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

Annual Report 2018

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INTRODUCTION

Centre for Stochastic Geometry and Advanced Bioimaging (CSGB) is a VKR Centre of Excellence, supported by the Villum Foundation. A main task is to advance the discipline of stochastic geometry, and thereby laying the mathematical foundations for novel methods of analyzing advanced bioimaging data. At the same time, we take up the concrete challenge of new types of bioimaging data.

CSGB has now been running for nine years. Since the beginning in April 2010, CSGB has functioned as an **inter-institutional collaboration** between the Universities of Aarhus, Aalborg and Copenhagen. Four research groups participate in CSGB: the stochastic geometry group (AU), the section for stereology and microscopy (AU), the spatial statistics group (AAU) and the image section (KU). In 2018, the stereology and microscopy group moved to Aarhus University Hospital, as part of the Core Centre for Molecular Morphology.

During 2018, two co-financed **PhD students** and two **postdocs** started at CSGB (page 12). Some of these appointments would not have been possible without additional funding, obtained by the CSGB staff. In 2018, the permanent staff took part in the organization of a number of **international workshops** and **PhD courses**, including *12th French-Danish Workshop on Spatial Statistics and Image Analysis in Biology, Workshop on Statistics for Data with Geometric Structure* and *Workshop on Shape Analysis, Stochastic Geometric Mechanics and Applied Optimal Transport*. For more details, see page 13 and 32.

A detailed account of the research results obtained in 2018 for each of the **six work packages**, that form the research plan of the second funding period of CSGB, may be found on page 18-29. An overview of the results is given on page 16. A description of four collaborative projects is provided on page 17. Important research published in 2018 concerns volume tensor estimation, statistical modelling of data on manifolds, determinantal point processes, point processes on directed linear networks, Lévy-based random fields and cryo-electron microscopy. A new collaborative project between the AAU group and the KU group was started in 2018, concerning extensions of *K*-functions to spatial patterns of curves.

Apart from the international workshops and PhD courses, **two internal CSGB workshops** were held in 2018, at Musholm (Korsør) and HUSET (Middelfart), respectively. The scientific program for these internal workshops may be found on page 34. The internal CSGB workshops are arranged alternately by the two AU groups, the AAU group and the KU group. The aim of these internal workshops has been 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.

2019 is a year of intense international activity for the CSGB staff, involving the organization of (i) *Workshop on Point Processes in Space, Time and Beyond*, (ii) *15th International Congress for Stereology and Image Analysis* and (iii) *20th Workshop on Stochastic Geometry, Stereology and Image Analysis*. More details about these scientific meetings may be found on page 32-33.

In the following pages, we inform in more detail our colleagues, 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 2018.

April 2019
Eva B. Vedel Jensen

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 2018 of 6 professors, 14 associate professors, 1 assistant professor, 5 postdocs and 16 PhD students, see page 40-41 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.

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 **Anders Rønn-Nielsen**

- 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

NEWS ABOUT STAFF

Christophe A.N. Biscio (AAU)

One of the very active members of the CSGB staff is Christophe A.N. Biscio. Together with Ottmar Cronie, Umeå University, and Raphaël Lachièze-Ray, Université Paris Descartes, he has in 2018 studied point processes on random environments such as unobserved 3D surfaces or fibers. This is relevant in medical imaging where motion paths in the brain are studied. Moreover, Christophe A.N. Biscio and Florent Bonneu, Avignon University, have investigated the rate of convergence of central limit theorems for statistics of spatial point processes. Christophe A.N. Biscio is participating in the CSGB work package **Spatial and spatio-temporal point processes**.

Jens R. Nyengaard (AU-bio)

Jens R. Nyengaard has in 2018 obtained additional funding from the Sino-Danish Center and Graduate School, Health, Aarhus University. Jens R. Nyengaard is vice-director of CSGB and leader of the AU-bio stereology and microscopy group. He is also one of the principal investigators of the work package **Point processes in bioimaging**. 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. Collaborative projects of this type concerns, for instance, *Neuronal Dendritic Trees* and *Spines* and *Synaptic Vesicles by FIB-SEM*. For more details, see page 17.

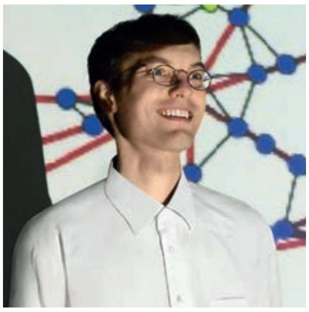
Stefan Sommer (KU)

During 2018, Stefan Sommer has obtained additional funding from the Villum Foundation Experiment Programme. The title of the project is *Daydreaming Algorithms*. Stefan Sommer has been a member of the CSGB staff since the very beginning in 2010. In the second funding period of CSGB (2015-2020), Stefan Sommer is one of the principal investigators of the **Random shapes** work package. During 2018, he has developed a technique for performing principal component analysis on manifolds, using stochastic processes and bridge sampling. A collaboration with Frank van der Meulen, Delft University of Technology, and Moritz Schauer, Leiden University, on sampling of stochastic bridges has also been initiated.

Jon Sporring (KU)

In October 2018, Jon Sporring was appointed full professor at Department of Computer Science, University of Copenhagen. Jon Sporring is involved in basic research within mathematical and medical image analysis, computer graphics, information theory and pattern recognition. Since the formation of CSGB in 2010, Jon has played a key role in a number of collaborative projects, in particular in the project on synaptic vesicles by Focused Ion Beam Scanning Electron Microscopy (FIB-SEM). He has made important contributions to the work packages **Point processes in bioimaging** and **Statistics for stochastic geometry models**. Together with CSGB researcher Sune Darkner, Jon Sporring has participated in the establishment of the Danish BioImaging Network.

APPOINTMENTS 2018



Christian Hirsch (AAU)
Christian Hirsch was hired as a postdoc at the AAU group in April 2018. Christian Hirsch has a PhD degree from Ulm University. The thesis concerns percolation and connectivity properties of spatial random networks. At CSGB, he has studied modern methods from spatial statistics and Monte Carlo simulations for research problems in the domains of topological data analysis and stochastic channel models. In particular, goodness of fit tests for point processes via topological data analysis have been developed. This project lies within the work package **Spatial and spatio-temporal point processes**. Christian Hirsch has strong competences in probability theory.

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**. The aim of the PhD study is to 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 needed to develop models where the temporal component of the data is taken into account.

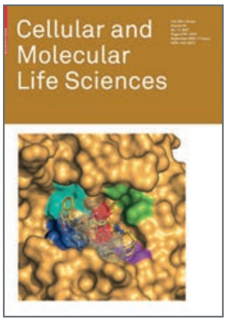
Mathias Højgaard Jensen (KU)
Mathias Højgaard Jensen has a master degree in mathematical statistics and probability theory from University of Copenhagen. The title of his master thesis is *Stochastic Processes in Manifolds and Fibre Bundles*. In September 2018, he started in a co-financed PhD position. Mathias Højgaard Jensen is associated to the KU group and works within the **Random shapes** work package. It is the plan that Mathias will continue and further develop the research project on *Stochastic Bridge Simulation on Manifolds*. This technique can be used for performing principal component analysis on manifolds.

Anne Marie Svane (AAU)
In September 2018, Anne Marie Svane started as a postdoc at the AAU group. She is participating in the **Spatial and spatio-temporal point processes** work package. Together with Christophe A.N. Biscio, Anne-Marie Svane is seeking to establish a functional central limit theorem for the persistence diagram associated with a spatial point process, as the observation window becomes increasingly large. This would allow goodness-of-fit tests for spatial point patterns based on the accumulated persistence function and other test statistics derived from the persistence diagram. Anne Marie is also associated with the work package entitled **Valuation theory**. Within this work package, she has in collaboration with CSGB researcher Markus Kiderlen given some attention to the project on *Isoperimetric Inequalities with Tensor Constraints*.

PUBLICATION HIGHLIGHTS 2018

During 2018, a number of papers written by members of the AAU group has been published or accepted for publication in absolute top international statistical journals, including *Bernoulli* and *Journal of the American Statistical Association*.

Members of the AU-bio group has published a paper on pyruvate dehydrogenase complex varants in the prestigious journal *Cellular and Molecular Life Sciences*. The results obtained in this paper is described in detail on page 28-29.



ORGANIZATION OF INTERNATIONAL WORKSHOPS AND PHD COURSES IN 2018

In 2018, the CSGB staff participated in the organization of a number of international workshops and PhD courses:

- The *12th French-Danish Workshop on Spatial Statistics and Image Analysis in Biology (SSIAB12)*, 23 – 25 May 2018, Aalborg, was organized by **Christophe Biscio** and **Ege Rubak (AAU)**. The workshop was devoted to spatial statistics and image analysis and their applications in biology (agriculture, medicine, ecology, environment…). Attendance was by invitation only. The program contained thirty scientific talks of 25 min. duration. For further details, see *http://people.math.aau.dk/~christophe/SSIAB12.html*.

- *Workshop on Statistics for Data with Geometric Structure*, 21 – 27 January 2018, Oberwolfach, was organized by **Aasa Feragen (KU)**, Thomas Hotz (Ilmenau), Stephan Huckemann (Göttingen) and Ezra Miller (Durham). A description of the background for organizing this workshop may be found on page 37.

- In 2018, **Jens R. Nyengaard (AU-bio)** took part in the organization of two international workshops on stereology and microscopy, and two PhD courses in stereology. The venues were, respectively, Bern, Oviedo, Tehran and Aarhus. Further details may be found on page 32.

- *Workshop on Shape Analysis, Stochastic Geometric Mechanics and Applied Optimal Transport*, 9 - 14 December 2018, Banff International Research Station, was organized by a team of international experts, including CSGB researcher **Stefan Sommer (KU)**. The background for organizing the workshop was the recent developments, highlighting the strong connections between shape analysis and the related fields of optimal transport and stochastic geometric mechanics, both very active fields in their own right. The workshop aimed at bringing together researchers in these three fields, to share methodological developments and open problems, and generally to link and accelerate research in all three fields. For further details, see *https://www.birs.ca/events/2018/5-day-workshops/18w5151*.

www.csgb.dk

RESEARCH

RESEARCH OVERVIEW 2018

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 2018 within each of these work packages. A detailed description of the research results obtained in 2018 may be found on page 18-29. On the following page, the present status of four collaborative projects is described.

One of the focus points within the **Valuation theory** work package has in 2018 been stereology of volume tensors and their implementation in optical microscopy. A new and simple method of estimating mean particle volume tensors from vertical sections has been developed for use in optical microscopy. In a design-based setting, where the vertical plane is uniformly rotated around the vertical axis, the method provides information about an index of elongation of the particles in the direction of the vertical axis. Methods of assessing the precision of the new estimator, based on a bootstrap procedure, are also provided. The research on uniqueness of measurement functions in integral geometric formulae has been continued in 2018.

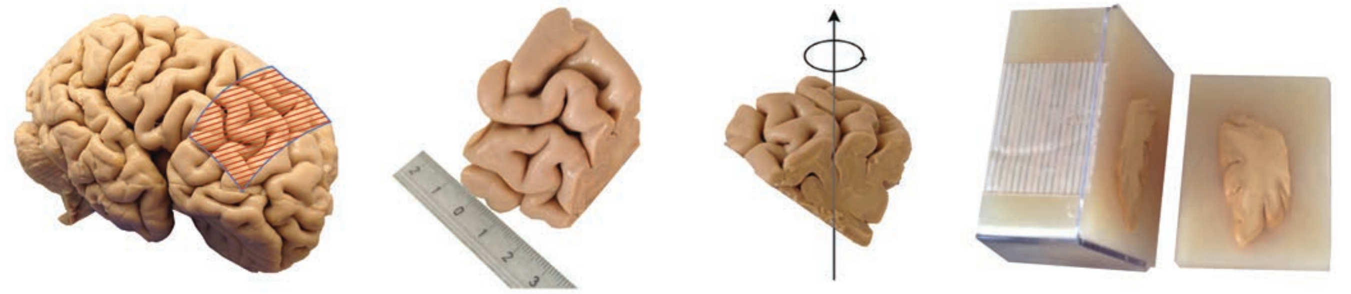
In the work package **Random shapes**, several contributions have been made to statistical modelling of data residing on a manifold. Using a generalization of a Gaussian process to data taking values in a Riemannian manifold, it has been possible to construct regression models and latent variable models for data on manifolds. In 2018, we also constructed a technique for performing principal component analysis on manifolds, using bridge sampling. The construction avoids linearization of the underlying space and incorporates curvature. Furthermore, extensive work has evolved around investigating the behaviour of Brownian motion on landmark shape spaces, the simplest, non-trivial type of shape spaces.

Several results on determinantal point processes have been published in 2018 within the work package **Spatial and spatio-temporal point processes**. Determinantal point process models have been developed for the sphere and also in a non-stationary setting. Inference for non-stationary processes may be based on an adaptive estimating function approach. The relation between the distribution of a determinantal point process and its reduced Palm distribution has also been studied in 2018. Statistical methodology for log Gaussian Cox processes has been developed for processes on the sphere. Several advances regarding statistics for spatial point processes were also made in 2018, including the derivation of a central limit theorem for summary statistics of point processes in a general setting and an improvement of an intensity estimator based on resampling of the observed point pattern.

A focus point within the work package **Point processes in bioimaging** has been development of point process models on directed linear networks with applications to neuronal dendritic trees in mind. The point processes are specified by the conditional intensity function and this approach makes it possible to derive the likelihood function for the point process. Two simulation algorithms are considered. The research on improved variance prediction in stereology has been continued in 2018. In continuation of the research on point process models of protein clusters, Cluster Marked Cluster point processes (CMCpps) have been studied in 2018.

The main contribution in 2018 to the work package **Statistics for stochastic geometry models** has been asymptotic results for mean value and variogram estimators in a Lévy-based random field model, defined on a discrete lattice. The asymptotics has been derived for the regime where the number of lattice sites, at which observations are made, is increasing to infinity. The CSGB group also started in 2018 to study Lévy-based models depending on both space and time. Here, a challenge has been that discontinuities are introduced in the resulting field when modelling present observations as based solely on noise from the past.

Within the work package **Algorithms**, the research on single particle cryo-electron microscopy has resulted in an important publication on pyruvate dehydrogenase complex (PDC) variants. PDC is one of the cell's largest enzymatic complexes and is subject to inherited genetic variations that may cause neurodevelopmental disorders in children. In particular, the research has shown that impairments in protein folding may contribute to functional impairments of variant PDC. In the project on digital grey-scale images, reconstruction of objects from noisy images at low resolution was studied in 2018.



Sampling from Brodmann Area 46 in the human cerebral cortex. For details, see Larsen *et al.* (*CSGB Research Report* **2018-12**).

COLLABORATIVE PROJECTS

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

During 2018, stereological estimation of volume tensors has been implemented on human brain tissue for the analysis by optical microscopy of neurons in layer III of the medial frontal gyrus of Brodmann Area 46 (Larsen *et al.*, *CSGB Research Report* **2018-12**). This area was chosen, since it has been the subject of studies related to schizophrenia and depression. The sampling of tissue is illustrated above. The new estimator uses measurements on a uniform sample of neurons. For each sampled neuron, the measurement is performed in a vertical plane passing through a reference point belonging to the neuron. In contrast to an earlier method, based on observation in several optical planes, the implemented method is not sensitive to tissue shrinkage. Furthermore, in the examples considered, the new estimator is more efficient than the one, using observation in several optical planes.

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

Focused Ion Beam Scanning Electron Microscopy (FIB-SEM) imaging is a technique that image materials section-by-section at nano-resolution, corresponding to pixels of width 5 nanometer. FIB-SEM is well suited for imaging ultrastructures within cells. Unfortunately, traditional setups introduce a slight sub-pixel translation from section to section, referred to as drift. Over multiple sections, the drift will change distance measures and geometric structures significantly. Popular correction approaches often involve standard image registration methods available in packages such as ImageJ or similar software. Using these methods, the images are transformed to maximize the similarity between consecutive sections. During 2018, we have in Stephensen *et al.* (2018, arXiv:1810.01159v1) shown how these standard approaches will significantly underestimate the drift and produce biased corrections as they tend to align the images such that the normal of planar biological structures are perpendicular to the sectioning direction. In our paper, we present a highly accurate correction method for estimating drift in isotropic electron microscopy images with visible vesicles.

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 2018, we have continued the large-scale investigation of this hypothesis for neurons in the Brodmann Area 46 (BA46) in human autopsy brains from normal, schizophrenic and depressed patients. After the AU-bio and AU-math groups have developed sampling procedures for collection of biopsies from BA46, CSGB staff member Nick Yin Larsen (AU-bio) has started cutting the biopsies in Beijing on a unique AutoCUT machine, which can collect thousands of sections. Section quality and the subsequent staining of the sections have turned out to be a challenge, but we still aim at automatic procedures for detecting the neurons in BA46. Here, the KU group is expected to 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)

Spine geometry is considered to reflect synapse function. It is therefore important to obtain reliable information in 3D about dendritic trees and the distribution of the spines on these trees. In Al-Absi *et al.* (2018, *J. Chem. Neuroanat.* **94**, 119-124), we have compared three types of reconstruction methods for suitably sampled pyramidal neurons in Golgi-stained mouse brains. Spine features such as spine volume, spine area, spine length and spine neck length were determined by an automatic method, a semi-automatic method and a manual method, respectively. In this study, the semi-automatic method was in line with the reliable, but slower manual method, and both methods were significantly different from the automatic method. The semi-automatic method was therefore the method of choice.

The same dendritic trees and spines have in Rasmussen & Christensen (*CSGB Research Report* **2018-11**) been analyzed, using point processes on directed linear networks. For more details, see page 24-25.

WP1

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

Valuation theory

During 2018, one of the focus points within this work package has been **stereology of volume tensors** and their implementation in optical microscopy.

As shown in the recent book chapter Kousholt *et al.* (2017), a simple stereological method of estimating mean particle volume tensors in 3D from vertical sections can be constructed. The method uses measurements in a single optical plane, passing through a reference point of each sampled particle, see Figure 1.

In Larsen *et al.* (2018), this new and simple method is presented to scientists working in optical microscopy. In a model-based setting, the method requires that the particle distribution is invariant under rotations around the vertical axis. Under rotational invariance, the vertical axis represents the average orientation of the particles in 3D and the mean particle shape can be estimated from observations in vertical planes. The implication of the rotational invariance assumption for stereological estimation of mean particle volume has also recently been discussed in Hasselholt *et al.* (2019).

For a single particle, the volume tensors of rank 0, 1 and 2 can be used to construct an ellipsoidal approximation to the particle, see Figure 2. Likewise, for a particle population, the mean particle volume tensors of rank 0, 1 and 2 can be combined into an ellipsoid, called the **Miles ellipsoid**, representing the 3D shape and orientation of the typical particle. (The Miles ellipsoid is named after Roger Miles who was a pioneer in the development of stereological methods for particle populations with arbitrarily shaped particles.) The concept of the Miles ellipsoid is illustrated in Figure 3. Under rotational invariance, the Miles ellipsoid is an ellipsoid of revolution around the vertical axis. This ellipsoid contains information about mean particle shape.

In a design-based approach, where the vertical plane is uniformly rotated around the vertical axis, it is not needed to assume rotational invariance. In this case, the method provides information about an index of elongation of the particles in the direction of the vertical axis. This set-up has been implemented on human brain tissue for the analysis of neurons in layer III of the medial frontal gyrus of Brodmann Area 46. Methods of assessing the precision of the new estimator, based on a bootstrap procedure, are also provided in Larsen *et al.* (2018). In the actual implementation, the new estimator shows similar precision as an earlier estimator (Ziegel *et al.*, 2015; Rafati *et al.*, 2016), based on an optical rotator design, but it is a factor 3 faster to collect the measurements for the new estimator. For more details about the implementation, see page 17.

The research on **uniqueness of measurement functions** in integral geometric formulae has been continued in 2018. The question examined is whether the measurement function appearing in Crofton's formula is unique. An equivalent question is to characterize the measurement functions φ for which

$$\int_{A(n,k)} \varphi(X \cap E)\,\mathrm{d}E = 0.$$

Here, X is a convex body in $\mathbb{R}^n$ and E is an affine subspace of $\mathbb{R}^n$ of dimension k. A main result obtained in 2018 is a characterization of local and even measurement functions φ, defined on convex bodies of dimension at most $0 < k < 3$, which satisfy the above integral equation. A proof of this result will appear in the forthcoming publication Eriksen & Kiderlen (2019).

The project on **isoperimetric inequalities with tensor constraints** was also given some attention in 2018 by CSGB researchers Markus Kiderlen and Anne Marie Svane. The paper Gardner & Kiderlen (2018) on a structural theory of operations between real-valued functions on subsets of $\mathbb{R}^n$ was published in the journal *Communications in Analysis and Geometry*.

References

Eriksen, R.K. & Kiderlen, M. (2019): Uniqueness of the measurement function in Crofton's formula. In preparation.

Gardner, R. & Kiderlen, M. (2018): Operations between functions. *Commun. Anal. Geom.* **26**, 787-855.

Hasselholt, S., Hahn, U., Jensen, E.B.V. & Nyengaard, J.R. (2019): Practical implementation of the planar and spatial rotator in a complex tissue – the brain. *J. Microsc.* **273**, 26-35. Has appeared in 2018 as *CSGB Research Report* **2018-09**.

Kousholt, A., Ziegel, J.F., Kiderlen, M. & Jensen, E.B.V. (2017): Stereological estimation of mean particle volume tensors in $\mathbb{R}^3$ from vertical sections. In *Tensor Valuations and their Applications in Stochastic Geometry and Imaging* (eds. E.B.V. Jensen and M. Kiderlen). *Lecture Notes in Mathematics* **2177**, pp. 423-434. Springer.

Larsen, N.Y., Ziegel, J.F., Nyengaard, J.R. & Jensen, E.B.V. (2018): Stereological estimation of particle shape from vertical sections. *CSGB Research Report* **2018-12**. Submitted.

Rafati, A.H., Ziegel, J.F., Nyengaard, J.R. & Jensen, E.B.V. (2016): Stereological estimation of particle shape and orientation from volume tensors. *J. Microsc.* **263**, 229-237.

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

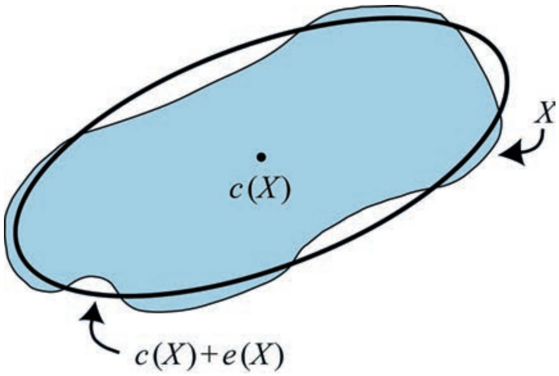


Figure 2
2D illustration of the ellipsoidal approximation to a particle X (blue). Here, $c(X)$ is the centre of gravity of X and $e(X)$ is a centred ellipsoid, approximating $X - c(X)$. If X is an ellipsoid, $X = c(X) + e(X)$.

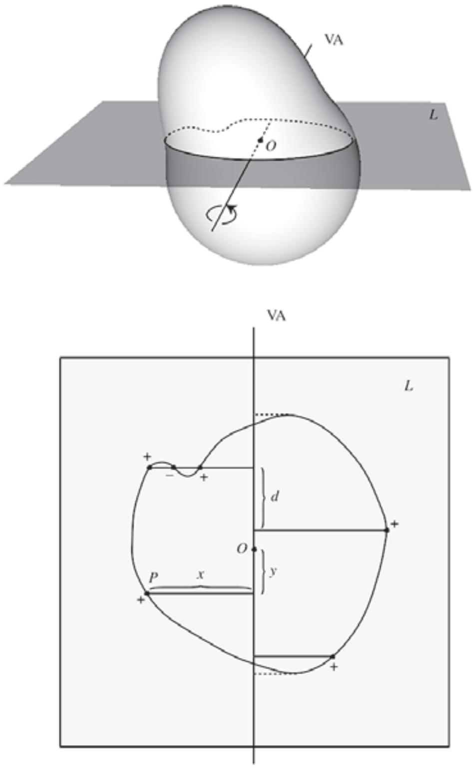


Figure 1
Upper: The particle is sectioned by a vertical plane, containing the vertical axis (VA) and passing through the reference point O of the particle.
Lower: The section is subsampled by a systematic set of half lines. The intersection points on a given half line are ordered according to decreasing distance to VA and are given alternating signs, starting with + for the most distant intersection point.

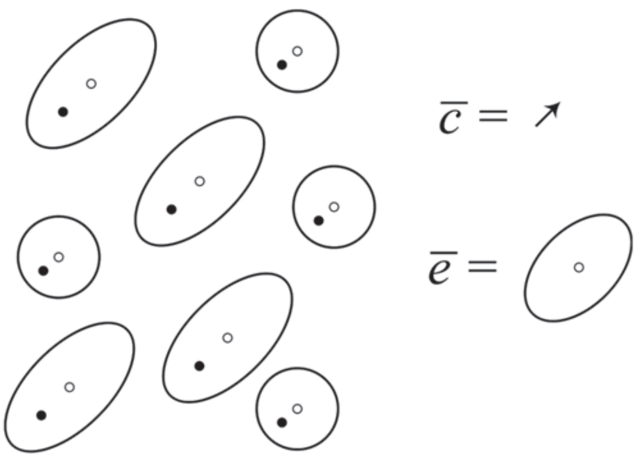


Figure 3
2D illustration of the displacement vector $\bar{c}$ and the Miles ellipsoid $\bar{e}$ for a particle population, consisting of an equal mixture of ellipses and circular disks. The centre of gravity of a particle is indicated by an open circle and the reference point by a closed circle.

WP2

Researchers
Ivan D'Annibale
Sune Darkner
Aasa Feragen
Ute Hahn
Tom Dela Haije
Mathias Højgaard Jensen
Line Kühnel
François Lauze
Anton Mallasto
Mads Nielsen
Rune Kok Nielsen
Jens R. Nyengaard
Andrew du Plessis
Stefan Sommer
Hans Jacob T. Stephensen

Random shapes

During 2018, several contributions have been made to the quantification of uncertainty in statistical models for complex data. One of the workhorses in this respect was the **Wrapped Gaussian Process** (WGP), which is a generalization of a Gaussian process to data taking values on a Riemannian manifold. This allowed us first to define a WGP regression model for manifold valued data, hence quantifying the regression model uncertainty (Mallasto & Feragen, 2018a). This approach was also used to define a WGP latent variable model, which allows stochastic submanifold learning. More precisely, when data is known to reside on a manifold, for instance due to invariances or constraints, the WGPLVM allows us to learn a stochastic data manifold, which is ensured to satisfy the constraints or invariances by being constrained to lie within the manifold (Mallasto *et al.*, 2019). Finally, comparison of Wrapped Gaussian Distributions (WGDs) on manifolds are enabled by the generalization of optimal transport to WGDs (Mallasto & Feragen, 2018b).

Within **diffusion MRI**, the importance of constraints and spherical sampling has been discussed in Dela Haije & Feragen (2018). Furthermore, it was shown in Holm *et al.* (2018) that uncertainty quantification plays a crucial part in performing population-wide tractography. This paper was based on the MSc thesis of Andreas N. Holm and is one of several examples of graduate students contributing actively to the research in this work package. Another example concerns a BSc thesis, which demonstrated a clear bias in classical algorithms for structural parcellation (Jensen *et al.*, 2018).

Finally, first results were obtained in stratified diffeomorphic image registration. Here, we utilize a pre-defined stratification of the image domain to define a piecewise-diffeomorphic deformation model which is able to model the topological changes explicitly defined by the stratification (Nielsen *et al.*, 2018).

In **statistics on nonlinear spaces**, activities have evolved around parametric statistics using stochastic processes, and stochastics on shape spaces. We constructed a technique for performing principal component analysis on manifolds, using stochastic processes and bridge sampling (Sommer, 2018). The construction avoids linearization of the underlying space and incorporates curvature by marginalization over all possible (stochastic) ways of coming from a mean to an observation. We have extended the stochastic shape model (Arnaudon *et al.*, 2018) to image data, including parameter estimation in the model (Kühnel *et al.*, 2018).

We have initiated collaboration with F. van der Meulen (Delft) and M. Schauer (Leiden) on **sampling of stochastic bridges**. These two researchers have worked extensively on sampling schemes for conditioned stochastic processes in the Euclidean setting, and we are currently extending their approaches to manifolds, including stochastic phase space flows where the processes are generally semi-elliptic. An important case concerns the application of this to landmark manifolds and more general shape spaces. As an outcome of this collaboration, F. van der Meulen will spend a six month sabbatical in Copenhagen in 2019, and we have received funding to explore extensions of the methods to infinite dimensional spaces.

Extensive work has evolved around investigating the behaviour of Brownian motion on landmark shape spaces, the simplest non-trivial shape space. This work has been carried out in collaboration with P. Harms, Freiburg. In particular, we wish to investigate Brownian completeness on landmark manifolds with Riemannian metric inherited from right-invariant metrics on the diffeomorphism group.

Several members of the KU-group associated with CSGB have contributed to an upcoming book (Pennec *et al.*, 2019) on nonlinear statistics shape analysis and applications in medical image analysis. The book is currently planned for publication in 2019.

References

Arnaudon, A., Holm, D.D. & Sommer, S. (2018): A geometric framework for stochastic shape analysis. Available at arXiv:1703.09971. *Found. Comput. Math.*, in press. DOI: 10.1007/s10208-018-9394-z.

Dela Haije, T. & Feragen, A. (2018): The importance of constraints and spherical sampling in diffusion MRI. Conference abstract from *ISMRM – 26th Annual Meeting for International Society for Magnetic Resonance in Medicine 2018.*

Holm, A.N., Feragen, A., Dela Haije, T. & Darkner, S. (2018): Deterministic group tractography with local uncertainty quantification. *Computational Diffusion MRI (CDMRI) Workshop at MICCAI 2018.*

Jensen, M.H., Thomsen, H., Liptrot, M., Kasenburg, N., Dorph-Petersen, K.-A., Darkner, S. & Feragen, A. (2018): Biases in classical structural parcellation. Conference abstract from *ISMRM – 26th Annual Meeting for International Society for Magnetic Resonance in Medicine 2018.*

Kühnel, L., Arnaudon, A., Fletcher, T. & Sommer, S. (2018): Stochastic image deformation in frequency domain and parameter estimation using moment evolutions. Submitted.

Mallasto, A. & Feragen, A. (2018a): Wrapped Gaussian process regression on Riemannian manifolds. *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition (CVPR) 2018,* pp. 5580-5588. Has also appeared as *CSGB Research Report* **2018-03**.

Mallasto, A. & Feragen, A. (2018b): Optimal transport distance between wrapped Gaussian distributions. Conference paper at *MaxEntropy 2018*.

Mallasto, A., Hauberg, S. & Feragen, A. (2019): Probabilistic Riemannian submanifold learning with wrapped Gaussian process latent variable models. Conference paper accepted for presentation at *22nd International Conference on Artificial Intelligence and Statistics (AISTATS 2019).*

Nielsen, R.K., Darkner, S. & Feragen, A. (2018): Explicit topological changes in piecewise-diffeomorphic image registration. Submitted.

Pennec, X., Fletcher, T. & Sommer, S. (2019, eds.): *Riemannian Geometric Statistics in Medical Image Analysis.* Elsevier. In press.

Sommer, S. (2018): An infinitesimal probabilistic model for principal component analysis of manifold valued data. *CSGB Research Report* **2018-02**. *Sankhya A*, in press. DOI: 10.1007/s13171-018-0139-5.

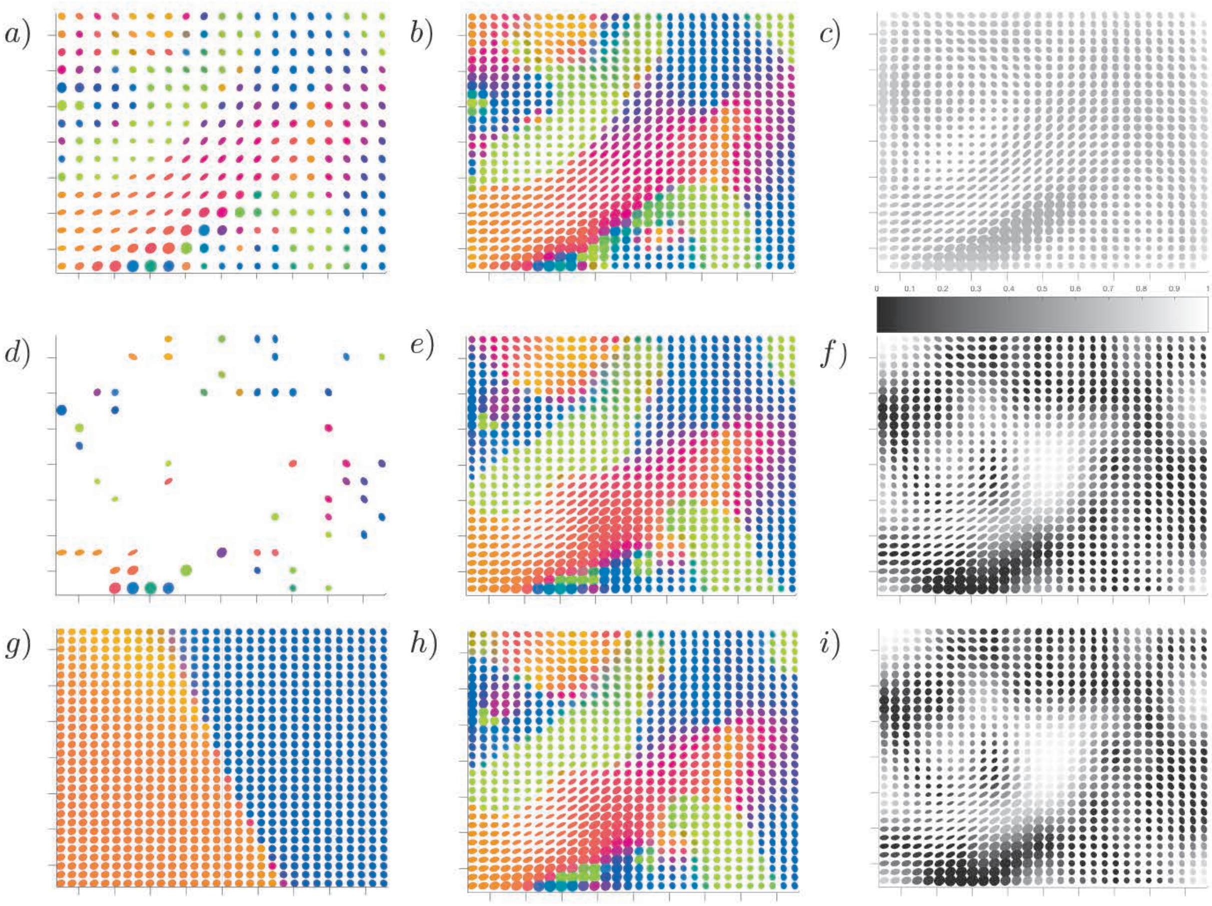


Figure 1
WGP regression on DTI data. Colours depict the direction of the largest eigen-vector of the respective tensors. For details, see Mallasto & Feragen (2018a).

WP3

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Spatial and spatio-temporal point processes

During 2018, a number of papers written by the CSGB researchers associated with WP3 have been accepted for publication or published in top international journals, including *Bernoulli*, *Journal of the American Statistical Association* and *Journal of Computational and Graphical Statistics*, see the list of references.

Within WP3, we have in 2018 published an important paper on **determinantal point process models** on the sphere (Møller *et al.*, 2018b). These are finite point processes exhibiting repulsiveness and with moment properties determined by a certain determinant. The appealing properties of such processes are reviewed, including their specific moment properties, density expressions and simulation procedures. In Lavancier *et al.* (2018), statistical inference for non-stationary determinantal point processes is developed. The suggested inference procedure is based on an adaptive estimating function approach. In the paper, asymptotic normality of estimating function estimators is established in a very general setting of non-stationary point processes. The relation between the distribution of a determinantal point process and its reduced Palm distribution is studied in Møller & O'Reilly (2018). The obtained results are used for quantifying repulsiveness of the point process.

Statistical methodology for log **Gaussian Cox processes** (LGCPs) has mainly been developed for LGCPs in the d-dimensional Euclidean space. In Cuevas-Pacheco & Møller (2018), this theory has been extended to LGCPs on the sphere and applied in the description of sky positions of galaxies. The related question of constructing covariance functions for random fields on spheres has been studied in Alegria *et al.* (2018). Structured **space-sphere point processes** and their K-functions have been considered in Møller *et al.* (2018a).

In Biscio & Waagepetersen (2018), a **central limit theorem** for summary statistics of point processes is established in a general setting and under weak conditions. The paper also provides an estimate of the asymptotic variance appearing in the central limit theorem which is required for example to assess the efficiency of an estimator in applications. Related work may be found in Biscio *et al.* (2018). Moreover, Christophe A.N. Biscio and Florent Bonneu, Avignon University, currently investigate the rate of convergence of central limit theorems for statistics of spatial point processes with the aim to assess the quality of a proposed estimator.

In Sporring *et al.* (2018), an extension of the K-functions, aiming at quantifying interactions in **spatial patterns of curves**, has been suggested. This extension involves differential geometric characteristics of the curves. Previous approaches were only based on curve length.

The CSGB researchers working in WP3 also made several advances regarding **statistics for spatial point processes**. In Baddeley *et al.* (2019), the recently developed leverage and influence diagnostics for Poisson processes are derived in a novel and much simpler way than previously, and everything is implemented as part of the open source package spatstat for the statistical software R. Mehdi Moradi *et al.* (2018) propose to apply an additional smoothing operation to a Voronoi intensity estimator, based on resampling the point pattern by independent random thinning. The resulting resample-smoothing estimator is very promising and simulation studies show that it may improve intensity estimation substantially. Stochastic quasi-likelihood methods for case-control point pattern data are developed in Xu *et al.* (2018). See also Choiruddin *et al.* (2018) and Gratzer & Waagepetersen (2018).

During 2018, the research on the accumulated persistence function as a functional summary of the persistence diagram (Biscio & Møller, 2019), quasi-likelihoods (Deng *et al.*, 2018), stability of generalized sampling (Jacobsen *et al.*, 2018), fast bandwidth selection (Jalilian & Waagepetersen, 2018) and iterated cluster point processes (Møller & Christoffersen, 2018) has been published or accepted for publication. The majority of this research has been described in earlier *CSGB Annual Reports*.

References

Alegria, A., Cuevas, F., Diggle, P. & Porcu, E. (2018): A family of covariance functions for random fields on spheres. *CSGB Research Report* **2018-08**.

Baddeley, A. Rubak, E. & Turner, R. (2019): Leverage and influence diagnostics for Gibbs spatial point processes. *Spat. Stat.* **15**, 15-48. DOI: 10.1016/j.spasta.2018.09.004.

Biscio, C.A.N. & Møller, J. (2019): The accumulated persistence function, a new useful functional summary statistic for topological data analysis, with a view to brain artery trees and spatial point process applications. Available at arXiv:1611.00630. To appear in *J. Comput. Graph. Stat.*

Biscio, C.A.N., Poinas, A. & Waagepetersen R. (2018): A note on gaps in proofs of central limit theorems. *Stat. Probab. Lett.* **135**, 7-10.

Biscio, C.A.N. & Waagepetersen, R. (2018): A general central limit theorem and subsampling variance estimator for α-mixing point processes. *CSGB Research Report* **2018-05**. To appear in *Scand. J. Stat.*

Choiruddin, A., Coeurjolly, J.F., & Letué, F. (2018): Convex and non-convex regularization methods for spatial point processes intensity estimation. *Electron. J. Stat.* **12**, 1210-1255.

Cuevas-Pacheco, F. & Møller, J. (2018): Log Gaussian Cox processes on the sphere. *Spat. Stat.* **26**, 69-82. Has also appeared as *CSGB Research Report* **2018-04**.

Deng, C., Waagepetersen, R.P., Wang, M. & Guan, Y. (2018): A fast spectral quasi-likelihood approach for spatial point processes. *Stat. Probab. Lett.* **133**, 59-64.

Gratzer, G. & Waagepetersen, R. (2018): Seed dispersal, microsites or competition - what drives gap regeneration in an old-growth forest? - An application of spatial point process modelling. *Forests* **9**, 230, 15 pages.

Jacobsen, R.D., Møller, J., Nielsen, M. & Rasmussen, M.G. (2018): Investigations of the effects of random sampling patterns on the stability of generalized sampling. *Appl. Comput. Harmon. A.* **45**, 453-461.

Jalilian, A. & Waagepetersen, R. (2018): Fast bandwidth selection for estimation of the pair correlation function. *J. Stat. Comput. Sim.* **88**, 2001-2011.

Lavancier, F., Poinas, A. & Waagepetersen, R. (2018): Adaptive estimating function inference for non-stationary determinantal point processes. Available at arXiv:1806.06231. Revised version submitted.

Mehdi Moradi, M., Cronie, O., Rubak, E., Lachièze-Rey, R., Mateu, J. & Baddeley, A. (2018): Resample-smoothing of Voronoi intensity estimators. Available at arXiv:1807.02590. *Stat. Comput.*, in press.

Møller, J., Christensen, H.S., Cuevas-Pacheco, F. & Christoffersen, A.D. (2018a): Structured space-sphere point processes and *K*-functions. *CSGB Research Report* **2018-10**. Submitted.

Møller, J. & Christoffersen, A.D. (2018): Pair correlation functions and limiting distributions of iterated cluster point processes. *J. Appl. Probab.* **55**, 789-809.

Møller, J., Nielsen, M., Porcu, E. & Rubak, E. (2018b): Determinantal point process models on the sphere. *Bernoulli* **24**, 1171-1201.

Møller, J. & O'Reilly, E. (2018): Couplings for determinantal point processes and their reduced Palm distributions with a view to quantifying repulsiveness. *CSGB Research Report* **2018-07**. Submitted.

Sporring, J., Waagepetersen, R. & Sommer, S. (2018): Generalizations of Ripley's *K*-function with application to space curves. Available at arXiv:1812.06870. Submitted.

Xu, G., Waagepetersen, R. & Guan, Y. (2018): Stochastic quasi-likelihood for case-control point pattern data. To appear in *J. Am. Stat. Assoc.*

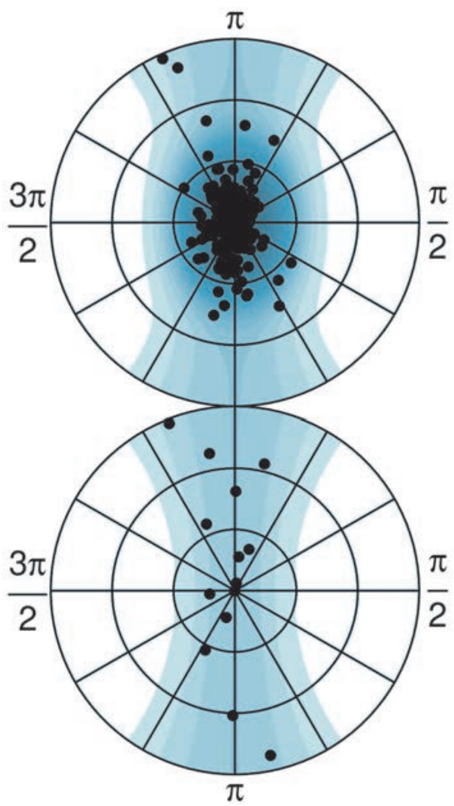

Figure 1
Plot of observed neuron orientations (dots) and a fitted mixture density (blue). Stereographic projection of the northern (top) and southern (bottom) hemisphere. For details, see Møller *et al.* (2018a).

WP4

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Point processes in bioimaging

Point processes on **linear networks** are important for modelling events or objects on real networks, such as neuronal dendritic trees. In recent years there have been a fair amount of papers on functional summary statistics and models for point processes specified on linear networks, see Baddeley *et al.* (2014), McSwiggan et al. (2016), Baddeley *et al.* (2017), Rakshit *et al.* (2017) and references therein. For ***K*-functions defined on such networks**, it is often required that the point process is second-order pseudostationary, meaning that the intensity is constant and the pair correlation function depends only on the geodesic distance. However, Baddeley *et al.* (2017) discuss the difficulties of finding such point processes, and Rakshit *et al.* (2017) discuss using alternative distance metrics and present analogues of the *K*-functions and pair correlation function with respect to these metrics. Further, Baddeley *et al.* (2014) present methods for analyzing multitype point processes on networks, and McSwiggan *et al.* (2016) address problems with existing kernel estimates of the intensity point processes and further develop a new kernel estimate eluding these problems.

In Rasmussen & Christensen (2018), we consider point processes on **directed linear networks**, i.e. networks consisting of line segments with an associated direction. Such directions appear naturally in neuronal dendritic trees, where the directions go from the root of the tree towards the leaves of the network. A point process on the network is formed by the locations of spines along the dendritic tree. Spines play a role in e.g. memory storage. Changes in the spine distribution and shape have been linked to neurological diseases (Irwin *et al.*, 2001). Only a few studies (Jammalamadaka *et al.*, 2013; Baddeley *et al.*, 2014) model the distribution of spines, using point processes on (undirected) linear networks.

In Rasmussen & Christensen (2018), we focus on point processes specified by a modified version of the **conditional intensity function** often used for point processes on the time line, see e.g. Chapter 7 in Daley & Vere-Jones (2003) for an introduction to these. On the time line, the conditional intensity is based on conditioning on the past, and for a directed linear network the directions enable us to modify the notion of past and thereby to extend the definition of a conditional intensity. The details are given in the paper Rasmussen & Christensen (2018) which also contains a derivation of the likelihood function for a point process specified by such a conditional intensity function. In the paper, two simulation algorithms are considered and methods for model checking based on residuals are discussed. Using the conditional intensity function, a number of models for point processes on directed linear networks can be defined, all inspired from similar models on the time line. The paper Rasmussen & Christensen (2018) also presents analyses of simulated datasets and a real dataset consisting of spines along a dendritic tree. Various aspects of the methodology are illustrated in Figures 1 and 2.

The research on **improved variance prediction in stereology** has been continued in 2018. The main focus is on variance prediction for Cavalieri type estimators with unequal spacing between sampling points. The classical Cavalieri estimator may have a severely inflated variance when the sampling points are not equidistant. To remedy this shortcoming, we measure the distances between the sampling points and use this information in the construction of a new estimator, involving Newton-Cotes quadratures. The positions of the sampling points are modelled by a stationary point process on the line. The variance inflation can be avoided if a Newton-Cotes quadrature of sufficiently high order is applied (Stehr & Kiderlen, 2019).

In 2018, the paper Andersen *et al.* (2018) on statistical inference for **point process models of protein clusters** has been published. In continuation of this research, Cluster Marked Cluster point processes (CMCpps) have been studied in 2018. CMCpps hold new potential for modelling of data from **super resolution microscopy**, where photo-blinking artifacts give rise to clusters of multiple appearances from the same molecule. These blinking artifacts complicate matters of counting proteins, and quantifying the degree of clustering between them.

References

Andersen, I.T., Hahn, U., Arnspang, E.C., Nejsum, L.N. and Jensen, E.B.V. (2018): Double Cox cluster processes – with applications to photoactivated localization microscopy. *Spat. Stat.* **27**, 58-73.

Baddeley, A., Jammalamadaka, A. & Nair, G. (2014): Multitype point process analysis of spines on the dendrite network of a neuron. *J. Roy. Stat. Soc. C* **63**, 673-694.

Baddeley, A., Nair, G., Rakshit, S. & McSwiggan, G. (2017): "Stationary" point processes are uncommon on linear networks. *Stat.* **6**, 68-78.

Daley, D.J. & Vere-Jones, D. (2003): *An Introduction to the Theory of Point Processes. Volume I: Elementary Theory and Methods.* 2nd edn. Springer, New York.

Irwin, S., Patel, B., Idupulapati, M., Harris, J., Crisostomo, R., Larsen, B., Kooy, F., Willems, P., Cras, P., Kozlowski, P., Swain, R., Weiler, I. & Greenough, W. (2001): Abnormal dendritic spine characteristics in the temporal and visual cortices of patients with fragile-X syndrome: a quantitative examination. *Am. J. Med. Genet.* **98**, 161-167.

Jammalamadaka, A., Banerjee, S., Manjunath, B. & Kosik, K. (2013): Statistical analysis of dendritic spine distributions in rat hippocampal cultures. *BMC Bioinformatics* **14**, 287.

McSwiggan, G., Baddeley, A. & Nair, G. (2016): Kernel density estimation on a linear network. *Scand. J. Stat.* **44**, 324-345.

Rakshit, S., Nair, G. & Baddeley, A. (2017): Second-order analysis of point patterns on a network using any distance metric. *Spat. Stat.* **22**, 129-154.

Rasmussen, J.G. & Christensen, H.S. (2018): Point processes on directed linear network. *CSGB Research Report* **2018-11**. Submitted.

Stehr, M. & Kiderlen, M. (2019): Asymptotic variance of Newton-Cotes quadratures based on randomized sampling points. In preparation.

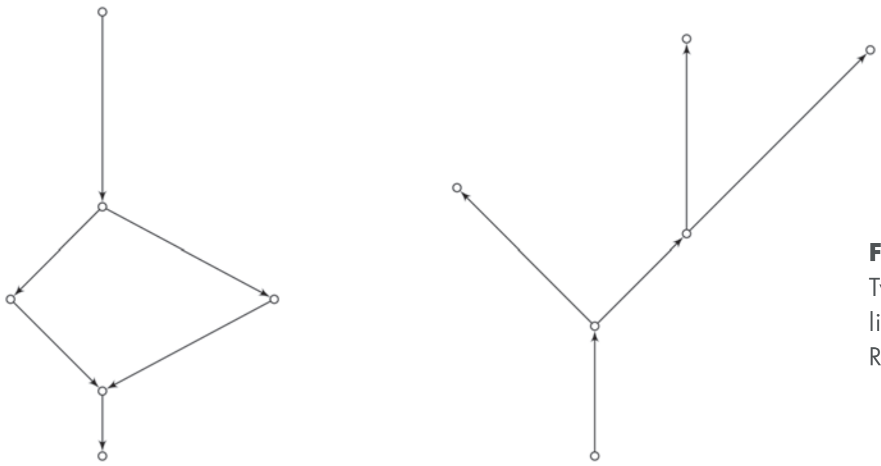

Figure 1
Two examples of directed linear networks. For details, see Rasmussen & Christensen (2018).

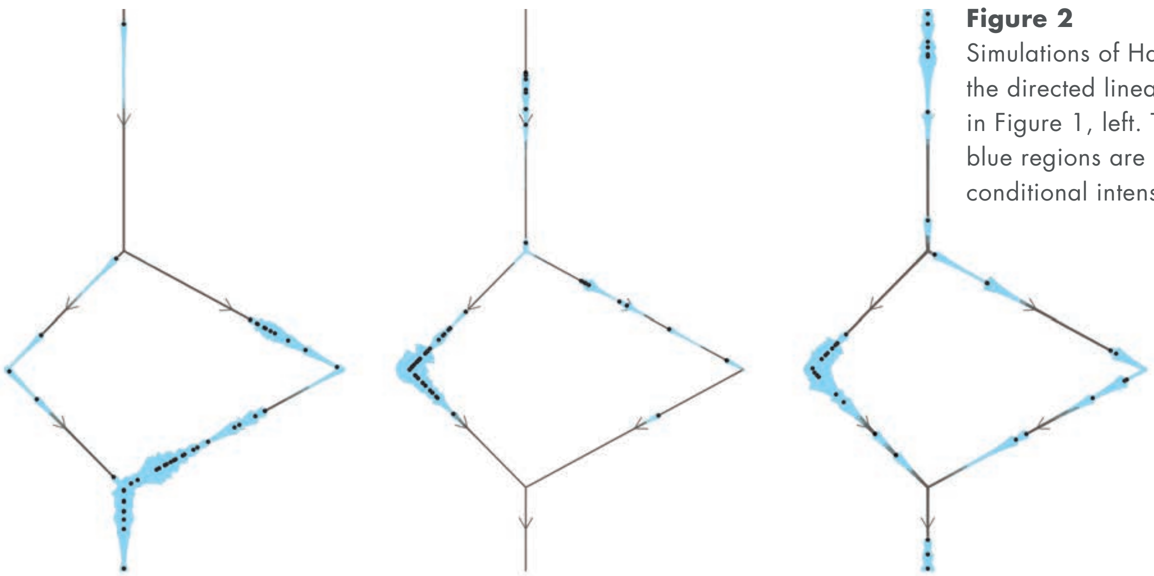

Figure 2
Simulations of Hawkes processes on the directed linear network, shown in Figure 1, left. The width of the blue regions are proportional to the conditional intensity.

WP5

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Statistics for stochastic geometry models

The basic modelling tool in the projects on **asymptotics for excursion sets** and **estimation of sample spacing** is Lévy-based random fields. If the fields are discretely indexed, they are defined by

$$X_i = \int_{\mathbb{R}^d} f(s-i)\, M(\mathrm{d}s), \qquad (1)$$

$i \in \mathbb{Z}^d$, where f is a kernel function and M is an infinitely divisible, independently scattered random measure on $\mathbb{R}^d$. Lévy-based models provide a flexible modelling framework that can be used in a range of modelling contexts, including modelling of turbulent flows, growth processes, Cox point processes and brain images (Barndorff-Nielsen & Schmiegel, 2004; Hellmund *et al.*, 2008; Jónsdóttir *et al.*, 2008, 2013).

Due to the tractability of Lévy-based models, it has been possible to derive tail asymptotics for the suprenum of such a field as well as asymptotics of excursion sets of the field. Results for the case where M is a convolution equivalent measure has recently been obtained in Rønn-Nielsen & Jensen (2016, 2017). The case of random measures with regularly varying tails were considered in Rosiński & Samorodnitsky (1993) and later further developed in Adler *et al.* (2010, 2013).

Motivated by applications in electron microscopy, we have in 2018 studied the asymptotic distribution of the following estimators of the mean value and the variogram of the random field,

$$S_\Gamma = \textstyle\sum_{i\in\Gamma} X_i \quad \text{and} \quad T_\Gamma(h) = \textstyle\sum_{i\in\Gamma}(X_i - X_{i+h})^2.$$

Here, $h \in \mathbb{Z}^d$ and Γ is a finite subset of $\mathbb{Z}^d$ with number of elements increasing to infinity in such a way that the ratio $\#\partial\Gamma/\#\Gamma$ goes to zero (Rønn-Nielsen & Jensen, 2018) where $\partial\Gamma$ is the notation used for the boundary of Γ. It is shown under mild regularity conditions that both S_Γ and $T_\Gamma(h)$ are asymptotically normally distributed. An important tool in the proof of the central limit theorem (CLT) obtained in Rønn-Nielsen & Jensen (2018) is a Lindeberg-type CLT from Heinrich (1988) on m_n-dependent random fields. Explicit expressions for the asymptotic variances are derived. It turns out that the asymptotic variance of $T_\Gamma(h)$ is equal to an approximate variance, earlier derived in Rønn-Nielsen *et al.* (2017). In the latter paper, the approximate variance was used in the assessment of the precision of a section spacing estimator in electron microscopy.

In El Machkouri *et al.* (2013), CLTs for random variables obtained by discretizing the integral in (1) is discussed. In particular, a CLT for S_Γ is derived which is a discrete analogue of the CLT we obtain. For second-order properties, El Machkouri *et al.* (2013) considers

$$\textstyle\sum_{i\in\Gamma} X_i X_{i+h},$$

but does not deal explicitly with the case where the mean of the field is unknown, as is done in Rønn-Nielsen & Jensen (2018).

In the case where the kernel function is isotropic, the variogram estimator $T_\Gamma(h)$ can be improved by taking into account that the variogram $\gamma(h)$ only depends on h through the length of h. Following exactly the same lines as in the proof for general kernel functions, a CLT for the improved estimator can be derived. Based on observations of the field within two parallel planes in 3D, this estimator has been used for estimation of the unknown distance between the two planes.

In 2018, the CSGB group (Stehr & Rønn-Nielsen, 2019) started a study of Lévy-based models depending on both space and time, generalizing the models appearing in Rønn-Nielsen & Jensen (2016, 2017). Here, a challenge has been that discontinuities are introduced in the resulting field when modelling present observations as based solely on noise in the past. Another ongoing project is to generalize the results in Rønn-Nielsen & Jensen (2016) to Lévy measures with exponential, not necessarily convolution equivalent tails. A future project will be to find the limiting extreme value distribution of the supremum under consideration in Rønn-Nielsen & Jensen (2016), when the index set increases.

References

Adler, R.J., Samorodnitsky, G. & Taylor, J.E. (2010): Excursion sets of three classes of stable random fields. *Adv. Appl. Probab.* **42**, 293-318.

Adler, R.J., Samorodnitsky, G. & Taylor, J.E. (2013): High level excursion set geometry for non-Gaussian infinitely divisible random fields. *Ann. Probab.* **41**, 134-169.

Barndorff-Nielsen, O.E. & Schmiegel, J. (2004): Lévy based tempo-spatial modelling with applications to turbulence. *Uspekhi Mat. Nauk.* **159**, 63-90.

El Machkouri, M., Volný, D. & Wu, W.B. (2013): A central limit theorem for stationary random fields. *Stoch. Proc. Appl.* **123**, 1-14.

Heinrich, L. (1988): Asymptotic behaviour of an empirical nearest-neighbour distance function for stationary Poisson cluster processes. *Math. Nachr.* **136**, 131-148.

Hellmund, G., Prokešová, M. & Jensen, E.B.V. (2008): Lévy-based Cox point processes. *Adv. Appl. Probab.* **40**, 511-529.

Jónsdóttir, K.Ý., Schmiegel, J. & Jensen, E.B.V. (2008): Lévy-based growth models. *Bernoulli* **14**, 62-90.

Jónsdóttir, K.Ý., Rønn-Nielsen, A., Mouridsen, K. & Jensen, E.B.V. (2013): Lévy-based modelling in brain imaging. *Scand. J. Stat.* **40**, 511-529.

Rosiński, J. & Samorodnitsky, G. (1993): Distributions of subadditive functionals of sample paths of infinitely divisible processes. *Ann. Probab.* **21**, 996-1014.

Rønn-Nielsen, A. & Jensen, E.B.V. (2016): Tail asymptotics for the supremum of an infinitely divisible field with convolution equivalent Lévy measure. *J. Appl. Probab.* **53**, 244-261.

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

Rønn-Nielsen, A. & Jensen, E.B.V. (2018): Central limit theorems for mean and variogram estimators in Lévy-based models. *CSGB Research Report* **2018-06**. Accepted for publication in *Adv. Appl. Probab.*

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

Stehr, M. & Rønn-Nielsen, A. (2019): Tail asymptotics for an infinitely divisible space-time model with convolution equivalent Lévy measure. In preparation.

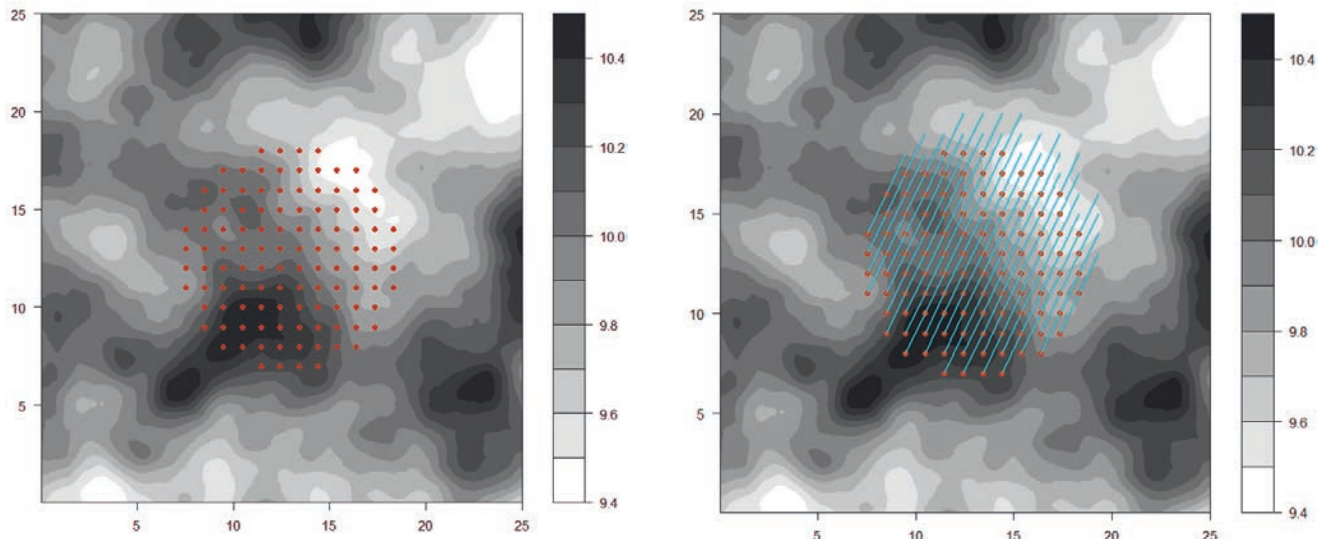

Figure 1
Left: The random field is observed at the set of sampling points Γ (red points). The central limit theorem (CLT) for mean and variogram estimators hold in an asymptotic scenario, where the number of elements in Γ increases to infinity in such a way that the ratio $\#\partial\Gamma/\#\Gamma$ goes to zero. Here, $\partial\Gamma$ is the notation used for the boundary of Γ.
Right: The variogram estimator uses pairs of sampling points with the same distance and direction. For details, see Rønn-Nielsen & Jensen (2018).

WP6

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Algorithms

In 2018, the project on **single particle cryo-electron microscopy** has resulted in a publication on pyruvate dehydrogenase complex variants, see Drakulic *et al.* (2018). The pyruvate dehydrogenase complex (PDC) is one of the cell's largest enzymatic complexes and is located in the inner matrix of mitochondria, the cell's powerhouses. PDC consists of multiple copies of five protein subunits that carry out a three-step enzymatic reaction essential for the metabolism of carbohydrates. In PDC, E1 subunits, tetramers of two E1α and two E1β proteins, are located in the outer shell of the complex and bound to the core in a distance *d* via linkers of the centrally located E2 core proteins. Besides multiple copies of E2 proteins, the core also contains some copies of the E3 binding protein (E3BP) that links E3 dimers in the outer shell to the core (Figure 1A).

PDC is subject to inherited genetic variations that cause neurodevelopmental disorders in children. A hot spot for genetic variations is found in the α subunit of the enzyme E1. Currently, the molecular mechanisms underlying the impairment of PDC function caused by E1α variants are poorly understood. In the recent years, we have developed a model system of PDC that now allowed us to engineer PDC variants with single amino acid substitutions and to characterize these PDC variants biochemically and by single-particle electron microscopy (Drakulic *et al.*, 2018). Particularly, we studied the variants A189V, M230V and R322C in yeast E1α corresponding to the pathogenic variants A169V, M210V and R302C, respectively, in human E1α. These variants have been attributed to three different functional regions of the E1α protein, namely, the heterodimer interface (A169V), the tetramer interface (M210V) and the phosphorylation loop of E1α (R302C; compare Figure 1A). Strikingly, these exemplary variants each cause unique structural alteration of PDC. The E1α A189V variant shows a more compact conformation with a reduced core-shell distance and underrepresentation of E1 (Figure 1B, first column). In contrast, the M230V variant shows a relatively more open conformation (Figure 1B, second column). Biochemical data also indicate that the M230V variant is particularly affected by low thiamin pyrophosphate (a form of vitamin B1) concentrations. The E1α R322C variant results in PDC complexes similar to control PDC (Figure 1B, third column); however, mass spectrometry shows that this variant of PDC is lacking E3 subunits, which abolishes overall functional activity. This far-reaching structural effect of the single amino acid substitution R322C on PDC is a novel and unexpected finding, as direct E1-E3 interactions in PDC are not known.

Furthermore, we found that impairments in protein folding may contribute to functional impairments of variant PDC. Any protein in the cell is required to be 'folded' into a well-defined three-dimensional structure as a prerequisite for correct function. So-called 'chaperonin' proteins assist other proteins in this process and facilitate folding. We show that these variant E1α proteins accumulate in the central mitochondrial chaperonin protein complex, the Hsp60 chaperonin (Figure 1C, left panel), but can be released upon ATP supplementation (Figure 1C, right panel).

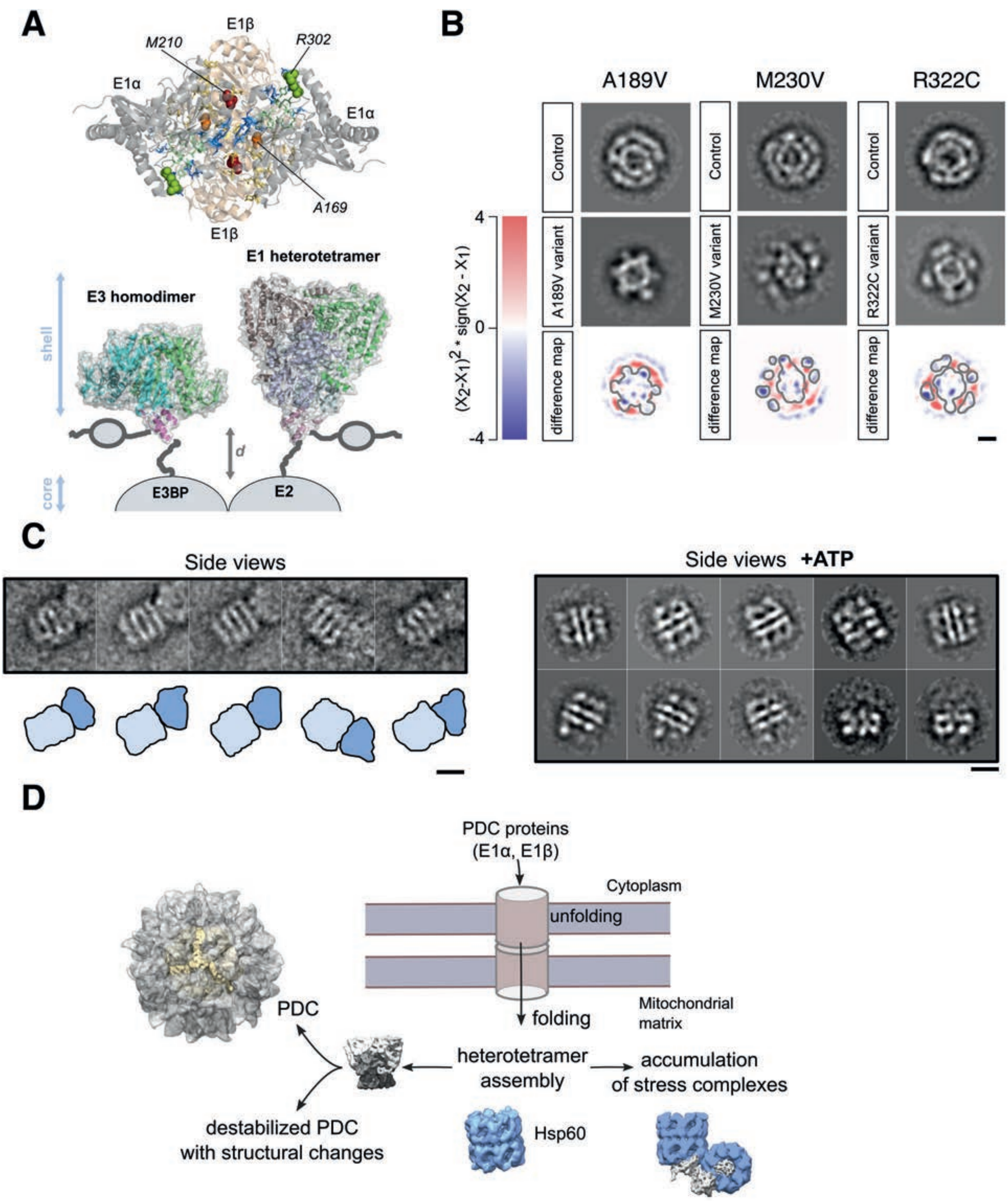
Together, these results suggest that different pathogenic variants of E1α induce characteristic changes in the shell including an overall structural impairment of the shell. Moreover, the lack of E3 found in the E1α R322C variant PDC indicates that single amino acid variations may alter the PDC protein interactions by hitherto unknown mechanisms such as for example changes in post-translational modifications. Moreover, the data suggest that the obligatory re-folding of proteins upon import into the mitochondria is impaired for variant E1α, which may further impede variant PDC function (Figure 1D).

In 2018, the research on **digital grey-scale images** resulted in the publication Svane & Feragen (2018).

References

Drakulic, S., Rai, J., Petersen, S.V., Golas, M.M. & Sander, B. (2018): Folding and assembly defects of pyruvate dehydrogenase deficiency-related variants in the E1α subunit of the pyruvate dehydrogenase complex. *Cell. Mol. Life Sci.* **75**, 3009-3026.

Svane, H. & Feragen, A. (2018): Reconstructing objects from noisy images at low resolution. To appear in the *Proceedings of the GbR2019 workshop.*



(A) Structure of the PDC subunit E1 (upper panel) and interactions of PDC proteins between core proteins (E2, E3BP) and shell proteins (E1 tetramers with two E1α and two E1β as well as E3 homodimers).

(B) Structural effects of the single-amino acid substitutions A189V (first column), M230V (second column), and R322C (third column). For each variant, a two-dimensional reconstruction of control PDC, variant PDC and an annotated difference map is shown. The scale bar corresponds to 100 Å at the specimen level.

(C) HSP60 chaperonin complexes bound to E1 (left panel), and HSP60 chaperonin upon ATP-dependent substrate protein release (right panel). Scale bars correspond to 100 Å at the specimen level.

(D) Model of the effects of impaired protein folding in variant E1α PDC. E1α refolding upon transport through the mitochondrial transport channel is impaired leading to reduced E1 tetramer assembly. Instead, 'stress complexes' consisting of partially folded E1 subunits and HSP60 complexes may accumulate. Formed E1 tetramers assemble into PDC complexes with destabilized shell and structural alterations in the shell including altered core-shell distances.

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CENTRE ACTIVITIES

OVERVIEW

PAST AND PLANNED INTERNATIONAL ACTIVITIES

INTERNATIONAL CONFERENCES, SYMPOSIA AND WORKSHOPS

- *International Workshop on Stereology*
  8 – 10 May 2018, Tehran
- *12th French-Danish Workshop on Spatial Statistics and Image Analysis in Biology*
  23 – 25 May 2018, Aalborg
- *Workshop on Quantitative Microscopy*
  20 – 24 August 2018, Bern
- *Workshop on Diffusion MRI and Stochastic Geometry*
  20 – 24 January 2019, Sandbjerg
- *Workshop on Point Processes in Space, Time and Beyond*
  13 - 16 May 2019, Skagen
- *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

- *Stereology Course*
  21 – 22 March 2018, Oviedo
- *Advanced Neuroscience Course*
  19 – 20 June 2018, Sino-Danish Center, Beijing
- *Interdisciplinary Summer School on Neuroimaging*
  16 – 26 July 2018, Aarhus
- *International PhD Course on Stereology*
  28 – 30 August 2018, Aarhus
- *PhD Course on Design and Analysis of Experiments*
  11 September – 24 October 2018, Aalborg
- *PhD Course on Bayesian Statistics, Simulation and Software*
  21 – 28 October 2018, Aalborg



From *12th French-Danish Workshop on Spatial Statistics and Image Analysis in Biology*, 23 – 25 May 2018, Aalborg, Denmark. Photo Ute Hahn.

15TH INTERNATIONAL CONGRESS FOR STEREOLOGY AND IMAGE ANALYSIS

27 – 30 MAY 2019, AARHUS UNIVERSITY, DENMARK

Scope of the congress

The 15th International Congress for Stereology and Image Analysis (ICSIA 2019) focuses on the transition from qualitative to quantitative descriptions of images from a range of imaging modalities in biology/medicine and materials science, using stereology and image analysis. ICSIA 2019 includes virtual materials design and reconstruction of microstructures investigated by quantitative microscopy, MRI, PET and other advanced imaging platforms. Time is also devoted to the development of advanced statistical/computational methods and the application of such methods in image analysis. ICSIA 2019 will put to test the development and use of methods for quantitative studies of structures from the atomic and molecular level up to a grand scale at the highest scientific level.

Structure of the congress and keynote speakers

ICSIA 2019 comprises invited presentations, minisymposia, free presentations and poster sessions.
The keynote speakers are

- Michael Klatt (Princeton)
- Mari Myllymäki (Helsinki)
- Emilio Porcu (Newcastle)
- Katja Schladitz (Kaiserslautern)
- Fei Sun (Beijing)

For further information, see *http://conferences.au.dk/icsia2019/*.

20TH WORKSHOP ON STOCHASTIC GEOMETRY, STEREOLOGY AND IMAGE ANALYSIS

2 – 7 JUNE 2019, SANDBJERG ESTATE, DENMARK

Scope of the workshop

This workshop is the 20th workshop in the series of biannual Workshops on Stochastic Geometry, Stereology and Image Analysis. These workshops constitute a principal forum for researchers working with random geometric objects. Since the beginning, the workshops have focused on both, the consolidation and advance of the title disciplines, and their development as valuable tools in a number of applied fields.

Structure of the workshop and invited speakers

The upcoming workshop will have longer talks by invited speakers and shorter contributed talks by participants, as well as a poster session. The invited speakers are

- Rémi Bardenet (Lille)
- Valentina Cammarota (Rome)
- Elisabetta Candellero (Rome)
- Peter F. Craigmile (Columbus)
- Frédéric Lavancier (Nantes)
- Thomas Richthammer (Paderborn)
- Patrick Rubin-Delanchy (Bristol)
- Vincent Tassion (Zürich)
- Benjamin Taylor (Lancaster)
- D. Yogeshwaran (Bangalore)

Photo Søren Petersen.

The workshop homepage *http://csgb.dk/activities/2019/sgsia2019/* contains further information.

INTERNAL CSGB WORKSHOPS

SIXTEENTH INTERNAL CSGB WORKSHOP

Musholm, Korsør, 31 May – 1 June 2018

TALKS

- Abdel-Rahman Al-Absi, AU-bio: *Recording and sorting of the electrical activity from acute brain slices using microelectrode array*
- Heidi Søgaard Christensen, AAU: *Structured space-sphere point processes and K-functions*
- Tom Dela Haije, KU: *Estimating orientations from diffusion MRI using fiber processes*
- Kristian Bjørn Hessellund, AAU: *Statistical analysis of multivariate point patterns using a case-control approach*
- Markus Kiderlen, AU-math: *The shape from moments problem: uniqueness and stability results*
- Line Kühnel, KU: *Noise estimation in stochastic image registration*
- Jens R. Nyengaard, AU-bio: *Volume tensor estimation with the planar rotator, its practical implementation and comparison with the optical rotator*
- Francisco Andrés Cuevas Pacheco, AAU: *Log Gaussian Cox processes on the sphere*
- Hans Jacob T. Stephensen, KU: *Model-based registration approach to correcting drifted FIB-SEM images*
- Helene Svane, AU-math: *Reconstruction from refined digital images*



From the *Sixteenth Internal CSGB Workshop*, 31 May – 1 June 2018, Musholm, Korsør.
Photo Karl-Anton Dorph-Petersen.

SEVENTEENTH INTERNAL CSGB WORKSHOP

HUSET, Middelfart, 8 – 9 November 2018

TALKS

- Abdel-Rahman Al-Absi, AU-bio: *Investigating the excitatory and the inhibitory synapses in animal models of schizophrenia*
- Rikke Eriksen, AU-math: *Uniqueness of the measurement function in Crofton's formula*
- Christian Hirsch, AAU: *Goodness of fit tests for point processes via topological data analysis*
- Louis Gammelgaard Jensen, AU-math: *Cluster marked cluster point processes*
- Mathias Højgaard Jensen, KU: *Stochastic bridge simulation on manifolds*
- Jens R. Nyengaard, AU-bio: *Gender differences in brain structure and function*
- Francisco Andrés Cuevas Pacheco, AAU: *A family of covariance functions for random fields on spheres*
- Jon Sporring, KU: *Ripley's K-function for space curves*
- Mads Stehr, AU-math: *Extremal properties over time of an infinitely divisible random field with convolution equivalent Lévy measure*

CSGB RESEARCH REPORTS 2018

1. Alegria, A., Cuevas, F., Diggle, P. & Porcu, E. (2018): A family of covariance functions for random fields on spheres. *CSGB Research Report* **2018-08**.

2. Biscio, C.A.N. & Waagepetersen, R. (2018): A general central limit theorem and subsampling variance estimator for α-mixing point processes. *CSGB Research Report* **2018-05**. To appear in *Scand. J. Stat.*

3. Cuevas-Pacheco, F. & Møller, J. (2018): Log Gaussian Cox processes on the sphere. *CSGB Research Report* **2018-04**. Has appeared as *Spat. Stat.* (2018) **26**, 69-82.

4. Hasselholt, S., Hahn, U., Jensen, E.B.V. & Nyengaard, J.R. (2018): Practical implementation of the planar and spatial rotator in a complex tissue - the brain. *CSGB Research Report* **2018-09**. Has appeared as *J. Microsc.* (2019) **273**, 26-35.

5. Kühnel, L., Arnaudon, A. & Sommer, S. (2018): Differential geometry and stochastic dynamics with deep learning numerics. *CSGB Research Report* **2018-01**.

6. Larsen, N.Y., Ziegel, J.F., Nyengaard, J.R. & Jensen, E.B.V. (2018): Stereological estimation of particle shape from vertical sections. *CSGB Research Report* **2018-12**. Submitted.

7. Mallasto, A. & Feragen, A. (2018): Wrapped Gaussian process regression on Riemannian manifolds. *CSGB Research Report* **2018-03**. Has appeared in *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition (CVPR) 2018*, pp. 5580-5588.

8. Møller, J., Christensen, H.S., Cuevas-Pacheco, F. & Christoffersen, A.D. (2018): Structured space-sphere point processes and K-functions. *CSGB Research Report* **2018-10**. Submitted.

9. Møller, J. & O'Reilly, E. (2018): Couplings for determinantal point processes and their reduced Palm distributions with a view to quantifying repulsiveness. *CSGB Research Report* **2018-07**. Submitted.

10. Rasmussen, J.G. & Christensen, H.S. (2018): Point processes on directed linear networks. *CSGB Research Report* **2018-11**. Submitted.

11. Rønn-Nielsen, A. & Jensen, E.B.V. (2018): Central limit theorem for mean and variogram estimators in Lévy-based models. *CSGB Research Report* **2018-06**. To appear in *Adv. Appl. Probab.*

12. Sommer, S. (2018): An infinitesimal probabilistic model for principal component analysis of manifold valued data. *CSGB Research Report* **2018-02**. *Sankhya A*, in press.

CSGB JOURNAL AND PROCEEDINGS PUBLICATIONS, BOOK CHAPTERS

Al-Absi, A.R., Christensen, H.S., Sanchez, C. & Nyengaard, J.R. (2018): Evaluation of semi-automatic 3D reconstruction for studying geometry of dendritic spines. *J. Chem. Neuroanat.* **94**, 119-124.

Andersen, I.T., Hahn, U., Arnspang, E.C., Nejsum, L.N. and Jensen, E.B.V. (2018): Double Cox cluster processes – with applications to photoactivated localization microscopy. *Spat. Stat.* **27**, 58-73.

Arnaudon, A., Holm, D. & Sommer, S. (2019): String methods for stochastic image and shape matching. *J. Math. Imaging Vis.* ***60***, 953-967.

Bay, V., Kjølby, B.F., Iversen, N.K., Mikkelsen, I.K., Ardalan, M., Nyengaard, J.R., Jespersen, S.N., Drasbek, K.R., Østergaard, L. & Hansen, B. (2018): Stroke infarct volume estimation in fixed tissue: comparison of diffusion kurtosis imaging to diffusion weighted imaging and histology in a rodent MCAO model. *PLoS One* **13**, s. e0196161.

Biscio, C.A.N., Poinas, A. & Waagepetersen R. (2018): A note on gaps in proofs of central limit theorems. *Stat. Probab. Lett.* **135**, 7-10.

Choiruddin, A., Coeurjolly, J. F., & Letué, F. (2018): Convex and non-convex regularization methods for spatial point processes intensity estimation. *Electron. J. Stat.* **12**, 1210-1255.

Clark, C.D., Ely, J.C., Spagnolo, M., Hahn, U., Hughes, A. & Stokes, C. (2018): Spatial organization of drumlins. *Earth Surf. Proc. Land.* **43**, 499-513.

Cuevas-Pacheco, F. & Møller, J. (2018): Log Gaussian Cox processes on the sphere. *Spat. Stat.* **26**, 69-82.

Darkner, S., Pai, A., Liptrot, M.G. & Sporring, J. (2018): Collocation for diffeomorphic deformations in medical image registration. *IEEE T. Pattern Anal.* **40**, 1570-1583.

Deng, C., Waagepetersen, R.P., Wang, M. & Guan, Y. (2018): A fast spectral quasi-likelihood approach for spatial point processes. *Stat. Probab. Lett.* **133**, 59-64.

Drakulic, S., Rai, J., Petersen, S.V., Golas, M.M. & Sander, B. (2018): Folding and assembly defects of pyruvate dehydrogenase deficiency-related variants in the E1α subunit of the pyruvate dehydrogenase complex. *Cell Mol. Life Sci.* **75**, 3009-3026.

du Plessis, A. & Wall, C.T.C. (2018): The moduli space of binary quintics. *Eur. J. Math.* **4**, 423-436.

Gardner, R. & Kiderlen, M. (2018): Operations between functions. *Commun. Anal. Geom.* **26**, 787-855.

Gratzer, G. & Waagepetersen, R. (2018): Seed dispersal, microsites or competition - what drives gap regeneration in an old-growth forest? - An application of spatial point process modelling. *Forests* **9**, 230, 15 pages.

Holm, A.N., Feragen, A. Dela Haije, T. & Darkner, S. (2018): Deterministic group tractography with local uncertainty quantification. *Computational Diffusion MRI (CDMRI) Workshop at MICCAI 2018.*

Jacobsen, R.D., Møller, J., Nielsen, M. & Rasmussen, M.G. (2018): Investigations of the effects of random sampling patterns on the stability of generalized sampling. *Appl. Comput. Harmon. A.* **45**, 453-461.

Jalilian, A. & Waagepetersen, R. (2018): Fast bandwidth selection for estimation of the pair correlation function. *J. Stat. Comput. Sim.* **88**, 2001-2011.

Kiderlen, M. & Rataj, J. (2018): Dilation volumes of sets of finite perimeter. *Adv. Appl. Probab.* **50**, 1095-1118.

Lauze, F., Dong, Y. & Dahl, A.B. (2018): Guest editorial: scale space and variational methods. *J. Math. Imaging Vis.* **60**, 1367-1368.

Le, L.T.M., Nyengaard, J.R., Golas, M.M. & Sander, B. (2018): Vectors for expression of signal peptide-dependent proteins in baculovirus/insect cell systems and their application to expression and purification of the high-affinity immunoglobulin gamma Fc receptor I in complex with its gamma chain. *Mol. Biotechnol.* **60**, 31–40.

Mallasto, A. & Feragen, A. (2018a): Wrapped Gaussian process regression on Riemannian manifolds. *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition (CVPR) 2018*, pp. 5580-5588.

Mallasto, A. & Feragen, A. (2018b): Optimal transport distance between wrapped Gaussian distributions. Conference paper at *MaxEntropy 2018*.

Meier, M., Andersen, K.J., Knudsen, A.R., Nyengaard, J.R., Hamilton-Dutoit, S. & Mortensen, F.V. (2018): Adaptive growth changes in the liver remnant are affected by the size of hepatectomy in rats. *Int. J. Exp. Pathol.* **99**, 150-157.

Møller, J. & Christoffersen, A.D. (2018): Pair correlation functions and limiting distributions of iterated cluster point processes. *J. Appl. Probab.* **55**, 789-809.

Møller, J., Nielsen, M., Porcu, E. & Rubak, E. (2018b): Determinantal point process models on the sphere. *Bernoulli* **24**, 1171-1201.

Orbes-Arteaga, M., Cardoso, M.J., Sørensen, L., Modat, M., Ourselin, S., Nielsen, M. & Pai, A. (2018): Simultaneous synthesis of FLAIR and segmentation of white matter hypointensities from T1 MRIs. *Conference on Medical Imaging with Deep Learning MIDL 2018*, 8 p.

Paternoster, V., Rajkumar, A.P., Nyengaard, J.R., Børglum, A.D., Grove, J. & Christensen, J.H. (2018): The importance of data structure in statistical analysis of dendritic spine morphology. *J. Neurosci. Meth.* **296**, 93-98.

Petersen, A., Petersen, S.V., Frische, S., Drakulic, S., Golas, M.M., Sander, B. & Fago, A. (2018): Hemoglobin polymerization via disulfide bond formation in the hypoxia-tolerant turtle Trachemys scripta: implications for antioxidant defense and O2 transport. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* **314**, R84–R93.

Quéau, Y., Durix, B., Wu, T., Cremers, D., Lauze, F.B. & Durou, J.-D. (2018): LED-based photometric stereo: modeling, calibration and numerical solution. *J. Math. Imaging Vis.* **60**, 313-340.

Sørensen, L. & Nielsen, M. (2018): Ensemble support vector machine classification of dementia using structural MRI and mini-mental state examination. *J. Neurosci. Meth.* **302**, 66-74..

Mathematisches Forschunginstitut Oberwolfach
Photo Eva B. Vedel Jensen.

WORKSHOP ON STATISTICS FOR DATA WITH GEOMETRIC STRUCTURE

21 – 27 January 2018, Oberwolfach

The organizers of this workshop were CSGB researcher Aasa Feragen (Copenhagen), Thomas Hotz (Ilmenau), Stephan Huckemann (Göttingen) and Ezra Miller (Durham).

Statistics for data with geometric structure is an active and diverse topic of research. Applications may involve manifold spaces and, in some cases, more complicated metric spaces like stratified spaces play a crucial role. As data sets become not only larger but also more complex, the need for theoretical and methodological progress in dealing with data on non-Euclidean spaces is growing. At the workshop, leading experts in the field presented great accomplishments of collaborations between statisticians, geometers and topologists. The open problems discussed at the workshop showed the need for an expansion of this interdisciplinary effort which could also strengthen the ties to computer science.

See also: https://www.mfo.de/occasion/1804

SELECTED TALKS BY CSGB STAFF IN 2018

Workshop on Statistics for Data with Geometric Structure
Oberwolfach | 21 – 27 January 2018
Stefan Sommer: Probabilistic inference on manifolds

Random Structures in Neuroscience and Biology
Herrsching | 26 – 29 March 2018
Jesper Møller: The cylindrical *K*-function and Poisson line cluster point processes

Stochastic Geometry Days
Paris | 14 – 18 May 2018
Eva B. Vedel Jensen: Precision of systematic sampling

12th French-Danish Workshop on Spatial Statistics and Image Analysis in Biology
Aalborg | 23 - 25 May 2018
Achmad Choiruddin: Sparse models for multivariate log-Gaussian Cox processes

12th French-Danish Workshop on Spatial Statistics and Image Analysis in Biology
Aalborg | 23 - 25 May 2018
Heidi Søgaard Christensen: Structured space-sphere point processes and *K*-functions

12th French-Danish Workshop on Spatial Statistics and Image Analysis in Biology
Aalborg | 23 - 25 May 2018
Andreas Dyreborg Christoffersen: Iterated cluster point processes

Meeting in the honor of Odile Macchi
Paris | 5 June 2018
Jesper Møller: Statistics for determinantal point process models and its usefulness

40th Conference on Stochastic Processes and their Applications (SPA 2018)
Gothenburg | 11 – 15 June 2018
Christophe Biscio: The accumulated persistence function, a new functional summary statistic for topological data analysis

4th Conference of the International Society for Nonparametric Statistics
Salerno | 11 – 15 June 2018
Aasa Feragen: Beyond trees: stratified spaces for variable topology data

9th International Workshop on Spatio-Temporal Modelling
Montpellier | 13 – 15 June 2018
Francisco Cuevas: Contours and dimples for the Gneiting class of space-time covariance functions

9th International Workshop on Applied Probability (IWAP 2018)
Budapest | 18 – 21 June 2018
Christophe Biscio: A general central limit theorem and subsampling variance estimator for α-mixing point processes

S4G Conference
Prague | 25 – 29 June 2018
Heidi Søgaard Christensen: Structured space-sphere point processes and *K*-functions

S4G Conference
Prague | 25 – 29 June 2018
Ute Hahn: On envelopes and multiple testing

Nordstat
Tartu | 26 – 29 June 2018
Stefan Sommer: Probabilistic inference on manifolds

International Statistical Ecology Conference (ISEC 2018)
St. Andrews | 2 - 6 July 2018
Achmad Choiruddin: Sparse models for multivariate log-Gaussian Cox processes

19th International Society for Serotonin Research Meeting
Cork | 15 – 19 July 2018
Jens Randel Nyengaard: Synaptic and mitochondrial plasticity of rat hippocampus follows treatment with Vortioxetine

Workshop on Probability and Statistical Modeling, and Applications: 9th Smögen Workshop
Smögen | 13 – 16 August 2018
Andreas Dyreborg Christoffersen: Iterated cluster point processes

Workshop on Probability and Statistical Modeling, and Applications: 9th Smögen Workshop
Smögen | 13 – 16 August 2018
Jesper Møller: Statistics for determinantal point process models and its usefulness

14th Iranian Statistics Conference
Shahrood | 25 – 27 August 2018
Rasmus Waagepetersen: Case control and regularized inference for multivariate log Gaussian Cox processes

Workshop on Image Analysis and Stereology with Applications in Biological and Social Sciences
Santander | 11 – 14 September 2018
Markus Kiderlen: Asymptotic variance of Newton-Cotes quadratures based on randomized sampling points

Workshop on Point Process Models
Texas A & M University | 27 – 28 September 2018
Jesper Møller: Statistics for determinantal point process models and its usefulness

6th Annual SDC Neuroscience and Neuroimaging Symposium
Beijing | 23 – 24 October 2018
Nick Yin Larsen: Characterization of columnarity and volume tensors of neurons in Brodmann Area 46 in normal, schizophrenic and depressive human autopsy brains

Van Dantzig Seminar
Delft | 26 October 2018
Stefan Sommer: Probabilistic approaches to geometric statistics

Dagstuhl Seminar Visualization and Processing of Anisotropy in Imaging, Geometry and Astronomy
Schloss Dagstuhl | 28 October – 2 November 2018
Aasa Feragen: Three cases of uncertainty

Dagstuhl Seminar Visualization and Processing of Anisotropy in Imaging, Geometry and Astronomy
Schloss Dagstuhl | 28 October – 2 November 2018
Tom Dela Haije: Enforcing necessary constraints for common diffusion MRI models using sum-of-squares optimization

Hangzhou International Human Resources Exchange and Cooperation Conference
Hangzhou | 9 – 11 November 2018
Jens Randel Nyengaard: A new strategy and target for anti-Alzheimer's disease drug PI01

Workshop on Convex Geometry and its Applications
Oberwolfach | 9 – 15 December 2018
Eva B. Vedel Jensen: Rotational Crofton formulae for Minkowski tensors


Christophe Biscio


Jens Randel Nyengaard


Francisco Cuevas


Tom Dela Haije


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Photo Karl-Anton Dorph-Petersen and Ute Hahn.

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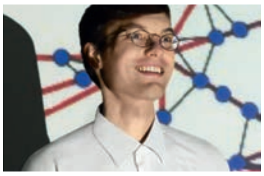
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CENTRE FOR **STOCHASTIC GEOMETRY** AND ADVANCED **BIOIMAGING**

Annual Report 2018, published April 2019

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