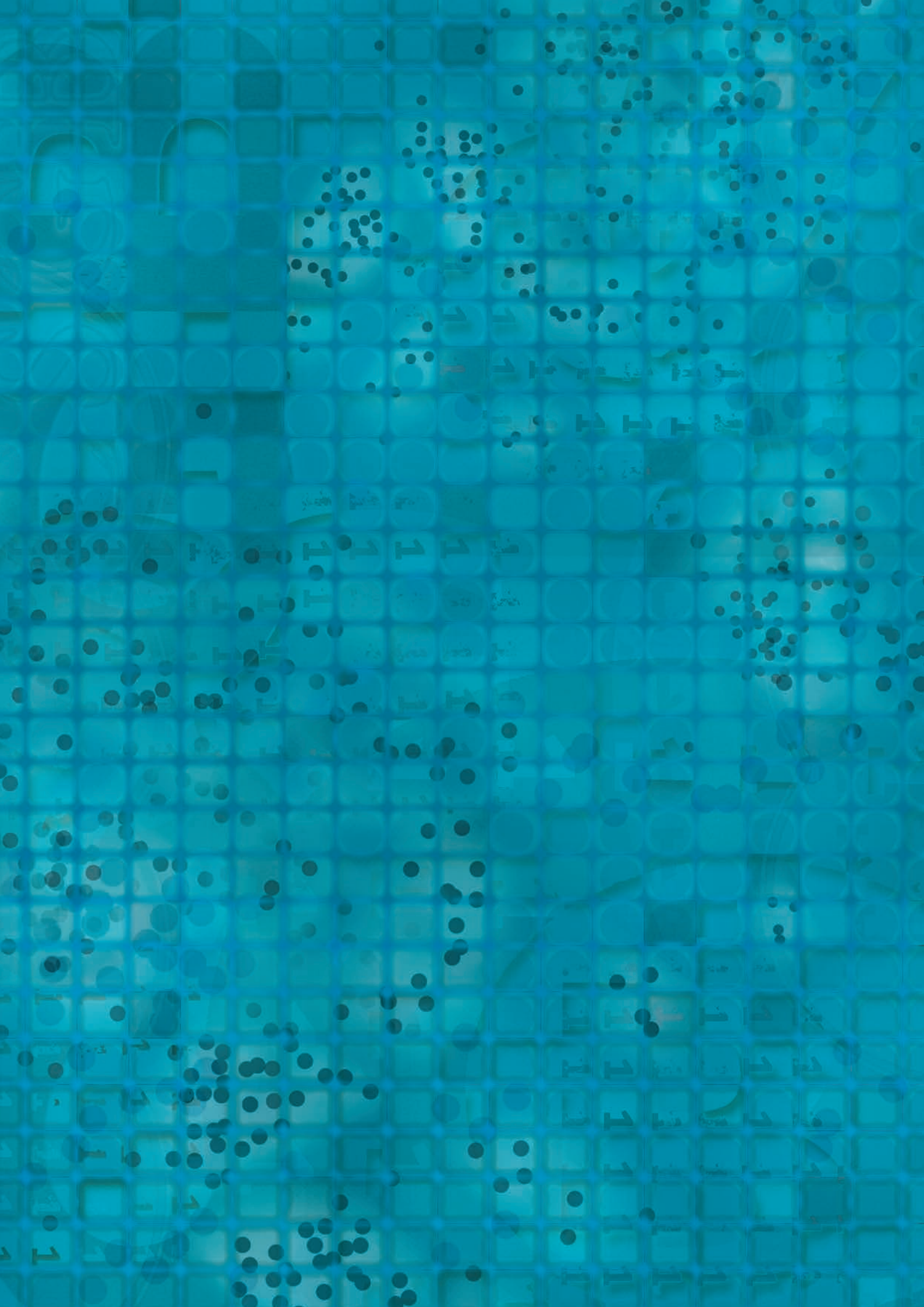
CSGB

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

Annual Report 2013



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Annual Report

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INTRODUCTION

Centre for Stochastic Geometry and Advanced Bioimaging (CSGB) was founded in 2010 as a VKR Centre of Excellence with the generous donation of 25 mill DKK from the Villum Foundation. The main aim of CSGB is to develop new mathematical, statistical and computational methods of analyzing advanced bioimaging data. A particular focus has been on the analysis of molecular microscopy data.

CSGB is an interdisciplinary collaboration between the **stochastic geometry group** at Department of Mathematics, Aarhus University, the **stereology and EM research laboratory**, Aarhus University, the spatial statistics group, Department of Mathematical Sciences, Aalborg University, and the **image group**, Department of Computer Science, University of Copenhagen.

With this annual report, I want to inform our colleagues, potential research students, the Danish funding partner and the Universities of Aarhus, Aalborg and Copenhagen about the research, organizational issues and international centre activities that took place at CSGB in 2013.

Since the establishment of CSGB in 2010, central elements of a theory of rotational integral geometry have been developed. A breakthrough in digital stereology has moved the focus of the research to grey-value images. Advanced statistical inference has been developed for a whole range of models for point processes and random geometric structures in shape spaces. New quantitative bioimaging techniques have been developed by fertile interdisciplinary research collaborations, a long-time investment.

At the same time, we have had the aim that the research should be of the highest quality to either of the disciplines involved in the collaborations. This is reflected in the high impact journals in which CSGB researchers publish, including *Bernoulli, Biometrika, IEEE Transactions on Pattern Analysis and Machine Intelligence, Journal of the American Statistical Association, Journal of Mathematical Imaging and Vision, Molecular Cell*, *Nature Neuroscience* and *Statistical Science*.

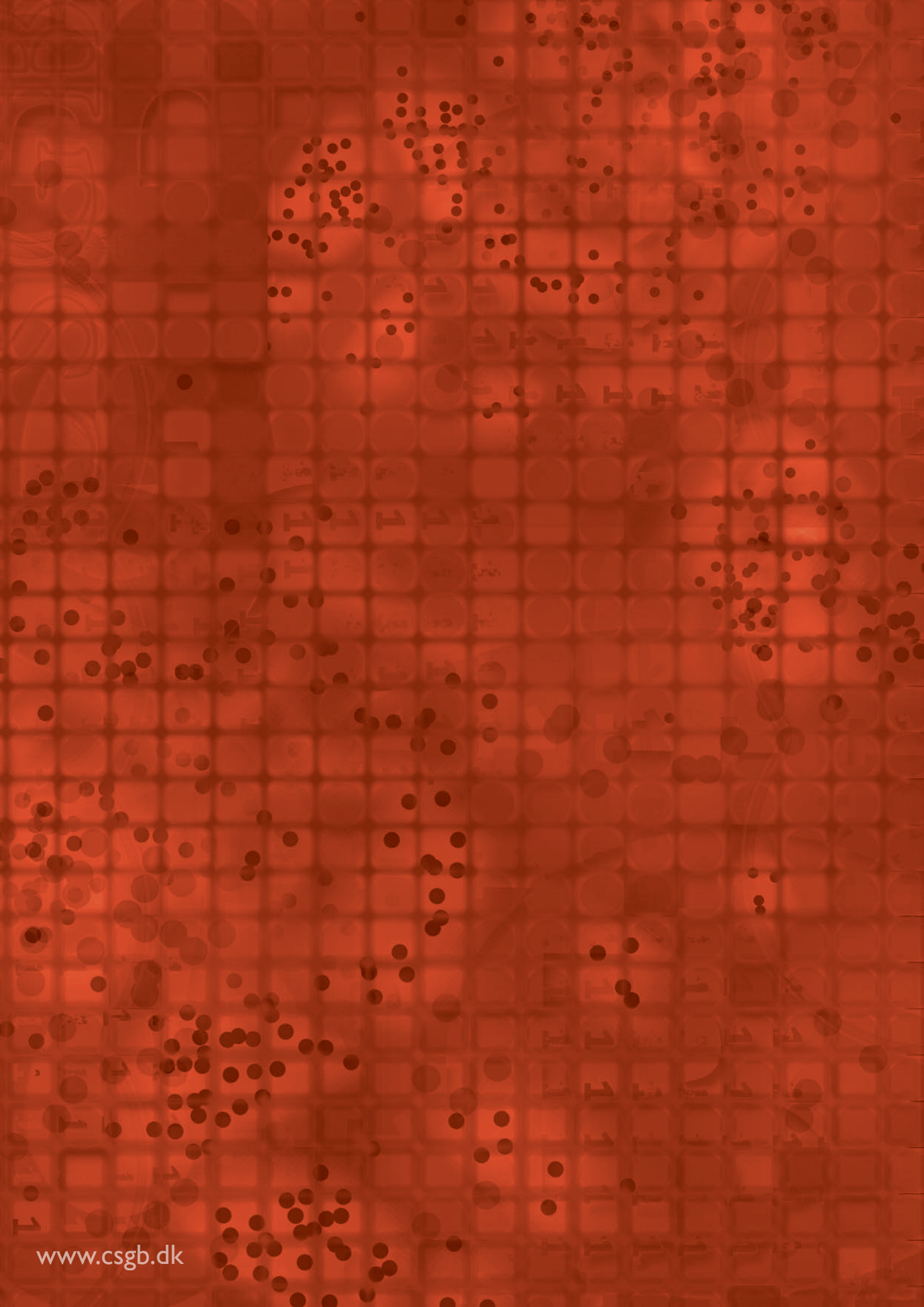
During the Centre period, a lab infrastructure for single-particle electron microscopy has also been built up that facilitates the preparation of multi-protein complexes. The projects running in the lab typically require the culturing of several tens of liters each week, followed by their application to a chain of purification steps involving the lab hardware.

In the beginning of this year, the Deutsche Forschungsgemeinschaft (DFG) granted a second funding period of the Research Unit entitled Geometry and Physics of Spatial Random Systems, for which CSGB is the international partner. Within CSGB, two of our young researchers, **Aasa Feragen** and **Kristjana Jónsdóttir**, have been appointed associate professors. The Rector of Aarhus University awarded in June 2013 Professor **Adrian Baddeley**, University of Western Australia, an honorary Professorship in Statistics at Department of Mathematics, AU. The Faculty of Science, University of Bern, awarded **Eva B. Vedel Jensen** a Doctor philosophiae honoris causa in December 2013.

During 2013, ten international activities were organized or co-organized by CSGB. This includes five international PhD courses which emphasizes the priorities of research training for CSGB. One of these PhD courses was the **Summer School on Topics in Space-Time Modeling and Inference** that took place 27 – 31 May 2013 at Department of Mathematical Sciences, Aalborg University. This summer school was arranged with the purpose to present the newest advances in space-time modeling and inference to an audience of junior researchers with a special interest in spatial statistics. The international lecturers were Professor **Peter J. Diggle** (Lancaster University), Professor **Tilmann Gneiting** (University of Heidelberg) and Professor **Peter F. Craigmile** (University of Glasgow).

March 2014

Eva B. Vedel Jensen



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ORGANIZATION AND STAFF

STAFF

Centre for Stochastic Geometry and Advanced Bioimaging – CSGB – is an interdisciplinary research collaboration between

- the stochastic geometry group, Department of Mathematics, AU
- the biomedical group, Stereology and EM Research Laboratory, AU
- the spatial statistics group, Department of Mathematical Sciences, AAU
- the image group, Department of Computer Science, KU

The four participating research groups are in the following denoted by **AU-math**, **AU-bio**, **AAU** and **KU**, respectively.

Since the establishment of CSGB on 1 April 2010, the four research groups have collaborated on developing new mathematical, statistical and computational methods of analyzing bioimaging data. The theoretical groups **AU-math**, **AAU** and **KU** have all now close bonds to the experimental group **AU-bio**, but have also established mutual collaborations on basic research questions within mathematics, statistics and computer science. In addition, a very active research training programme has been arranged.

The staff consisted in 2013 of 7 professors, 16 associate professors, 8 postdocs and 12 PhD students,
see page 52 – 53 for details.

ORGANIZATION

The research of CSGB is organized along three streams of research, coordinated by senior researchers of the Centre. Each stream contains three research projects; the principal investigator(s) of each research project is (are) indicated in the diagram below.

The projects in the left column are mainly focused on mathematical issues, the middle column on statistical issues and the right column on bioimaging issues. The activities in 2013 within each of these nine research projects are presented on page 22 – 39. A number of the research projects involve the participation of at least two of the four research groups in CSGB. On page 20 – 21, the focus is on these collaborative aspects.

Integral geometry and advanced stereology Eva B. Vedel Jensen Markus Kiderlen	**Statistics of stochastic geometry models** Jesper Møller Jens Ledet Jensen	**Advanced bioimaging** Jens R. Nyengaard Mads Nielsen
Rotational integral geometry Eva B. Vedel Jensen	**Spatial and spatio-temporal point processes** Jesper Møller Rasmus P. Waagepetersen	**Non-uniform sampling** Ute Hahn Jens R. Nyengaard
Digital stereology Markus Kiderlen	**Space-time lattice data** Mads Nielsen Kristjana Jónsdóttir	**Fluorescence microscopy taken to the molecular level** Jens R. Nyengaard Rasmus P. Waagepetersen
Topological properties Andrew du Plessis	**Random shapes** Francois Lauze Mads Nielsen	**Molecular cryo-EM** Monika Golas, François Lauze, Björn Sander

NEWS ABOUT STAFF

Sami Brandt (KU)

Sami Brandt (KU) has started a new appointment in the company 3Shape from 1 March 2014. He will continue to be a member of the image group, KU, as part-time associate professor. Sami has been working in the CSGB team developing new algorithms for reconstruction of macromolecules from **Cryo-EM** data. He has a Doctor of Science degree in computer science from Helsinki University of Technology.

Aasa Feragen (KU)

Aasa Feragen has been appointed associated professor 1 February 2014 at Department of Computer Science, KU. Aasa Feragen received her PhD degree in mathematics from the University of Helsinki in 2010. Her research interests include the mathematical modelling of structured data such as trees and networks, and the development of statistical and machine learning methodology for their analysis. Aasa is mainly working in the CSGB project entitled **Random shapes**.

Stefan Sommer (KU)

Stefan Sommer has been appointed assistant professor 1 June 2013 at Department of Computer Science, KU. Stefan received a master degree in mathematics in 2008 and a PhD degree in computer science in 2011 from University of Copenhagen. His research interests include deformation modelling and statistics of deformations. Stefan has mainly contributed to the research within the CSGB project entitled **Random shapes.**

Sine Flarup Budtz (AU-bio)

Sine Flarup Budtz has been appointed part-time software developer 1 February 2013 at Stereology and EM Research Laboratory, AU. Sine has a master degree in computer science from Aarhus University. One of her main tasks has been to implement the new local stereological techniques for estimating tensors in optical microscopy, using computerized microscopes. This is a subproject of the **Rotational integral geometry** project.

Kristjana Ýr Jónsdóttir (AU-math)

Kristjana Ýr Jónsdóttir has been appointed associate professor 1 September 2013 at Department of Mathematics, AU. Kristjana received her PhD degree in mathematical statistics from Aarhus University in 2006. After the PhD degree, she continued as a postdoc at the MINDLab (UNIK) Centre. Kristjana has mainly contributed to the research within the CSGB project entitled **Space-time lattice data**. Especially important are the results concerning Lévy-based modelling.

NEWS ABOUT STAFF

Honorary professorship in statistics

The Rector of Aarhus University awarded 1 June 2013 **Professor Adrian Baddeley,** University of Western Australia, an honorary Professorship in Statistics at Department of Mathematics, AU. With this title, Aarhus University wished to honour Adrian Baddeley as an internationally highly estimated researcher.

Adrian Baddeley is a **close collaborator** of a number of scientists at CSGB. Together with Eva B. Vedel Jensen, he has written a monograph entitled Stereology for Statisticians in the Chapman & Hall series on Statistics and Applied Probability. Right now he is working on a Springer R-book entitled **Analysing spatial point patterns in R** where CSGB researcher Ege Rubak is among the co-authors.

The **honorary professorship** is in recognition of this fruitful and constructive collaboration.

Symposium in honour of Adrian Baddeley
7 – 8 November 2013, Aarhus

To celebrate, a symposium in honour of Adrian Baddeley was arranged 7 - 8 November 2013. As part of the symposium, Adrian Baddeley gave an inaugural lecture 7 November at 2 p.m. The focus of the symposium was on spatial point processes.

The invited speakers included:

- **Jean-Francois Coeurjolly** (Laboratoire Jean Kuntzmann, Grenoble)
- **David Dereudre** (Laboratoire Paul Painlevé, Lille)
- **Frédéric Lavancier** (Université de Nantes)
- **Tomás Mrkvicka** (University of South Bohemia)
- **Mari Myllymäki** (Aalto University)
- **Ege Rubak** (Aalborg University)
- **Aila Särkkä** (Chalmers University of Technology, Gothenburg)
- **Marie-Colette van Lieshout** (CWI Amsterdam)
- **Sergei Zuyev** (Chalmers University of Technology, Gothenburg)

SPECIAL ISSUE OF JMIV

Papers for a special issue of **Journal of Mathematical Imaging and Vision** (JMIV), entitled Geometry and Statistics: Manifolds and Stratified Spaces, have been collected during 2013. The special issue is aimed as an overview of current results and problems from **geometry and statistics of nonlinear data spaces**, to serve as a coherent source of information for the broader statistics and imaging communities. The editors of this issue are Andrew du Plessis, Eva B. Vedel, Aasa Feragen, Mads Nielsen and Francois Lauze.

Manifolds and stratified spaces are large families of nonlinear geometric spaces, used for mathematical modelling of real data. When the data is modelled in such spaces, standard operations such as interpolation, averaging, principal components or hypothesis testing are no longer straightforward or even neccessarily well-defined. This special issue aims to capture the **state-of-the-art in statistics on manifolds and stratified spaces**, drawing on scientific communities as diverse as mathematical statistics, geometry, image analysis and computational biology.

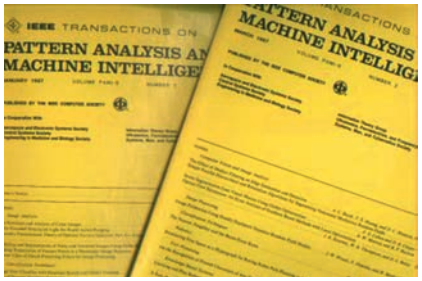
Many of the contributions to this special JMIV issue are based on lectures given at the CSGB workshop held 8 – 12 October 2012 at Sandbjerg Estate. A number of activities have taken place in this community, as a spin-off of the **Sandbjerg workshop**:

- In September 2014, Aasa Feragen is co-organizing an Oberwolfach mini-workshop on Stratified Statistics together with Steve Marron (University of North Carolina, Chapel Hill), Ezra Miller (Duke) and Stephan Huckemann (University of Göttingen)
- Stefan Sommer has been visiting Xavier Pennec, INRIA, for one month in January 2014
- For the academic year of 2013/14, Sarang Joshi is visiting professor at the image group
- Nicholas Chabron has been attracted to the image group as postdoc, partly funded by CSGB
- An agreement to make a biannual follow up as a MICCAI workshop on the Mathematical Foundation of Computational Anatomy
- Aasa Feragen has visited several participants of the workshop for shorter research visits

HIGHLIGHTS

Two papers have been published by members of the image group, KU, in one of the absolute best journals (2011 journal impact factor is 4.9). The papers represent the cornerstone in the development of numerical methods for non-rigid registration based on mutual information, and the construction of a metric space of geometric trees, both topics being part of the CSGB project **Random shapes**.

- Darkner, S. & Sporring, J. (2013): Locally orderless registration. *IEEE Transactions on Pattern Analysis and Machine Intelligence* **35**, 1437-1450.
- Feragen, A., Lo, P.C.P., de Bruijne, M., Nielsen, M. & Lauze, F. (2013): Toward a theory of statistical tree-shape analysis. *IEEE Transactions on Pattern Analysis and Machine Intelligence* **35**, 2008-2021.



One of the papers on multivariate point process modelling, written jointly by Rasmus Waagepetersen (AAU) and Y. Guan (University of Miami) among others, has in 2013 been published in the prestigious Journal of the American Statistical Association. The research is part of the CSGB project **Spatial and spatio-temporal point processes**.

- Huang, H., Ma, X., Waagepetersen, R., Holford, T., Wang, R., Risch, H., Mueller, L. & Guan, Y. (2013): A new estimation approach for combining epidemiological data from multiple sources. *J. Amer. Statist. Assoc.* **94**, 2436-2443.

INTERNATIONAL COLLABORATION

CSGB is the international research partner of the Research Unit entitled **Geometry and Physics of Spatial Random Systems**, supported by the Deutsche Forschungsgemeinschaft (DFG). The German nodes are the stochastic geometry group (led by Günter Last), Department of Mathematics, Karlsruhe Institute of Technology, and the theoretical physics group (led by professor Klaus Mecke), Institute for Theoretical Physics, Friedrich-Alexander-Universität. In 2013, an internal GPSRS workshop was arranged 8 – 10 April in Aarhus. This workshop was followed by an international conference on geometry and physics of spatial random systems, arranged by the Research Unit in Freudenstadt (Black Forest) 9 – 13 September 2013, see the group photo. This interdisciplinary workshop had about 80 participants mainly from mathematics, physics and statistics. In December 2013, a midterm evaluation of the Research Unit was performed by an international committee. On the basis of a very positive review, DFG has granted a second funding period of the Research Unit.

HONOURS

The Faculty of Science, University of Bern, has awarded **Eva B. Vedel Jensen** a Doctor philosophiae honoris causa. This high-level academic recognition granted by the University of Bern was marked by a graduation ceremony on Saturday 7 December 2013.

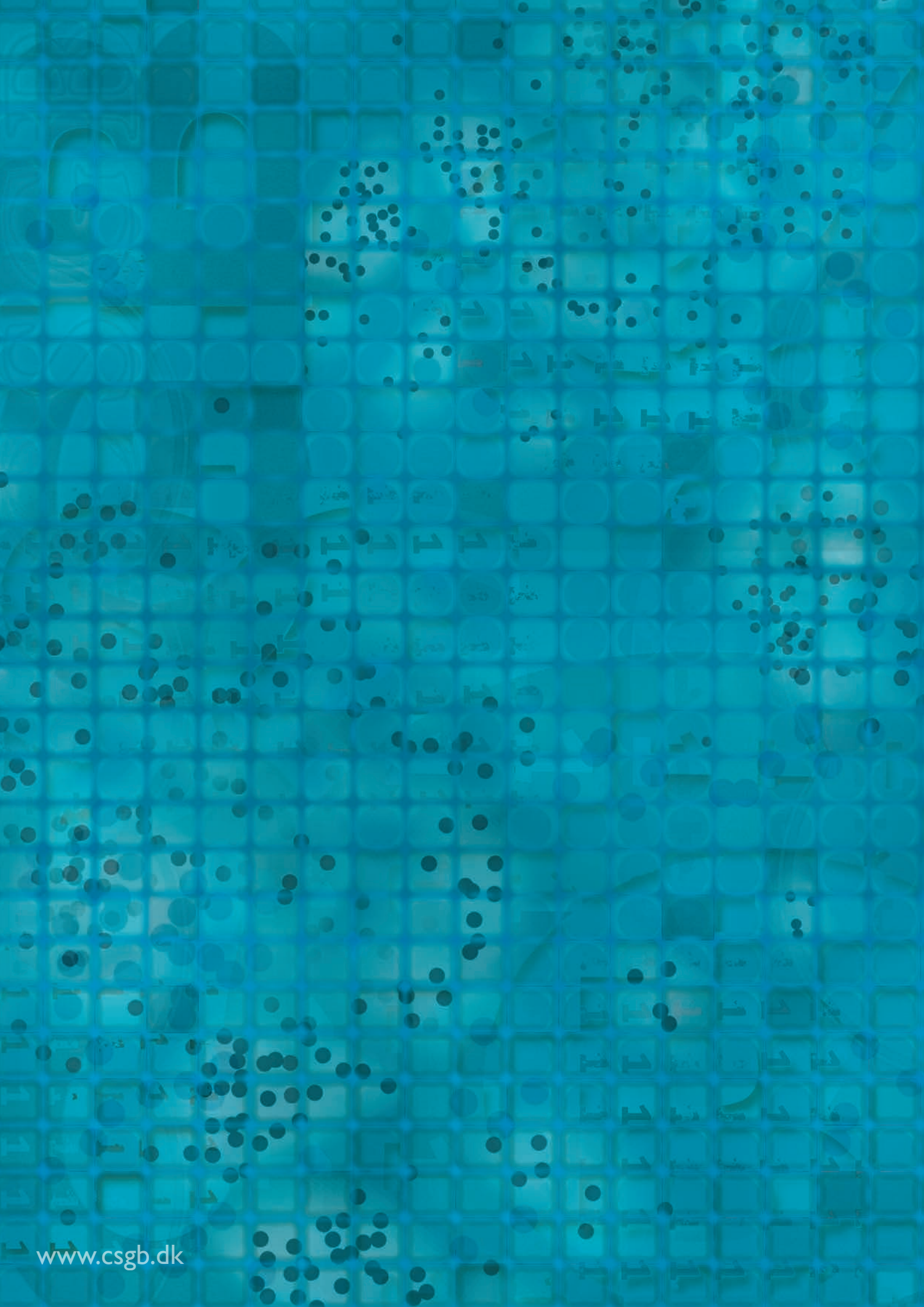
The established relationship with University of Bern goes back to the nineteen-eighties where Eva B. Vedel Jensen attended an international stochastic geometry workshop in Bern, organized by Professor of Anatomy Ewald R. Weibel and Professor of Statistics Luis M. Cruz-Orive. This workshop became very important for the further development of the field of stereology and stochastic geometry. The close connection to Institute of Anatomy, Bern, is nowadays via the Microscopy Imaging Center (MIC). Eva B. Vedel Jensen has also an established scientific relationship to Department of Mathematics and Statistics, Bern, especially with Professor **Ilya Molchanov** and Professor **Johanna F. Ziegel**.

AWARDS

Information Processing in Medical Imaging (IPMI) is a very competitive biannual conference where the oral papers have unlimited discussion time. The Francois Erbsmann prize is thus one of the most prestigious prizes in medical image analysis, and is handed out every second year to a young researcher presenting at the podium of IPMI.

At IPMI 2013, **Aasa Feragen** (KU) was runner-up for the Erbsmann prize for her presentation of the paper *Tree-space statistics and approximations for large-scale analysis of anatomical trees*. The paper is written jointly with Megan Owen, Jens Petersen, Mathilde M.W. Wille, Laura H. Thomsen, Asger Dirksen and Marleen de Bruijne.

Jon Sporring (KU) was second author on the paper receiving the Erbsmann prize at IPMI 2013 with the presesentation by Herve Lombaert of the paper entitled *Diffeomorphic spectral matching of cortical surfaces*. The third author of the paper is Kaleem Siddiqi (McGill University).



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RESEARCH

RESEARCH HIGHLIGHTS

Below, research highlights obtained since the establishment of CSGB in 2010 is presented. A more detailed description of research results obtained in 2013 may be found on page 22 – 39. For earlier results, the reader is referred to CSGB Annual Reports 2010, 2011 and 2012.

Since the establishment of CSGB in 2010, central elements of a theory of **rotational integral geometry**, dual to the theory of translative integral geometry, has been developed for Minkowski tensors. Most importantly, a genuine rotational Crofton formula for integrated Minkowski tensors has been derived (Auneau-Cognacq et al., 2013). This theory makes it possible to go beyond classical global analysis of a biostructure that often leaves subtle changes in the spatial arrangement of the structure unnoticed. The new theoretical results have been used to develop flexible local methods of describing cell position, cell orientation and cell shape (Jensen & Ziegel, 2014). See Thórisdóttir & Kiderlen (2013) for a treatment of the classical Wicksell's problem in a local setting.

During the first funding period of CSGB, it was a breakthrough in **digital stereology** when we managed to extend a first-order asymptotic formula for configuration counts to a second-order expansion. This important result has been used in Svane (2014a) to show that in dimensions two or higher there exists no local multigrid convergent algorithm on the family of convex polytopes for estimating intrinsic volumes, except in the special case of ordinary volume. This result emphasizes the importance of considering algorithms that use the additional information in grey-valued images stringently (Svane, 2014b). Further advances may be found in Ziegel *et al.* (2011) and Kampf & Kiderlen (2013)

Statistical inference has been developed for a whole range of **point process models**, the fundamental building blocks of most stochastic geometry models. Examples are Baddeley et al. (2011, 2013), Couerjolly et al. (2012), Lavancier et al. (2012), Jalilian et al. (2013) and Huang et al. (2013). For inhomogeneous point processes, statistical methods of distinguishing various ways of inhomogeneity have been established, see also Hahn (2012). Statistical inference on **shape spaces** has been developed in a series of papers. Cornerstones are here numerical methods for non-rigid registration based on mutual information, construction of a metric space of geometric trees and statistical analysis in curved spaces by exact geodesic analysis (Darkner & Sporring, 2013; Feragen *et al.*; 2013a, b; Sommer *et al.*, 2013a, b).

During the Centre period, stochastic geometry models have been introduced for modelling of various microscopy and, more generally, bioimaging data. Point process models have thus been used in the analysis of spatial arrangements of cells relating to minicolumns and protein interactions, see the description of the collaborative projects under the heading point processes on page 21.

New quantitative microscopy techniques have been developed as collaborative projects (Stark et al., 2011; Rasmusson et al., 2013). Another concrete example is given under the heading **non-uniform sampling** on page 20. New stochastic geometry models and methods of analysis has been developed for advanced microscopy experiments that give access to the molecular level, including laser scanning microscopy and cryo-EM, see the description of the collaborative projects **fluorescence microscopy taken to the molecular level** and **molecular cryo-EM** on page 20 and 21, respectively.

PUBLICATION HIGHLIGHTS

Auneau-Cognacq, J., Ziegel, J. and Jensen, E.B.V. (2013): Rotational integral geometry of tensors valuations. *Adv. Appl. Math.* **50**, 429-444.

Baddeley, A.J., Coeurjolly, J.-F., Rubak, E. & Waagepetersen R. (2013): A logistic regression estimating function for Gibbs point processes. *CSGB Research Report* **13-02**. To appear in *Biometrika*.

Baddeley, A., Rubak, E. & Møller, J. (2011): Score, pseudo-score and residual diagnostics for goodness-of-fit of spatial point process models. *Statist. Sci.* **26**, 613-646.

Couerjolly, J.-F. & Møller, J. (2012): Variational approach for spatial point process intensity estimation. *CSGB Research Reports* **12-09**. To appear in *Bernoulli*.

Darkner, S. & Sporring, J. (2013): Locally orderless registration. *IEEE Transactions on Pattern Analysis and Machine Intelligence* **35**, 1437-1450.

Feragen, A., Lo, P.C.P., de Bruijne, M., Nielsen, M. & Lauze, F. (2013a): Toward a theory of statistical tree-shape analysis. *IEEE Transactions on Pattern Analysis and Machine Intelligence* **35**, 2008-2021.

Feragen, A., Owen, M., Petersen, J., Wille, M.M.W., Thomsen, L.H., Dirksen, A. & de Bruijne, M. (2013b): Tree-space statistics and approximations for large-scale analysis of anatomical trees. *23rd International Conference on Information Processing in Medical Imaging (IPMI 2013). LNCS* **7917**, 74-85.

Golas, M.M.*, Sander, B.*, Bessonov, S., Grote M., Wolf, E., Kastner, B., Stark, H. & Lührmann, R. (2010): 3D cryo-EM structure of an active step I spliceosome and localization of its catalytic core. *Molecular Cell* **40**, 927-938.

Hahn, U. (2012): A studentized permutation test for comparison of spatial point patterns. *J. Amer. Statist. Assoc.* **107**, 754-764.

Huang, H., Ma, X., Waagepetersen, R., Holford, T., Wang, R., Risch, H., Mueller, L. & Guan, Y. (2013): A new estimation approach for combining epidemiological data from multiple sources. *J. Amer. Statist. Assoc.* **94**, 2436-2443.

Jalilian, A., Guan, Y. & Waagepetersen, R. (2013): Decomposition of variance for spatial Cox processes. *Scand. J. Statist.* **40**, 119-137.

Jensen, E.B.V. and Ziegel, J.F. (2014): Local stereology of tensors of convex bodies. *Methodol. Comput. Appl. Prob.*, in press.

Kampf, J. & Kiderlen, M. (2013): Large parallel volumes of finite and compact sets in *d*-dimensional Euclidean space. *Documenta Math.* **18**, 275-295.

Lavancier, F., Møller, J. & Rubak, E. (2012): Statistical aspects of determinantal point processes. *CSGB Research Reports* **12-04**, submitted.

Rasmusson, A., Hahn, U., Larsen, J.O., Gundersen, H.J.G., Jensen, E.B.V. & Nyengaard, J.R. (2013): The spatial rotator. *J. Microsc.* **250**, 88-100.

Sommer, S., Lauze, F., Nielsen, M. & Pennec, X. (2013a): Sparse multi-scale diffeomorphic registration: the kernel bundle framework. *J. Math. Imaging Vis.* **46**, 292-308.

Sommer, S., Nielsen, M., Darkner, S. & Pennec, X. (2013b): Higher-order momentum distributions and locally affine LDDMM registration. *SIAM Journal on Imaging Sciences* **6**, 341-367.

Stark, A.K., Gundersen, H.J.G., Gardi, J.E., Pakkenberg, B. & Hahn, U. (2011): The saucor, a new stereological tool for analysing the spatial distributions of cells, exemplified by human neocortical neurons and glial cells. *J. Microsc.* **242**, 132-147.

Svane, A.M. (2014a): On multigrid convergence of local algorithms for intrinsic volumes. *J. Math. Imaging Vis.* **49**, 148-172.

Svane, A.M. (2014b): Estimation of intrinsic volumes from digital grey-scale images. *J. Math. Imaging Vis.* **49**, to appear.

Thórisdóttir, Ó. & Kiderlen, M. (2013): Wicksell's problem in local stereology. *Adv. Appl. Probab.* **45**, 925-944.

Ziegel, J., Jensen, E.B.V. & Dorph-Petersen, K.-A. (2011): Variance estimation for generalized Cavalieri estimators. *Biometrika* **98**, 187-198.

COLLABORATIVE PROJECTS

When developing the research plan of CSGB during 2009, it was realized that a number of the planned research projects required the participation of at least two of the four research groups. The diagramme to the right shows the actual structure of the collaboration as it has evolved during the four year period, since the start of CSGB. Compared to the original digramme, only one project, Digital stereology, has remained a pure AU-math project. The other collaborative projects have been established, sometimes with a changed or extended combination of collaborative partners.

Below, we present some of the results obtained in these collaborative projects.

Random fields

A close collaboration between the AU and KU groups within the collaborative project **random fields** has resulted in a new statistical method of estimating the thickness of ultra thin sections obtained by transmission electron microscopy, see Sporring *et al.* (2014). After correction for intensity inhomogeneity, it is feasible to assume that the pixel values are realizations from a 3D stationary and isotropic random field $F = \{F(x_{ijk})\}$. The unknown distance in the z-direction is estimated, by combining a detailed statistical analysis of the random field with the knowledge of the distance between grid points in the x- and y-directions. This project is part of a larger investigation of the spatial distribution of synaptic vesicles.

Sporring, J., Khanmohammadi, M., Darkner, S., Nava, N., Nyengaard, J.R. & Jensen, E.B.V. (2014): Estimating the thickness of ultra thin sections for electron microscopy by image statistics. To appear in the *Proceedings of the 2014 IEEE International Symposium on Biomedical Imaging*, Beijing, 29 April – 2 May 2014.

Fluorescence microscopy

A new approach to the analysis of Förster resonance energy transfer (FRET) microscopy data, involving a detailed modelling of the measurement noise, has been developed in the collaborative project entitled **fluorescence microscopy taken to the molecular level**, see Jensen *et al.* (2012). The focus has been on the possibility of estimating from single cells the equilibrium dissociation constant K_d, a measure of the average protein-protein interaction strength. Estimation of the intrinsic FRET efficiency E_m, a measure of the average donor-acceptor distance, has also been considered. In Jensen *et al.* (2012), it is demonstrated for a population of cells that the intercellular variability in the estimates of K_d (and E_m) cannot be explained by the measurement noise.

Hooghoudt, J.-O. & Waagepetersen, R.P. (2014): A Bayesian approach to inferring the spatial distribution of intracellular proteins from fluorescence resonance energy transfer data. In preparation.

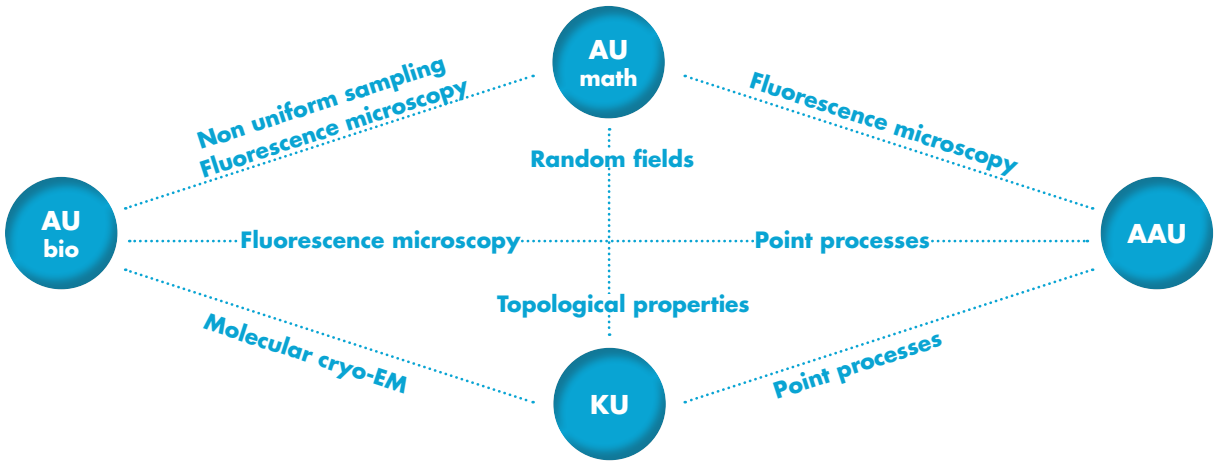
Jensen, J.L., Raarup, M.K. & Rubak, E. (2012): Estimating protein-protein interaction affinity in single living cells using Förster resonance energy transfer measurements. *CSGB Research Report* **12-12**. Submitted.

Non uniform sampling

The collaborative project on **non-uniform sampling** has resulted in new quantitative microscopy techniques (Andersen *et al.*, 2014). The starting point of the investigations has been the use of PPS sampling in microscopy where vanishing auxiliary variables are a common phenomenon, see Keller *et al.* (2013). Since PPS sampling requires positive auxiliary variables, it has earlier been suggested in the microscopy literature to add a small positive constant ε to the auxiliary variables. Then, all sampling units become accessible by PPS sampling, but, depending on the choice of ε, this procedure may lead to extremely large estimator variances. In Andersen *et al.* (2014), optimal ways of choosing ε are established.

Andersen, I.T., Hahn, U. & Jensen, E.B.V. (2014): Vanishing auxiliary variables in PPS sampling – with applications to microscopy. *CSGB Research Report* **14-01**. Submitted.

Keller, K.K., Andersen, I.T., Andersen, J.B., Hahn, U., Stengaard-Pedersen, K., Hauge, E.M. & Nyengaard, J.R. (2013): Improving efficiency in stereology: a study applying the proportionator and the autodisector on virtual slides. *J. Microsc.* **251**, 68-76.



Molecular cryo-EM

In single-particle **electron cryo-microscopy** (cryo-EM), the goal is to estimate the three-dimensional structure of a macromolecular complex from randomly oriented projection images with very low SNR. For the angular reconstitution, we have investigated the uncalibrated, affine projection geometry between two views without point correspondences and derived the relation between the common lines and epipolar geometry (Brandt *et al.*, 2012). The two-view estimates are used for estimating the N-view geometry, which is intended to initialize the reconstruction problem. We have proposed a sound statistical reconstruction algorithm, based on maximum a posteriori (MAP) estimation of the particle structure from the marginal posterior (Brandt *et al.*, 2013).

Brandt, S.S., Jensen, K.H. & Lauze, F.B. (2012): Bayesian epipolar geometry estimation from tomographic projections. *11th Asian Conference on Computer Vision*, South Korea, 231-242.

Brandt, S.S., Jensen, K.H. & Lauze, F.B. (2013): On the Bayesian reconstruction method for randomly oriented particles in cryo-EM. *10th International Symposium on Biomedical Imaging*, San Francisco, CA, pp. 1166-1169.

Topological properties

In a collaborative project, concerning extraction of **topological properties** in Diffusion Weighted Imaging (DWI), mathematical methods for analysis of brain connectivity through DWI is under development. Two different approaches have been considered: (1) model-free biomarkers for disease prediction and (2) graph-based methods for extracting brain connectivity networks (Liptrot & Lauze, 2014; Kasenburg et al., 2014). This forms the basis for several future research projects, including model-free learning of texture-like biomarkers for DWI and a mathematical framework for multiscale analysis of DWI texture, and stratified statistics for voxel-based multi-tensor morphology and visualization.

Kasenburg, N., Liptrot, M., Borgwardt, K.M., Ørting, S.N., Nielsen, M. & Feragen, A. (2014): Graph-based fibre tractography computing shortest paths between regions of interest. Extended abstract at ISMRM 2014.

Liptrot, M. & Lauze, F. (2014): A model-free unsupervised method to cluster brain tissue directly from DWI volumes. Extended abstract at ISMRM 2014.

Point processes

Point processes have been used in the study of spatial arrangement in collaborative projects, concerning the minicolumn hypothesis (Rafati *et al.*, 2014) and protein interactions (Hooghoudt & Waagepetersen, 2014). Various statistical methods for testing the existence of minicolumns in three-dimensional point patterns consisting of cell centers have been developed. The new methods are based on nearest neighbour distances, anisotropic summary statistics and Delaunay tessellations. The application relating to protein interactions is described on pages 36 – 37.

Hooghoudt, J.-O. & Waagepetersen, R.P. (2014): A Bayesian approach to inferring the spatial distribution of intracellular proteins from fluorescence resonance energy transfer data. In preparation.

Rafati, A.H., Safavimanesh, F., Dorph-Petersen, K.-A., Rasmussen, J.G., Møller, J., & Nyengaard, J.R. (2014): The degree of columnarity: An index for spatial quantification of minicolumns in cerebrel cortex. In preparation.

ROTATIONAL INTEGRAL GEOMETRY

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In 2013, our research in rotational integral geometry has been focused on the invariator principle in convex geometry. Furthermore, a new surface area estimator valid for non-convex particles and based on measurements in central planar sections has been developed and implemented in optical microscopy.

The invariator principle (Cruz-Orive, 2005) is a measure decomposition that was rediscovered in local stereology in 2005 and has since then been used widely in stereology. Using this principle, it is possible to generate a motion invariant line in 3D via an isotropic plane passing through a fixed point. This possibility opens up for a wide range of new measurement techniques in **optical microscopy**, relating especially to particle surface area estimation. In Thórisdóttir & Kiderlen (2013), an exposition of invariator results are given where existing formulae are generalized and new ones proposed. In particular, new rotational Crofton-type formulae are obtained for support measures by combining the invariator principle and classical Crofton formulae.

The work presented in Thórisdóttir & Kiderlen (2013) includes natural generalizations that apparently have not been treated in the literature yet. The major new contribution is to combine the invariator and concepts from **Morse theory** for obtaining a new and more explicit rotational Crofton formula. What is different and appealing with this new formula is that the measurement functional on the section of the object may be written entirely in terms of so-called critical values and their indices.

In Thórisdóttir *et al.* (2013), these results are used to construct a new stereological estimator of surface area from central planar sections that is valid for non-convex particles. The estimator is called the **Morse type surface area estimator**. The estimator is based on a two-stage sampling procedure. For each sampled particle, an optical section through a fixed reference point of the particle is generated. In this section, a modification of the area tangent count by DeHoff (1967) is used.

For a given section profile and a given direction in the section plane, a sweeping line is used and all tangents to the section profile are recorded, together with their type (if they represent a positive or a negative tangent) and their distance to the origin. We call the distance of a tangent from the origin a **critical value** and the type an **index**. See Figure 1 for an illustration. The new estimator can be written entirely in terms of these indices and critical values.

The Morse type estimator generalizes Cruz-Orive's pivotal estimator of surface area for convex particles (Cruz-Orive, 2005, 2011) to non-convex particles. The estimator is well suited for computer assisted confocal microscopy. Interactive software has been developed that allows the user to efficiently obtain the estimator. An application is shown in Figure 2. A detailed study of the efficiency of the Morse type surface area estimator may also be found in Thórisdóttir *et al.* (2013). The various profile shapes considered in the simulation study is shown in Figure 3.

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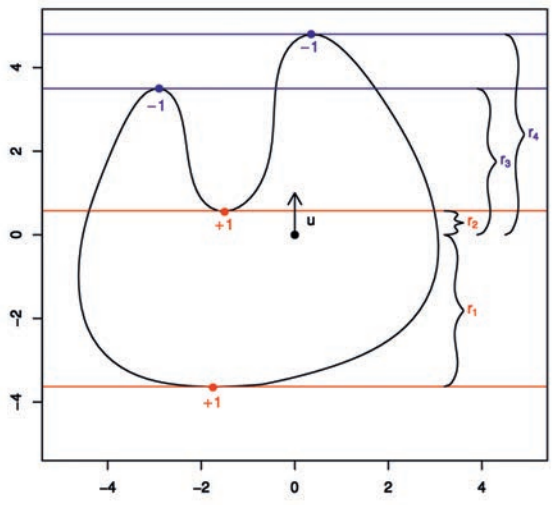


Figure 1: Critical levels and indices for a given direction u in a section profile. Positive tangents are colored red while negative tangents are colored blue.

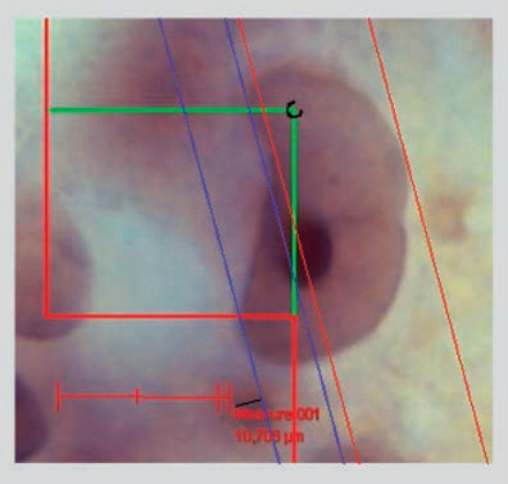
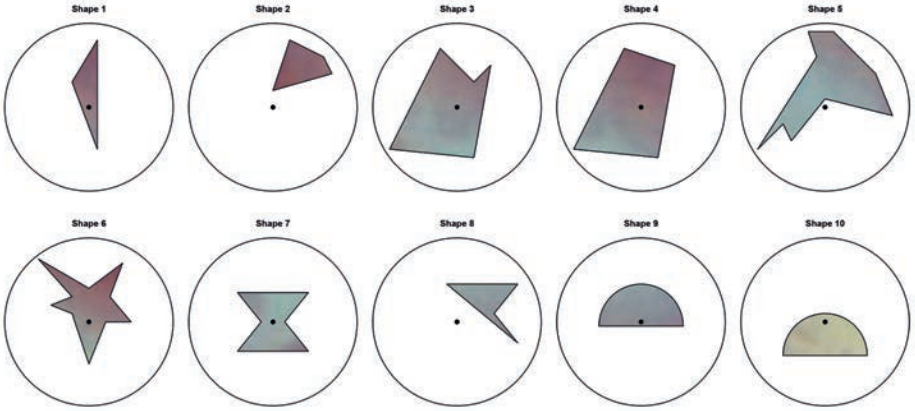


Figure 2: An illustration of the expert-assisted procedure on one section profile through a nucleolus of the nucleus of a giant-cell glioblastoma.

Figure 3: Polygons and half-circles.



DIGITAL STEREOLOGY

Modern stereology makes increasingly use of semi-automized or automized image analysis to reduce the workload needed for the quantitative analysis of biological samples.

In Dvorák & Jensen (2013), we investigated local surface area estimators of objects from sections with isotropic test planes. We could show there, that supervised automatic - and hence fast - segmentations of the section profile of the object can be used to obtain stable estimators. Another example are the fundamental stereological formulae, which require the measurement of intrinsic volumes such as area, boundary length or Euler-Poincaré characteristic of planar sections of the object. In digital stereology, we examine if these quantities can be derived in a reliable way from digital images of the profiles.

Popular algorithms to determine intrinsic volumes of an object in n-dimensional space from **black & white digital images** are based on counts of the numbers of occurrences of $k \times k \times \cdots \times k$ configurations. There are 2^{k^n} configurations, i.e. possibilities to colour the k^n pixels of a cube with a side length of k pixels. The intrinsic volumes are then estimated by linear combinations of the configuration counts. Implementations are extremely fast and simple, as the estimators are only relying on local information and can be calculated by filtering the image in linear time, see Ohser & Mücklich (2000).

Clearly, such local algorithms are biased when the resolution is finite, but it was unknown if they yield the correct result asymptotically, that is, when the resolution tends to infinity. In Svane (2013a), it is shown that **all local algorithms** for any of the intrinsic volumes other that the ordinary volume are asymptotically biased. For the special case of surface area measure in 2D and 3D this was already conjectured by Kenmochi & Klette (2000).

For this very strong result, **convex polytopes** can be used **as counterexamples**. Roughly speaking, $k \times k \times \cdots \times k$ configurations are only able to capture a finite number of slopes of the sides of the polytopes, and therefore even 'almost all' polytopes are counterexamples (under some technical restrictions and with a suitable natural measure on the family of convex polytopes). Although the bias may be acceptable in some applications - the best surface area estimator in 3D based on $2 \times 2 \times 2$ configurations has an asymptotic worst case error of 4.7% - this result shows the need for improved digital algorithms.

The above algorithms for black & white images are often applied to **thresholded grey-value images**, thus disregarding a large amount of image information. This observation led us to investigate local algorithms defined directly for grey-value images. We adopted the two-step grey-value digitization model from Stelldinger & Köthe (2006), where the exact continuous object is first blurred by the camera objective and subsequently the blurred object is digitized, see Figure 1. The first step is modelled mathematically by a convolution with a rotationally symmetric point spread function (PSF).

Using the full grey-value information, we showed in Svane (2013b) that **asymptotically unbiased local algorithms** for surface area and the integral of mean curvature exist. In the light of the negative results for black & white images this is quite remarkable. Both algorithms work with $k = 1$, meaning that no neighborhood relations are required here. For instance, for any $0 < \beta < \frac{1}{2}$ the number of pixels with grey values in the interval $[\frac{1}{2} - \beta, \frac{1}{2} + \beta]$ is up to a known normalization an asymptotically unbiased estimator of the surface area of the object. A 2D illustration is given in Figure 2.

For the first time, our work establishes non-trivial examples of asymptotically unbiased local algorithms for intrinsic volumes. To assess the reliability of these algorithms, we are currently investigating their asymptotic variance by generalizing the Kendall-Matheron variance formula for systematic sampling to our setting.

Figure 1: The grey-value digitization model: the original object (left), the blurred object after convolution with a Gaussian PSF (middle), and its subsequent digitization (right).

Researchers

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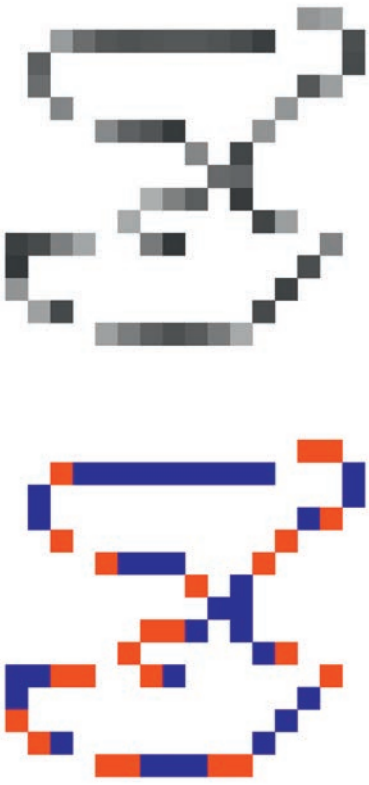

Figure 2: The pixels with grey-value in the interval [0.25,0.75]. Their number is, up to a factor, an asymptotically unbiased estimator of the perimeter of the underlying set (upper). Lower: If the same pixels are counted, but positive (blue) when the grey-value is below 0.5, and negative (red) otherwise, an asymptotically unbiased estimator of the Euler-Poincaré characteristic can be obtained.

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TOPOLOGY AND DIGITAL IMAGE ANALYSIS

It is crucial for the analysis of microscopy results that the interplay between objects in the real world and their digital representations is well understood. In the previous project Digital stereology the aim is to estimate quantitative characteristics of planar or spatial objects, such as volume, surface area, integral of mean curvature and Euler-Poincaré characteristic. In this project, we aim at reconstructing the full differential-geometric structure of the boundary of the object.

2-D reconstruction
Given an object in two dimensions with a smooth boundary, any digitization of sufficiently high resolution of the object preserves its topology; the required resolution is related to the curvature of the boundary, see Figure 1. This is in particular true for digitizations based on **pixel** and **cellular approximations**, see Pavlidas (1982). (The pixel approximation is the union of pixels with centre point in the object while the cellular approximation is the union of pixels with all vertices lying in the object.) However, reconstructing the differential-geometric structure of the object, and in particular of its boundary, is substantially more difficult, even at high resolutions.

A new approach to this question has had considerable success. The basis of the new approach is that advances in digital imaging imply that a pixel represents rather faithfully the light intensity falling on the whole of the corresponding lattice square in the sensor, rather than just being a sampling of it. This leads to new methods of **boundary reconstruction** based both on differential-geometric and integral-geometric considerations. The new methods are based on information from a **digital grey-value image** which to each point p in a lattice associates the areal fraction of the object inside the lattice square centred at the point p (du Plessis, 2014). In practice, these methods work well for objects with boundaries smooth enough to guarantee that the topology of the object is captured. The result is a smooth reconstruction of the object whose area in each lattice square is as good an approximation to the corresponding area of the original object as the accuracy of the image modality in question permits.

3-D reconstruction
Given an object in three dimensions with a smooth boundary, many reconstructions of digitizations of sufficiently high resolution of the object preserve its topology; the required resolution is again related to the curvature of the boundary. This is a fairly recent result Stelldinger *et al.* (2007), and is much more difficult to establish than the corresponding statement in two dimensions, see above.

In a close collaboration between CSGB researchers Andrew du Plessis and Sabrina Tang Christensen, work has begun towards adapting the new methods described above for the two-dimensional case to the three-dimensional case. The mathematical difficulties are considerable, since both the differential geometry of the boundary surface and the **combinatorics** of its relation to the lattice structure are **very much more complicated** than in the two-dimensional case. One of the difficulties we encounter when trying to generalize the work done in dimension two lies in the construction of a vector field on the digitization of the three-dimensional body, see Figure 2. Where the two-dimensional construction involves few special cases, they come in abundances in dimension three due to the many types of vertices that arise here. In fact, determining the possible vertices poses a challenge in itself. To begin with, at least, it will probably be necessary to assume high resolution; so that, for example, the often-used method of marching cubes can be adapted to give a sufficiently good first approximation to a reconstruction to allow the differential- and integral-geometric ideas used in two dimensions to be brought into play.

Researchers

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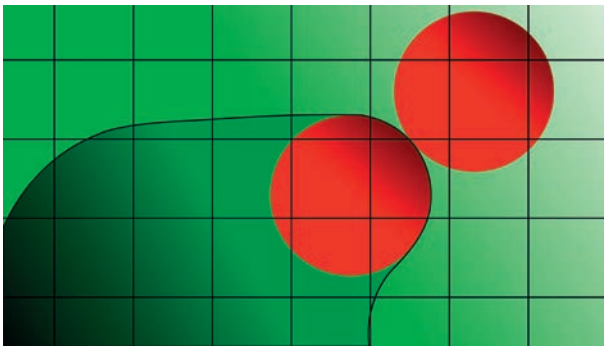

Figure 1:
A digitization of the dark green body is obtained, based on the pixels represented by the black grid. The resolution of the digitization corresponds to the side length of the pixels. For preservation of topology, the side length must not exceed the radius of regularity (the radius of the two red balls) of the body.

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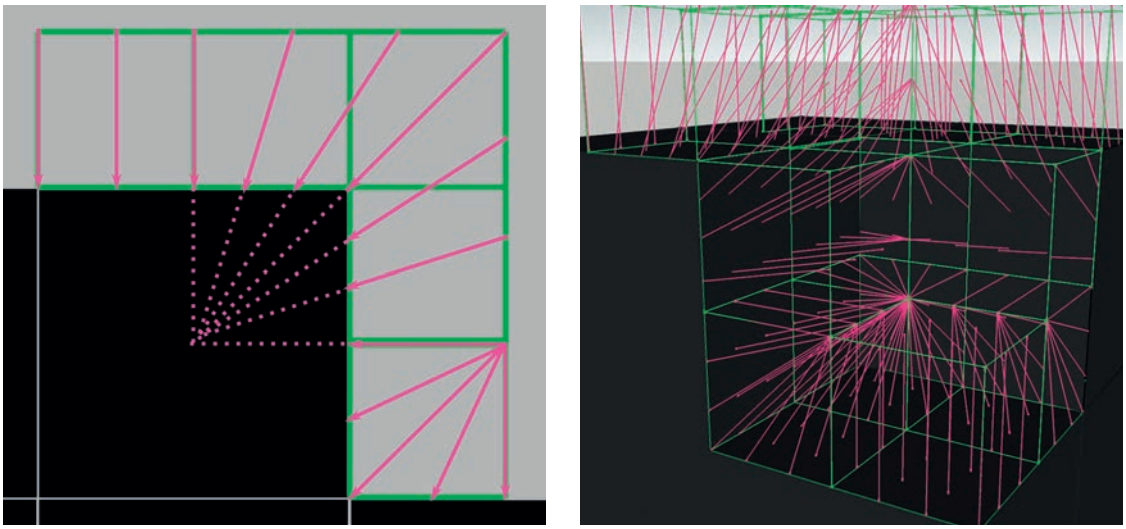


Figure 2:
To the left, the directions of vectors in the vector field imposed on the black digitization are illustrated. These in fact cover all the special cases. To the right, the generalization to dimension three is shown for just two types of vertices.

SPATIAL AND SPATIO-TEMPORAL POINT PROCESSES

In 2013, Rasmus Waagepetersen and Ege Rubak completed joint work with Adrian Baddeley (University of Western Australia) and Jean-Francois Couerjolly (University of Grenoble) on **logistic regression estimating functions** for spatial Gibbs point processes, see Baddeley *et al.* (2013). These estimating functions are closely related to the well-known pseudo-likelihood estimating function. However, in contrast to the usual implementations of pseudo-likelihood, the logistic regression estimating functions are always unbiased. They are moreover computationally efficient and can be implemented, using standard statistics software for generalized linear models.

Two projects on **multivariate point process modelling** have been continued in cooperation with Yongtao Guan (University of Miami), Abdollah Jalilian (Razi University) and Jorge Mateu (Universitat Jaume I). Two modelling strategies have been considered: one based on shot-noise Cox processes and so-called product fields and one based on multivariate log Gaussian Cox processes, see also Huang *et al.* (2013). Major issues in these projects were computational problems in relation to model fitting and optimal extraction of biologically relevant information from the models. Moreover, point process modelling in tropical rain forest ecology has been considered in cooperation with Guochun Shen (East China Normal University), see Shen *et al.* (2013). A particular focus point has here been the impact of scale when quadrat count methods are used to quantify spatial variation in patterns of trees.

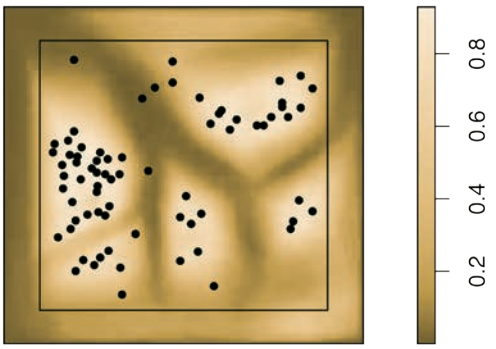
New models for cluster point processes within 'territories' modelled by planar Voronoi cells have been developed in Møller & Rasmussen (2013). The nuclei of the Voronoi cells are generated by a latent Poisson process. Conditional on the territories/cells, the clusters are independent Poisson processes whose points may be aggregated around or away from the nuclei and along or away from the boundaries of the cells. In Møller & Rasmussen (2013), it is also discussed how to account for edge effects when observing the superposition of clusters within a bounded region. Bayesian inference for a particular flexible model is discussed in connection to a botanical example.

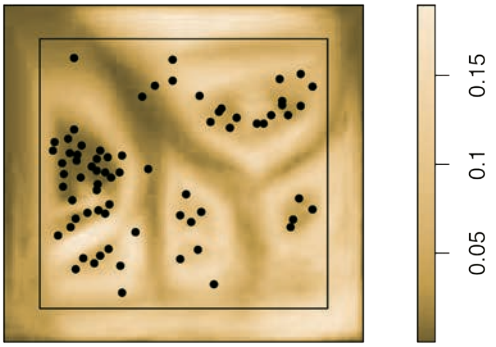
The Johnson-Mehl germination-growth model is a spatio-temporal point process model which, in particular, is used for modelling of neurotransmitters data. However, parametric Johnson-Mehl models fitted by maximum likelihood have not yet been evaluated for such data by means of functional summary statistics. In Møller & Ghorbani (2013), four such functional summary statistics adapted to the **Johnson-Mehl model** are developed. Two of them are based on the second-order properties while the other two are based on the nuclei-boundary distances for the associated Johnson-Mehl tessellation. The theoretical properties of the functional summary statistics are investigated in Møller & Ghorbani (2013). Furthermore, non-parametric estimators are suggested, and their usefulness for model checking is examined in a simulation study and in an actual application of Johnson-Mehl models to a neurotransmitters dataset.

The standard **Hawkes process** is constructed from a homogeneous Poisson process and the same exciting function is used for different generations of offspring. In collaboration with Raul Fierro (Pontificia Universidad Catolica de Valparaıso) and Victor Leiva (Universidad de Valparaıso), an extension of this process with different exciting functions has been suggested in Fierro *et al.* (2013). This extension may well be important in a number of fields; in particular in seismology, where main shocks produce aftershocks with possibly different intensities. The main results in Fierro *et al.* (2013) relate to the asymptotic behaviour of this extension of the Hawkes process. The results allowed us to analyze the asymptotic behaviour of the process when unpredictable marks are considered.

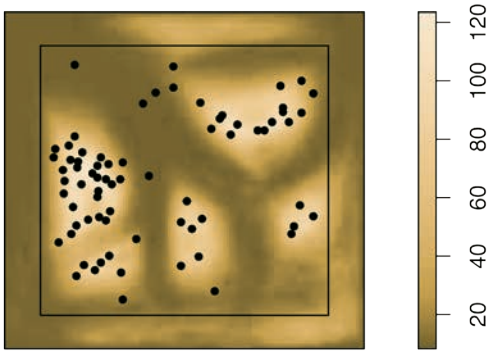
The minicolumn project detailed in the CSGB Annual Report 2012 continued to play an important part of the research in 2013. Finally, the papers Coeurjolly & Rubak (2013), Jalilian *et al.* (2013) and Rasmussen (2013) have appeared in 2013.

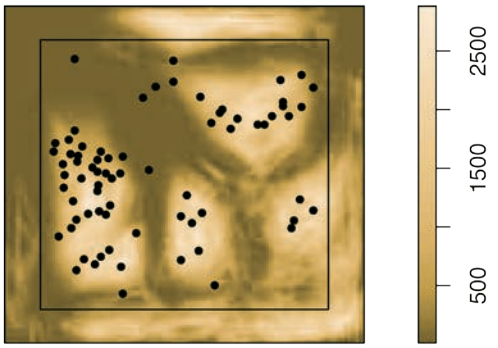
Posterior mean (upper) and variance (lower) of the function 1-α/Λ. The windows W_{ext} and W are shown as rectangles. From Møller & Rasmussen (2013).





Upper plot: Posterior mean of Λ(x). Lower plot: Posterior variance of Λ(x). The windows W_{ext} and W are shown as rectangles. in both plots. From Møller & Rasmussen (2013).





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SPACE-TIME LATTICE DATA

The research on **Lévy-based modelling** of lattice data in bioimaging has continued in 2013. Lévy-based random fields are at the same time analytically tractable and flexible. The Lévy-based approach can produce a wide range of non-Gaussian random fields. This is important in relation to modelling of brain imaging data, as shown in Jónsdóttir *et al.* (2013). Another advantage of the Lévy-based approach is that it can be used for producing random particles of varying shape with known statistical properties. **Lévy particles** are thus an important tool when testing new methods. For instance, in Jónsdóttir & Jensen (2013) planar Lévy particles have been used in a study of a new method of error prediction in circular systematic sampling. Right now, spatial Lévy particles, as those shown in Figure 1, are used in simulation studies of the statistical properties of new stereological estimators of Minkowski tensors. It may even be possible to obtain further results for the extremal properties of Lévy-based random fields but this question is still largely open.

During 2013, a close collaboration between AU-bio, AU-math and KU has resulted in a new statistical method of **estimating the thickness of ultra thin sections obtained by electron microscopy**. Available for observation is serial sections obtained by transmission electron microscopy. Two such neighbour sections are shown in Figure 2. In an attempt to create a 3D reconstruction from the serial sections, it is, of course, important to know the distance between neighbour sections. The intended distance is 45 nm. However, visual inspection of the sections indicate that the distance between sections may vary dramatically.

The idea is now first to correct for intensity inhomogeneity within each section and then align neighbouring images by an affine warp. After this procedure, it is feasible to assume that the pixel values are realizations from a 3D stationary and isotropic random field $F = \{F(x_{ijk})\}$. Here, $\{F(x_{ijk})\}$ is the realized value of the random field at the grid point x_{ijk} in 3D, where *i* and *j* refer to the position of the grid point inside the section, while *k* refers to the number of the section. The distance between two grid points belonging to the same section is known (observable) while the distance between two aligned grid points x_{ijk} and $x_{ij(k+1)}$ from the neighbour sections k and $k+1$ is equal to the **unknown local section thickness**.

Under stationary and isotropy of the random field *F*, the joint distribution of $(F(x), F(y))$ only depends on the distance r between x and y. We assume that there exists a strictly monotone function $m(r)$ of r. For instance, one may use the variogram of the random field, defined for two points x and y with mutual distance r by

$$m(r) = E(F(x) - F(y))^2/2.$$

We may estimate the function *m*, using observations of the random field within the sections. Combining aligned grid points on two neighbour sections we may also calculate an estimate $\widehat{m}(\Delta)$ where Δ is the unknown distance between the two neighbour sections. The estimate of Δ then becomes $m^{-1}(\widehat{m}(\Delta))$.

This method has been implemented in Sporring *et al.* (2014).

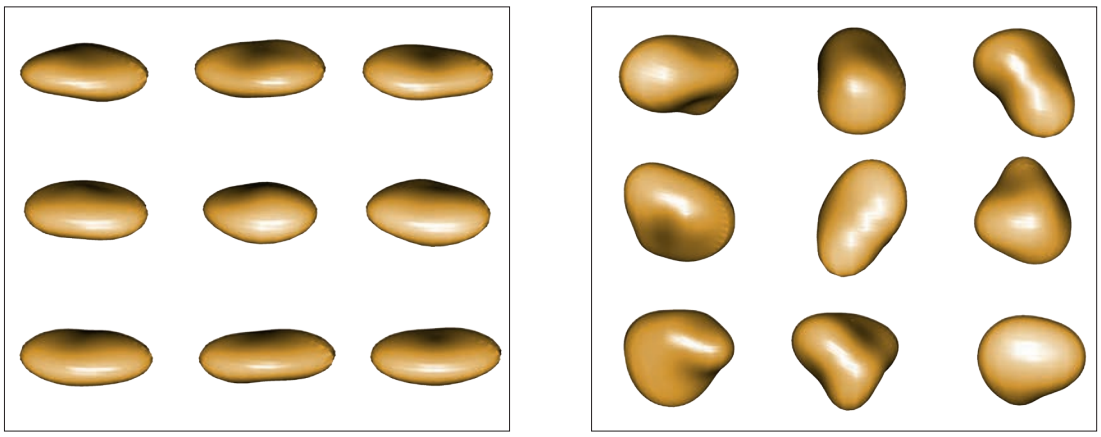
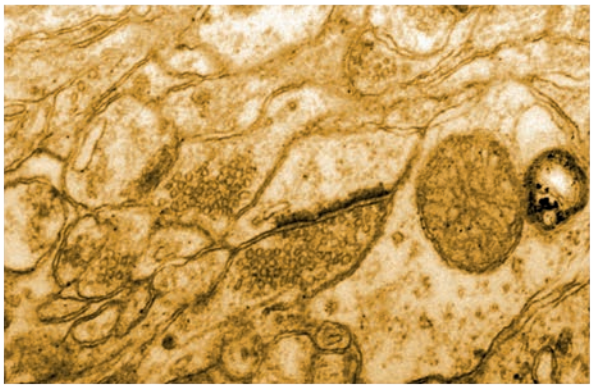
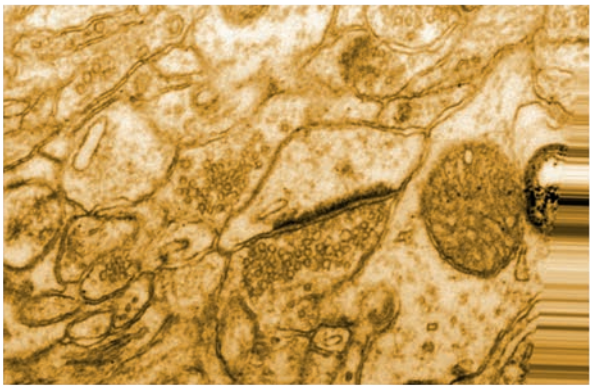


Figure 1: Lévy particles with von Mises-Fisher kernel and Gamma Lévy basis.



(a)



(b)

Figure 2: The cerebral cortex of a rat as viewed by serial section transmission electron microscopy. The images (a) and (b) show section 17 and 18 from the dataset called 10.1.top.syn3.5 after intensity inhomogeneity correction and registration.

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RANDOM SHAPES

The work on random shapes has been concentrated on the two major applications of non-rigid registration and on the construction, analysis and application of a metric space of **geometric trees**. The latter has been further analyzed and applied to data from airways of COPD patients. The tree space construction, as now published in Pattern Analysis Machine Intelligence (PAMI), has been shown to be geodesically complete, and to have so-called sticky means due to the unbounded negative curvature at special locations (Feragen *et al.*, 2013a). Furthermore, the analysis using the tree space construction in polynomial time is so far not possible without simplifications such as labeled leaves in the tree. This has led to the use of reproducing Hilbert space kernels in a machine learning framework, for simpler computations (Feragen *et al.*, 2013b).

The work on **non-rigid registration** has been published in several contributions. Darkner and Sporring have developed the locally orderless images view on the numerical implementation of information theoretic measures of image matching like the mutual information (Darkner & Sporring, 2013). Sommer and co-workers have further developed the kernel bundle framework for describing the Large Deformation Diffeomorphic Metric Mapping (LDDMM). Here, higher order momentum kernels have been introduced and the solution provided in the LDDMM framework (Sommer *et al.*, 2013a) and the kernel bundle applied to kernels at various scales simultaneously has been developed (Sommer *et al.*, 2013b). Pai and coworkers have developed the cube-propagation framework for computing volume changes along the non-rigid registration and shown superior separation of Alzheimer's patients and normal controls compared to numerical volume integration of the Jacobian determinant (Pai *et al.*, 2013).

The common idea behind the development of the tree space framework and the further development of the LDDMM framework is to create **a metric space of geometric trees and diffeomorphisms**, respectively. A metric is the underlying necessary structure for construction of statistical tests and machine learning methodologies. For all applications where the output is a tree/diffeomorphism, respectively, the analysis of the space and its geodesic structure is necessary. Sommer and co-workers have contributed to the statistical analysis in curved spaces by studying exact principle geodesic analysis (Sommer *et al.*, 2013c) and dimensionality reduction in curved spaces by the iteration frame bundle methodology (Sommer, 2013).

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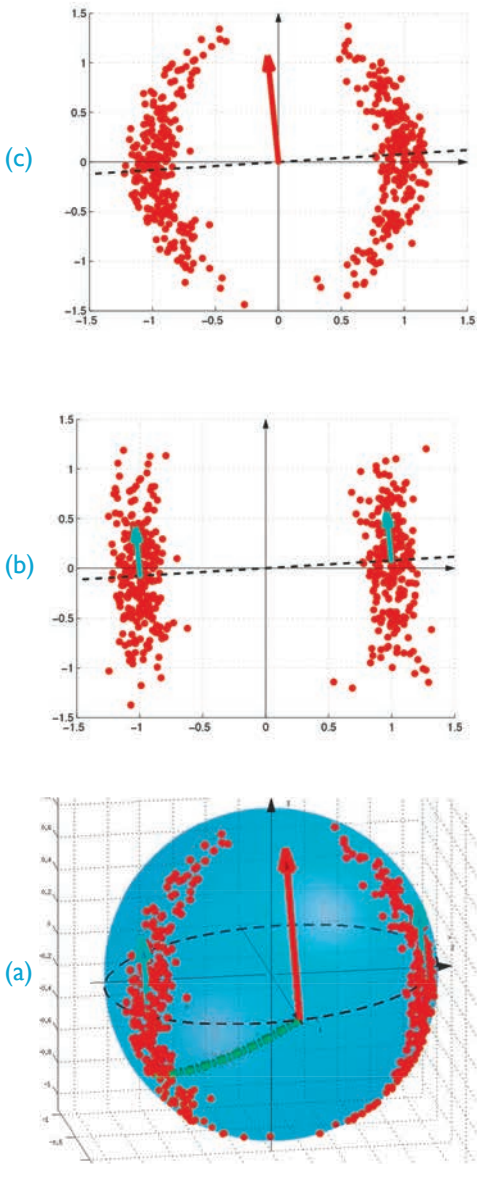
Sommer, S., Nielsen, M., Darkner, S. & Pennec, X. (2013a): Higher-order momentum distributions and locally affine LDDMM registration. *SIAM Journal on Imaging Sciences* **6**, 341-367.

Figure 1:
A bimodal distribution on S^2 constructed from Gaussian distributions in the tangent space at the two modes. With HCA, the first horizontal component (black dotted in (a,b)) is the geodesic between the modes. The second horizontal component (blue vectors) is parallel transported along the first component and the analysis is performed relative to the first component. With PGA (c), the curvature skews the centralized linearization giving a curved view of the distributions. Since geodesics curve towards the modes (green dotted in (a)), variance along the second PGA component (red vector) is over-estimated. In higher dimensions, components may flip. See Sommer (2013).



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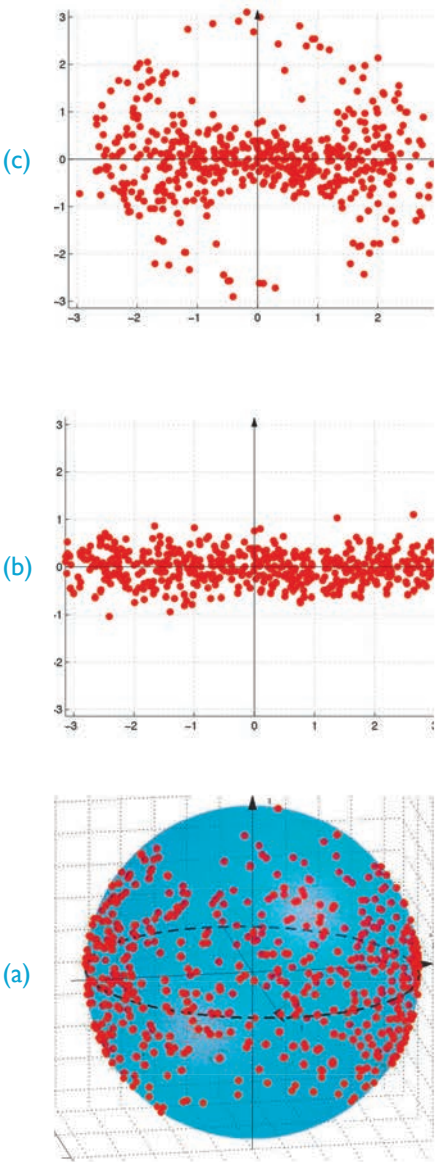

Figure 2:
Illustrating a diffusion starting at the equator, 2^9 points are sampled uniformly around equator with normally distributed vertical position (variance 0.35^2). (a) HCA captures the center of mass in the first component (black dotted in (a)), and it estimates the vertical correct variance (0.34^2). (c) The curvature and centralized analysis distorts the PGA visualization, and the variance is over-estimated (1.75^2). From Sommer (2013).

NON-UNIFORM SAMPLING

Researchers

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Jens R. Nyengaard
Johanna F. Ziegel

During 2013, the research on vanishing auxiliary variables in PPS sampling has been finalized (Andersen *et al.*, 2014). The starting point of the investigations has been the use of PPS sampling in microscopy where **vanishing auxiliary variables** are a common phenomenon and, accordingly, part of the population is not accessible, using PPS sampling. For instance, in Keller *et al.* (2013), it was shown that 5% of the population total is associated with vanishing auxiliary variables. Since PPS sampling requires positive auxiliary variables, it has earlier been suggested in the microscopy literature to add a small positive constant ε to the auxiliary variables (Gardi *et al.*, 2008). Then, all sampling units become accessible by PPS sampling, but, depending on the choice of ε, this procedure may lead to extremely large estimator variances.

In Andersen *et al.* (2014), optimal ways of choosing ε are established. A sampling design for a finite population of N units is considered for which the sampling probabilities of the first $N_0 < N$ units are zero. The sample is a random subset of the population with n elements, say. The sampling design is modified such that the resulting sample still has size n and such that the sampling probabilities of the first N_0 units are equal to a positive constant while the sampling probabilities of the remaining units are proportional to the original sampling probabilities. Under mild regularity conditions, the **optimal design** of this type is derived. This result, which has independent interest in sampling theory, can be used to determine an optimal value of ε in the original problem described above.

Under a **proportional regression model**, the optimality results simplify. This framework, where both design and model play a role, is often referred to as a model assisted approach (Särndal *et al.*, 2003). The robustness of the optimal design against parameter misspecification and departures from proportionality is also investigated in Andersen *et al.* (2014). An analysis of microscopy data, using the developed methods, is presented which shows that an important gain in efficiency may be obtained by choosing an optimal ε.

Another line of research in 2013 within the non-uniform sampling project has concerned the possibility for designing 2D non-uniform systematic sampling that respect the spatial information available. In designs like the proportionator (Gardi *et al.*, 2008), which is used in microscopy, all spatial information is lost, prior to sampling. In an attempt to preserve the spatial information available, a genuine 2D sampling procedure has been considered which is a generalization of the non-uniform sampling in 1D, suggested in Dorph-Petersen *et al.* (2000). The 2D non-uniform systematic sampling design yields zero estimator variance under optimal auxiliary information about the measurement function of interest. However, simulation results show that in set-ups which resemble sampling situations in microscopy (estimation of total number of cells in a section, estimation of the area of a tissue of interest), the proposed design does not substantially improve efficiency compared to standard non-uniform sampling designs such as sampling proportional to size with replacement. The results may be found in Andersen & Ziegel (2014).

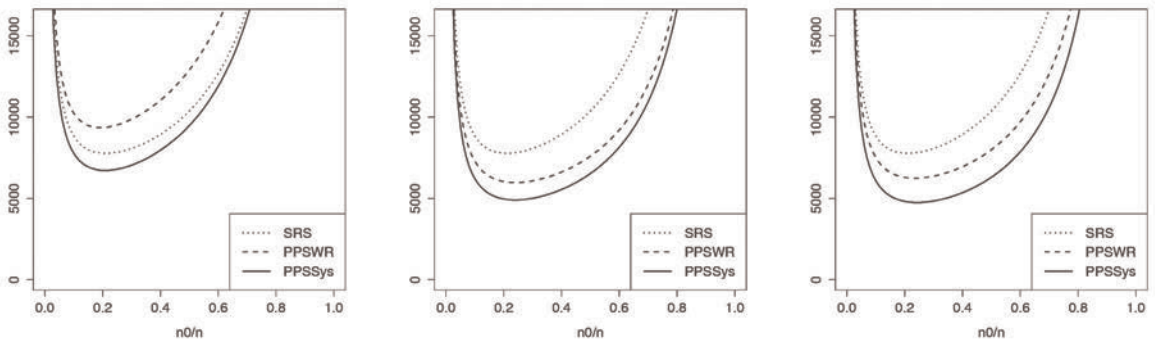

Figure 2:
The mean variance under simple random sampling (SRS), PPS sampling with replacement (WR) and systematic PPS sampling is shown for three different regression relationships (left to right), as a function of the sample proportion in Stratum 0. From Andersen *et al.* (2014).

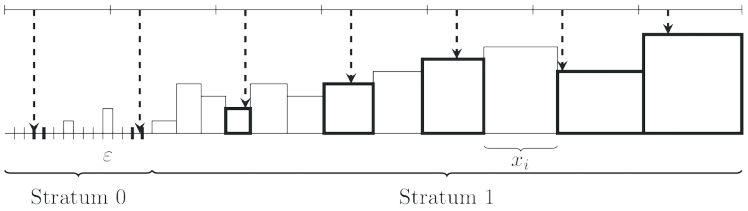

Figure 1:
Illustration of ε-corrected systematic PPS sampling, where a small positive constant ε has been added to each sampling unit with associated auxiliary variable equal to zero. Stratum 0 consists of the sampling units with vanishing auxiliary variable while Stratum 1 is the remaining part of the population. From Andersen *et al.* (2014).

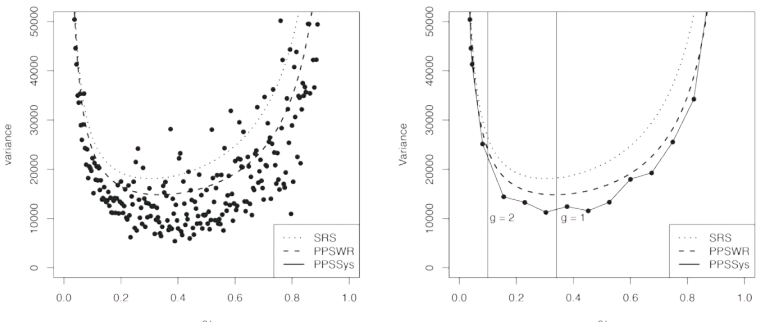

Figure 3:
Left: The variance of stratified SRS (dotted), stratified PPS WR (stippled) and systematic PPS with a balanced ordering of the auxiliary variable as a function of the sample proportion in Stratum 0. Right: The same plot, except that the variance is based on binned data. From Andersen *et al.* (2014).

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FLUORESCENCE MICROSCOPY TAKEN TO THE MOLECULAR LEVEL

In 2013, we have focused on modelling af **cellular protein interactions**, using spatial point process models. The data are obtained by FRET microscopy which is the preferred tool to obtain indirect information concerning the distribution of intracellular proteins (Periasamy, 2001). In a typical FRET experiment, three emission channels are measured, resulting in three pixel images. One of the channels is only active if proteins interact at a small scale (Clegg, 1995). In a typical FRET experiment, proteins are labelled by **donor** and **acceptor** molecules. Here, donor molecules, being continuously excited due to a laser beam, have the possibility to de-excite by transferring their surplus of energy to an acceptor (in case in close vicinity of the donor), instead of emitting a photon. Although the interactions between acceptor and donor proteins are at the molecular level (1-10 nm), the pixel resolution of FRET microscopy is typically 200x200 nm^2.

We have derived a **statistical model for FRET pixel intensity data** (3-channels), given a protein configuration, see also Corry *et al.* (2005). In this model, incoming streams of photons are absorbed and redistributed among proteins according to probabilities depending on their spatial configurations. The photon streams are modeled by Poisson processes. By using the labeling theorem for Poisson processes, we are able to derive an explicit model for the intensities in the pixels of each channel image. Further, by specifying a spatial point process model for the distribution of proteins and combining this with the intensity model, a complete stochastic model for the generation of FRET pixel intensity data is obtained. This allows us, by Bayesian inference and Markov Chain Monte Carlo (Møller & Waagepetersen 2003; Gamerman & Lopes, 2006), to draw quantitative statements concerning the protein arrangement at an inner pixel level, see Figure 1. The results will be presented in Hooghoudt *et al.* (2014).

Currently, we are assessing the performance of the proposed methodology on synthetic data, generated by Poisson, clustered and repulsive point processes. Furthermore, we want to test our method on real FRET datasets. Therefore, a collaboration has been developed between Dr. Margarida Barroso from Albany Medical Center in Albany, NY. We have visited Dr. Barroso's lab in the summer of 2013 to learn about transferrin (iron binding proteins) endocytic trafficking in cancer vs. normal cells (Talati *et al.*, 2013). During this stay, we have collected **FRET datasets** in different types of cells (cancer and normal epithelial cells) as well as in vitro random distributions of transferrin bound to polylysine slides. Analysis of these FRET datasets by our method allows for establishment of quantitative methods to evaluate the organization and distribution of Transferrin-receptor complexes (proteins transporting transferrin into the cell) in cancer vs. normal cells.

Researchers

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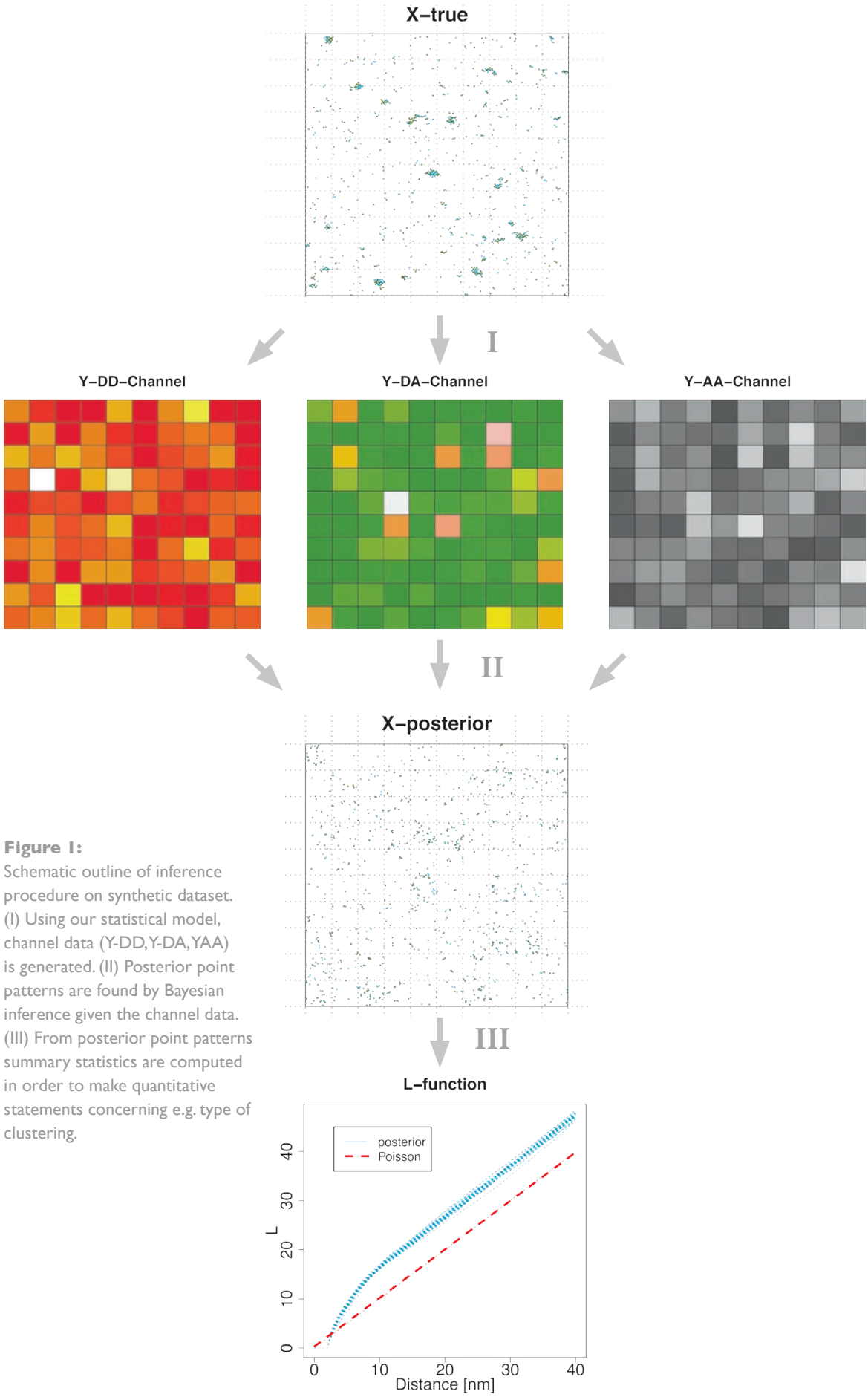

Figure 1:
Schematic outline of inference procedure on synthetic dataset. (I) Using our statistical model, channel data (Y-DD, Y-DA, YAA) is generated. (II) Posterior point patterns are found by Bayesian inference given the channel data. (III) From posterior point patterns summary statistics are computed in order to make quantitative statements concerning e.g. type of clustering.

MOLECULAR CRYO-EM

The vast majority of proteins in living cells binds other cellular molecules. Typically, interactions are formed to other proteins, with the specific sites of interaction termed protein-protein interfaces. Among the multitude of protein-protein interactions (PPIs) inside the cell, a huge variation in terms of lifetime and binding strength is found. Multi-protein assemblies containing multiple PPIs are referred to as '**molecular machines**' and are classically characterized by a set of rather stable interactions. Assembling multiple proteins in one entity enables the cell to perform more sophisticated cellular functions than could be accomplished by individual proteins alone.

Importantly, whenever the cell must adhere to a regulated temporal order of events, the ability of proteins to form transient PPIs is essential. **Transiently interacting proteins** are characterized by a regulated, limited lifetime of their interactions, which makes a molecular and structural analysis of these key players in cellular regulation processes challenging. However, a better structural understanding of transient PPIs will give researchers better possibilities to influence PPIs, for instance to design novel drugs that specifically act on signaling pathways disturbed in diseased states. In this respect, kinases, i.e. proteins that add phosphate groups to specific amino acid moieties of other proteins, are of special interest as primary targetable enzymes that can turn protein surfaces into interfaces. In human, there are >500 kinases while in the model yeast **Saccharomyces cerevisiae**, >100 kinases are found. It is estimated that up to one third of the proteins found in the cell can undergo phosphorylation as a means of their regulation.
We have developed a set of stable genetic modifications that allows us to study a kinase-controlled macromolecular complex composed of proteins that exhibit stable permanent, weak permanent as well as transient PPIs in a model system. For the structural study of this complex, S. cerevisiae pyruvate dehydrogenase, we employ molecular cryo-EM, a technique that aims at analyzing the three-dimensional (3D) structures of cellular macromolecular assemblies. As an important prerequisite for high-quality structural studies, **purification strategies** that on the one hand are mild in order to preserve PPIs and on the other hand yield sufficient amounts of pure material are required. To this end, we established a purification method employing automated **liquid affinity chromatography** that allowed purifying decent amounts of biochemically pure material (compare with Figure 1A) suitable for structural studies. This purification method turned out to show a considerably improved scalability which means that higher amounts of particles can be obtained. We could acquire image data sets and subjected these to statistical single-particle analyses. Some average images representing **clusters of similar particle views** are shown in Figure 1B. While the majority of discontinuities seen at the outline of the particle appear to be caused by absence of weakly interacting envelope proteins, some outer densities may possibly represent interactions to regulatory proteins.

Thus, we next ask whether the location of transient binding partners such as kinases can be detected in these particles. To this end, the use of purposive purification strategies that maximize the chance to visualize these **rare binding events** are essential. We therefore work on the purification of particles from yeast strains carrying different purification tags on the particle's core proteins and its regulatory kinases,

Researchers
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Jay Rai
Björn Sander

respectively. Furthermore, we carry out experiments in order to introduce double affinity tags that are split over a pair of proteins. Such modification strategies will facilitate to establish multi-step purification procedures in which complexes containing both proteins can sequentially be enriched. As further advantage, these tags are also well suitable for immunoblotting experiments in order to verify the identity of additional proteins. The detection of substoichiometric components of macromolecular assemblies by a combination of biochemical and structural methods will thus be a focus in the coming time.

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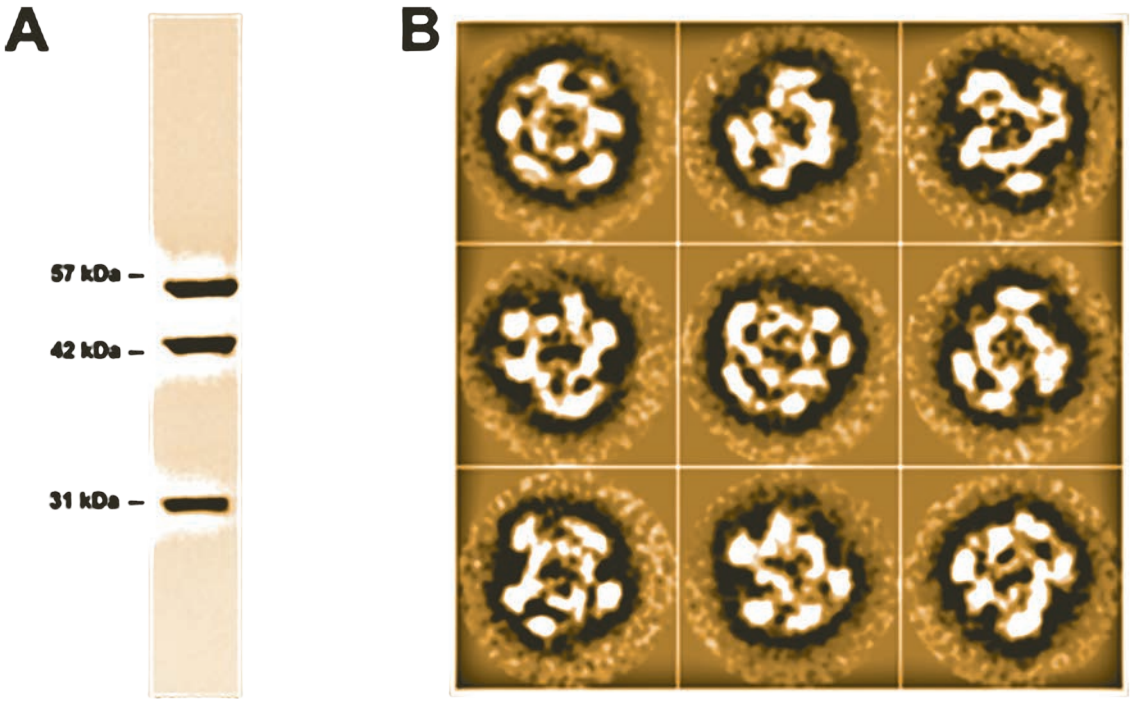
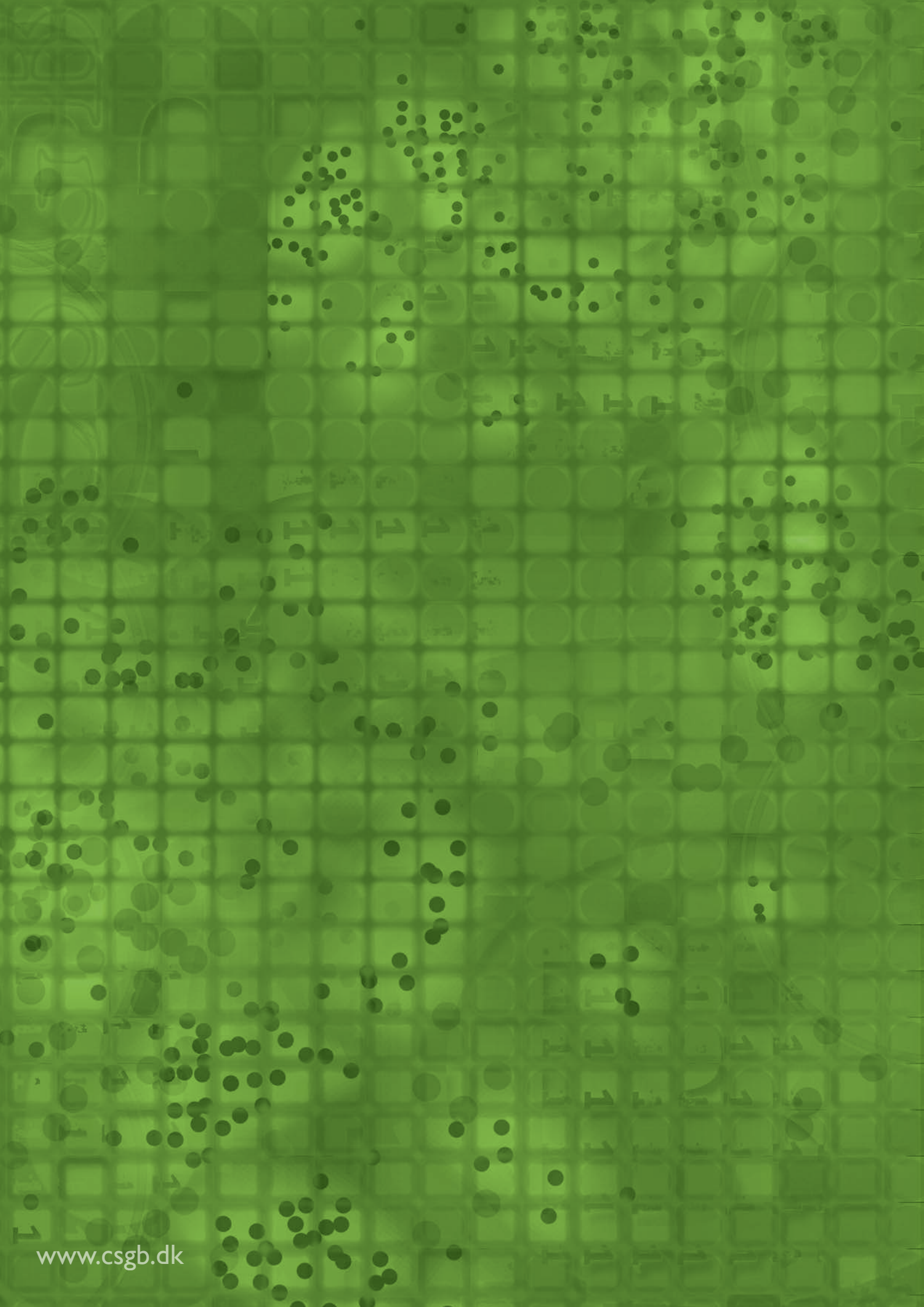


Figure 1:
Characterization of the *S. cerevisiae* pyruvate dehydrogenase complex. (A) Protein composition of the purified complexes. (B) Representative class averages upon single-particle image analysis of the macromolecular complexes.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CENTRE ACTIVITIES








OVERVIEW

PAST AND PLANNED INTERNATIONAL ACTIVITIES

International conferences and workshops

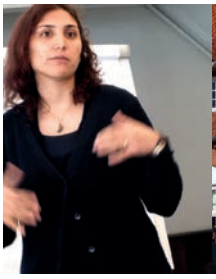
- *Joint EMS-DMF Mathematical Weekend*, 5 – 7 April 2013, Aarhus
- *GPSRS Workshop*, 8 – 10 April 2013, Aarhus
- *Workshop on Quantitative Microscopy*, 26 – 30 August 2013, Bern
- *Workshop on Tensor Valuations in Stochastic Geometry and Imaging*, 21 - 26 September 2014, Sandbjerg

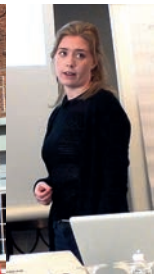
International symposia

- *Minisymposium on Sampling and Stereology*, 31 January 2013, Aarhus
- *Symposium in Honour of Adrian Baddeley*, 7 – 8 November 2013, Aarhus

International PhD courses

- *Courses on Quantitative Medical Graphics*, 6 and 13 March 2013, Aarhus
- *Summerschool on Topics in Space-Time Modelling and Inference*, 27 - 31 May 2013, Aalborg
- *Summerschool on Tensors and Tensor Fields in Imaging*, 19 – 23 August 2013, Marstal
- *Stereology Course*, 2 September 2013, Cambridge
- *Stereology Course*, 24 – 26 September 2013, Sandbjerg
- *International PhD Course on Inverse Problems with Applications in Tomography and Imaging*, 16-20 June 2014, Copenhagen




Sixth Internal CSGB workshop - Brøndums Hotel, Skagen

The internal CSGB workshops are held twice a year. They are arranged alternately by the two Aarhus groups (the stochastic geometry group and the biomedical group), the spatial statistics group at Aalborg University and the image group at University of Copenhagen.

The aim of these internal workshops is to discuss the present status of the CSGB research projects by presentations by the members of CSGB and to plan the further progress of the research projects. Furthermore, new activities arranged by CSGB such as workshops, courses, establishment of new international contacts, etc. are also discussed at these internal workshops. The Sixth Internal CSGB workshop was arranged by the spatial statistics group and took place at Brøndums Hotel, Skagen, 2 - 3 May 2013.

An important purpose of the internal workshops is **training of young researchers.** At the workshops they get the opportunity to present and discuss their work in an informal atmosphere.

WORKSHOP 2014

TENSOR VALUATIONS IN STOCHASTIC GEOMETRY AND IMAGING

21-26 SEPTEMBER 2014, SANDBJERG ESTATE, SØNDERBORG, DENMARK

WORKSHOP ON TENSOR VALUATIONS AT SANDBJERG MANOR 2014

The workshop is arranged jointly by CSGB and GPSRS, the DFG supported Research Unit Geometry and Physics of Spatial Random Systems.

SCOPE AND STRUCTURE OF THE WORKSHOP

This workshop is dedicated to the mathematical theory and the application of tensor valuations in stochastic geometry and imaging. The workshop is a result of our desire to bring together researchers from stochastic geometry and imaging, who have an interest in the underlying mathematical theory of tensor valuations, along with mathematicians who have an interest in the (potential) application areas of tensor valuations.

Also in recent years, there have been very important advances in the mathematical theory of tensor valuations, for instance, concerning the algebraic structure of tensor valuations and the characterization of local tensor measures. At the same time, tensor valuations are starting to be used in a number of research areas, primarily with the purpose of quantifying the morphology and anisotropy of complex spatial structures.

At the workshop, overview lectures will be given by experts in the field. The workshop will also have shorter research talks.

Invited speakers

- Semyon Alesker (Tel Aviv)
- David Cohen-Steiner (INRIA, Sophia Antipolis)
- Daniel Hug (Karlsruhe)
- Monika Ludwig (Wien)
- Quentin Mérigot (Grenoble)
- Rolf Schneider (Freiburg)
- Gerd Schröder-Turk (Erlangen)
- Franz Schuster (Wien)

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Find more information: www.csgb.dk









CSGB RESEARCH REPORTS 2013

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

1. Baddeley, A.J., Coeurjolly, J.F., Rubak, E. & Waagepetersen, R. (2013): A logistic regression estimating function for Gibbs point processes. *CSGB Research Report* **13-02**. To appear in *Biometrika*.

2. Fierro, R., Leiva, V. & Møller J. (2013): The Hawkes process with different excitation functions and its asymptotic behaviour. *CSGB Research Report* **13-10**. To appear in *J. Appl. Probab.*

3. Hahn, U. & Jensen, E.B.V. (2013): Inhomogeneous spatial point processes with hidden second-order stationarity. *CSGB Research Report* **13-07**. Submitted.

4. Kiderlen, M. & Hörig, M. (2013): Matérn's hard core models of types I and II with arbitrary compact grains *CSGB Research Report* **13-05**. Submitted.

5. Møller, J. & Ghorbani, M. (2013): Functional summary statistics for the Johnson-Mehl model. *CSGB Research Report* **13-03**. To appear in *J. Statist. Comput. Sim.*

6. Møller, J. & Rasmussen, J.G. (2013): Spatial cluster point processes related to Poisson-Voronoi tesselations. *CSGB Research Report* **13-09**. To appear in *Stoch. Env. Res. Risk A*.

7. Svane, A.M. (2013a): On multigrid convergence of local algorithms for intrinsic volumes. *CSGB Research Report* **13-01**. To appear in *J. Math. Imaging Vis.*

8. Svane, A.M. (2013b): Estimation of intrinsic volumes from digital grey-scale images. *CSGB Research Report* **13-04**. To appear in *J. Math. Imaging Vis*.

9. Thórisdóttir, Ó. & Kiderlen, M. (2013): The invariator principle in convex geometry. *CSGB Research Report* **13-06**. To appear in *Adv. Appl. Math.*

10. Thórisdóttir, Ó., Rafati, A.H. & Kiderlen, M. (2013): Estimating the surface area of non-convex particles from central planar sections. *CSGB Research Report* **13-08**. Submitted.

CSGB MISCELLANEA 2013

The CSGB miscellanea series contains various internal publications such as lecture notes, conference abstracts, etc. Two such publications appeared in 2013.

1. Jensen, E.B.V. (2013): Rotational integral geometry and local stereology – with a view to image analysis. *CSGB Miscellanea* **07**. 24 pages.
2. Baddeley, A. (2013): Joining the dots - inaugural lecture 7 November 2013. *CSGB Miscellanea* **08**. 96 pages.

In this context, we also want to mention the following review paper:

> Møller, J. & Stoyan, D. (2013): Stochastic geometry and random tessellations. To appear in *Tessellations in the Sciences*: *Virtues, Techniques and Applications of Geometric Tilings*, Eds. R. van Weijgaert, G. Vegter, V. Icke and J. Ritzerveld, Springer-Verlag.

written by CSGB researcher Jesper Møller and Professor Dietrich Stoyan, the grand-old-man of stochastic geometry.

Minisymposium on Sampling and Stereology

On 31 January 2013, a minisymposium on *Sampling and Stereology* was held at Department of Mathematics, Aarhus University. The invited speakers were (left) Yves Tillé (University of Neuchâtel) and (right) Johanna F. Ziegel (University of Bern). At the minisymposium, Ina Trolle Andersen, Eva B. Vedel Jensen and Jens R. Nyengaard from CSGB also gave talks about stereology, from a sampling point of view. The next day, there was a lively discussion (middle) on the use of sampling in modern stereology and the possibilities of implementing advanced spatially balanced sampling in stereology. It was agreed that AU-bio provides data for such analysis.

Seventh Internal CSGB Workshop - Aarhus

The Seventh Internal CSGB Workshop was arranged by the biomedical group and took place in the main building of Aarhus University, 14 – 15 November 2013. Nine research talks were given, this time also by senior researchers. In the evening, a guided tour to Den Gamle By was arranged. At the end of the workshop, an administrative meeting took place where the possibilities were discussed for an extension of CSGB beyond the present funding period that terminates 31 March 2015.








CSGB JOURNAL AND PROCEEDINGS PUBLICATIONS, BOOK CHAPTERS

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Feragen, A., Kasenburg, N., Petersen, J., de Bruijne, M. & Borgwardt, K. (2013): Scalable kernels for graphs with continuous attributes. *Advances in Neural Information Processing Systems* **26**, 1-9.

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Ghorbani, M. (2013a): Cauchy cluster process. *Metrika* **76**, 697-706.

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Keller, K.K., Andersen, I.T., Andersen, J.B., Hahn, U., Stengaard-Pedersen, K., Hauge, E.M. & Nyengaard, J.R. (2013): Improving efficiency in stereology: a study applying the proportionator and the autodisector on virtual slides. *J. Microsc.* **251**, 68-76.

Jalilian, A., Guan, Y. & Waagepetersen, R. (2013): Decomposition of variance for spatial Cox processes. *Scand. J. Statist.* **40**, 119-137.

Jacobsen, C.R. & Nielsen, M. (2013): Stylometry of paintings using hidden Markov modelling of contourlet transforms. *Signal Processing* **93**, 579-591.

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Miller, T., van Colen, G., Sander, B., Golas, M.M., Uezguen, S., Weigandt, M. & Goepferich, A. (2013): Drug loading of polymeric micelles. *Pharm. Res.* **30**, 584-595.

Pai, A.S.U., Sørensen, L., Darkner, S., Mysling, P., Jørgensen, D.R., Dam, E.B., Lillholm, M., Oh, J., Chen, G., Suhy, J., Sporring, J. & Nielsen, M. (2013): Cube propagation for focal brain atrophy estimation. *Proceedings from the 10th IEEE International Symposium on Biomedical Imaging: from Nano to Macro*, pp. 402-405.

Piuze, E., Lombaert, H., Sporring, J. & Siddiqi, K. (2013): Cardiac fiber inpainting using Cartan forms. Proceedings of MICCAI 2013, Nagoya, Japan, 22-26 September 2013, Part II (eds. Kensaku Moru, Ichiro Sakuma, Yoshinobu Sato, Christian Barillot, Nassir Navab). *Lecture Notes in Computer Science* **8150**, 509-517. Springer.

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Prokesová, M. & Jensen, E.B.V. (2013): Asymptotic Palm likelihood theory for stationary point processes. *Ann. Inst. Statist. Math.* **65**, 387-412.

Quéau, Y., Lauze, F. & Durou, J.-D. (2013): Solving the uncalibrated photometric stereo problem using total variation. Scale Space and Variational Methods in Computer Vision (eds. Arjan Kuijper, Kristian Bredies, Thomas Pock, Horst Bischof). *Lecture Notes in Computer Science* **7893**, 270-281. Springer.

Rasmusson, A., Hahn, U., Larsen, J.O., Gundersen, H.J.G., Jensen, E.B.V. & Nyengaard, J.R. (2013): The spatial rotator. *J. Microsc.* **250**, 88-100.

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Shen, G., He, F., Waagepetersen, R., Sun, I.-F., Hao, Z., Chen, Z.-S. & Yu, M. (2013): Quantifying effects of habitat heterogeneity and other cluster processes on spatial distributions of tree species. *Ecology* **94**, 2436-2443.

Sommer, S.H. & Johannsson, H. (2013): Real-time thevenin impedance computation. *Innovative Smart Grid Technologies (ISGT), 2013 IEEE PES*, 1-6.

Sommer, S.H. (2013): Horizontal dimensionality reduction and iterated frame bundle development. Geometric Science of Information (eds. Frank Nielsen, Frederic Barbaresco). *Lecture Notes in Computer Science* **8085**, 76-83.

Sommer, S.H., Lauze, F., Nielsen, M. & Pennec, X. (2013): Sparse multi-scale diffeomorphic registration: the kernel bundle framework. *J. Math. Imaging Vis.* **46**, 292–308.

Sommer, S.H., Nielsen, M., Darkner, S. & Pennec, X. (2013): Higher-order momentum distributions and locally affine LDDMM registration. *SIAM Journal on Imaging Sciences* **6**, 341-367.

Thórisdóttir, Ó. & Kiderlen, M. (2013): Wicksell's problem in local stereology. *Adv. Appl. Prob.* **45**, 925-944.









CSGB SEMINARS

31 January 2013 | Johanna F. Ziegel (University of Bern): **Precision estimation for stereological volumes**

31 January 2013 | Yves Tillé (University of Neuchâtel): **Doubly balanced spatial sampling with spreading and restitution of auxiliary totals**

31 January 2013 | Eva B. Vedel Jensen (Aarhus University): **Introduction to stereology**

16 May 2013 | Jonatan Andrey González Monsalve (Universitat Jaume 1, Spain): **Spatio-temporal ANOVA for replicated point patterns**

24 May 2013 | Astrid Kousholt (Aarhus University): **Stokastiske lukkede mængder og buffons nåleproblem**

16 September 2013 | Nicolas Charon (ENS Cachan, Paris): **Estimating shape variability of submanifold datasets**

10 October 2013 | Julia Hörrmann (Karlsruhe Institute of Technology): **Shape reconstruction from moments**

18 November 2013 | Martin Bauer (University of Vienna): **Riemannian geometry of shape spaces**

18 November 2013 | Klas Modin (Chalmers University of Technology): **Optimal information transport, Fisher-Rao metrics and image registration**

28 November 2013 | Viktor Benes (Charles University, Prague): **Some aspects of point process space-time modelling and statistics**

16 December 2013 | Peter Craigmile (Ohio State University): **One dimensional wavelet transforms**

16 December 2013 | Stephen M. Pizer (University of North Carolina): **Interclass statistical tests on objects via S-reps**

17 December 2013 | Peter Craigmile (Ohio State University): **Representing stochastic processes using wavelets**

18 December 2013 | Peter Craigmile (Ohio State University): **Two dimensional wavelet transforms for gridded data**

Summer School 2013

Topics in Space-Time Modeling and Inference
27 – 31 May 2013

Department of Mathematical Sciencess
Aalborg University

This summer school was arranged with the purpose to present the newest advances in space-time modeling and inference the an audience of junior researchers with a special interest in spatial statistics. The mode of presentations was a combination of lectures, software demonstrations and, for those who had their own computers loaded with the R software, opportunities were given to try the methods out in practice. The junior participants were also given the possibility to shortly present a poster. This was followed by a poster discussion session.

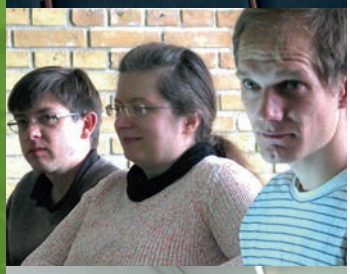
Programme

Professor Peter J. Diggle | Lancaster University
Statistical models and methods for space-time point processes

Professor Tilmann Gneiting | University of Heidelberg
Covariance models for spatial and space-time data

Professor Peter F. Craigmile | University of Glasgow
Time-frequency methods for spatio-temporal data

Professor Rasmus P. Waagepetersen | Aalborg University
Statistical models and methods for spatial point processes






CSGB VISITORS

Johanna F. Ziegel (University of Bern)
27 January – 1 February 2013

Yves Tillé (Université de Neuchâtel)
30 January – 2 February 2013

Martin Englund (University of Lund)
15 March 2013

Alexandre Falcao (Instituto de Computacao, Brazil), 15 March 2013

Octavio Arizmendi (Saarland University)
5 – 7 April 2013

Serban Belinschi (University of Waterloo, Canada), 5 – 7 April 2013

Fred Espen Benth (Univeristy of Oslo)
5 – 7 April 2013

Philippe Biane (France)
5 – 7 April 2013

Susanne Ditlevsen (University of Copenhagen), 5 – 7 April 2013

Ion Nechita (CNRS, Toulouse)
5 – 7 April 2013

Roland Speicher (Saarland University, Germany), 5 – 7 April 2013

Francois Baccelli (Texas, Austin)
5 – 10 April 2013

Bruno Ebner (Karlsruher Institute für Technologie), 7 – 10 April 2013

Fabian Gieringer (Karlsruher Institute für Technologie), 7 – 10 April 2013

Daniel Hug (Karlsruher Institute für Technologie), 7 – 10 April 2013

Julia Hörrmann (Karlsruher Institute für Technologie), 7 – 10 April 2013

Michael Klatt (Universität Erlangen-Nürnberg), 7 – 10 April 2013

Günter Last (Karlsruher Institute für Technologie), 7 – 10 April 2013

Klaus Mecke (Universität Erlangen-Nürnberg), 7 – 10 April 2013

Eva Ochsenreither (Karlsruher Institute für Technologie), 7 – 10 April 2013

Andreas Reichenbacher (Karlsruher Institute für Technologie)
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Gerd Schröder-Turk (Universität Erlangen-Nürnberg), 7 – 10 April 2013

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René Wittmann (Universität Erlangen-Nürnberg), 7 – 10 April 2013

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Jonatan Andrey González Monsalve (Universitat Jaume I, Spain)
9 - 25 May 2013

Peter F. Craigmile (University of Glasgow)
27 - 31 May 2013

Peter Diggle (Lancaster University)
27 - 31 May 2013

Tilmann Gneiting (University of Heidelberg), 27 - 31 May 2013

David John Hunter (University of Sydney), 26 June 2013

Wiro Niessen (Biomedical Imaging Group Rotterdam), 26 June 2013

Luc Florac (Eindhoven University of Technology), 18 - 23 August 2013

Sarang Joshi (University of Utah) 1 August 2013 - 31 July 2014

Hans Knutsson (Linköpings Universitet) 18 - 23 August, 2013

Marco Loog (University of Technology, Netherlands), 18 - 23 August, 2013

Steen Markvorsen (Technical University of Denmark), 18 - 23 August 2013

Gerard Medioni (University of Southern California), 18 - 23 August

Nicolas Charon (ENS Cachan, Paris) 16 - 20 September 2013

Julia Hörrmann (Karlsruhe Institute of Technology), 1 October - 30 November 2013

Anders Rønn-Nielsen (University of Copenhagen), 7 - 10 October 2013

Rasmus Larsen (Technical University of Denmark), 18 October 2013

Wiro Niessen (Biomedical Imaging Group Rotterdam), 18 October 2013

Michaela Prokesova (Charles University, Prague), 21 – 25 October 2013

Anders Rønn-Nielsen (University of Copenhagen), 28 October – 1 November 2013

Mari Myllymäki (Aalto University) 5 – 9 November 2013

Adrian Baddeley (University of Western Australia, Perth), 4 – 16 November 2013

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Aila Särkkä (Chalmers University of Technology, Gothenburg) 6 – 8 November 2013

Sergei Zuyev (Chalmers University of Technology, Gothenburg) 6 – 8 November 2013

Jean-Francois Coeurjolly (Laboratoire Jean Kuntzmann, Grenoble) 6 – 9 November 2013

Frédéric Lavancier (Université de Nantes) 6 – 9 November 2013

Marie-Colette van Lieshout (CWI Amsterdam), 6 – 9 November 2013

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

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