random shapes

In 2015, new results were obtained within the random shapes work package in several directions, including (i) statistics in manifolds and stratified spaces, (ii) statistical modelling of random variation in functional and imaging data, and (iii) tractography and fibre path modelling in diffusion weighted imaging.

Relating to **inference in general non-linear spaces**, it was shown in Feragen *et al.* (2015a) that geodesic exponential kernels are not generally positive definite in curved geodesic spaces, implying that such kernels cannot generally be used for machine learning on manifold and other curved spaces. This finding was in distinct contrast to popular recent work in computer vision, and the result attracted quite some interest.

An important special case of non-linear statistics takes place in tree-space, which is a non-linear space of **tree-structured shapes**. During 2015, Amenta *et al.* (2015) have obtained new visualization methods for variation in tree-structured data, while an automatic anatomical airway tree labelling algorithm, based on non-linear tree geodesics, is presented in Feragen *et al.* (2015b). This algorithm was shown to perform as well as a human expert, and the resulting labelling algorithm has subsequently been used in clinical research.

In 2015, we have also explored the link between sub-Riemannian fibre bundle geometry, stochastic models in non-linear manifolds, and non-linear statistics. Stefan Sommer was awarded an honourable mention for his work on defining **families of distributions on manifolds** at the 2015 IPMI medical imaging conference (Sommer, 2015a). The resulting evolution equations for the most probable paths of the stochastic processes were treated in Sommer (2015b), and, in collaboration with Anne Marie Svane (AU-math), the relation between holonomy, stochastic development, and anisotropy of normal distributions generalized to manifolds were explored further in Sommer & Svane (2016). Relations between symmetry reduction in geometric mechanics, image registration, and **diffeomorphism groups** were investigated in Sommer & Jacobs (2015). Developments in multiscale image registration with stationary velocity fields and kernel framework have led to the state-of-the-art registration framework (Pai *et al.*, 2015). Mixed-effects models for simultaneous modelling of warp and amplitude variation developed in collaboration with Lars Lau Raket (MATH, Copenhagen) have been applied in clinical settings in Mieritz *et al.* (2015). We are currently extending these models further to warp-dependent imaging data.

Relating to **diffusion weighted imaging** (DWI), several new developments took place in 2015: Hauberg *et al.* (2015b) and Kasenburg *et al.* (2016) presented two new, and closely related, shortest-path tractography algorithms, which aim to estimate physical connection pathways in the brain. The first algorithm is able to incorporate spatial priors into the estimation procedure. The second algorithm estimates, as opposed to the state-of-the-art, not just the most likely brain fibre pathway, but an entire **probability distribution over pathways**. In particular, the uncertainty of the distribution is directly linked to the uncertainty of the data through a novel random Riemannian metric formulation. This new tractography formulation therefore leads to new and potentially very useful modelling possibilities. Finally, the paper Kasenburg *et al.* (2015a), which was developed in collaboration with Ute Hahn (AU-math), describes statistical tests for significance on the resulting fibre pathways, while Kasenburg *et al.* (2015b) presents tools for interpretable machine learning on brain connectivity networks constructed using these tractography methods.

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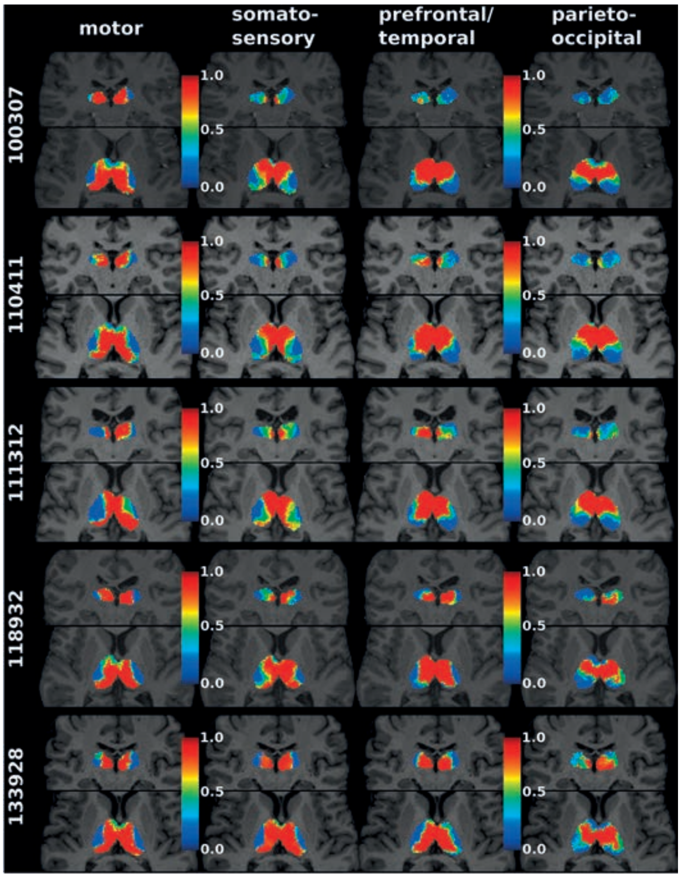

Figure:
Soft segmentations of the thalamus for four target regions (the motor, somatosensory, prefrontal/temporal and parieto-occipital zones, respectively) in five subjects. Regions indicated by low confidence *p*-values (blue) are more likely to be connected to the respective target region than regions indicated by high *p*-values (red). For details, see Kasenburg *et al.* (2015a).

WP3

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Spatial and spatio-temporal point processes

In 2015, a monograph (Baddeley *et al.*, 2015) and a total of eight papers on spatial and spatio-temporal point processes have been published or accepted for publication in **top international statistical journals** (Chang *et al.*, 2015; Guan *et al.*, 2015; Jalilian *et al.*, 2015; Lavancier & Møller, 2015; Lavancier *et al.*, 2015; Møller & Rasmussen, 2015; Suryaprakash *et al.*, 2015; Waagepetersen *et al.*, 2015). Moreover, six papers have been submitted for publication. The CSGB researchers associated with this work package have also during 2015 contributed decisively to the work package **point processes in bioimaging**, see page 26-27.

The publication of the **monograph** Baddeley *et al.* (2015) represents one of the highlights of 2015, see the more detailed description of the event on page 14. Below, we review part of the research presented in the papers. A detailed description of some of the papers can be found in earlier annual reports.

The research on **determinantal point processes** (**DPPs**), now published in Lavancier *et al.* (2015), has in 2015 been extended to point processes on the sphere. Such processes have rarely been studied in the literature, though the sphere serves as a good approximation of planet Earth. In Møller *et al.* (2015), the spectral representation of the kernel of an isotropic **DPP defined on the sphere** is completely characterized and strategies for developing new models, including a useful spectral approach, are discussed. Furthermore, Møller & Rubak (2016) provide a rigorous description of Palm distributions and functional summary statistics for point processes on the sphere and relate this theory to DPPs.

Optimal parametric estimation procedures for first and second order properties of a spatial point process are studied in Deng *et al.* (2015) and Guan *et al.* (2015), and for parametric Gibbs point processes using the Takacs-Fiksel method in Coeurjolly *et al.* (2015a). The latter paper obtains considerable improvements for specific cases of repulsive Gibbs point processes.

Palm distributions is a fundamental concept for spatial point processes. Palm distributions can be quite complex but in case of log Gaussian Cox processes (LGCPs), Coeurjolly *et al.* (2015b) establish a strikingly simple fact: that the Palm distribution of a LGCP is itself a LGCP with the same covariance of the Gaussian field as for the original process but with a modified mean function for the Gaussian field. The purpose of Coeurjolly *et al.* (2015c) is to give a gentle tutorial to Palm distributions specified by probability densities.

Lavancier & Møller (2015) consider a dependent thinning of a regular point process with the aim of obtaining **aggregation on the large scale and regularity on the small scale** in the resulting target point process of retained points. Various parametric models for the underlying processes are suggested and the properties of the target point process are studied. The paper extends previous work by Dietrich Stoyan on interrupted point processes, and it studies in detail simulation and inference procedures when a realization of the target point process is observed, depending on whether the thinned points are observed or not.

The research on **multivariate spatial point processes**, dealing with multivariate log Gaussian Cox processes and product-shot-noise Cox processes, have been published in Jalilian *et al.* (2015) and Waagepetersen *et al.* (2015). Several approaches to sparse modelling of multivariate log Gaussian Cox point processes have been considered. These involve a version of the fused lasso where similarity is promoted for certain weight parameters associated to different species.

During 2015, Jesper Møller and Jakob G. Rasmussen have started a collaboration with Ethan Anderes, University of California at Davis, on **random fields and point processes on graphs** with Euclidean edges.

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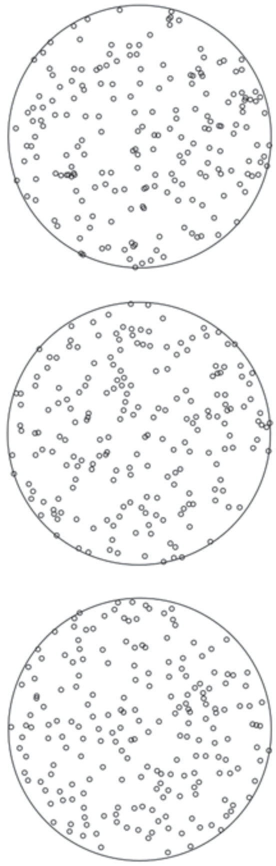

Figure 1:
Northern hemisphere of three spherical point patterns projected to the unit disc with an equal-area azimuthal projection. Each pattern is a simulated realization of a determinantal point process (DPP) on the sphere with mean number of points equal to 400.
(Upper) Complete spatial randomness (Poisson process).
(Middle) Multiquadric model.
(Lower) Most repulsive DPP. For more details, see Møller *et al.* (2015).

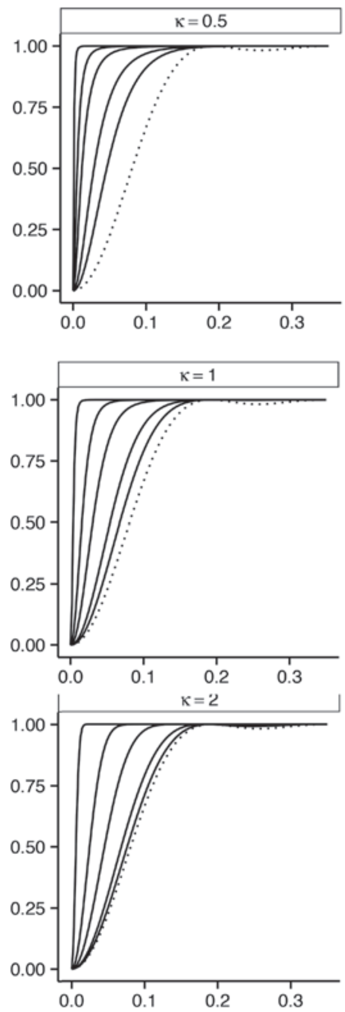

Figure 2:
Approximate pair correlation functions for determinantal point process (DPP) models on the sphere. The dotted line corresponds to the most repulsive DPP. For more details, see Møller *et al*. (2015).

WP4

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Point processes in bioimaging

During the first funding period of CSGB, point process tools for analyzing the **minicolumn hypothesis** in the cerebral cortex of the brain have been developed, see Møller *et al.* (2015) and Rafati *et al.* (2016). These developments include a cylindrical *K*-function and a new model, the Poisson line cluster point process, describing 3D point patterns of locations of (pyramidal and non-pyramidal) neurons. The challenge in the second funding period of CSGB is to extend our methods and models to more complicated data such as two-point pattern data of neurons.

Nodule identification and classification from confocal microscopy have been studied, using directional analysis of planar point processes. Legume symbiosis with rhizobia results in the formation of a specialized organ, the root nodule. The interest is in the early stage of formation of root nodules (nodule primordia), where nodules are difficult to distinguish from structures that will later develop into lateral roots that do not house rhizobia. The preliminary investigations call for further development of the point process tools, either in the direction of a more sensitive correlation analysis or 3D point process analysis.

In relation to the project on **protein clusters**, we have in collaboration with the group of Lene Niemann Nejsum, AU, started in fall 2015 a pilot study, which involves PALM (Photo Activated Localization Microscopy) data from patterns of protein clusters in control and hormone treated cells. These data consist of points in space and time, representing fluorescent molecules. The literature usually assumes that PALM detects individual molecules independently of each other. As we could show with statistical methods for marked point processes, this assumption does not hold for the present data. In intense collaboration with the group of Lene N. Nejsum, we are currently focusing on finding an appropriate alternative model that takes the dependence structure of the data into account.

The spatial interactions of **synaptic vesicles** have been assessed in Khanmohammadi *et al.* (2015), using a detailed characterization of size, shape and orientation of the synaptic vesicles. 3D representations of synapses obtained from a set of publicly available FIB-SEM images were analyzed. The configurations of synaptic vesicles were regarded as marked point processes where the points are the centres of the vesicles and the mark of the vesicle is given by its size, shape and orientation characteristics. Statistics for marked point processes are employed to study spatial interactions between vesicles. The vesicles in excitatory synapses appear to be of oblate ellipsoidal shape, while in inhibitory synapses of prolate ellipsoidal shape. There is strong evidence of spatial alignment in the orientations of synaptic vesicles and of repulsion between them only in excitatory synapses. Figures 1-3 illustrate the developed methodology in Khanmohammadi *et al.* (2015).

Motivated by analysis of **patterns of megakaryocytes in bone marrow**, a new model class for point processes, Matérn thinned Cox processes, has been developed in Andersen & Hahn (2015). These point processes show repulsion on a small scale, but clustering on a larger scale. The processes are obtained by Matérn thinning of a clustered Cox point process (by contrast, Lavancier & Møller (2015) thin a repulsive point process in order to achieve clustering behaviour at a larger scale; for more details, see work package WP3). Theoretical expressions for second order summary statistics of the Matérn thinned Cox point processes are derived in Andersen & Hahn (2015). These expressions are computationally infeasible, but we found a good approximation that makes it possible to calculate the theoretical pcf for shot noise Cox processes. This allows fitting the model by the minimum contrast method.

The research from the first funding period of CSGB, concerning the **spatial distribution of proteins** within cells based on fluorescence resonance energy transfer data (**FRET**), has been reviewed in Hooghoudt (2015).

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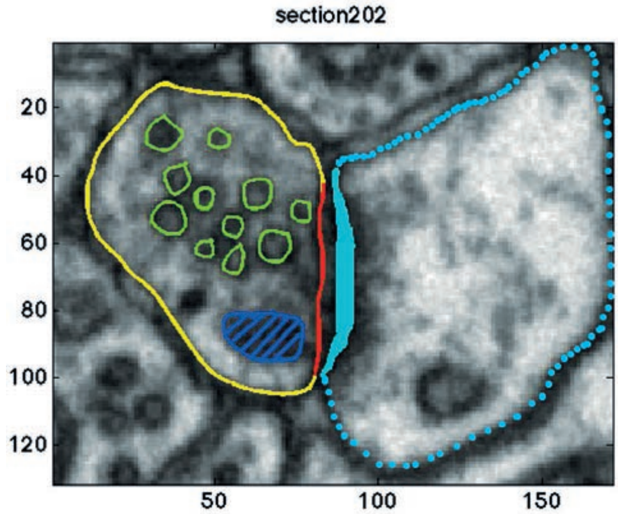

Figure 1: Annotation of the objects of interests in one sample section of the data.
The synaptic vesicles, the mitochondria, the pre-synaptic membrane, the post-synaptic membrane, the active zone, and the post synaptic density (PSD) are shown in green, dark blue, yellow, blue, red and cyan, respectively. From Khanmohammadi *et al.* (2015).

Figure 2: A 3D view of the pre-synaptic compartments of one of the synapses including the active zone (red), the mitochondria (blue), the centers of the synaptic vesicles (black dots) and the slices (cyan) parallel to the active zone surface. For better visualization one of the bands is shown in green. From Khanmohammadi *et al.* (2015).

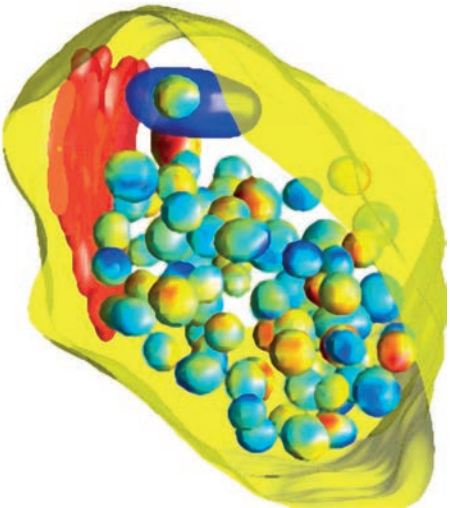

Figure 3: A simulation of the null model.
The pre-synaptic membrane, active zone and mitochondria are shown in yellow, red and dark blue, respectively. Vesicles are shown with interpolated colours, where the variation of colour serves to better show the three-dimensional features. From Khanmohammadi *et al.* (2015).

WP5

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Statistics for stochastic geometry models

The main advances in 2015 within this work package concern **Monte Carlo envelope tests for random closed sets**. The focus has been on tests for spatial point processes. The background for this research is that goodness of fit for spatial point process models is often assessed via summary functions, such as the *K*-, *J*- or pair correlation function. In order to compare the observed summary function with simulated counterparts from the model under question, it seems natural to draw a pointwise central envelope. This way, it becomes directly evident at which spatial scale the observed pattern deviates from the model, if at all. However, albeit a popular method, this does not constitute a proper statistical test, as pointed out by Loosmore & Ford (2006).

In Myllymäki *et al.* (2015), a new solution is presented to construct a simultaneous envelope such that, under the null hypothesis, the observed curve leaves the envelope with a given probability α. To this envelope corresponds an interval for the *p*-value of the observed function. One would need a large number of simulations in order to obtain a small interval from straightforward application of the envelope test, therefore we also suggested a related test that always yields a single *p*-value, even for a moderate number of simulations.

With this new test, it has become feasible to apply the idea to more general situations:

- In Mrkvička *et al.* (2015a), we demonstrate how this principle can be used to improve the power of goodness of fit tests by basing the test on several summary functions simultaneously. An example can be seen in Figure 1. In the same paper, we tested whether a Boolean model fits a given microscopical structure, using Minkowski functionals.

- In Mrkvička *et al.* (2015b), envelope tests are extended to higher dimensional functions, with the particular application to spatial residuals. Figure 2 shows a goodness of fit test for a point pattern using residuals as defined in Baddeley *et al.* (2005).

- A paper on using the envelope method for comparison of groups is in preparation.

During 2015, we have also studied **asymptotics for excursion sets**, relating to extremal properties of random fields. (An excursion set of a random field is the set of points at which the value of the random field exceeds a certain level.) Excursion sets is a very difficult study field of probability theory. Nevertheless, we aim at getting insight into the asymptotic size of the excursion set of a random field defined as an integral with respect to an infinitely divisible, independently scattered random measure. Such random fields fill a gap in the literature. By using techniques from Rønn-Nielsen & Jensen (2014), we have during 2015 managed to obtain new results concerning the asymptotic size of excursion sets such as the probability that the excursion set contains (i) a ball of a given radius, (ii) a line segment of a given length and (iii) a pair of points at a given mutual distance. Some of the technical details need still to be worked out.

Inspired by a concrete collaboration during CSGB I between CSGB researchers from AU-math, AU-bio and KU concerning estimation of the thickness of ultra thin sections in electron microscopy, see Sporring *et al.* (2014), we have in 2015 studied **estimation of sample spacing in stochastic processes**. More specifically, we have investigated the statistical properties of an estimator of sample spacing in stationary, isotropic random fields. In particular, we have derived the variance of the estimator for a large class of random fields, given as a kernel smoothing of a so-called Lévy basis. The results will be presented in Rønn-Nielsen *et al.* (2016).

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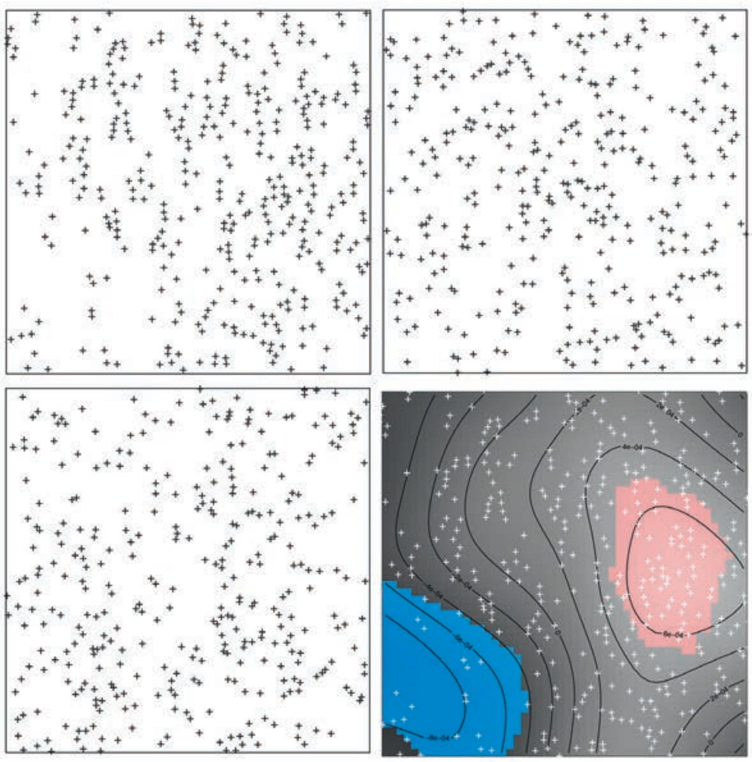

Figure 2: Application of the envelope test to a residual field. (Upper left) Another point pattern showing locations of intermembraneous particles in freeze fracture microscopy, data from Schladitz *et al.* (2003, *J. Microsc.* **211**, 137-153). (Upper right and lower left) Plots show realizations of a fitted Gibbs hard core model. (Lower right) Contour plot of the smoothed residual field together with the original data. A simultaneous envelope has been calculated from 9999 simulations of the fitted model. Areas where the observed residuals leave the envelope are marked in blue and red.

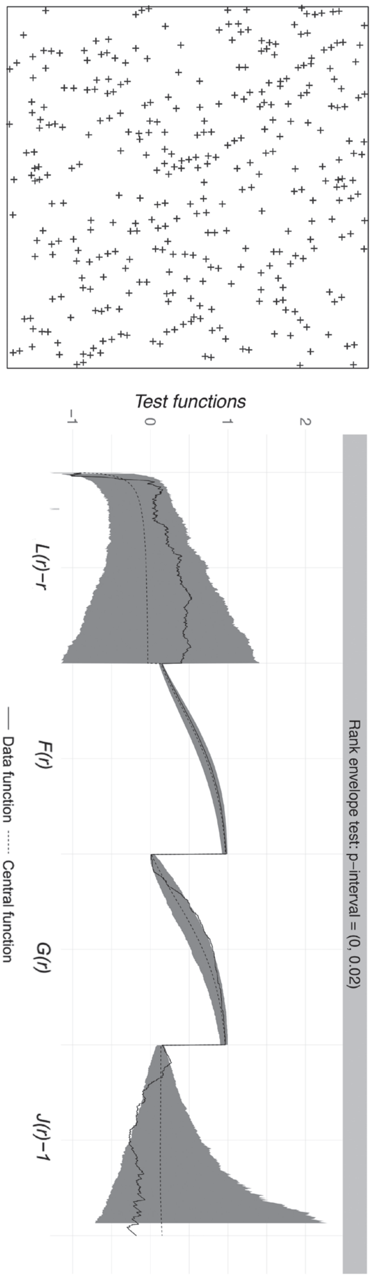

Figure 1: Goodness of fit test using several summary functions simultaneously.
(Upper) A point pattern showing locations of intermembraneous particles in freeze fracture microscopy, data from Schladitz *et al.* (2003, *J. Microsc.* **211**, 137-153).
(Lower) Simultaneous envelope goodness of fit test for a fitted Gibbs hard core model, using the *L*-, *F*-, *G*- and *J*-function, based on 9999 simulations.

WP6

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Algorithms

It was shown in the first funding period of CSGB that local algorithms for estimating geometric functionals from black-and-white images, the simplest and most common type of algorithms, are typically biased (Svane, 2014a). The proof relies on a second order formula for the mean, which was finally published in 2015 (Svane, 2015a). Instead, local algorithms for **grey-scale images** is one of the focus points in the new funding period. It was discovered in CSGB I that grey-values can be used to define unbiased algorithms for computation of surface area and integrated mean curvature (Svane, 2014b). An extension to estimation of **Minkowski tensors** was published in 2015 (Svane, 2015b), as well as a formula for the asymptotic variance of the surface area estimator (Svane, 2015c).

The research on black-and-white images was also continued in 2015 together with our German colleagues within the DFG Research Unit GPSRS. A major breakthrough was the use of parallel volumes to define asymptotically unbiased estimators for intrinsic volumes and Minkowski tensors (Hug *et al.*, 2016). The algorithms have a simple formulation, using **Voronoi cells** associated with the image, see Figures 1-3, and the computation time is still moderate.

In CSGB I, local algorithms for 2D **Boolean models** were developed in Svane (2014c). Such algorithms were extended in 2015 to 3D in a collaborative project with Julia Hörrmann, Bochum. The resulting optimal algorithms for estimating specific intrinsic volumes from 3D Boolean models are presented in Hörrmann & Svane (2016).

During 2015, we have also studied **shape reconstruction from finitely many surface tensors** for convex bodies in *n*-dimensional space. The shape of a convex body *K* with non-empty interior is uniquely determined by all its surface tensors. In general, however, it is only possible to obtain an approximation of the shape of *K* from finitely many surface tensors (Kousholt & Kiderlen, 2016).

To reconstruct the shape of an unknown convex body K_0, we consider the (infinite dimensional) minimization problem

$$\min_K \|\phi_s(K_0) - \phi_s(K)\|^2, \qquad (1)$$

where the minimization is over all convex bodies *K*, and $\phi_s(K)$ is the vector of all components of the surface tensors of *K* up to rank $s \in \mathbb{N}$. A solution to (1) is a convex body with surface tensors identical to the surface tensors of K_0 up to rank *s*. Using that the set of solutions to (1) contains a polytope with at most m_s facets ($m_s = 2s + 1$ in the planar case, while $m_s = (s+1)^2$ in 3D), the minimization problem (1) can be reduced to a finite dimensional minimization problem. For a sequence $(\widehat{K}_s)_s$ of reconstructions of K_0, a stability result yields that the shape of $\widehat{K}_s$ converges to the shape of K_0.

When only noisy measurements are available for the reconstruction, harmonic intrinsic volumes, as introduced in Hörrmann (2014), may be used instead of surface tensors. Using properties of spherical harmonics, the consistency of the reconstruction algorithm can be established under certain assumptions on the variance of the noise variables.

Shape reconstruction of 2-dimensional convex bodies are treated in Kousholt & Kiderlen (2016), whereas the general case of reconstruction of *n*-dimensional convex bodies will be treated in Kousholt (2016). An illustration of the reconstruction of an ellipsoid may be found in Figures 4-5.

In 2015, the AU-math and AU-bio groups have studied **algorithms for single particle cryo-electron microscopy**. Already at a two-dimensional level, classification is required to visualize features that in the individual images would be masked by noise. In the recent years, several expectation-maximization techniques have been proposed that aim at finding a maximum likelihood estimate of the structures underlying a data set. Many samples that we currently image still challenge state-of-the-art methods, and thereby serve as test beds for the methods that we develop and implement.

Methods for tomographic **reconstruction of incomplete micro CT images**, based on the inverse Radon transform or algebraic methods, have during 2015 been studied by the KU group.

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Svane, A.M. (2015b): Estimation of Minkowski tensors from digital grey-value images. *Image Anal. Stereol.* **34**, 51-61.

Svane, A.M. (2015c): Asymptotic variance of grey-scale surface area estimators. *Adv. Appl. Math.* **62**, 41-73.

Figure 1:
A disk (blue) and its parallel set (light blue).

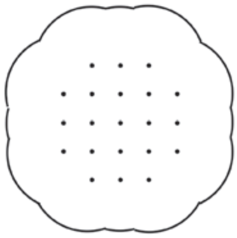

Figure 2:
A digital black-and-white image of the disk and the parallel set of the point set.

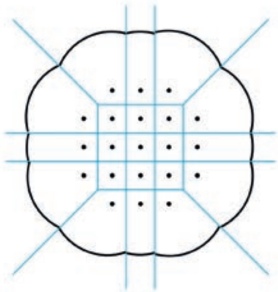

Figure 3:
The Voronoi cells associated to the image are used in the Voronoi algorithm in Hug *et al.* (2016).

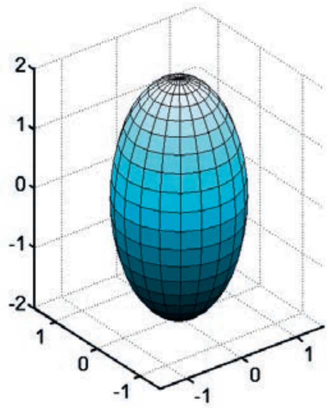

Figure 4:
Ellipsoid with semi-axes (1, 0, 0), (0, 1, 0) and (0, 0, 2).

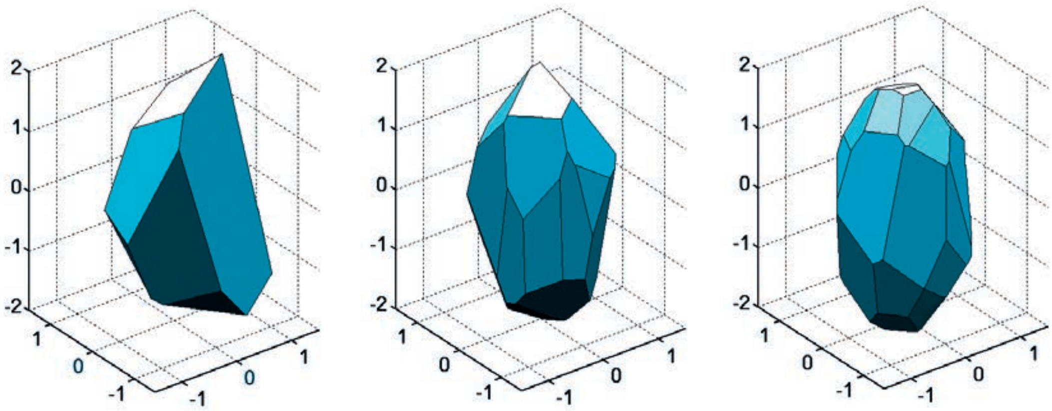

Figure 5:
Reconstructions of the ellipsoid in Figure 4 based on surface tensors up to rank $s = 2, 4, 6$.

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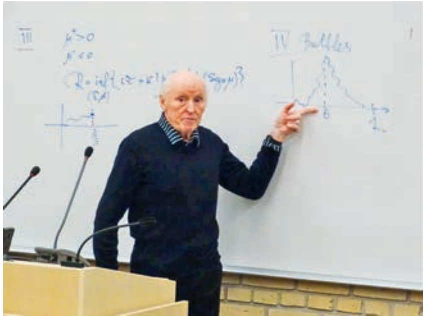
CENTRE ACTIVITIES

OVERVIEW – PAST AND PLANNED INTERNATIONAL ACTIVITIES



From the *Aarhus Conference on Probability, Statistics and their Applications*, 15 – 19 June 2015. The lecturer to the left is Albert Shiryaev (Moscow).

International conferences and workshops

Curves and Tree Statistics Workshop | 21 May 2015, Copenhagen

Workshop on Mathematical and Statistical Analysis of Spatial Data | 1 – 3 June 2015, Aalborg University

Scandinavian Conference on Image Analysis
15 – 17 June 2015, IT University of Copenhagen

Aarhus Conference on Probability, Statistics and their Applications | 15 – 19 June 2015, Aarhus University

The useR! Conference 2015 | 30 June – 3 July 2015, Aalborg University

Shape Analysis Workshop | 27 July – 1 August 2015, Grundsund, Sweden

Workshop on Quantitative Microscopy | 17 – 21 August 2015, Bern University

SIMBAD 2015 – 3rd International Workshop on Similarity-Based Pattern Analysis and Recognition | 12 – 14 October 2015, Copenhagen

Workshop on Stochastic Geometry, Stereology and their Applications | 5 – 10 June 2016, Sandbjerg

Workshop on Geometry and Stochastics of Nonlinear, Functional and Graph Data | 15 – 19 August 2016, Rønne

International PhD Courses

A total of **eight stereology courses** have been held in 2015, the majority being PhD courses. A detailed description may be found on page 15. In addition, we have organized the following PhD courses:

Quantitative Medical Graphics | 8 April 2015, Aarhus University

Analysing spatial point patterns with R | 21 – 22 April 2015, Aalborg University

International Summer School on Convex & Discrete Optimization | 17 – 21 August 2015, Sønderborg

Selected CSGB seminars

26 February 2015 | Eva B. Vedel Jensen (Aarhus University)
Rotational integral geometry and its applications in stereology

23 April 2015 | Markus Kiderlen (Aarhus University)
Rotational Crofton formulae

21 May 2015 | Xavier Descombes (INRIA, Sophia-Antipolis, France) | An extension of the elastic shape metric for comparing axonal trees

21 May 2015 | Anuj Srivastava (Florida State University, USA) | Analyzing shapes of certain trees using elastic curve methods

25 June 2015 | Richard Gardner (Western Washington University, USA) | The Orlicz-Brunn-Minkowski theory

18 November 2015 | Chloe-Agathe Azencott (MINES Paris Tech) | Large-scale network-guided feature selection for precision medicine

15 December 2015 | Martins Bruveris (Brunel University)
Riemannian geometry of the diffeomorphism group

Workshop on Geometry and Stochastics of Nonlinear, Functional and Graph Data

15 – 19 August 2016, Green Solution House, Rønne, Denmark

This workshop is arranged jointly by the stochastic geometry group, AU, and the image section, KU.

SCOPE OF THE WORKSHOP

The field of **nonlinear statistics** (NS) seeks to answer the fundamental questions that arise when defining new statistical models and tools in nonlinear spaces. The field spans from theoretical statistics and geometry to the development of data analysis tools that are directly applicable to actual data. A typical application area is bioimaging.

NS is a rapidly evolving research field. While there is a deep understanding of the mathematical and computational aspects of many data types living in nonlinear spaces, a detailed understanding of random variation in these spaces and how to handle randomness statistically is largely missing.

With this workshop, we want to reach out to key researchers in two closely related fields: **functional data analysis** (FDA), and **random topology and graphs** (RTG). The recent movement in FDA towards increasingly complex data structures has paved the way for a deeper statistical understanding of practical and commonly used methods in NS. The study of statistical properties of random graphs is closely related to NS through concepts like manifold learning, dimensionality reduction and topological data analysis. Complex topological properties of data living in nonlinear spaces, such as persistent homology, are studied in random topology.

The two fields FDA and RTG share problems and methodology, unresolved questions, and technical solutions with NS, and it is our belief, backed by world-leading experts in all three fields, that extended collaboration will lead to new results and development beyond the current state-of-the-art in these areas.

Green solution house

INVITED SPEAKERS

Robert Adler
(Technion, Haifa)

Benjamin Eltzner
(Institute for Mathematical Stochastics, Göttingen)

Tom Fletcher
(University of Utah)

Thomas Hotz
(TU Ilmenau)

Stephan Huckemann
(Institute for Mathematical Stochastics, Göttingen)

Sarang Joshi
(University of Utah)

Sungkyu Jung
(University of Pittsburgh)

Steve Marron
(University of North Carolina at Chapel Hill)

Hans-Georg Müller
(University of California, Davis)

Xavier Pennec
(INRIA Sophia Antipolis)

Mathew Penrose
(University of Bath)

Stephen M. Pizer
(UNC)

Anastasios Sidiropoulos
(Ohio State University)

Anuj Srivastava
(Florida State University)

Jonathan Taylor
(Stanford University)

Christoph Thäle
(Ruhr Universität Bochum)

Jane Ling Wang
(University of California, Davis)

Yu (Ryan) Yue
(CUNY)

Joseph Yukich
(Lehigh University)

Further information, see **http://csgb.dk/activities/2016/geometry/**

CSGB RESEARCH REPORTS 2015

CSGB has its own research report series that mainly publishes mathematical and statistical manuscripts. The major part of these manuscripts will later appear in international journals. The publication traditions are different in computer science and biology for which reason publications by CSGB researchers from these fields will appear directly in international journals, proceedings, etc.

1. Andersen, I.T. & Hahn, U. (2015): Matérn thinned Cox processes. *CSGB Research Report* **2015-08**. Has appeared as *Spat. Stat.* (2016) **15**, 1-21.

2. Coeurjolly, J.-F., Guan, Y., Khanmohammadi, M. & Waagepetersen, R. (2015): Towards optimal Takacs-Fiksel estimation. *CSGB Research Report* **2015-15**. Submitted.

3. Coeurjolly, J.-F., Møller, J. & Waagepetersen, R. (2015a): Palm distributions for log Gaussian Cox processes. *CSGB Research Report* **2015-09**. Submitted.

4. Coeurjolly, J.-F., Møller, J. & Waagepetersen, R. (2015b): Conditioning in spatial point processes. *CSGB Research Report* **2015-14**. Submitted.

5. Gardner, R.J. & Kiderlen, M. (2015): Operations between functions. *CSGB Research Report* **2015-11**. Submitted.

6. Hahn, U. (2015): A note on simultaneous Monte Carlo tests. *CSGB Research Report* **2015-06**. Submitted.

7. Jacobs, H.O. & Sommer, S. (2015): Higher-order spatial accuracy in diffeomorphic image registration. *CSGB Research Report* **2015-02**.

8. Jalilian, A., Guan, Y., Mateu, J. & Waagepetersen, R. (2015): Multivariate product-shot-noise Cox point process models. *CSGB Research Report* **2015-05**. Has appeared in *Biometrics* (2015) **71**, 1022-1033.

9. Kousholt, A. & Kiderlen, M. (2015): Reconstruction of convex bodies from surface tensors. *CSGB Research Report* **2015-10**. Has appeared as *Adv. Appl. Math.* (2016) **76**, 1-33.

10. Lavancier, F. & Møller, J. (2015): Modelling aggregation on the large scale and regularity on the small scale in spatial point pattern datasets. *CSGB Research Report* **2015-07**. To appear in *Scand. J. Stat.*

11. Møller, J., Safavimanesh, F. & Rasmussen, J.G. (2015): The cylindrical *K*-function and Poisson line cluster point processes. *CSGB Research Report* **2015-03**. Submitted.

12. Møller, J., Nielsen, M., Porcu, E. & Rubak, E. (2015): Determinantal point process models on the sphere. *CSGB Research Report* **2015-13**. Submitted.

13. Rafati, A.H., Ziegel, J.F., Nyengaard, J.R. & Jensen, E.B.V. (2015): Stereological estimation of particle shape and orientation from volume tensors. *CSGB Research Report* **2015-12**. To appear in *J. Microsc.* DOI: 10.1111/jmi.12382.

14. Sommer, S. & Jacobs, H.O. (2015): Symmetry in image registration and deformation modeling. *CSGB Research Report* **2015-01**. Has appeared as *Symmetry* (2015) **7**, 599-624.

15. Waagepetersen, R., Guan, Y., Jalilian, A. & Mateu, J. (2015): Analysis of multi-species point patterns using multivariate log Gaussian Cox processes. *CSGB Research Report* **2015-04**. Has appeared as *Appl. Statist.* (2015) **65**, 77-96.

Workshop on Mathematical and Statistical Analysis of Spatial Data

1–3 June 2015, Aalborg University

SCOPE OF THE WORKSHOP

Spatial statistics is concerned with statistical analysis of three types of spatial data: observations measured at a fixed set of sites, random point patterns, and random geometrical objects. The first type of data is analysed by means of random field models, while point process models are appropriate for the second type. The last type of data is handled by methods of stochastic geometry. Spatial statisticians are challenged with the need for increasingly complicated mathematical models which a) account for non-stationary variation, b) describe complex interactions at different scales and c) include attributes associated to the points or pixels. For data sets of moderate size, spatial statisticians typically apply a direct statistical modelling of the data, but for huge data sets this is not feasible with existing spatial models due to excessive computing time and a lack of efficient procedures.

Harmonic analysis is a branch of mathematical analysis that studies representations of signals as superpositions of elementary signals. A signal such as an image has countless possible representations and the goal is to find a cost effective representation. Cost effective means reducing storage requirements while keeping only 'relevant features' of the data. Such representations are also referred to as sparse representations. A sparse representation enables compression of the signal (e.g. music stored in the mp3-format) and can also be used to extract hidden structures of particular interest. Harmonic analysts are challenged with the need for new and more cost effective representation methods, which a) are adapted to capture specific structures such as edges and b) capture complex interaction on different scales, thus allowing sophisticated statistical modelling.

The aim of this workshop was to explore the **interface between spatial statistics and harmonic analysis** with the purpose of developing new methods and algorithms for sparse representation and statistical analysis of spatial data.

Topics included (but were not restricted to)

- spatial modelling of wavelet representations of images
- compressed sensing in combination with advanced statistical modelling
- multi-scale spatial analysis for sparse representation data at different resolutions
- applications of mathematical analysis in spatial point process theory
- sparse models for multivariate spatial data

The talks aimed at fostering learning and exchange of ideas between the communities of spatial statisticians and harmonic analysts. There was ample time for discussions between the talks.

INVITED SPEAKERS

Thomas Arildsen
(Aalborg University)

Bubacarr Bah
(University of Texas at Austin, USA)

Peter Craigmile
(Ohio State University, USA)

Marc Genton
(King Abdullah University of Science and Technology, Saudi Arabia)

Rémi Gribonval
(Centre de Recherche INRIA, Rennes, France)

Anders Hansen
(University of Cambridge, United Kingdom)

William Kleiber
(University of Colorado, USA)

Jakob Lemvig
(Danish Technical University)

Finn Lindgren
(University of Bath, United Kingdom)

Jesper Møller
(Aalborg University)

Doug Nychka
(University Corporation for Atmospheric Research, USA)

Emilio Porcu
(University Federico Santa Maria, Chile)

From the canoe excursion to Lindenborg Å. The excursion started in Rebild Bakker.

CSGB JOURNAL AND PROCEEDINGS PUBLICATIONS, BOOK CHAPTERS

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Feragen, A., Lauze, F. & Hauberg, S. (2015): Geodesic exponential kernels: when curvature and linearity conflict. In *Proceedings of IEEE Conference on Computer Vision and Pattern Recognition (CVPR) 2015*, pp. 3032-3042.

Feragen, A., Petersen, J., Owen, M., Lo, P., Hohwu Thomsen, L., Wille, M.M., Dirksen, A. & de Bruijne, M. (2015): Geodesic atlas-based labeling of anatomical trees: application and evaluation on airways extracted from CT. *IEEE T. Med. Imaging* **34**, 1212-1226.

Foldager, C.B., Nyengaard, J.R., Lind, M. & Spector, M. (2015): A stereological method for the quantitative evaluation of cartilage repair tissue. *Cartilage* **6**, 123-132.

Guan, Y., Jalilian, A. & Waagepetersen, R. (2015): Quasi-likelihood for spatial point processes. *J. Roy. Stat. Soc. B* **77**, 677-697.

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Kousholt, A., Kiderlen, M. & Hug, D. (2015): Surface tensor estimation from linear sections. *Math. Nachr.* **288**, 1647-1672.

Lavancier, F., Møller, J. & Rubak, E. (2015): Determinantal point process models and statistical inference. *J. Roy. Stat. Soc. B* **77**, 853-877.

Lin, T.Y., Voronovsky, A., Raabe, M., Urlaub, H., Sander, B. & Golas, M.M. (2015): Dual tagging as an approach to isolate endogenous chromatin remodeling complexes from Saccharomyces cerevisiae. *Biochim. Biophys. Acta* **1854**, 198-208.

Mieritz, M.G., Raket, L.L., Hagen, C.P., Nielsen, J.E., Talman, M.-L.M., Petersen, J.H., Sommer, S.H., Main, K.M., Jørgensen, N. & Juul, A. (2015): A longitudinal study of growth, sex steroids and IGF-1 in boys with physiological gynaecomastia. *J. Clin. Endocr. Metab.* **100**, 3752-3759.

Møller, J. & Rasmussen, J.G. (2015): Spatial cluster point processes related to Poisson-Voronoi tessellations. *Stoch. Env. Res. Risk A.* **29**, 431-441.

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Pai, A.S.U., Klein, S., Sommer, S.H., Sørensen, L., Darkner, S., Sporring, J. & Nielsen, M. (2015): Adaptive time-stepping in diffeomorphic image registration with bounded inverse consistency error. In *Proceedings of Medical Image Computing and Computer-Assisted Intervention (MICCAI) 2015. Lecture Notes in Computer Science* **9349**, pp. 35-47.

Pausinger, F. & Svane, A.M. (2015): A Koksma-Hlawka inequality for general discrepancy systems. *J. Complexity* **31**, *773-797*.

Piuze, E., Sporring, J. & Siddiqi, K. (2015): Maurer-cartan forms for fields on surfaces : application to heart fiber geometry. *IEEE T. Pattern Anal.* **37**, 2492-2504.

Quéau, Y., Lauze, F.B. & Durou, J.-D. (2015): Solving uncalibrated photometric stereo using total variation. *J. Math. Imaging Vis.* **52**, 87-107.

Sommer, S.H. (2015a): Anisotropic distributions on manifolds: template estimation and most probable paths. In *Proceedings of Information Processing in Medical Imaging: 24th International Conference (IPMI) 2015. Lecture Notes in Computer Science* **9123**, pp. 193-204. Springer.

Sommer, S.H. (2015b): Evolution equations with anisotropic distributions and diffusion PCA. In *Proceedings of Geometric Science of Information: Second International Conference. Lecture Notes in Computer Science* **9389**, pp. 3-11. Springer.

Sommer, S.H. & Jacobs, H.O. (2015): Reduction by Lie group symmetries in diffeomorphic image registration and deformation modelling. *Symmetry* **7**, 599-624.

Svane, A.M. (2015a): Local digital algorithms for estimating the integrated mean curvature of *r*-regular sets. *Discrete Comput. Geom.* **54**, 316-338.

Svane, A.M. (2015b): Estimation of Minkowski tensors from digital grey-value images. *Image Anal. Stereol.* **34**, 51-61.

Svane, A.M. (2015c): Asymptotic variance of grey-scale surface area estimators. *Adv. Appl. Math.* **62**, 41-73.

Suryaprakash, V., Møller, J. & Fettweis, G.P. (2015): On the modeling and analysis of heterogeneous radio access networks using a Poisson cluster process. *IEEE T. Wirel. Commun.* **14**, 1035-1047.

Waagepetersen, R., Guan, Y., Jalilian, A. & Mateu, J. (2015): Analysis of multi-species point patterns using multivariate log Gaussian Cox processes. *Appl. Statist.* **65**, *77-96*.

Ziegel, J.F., Nyengaard J.R. & Jensen, E.B.V. (2015): Estimating particle shape and orientation using volume tensors. *Scand. J. Stat.* **42**, 813-831.

Ziomkiewicz, I., Sporring, J., Günther-Pomorski, T. & Schulz, A. (2015): Novel approach to measure the size of plasma-membrane nanodomains in single molecule localization microscopy. *Cytom. Part A* **87**, 868-877.

THREE 2015 INTERNATIONAL EVENTS

Curves and Tree Statistics Workshop
21 May 2015, University of Copenhagen

Professor Anuj Srivastava, Florida State University, Research Director Xavier Descombes, INRIA, Sophia-Antipolis, France, and eight researchers from the Image Section, KU, participated in this mini-workshop. The focus was on statistics on spaces of complex objects exhibiting non linear variations. The themes ranged from abstract problems such as kernels or diffusion on Riemannian manifolds, to more concrete ones, in particular (but not limited to) different types of geometric trees.

Shape Analysis Workshop
27 July – 1 August 2015, Grundsund, Sweden

This workshop, organized by Klas Modin and Stefan Sommer, took place in Grundsund, Sweden, in the archipelago of Western Sweden. The workshop was the third edition of the Shape Analysis workshops, continuing the earlier workshops in Foxton Beach, New Zealand, 2013, and in Bad Gastein, Austria, 2014.

The aim was to bring together a group of researchers with backgrounds ranging from differential geometry to applied medical image analysis to discuss questions of common interest. Topics discussed at the workshop included infinite-dimensional Riemannian geometry, shape analysis, image matching, computational anatomy and topological hydrodynamics.

Proceedings may be found at http://dx.doi.org/10.5281/zenodo.33558.

International Summer School on Convex & Discrete Optimization
17 – 21 August 2015, Sønderborg

The summer school was organized in collaboration between the Image Section, Department of Computer Science, University of Copenhagen, and the Image Analysis and Computer Graphics section, DTU Compute, Technical University of Denmark. The summer school gave a comprehensive overview of discrete and convex optimization with a focus on applications within imaging, involving topics such as Markov random fields, graphical models, convex optimization using duality, linear programming and relaxations, binary and multiple label problems, optimization in metric spaces and much more, plus a range of applications.

INTERNAL CSGB WORKSHOPS

The internal CSGB workshops are held twice a year. They are arranged alternately by the two Aarhus groups (the Stochastic Geometry and the Biomedical groups), the Spatial Statistics group at Aalborg University, and the Image Section at Department of Computer Science, University of Copenhagen.

The aim of these internal workshops is to discuss the present status of the CSGB research projects by presentations by the members of CSGB and to plan the further progress of the research projects. Furthermore, new activities arranged by CSGB such as workshops, courses, establishment of new international contacts, etc. are also discussed at these internal workshops. An equally important aim of the internal workshops is to tighten the connections between the researchers associated to CSGB.

In 2015, the following internal workshops were arranged

Tenth Internal CSGB Workshop
7 – 8 May 2015, Gl. Vraa Slot

Eleventh Internal CSGB Workshop
26 – 27 November 2015, Moesgaard Museum

CSGB VISITORS - 2015

Abd EL–Rahman AL–Absi (University of Aleppo, Syria) | 15 August 2014 - 15 February 2015

Ayse Ikinci (Karadeniz Technical University, Turkey)
18 August 2014 - 13 August 2015

Abdollah Jalilian (Razi University, Iran)
11 March - 3 April 2015

Adrian Baddeley (Curtin University, Perth, Australia)
12 - 25 April 2015

Anuj Srivastava (Florida State University, USA)
21 May 2015

Xavier Descombes (INRIA, Sophia-Antipolis, France)
21 May 2015

Bubacarr Bah (University of Texas at Austin, USA)
31 May - 3 June 2015

Haakon Christopher Bakka (NTNU, Trondheim, Norway) | 31 May - 3 June 2015

Brahim Boussidi (Université de Bretagne, France)
31 May - 3 June 2015

Jorge Clarke (University Federico Santa Maria, Chile)
31 May - 3 June 2015

Peter F. Craigmile (Ohio State University, USA)
31 May - 3 June 2015

Geir-Arne Fuglstad (NTNU, Trondheim, Norway)
31 May - 3 June 2015

Marc Genton (King Abdullah University of Science and Technology, Saudi Arabia) | 31 May - 3 June 2015

Rémi Gribonval (Centre de Recherche INRIA, Rennes, France) | 31 May - 3 June 2015

William Kleiber (University of Colorado, USA)
31 May - 3 June 2015

Jakob Lemvig (DTU, Denmark)
31 May - 3 June 2015

Finn Lindgren (University of Bath, United Kingdom)
31 May - 3 June 2015

Dough Nychka (IMAGe, USA)
31 May - 3 June 2015

Emilio Porcu (University Federico Santa Maria, Chile)
31 May - 3 June 2015

Brian Reich (North Carolina State University, USA)
31 May - 3 June 2015

Bogdan Roman (University of Cambridge, England)
31 May - 3 June 2015

Ying Sun (King Abdullah University of Science and Technology, Saudi Arabia) | 31 May - 3 June 2015

Yongtao Guan (University of Miami School of Business, USA) | 1 - 26 June 2015

Christoph Busch (Gjøvik University College, Norway)
14 - 17 June 2015

Dorin Comaniciu (Siemens Corporate Technology, USA) | 14 - 17 June 2015

Tim Cootes (University of Manchester, United Kingdom)
14 - 17 June 2015

Robert Jenssen (University of Tromsø, Norway)
14 - 17 June 2015

Thomas B. Moeslund (Aalborg University, Denmark)
14 - 17 June 2015

Carolina Wählby (Uppala University, Sweden)
14 - 17 June 2015

Kalle Åström (Lund University, Sweden)
14 - 17 June 2015

Richard J. Gardner (Western Washington University, USA) | 14 - 27 June, 2015

Fred Espen Benth (University of Oslo, Norway)
15 – 19 June 2015

José Manuel Corcuera (Universitat de Barcelona, Spain) |15 – 19 June 2015

Gérard Letac (Université Paul Sabatier, Toulouse, France) |15 – 19 June 2015

Albert Shiryaev (Steklov Mathematical Institute, Moscow, Russia) | 15 – 19 June 2015

Robert Stelzer (Ulm University, Germany)
15 – 19 June 2015

Adrian Baddeley (Curtin University, Perth, Australia)
27 June – 6 July 2015

Dianne Cook (Monash University, Melbourne, Australia)
30 June - 3 July 2015

Susan Holmes (Stanford University, USA)
30 June – 3 July 2015

Thomas Lumley (University of Auckland, New Zealand) | 30 June - 3 July 2015

Martin Andersen (DTU, Denmark)
17 – 21 August 2015

Yiqiu Dong (DTU, Denmark)
17 – 21 August 2015

Richard Hartley (Australian National University)
17 – 21 August 2015

Fredrik Kahl (Chalmers University of Technology)
17 – 21 August 2015

Henrik Aanæs (DTU, Denmark)
17 – 21 August 2015

Anders Rønn-Nielsen (University of Copenhagen, Denmark) | 30 September - 2 October 2015

Nina Balcan (Carnegie Mellon University, USA)
12 – 14 October 2015

Barbara Hammer (Bielefeld University, Germany)
12 – 14 October 2015

Morten Mørup (DTU, Denmark)
12 – 14 October 2015

Chloe-Agathe Azencott (MINES Paris Tech)
17 – 18 November 2015

Thordis Linda Thorarinsdottir (Norwegian Computing Center, Norway) | 19 - 22 October 2015

PhD course: Analysing spatial point patterns with R

21 – 22 April 2015, Aalborg University

On 21 – 22 April 2015 **Adrian Baddeley** gave a two-day PhD course at Aalborg University entitled *Analysing spatial point patterns with R*. The course had a strong focus on hands-on exercises using the comprehensive R package **spatstat**. No prior knowledge about spatial statistics was required, but basic familiarity with R and ordinary statistical concepts were prerequisites for attending the course.

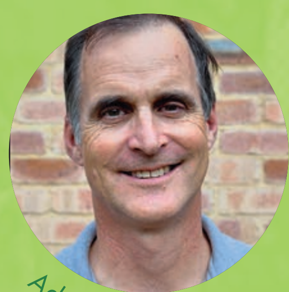
Description

Spatial point pattern data sets are becoming more common across many fields of research. However, statistical methodology for analysing these data has not been widely disseminated.

The course *Analysing spatial point patterns with R* provided a practical introduction to the analysis of spatial point patterns with a strong focus on hands-on exercises. The course gave an in-depth introduction to spatstat, which is an R-package for analysing spatial point patterns. The package supports a complete statistical analysis of spatial point pattern data: data input and inspection, calculations, plotting, exploratory data analysis, hypothesis tests, model-fitting, simulation, Monte Carlo methods and model diagnostics. The course treated all these subjects.

The course had the following goals:

- Understand basic statistical concepts used in spatial point pattern analysis.
- Get an overview of the capabilities of spatstat and how to find your way around.
- Learn how to conduct a basic analysis of a point pattern dataset.



Adrian Baddeley

APPENDIX

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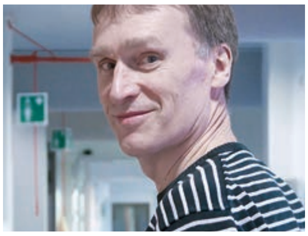
Jesper Møller (JM)
Mads Nielsen (MN)
Jens R. Nyengaard (JRN)
Rasmus P. Waagepetersen (RPW)


EBVJ


JM


MN


JRN


RPW

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Aasa Feragen (AF)
Monika Golas (MG)
Ute Hahn (UH)
Kristjana Ý. Jónsdóttir (KYJ)
Markus Kiderlen (MK)
François Lauze (FL)
Andrew du Plessis (AP)
Jakob G. Rasmussen (JGR)
Ege Rubak (ER)
Björn Sander (BS)
Jon Sporring (JS)


JBA


KADP


AF


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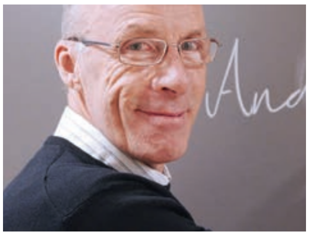
FL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SFB

CENTRE FOR **STOCHASTIC GEOMETRY**
AND ADVANCED **BIOIMAGING**

Annual Report 2015, published May 2016

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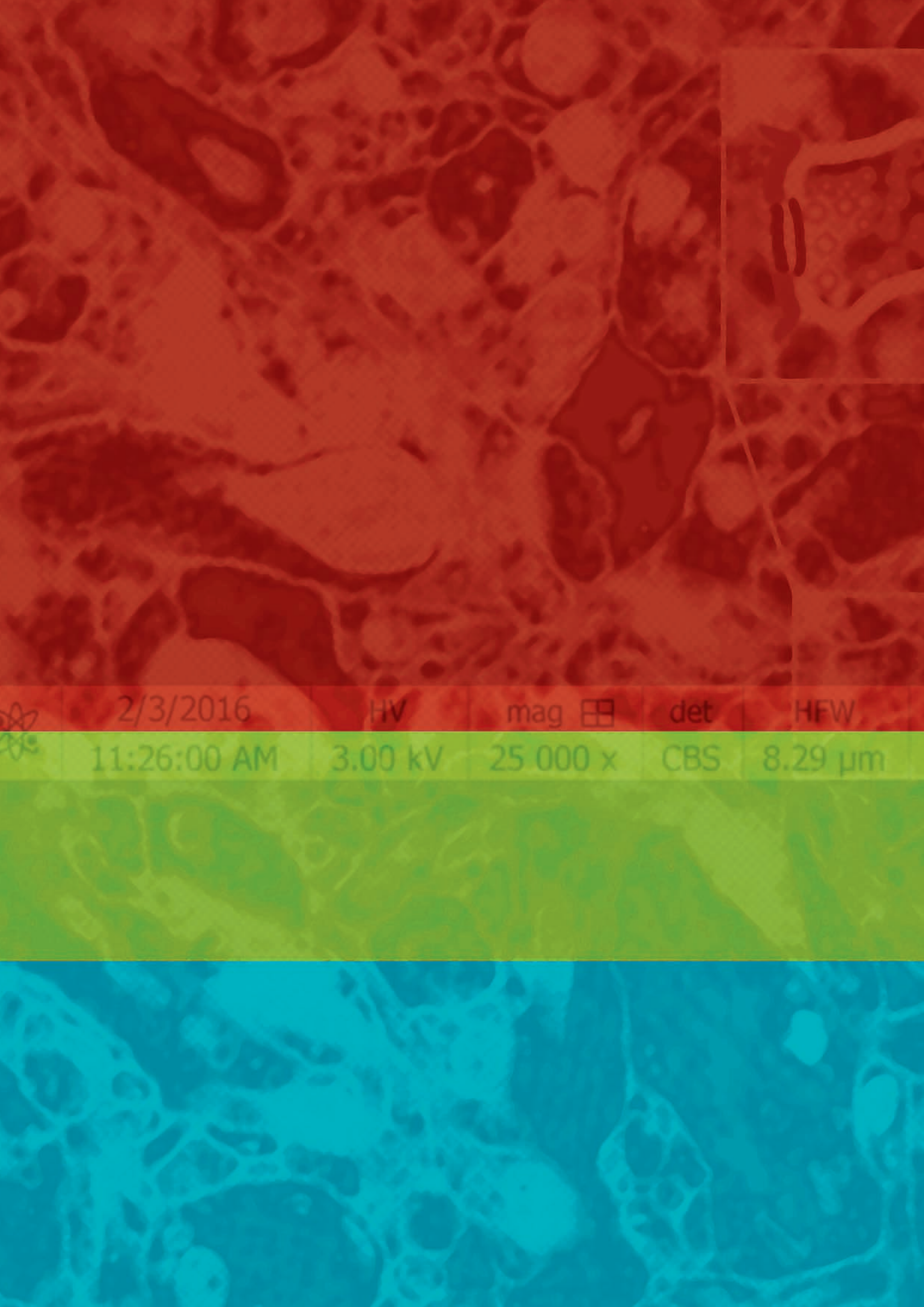
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