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

Annual Report 2017

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

Annual Report 2017, published April 2018

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INTRODUCTION

Centre for Stochastic Geometry and Advanced Bioimaging (CSGB) is a VKR Centre of Excellence. CSGB was established 1 April 2010 with a grant from the Villum Foundation of DKK 25 million. A second funding period started in 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 new statistical methods of analyzing advanced bioimaging data. Bioimaging data are extremely challenging to analyze, because of their complexity and huge size. In CSGB, the focus is on microscopy data, giving access to the molecular level, and on diffusion MRI data.

CSGB joins **four Danish research groups** at the Universities of Aarhus, Aalborg and Copenhagen: the stochastic geometry group (AU), the section for stereology and microscopy (AU), the spatial statistics group (AAU) and the image section (KU). The short geographical distance between the research groups 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.

During 2017 and the beginning of this year, five new **PhD students** and two new **postdocs** started at CSGB (page 12-13). Three of the new staff members come from abroad. Some of these new appointments would not have been possible without the additional funding that recently has been obtained by CSGB staff member Aasa Feragen.

Research-wise, 2017 was a year of many **publication highlights**. First of all, the Springer Lecture Notes on *Tensor Valuations and their Applications in Stochastic Geometry and Imaging* was published. The challenging project on Bayesian analysis of FRET data resulted in a paper in the recognized journal *Annals of Applied Statistics*. Two papers written by CSGB staff members appeared in the proceedings of IPMI 2017, a top medical imaging conference, and one paper in the proceedings of NIPS 2017, the most prestigious conference in machine learning with very low acceptance rate.

A detailed account of the research results obtained in 2017 for each of the six work packages, that form the research plan of the second funding period of CSGB, may be found on page 20-31. An overview of the results is given on page 18. A description of four collaborative projects is provided on page 19.

During 2017, we have organized four international **conferences** and **workshops**, and four international **PhD courses** (page 34). In 2017, the KU group was granted organization of the IPMI 2021 conference. In early 2018, we were informed that our proposal for hosting the *International Congress for Stereology and Image Analysis* was selected by the board of the International Society for Stereology and Image Analysis. The conference will take place 27 - 30 May 2019.

On 15 November 2017, a **follow-up meeting** between CSGB and the Villum Foundation took place. In 2017, a theme of the follow-up meetings between the VKR centres of excellence and the Villum Foundation was research integrity. This theme was present during the whole follow-up meeting on 15 November 2017. The future of CSGB beyond the present funding period (2015-2020) was also discussed.

In the following pages, we inform in more detail our colleagues, potential research students, the Danish funding partner and the Universities of Aarhus, Aalborg and Copenhagen about the organization, research and other centre activities that took place at CSGB in 2017.

April 2018
Eva B. Vedel Jensen

www.csgb.dk

ORGANIZATION AND STAFF

ORGANIZATION AND STAFF

STAFF

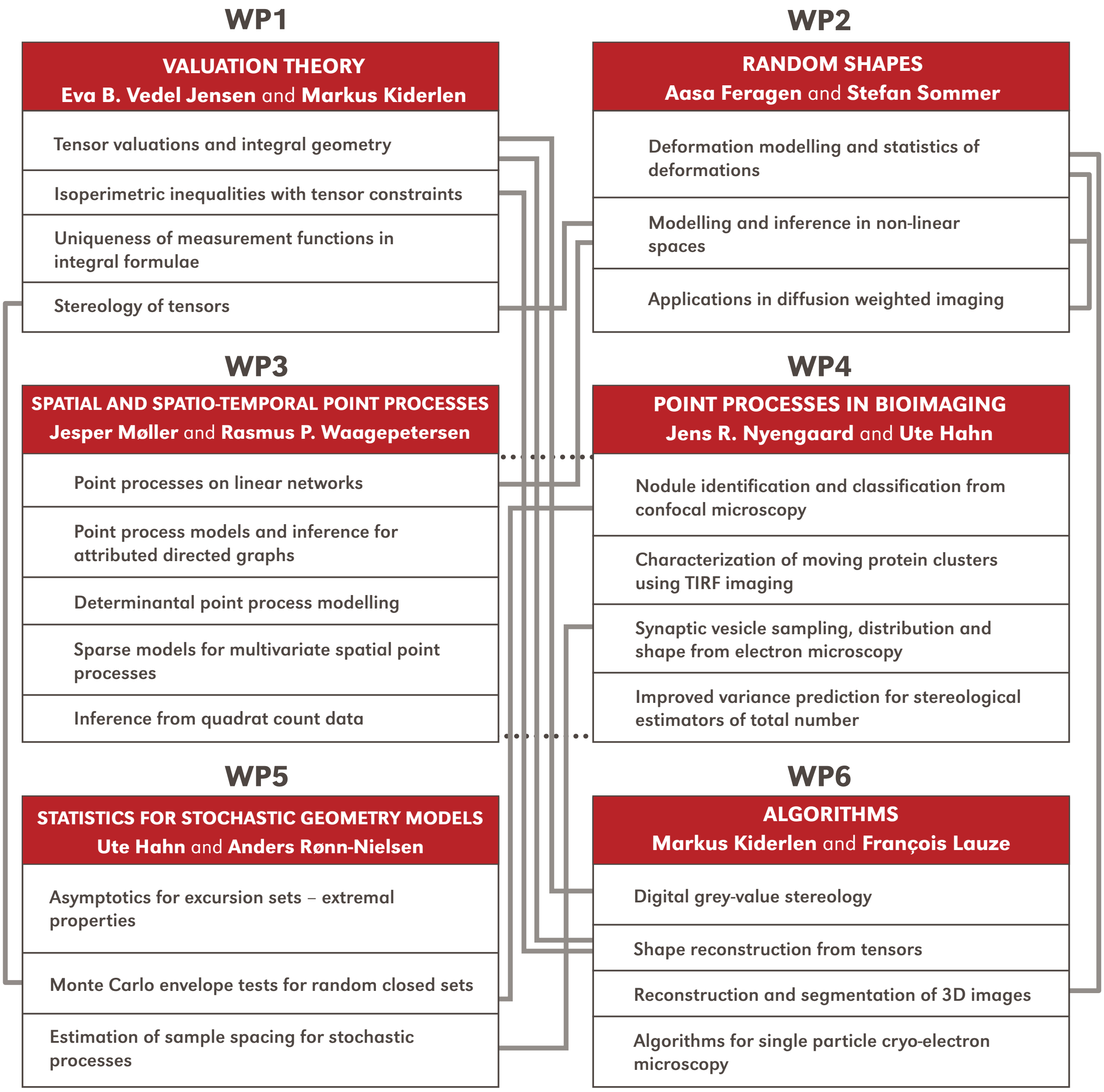
Centre for Stochastic Geometry and Advanced Bioimaging (CSGB) unites four Danish research groups

- **AU-math:** Stochastic Geometry Group, Department of Mathematics, AU
- **AU-bio:** Section for Stereology and Microscopy, Department of Clinical Medicine, AU
- **AAU:** Spatial Statistics Group, Department of Mathematical Sciences, AAU
- **KU:** Image Section, Department of Computer Science, KU

The staff consisted in 2017 of 5 professors, 15 associate professors, 2 assistant professors, 4 postdocs and 14 PhD students, see page 44-45 for details.

RESEARCH PLAN

The research is in the second funding period of CSGB (1 April 2015 – 31 March 2020) organized in six work packages, see the diagram below. The principal investigators of the work packages are also shown in the diagram, just below the title of the work packages.



NEWS ABOUT STAFF

Aasa Feragen (KU)
Aasa Feragen has in 2017 obtained additional funding, this time from the Novo Nordisk Foundation. As mentioned in *CSGB Annual Report* **2016**, she has also recently obtained funding from the Villum Foundation and the Lundbeck Foundation. Aasa Feragen is one of the principal investigators of the **Random shapes** work package. She is in charge of the project *Image Registration with Topological Differences through Stratified Diffeomorphisms* that has been strengthened by the additional funding. Aasa Feragen is also involved in applications in diffusion MRI, in particular modelling and uncertainty quantification for diffusion MRI data.

Jesper Møller (AAU)
Jesper Møller has in 2017 obtained additional funding from the Danish Council for Independent Research (DFF). The title of the funded project is *Point Processes in Space and Beyond*. Jesper Møller is leading the AAU spatial statistics group and one of the principal investigators of the work package **Spatial and spatio-temporal point processes**. Together with the rest of the AAU group, he also plays a decisive role in the work package **Point processes in bioimaging** that involves a number of collaborative projects between the four research groups participating in CSGB. The AAU group is in the process of organizing in Aalborg an international conference with the same title as the DFF project title. The conference will take place 13 – 16 May 2019.

Anders Rønn-Nielsen (AU-math)
Anders Rønn-Nielsen has recently been appointed principal investigator of the work package **Statistics for stochastic geometry models**. Anders is one of the main contributors to this work package where he in particular uses his skills in probability theory to study the asymptotic behaviour of excursions sets for non-Gaussian random fields.
The random fields considered are infinitely divisible with convolution equivalent Lévy measure. He replaces as principal investigator Kristjana Ýr Jónsdóttir who in 2016 decided to move back to her home country Island. During 2017, Anders Rønn-Nielsen moved from Department of Mathematical Sciences, University of Copenhagen, to Department of Finance, Copenhagen Business School, where he holds an associate professorship.

Stefan Sommer (KU)
In April 2017, Stefan Sommer was promoted from assistant to associate professor at Department of Computer Science, University of Copenhagen. He has been a member of the CSGB staff since the very beginning in 2010, first as PhD student, then as assistant professor and now as associate professor. In the second funding period of CSGB (2015-2020), Stefan Sommer is one of the principal investigators of the **Random shapes** work package. During 2017, Stefan Sommer and coworkers have developed a general framework for including noise in shape models. The research on large deformation models and stochastic development regression on non-linear manifolds has also been published in 2017.

APPOINTMENTS 2017/2018

Achmad Choiruddin (AAU)
Achmad Choiruddin has a double master degree from 2014 in applied mathematics and statistics from Institut Teknologi Sepuluh Nopember, Indonesia, and University Aix-Marseille, France. He obtained a PhD degree from University Grenoble Alpes in 2017 with a thesis entitled *Feature Selection for Spatial Point Processes*. Achmad Choiruddin has been a postdoc at the AAU group since 1 September 2017. He is participating in the work package **Spatial and spatio-temporal point processes**. More specifically, he is involved in the development of sparse models for spatial point processes. Achmad Choiruddin contributes with his competences in spatial regression models and LASSO-type methods for spatial point processes.

Ivan D'Annibale (KU)
Ivan D'Annibale earned his master of science degree in mathematics from Sapienza, University of Rome. The title of the master thesis was *Chern-Simons and Stacks Morphisms*. He has a strong theoretical background in differential geometry and topology. Ivan D'Annibale is interested in applications of geometry, topology and ideas from physics to questions from biology. In May 2017, he started as a PhD student at the KU group. His PhD project entitled *Image Registration with Topological Differences through Stratified Diffeomorphisms* lies within the **Random shapes** work package. Transformations linking a pair of images are usually diffeomorphisms between manifolds. In the PhD project, the aim is to study more general objects, allowing for singularities.

Tom Dela Haije (KU)
Tom Dela Haije has a master degree in biomedical engineering from Eindhoven University of Technology. In 2017, he obtained a PhD degree in mathematics with a thesis entitled *Finsler Geometry and Diffusion MRI*, also from Eindhoven University of Technology. Tom Dela Haije was hired as a postdoc at the KU group in March 2017. Tom Dela Haije is participating in the **Random shapes** work package. He is engaged with applications in diffusion MRI, in particular focusing on modelling and uncertainty quantification for data obtained from this type of image modality. The research on geometry in diffusion MRI has been significantly strengthened by the hiring of Tom Dela Haije.

Louis Gammelgaard Jensen (AU-math)
Louis Gammelgaard Jensen has a bachelor degree in mathematical statistics from Aarhus University. He started as PhD student (4+4 programme) at the AU-math group in February 2018. The title of his PhD project is *Statistical Models and Analysis Methods for Super-Resolution Microscopy*. The project is part of the work package **Point processes in bioimaging**. It is the plan that Louis Gammelgaard Jensen will continue and further develop the research earlier taken place at CSGB on statistical modelling and inference for PALM (photoactivated localization microscopy) data. In particular, it is planned to develop models where the temporal component of the data is taken into account.

Kristian Bjørn Hessellund (AAU)
Kristian Bjørn Hessellund has a master degree in mathematical statistics from Aalborg University. He started as a PhD student at the AAU group in September 2017. His project lies within the work package **Spatial and spatio-temporal point processes**. The title of the project is *Statistical Analysis of Multivariate Point Patterns using a Case-Control Approach*. The aim is to propose a new method for analyzing multi-type (multivariate) point patterns, considering the different types of points as cases relative to some control pattern. Exploratory functions called cross-summary statistics are an integral part of the approach. Kristian Bjørn Hessellund has also a bachelor degree in sports science.

Rune Kok Nielsen (KU)
Rune Kok Nielsen has a bachelor degree in computer science from University of Copenhagen. Since September 2017, he has been a PhD student (4+4 programme) at the KU group. Rune Kok Nielsen is working under the same project heading as Ivan D'Annibale, *Image Registration with Topological Differences through Stratified Diffeomorphisms*, within the work package **Random shapes**, but his emphasis will be on more concrete image processing and machine learning aspects of the project. Rune Kok Nielsen has strong competences in these two disciplines as well as in systems engineering.

Hans Jacob Teglbjærg Stephensen (KU)
In August 2017, Hans Jacob Teglbjærg Stephensen defended his master thesis entitled *Biophysical Parameter Estimation using Image Analysis — Distribution of Organelles using Shortest Path Metrics on the Intracellular Space of the Neuron Active Zone*. Immediately after the defence, he was hired as PhD student at the KU group. The title of his PhD project is *Geometric Models and Stochastic Geometry of Subcellular Structures*. The project is part of the work package **Point processes in bioimaging** and involves collaboration between the KU, AU-bio and AAU groups. An important application area of the PhD project is in the study of the spatial distribution of synaptic vesicles, obtained by FIB-SEM (focused ion beam scanning electron microscopy).

ORGANIZATION AND STAFF

NEWS ABOUT STAFF/EVENTS 2017

PUBLICATION HIGHLIGHTS 2017

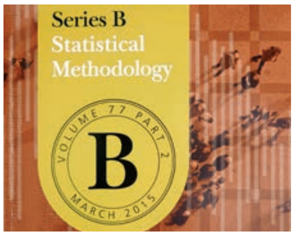
The volume in the Springer Lecture Notes in Mathematics Series, entitled *Tensor Valuations and their Applications in Stochastic Geometry and Imaging*, has been published in 2017. Publication details may be found under WP1, page 20-21. In 15 chapters, edited by **Eva B. Vedel Jensen** and **Markus Kiderlen**, a comprehensive overview of the modern theory of tensor valuations is given. See also http://www.springer.com/gp/book/9783319519500.

A paper written by **Anton Mallasto** and **Aasa Feragen** was in 2017 accepted for publication in the proceedings of the *Conference on Neural Information Processing Systems (NIPS) 2017*. NIPS is the most prestigious conference in machine learning with very low acceptance rate. Publication details may be found under WP2, page 22-23.

Two papers with **Line Kühnel** and **Stefan Sommer** as coauthors were accepted for publication in the proceedings of the *Information Processing in Medical Imaging (IPMI) 2017 Conference*, a top medical imaging conference. Publication details may be found under WP2, page 22-23.

In 2017, a challenging collaborative project on Bayesian analysis of FRET data resulted in a paper in the recognized journal *Annals of Applied Statistics*. Amongst the authors of this paper was **Jan-Otto Hooghoudt** and **Rasmus Waagepetersen**. Publication details may be found under WP4, page 26-27.

One of the absolute highlights in 2017 was the publication in the prestigious *Journal of the Royal Statistical Society B* of a paper on envelope testing for spatial processes, see WP5, page 28-29. The research team behind this paper includes CSGB researcher **Ute Hahn**.



FOLLOW-UP MEETING - 15 NOVEMBER 2017

On 15 November 2017, a follow-up meeting took place at Department of Mathematics, Aarhus University, between CSGB and the Villum Foundation.

From the Villum Foundation, the following participated: Director of Science Thomas Sinkjær, Professor Anja Boisen (DTU, member of the Foundation's board), Professor Poul Henrik Damgaard (KU, member of the Foundation's technical and natural sciences committee), Professor Peter Landrock (member of the Foundation's board) and Senior Adviser Lars Arnskov Olsen. From CSGB, thirty staff members participated, representing about 70% of the staff.

After an introduction by Director of Science Thomas Sinkjær, Eva B. Vedel Jensen gave a brief overview of CSGB, including the present staff, new appointments, status of the work packages and selected highlights since last follow-up meeting. This overview was followed by a presentation of two of the collaborative projects at CSGB:

- **Karl-Anton Dorph-Petersen** (AU-bio) and **Jesper Møller** (AAU): *The minicolumn hypothesis*
- **Stine Hasselholt** (AU-bio) and **Jon Sporring** (KU): *Synaptic vesicles by FIB-SEM*

In 2017, a theme of the follow-up meetings between the VKR centres of excellence and the Villum Foundation was reearch integrity. This theme was present during the whole follow-up meeting on 15 November 2017. The research environment of CSGB was described, including the supervision of junior researchers (mentoring and guidance, co-authorship), local weekly meetings (informal presentations by the junior researchers, mixed audiences), the internal CSGB workshops (including special junior meetings) and the role of the annual reports (information for colleagues, internal purposes).
The future of CSGB beyond the present funding period (2015-2020) was also discussed.

AWARDS AND RECOGNITION

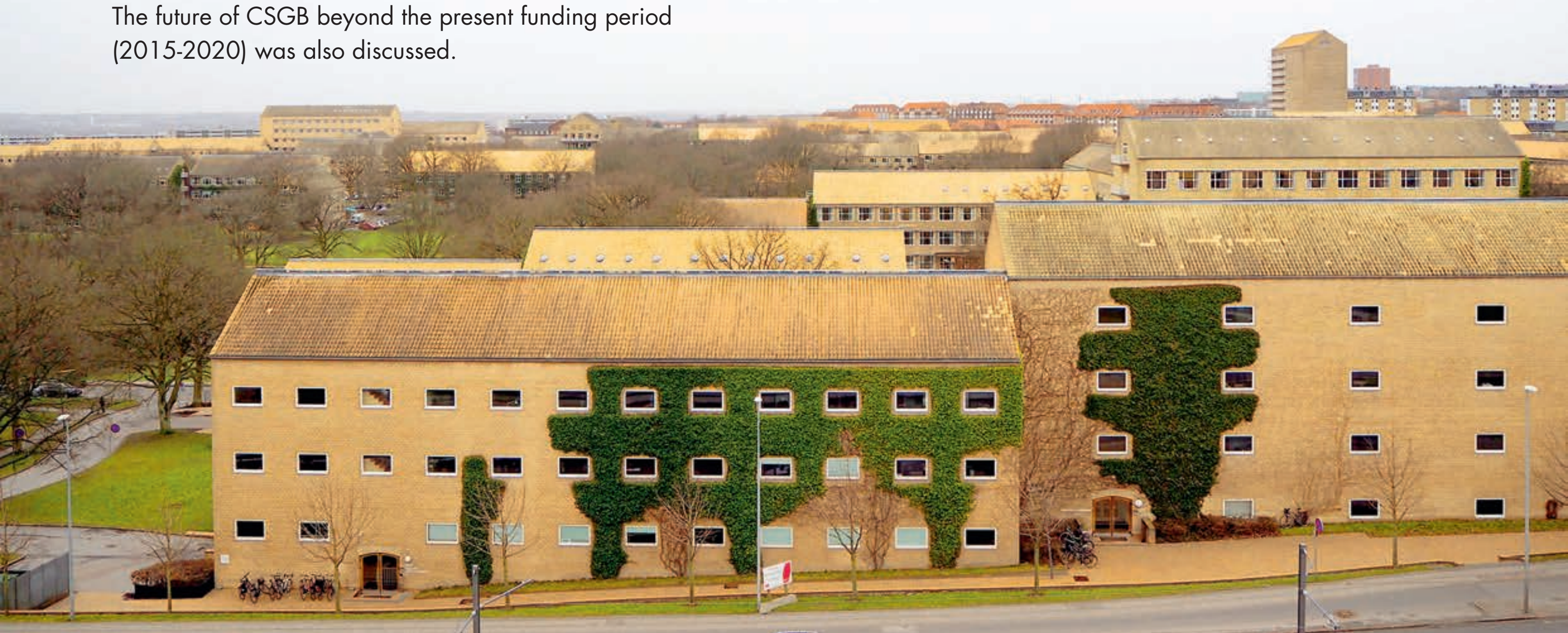
In 2017, the KU group was granted the organization of the *Information Processing in Medical Imaging (IPMI) 2021 Conference*. IPMI is among the most prestigious medical imaging conferences. The organizing team consists of Mads Nielsen (KU), Julia Schnabel (Kings College), Aasa Feragen (KU, programme committee chair), Stefan Sommer (KU, general chair). The conference will take place at the Danish island of Bornholm.

In early 2018, we were informed that our proposal for hosting the *International Congress for Stereology and Image Analysis (ICSIA)* was selected by the members of the International Society for Stereology and Image Analysis board. The conference will take place in Aarhus 27 – 30 May 2019. The organization team includes members from the AU-math, AU-bio, AAU and KU groups.

SOFTWARE

Ege Rubak (AAU) and coworkers have developed the software s2 (https://github.com/spatstat/s2) and spatstat.sphere (https://github.com/spatstat/spatstat.sphere). Spherical geometry calculations may be performed by s2 in R, while spatstat.sphere performs analysis of spatial point processes on the sphere.

Stefan Sommer (KU) and coworkers have developed the software Theano Geometry (https://bitbucket.org/stefansommer/theanogeometry). The software uses the Theano framework in an efficient implementation of differential geometry and non-linear algorithms.



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RESEARCH

RESEARCH OVERVIEW 2017

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 give an overview of the research taken place in 2017 within each of these work packages. A detailed description of the research results obtained in 2017 may be found on page 20-31. On the following page, the present status of four collaborative projects is described.

The research within the work package **Valuation theory** has in 2017 been focused on uniqueness of measurement functions in integral geometric formulae. This question has been triggered by the observation that two apparently very different measurement functions may essentially coincide. In integral geometric language, we have asked for uniqueness of the measurement function in the classical (affine) Crofton formula. Uniqueness holds if the measurement function is continuous, motion invariant and additive. However, if the motion invariance is weakened to translation invariance, uniqueness does no longer hold. Riemann-Liouville integrals play a role in the case where the section is a line.

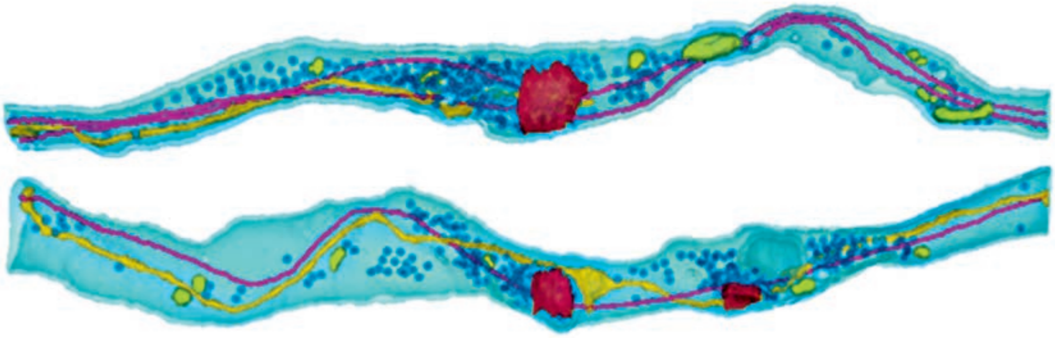
In the **Random shapes** work package, a general framework for including noise in shape models with geometry inherited from the diffeomorphism group has been developed. The proposed stochastic model is a natural extension of the deterministic set-up and has a rich geometric structure. Likelihood based statistics of landmark configurations was also investigated further in 2017. Advances were made on uncertainty quantification in non-linear statistics. These results allow us to take into account the uncertainty of estimated brain connectivity when analyzing images from diffusion MRI. The research on diffusion MRI also resulted in two contributions on scalable reconstruction of higher order cumulants.

Parametric classes of isotropic covariance functions on linear networks have been developed in 2017 within the work package **Spatial and spatio-temporal point processes**. Moreover, Gaussian random fields and log Gaussian Cox processes have been constructed on such networks. In 2017, a number of new estimation procedures for spatial point processes have also been developed, including an orthogonal series estimator of the pair correlation function, a fast spectral quasi-likelihood estimator of the intensity function and a second-order quasi-likelihood estimation procedure. Finally, pair correlation functions and limiting distributions for iterated cluster point processes have been derived.

The research within the work package **Point processes in bioimaging** has been focused on (i) improved estimation in Cavalieri designs and (ii) point process modelling of protein clusters. The background for the research on improved estimation in Cavalieri designs is the observation that unequal spacing significantly affects the asymptotic variance of the Cavalieri estimator. In 2017, a new Cavalieri type estimator with improved variance behaviour has been constructed. The estimator uses information about the actual section spacing. During 2017, we have also developed new point process models for PALM data. The processes, denoted double Cox cluster processes, can describe clustering at two different scales.

Within the work package **Statistics for stochastic geometry models**, the research on asymptotics for excursion sets has been published in 2017. A new method of estimating sample spacing for stochastic processes has also been published in 2017. The project on Monte Carlo envelope tests resulted in two publications, one of them in the prestigious *Journal of the Royal Statistical Society B*. During 2017, the research on envelope testing focused on an extension of the envelope method for the comparison of groups of functional data. The initial application being summary statistics estimated on point patterns, the method is applicable in a much broader context.

The work package **Algorithms** involves the development of computer-intensive algorithms, including a study of their mathematical and statistical properties. During 2017, we have developed further the project on reconstructing a 3-dimensional black object, or determining topological features of it, from a digital grey-scale image. The focus has been on objects that are *r*-regular. An important step has been to determine the configurations of black and non-black voxels that cannot occur in the digitization of such an object. In 2017, a number of papers, dealing with other research questions in this work package, has also been published, including papers on shape reconstruction from surface tensors and estimation of Minkowski tensors from digital images.



COLLABORATIVE PROJECTS

Stereology of tensors by optical microscopy (AU-bio/AU-math)

During 2017, a main focus in this project has been on implementation in optical microscopy of a new stereological estimator of mean particle volume tensors from vertical sections. A manuscript is in preparation that presents the new method for researchers, using microscopy. The measurements required for the estimation can be given in explicit form for particles in 3D. For cases where the intersections between the particles and the vertical section are not available as digital images, procedures have been developed for such digitization. The resulting estimators of mean particle volume tensors give information about particle shape and related characteristics. The new method works if the tissue under investigation satisfies the restricted isotropy assumption. This assumption may be relaxed if the vertical section has a uniform rotation around the vertical axis.

The minicolumn hypothesis (AU-bio/AU-math/AAU/KU)

The minicolumn hypothesis in neuroscience claims that neurons and other brain cells have a columnar arrangement, perpendicular to the surface of the brain. In 2017, we have initiated a larger investigation of this hypothesis for neurons in the Brodmann Area 46 (BA46) in human autopsy brains. The AU-bio and AU-math groups have developed sampling procedures for collection of biopsies from BA46. After embedding in Epon, several staining techniques of the biopsies have been tested. The most optimal technique with a signal-to-noise ratio of approximately 1.5 has been chosen in collaboration with the KU group. The cutting of biopsies will take place in Beijing, China, on a unique AutoCUT machine, which can collect thousands of sections, using automatic microscopy software. We aim at automatic procedures for detecting the neurons in BA46. Here, the KU group will again play an important role while the AAU group will contribute with statistical analysis of the spatial distribution of the neurons, using marked point processes.

Neuronal dendritic trees and spines (AU-bio/AAU)

Neuron synapse function has repeatedly been shown to be related to spine geometry. Spines are highly plastic protrusions on the dendrites that can rapidly and dramatically react to several disorders. Therefore, it is of interest to reconstruct in 3D dendritic trees and study the distribution of the spines on these trees. The manual reconstruction method is subjective and time consuming. The more recent automatic reconstruction method lacks the necessary accuracy. Therefore, the less time consuming semi-automatic method represents an important alternative for 3D reconstruction. A paper is in preparation where the three types of reconstruction methods are compared for suitably sampled neurons in Golgi stained mouse brains. This investigation involves the AU-bio and AAU groups. We expect to submit the paper during 2018. For appropriately reconstructed dendrites and spines, the next step is to develop spatial marked point process models, describing the relationship between characteristics of the dendrite trees and the spines. One possibility is point processes on graphs.

Synaptic vesicles by FIB-SEM (AU-bio/AAU/KU)

Focused ion beam scanning electron microscopy (FIB-SEM) offers details at sub-cellular level of dynamic processes frozen in time. Neurons are of particular interest to us, since they independently are simple but collectively have complex behaviour. One process of interest is neuronal communication, and for some time we have studied first- and second-order statistics of vesicles near the synaptic cleft. Some of our recent research results have been published in Khanmohammadi *et al.* (2017, *J. Microsc.* **265**, 101-110). The list of authors include researchers from both the AU-bio group and the KU group. A next step is to extend our approach to other ultrastructures than the vesicles: endoplasmic reticulum, endosome, mitochondria and other tubular structures. Our goal is to develop a modelling approach that includes all these structures visible in FIB-SEM images.

WP1

Researchers
Johnny B. Andersen
Karl-Anton Dorph-Petersen
Rikke Krog Eriksen
Eva B. Vedel Jensen
Markus Kiderlen
Nick Larsen
Jens R. Nyengaard
Andrew du Plessis
Mads Stehr
Johanna F. Ziegel

Valuation theory

In 2017, one of the absolute highlights was the publication in the Springer Series, *Lecture Notes in Mathematics*, of the **volume on tensor valuations** and their applications in stochastic geometry and imaging, see Jensen & Kiderlen (2017a). This volume gives an up-to-date introduction to tensor valuations and their applications. Starting with classical results concerning scalar-valued valuations on the families of convex bodies and convex polytopes, it proceeds to the modern theory of tensor valuations. Product and Fourier-type transforms are introduced and various integral formulae are derived. New and well-known results are presented, together with generalizations in several directions, including extensions to the non-Euclidean setting and to non-convex sets. A variety of applications of tensor valuations to models in stochastic geometry, to local stereology and to imaging are also discussed. Jensen & Kiderlen (2017b), Kousholt *et al.* (2017) and Svane (2017) appear as chapters in this volume.

Otherwise, the research within this work package has in 2017 been focused on **uniqueness of measurement functions** in integral geometric formulae. This question has been triggered by the following observation. Established methods in local stereology allow to estimate the surface area of an object K in 3D from a section with a randomized isotropic plane L_2 through a fixed reference point. The function φ of the section profile, which yields an unbiased estimator of the surface area of K, is called measurement function. It was explicitly given in Jensen & Gundersen (1987), where the estimator $\varphi(K \cap L_2)$ was named **surfactor**. Later, based on the invariator principle, an apparently different measurement function was derived in Cruz-Orive (2005). The CSGB group has shown (Thórisdóttir & Kiderlen, 2014) that the two measurement functions essentially coincide. This motivates the general question if measurement functions are essentially unique. Uniqueness can only be expected under additional geometric assumptions, as a random variable is only in trivial cases determined by its mean.

For convex objects K, Jensen & Kiderlen (2017b) showed a result for sections with a **random line** L_1 instead of the two-dimensional plane L_2 above. It is not required that the target is the surface area, nor is the restriction to three-dimensional space essential. If φ and φ' are two rotation invariant measurement functions such that the expectations

$$\mathbb{E}\,\varphi(K \cap L_1) = \mathbb{E}\,\varphi'(K \cap L_1)$$

coincide for all compact, convex sets K, then $\varphi = \varphi'$. Such measurement functions are very common in applications, when the target is a rotation invariant functional of K, for instance, an intrinsic volume.

Ongoing work (Eriksen & Kiderlen, 2018) focuses on uniqueness of the measurement function when K is sampled with a suitably **randomized affine plane** E_k of dimension k, see Figure 1. In integral geometric language, we ask for uniqueness of the measurement function in the classical Crofton formula: if E_k is an IUR plane (isotropic uniform random), under what conditions does

$$\mathbb{E}\,\varphi(K \cap E_k) = \mathbb{E}\,\varphi'(K \cap E_k)$$

imply that $\varphi = \varphi'$? When φ and φ' are continuous (with respect to the Hausdorff metric), motion invariant and additive, uniqueness holds, as they must be linear combinations of intrinsic volumes by Hadwiger's theorem (Schneider, 2014), and the coefficients must coincide due to the classical Crofton formula. However, if the motion invariance is weakened to translation invariance, uniqueness does no longer hold, and a whole family of counterexamples can be constructed.

When the Crofton formula with lines ($k = 1$) is considered, a result analogous to the one for the local case can be established: If both functionals φ and φ' are motion invariant, and $\mathbb{E}\,\varphi(K \cap E_1) = \mathbb{E}\,\varphi'(K \cap E_1)$, then φ essentially coincides with φ'. In this linear case, the expectations can be reduced to a **Riemann-Liouville integral**, and known injectivity properties of the corresponding transform can be exploited.

During 2017, the research on rotational Crofton formulae and some affine counterparts has been published, see Svane & Jensen (2017). The formulae show how rotational averages of intrinsically defined Minkowski tensors on sections passing through the origin are related to the geometry of the sectioned set. See also the *CSGB Research Report* Kiderlen & Rataj (2017) on dilation volumes of sets with finite perimeter.

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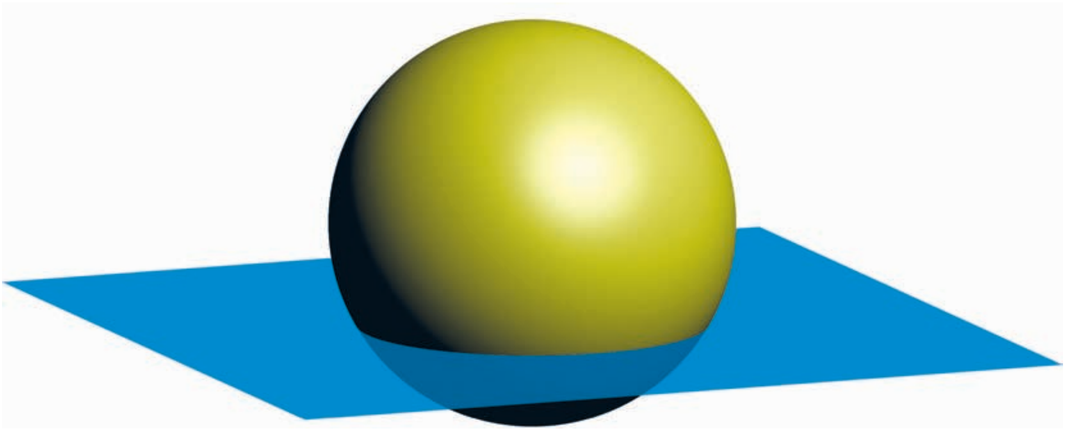

Figure 1
An illustration of the fundamental relations in stereology: the surface area of the 3D object can be estimated unbiasedly, measuring the perimeter of the section profile in a random (IUR) plane.

WP2

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Random shapes

In this work package, we study random shapes that reside in non-linear spaces. The aim is to develop statistical and computational tools for analyzing data in such spaces. Examples are manifolds, stratified spaces and general metric spaces. Most tools have to be developed anew for non-linear domains, as their usual definitions require Euclidean structure. This includes theoretical properties like consistency and uniqueness, as well as computational tools and heuristics from combinatorics and computational geometry.

Random shapes have been the focus of several papers and talks as well as software development in 2017. Continued collaboration between the KU group and Department of Mathematics, Imperial College, London, resulted in the submission of the paper Arnaudon *et al.* (2017b) that introduces a general framework for including **noise in shape models** with geometry inherited from the diffeomorphism group. The deterministic set-up uses the action of the diffeomorphism group and a right-invariant metric to induce geometries on shape spaces. The proposed stochastic model continues this by adding right-invariant stochastic noise to the shape evolutions. This gives a rich geometric structure, including a stochastic Euler-Poincaré principle for reducing dynamics of extremal paths. The model was in Arnaudon *et al.* (2017c) extended to the stochastic metamorphosis case. In metamorphosis, the action of the diffeomorphism group is accompanied by internal changes of the shape itself. For functional data, both the phase and the amplitude can vary in metamorphosis. In stochastic metamorphosis, a stochastic model is applied to both phase and amplitude variation while keeping the geometric properties of the original method.

In Arnaudon *et al.* (2017d), the stochastic model was related to **string methods** used for rare event sampling in physics. The main purpose was to link the method to a classical optimization algorithm for the deterministic case that progressively "shortens" a string between to shapes. With stochasticity, the matching takes the form of a progressively tightening of a randomly vibrating string of shapes.

Likelihood based statistics of landmark configurations was investigated in Sommer *et al.* (2017), using the guided diffusion approach. This work should be seen as part of a wider effort of introducing a more probabilistic approach to statistics of manifold-valued non-linear data. Instead of using geodesics and Riemannian distances as the main vehicles for statistics, we wish to base non-linear statistics on **likelihoods** and maximum a posteriori estimation.

During 2017, further advances were made on uncertainty quantification in non-linear statistics. The paper Mallasto & Feragen (2017a) endows the space of Gaussian Processes (GPs) with a Wasserstein metric and proves asymptotic results on how it relates to the well-known Wasserstein spaces of Gaussian distributions and their statistics. This allows us to perform basic statistical operations on structural brain connectivity from **diffusion MRI**, while respecting the uncertainty of the estimated brain connectivity. In Mallasto & Feragen (2017b), a GP regression algorithm has been defined for manifold-valued data, allowing uncertainty quantification for manifold-valued regression.

The research on diffusion MRI has resulted in two contributions on scalable reconstruction of higher order cumulants (Dela Haije & Feragen, 2017a, b), which will be used for subsequent analysis.

In Kühnel & Sommer (2017a) and Kühnel *et al.* (2018), the Theano geometry framework for performing differential geometric computations has been developed, using the automatic differentiation features of modern deep learning methodology. The shift away from hand derived and implemented derivatives allows computations of a complexity that was previously infeasible to implement in practice.

During 2017, the research on **large deformation models** and stochastic development regression on non-linear manifolds has been published in Arnaudon *et al.* (2017a) and Kühnel & Sommer (2017b). This research was already described in *CSGB Annual Report* **2016**.

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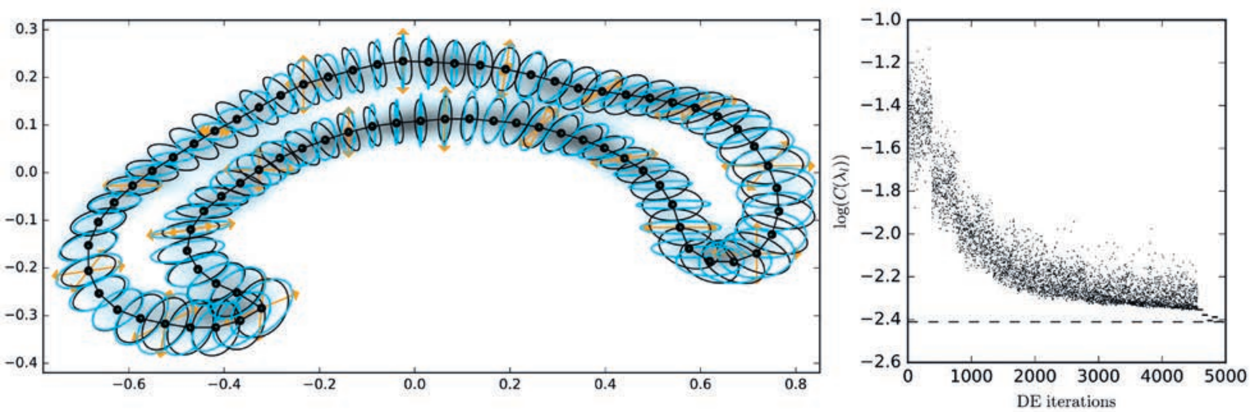

Figure 1
Corpus callosum estimation with moment matching. For details, see Arnaudon *et al.* (2017a).

WP3

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Spatial and spatio-temporal point processes

The CSGB researchers associated with this work package have during 2017 also contributed to the work package WP4 on point processes in bioimaging. Most importantly, research on Bayesian analysis of the spatial distribution of proteins from FRET data has been published, see page 26-27.

Within WP3, we have during 2017 developed parametric classes of covariance functions on **linear networks** and their extension to graphs with Euclidean edges, see Anderes *et al.* (2017). The covariance functions are isotropic in the sense that they only depend on a new metric that extends the classical resistance metric on the vertices of a weighted graph to both the vertices and edges of any graph with Euclidean edges. The paper Anderes *et al.* (2017) has been submitted to the prestigious *Annals of Statistics*. Moreover, in two newly started projects, Gaussian random fields and log Gaussian Cox processes are constructed on such graphs, and the possibility for deriving further models has been investigated when considering **directed graphs** with Euclidean edges.

The pair correlation function is a fundamental spatial point process characteristic that, given the intensity function, determines second-order moments of the point process. Non-parametric kernel estimators are popular, but especially for clustered point patterns the estimators suffer from bias for small spatial lags. In Jalilian *et al.* (2017), we introduce a new **orthogonal series estimator**, which is consistent and asymptotically normal. Our simulations further show that the new estimator can outperform the kernel estimators, in particular for Poisson and clustered point processes.

In applications of spatial point processes, it is often of interest to fit a parametric model for the intensity function. A **quasi-likelihood type estimating function**, that is optimal within a certain class of first-order estimating functions, has recently been introduced. However, depending on the choice of certain tuning parameters, the implementation of the method can be very demanding, both in terms of computing time and memory requirements. Using a novel spectral representation, we construct in Deng *et al.* (2018) an implementation that is computationally much more efficient than seen before in the literature.

Applications of spatial point processes to **large and complex data sets** with inhomogeneities, as encountered e.g. in tropical rain forest ecology, call for estimation methods that are both statistically and computationally efficient. In Deng *et al.* (2017), we propose a novel second-order quasi-likelihood procedure for estimating the parameters in a second-order intensity reweighted stationary spatial point process. The procedure represents a considerable gain in computational efficiency compared to existing methods. An application to a tropical rain forest data set further illustrates the advantages of our procedure.

In Møller & Christoffersen (2017), a **Markov chain of point processes** is studied for which each state is a superposition of an independent cluster process with the previous state as its centre process together with some independent noise process. The model may be used for describing a reproducing population. Closed term expressions of the first- and second-order moments are derived for any state. In a special case, the pair correlation functions converge, as the Markov chain progresses, but it has not been shown whether the Markov chain has an equilibrium distribution with this particular pair correlation function and how it may be constructed. Assuming the same reproducing system, we construct an equilibrium distribution by a coupling argument.

Also the publication of various other papers is worth mentioning: the technical paper Biscio *et al.* (2018) on central limit theorems motivated by applications of spatial point process models, the papers Coeurjolly *et al.* (2017a, b) on Palm distributions and the comprehensive review paper Møller & Waagepetersen (2017) on recent developments in statistics for spatial point patterns. Some of this research have been described in previous *CSGB Annual Reports*. See also the *CSGB Research Report* Waagepetersen & Jalilian (2017) on fast bandwidth selection.

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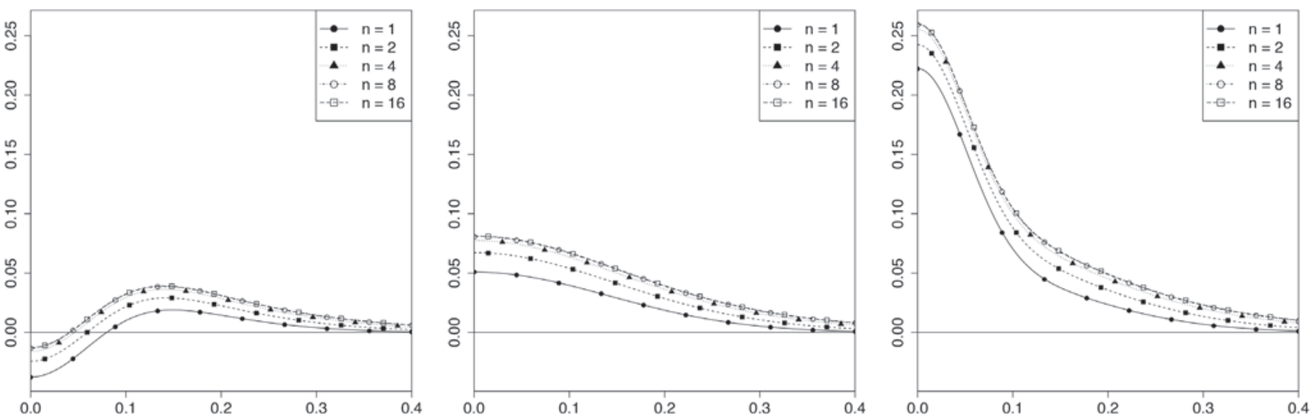

Figure 1
In each of the three plots, the pair correlation functions (minus 1) are shown for the *n*th generation of the Markov chain when the noise processes are either determinantal, Poisson or weighted permanental point processes (left to right). The model parameters, the Gaussian offspring probability density functions and further details may be found in Møller & Christoffersen (2017). The solid horizontal line is the theoretical pair correlation function (minus 1) for a Poisson process.

WP4

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Point processes in bioimaging

In 2017, the research within this work package has been focused on **improved variance prediction in stereology** and point process **modelling of protein clusters**.

The starting point for the research on variance prediction has been the classical Cavalieri method (Baddeley & Jensen, 2004, Section 13.2) that allows estimating the volume of a compact object K in three-dimensional space from area measurements in equidistant parallel planar sections, see Figure 1. In applications, however, precise equidistant spacing may be difficult to achieve. In earlier CSGB research (Ziegel *et al.*, 2010, 2011), the effect of random variability in section spacing has thus been studied, showing that the generalized Cavalieri estimator (which pretends that the sections are equidistant although they are not) is still unbiased when the stack of parallel planes is stationary.

However, the **variance contribution from unequal spacing** can be significant. The precise variance behaviour depends on the smoothness of the function $f(x)$ that measures the area of $K \cap H_x$, where H_x is a plane at position x parallel to the sampling planes. We say that f is $(m,1)$-piecewise smooth, if its derivatives up to order $m-1$ exist and are continuous, whereas the mth order derivative has a finite number of jumps of finite size. If f is $(m,1)$-piecewise smooth, the variance of the classical Cavalieri estimator decreases with t^{α}, $\alpha = 2m+2$, when the interplane distance t tends to 0. Compared to this, the variance of the generalized Cavalieri estimator cannot be better than t^3- even if f is very smooth!

To remedy this shortcoming, it was suggested in Kiderlen & Dorph-Petersen (2017) to measure the distances between consequtive sections. Together with the area measurements, this allows to employ a classical Newton-Cotes quadrature rule of some given order n to obtain a better estimator $\widehat{V}_n$. It was shown that the estimators $\widehat{V}_n$ are unbiased when $n \leq 2$, and promising simulations (Figure 2) suggested a better variance behaviour than that of the generalized Cavalieri estimator.

In 2017, the CSGB group (Stehr & Kiderlen, 2017) started an in-depth study, showing that all estimators $\widehat{V}_n$ are unbiased (assuming a suitable integrability condition). The main finding to date is that an $(m,1)$-piecewise smooth function f leads to variance behaviour of order at least t^{2m+2}, if the quadrature rule has an order of m or larger. Typically, the function f associated to a three-dimensional object is $(m,1)$-piecewise smooth with $m=1$. In this case, already the simple trapezoidal quadrature ($n=1$) is sufficient to replicate the asymptotic rate of the classical Cavalieri estimate. Interestingly, the use of refined Euler-MacLaurin formulae in earlier work was not sufficient for proofs. We therefore adapted the classical **Peano kernel representation** to our setting.

Related research concerning variance prediction of **number estimators**, based on systematic sampling, has also been initiated in 2017.

During 2017, statistical inference for **point process models of protein clusters** has been developed, see Andersen *et al.* (2017). The individual proteins, observed using photoactivated localization microscopy (PALM), may appear as small artificial clusters of points, due to multiple blinking of individual fluorophores. The proteins may also cluster together, and in such cases a pertinent model for a PALM point pattern shows clustering at two different scales. In Andersen *et al.* (2017), a model-based framework for analysis of PALM data is developed. The focus is on a subclass of independent cluster processes, denoted double Cox cluster processes (DCCPs), for which both the parent process (of proteins) and the observed process are Cox cluster processes. Parametric models for DCCPs with a Neyman-Scott process as parent process are developed together with statistical inference procedures, based on moment methods. To illustrate the proposed methodology, a data set from a PALM acquisition is analyzed. In contrast to earlier model-free methods, the analysis provides information, directly relating to the performance of the proteins.

The research on Bayesian inference of spatial distributions of proteins from three-cube Förster Resonance Energy Transfer (FRET) data, initiated in the first funding period of CSGB, has been published in Hooghoudt *et al.* (2017).

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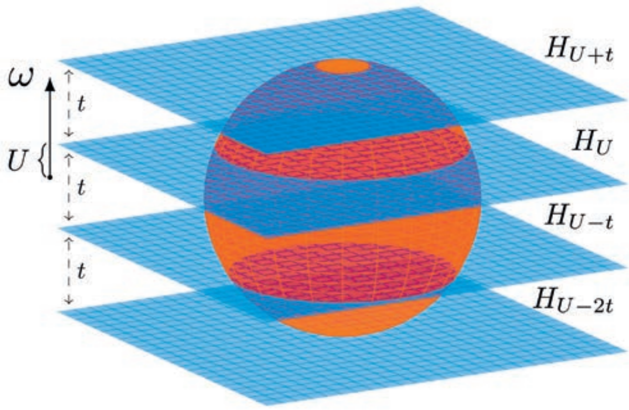

Figure 1
Illustration of the Cavalieri method of sampling an object with a stationary stack of planes. In the classical setting, the interplane distances are constant. For the more refined estimators described in the main text, irregular spacing is allowed.

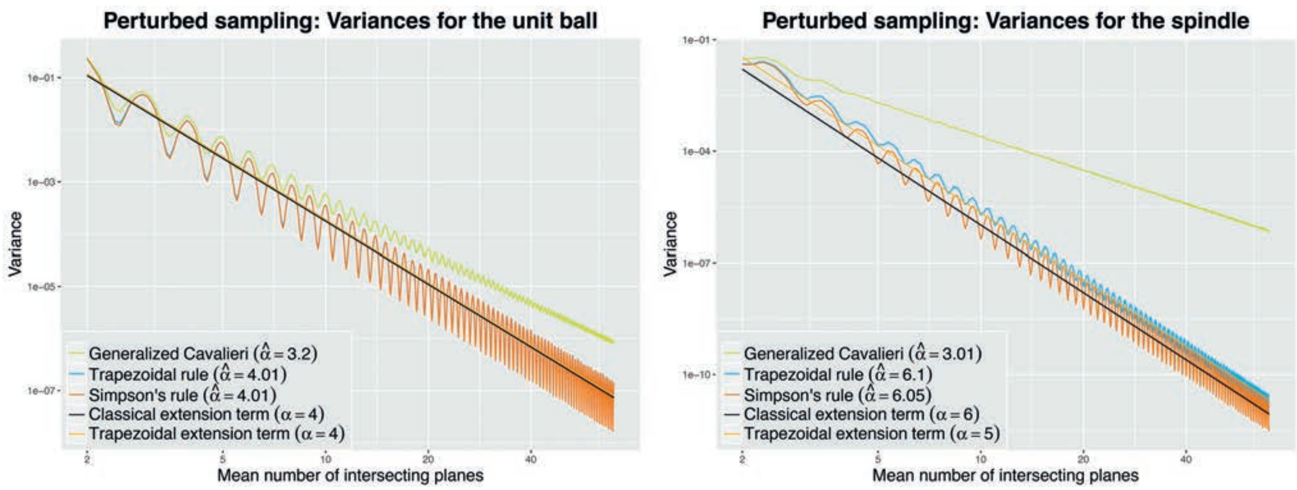

Figure 2
Variance comparison on a log-log scale. The asymptotic order α has been estimated numerically through a least squares approximation.
Left: The object K is the unit ball with corresponding f being (1,1)-piecewise smooth. Note the improved asymptotic performance of the quadrature rules compared to the generalized Cavalieri estimator.

Right: The object K is a spindle shaped body of revolution with corresponding f being (2,1)-piecewise smooth. Note that the order of the trapezoidal rule is 5, and thus even better that the exponent $2n + 2 = 4$ mentioned in the main text.

WP5

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Statistics for stochastic geometry models

During 2017, the paper Rønn-Nielsen & Jensen (2017) on **asymptotics for excursion sets** of random fields has been published. The random fields considered in this paper are infinitely divisible with convolution equivalent Lévy measure. The asymptotic probability that the excursion set contains a rotation of an object with fixed radius has been computed. Examples of this object are a ball of a given radius and a line segment of a given length.

The paper on **estimation of sample spacing for stochastic processes** has also been published in 2017, see Rønn-Nielsen *et al.* (2017). The work has been motivated by an application in electron microscopy, where ultra-thin microscopy sections are analyzed. An estimator of the section distance is proposed, using a random field approach. Furthermore, an approximation to the variance of the estimator is derived under the tractable, yet flexible, class of Lévy-based random fields models. During 2017, we succeeded in showing asymptotic normality of the estimator under an expanding window regime. In fact, apart from a scaling, the asymptotic variance is equal to the approximation to the variance suggested in Rønn-Nielsen *et al.* (2017). An important tool in the proof of the central limit theorem is a theorem from Heinrich (1988) on m_n-dependent random fields. These results will appear in Rønn-Nielsen & Jensen (2018).

In 2017, two papers on **Monte Carlo envelope tests** have been published (Mrkvička *et al.*, 2017; Myllymäki *et al.*, 2017). The paper Myllymäki *et al.* (2017) in the prestigious *Journal of the Royal Statistical Society B* has already received 49 citations, according to Google.

Research focused in 2017 on an extension of the envelope method for the comparison of groups of functional data. The initial application being summary statistics estimated on point patterns, the method is applicable in a much broader statistical context. The idea is to find a characteristic functional statistics that carries information on the difference between groups. This characteristic function should have a distribution that depends on whether the null hypothesis, that the groups represent samples from the same distribution, is true or not. For the test, samples from the null hypothesis are obtained by random relabelling. In large scale simulation studies, we compared several suggestions, and it turned out, that the simplest idea, namely concatenating the mean functions of each group into one, was the most powerful in most cases. This method is illustrated with an example in Figure 1. Our test also turned out to be more powerful than the popular nonparametric test proposed by Cuevas *et al.* (2004). A preliminary version of our paper can be found on arXiv (Mrkvička *et al.*, 2016). We plan to include advances in the theoretical foundations in the final version of the paper.

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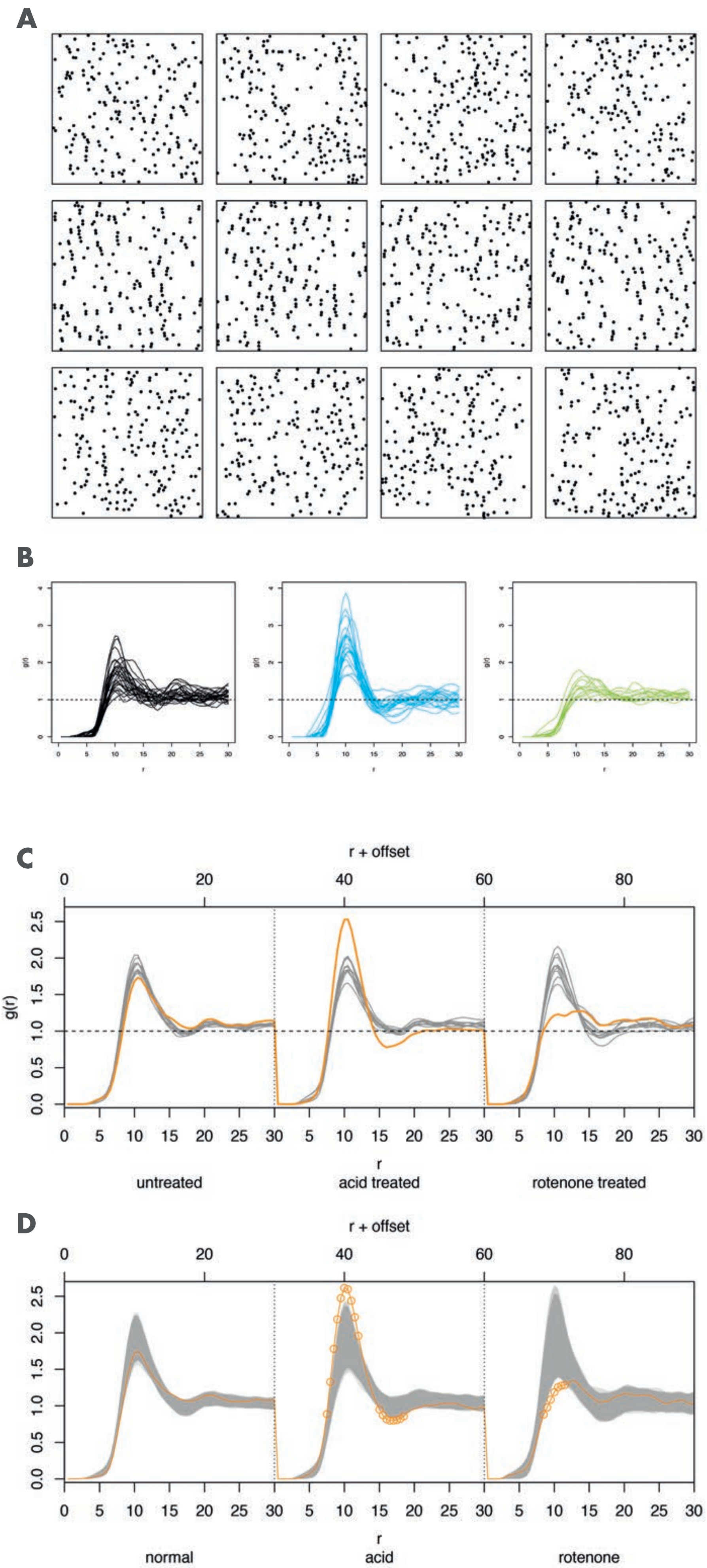

Figure 1

A:
Example point patterns for freeze fracture preparation of intermembraneous particles, from Schladitz *et al.* (2003, *J. Microsc.* **211**, 137–153).

B:
Estimated pair correlation functions.

C:
Concatenated group means (red) and group means after relabelling (grey).

D:
Envelope test, highly significant result (p=0.0001), significant deviations indicated by circles.

WP6

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Algorithms

Reconstruction of a 3-dimensional black object X on white background from a **digital grey-scale image** of the object is an important task in image analysis. Such an image may be formed by placing the object in a cubic grid and then colouring each grid cube a shade of grey corresponding to the fraction of the cube that is covered by the object. The digitization or digital image of X is now the resulting collection of grey-scale cubes (voxels). A 2D illustration may be found in Figure 1.

In the second funding period of CSGB, we have developed further the project from CSGB I on reconstructing the original object or determining topological features of it from a digital grey-scale image (Christensen, 2016). One of the aims is to develop an efficient reconstruction algorithm for sufficiently nice objects, namely objects that are r–regular for some $r > 0$. Although r–regular objects are not in general smooth manifolds, they can be approximated by such sets.

For the reconstruction, our first goal has been to investigate what a digital image of an r–regular set reveals about the topology of the original set. We have considered a grid where each pixel has side length d. Following the general ideas in Christensen (2016), we have shown that if X is an r–regular object with $d\sqrt{3} < r$, it is possible to modify the set of black digitization voxels slightly to get a set Z that is **ambiently isotopic** to the original object X.

In order to prove this result, it is needed to determine the configurations of black and non–black voxels that cannot occur in the digitization of the object. We have shown that the 6 configurations in Figure 2 cannot occur in the digital image of an r–regular object with $d\sqrt{3} < r$. Together with modifications of Theorem 2.1, Theorem 2.10 and Proposition 2.30 in the thesis Christensen (2016) to fit our slightly different digitization, this is enough to apply her thesis to our situation and obtain a set Z that is ambiently isotopic to X.

Our goal for the reconstruction part has been to use the digitization of X to construct an object $Y(X)$ that is close to the original set X. If possible we would like the reconstruction $Y(X)$ to have the same digitization as X and be s–regular for some s that is close to r.

Until now, we have investigated the equivalent 2–dimensional problem. Here, we consider a digitization of a 2–dimensional black r–regular object X, and we suppose that the pixels of this digitization have side length d with $d\sqrt{2} < r$. The question is now how the pixels of the digitization can be used to reconstruct the original object.

The idea that we are working on is to determine where the boundary of the original set X intersects each pixel edge. So far we know for most of the pixels which pixel edges are intersected by ∂X. We then intend to approximate the exact intersection points on these pixel edges to get a set of points close to ∂X, and then approximate the boundary ∂X by an interpolation of arc segments through these points. An illustration of the method is shown in Figure 3.

In 2017, a number of papers, dealing with other research questions in this work package, has also been published:

- Algorithms for **shape reconstruction from surface tensors** of n-dimensional convex bodies are presented in Kousholt (2017). Consistency results are available for these algorithms. The proof of the consistency is based on a stability result, stating that the Hausdorff metric of two (appropriately translated) convex bodies with the same surface tensors up to rank r decreases as a negative power of r.
- A global digital algorithm for **estimating Minkowski tensors** has been published (Hug *et al.*, 2017). The algorithm is based on a Voronoi decomposition of the pixel/voxel midpoints of the digitization and the inversion of a local Steiner formula.
- The research on optimal algorithms for estimating specific intrinsic volumes for 3D Boolean models has been published (Hörrmann & Svane, 2017).
- Two papers on **reconstruction and segmentation of 3D images** have been published (Hansen & Lauze, 2017; Lauze *et al.*, 2017).

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Hansen, J.D.K. & Lauze, F. (2017): Local mean multiphase segmentation with HMMF models. In: *Proceedings of the International Conference on Scale Space and Variational Methods in Computer Vision (SSVM 2017). Lecture Notes in Computer Science* **10302**, pp. 396-407.

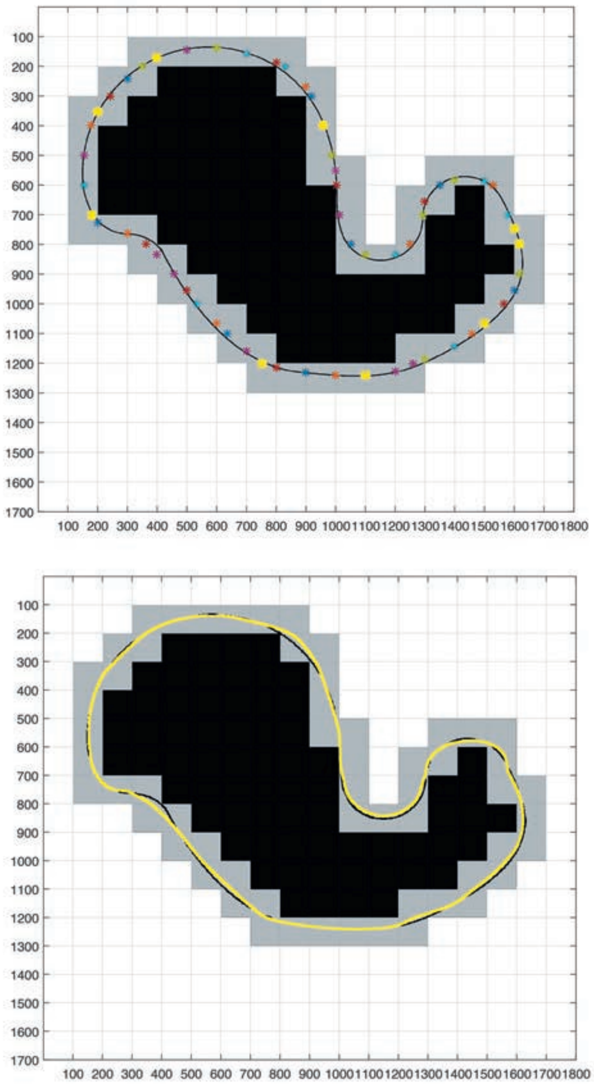

Figure 3: In this 2D illustration, all grey pixels have the same shade of grey for the sake of clarity. (Top) The coloured points are our candidates for intersection points between the boundary and the pixel edges. The black line is the boundary of the original object. (Bottom) The coloured points are used to approximate the boundary of the original set (black curve) by a curve (yellow).

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Hörrmann, J. & Svane, A.M. (2017): Local digital algorithms applied to Boolean models. *Scand. J. Stat.* **44**, 369-395.

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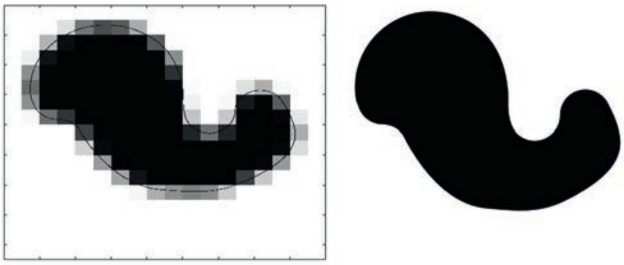

Figure 1: Illustration in 2D of an r-regular set (right) together with its grey-scale digitization (left). The black curve in the left figure marks the boundary of the original set.

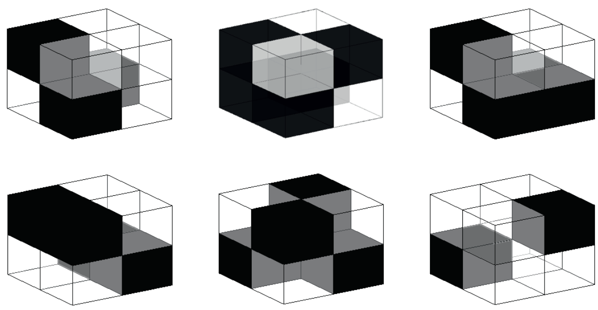

Figure 2: These six configurations of black and non-black voxels cannot occur when an r-regular object is digitized by a lattice where each lattice cube has side length d and $d\sqrt{3} < r$.

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CENTRE ACTIVITIES

OVERVIEW
PAST AND PLANNED INTERNATIONAL ACTIVITIES

INTERNATIONAL CONFERENCES, SYMPOSIA AND WORKSHOPS

- 6th International Conference on Scale Space and Variational Methods in Computer Vision
  4 –7 June 2017, Kolding
- Stereology Workshop
  14 – 20 August 2017, Bern
- Workshop on Diffusion DeKay
  13 November 2017, Copenhagen
- Workshop on Points in Space and Time
  14 December 2017, Aalborg
- 12th French-Danish Workshop on Spatial Statistics and Image Analysis in Biology
  23 – 25 May 2018, Aalborg
- International Conference on Point Processes in Space and Beyond
  13 - 16 May 2019, Aalborg
- 15th International Congress for Stereology and Image Analysis
  27 – 30 May 2019, Aarhus
- 20th Workshop on Stochastic Geometry, Stereology and Image Analysis
  2 – 7 June 2019, Sandbjerg

INTERNATIONAL PHD COURSES

- Statistical Models and Methods for Spatial Point Processes
  5 – 8 February 2017, Les Diablerets
- International PhD Course in Nonlinear Statistics
  12 – 16 June 2017, Copenhagen
- International Summer School on Graphical Models
  14 – 18 August 2017, Tjärö
- Course on Quantitative Digital Pathology: Stereology
  23 – 25 October 2017, Seattle
- PhD Course on Stereology
  31 October – 2 November 2017, Aarhus

From the *International Summer School on Graphical Models*, 14 – 18 August 2017, Tjärö, Sweden.

INTERNATIONAL SUMMER SCHOOL ON GRAPHICAL MODELS
14 – 18 AUGUST 2017, TJÄRÖ

Scope of the summer school
At this summer school, four internationally renowned experts gave a week-long course on graphical models together with local teachers from Copenhagen. The course consisted of the following parts:

- A crash course on the basics of graphical models
- A theoretical insight in the challenges of graphical models
- A practical session with hands-on exercises
- Applications of graphical models in image analysis

The participants were a good mix of local students and international participants. In addition to bringing international expertise into the Danish research groups, the summer school also provided an important networking opportunity for the students.

Summer School on Graphical Models

Image Analysis and Computer Graphics

Structure of the summer school
The summer school consisted of 5 days of lectures and exercises. The students were expected to read a predefined set of scientific articles on graphical models prior to the course. Additionally, the students were asked to bring a poster presenting their research field.

Organizers and financial support
The summer school was organized jointly by the Image Section at University of Copenhagen, and the Image Analysis and Computer Graphics Section at the Technical University of Denmark.

Venue
The summer school was held at Tjärö in Sweden, an idyllic island in the archipelago of Hällaryd, located about 15 kilometers east of Karlshamn.

THE FOUR SPEAKERS

Christoph Lampert is a professor at the Institute of Science and Technology Austria (IST Austria). His research on computer vision and machine learning has won several international and national awards, including the best paper prize at CVPR 2008. Christoph's publication records span a broad range of topics within both theoretical and applied machine learning, with particular focus on computer vision.

Nikos Paragios is professor in applied mathematics and computer science, director of the Center for Visual Computing of École Centrale de Paris, and scientific leader of GALEN group of École Centrale de Paris/ Inria at the Saclay, Ile-de-France Unit. His research interests include image processing, computer vision and medical image analysis, and his publication list includes many examples of highly interesting applications of graphical models within these areas.

Steffen L. Lauritzen is a professor at Department of Mathematical Sciences, University of Copenhagen, and Emeritus Professor of Statistics at the University of Oxford. He is one of the leading experts in the world on graphical models. His research is primarily within mathematical statistics but often associated with development of methodology for specific areas of application, for example in connection with forensic genetics.

Jonas Peters is associate professor at Department of Mathematical Sciences, University of Copenhagen. His work focuses on causal inference: learning causal structures either from purely observational data or from a combination of observational and interventional data. Causal inference is a growing subject with many unresolved questions. Despite his young age, Jonas Peters has already established himself as an important contributor to this field.

THREE 2017 INTERNATIONAL EVENTS

6th International Conference on Scale Space and Variational Methods in Computer Vision, 4 – 7 June 2017, Kolding

This conference, organized by CSGB researcher François Lauze together with Yiqiu Dong and Anders Bjorholm Dahl from DTU Compute, Technical University of Denmark, took place at Hotel Koldingfjord in Denmark. The conference was the sixth edition of the SSVM conferences.

Refereed proceedings from the conference contain 55 full papers, organized in the following topical sections: scale space and PDE methods; restoration and reconstruction; tomographic reconstruction; segmentation; convex and non-convex modelling and optimization in imaging; optical flow, motion estimation and registration; 3D vision.

International PhD Course in Nonlinear Statistics 12 – 16 June 2017, Copenhagen

Aasa Feragen and Stefan Sommer from the Image Section organized this summer school in Copenhagen.

The focus was on nonlinear statistics, an increasingly active research field at the intersection of geometry, statistics, machine learning and algorithmics. Nonlinear statistics seeks to answer fundamental questions that arise when defining new statistical models and tools for analysis of data that exhibits nonlinearity. Such data is becoming increasingly prevalent in diverse fields including computational anatomy, phylogenetics and computational biology.

Invited lecturers were Anuj Srivastava (Florida State University), Tom Nye (Newcastle University) and Tom Fletcher (University of Utah).

International Conference on Geometry and Physics of Spatial Random Systems, 11 – 15 September 2017, Bad Herrenalb

This conference borrowed its name from a DFG funded German Research Unit with nodes in Karlsruhe and Erlangen. CSGB has since 2011 been the international research partner of this Research Unit.

The focus of the conference was on modelling of spatial systems with disorder, using advanced concepts from integral and stochastic geometry. Topics included cellular matter, random packings, random fields, percolation, tensor valuations, Boolean models, random tessellations and stereology.

WORKSHOP ON POINTS IN SPACE AND TIME

14 December 2017, Aalborg

This workshop on points in space and time took place at Department of Mathematical Sciences, Aalborg University, on 14 December 2017. The workshop celebrated the scientific achievements of **Jesper Møller** that has created the famous spatial statistics group in Aalborg.

The main research contributions of Jesper Møller are in spatial statistics (spatial and spatio-temporal point processes, random field models), computational statistics (Markov chain Monte Carlo methods and perfect simulation) and stochastic geometry (random tessellations and other random set models). He is leading the research group in statistics at Department of Mathematical Statistics, Aalborg University, which counts approx. 12 researchers and teachers. He has been project leader for numerous research projects. For decades, Jesper Møller has been internationally very recognized and highly cited. At the latest, Jesper Møller and the remaining spatial statistics group in Aalborg have shown a serious commitment in CSGB.

Scientific programme

The scientific programme of the workshop consisted of longer talks by five invited speakers. There was a lively discussion between the talks. The workshop represented a happy gathering of researchers, some of them had known each other for a very long time.

Speakers and lecture titles

- Eva B. Vedel Jensen (Aarhus University, Denmark):
  Double Cox cluster processes - with applications to photoactivated localization microscopy

- Frédéric Lavancier (Nantes University, France):
  Approximation of the intensity of a pairwise interaction Gibbs point process

- Emilio Porcu (Newcastle University, United Kingdom):
  Modeling temporal phenomena evolving over spheres

- Ethan Anderes (University of California at Davis, USA):
  Isotropic random fields and point processes on graphs and their edges

- Christian Hirsch (Aalborg University, Denmark):
  Continuum percolation in device-to-device networks

Rasmus Waagepetersen at the welcome ceremony.

Sergei Zuyev with Jesper Møller in a coffee break.

Kristian Hirch at the end of his talk.

At the dinner, from left to right: Jesper Møller, Hanne Møller Petersen, Emilio Porcu and Francisco Cuevas.

INTERNAL CSGB WORKSHOPS

FOURTEENTH INTERNAL CSGB WORKSHOP

Hotel Hvide Hus, Aalborg, 4 – 5 May 2017

TALKS

- Abdel-Rahman Al-Absi, AU-bio: *Different methods for 3D reconstruction of neurons*
- Ina Trolle Andersen, AU-math: *Processes of spatial points with multiple noisy appearances*
- Andreas Dyreborg Christoffersen, AAU: *Iterated cluster processes*
- Stine Hasselholt, AU-bio: *Estimation of cell volume in the brain – practice and potential bias*
- Matthew Liptrot, KU: *Streamlets and persistent homology*
- Anton Jussi Olavi Mallasto, KU: *Wasserstein distance between Gaussian processes*
- Jens R. Nyengaard, AU-bio: *Sampling and analysis of nerve fibres from corneal confocal microscopy II*
- Stefan Sommer, KU: *A geometric framework for stochastic shape analysis*
- Mads Stehr, AU-math: *The Cavalieri estimator with unequal section spacing revisited*
- Rasmus Waagepetersen, AAU: *Orthogonal series estimation of the pair correlation function of a spatial point process*

FIFTEENTH INTERNAL CSGB WORKSHOP AND FOLLOW-UP MEETING WITH THE VILLUM FOUNDATION

Department of Mathematics, Aarhus University, 15 - 16 November 2017

TALKS

- Achmad Choiruddin, AAU: *Estimation of intensity functions for point processes by means of LASSO methods*
- Ivan D'Annibale, KU: *Attempts in sliding motion*
- Karl-Anton Dorph-Petersen, AU-bio, and Jesper Møller, AAU: *The minicolumn hypothesis*
- Rikke Eriksen, AU-math: *Uniqueness of the measurement function in Crofton's formula*
- Stine Hasselholt, AU-bio, and Jon Sporring, KU: *Synaptic vesicles by FIB-SEM*
- Nick Yin Larsen, AU-bio: *Characterization of minicolumns and volume tensors of neurons in Brodmann Area 46 in normal, schizophrenic and depressive human autopsy brains*
- Anders Rønn-Nielsen, AU-math: *Estimation and central limit theorems for Lévy-based random fields*
- Hans Jacob T. Stephensen, KU: *Distribution of organelles using shortest path metrics on the intracellular space of the neuron active zone*
- Helene Svane, AU-math: *Reconstruction from refined digital images*

From the *Fourteenth Internal CSGB Workshop*, 4 – 5 May 2017, Hotel Hvide Hus, Aalborg.

CSGB RESEARCH REPORTS 2017

1. Anderes, E., Møller, J. & Rasmussen, J.G. (2017): Isotropic covariance functions on graphs and their edges. *CSGB Research Report* **2017-10**. Submitted.

2. Andersen, I.T., Hahn, U., Arnspang, E.C., Nejsum, L.N. & Jensen, E.B.V. (2017): Double Cox cluster processes – with applications to photoactivated localization microscopy. *CSGB Research Report* **2017-09**. Submitted.

3. Arnaudon, A., Holm, D.D., Pai, A. & Sommer, S. (2017): A stochastic large deformation model for computational anatomy. *CSGB Research Report* **2017-02**. Has appeared in *Proceedings of the International Conference on Image Processing in Medical Imaging (IPMI 2017). Lecture Notes in Computer Science* **10265**, pp. 571-582. Springer.

4. Arnaudon, A., Holm, D.D. & Sommer, S. (2017a): A geometric framework for stochastic shape analysis. *CSGB Research Report* **2017-06**. Submitted.

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6. Biscio, C.A.N., Poinas, A. & Waagepetersen, R. (2017): A note on gaps in proofs of central limit theorems. *CSGB Research Report* **2017-12**. Has appeared as *Stat. Probab. Lett.* (2018) **135**, 7-10.

7. Hooghoudt, J.-O., Barroso, M. & Waagepetersen, R. (2017): Toward Bayesian inference of the spatial distribution of proteins from three-cube Förster resonance energy transfer data. *CSGB Research Report* **2017-05**. Has appeared as *Ann. Appl. Stat.* (2017) **11**, 1711-1737.

8. Jalilian, A., Guan, Y. & Waagepetersen, R. (2017): Orthogonal series estimation of the pair correlation function of a spatial point process. *CSGB Research Report* **2017-01**. *Stat. Sinica*, in press. DOI:10.5705/ss.202017.0112.

9. Kiderlen, M. & Dorph-Petersen, K.-A. (2017): The Cavalieri estimator with unequal section spacing revisited. *CSGB Research Report* **2017-04**. Has appeared as *Image Anal. Stereol.* (2017) **36**, 133-139.

10. Kühnel, L. & Sommer, S. (2017): Stochastic development regression on non-linear manifolds. *CSGB Research Report* **2017-03**. Has appeared in *Proceedings of the International Conference on Image Processing in Medical Imaging (IPMI 2017). Lecture Notes in Computer Science* ***10265***, pp. 53-64. Springer.

11. Kiderlen, M. & Rataj, J. (2017): Dilation volumes of sets of finite perimeter. *CSGB Research Report* **2017-08**. Submitted.

12. Møller, J. & Christoffersen, A.D. (2017): Pair correlation functions and limiting distributions of iterated cluster point processes. *CSGB Research Report* **2017-11**. Submitted.

13. Waagepetersen, R. & Jalilian, A. (2017): Fast bandwidth selection for the estimation of the pair correlation function. *CSGB Research Report* **2017-07**. Accepted for publication in *J. Stat. Comput. Sim.*

CSGB JOURNAL AND PROCEEDINGS PUBLICATIONS, BOOK CHAPTERS

Ardalan, M., Rafati, A.H., Nyengaard, J.R. & Wegener, G. (2017): Rapid antidepressant effect of ketamine correlates with astroglial plasticity in the hippocampus. *Brit. J. Pharmacol.* **174**, 483-492.

Arnaudon, A., Holm, D.D., Pai, A. & Sommer, S. (2017): A stochastic large deformation model for computational anatomy. *Proceedings of the International Conference on Image Processing in Medical Imaging (IPMI 2017). Lecture Notes in Computer Science* **10265**, pp. 571-582. Springer.

Coeurjolly, J.-F., Møller, J. & Waagepetersen, R. (2017a): A tutorial on Palm distributions for spatial point processes. *Int. Stat. Rev.* **85**, 404-420.

Coeurjolly, J.-F., Møller, J. & Waagepetersen, R. (2017b): Palm distributions for log Gaussian Cox processes. *Scand. J. Stat.* **44**, 192–203.

Deng, C., Guan, Y., Waagepetersen, R. & Zhang, J. (2017): Second-order quasi-likelihood for spatial point processes. *Biometrics* **73**, 1311-1320.

Greisen, S.R., Yan, Y., Hansen, A.S., Venø, M.T., Nyengaard, J.R., Moestrup, S.K., Hvid, M., Freeman, G.J., Kjems, J. & Deleuran, B. (2017): Extracellular vesicles transfer the receptor programmed death-1 in rheumatoid arthritis. *Front Immunol.* **8**, 851.

Hansen, J.D.K. & Lauze, F. (2017): Local mean multiphase segmentation with HMMF models. In: *Proceedings of the International Conference on Scale Space and Variational Methods in Computer Vision (SSVM 2017). Lecture Notes in Computer Science* **10302**, pp. 396-407.

Hooghoudt, J.-O., Barroso, M. & Waagepetersen, R. (2017): Toward Bayesian inference of the spatial distribution of proteins from three-cube Förster resonance energy transfer data. *Ann. Appl. Stat.* **11**, 1711-1737.

Hug, D., Kiderlen, M. & Svane, A.M. (2017): Voronoi-based estimation of Minkowski tensors from finite point samples. *Discrete Comput. Geom.* **57**, 545-570.

Hörrmann, J. & Svane, A.M. (2017): Local digital algorithms applied to Boolean models. *Scand. J. Stat.* **44**, 369-395.

Inui, K., Zhao, Z., Yuan, J., Jayaprakash, S., Le, L.T., Drakulic, S., Sander, B. & Golas, M.M. (2017): Stepwise assembly of functional C-terminal REST/NRSF transcriptional repressor complexes as a drug target. *Protein Sci.* **26**, 997–1011.

Jensen, E.B.V. & Kiderlen, M. (2017a, eds.): *Tensor Valuations and their Applications in Stochastic Geometry and Imaging. Lecture Notes in Mathematics* **2177**. Springer.

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Khanmohammadi, M., Darkner, S., Nava, N., Nyengaard, J.R., Wegener, G., Popoli, M. & Sporring, J. (2017): 3D analysis of synaptic vesicle density and distribution after acute foot-shock stress by using serial section transmission electron microscopy. *J. Microsc.* **265**, 101–110.

Kiderlen, M. & Dorph-Petersen, K.-A. (2017): The Cavalieri estimator with unequal section spacing revisited. *Image Anal. Stereol.* **36**, 133-139.

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Kühnel, L. & Sommer, S. (2017a): Computational anatomy in Theano. *Graphs in Biomedical Image Analysis, Computational Anatomy and Imaging Genetics. GRAIL 2017, MFCA 2017, MICGen 2017. Lecture Notes in Computer Science* **10551**, pp. 164-176. Springer.

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Mallasto, A. & Feragen, A. (2017): Learning from uncertain curves: The 2-Wasserstein metric for Gaussian processes. *Advances in Neural Information Processing Systems* **30** (NIPS).

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Mrkvička, T., Myllymäki, M. & Hahn, U. (2017): Multiple Monte Carlo testing, with applications in spatial point processes. *Stat. Comp.* **27**, 1239–1255.

Myllymäki, M., Mrkvička, T., Grabarnik, P., Seijo, H. & Hahn, U. (2017): Global envelope tests for spatial processes. *J. Roy. Stat. Soc. B* **79**, 381-404.

Møller, J. & Waagepetersen, R. (2017): Some recent developments in statistics for spatial point patterns. *Annual Review of Statistics and Its Applications* **4**, 317-342.

Pai, A.S.U., Sommer, S.H., Raket, L.L., Kühnel, L., Darkner, S., Sørensen, L. & Nielsen, M. (2017): A statistical model for simultaneous template estimation, bias correction, and registration of 3D brain images. In *Proceedings of MICCAI 2016. Lecture Notes in Computer Science* **10081**, pp. 151-159. Springer.

Prokešová, M., Dvořák, J. & Jensen, E.B.V. (2017): Two-step estimation procedures for inhomogeneous shot-noise Cox processes. *Ann. Inst. Statist. Math.* **69**, 513-542.

Rønn-Nielsen, A. & Jensen, E.B.V. (2017): Excursion sets of infinitely divisible random fields with convolution equivalent Lévy measure. *J. Appl. Prob.* **54**, 833-851.

Rønn-Nielsen, A., Sporring, J. & Jensen, E.B.V. (2017): Estimation of sample spacing in stochastic processes. *Image Anal. Stereol.* **36**, 43-49.

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Sommer, S.H. & Svane, A.M. (2017): Modelling anisotropic covariance using stochastic development and sub-Riemannian frame bundle geometry. *J. Geom. Mech.* **9**, 391-410.

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Sørensen, L., Igel, C., Pai, A.S.U., Balas, I., Anker, C., Lillholm, M. & Nielsen, M. (2017): Differential diagnosis of mild cognitive impairment and Alzheimer's disease using structural MRI cortical thickness, hippocampal shape, hippocampal texture, and volumetry. *NeuroImage Clin.* **13**, 470-482.

Yuan, J., Llamas, N., Sander, B. & Golas, M.M. (2017): Synergistic anti-cancer effects of epigenetic drugs on medulloblastoma cells. *Cell Oncol.* **40**, 263–279.

CSGB VISITORS - 2017

Alessandra Conte (University of Milano, Italy)
1 January – 30 June 2017

Rachel L. Zemans (University of Michigan, USA)
1 – 28 February 2017

Qichao Zhang (Shanghai Advanced Research Institute, China) | 1 February – 30 April 2017

Fei Yan (Chinese Academy of Sciences, Beijing, China)
1 February – 30 April 2017

Juan Alonso (Universidad Politécnica de Madrid, Spain)
15 March – 31 August 2017

Maurizio Falcone (Rome La Sapienza University, Italy)
4 – 7 June 2017

Per Christian Hansen (Technical University, Denmark)
4 – 7 June 2017

Marco Loog (Delft University of Technology, Holland)
4 – 7 June 2017

Christine De Mol (Université Libre de Bruxelles, Belgium)
4 – 7 June 2017

Tom Fletcher (University of Utah, USA)
12 - 16 June 2017

Tom Nye (Newcastle University, United Kingdom)
12 - 16 June 2017

Anuj Srivastava (Florida State University, USA)
12 - 16 June 2017

Richard J. Gardner (Western Washington University, USA) | 14 June - 1 July 2017

Javad Sadeghinezhad (University of Tehran, Iran)
1 July – 1 September 2017

Sarang Joshi (University of Utah, USA)
3 - 4 July 2017

Gopalakrishnan Dhanabalan (Karolinska Institutet, Stockholm, Sweden) | 1 – 31 August 2017

Selfi Handayani (Sebelas Maret University, Indonesia)
1 August – 30 November 2017

Christoph H. Lampert (Institute of Science and Technology, Austria) | 14 – 18 August 2017

Steffen L. Lauritzen (University of Copenhagen, Denmark) | 14 – 18 August 2017

Nikos Paragios (École Centrale Paris, France)
14 – 18 August 2017

Jonas Peters (University of Copenhagen, Denmark)
14 – 18 August 2017

Jan Rataj (Charles University, Praha, Czech Republic)
20 August - 1 September 2017

Mohammadali Khosravifard (Isfahan University of Technology, Iran) | 1 September 2017 – 30 April 2018

Alex Bronstein (Technion, Israel)
9 October 2017

Rémi Bardenet (University of Lille, France)
29 October – 5 November 2017

Ottmar Cronie (Umeå University, Sweden)
5 - 10 November 2017

Mehdi Moradi (Jaume I University, Spain)
5 - 11 November 2017

Ethan Anderes (University of California at Davis, USA)
13 – 15 December 2017

Claes Anderson (Chalmars University of Technology, Sweden) | 13 – 15 December 2017

Frédéric Lavancier (Nantes University, France)
13 – 15 December 2017

Arnaud Poinas (Nantes University, France)
13 – 15 December 2017

Emilio Porcu (Newcastle University, United Kingdom)
13 – 15 December 2017

Aila Särkkä (Chalmars University of Technology, Sweden)
13 – 15 December 2017

SELECTED INVITED TALKS - 2017

Second Latin-American Conference on Statistical Computing
Valparaiso | 9-11 March 2017
Rasmus Waagepetersen: Quasi-likelihoods for spatial point processes

Small Workshop on Big Data
Melbourne | 13 - 15 March 2017
Ege Rubak: Point patterns on the sphere - statistical methodology and computation

Geometrical and Topological Structures of Information
Marseilles | 28 August – 1 September 2017
Aasa Feragen: From tree-spaces to stratified data spaces

International Conference on Geometry and Physics of Spatial Random Systems
Bad Herrenalb | 10 – 15 September 2017
Eva B. Vedel Jensen: Processes of spatial points with multiple noisy appearances

12th European Congress for Stereology and Image Analysis
Kaiserslautern | 11 – 14 September 2017
Ute Hahn: Spatial point processes in stereology and bioimaging

12th European Congress for Stereology and Image Analysis
Kaiserslautern |11 – 14 September 2017
Jens Randel Nyengaard: Improved sampling and analysis of images in corneal confocal microscopy

5th Annual SDC Neuroscience & Neuroimaging Symposium
Beijing | 24 – 26 September 2017
Jens Randel Nyengaard: Vortioxetine rapidly induces synaptic and mitochondrial plasticity of the rat hippocampus

Shape Analysis and Computational Anatomy, Isaac Newton
Cambridge | 13 – 17 November 2017
Stefan Sommer: Statistical inference in nonlinear spaces via maximum likelihood and diffusion bridge simulation

Inferential Challenges for Large Spatio-Temporal Data Structures
Banff | 3 – 8 December 2017
Rasmus Waagepetersen: Analysis of multi-species point patterns using multivariate log Gaussian Cox processes

Workshop on Points in Space and Time
Aalborg | 14 December 2017
Eva B. Vedel Jensen: Double Cox cluster processes – with applications to photoactivated localization microscopy

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