Annual Report 2018

Centre for Image Analysis

Centrum för bildanalys

Cover:
CBA collaboration partners across the world. For further information see Section 5.6.

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Anton Axelsson
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Edited by:
Gunilla Borgefors, **Filip Malmberg**, Ingela Nyström, Leslie Solorzano, Johan Öfverstedt

Centre for Image Analysis, Uppsala, Sweden

Contents

1 Introduction

The Centre for Image Analysis (CBA) conducts research and graduate education in computerised image analysis and perceptualisation. Our role is to develop theory in image processing as such, but also to develop better methods, algorithms and systems for various applications. We have found applications primarily in digital humanities, life sciences, and medicine. In addition to our own research, CBA contributes to image technology promotion and application in other research units and society nationally as well as internationally.

1.1 General background

CBA was founded in 1988 and was until 2014 a collaboration between Uppsala University (UU) and the Swedish University of Agricultural Sciences (SLU). From an organisational point of view, CBA was an independent entity within our host universities until 2010. Today, we are hosted by the Disciplinary Domain of Science and Technology and belong to one of five divisions within the Department of Information Technology (IT), the Division of Visual Information and Interaction (Vi2). The organisational matters are further outlined in Section 2.

A total of 37 persons within Vi2 were active in CBA research during 2018: 16 PhD students and 21 seniors (of which 3 are Professor Emeriti). Many of us have additional duties to research, for example, teaching, appointments within the Faculty, and leave for work outside academia, so the number 37 is not full-time equivalents. A complement to the CBA researchers are the 15 Master students who completed their thesis work with supervision from CBA during 2018. The number of staff in the CBA corridor fluctuates over the year thanks to that we have world class scientists visiting CBA and CBA staff visiting their groups, for longer or shorter periods, as an important ingredient of our activities. A successful example of collaboration we have is with the Division of Radiology, where two of our staff members work part time at the Uppsala University Hospital in order to be close to radiology researchers and also have funding from there.

We are particularly pleased with the recruitment of two senior lecturers in computerised image analysis, one of whom was directly promoted to full professor. This is an important strategic step to ensure the future of our subject at the Department, Faculty as well as Uppsala University.

The activity level continued to be high in 2018, for example, the 16 PhD students in the subject Computerised Image Processing. There were no PhD defenses during 2018; however, five are planned for 2019. In addition, we had a total of 77 ongoing research projects of which 22 are new for 2018. Our projects are involving as many as 40 international and close to 50 national collaboration partners. One way to measure our results is to acknowledge our 20 journal papers and 15 fully reviewed conference papers.

Traditionally, a large group from us participated in the annual national symposium organised by the Swedish Society for Automated Image Analysis (SSBA), which in March 2018 was hosted by KTH. CBA accounted for 25 of the 140 participants from academia, local students, and industry – a proof as good as any that CBA is the largest academic image analysis group in Sweden.

We are very active in international and national societies and are pleased that our leaders are recognised in these societies. Ingela Nyström has been a member of the Executive Committee of the International Association of Pattern Recognition (IAPR), since 2008 (President 2014–2016). After ten years as ExCo member, Nyström concluded her terms in August at the ICPR 2018. We are also closely involved in the Network of EUropean BioImage Analysis (NEUBIAS), where Nataša Sladoje and Carolina Wählby serve as members of the management committee. In the newly started COMULIS (Correlated Multimodal Imaging in Life Sciences) COST Action, Sladoje serves as a member of the core group.

Nationally, CBA has two board members in the Swedish Society for Automated Image Analysis (SSBA), Ida-Maria Sintorn as Chair and Robin Strand as Vice-Chair. They both served as Swedish

representatives on the IAPR Governing Board meeting at ICPR 2018. Additionally at ICPR, Strand was awarded best paper of the track on *Biomedical Imaging and Bioinformatics*. Other examples of national committee appointments are that Carolina Wählby serves on the board of Swedish Bioimaging and Ingela Nyström is Vice-Chair of the Council for Research Infrastructure (RFI) within the Swedish Research Council.

During the last few years, we have been active on both national and local level to establish biomedical image analysis and biomedical engineering as more well-supported strategic research areas. The UU Faculties of Science and Technology, Medicine, and Pharmacy have formed the new centre Medtech Science and Innovation together with the UU Hospital. We are looking forward to the increased funding and collaboration opportunities we expect to be the results of this new structure. Our image analysis support for researchers within life science continues to develop with the national SciLifeLab facility within BioImage Informatics, with Carolina Wählby as director and Petter Ranefall as head.

CBA has several elected members of learned socities. Ewert Bengtsson, Gunilla Borgefors, Christer Kiselman, and Carolina Wählby are elected members of the Royal Society of Sciences in Uppsala. Christer Kiselman is elected member and Ingela Nyström is elected as well as board member of the Royal Society of Arts and Sciences of Uppsala. In addition, Ewert Bengtsson, Gunilla Borgefors, and Carolina Wählby are elected members of the Royal Swedish Academy of Engineering Sciences (IVA).

Gunilla Borgefors continued during 2018 as the Editor-in-Chief for the journal Pattern Recognition Letters. Researchers at CBA also serve on several other journal editorial boards, scientific organisation boards, conference committees, and PhD dissertation committees. In addition, we take an active part in reviewing grant applications and scientific papers submitted to conferences and journals.

This annual report is available in printed form as well as on the CBA webpage, see `http://www.cb.uu.se/annual_report/AR2018.pdf`.

1.2 CBA research

The objective of CBA is to carry out research in computerised image analysis and perceptualisation. We are pursuing this objective through a large number of research projects, ranging from fundamental mathematical methods development, to application-tailored development and testing in, for example, biomedicine. We also have interdisciplinary collaboration with the humanities mainly through our projects on handwritten text recognition. In addition, we develop methods for perceptualisation, combining computer graphics, haptics, and image processing. Some of our projects lead to entrepreneurial efforts, which we interpret as a strength of our resaerch.

Our research is organised in many projects of varying size, ranging in effort from a few person months to several person years. There is a lot of interaction between different researchers; generally, a person is involved in several different projects in different constellations with internal and external partners. See Section 5 for details on and illustrations of all our research projects on the diverse topics.

1.3 How to contact CBA

CBA maintains a home-page (`http://www.cb.uu.se/`). There you can find all the annual reports, lists of all publications since CBA was founded in 1988, and other material. Note that our seminar series is open to anyone interested. Please join us on Mondays at 14:15. Staff members have their own homepages, which are found within the UU structure. On these, you can usually find detailed course and project information, etc.

The Centre for Image Analysis (Centrum för bildanalys, CBA) can also be reached by visiting us or by mail to:

Visiting address: Lägerhyddsvägen 2
Polacksbacken, ITC, building 2, floor 1
Uppsala
Postal address: Box 337
SE-751 05 Uppsala
Sweden

2 Organisation

CBA is from 2016 hosted by Department of Information Technology in the Division for Visual Information and Interaction (Vi2). In the beginning, CBA was an independent entity belonging equally to Uppsala University (UU) and the Swedish University of Agricultural Sciences (SLU). However, multiple reorganisations at both universities eventually led to the current situation, where SLU in no longer involved. Even so, CBA is today Sweden's largest single academic group for image analysis, with a strong position nationally and internationally. We have, in fact, grown during the last years. This successful operation shows that centre formations in special cases are worth investing in and preserving long-term. Ingela Nyström headed both Vi2 and CBA 2012–2018.

The Board of the Disciplinary Domain of Science and Technology (TekNat) has a nestablished instruction for CBA with description of objectives, mission, organisation, board, and roles of the director. The board appointed is

- Teo Asplund, Dept. of Information Technology *(PhD student representative)*
- Anders Brun, Dept. of Information Technology
- Elna-Marie Larsson, Dept. of Surgical Sciences; Radiology *(until 2018-06-30)*
- Joel Kullberg, Dept. of Surgical Sciences; Radiology *(from 2018-07-01)*
- Nikolai Piskunov, Dept. of Physics and Astronomy *(Vice-chair)*
- Robin Strand, Dept. of Information Technology
- Carolina Wählby, Dept. of Information Technology *(Chair)*
- Maria Ågren, Dept. of History

The general research subject of CBA and its PhD subject is Computerised Image Analysis, including both theory and applications. More specifically, our areas of particular strength is

- Theoretical image analysis, mainly based on discrete mathematics
- Digital humanities
- Quantitative microscopy
- Biomedical image analysis
- Visualisation and haptics

As image analysis currently is finding widespread application in research in many fields as well as in society in general, we believe there is a need for a centre with a strong application profile, especially in biomedical and handwritten document applications, based on equally strong roots in fundamental image analysis research. After 30 years, CBA has long experience and is more than ever at the research front.

2.1 Finances

After the re-organisation, where CBA became part of the Division of Visual Information and Interaction (Vi2) at the Department of Information Technology, the CBA economy is not separate, but integrated in activities as well as organisation. Hence, we report how this is financed as a whole. The total expenditure for Vi2 was 44.3 million SEK for 2018, where the largest cost is personnel. To cover this, 44% came from

external sources, 28% from UU faculty funding, and 21% from undergraduate education. The remaining % were covered by funds balanced from previous years.

Even though CBA as a centre does not organise undergraduate education, Vi2 offers undergraduate education with several courses on Image Analysis, Computer Graphics, and Scientific Visualisation as well as Human-Computer Interaction themes. Most of us teach up to 20%, while some Senior Lecturers teach more.

The economy in Table 1 summarises the overall economy for Vi2 in 2018. The same numbers for income and costs are also given as pie charts in Figure 1. Who finances each project can be ascertained in Section 5, where all projects are listed. Project grants that have been received but not used are directly balanced to next year, and are thus not included in the income–cost tables.

Table 1: Vi2 income and costs for 2018 in kSEK.

Income		**Costs**	
UU	12214	Personnel	29960
UU undergraduate education	9098	Equipment	366
Governmental grants[1]	14272	Operating expenditure[4]	2777
Non-governmental grants[2]	5511	Rent	2023
Contracts[3]	3173	University overhead	13612
Total income	**44268**	**Total cost**	**48738**

[1] The Swedish Research Council, Vinnova, SSF, etc.
[2] Research foundations, EU
[3] Internal invoices from UU and compensations
[4] Including travel and conferences

Within UU, we have financial support from SciLifeLab, the Centre for Interdisciplinary Mathematics (CIM), eSSENCE as well as strategic funds from the IT department as a supplement to the faculty funds

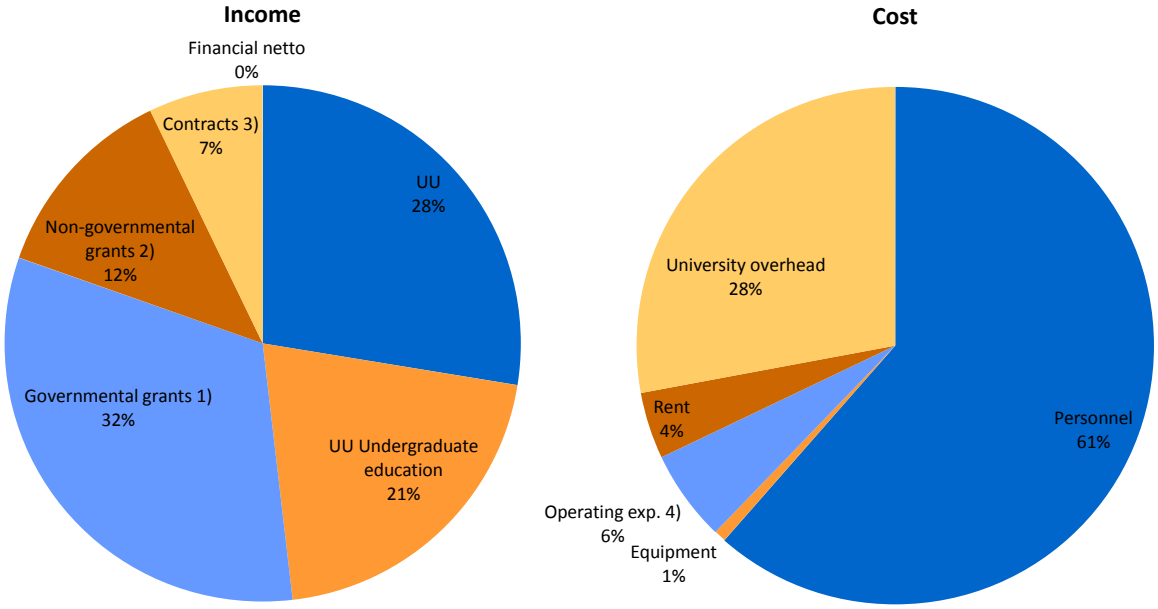

Figure 1: Vi2 income (left) and costs (right) for 2018.

that came to the research program Image analysis and human-computer interaction (so-called FFF). We note that the share of external funding is increasing year by year. The funding agencies are, for example, the Swedish Research Council, the Swedish Foundation for Strategic Research, Vinnova, the European Research Council, and the Riksbankens jubileumsfond. It should be noted that the imbalance between income and cost reflects that during 2018 recruitments of new PhD students and PostDocs on grants received in previous years were made.

2.2 Staff, CBA

People affiliated with CBA and employed by the Department of Information Technology during 2018:

Amin Allalou, PhD, Researcher
Teo Asplund, Graduate Student
Ewert Bengtsson, Professor Emeritus
Karl Bengtsson Bernander, Graduate Student
Ludovic Blache, PhD, PostDoc
Maxime Bombrun, PhD, PostDoc
Gunilla Borgefors, Professor Emerita
Eva Breznik, Graduate Student
Anders Brun, PhD, Researcher
Sukalpa Chanda, PhD, PostDoc
Heung-Kook Choi, Professor, Guest Researcher
Ashis Kumar Dhara, PhD, PostDoc
Anindya Gupta, PhD, PostDoc
Anders Hast, Docent and Excellent Teacher, Senior Lecturer
Raphaela Heil, Graduate Student
Christer O. Kiselman, Professor Emeritus
Anna Klemm, PhD, Bioinformatician
Nadezdha Koriakina, Graduate Student
Joakim Lindblad, PhD, Researcher
Filip Malmberg, Docent, Researcher
Damian Matuszewski, Graduate Student
Fredrik Nysjö, Graduate Student
Ingela Nyström, Professor, Director
Gabriele Partel, Graduate Student
Nicolas Pielawski, Graduate Student
Kalyan Ram Ayyalasomayajula, Graduate Student
Petter Ranefall, Docent, Bioinformatician
Sajith Sadanandan Kecheril, Graduate Student
Stefan Seipel, Professor, UU and University of Gävle
Ida-Maria Sintorn, Docent, Senior Lecturer
Nataša Sladoje, Docent, Senior Lecturer
Leslie Solorzano, Graduate Student
Robin Strand, Professor
Amit Suveer, Graduate Student
Ekta Vats, PhD, PostDoc
Elisabeth Wetzer, Graduate Student
Håkan Wieslander, Graduate Student
Tomas Wilkinson, Graduate Student
Carolina Wählby, Professor
Hangqin Zhang, PhD, PostDoc
Johan Öfverstedt, Graduate Student

The e-mail address of the staff is `Firstname.Lastname@it.uu.se`

Docent degrees from CBA

1. Lennart Thurfjell, 1999, UU
2. Ingela Nyström, 2002, UU
3. Lucia Ballerini, 2006, UU
4. Stina Svensson, 2007, SLU
5. Tomas Brandtberg, 2008, UU
6. Hans Frimmel, 2008, UU
7. Carolina Wählby, 2009, UU
8. Anders Hast, 2010, UU
9. Pasha Razifar, 2010, UU
10. Cris Luengo, 2011, SLU
11. Robin Strand, 2012, UU
12. Ida-Maria Sintorn, 2012, UU
13. Nataša Sladoje, 2015, UU
14. Petter Ranefall, 2016, UU
15. Filip Malmberg, 2017, UU

CBA staff appointed Excellent Teachers

1. Anders Hast 2014, UU

3 Undergraduate education

CBA either supervises or reviews many Master and some Bachelor theses each year, as our subjects are useful in many different industries or for other research groups and are also popular with the students. This year, we were involved in 15 theses, mostly as reviewers. Five were performed in co-operation with industries and nine together with other researchers groups, both needing image analysis applications. CBA is also responsible for or participate in many undergraduate courses, where subjects range from Image Analysis, Computer Graphics, Scientific Visualization, Machine Learning, and Medical Informatics, to Programming (course examiners in bold).

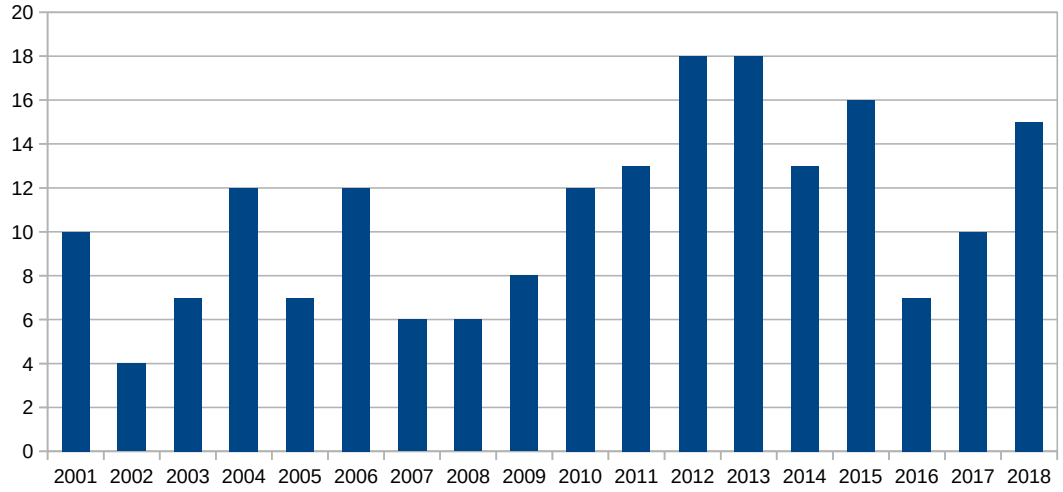

Figure 2: The number of Master theses from CBA 2001-2018.

1. **Computer Assisted Image Analysis II, 10p**
   Nataša Sladoje, Teo Asplund, Carolina Wählby, Robin Strand, Filip Malmberg, Anders Brun, Joakim Lindblad, Anna Klemm, Damian Matuszewski, Kalyan Ram Ayyalasomayajula, Johan Öfverstedt
   Period: 20180101–20180331
2. **Program Design and Data Structures, 20 hp**
   Eva Breznik
   Period: 20180101–20181231
3. **Machine Learning, 10 hp**
   Teo Asplund, Damian Matuszewski
   Period: 20180118–0601
4. **Computer Graphics, 10 hp**
   Anders Hast, Filip Malmberg, Fredrik Nysjö
   Period: 20180320–0529
5. **Scientific Visualization, 5 hp**
   Anders Hast, Fredrik Nysjö, Stefan Seipel, Raphaela Heil
   Period: 20180903 - 1018
6. **Computer Programming I, 5 hp**
   Johan Öfverstedt
   Period: 20180903–1025
7. **Programming, 10 hp**
   Teo Asplund
   Period: 20180903–1220

8. **Maintenance Programming, 5 hp**
   Raphael Heil (Teaching assistant)
   Period: 20180903 - 1017

9. **Medical Informatics, 5 hp**
   Robin Strand, Ingela Nyström
   Period: 20180904–1022

10. **Project in Computational Science, 1TD307, 15 hp**
    Joakim Lindblad, Nataša Sladoje
    Period: 20181001–20190109

11. **Algorithms and Datastructures II, 5 hp**
    Elisabeth Wetzer
    Period: 20181003–20190104

12. **Advanced Software Design, 5 hp**
    Raphael Heil (Teaching assistant)
    Period: 20181030 - 20190118

13. **Computer-Assisted Image Analysis I, 5 hp**
    Filip Malmberg, Joakim Lindblad, Nataša Sladoje, Robin Strand, Eva Breznik, Nicolas Pielawski, Tomas Wilkinson, Elisabeth Wetzer
    Period: 20181101–20190109

14. **Bioinformatics for Masters Students: Getting to grips with gene expression, data mining and image analysis, 1 hp**
    Ida-Maria Sintorn
    Period: 20181115

3.1 Bachelor theses

1. *Date:* 201805
   Image Analysis for Quantification of Cell Interactions
   Student: Valeriia Ladyhina
   Supervisor: Carolina Wählby
   Reviewer: Staffan Johansson, Dept. of Medical Biochemistry and Microbiology, UU
   Publisher: BSc thesis, Molecular Medicine programme at UU
   Abstract: Bone marrow (BM) is a complex of several structured micro-environmental formations that are called niches. These niches include two groups of cells: hematopoietic cells and non-hematopoietic so-called stromal cells. The functions of these niches are diverse and represented by controlling of a pool of hematopoietic stem cells, differentiation of hematopoietic cells and maintenance of immunological memory. However, the composition of different BM niches is not fully understood, due to the complexity of molecular and cellular structure, as well as the lack of suitable histological multiplexing methods. This study represents the development of methods for analysis of images of mice BM sections obtained by multi-epitope-ligand-cartography (MELC) in order to identify cell-cell interactions. The automated CellProfiler pipeline is used for the segmentation of irregular net-like structures of stromal cells and the accuracy of the automated analysis is evaluated in comparison to manual analysis of localization of somata and processes. In addition, we propose a method for automatic evaluation of object colocalization and heterogeneity of distribution of leptin receptor (LpR), BP-1 and VCAM-1 expression in the stromal network and demonstrate the correctness of the designed algorithm. In summary, this approach is suitable for spatial analysis of complex tissue structures.

3.2 Master theses

1. *Date:* 201801
   Designing a lightweight convolutional neural network for onion and weed classification
   Student: Niklas Bäckström
   Supervisor: Lars Asplund, Unibap AB

Reviewer: Carolina Wählby
Publisher: UPTEC F 17050
Abstract: The data set for this project consists of images containing onion and weed samples. It is of interest to investigate if Convolutional Neural Networks can learn to classify the crops correctly as a step in automatizing weed removal in farming. The aim of this project is to solve a classification task involving few classes with relatively few training samples (few hundred per class). Usually, small data sets are prone to overfitting, meaning that the networks generalize bad to unseen data. It is also of interest to solve the problem using small networks with low computational complexity, since inference speed is important and memory often is limited on deployable systems. This work shows how transfer learning, network pruning and quantization can be used to create lightweight networks whose classification accuracy exceeds the same architecture trained from scratch. Using these techniques, a SqueezeNet v1.1 architecture (which is already a relatively small network) can reach 1/10th of the original model size and less than half MAC operations during inference, while still maintaining a higher classification accuracy compared to a SqueezeNet v1.1 trained from scratch ($96.9 \pm 1.35\%$ vs $92.0 \pm 3.11\%$ on 5-fold cross validation)

2. *Date:* 201801
Building a high throughput microscope simulator using the Apache Kafka streaming framework
Student: Lovisa Lugnegård
Supervisor: Andreas Hellander, Dept. of IT
Reviewer: Carolina Wählby
Publisher: UPTEC F, ISSN 1401-5757 ; 18002
Abstract: Today microscopy imaging is a widely used and powerful method for investigating biological processes. The microscopes can produce large amounts of data in a short time. It is therefore impossible to analyse all the data thoroughly because of time and cost constraints. HASTE (Hierarchical Analysis of Temporal and Spatial Image Data) is a collaborative research project between Uppsala University, AstraZeneca and Vironova which addresses this specific problem. The idea is to analyse the image data in real time to make fast decisions on whether to analyse further, store or throw away the data. To facilitate the development process of this system a microscope simulator has been designed and implemented with large focus on parameters relating to data throughput. Apart from building the simulator the framework Apache Kafka has been evaluated for streaming large images. The results from this project are both a working simulator which shows a performance similar to that of the microscope and an evaluation of Apache Kafka showing that it is possible to stream image data with the framework.

3. *Date:* 201804
Image analysis tool for geometric variations of the jugular veins in ultrasonic sequences - Developement and Evaluation
Student: Arvid Westlund
Supervisor: Petter Holmlund, Dept. of Radiation Sciences, Umeå University
Reviewer: Gunilla Borgefors
Partner(s): Jan Malm and Anders Eklund, Dept. of Biomedical Engineering, Umeå University
Publisher: Uppsala University, UPTEC F 18007
Abstract: The aim of this project is to develop and perform a first evaluation of a software, based on the active contour, which automatically computes the cross-section area of the internal jugular veins through a sequence of 90 ultrasound images. The software is intended to be useful in future research in the field of intra cranial pressure and its associated diseases. The biomechanics of the internal jugular veins and its relationship to the intra cranial pressure is studied with ultrasound. It generates data in the form of ultrasound sequences shot in seven different body positions, supine to upright. Vein movements in cross section over the cardiac cycle are recorded for all body positions. From these films, it is interesting to know how the cross-section area varies over the cardiac cycle and between body positions, in order to estimate the pressure. The software created was semi-automatic, where the operator loads each individual sequence and sets the initial contour on the first frame. It was evaluated in a test by comparing its computed areas with manually estimated areas. The test showed that the software was able to track and compute the area with a satisfactory accuracy for a variety of sequences. It is also faster and more consistent than manual measurements. The most difficult sequences to track were small vessels with narrow geometries, fast moving walls, and blurry edges. Further development is required to correct a few bugs in the algorithm. Also, the improved algorithm should be evaluated on a larger sample of sequences before using it in research.

4. **Groupwise whole-body MR image registration guided by zero-average volume changes**
   Date: 201805
   Student: Martino Pilia
   Supervisor: Joel Kullberg, Dept. of Surgical Sciences
   Reviewer: Robin Strand
   Publisher: UPTEC IT 18015
   Abstract: Imiomics (imaging-omics) is an image analysis technique developed at Uppsala University that allows statistical analysis of whole-body image data from scans of multiple subjects. The process requires a common coordinate system for all the images, currently obtained by manually selecting a subject from the cohort with average anatomical parameters, to which all the subjects are registered.While a wide collection of groupwise registration methods has been proposed in the field of neuroimaging, the different nature of whole-body image registration and its specific problems do not allow their direct application without further adaption. This work proposes an approach that refines a manual initial choice of the reference, warping it with a deformation field that brings the voxel-wise average volume change associated to the mapping of all the images in the cohort to zero. A method for the generation of deformation fields with known volume changes was implemented, and experiments on synthetic and real data were performed in order to evaluate the impact of this approach on the quality of the registration. Results on fat/water separated whole-body magnetic resonance (MR) images show a decrease of the registration error of about 8% in terms of inverse consistency and mean squared error.

5. *Date:* 201806
   Web application for visualization of large bacterial growth image data
   Student: Julia Lundgren
   Supervisor: Amin Allalou
   Reviewer: Carolina Wählby
   Publisher: ISSN: 1401-2138, UPTEC BIO** ***
   Abstract: The aim of this master thesis was to facilitate the visualization of Q-lineaś high- resolution bacterial growth image data. The primary request was a tool for faster and smoother zoom and navigation within the images. A web application was developed for this purpose. By keeping a continuous communication with the users all the way from planning to evaluation of the finished product, the project managed to identify the major problems experienced by the users and implement solutions that solved them. Some of the main issues that were addressed were long time for loading the images, lack of overview during visualization and scattered result and metadata. The application was built in JavaScript with Node.js and Express.js, the open source JavaScript viewer OpenSeadragon was used for visualization of high-resolution images and MongoDB was used as database to store experiment information.

6. *Date:* 201806
   Interpretation of meteorological data in a GIS-based simulation environment
   Student: Charlotta Jaunviksna
   Supervisor: Petter Bivall, Swedish Defence Research Agency
   Reviewer: Stefan Seipel
   *Publisher:*UPTEC F, ISSN 1401-5757 ; 18034
   Abstract: The main object of this thesis was to investigate the possibility of integrating a visualization of meteorological data in an interactive GIS-based simulation environment. The work was carried out at at the Swedish Defence Research Agency (FOI). Focus was put on meteorological parameters affecting radar signals. The task consisted of mapping of existing visualization methods used for weather and investigating suitable data sources and structures. Furthermore, the work was implemented in Java and NASA's API WorldWind. The result was evaluated through a semi-structured interview held with a focus group at FOI. The data chosen was model data describing precipitation rate from the European organization ECMWF's open database. A software module was developed to decode and structure the data which were later fetched and visually represented using symbols from the MIL-STD-2525 standard. The main conclusion drawn from the interview was that the proposed implementation was suitable for some scenarios. Alternative visualisations have to be developed from which the user will be able to choose from. The data module serves together with the symbols as a good start for further visualizaiton work.

7. *Date:* 201806
   A Metric for Perceptual Distance between Bidirectional Reflectance Distribution Functions

Student: David Ryman
Supervisor: Jacob Self, Precisit.
Reviewer: Filip Malmberg
Publisher: ISSN 1401-5749, UPTEC IT
Abstract: Bidirectional reflectance distribution functions (BRDFs) are used in the rendering equation to simulate light reflections in physically realistic way. A reflectance metric defines distances between all possible pairs of BRDFs. Deriving a perceptually based reflectance metric which accurately predicts how humans perceive differences in the reflective properties of surfaces has been explicitly state as an open research for over a decade. This work builds upon previous insights on the problem and combines them with new idea, defining the new Projective Area Weighted CIELAB (PAWCIELAB) metric. To evaluate the performance of the PAWCIELAB metric, it was experimentally tested against an existing state-of-the-art metric, and the results indicate that the PAWCIELAB metric is the better reflectance metric with respect to human perception. The PAWCIELAB metric is useful in any application involving humans and light reflections, for example: 3D graphics applications and quality assurance of reflectance properties in a product. There is also room for improvement and extensions of the PAWCIELAB metric, which is described in the future work section at the end of this report.

8. *Date:* 201806
Image Registration for Improved Analysis of Multi-Parametric MRI of Chronic Kidney Disease
Student: Matilda Jonsson
Supervisor: Joel Kullberg, Dept. of Surgical Sciences
Reviewer: Robin Strand
Publisher: UPTEC X 18 027
Abstract: Chronic kidney disease (CKD), a global health problem with 10% global prevalence and 14% prevalence in the US, is causing major medical costs. The renal glomerular filtration rate is decreased and the renal function is affected in patients being diagnosed having CKD.

   Magnetic resonance imaging (MRI) allows non-invasive characterisation of tissue. MRI techniques that have been applied in studies of CKD include diffusion weighted imaging (DWI), perfusion measurements, T1-mapping and T2*-mapping, also known as blood-oxygen-level-dependent (BOLD). These methods have been found promising in assessing structural and functional variations associated to CKD.

   In this work, image registration was applied to series of source images for DWI and T1-mapping scans from 29 CKD patients and 20 healthy volunteers. Registration was applied within image series and kidney-wise to reduce motion artefacts, primarily caused by respiration during the image acquisition. An affine 3D image registration algorithm was customised to the DWI image series and a rigid 2D image registration algorithm was applied to the T1-mapping series. Evaluation was made visually and numerically, including mean squared error measure (MSE) of curve fitting models. Both methods demonstrated improvements in correction for motion after image registration. Images after registration had reduced MSE, especially around the edges of the kidneys, indicating that effects of motion in head-to-feet direction was reduced. Furthermore, cortex median signal measurements were decreased after registration for DWI images, $\sim$6,4% for healthy subjects and $\sim$5,2% for CKD patients, while no significant changes were found in the T1-mapping results in the comparison of healthy subjects and CKD patients.

9. *Date:* 201807
Generalized counting of tool inserts on different carriers
Student: Oskar Nilsson
Supervisor: Fredrik Engberg, Sandvik Coromant
Reviewer: Carolina Wählby
Publisher: UPTEC F 18022
Abstract: This thesis describes the theory and method to count tool inserts on different carriers. This is done by using a 3D camera that gives a set of (x,y,z) points. By analyzing the z-value we can draw conclusions of how many inserts are present in the picture.
In the production of tool inserts, one is afraid that different orders get mixed up. One way to identify this is to count every insert in a specific part of the production and compare that number to how many inserts it should be. If it differs, we have identified either a surplus of inserts - orders are mixed up, or a shortage of inserts. Which means that some inserts have dissapeared. With these numbers we can identify in which operations of production these mistakes happen and try to correct them.

The solution is based on parameters that are easily obtained from the order data. I have developed a method to estimate how accurate the counting is based on mean values of the z-value. The accuracy is 100% as long as the 3D image is relatively free from noise. If it is not, we will detect that and grab a new image with different exposure time for example.

10. *Date:* 201807
Study and Analysis of Convolutional Neural Networks for Pedestrian Detection in Autonomous Vehicles
Student: Louise Augustsson
Supervisor: Detlef Scholle, Alten Sverige AB
Reviewer: Carolina Wählby
Publisher: UPTEC F, ISSN 1401-5757 ; 18020
Abstract: The automotive industry is heading towards more automation. This puts high demands on many systems like Pedestrian Detection Systems. Such systems need to operate in real time with high accuracy and in embedded systems with limited power, memory resources and compute power. This in turn puts high demands on model size and model design. Lately Convolutional Neural Networks (ConvNets) have dominated the field of object detection and therefore it is reasonable to believe that they are suited for pedestrian detection as well. Therefore, this thesis investigates how ConvNets have been used for pedestrian detection and how such solutions can be implemented in embedded systems on FPGAs (Field Programmable Gate Arrays). The conclusions drawn are that ConvNets indeed perform well on pedestrian detection in terms of accuracy but to a cost of large model sizes and heavy computations. This thesis also comes up with a design proposal of a ConvNet for pedestrian detection with the implementation in an embedded system in mind. The proposed network performs well on pedestrian classification and the performance looks promising for detection as well, but further development is required.

11. **Stochastic based football simulation using data**
Date: 201808
Student: Ricky Cheung
Supervisor: David Sumpter, Dept. of Mathematics
Reviewer: Robin Strand
Publisher: UPTEC F 18052
Abstract: This thesis is an extension of a football simulator made in a previous project, where we also made different visualizations and simulators based on football data. The goal is to create a football simulator based on a modified Markov chain process, where two teams can be chosen, to simulate entire football matches play-by-play. To validate our model, we compare simulated data with the provided data from Opta. Several adjustments are made to make the simulation as realistic as possible. After conducting a few experiments to compare simulated data with real data before and after adjustments, we conclude that the model may not be adequately accurate to reflect real life matches.

12. *Date:* 201808
Improving recall of in situ sequencing by self-learned features and classical image analysis Techniques
Student: Giorgia Milli
Supervisor: Elisa Ficarra, Politecnico di Torino, Italy
Assistant Supervisor: Carolina Wählby, Gabriele Partel
Reviewer: Carolina Wählby
Publisher: Politecnico di Torino, Italy
Abstract: Image-based sequencing method to decode mRNA fragments directly in fixed tissue sam- ples allows to carry out the gene expression profile preserving morphological and spatial information of cells and tissues. This approach called in situ sequencing makes it possi- ble to directly visualize, at sub-cellular resolution, where in a tissue sample a given gene is active, to quantify its expression, and to distinguish among many different cell types at the same time. Such information are fundamental to gain a better understanding about tissue and disease development (such as cancer) and cells interplay. Since each gene is composed by a specific sequence of bases, the search is addressed to targeted se- quences which must be decoded over multiple staining and imaging cycles, and retrieved by processing multichannel fluorescent biological images of the analyzed samples. How- ever, signal density, high signal to noise ratio, and microscopeś resolution limits make decoding challenging. The state-of-art approach for signal decoding has led to low signal recall in efforts to maintain high sensitivity. The main issues related to the state-of-art technique concern difficul-

ties in distinguishing signals in more dense regions, the lack of a proper handling for local misalignments among signals belonging to different sequenc- ing cycles and the inability of processing 3D datasets. In this thesis a new approach has been implemented in order to face the state-of-art issues and increase recall at maintained sensitivity. Here signal candidates are included in the first processing steps and provided with their true-signal probability by an opportunely trained classifier. Signal candidates and their probability predictions are then fed to a decoding approach searching for signal candidates across sequencing cycles. Finally, the decoded sequences are provided with a quality measure indicating their reliability based on the classifier probabilities. In order to find the best solution, either a support vector machine and convolutional neural net- work have been tested as classifier. A window-based search has been designed for the sequence decoding. The developed sequence decoding method looks for the optimal paths representing the decoded signal sequences by combining intensity, probability and spatial distance. Multiple quality metrics have been tested to find out which one allowed to obtain the highest signal recall. All the possible combinations of the new proposed pipeline have been evaluated in relation of the state-of-art. Using the support vector machine as classifier has led to a consistent decrease in signal recall (20%) compared to the state-of- art pipeline. On the other hand, using the convolutional neural network has led to an improvement (31%). The obtained results demonstrated an evident advantage in using a classifier based on self-learned features and the need of a sequence decoding approach less dependent on signal probability predictions. The new proposed approach solves all the state-of-art issues and has the potential of significantly improve further analysis of spatial statistics in in situ sequencing experiments.

13. *Date:* 201809
Automatic Image Recomposition
Student: Jakob Andersson
*Supervisors:*Vladimir Curic, Alexis Boucharin
Reviewer: Filip Malmberg
Publisher: UPTEC F, ISSN: 1401-5757
Abstract: This thesis presents a method to perform automatic image improvements, utilizing image analysis techniques and smartphone sensor data. The project includes both the development of an image improvement implementation and a comparison between alternative methods to achieve the improvement. By reading the smartphone's accelerometer data at the time of image capture, the orientation of the phone can be detected and used as a parameter for rotational correction. To make sure that objects of interest are kept and framed correctly within the image, saliency maps and face detection is utilized to pinpoint their exact location.

14. **Building a user interface with MATLAB Guide for MRI data volumes in Imiomics**
Date: 201809
Student: Anna Larsson
Supervisor: Robin Strand
Reviewer: Joel Kullberg, Dept. of Surgical Sciences
Publisher: UPTEC IT 18017
Abstract: In this thesis project, a graphical user interface (UI) was built with the purpose of visualizing MRI data volumes that are used within Imiomics.

Imiomics is an ongoing research project that is a collaboration between several departments at Uppsala University. It involves handling a great number of medical imaging volumes which are whole-body MRI scans. In short, the work started within the Imiomics project might lead to new ways to diagnose certain medical conditions, using scans and image analysis instead of invasive procedures.

The aim of this thesis project has been to create a UI that helps visualize and compare these image volumes to each other. The purpose of the UI is to enable quality control of the processed images and to facilitate nmedical interpretation of large cohort study findings.

The UI was built in MATLAB's development environment for graphical user interfaces, GUIDE. GUIDE is relatively easy to learn, fast to work with, and suitable for making prototypes for UIs containing data that is already handled in MATLAB.

Based on requirements from the users, the UI was divided into two modules with functionality that complement each other: One for studying correlation maps, and one for comparing image volumes before and after performing the image analysis operations in the Imiomics pipeline.

Towards the end of the project, a user test was organized. Members of the research group tested the UI and gave written feedback, and based on their suggestions several improvements were made. All user feedback is summarized in the report.

15. **Water and Fat Image Reconstruction from MRI Raw Multi Coil Data**
Date: 201810
Student: Michael Wijaya Saputra
Supervisor: Jonathan Andersson, Dept. of Surgical Sciences
Reviewer: Robin Strand
Publisher: UPTEC IT 18053
Abstract: In MRI, water and fat signal separation with robust techniques are often helpful in the diagnosis using MRI. Reliable separation of water and fat will help the doctor to get accurate diagnoses such as the size of a tumour. Moreover, fat images can also help in diagnosing the liver and heart condition. To perform water and fat separation, multiple echoes, i.e. measurements of the raw MR signal at different time points, are required. By utilizing the knowledge of the expected signal evolution, it is possible to perform the separation. A main magnetic field is used in MRI. This field is not perfectly homogeneous. Estimating the non-homogeneities is crucial for correcting the separation signal. This thesis used the method of "Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation" (IDEAL). The aims of the thesis are developed a method which reconstruct fat or water MRI images from raw multi-coil image data and evaluate the method's accuracy and speed by comparing with an available, implemented reconstruction method. In particular, the stability to so called swap artefacts will be analysed. Estimated field maps or inhomogeneity fields are one important and essential step, but there exist multiple local minima. To avoid choosing the incorrect minima, the initial estimation of the field map had to be close to the actual field map value. Neighbouring pixels would have a similar field map values, since the inhomogeneity field was smoothly varying. As such, we carried out the combination of IDEAL algorithms with a region growing method. We implemented the method to do the water and fat separation from a raw image consisting of multi-coil data and multi- echo. The proposed method was tested and the region growing method shows a significantly improved separation of water and fat, when compared to the traditional method without region growing.

4 Graduate education

We offer several PhD courses each year, both for our own PhD students and for others needing our expertise as tools. This year, there were seven courses, which is more than usual. There were no PhD examinations this year, but we confidently expect five during 2019.

4.1 Graduate courses

1. **Classical & Modern Papers in Image Analysis, 10 hp**
   Examiner: Nataša Sladoje
   Period: 20180101–1231
   Description: Presentations and discussions of classical or modern papers in image processing. The course is given continuously and organized at CBA. Participants are PhD students at CBA.

2. **Quantitative Imaging in Cell Biology, 5 hp**
   Examiner: Carolina Wählby
   Lecturer(s): Carolina Wählby + participating PhD students
   Period: 20180212–0309
   Description: A reading course focused on how microscopy data is formed and what aspects of the sample preparation and imaging that will influence later extraction of quantitative information from the image data. The participating PhD students took turns in presenting different chapters of the book "Quantitative Imaging in Cell Biology, Editors: Jennifer Waters Torsten Wittmann", followed by discussion a of questions posted by the other students. All students were also asked to write a "thesis chapter style" summary on microcopy techniques related to their own research.

3. **Advanced Electron Microscopy, 5 hp**
   Lecturer: Ida-Maria Sintorn
   Period: 20180212–0309
   Description: The course provided a general introduction to scanning- and transmission electron microscopy. Lectures and labs were dedicated to special electron microscopy and focused ion beam techniques. Lecturers from the Ångström laboratory, the Biomedical Center, the Swedish University of Agricultural Science, the Information Technology Center, Stockholm University and the Geocentrum contributed to this course. The course was an interdisciplinary course, open to participants from all fields where electron microscopy is used. Ida-Maria Sintorn contributed with a lecture and examination task on image processing.

4. **Graph Based Image Processing and Combinatorial Optimization, 3 hp**
   Examiner: Filip Malmberg
   Lecturer(s): Filip Malmberg, Chris Ciesielski
   Period: 20180903–20180926
   Description: Graphs have emerged as a unified representation for image analysis and processing. Many powerful image processing methods have been formulated on pixel adjacency graphs, i.e., a graph whose vertex set is the set of image elements (pixels), and whose edge set is determined by an adjacency relation among the image elements. Due to its discrete nature and mathematical simplicity, this graph based image representation lends itself well to the development of efficient, and provably correct, methods for image processing. In this course, we will give an overview of recent developments in this field.

5. **Deep Learning, 7.5 hp**
   Examiner: Joakim Lindblad
   Period: 20180928–1231
   Description: Seminar style course on the fundamentals of Deep Learning. Participants are presenting chapters of the book, selected texts, or project works.
   Course is given continuously and organized at CBA. Participants are mainly PhD students at CBA.
   Main course literature: "Deep Learning", Goodfellow, Bengio, Courville, 2016.

6. **Digital Image Analysis for Scientific Applications, 8 hp**
   Examiner: Robin Strand
   Lecturer(s): Robin Strand, Mariëlle Jansen,Elisabeth Wetzer, Filip Malmberg, Carolina Wählby, Ida-Maria Sintorn, Anindya Gupta, Anna Klemm

Period: 20181002–1128
Description: This course aimed at giving doctoral students from different disciplines sufficient understanding to solve basic computerized image analysis problems. The course offered an introduction to a number of freely available software tools (CellProfiler, ImageJ and ilastik), preparing the students to start using computerized image analysis in their own research.

7. **Scientific Visualisation, 5 hp**
Examiner: Anders Hast
Lecturer(s): Alexandru C. Telea, Anders Hast, Fredrik Nysjö, Raphaela Heil
Period: 20181126–1130
Description: The Swedish eScience Education graduate course on Scientific Visualisation was held in Uppsala, and about 10 PhD students and 2 staff members of UPPMAX was following the course. The author of the text book Data Visualization: Principles and Practice, prof. Alexandru C. Telea was the main teacher, together with our own teachers.

5 Research

We here make an attempt to list our research activities as a 77 separate projects. Some are quite small, but still distinct, while some are big multi-national projects. In 2018, 22 new projects where started, while a similar number was finished in 2017. In Section 5.1, we list the theoretical projects that are not aimed at a particular application, but take the subject itself forward. In addition to the younger scientists, Prof. Emeritus Christer Kiselman contributes with a number of mathematical projects. However, most of our projects are aimed at specific applications, especially biomedical applications. Another reasonably large application area is Digital Humanities, mainly in the form of analysis of old, handwritten manuscripts. In almost all application projects, we co-operate with experts in the application area. In Section 5.2, we list the medical applications that concerns whole-body or organ investgations, together with surgical planning. We use many different imaging modalities and the tools used here are 3D image analysis, haptics, and visualization. In Section 5.3, we list the projects that investigate cells or proteins using a microscope, often in a time-series. Many of the projects are generated by our participation in the large Swedish co-operation project SciLifeLab, where we provide image analysis support to researchers within life science via our SciLifeLab BioImage Informatics Facility. This is the area where we have the most of the new projects. Also in Section 5.4, we list projects using microscopic images, but here on whole tissues or organisms. The most used model organism is the zebra fish. Also in this area, there are many new projects. Finally in Section 5.5, we list various projects involving humanities. As mentioned above, the largest application is analyzing old, handwritten documents using Image Analysis and Pattern Recognition.

In Section 5.6, we have collected all our research partners, international and national, with whom we had active co-operation, in the form of either a joint project or a joint publication, during 2018.

5.1 Mathematical and geometric theory

1. **Precise image-based measurements through irregular sampling**
   Teo Asplund, Robin Strand, Gunilla Borgefors
   Partner: Cris Luengo-Flagship Biosciences Inc., Westminster, Colorado, USA, Matthew Thurley-Luleå University of Technology, Luleå, Sweden
   Funding: Swedish Research Council
   Period: 20150401–
   Abstract: We develop mathematical morphology on irregularly sampled signals. This is beneficial for a number of reasons: 1. Irregularly sampled signals would traditionally have to be resampled onto the regular grid to allow morphology to be applied, however, such resampling can require interpolating data where the original signal contained large holes. This can lead to very poor performance. 2. The morphological operators depend on suprema/infima in the signal. A regularly sampled signal is likely to miss these. 3. The operators produce lines along which the derivative is not continuous, thereby introducing unbounded frequencies and breaking the correspondence between the sampled signal and the continuous bandlimited one. 4. The structuring element is limited by the sampling grid. We have shown that moving to morphology on irregularly sampled signals can yield results that better approximate continuous morphology, on regularly sampled signals, than the traditional morphological operators, yielding more accurate measurements both in 1D- and 2D grayscale morphology. We have also applied the developed methods to irregularly sampled data, such as 3D point clouds. See Figure 3.

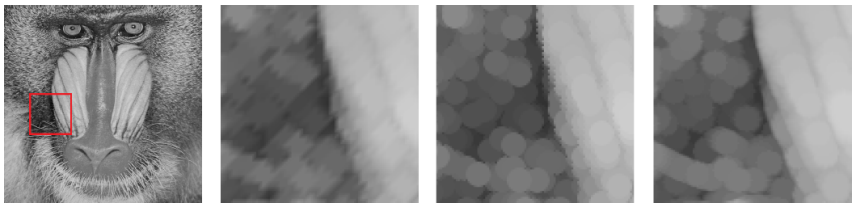

Figure 3: Precise Image-Based Measurements through Irregular Sampling

2. **Feature point descriptors for image stitching**
   Anders Hast, Ida-Maria Sintorn, Damian J. Matuszewski, Carolina Wählby
   Partner: Vironova AB; Dept. of Electronic Computers RSREU, Ryazan, Russia
   Funding: TN-faculty; UU; Science for Life Laboratory
   Period: 20150101–
   Abstract: When microscopy images are to be put together to form a larger image than one field of view, images are stitched together based on key point features in the images. Several methods for matching these images exist, but are often general in the sense that they can handle scale and rotation, which are not present in this particular case. Therefore, these methods are like cracking a nut with a sledge hammer, and we have investigated how simpler and therefore more efficient and also faster methods can be developed and applied for solving this task. Several key point descriptors have been investigated that are based on new sampling strategies and also new ways of combining these samples, using for instance elements of the Fourier transform, instead of histograms of gradients etc. During 2018, a paper entitled ”A Fast Fourier based Feature Descriptor and a Cascade Nearest Neighbour Search with an Efficient Matching Pipeline for Mosaicing of Microscopy Images” was published in Pattern Recognition and Image Analysis, 28(2). `https://doi.org/10.1134/S1054661818020050`. See Figure 4.

3. **Digital distance functions and distance transforms**
   Robin Strand, Gunilla Borgefors
   Partner: Benedek Nagy - Dept. of Computer Science, Faculty of Informatics, University of Debrecen, Hungary; Nicols Normand, IRCCyN - University of Nantes, France
   Funding: TN-faculty, UU
   Period: 19930901–
   Abstract: The distance between any two grid points in a grid is defined by a distance function. In this project, weighted distances have been considered for many years. A generalization of the weighted distances is obtained by using both weights and a neighborhood sequence to define the distance function.

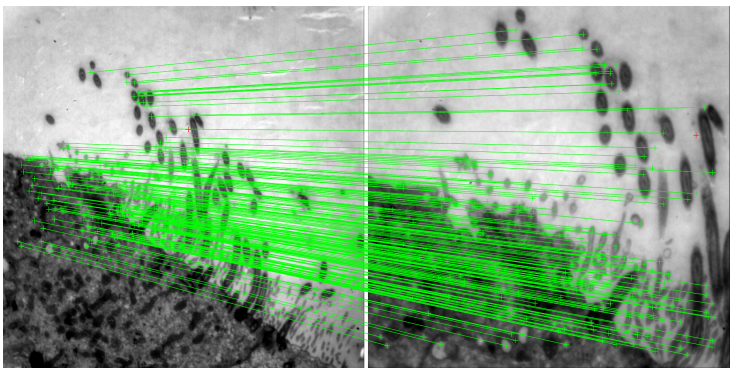

Figure 4: Feature Point Descriptors for Image Stitching

The neighborhood sequence allows the size of the neighborhood to vary along the paths. A manuscript on distance functions based on multiple types of weighted steps combined with neighborhood sequences has been produced in collaboration with Strand, Nagy and Normand. The manuscript holds (mainly theoretical) results on for example metricity and parameter optimization. The figure illustrates the shapes of disks with different number of weights, when the optimization criterion is roundness in the Euclidean sense. See Figure 5.

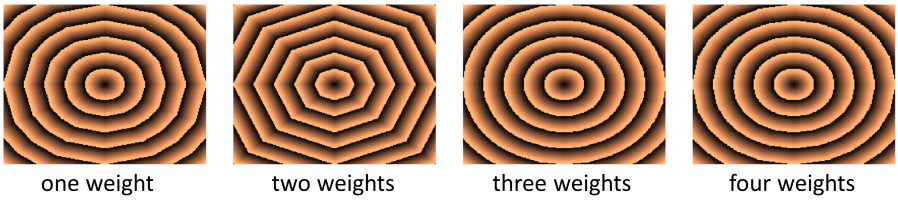

Figure 5: Digital Distance Functions and Distance Transforms

4. **Image enhancement based on energy minimization**
   Nataša Sladoje, Joakim Lindblad, Amit Suveer, Ida-Maria Sintorn, Anindya Gupta
   Partner: Buda Bajić, Faculty of Engineering, University of Novi Sad, Serbia
   Funding: Swedish Governmental Agency for Innovation Systems (VINNOVA); TN-faculty, UU; Swedish Research Council
   Period: 201409—-
   Abstract: A common approach to solve the ill-posed problem of image restoration is to formulate it as an energy minimization problem. A priori knowledge is, typically, included through a regularization component. Total variation is among most popular approaches, due to simplicity and generally good performance. We have studied performance of energy minimization based restoration for enhancing images degraded with blur and different types of noise. A comparative study of performances of different denoising methods on TEM images of cilia was presented at IEEE International Symposium on Biomedical Imaging - ISBI 2018. The title of the paper was “Denoising of Short Exposure Transmission Electron Microscopy Images for Ultrastructural Enhancement”. See Figure 6.

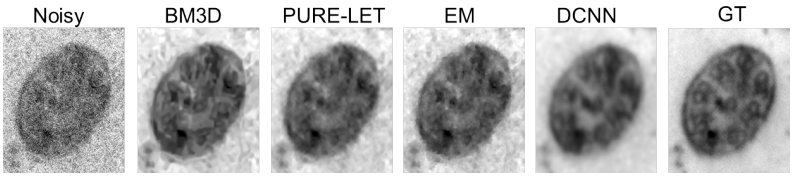

Figure 6: Image Enhancement Based on Energy Minimization

5. **Regional orthogonal moments for texture analysis**
   Ida-Maria Sintorn
   Partner: Vironova AB; Sven Nelander, Dept. of Immunology, Genetics and Pathology, UU
   Funding: Swedish Research Council
   Period: 201501—-
   Abstract: The purpose of this project is to investigate and systematically characterize a novel approach for texture analysis, which we have termed Regional Orthogonal Moments (ROMs). The idea is to combine the descriptive strength and compact information representation of orthogonal moments with the well-established local filtering approach for texture analysis. We will explore ROMs and quantitative texture descriptors derived from the ROM filter responses, and characterize them with special consideration to noise, rotation, contrast, scale robustness, and generalization performance, important factors in applications with natural images. In order to do this we will utilize and expand available image texture datasets and adapt machine learning methods for microscopy image prerequisites. The two main applications for which we will validate the ROM texture analysis framework are viral pathogen detection and identification in MiniTEM images, and glioblastoma phenotyping of patient specific cancer stem cell cultures for disease modeling and personalized treatment. During 2016, a paper comparing and evaluating several ROM filter banks on a number of different texture datasets was submitted and is awaiting the review response.

6. **Distance measures between images based on spatial and intensity information, with applications in biomedical image processing**
   Johan Öfverstedt, Nataša Sladoje, Joakim Lindblad
   Partner: Ida-Maria Sintorn, Vironova AB
   Funding: Swedish Governmental Agency for Innovation Systems (VINNOVA), TN-faculty
   Period: 20170101–
   Abstract: Many approaches to solving fundamental image analysis problems, such as template matching, image registration, classification and image retrieval are based on some numeric measure of distance (or similarity) between images. This project is focused on a family of such distance measures which are based on the combination of intensity and spatial information. We have studied the distance measures in the context of affine image registration, developing a powerful, symmetric, intensity interpolation-free registration framework which exhibits excellent performance with large regions of convergence enabling successful local optimization. This work has resulted in the paper "Fast and Robust Symmetric Image Registration Based on Intensity and Spatial Information". Our next aim is to extend the framework to support deformable transformation models and multi-modal imaging scenarios. Another outcome of this project is the paper "Stochastic Distance Transform", which introduces a novel type of distance transform which is robust to noise and other spurious structures. Presentations related to the project includes oral presentations at SSBA2018, in Stockholm, on the topic of "Distance Between Vector-valued Images based on Intersection Decomposition with Applications in Object Detection", and at NEUBIAS2018, in Szeged, on the topic of "Improved Distance Measures Between Images and their Performance in Biomedical Applications". See Figure 7.

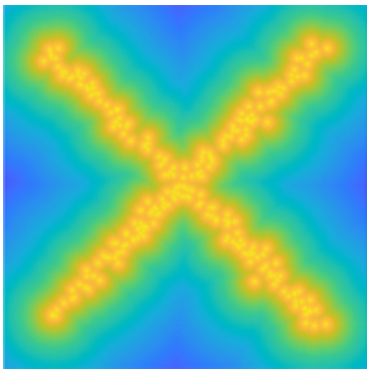

Figure 7: Distance Measures Between Images Based on Spatial and Intensity Information, with Applications in Biomedical Image Processing

7. **The mimimum barrier distance**
   Robin Strand, Filip Malmberg
   Partner: Punam K. Saha, Dept. of Electrical and Computer Engineering and the Dept. of Radiology, University of Iowa, IA, USA; Krzysztof C. Ciesielski, Dept. of Mathematics, West Virginia University, Morgantown, WV, USA; Dept. of Radiology, MIPG, University of Pennsylvania, PA, USA; Stan Sclaroff, Dept. of Computer Science, Boston University, USA; Jianming Zhang, Adobe Research, San Jose, USA
   Funding: TN-Faculty, UU
   Period: 201103–
   Abstract: This project studies the minimum barrier distance (MBD), given by the difference between the maximum and minimum values that has to be passed to go from one point to another, and the related Boolean Map Distance (BMD). Theoretical properties as well as efficient computational solutions for the MBD and BMD have been developed. During 2018, Filip Malmberg, together with Jianming Zhang and Stan Sclaroff, wrote a book for Springer Verlag on estimating visual saliency using the MBD and BMD. The book is scheduled for publication in january 2019. See Figure 8.

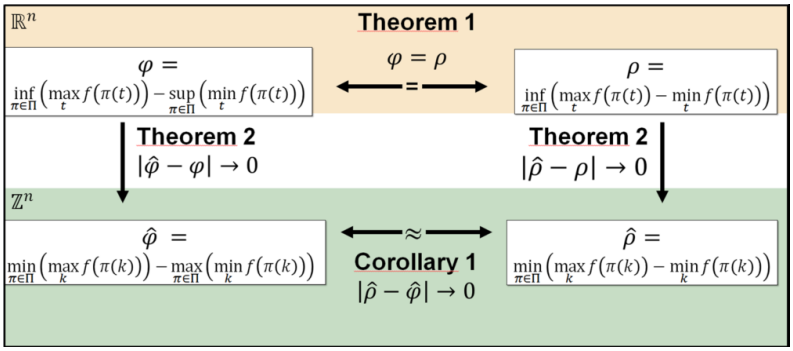

Figure 8: The Mimimum Barrier Distance

8. **Robust learning of geometric equivariances**
   Karl Bengtsson Bernander, Nataša Sladoje, Joakim Lindblad
   Funding: WASP (Wallenberg AI, Autonomous Systems and Software Program)
   Period: 201809–
   Abstract: The proposed project builds on, and extends recent works on Geometric deep learning and aims at combining it with Manifold learning, to produce truly learned equivariances without the need for engineered solutions and maximize benefits of shared weights (parameters to learn). A decrease of the number of parameters to learn leads to increased performance, generalizability and reliability (robustness) of the network. An additional gain is in reducing a risk that the augmented data incorporates artefacts not present it the original data. A typical example is textured data, where interpolation performed in augmentation by rotation and scaling unavoidably affects the original texture and may lead to non-reliable results. Reliable texture-based classification is, on the other hand, in many cases of high importance in biomedical applications. This project is conducted within AI-Math track of WASP –the Wallenberg Artificial Intelligence, Autonomous Systems and Software Program, a major Swedish national initiative for strategically motivated basic research, education and faculty recruitment. In 2018 we have performed a literature study to identify existing solutions and evaluate their theoretical properties and performance. We will proceed with designing solutions aimed at addressing shortcomings of existing models. We have also attended WASP Winter conference in Gothenburg. See Figure 9.

9. **Efficient isosurface rendering for visualization**
   Fredrik Nysjö, Filip Malmberg, Ingela Nyström
   Funding: TN Faculty, UU
   Period: 201801–
   Abstract: Efficient real-time rendering of isosurfaces in large volume datasets can be a challenge, especially for virtual reality applications that require low latency and high update rates. We developed an efficient hybrid rendering method, RayCaching, that combines rasterisation and raycasting to amortise the cost of

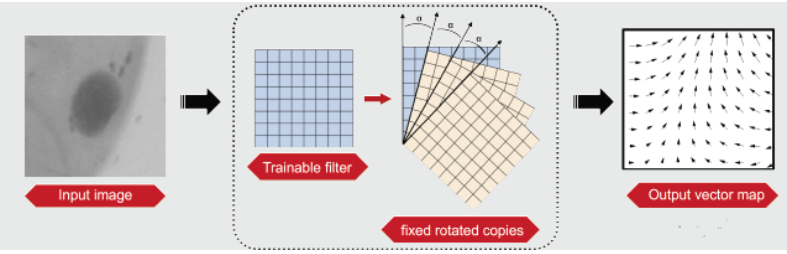

Figure 9: Robust learning of geometric equivariances

rendering a volume over several frames. The work was presented at SSBA 2018, and has been submitted for publication. See Figure 10.

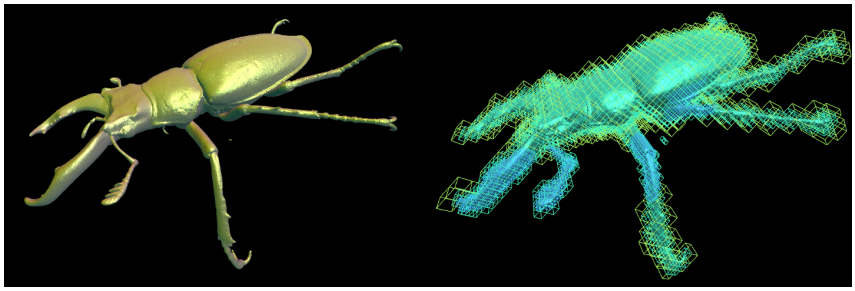

Figure 10: Efficient isosurface rendering for visualization

10. **COMULIS (Correlated Multimodal Imaging in Life Sciences) - COST Action 17121**
Nataša Sladoje, Joakim Lindblad
Partner: COMULIS network with 150 members from 35 countries
Funding: EU Framework Programme Horizon 2020
Period: 20181012–
Abstract: COMULIS is a EU funded COST Action that aims at fueling urgently needed collaborations in the field of correlated multimodal imaging (CMI), promoting and disseminating its benefits through showcase pipelines, and paving the way for its technological advancement and implementation as a versatile tool in biological and preclinical research. CMI combines two or more imaging modalities to gather information about the same specimen and to create a composite view of the sample with multidimensional information about its macro-, meso- and microscopic structure, dynamics, function and chemical composition. No single imaging technique can reveal all these details; CMI is the only way to understand biomedical processes and diseases holistically. CMI relies on the joint multidisciplinary expertise from biologists, physicists, chemists, clinicians and computer scientists, and depends on coordinated activities and knowledge transfer between academia and industry, and instrument developers and users. We have been actively participating in different activities organized within this recently initiated and rapidly growing network. Sladoje is engaged in the COMULIS Core Group as a Leader of WG4 (Correlation Software), and Sladoje and Lindblad are managing committee members. See Figure 11.

11. **Complex convexity**
Christer O. Kiselman
Funding: Université de Nice 1967-10-01 — 1968-09-30; Uppsala University 1968-10-01 — 2006-04-30.
Period: 19671001–
Abstract: A bounded open set with boundary of class C^1 which is locally weakly lineally convex is weakly lineally convex, but, as shown by Yurii Zelinskii, this is not true for unbounded domains. We construct explicit examples, Hartogs domains, showing this. Their boundary can have regularity $C^{1,1}$ or C^∞. Obstructions to constructing smoothly bounded domains with certain homogeneity properties are presented. A current activity is a study of one-sided regularity of subsets of $\mathbf{R}^n$ or $\mathbf{C}^n$. Preliminary results on this kind of regularity were presented at a conference on 2015 September 16. There are several publications in this

Figure 11: COMULIS (Correlated Multimodal Imaging in Life Sciences) - COST Action 17121

project. The latest publication appeared in March 2016 (16-1). A manuscript was submitted in September 2018 and is now under consideration for possible publication in Poland. Advisors: Jan Boman, Ragnar Sigurdsson, Mats Andersson.

12. **Discrete convolution equations**
Christer O. Kiselman
Partner: Advisors: Jan Boman, Ragnar Sigurdsson
Period: 20120111–
Abstract: We study solvability of convolution equations for functions with discrete support in $mathbf R^n$, a special case being functions with support in the integer points. The more general case is of interest for several grids in Euclidean space, like the body-centred and face-centered tesselations of three-space, as well as for the non-periodic grids that appear in the study of quasicrystals. The theorem of existence of fundamental solutions by de Boor, Höllig & Riemenschneider is generalized to general discrete supports, using only elementary methods. We also study the asymptotic growth of sequences and arrays using the Fenchel transformation. Estimates using the Fourier transformation have been studied. Now duality of convolution will be investigated. A study of quasicrystals is part of this project.

13. **How to best fold a triangle**
Christer O. Kiselman
Partner: Bo Senje, Högskolan i Halmstad
Funding: Uppsala University 2005 — 2006-04-30
Period: 200504—-
Abstract: We fold a triangle once along a straight line and study how small the area of the folded figure can be. It can always be as small as the fraction $2-\sqrt{2}$ of the area of the original triangle. This is best possible: For every positive number ε there are triangles that cannot be folded better than $2-\sqrt{2}-\varepsilon$.

14. **Elements of digital geometry, mathematical morphology, and discrete optimization**
Christer O. Kiselman
Partner: Hania Uscka-Wehlou, Shiva Samieinia, Adama Arouna Koné.
Period: 20020111–
Abstract: A book on fundamentals of three related fields of knowledge: digital geometry, mathematical morphology, and discrete optimization.

15. **Convexity of marginal functions in the discrete case.**
Christer O. Kiselman
Partner: Shiva Samieinia, Intercard
Period: 201001–
Abstract: We define, using difference operators, classes of functions defined on the set of points with integer coordinates which are preserved under the formation of marginal functions. The duality between classes of functions with certain convexity properties and families of second-order difference operators plays an important role and is explained using notions from mathematical morphology.

16. **Existence of continuous right inverses to linear mappings in elementary geometry**
Christer O. Kiselman
Partner: Erik Melin, Comsol AB
Period: 20050908–
Abstract: A linear mapping of a compact convex subset of a finite-dimensional vector space always possesses a right inverse, but may lack a continuous right inverse even if the set is smoothly bounded. Examples showing this are given, as well as conditions guaranteeing the existence of a continuous right inverse, also for other sets.

17. **Digital hyperplanes**
Christer O. Kiselman
Partner: Adama Arouna Koné, École Normale d'Enseignement Technique et Professionnel (ENETP).
Period: 20100111–
Abstract: Digital planes in all dimensions are studied. The general goal is to generalize to any dimension the results of Kiselman's 2011 paper in Mathematika (11-1).

18. **Mathematical concepts and their linguistic expression in a multicultural setting**
Christer O. Kiselman
Partner: Project manager: Hania Uscka-Wehlou. Partners: Christer O. Kiselman, Adama Arouna Koné, Fanja Rakontondrajao, Xiaoqin Wang. Advisors: Lars Mouwitz, Amites Rasho, Shiva Samieinia.
Period: 20160401–
Abstract: To study the relation between mathematical concepts and their expression in several languages. Special attention is devoted to the use of non-native languages.

5.2 Medical image analysis, diagnosis and surgery planning

19. **Imiomics - Large-scale analysis of medical volume images**
Robin Strand, Filip Malmberg, Eva Breznik
Partner: Joel Kullberg, Håkan Ahlström, Dept. of Surgical Sciences
Funding: Faculty of Medicine, UU; VR grant 2016-01040; AstraZeneca
Period: 201208–
Abstract: In this project, we mainly process magnetic resonance tomography (MR) images. MR images are very useful in clinical use and in medical research, e.g., for analyzing the composition of the human body. At the division of Radiology, UU, a huge amount of MR data, including whole body MR images, is acquired for research on the connection between the composition of the human body and disease. To compare volume images voxel by voxel, we develop a large scale analysis method, which is enabled by image registration methods. These methods utilize, for example, segmented tissue and anatomical landmarks. Based on this idea, we have developed Imiomics (imaging omics) – an image analysis concept, including image registration, that allows statistical and holistic analysis of whole-body image data. The Imiomics concept is holistic in three respects: (i) The whole body is analyzed, (ii) All collected image data is used in the analysis and (iii) It allows integration of all other collected non-imaging patient information in the analysis. During 2018, the registration method was improved. Also, manuscripts on correlations to non-imaging parameters in the POEM cohort and anomaly detection in oncology were produced. See Figure 12.

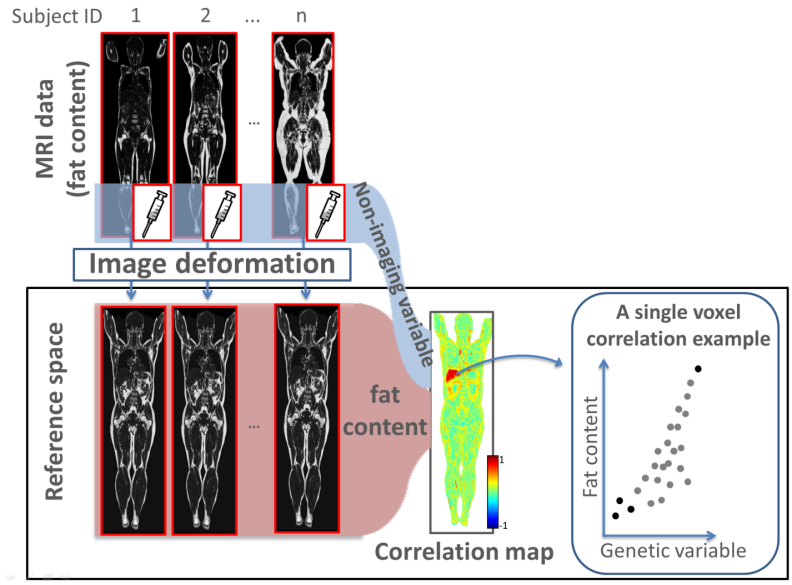

Figure 12: Imiomics - Large-Scale Analysis of Medical Volume Images

20. **Interactive deep learning segmentation for decision support in neuroradiology**
Ashis Kumar Dhara, Robin Strand, Filip Malmberg
Partner: Johan Wikström and Elna-Marie Larsson, Dept. of Surgical Sciences, Radiology, UU
Funding: Swedish Research Council
Period: 20150501–
Abstract: Many brain diseases can damage brain cells (nerve cells), which can lead to loss of nerve cells and, secondarily, loss of brain volume. Technical imaging advancements allow detection and quantification of very small tissue volumes in magnetic resonance (MR) neuroimaging. Due to the enormous amount of information in a typical MR brain volume scan interactive tools for computer aided analysis are absolutely essential for this task. Available interactive methods are often not suited for this problem. Deep learning by convolution neural networks has the ability to learn complex structures from training data. We develop, analyze and evaluate interactive deep learning segmentation methods for quantification and treatment response analysis in neuroimaging. Interaction speed is obtained by dividing the segmentation procedure into

an offline pre-segmentation step and an on-line interactive loop in which the user adds constraints until satisfactory result is obtained. The overarching aim is to allow detailed correct diagnosis, as well as accurate and precise analysis of treatment response in neuroimaging, in particular in quantification of intracranial aneurysm remnants and brain tumor growth. In 2018, conference papers were presented at the BraTS workshop at MICCAI and at the ICPR conference, at which a best paper award was received. See Figure 13.

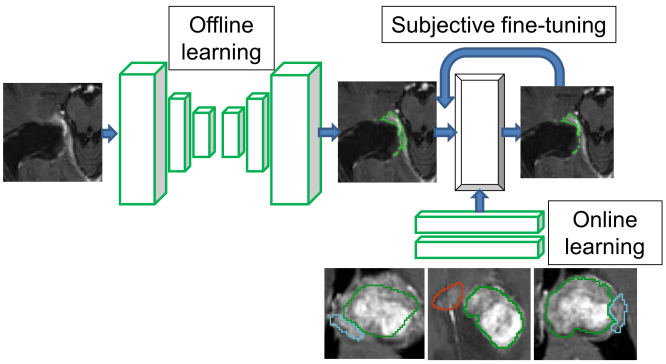

Figure 13: Interactive deep learning segmentation for decision support in neuroradiology

21. **Interactive segmentation and analysis of medical images**
Filip Malmberg, Robin Strand, Ingela Nyström
Partner: Joel Kullberg, Håkan Ahlström
Funding: TN Faculty, UU
Period: 201106–
Abstract: Three-dimensional (3D) imaging technique such as computed tomography (CT) and magnetic resonance imaging (MRI) are now routinely used in medicine. This has lead to an ever increasing flow of high-resolution, high-dimensional, image data that needs to be qualitatively and quantitatively analyzed. Typically, this analysis requires accurate segmentation of the image. At CBA, we have been developing powerful new methods for interactive image segmentation. In this project, we seek to employ these methods for segmentation of medical images, in collaboration with the Dept. of Surgical Sciences at the Uppsala University Hospital. A publicly available software for interactive segmentation, emphSmartPaint, can be downloaded from `http://www.cb.uu.se/~filip/SmartPaint/`. To date, this software has been downloaded more than 1500 times. During 2018, this software was used for segmentation in several research studies at the Division of Radiology, Dept. of Surgical Sciences, UU. See Figure 14.

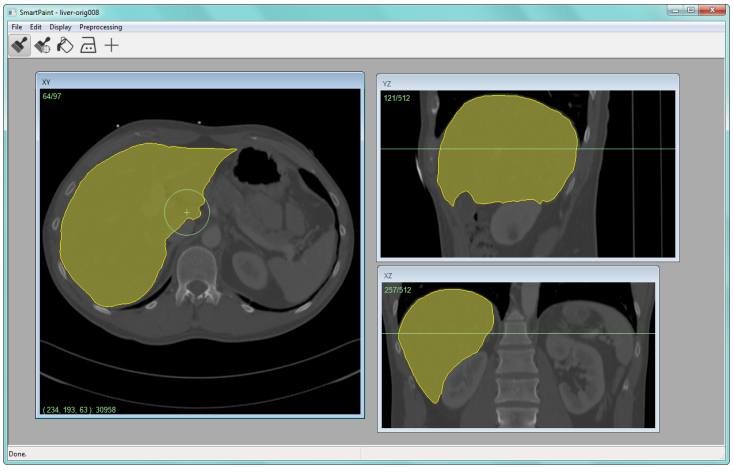

Figure 14: Interactive segmentation and analysis of medical images

22. **Methods for combined MR and radiation therapy equipment**
Robin Strand
Partner: Anders Ahnesjö, David Tilly, Dept. of Immunology, Genetics and Pathology, UU. Samuel Fransson, Håkan Ahlström, Dept. of Surgical Sciences, Radiology, UU
Funding: Vinnova; Barncancerfonden; TN-faculty, UU
Period: 20160601–
Abstract: Uppsala University and Hospital are current investing in image guided radiotherapy. An important component in the strategy is a combined MR scanner and treatment unit, enabling MR imaging right before and during treatment making it possible to adjust for internal motion. In this project, we develop methods for fast detection and quantification of motion for real-time adjustment of the radiation therapy in the combined MR scanner and treatment unit. A manuscript on the use of a motion model in radiation therapy was finalized and submitted. See Figure 15.

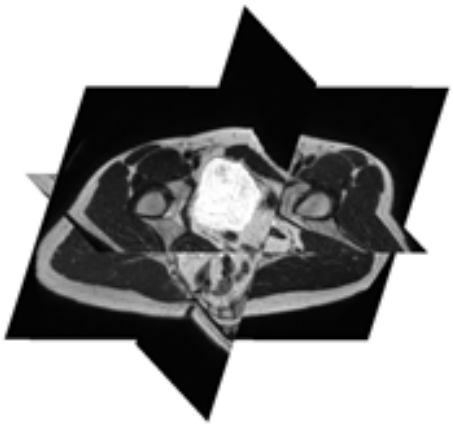

Figure 15: Methods for Combined MR and Radiation Therapy Equipment

23. **Image processing for virtual design of surgical guides and plates**
Fredrik Nysjö, Filip Malmberg, Ingrid Carlbom, Ingela Nyström
Partner: Andreas Thor, Andres Rodriguez Lorenzo, UU Hospital; Daniel Buchbinder, Mt Sinai-Beth Israel Hospital, New York; Pontus Olsson; Savantic AB, Stockholm
Funding: -
Period: 201503–
Abstract: An important part of virtual planning for reconstructive surgery, such as cranio-maxillofacial (CMF) surgery, is the design of customized surgical tools and implants. In this project, we are looking into how distance transforms and constructive solid geometry can be used to generate 3D printable models of surgical guides and plates from segmented computed tomography (CT) images of a patient, and how the accuracy and precision of the modelling can be improved using grayscale image information in combination with anti-aliased distance transforms. Another part of the project is to develop simple and interactive tools that allow a surgeon to create such models. Previously, we implemented a set of design tools for bone reconstruction in our existing surgery planning system HASP. When removing a tumor, a soft tissue defect in the face is also created. To reconstruct this defect, vascularized tissue is usually transplanted from other parts of the body. We developed a method to estimate the shape and dimensions of soft tissue resections from CT data, and a sketch-based interface for the surgeon to paint the resection contour on the patient. We also investigated numerical finite element models to simulate the non-rigid behavior of the soft tissue flap during the reconstruction. See Figure 16.

24. **Coverage model and its application to high precision medical image processing**
Nataša Sladoje, Joakim Lindblad
Partner: Buda Bajić, Slobodan Dražić, Faculty of Technical Sciences, University of Novi Sad, Serbia
Funding: Swedish Governmental Agency for Innovation Systems (VINNOVA); TN-faculty, UU; Swedish Research Council
Period: 201409—-

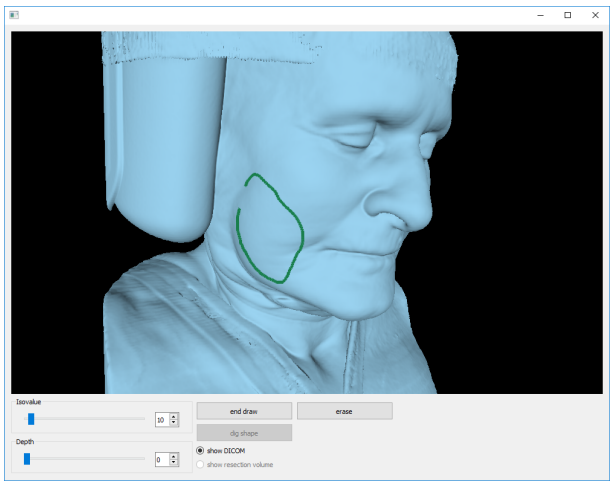

Figure 16: Image processing for virtual design of surgical guides and plates

Abstract: The coverage model, which we have been developing for several years now, provides a framework for representing objects in digital images as spatial fuzzy sets. Membership values indicate to what extent image elements are covered by the imaged components. The model is useful for improving information extraction from digital images and reducing problems originating from limited spatial resolution. We have by now developed methods for estimation of a number of features of coverage representation of shapes and demonstrated their increased precision and accuracy, compared to the crisp representations. Our focus is also on the development of segmentation methods which result in coverage segmentation. During 2018 we have prepared and submitted a journal publication on a coverage segmentation method based on energy minimization, which improves and generalizes our previously published results. The improved method is applicable to blurred and noisy images, and provides coverage segmentation at increased spatial resolution, while preserving thin fuzzy object boundaries. We have suggested a suitable global optimization scheme to address a challenging non-convex optimization problem. We have evaluated the method on several synthetic and real images, confirming its very good performance. Both Buda and Slobodan have started writing their PhD theses, expected to be defended in 2019. See Figure 17.

(a) Original, 54×106 px (b) Sensed, 27×53 px (c) Segmented, 54×106 px

Figure 17: Coverage Model and its Application to High Precision Medical Image Processing

25. **HASP: Haptics-Assisted Surgery Planning**
Ingrid Carlbom, Pontus Olsson, Fredrik Nysjö, Johan Nysjö, Ingela Nyström
Partner: Daniel Buchbinder, Icahn School of Medicine at Mount Sinai, New York, NY, USA; Andreas Thor, Johanna Nilsson, Dept. of Surgical Sciences, Oral & Maxillofacial Surgery, UU Hospital; Andres Rodriguez Lorenzo, Dept. of Surgical Sciences, Plastic Surgery, UU Hospital
Funding: BIO-X 1.5M SEK; Thuréus Stiftelsen: 150 K SEK, TN Faculty, Med Faculty, UU
Period: 201501–
Abstract: The goal of HASP, our haptics assisted surgery planning system, is to put the planning process for complex head and neck surgery into the hands of the surgeon. During 2018, we continued evaluating HASP and the BoneSplit segmentation software both at the Uppsala University Hospital and at Mount Sinai Beth Israel in NYC. At the UU Hospital, a trauma study using HASP was completed during 2018. We evaluated the haptic model in HASP on CT data from a scanned plastic skull and ten retrospective cases. For the plastic skull, we compared accuracy and precision between users, whereas for the retrospective cases we

compared precision only. The study is currently in process of being submitted for publication. At Mount Sinai Beth Israel the focus has been validation of the accuracy of HASP with 12 retrospective cases and eight prospective cases. For each case, we produce a neomandible from resin models generated by a 3D printer of the mandible, cutting guides, fibula, and case-specific plates, that are cut and glued together. CT models of the reconstructed resin neomandible were compared with the HASP neomandible, to verify their correspondence. The study was completed during 2018, and is currently in process of being submitted for journal publication. See Figure 18.

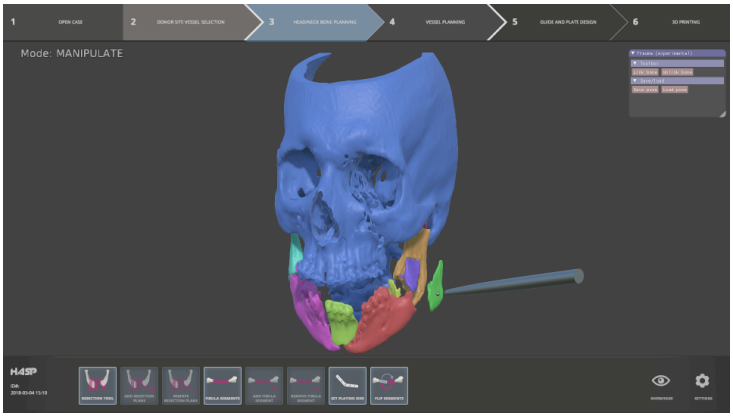

Figure 18: HASP: Haptics-Assisted Surgery Planning

26. **Virtual surgical planning for soft tissue resection and reconstruction**
Ludovic Blache, Filip Malmberg, Fredrik Nysjö, Ingela Nyström, Ingrid Carlbom
Partner: Andres Rodriguez Lorenzo, Andreas Thor, Dept. of Surgical Sciences, UU Hospital
Funding: TN Faculty
Period: 201610–
Abstract: With the increasing use of 3D models and CAD technologies in the medical domain, virtual surgical planning is now frequently used. Most of current solutions focus on bone surgical operations. However, for head and neck oncologic resection, soft tissue ablation and reconstruction are common operations. By removing the tumor, a defect in the face is created consisting of different tissue layers. To reconstruct this defect it is usually needed to transplant vascularized tissue from other parts of the body. In collaboration with the Dept. of Surgical Science at the UU Hospital, we aim at providing a virtual planning solution for such surgical operations. We developed a new method to estimate the shape and dimensions of soft tissue resections. Our approach takes advantage of a simple sketch-based interface, which allows the user to paint the contour of the resection on a patient specific 3D model reconstructed from a CT scan. The volume is then virtually cut and carved following this pattern to provide a 3D model of the resected volume. We then seek to develop a numerical model, based on finite element method, to simulate the non-rigid behavior of the soft tissue flap during the reconstruction process. See Figure 19.

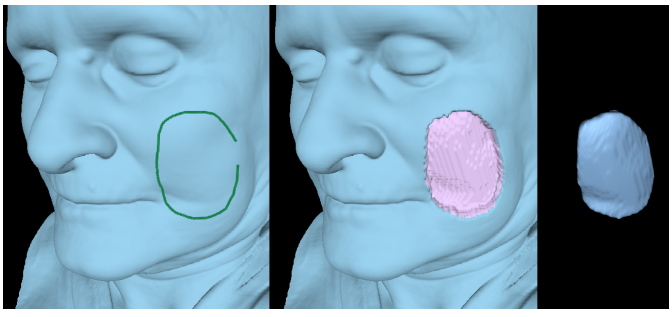

Figure 19: Virtual surgical planning for soft tissue resection and reconstruction

27. **Statistical considerations in whole-body MR analyses**
Eva Breznik, Robin Strand, Filip Malmberg
Partner: Joel Kullberg, Håkan Ahlström, Division of Radiology, Dept. of Surgical Sciences, UU
Funding: Centre for Interdisciplinary Mathematics, CIM, UU; TN-Faculty, UU
Period: 201609–
Abstract: In this project, the focus is on testing and developing methods for Imiomics, to facilitate utilization of whole-body MR images for medical purposes. For inference about activated areas, present in the image, statistical tests are done on series of images at every voxel. This introduces accuracy and reliability problems when drawing conclusions regarding the images or multi-voxel areas as a whole, due to the large number of tests that are considered at the same time. The solution to this problem is a proper multiple testing correction method. Therefore we need to test the existing ones on our specific datasets and explore possibilities of new ones, specifically tailored to our problem. See Figure 20.

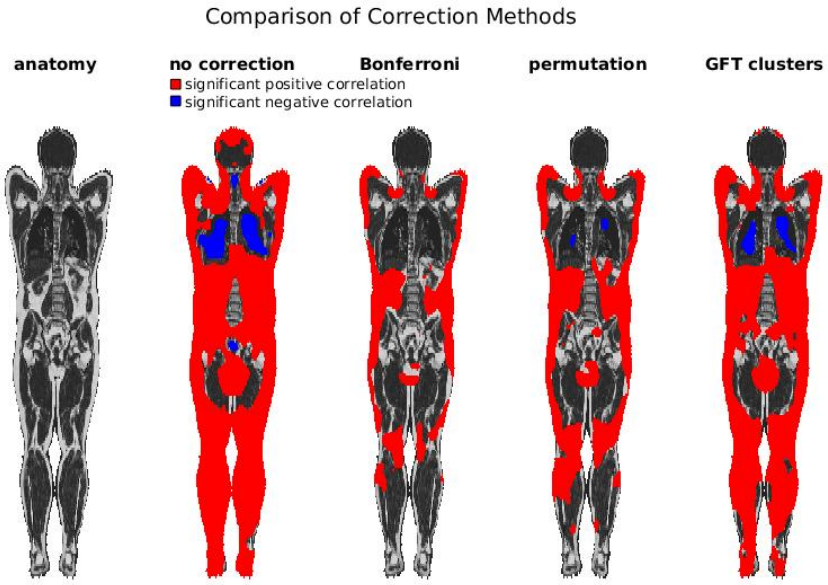

Figure 20: Statistical Considerations in Whole-Body MR Analyses

28. **Abdominal organ segmentation**
Eva Breznik, Robin Strand, Filip Malmberg
Partner: Joel Kullberg, Håkan Ahlström, Division of Radiology, Dept. of Surgical Sciences, UU
Funding: Centre for Interdisciplinary Mathematics, CIM, UU; TN-Faculty, UU
Period: 201706–
Abstract: We focus on improving the existing registration method for whole-body scans by including segmentation results as prior knowledge. Segmentation of the organs in the abdomen is a daunting task, as the organs vary a lot in their properties and size. And having a robust method to segment a number of them would not only be useful in clinical setting, but it could also help guide the registration method in those areas, which are most challenging to register. To develop an appropriate method we apply convolutional neural networks and explore ways of including prior knowledge in the process (via better sampling strategies and direct injection of anatomical information with landmarks and patch locality). Preliminary results on improvements we achieved by integrating anatomical (spatial) knowledge within a fully convolutional network were presented at SSDL 2018 in Göteborg. See Figure 21.

Figure 21: Abdominal organ segmentation

29. **KNIME support for High-Content Screening**
Anna Klemm
Partner: Jordi Carreras Puigvert, Oscar Fernandez Capetillo, Karolinska Institutet, Stockholm
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20181025–
Abstract: KNIME is a free and open-source data analytics platform. It is very suitable to sort, filter, analyze and display data obtained in High Content Screens. In this project data-normalization, filtering and data visualization tools were used. See Figure 22.

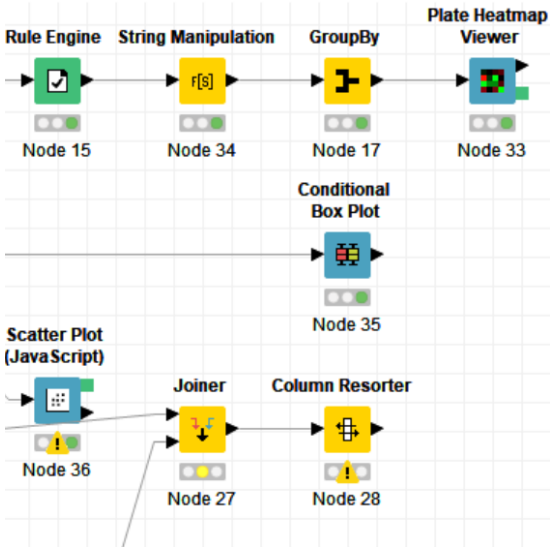

Figure 22: KNIME support for High-Content Screening

30. **Visualization of convolutional neural network class activations in automated oral cancer detection for interpretation of malignancy associated changes**
Nadezhda Koriakina, Joakim Lindblad, Nataša Sladoje, Ewert Bengtsson
Partner: Eva Darai Ramqvist - Pathology and Cytology, Karolinska Institute, Stockholm, Sweden; Jan-Michaél Hirsch - Surgical Sciences, Oral & Maxillofacial Surgery, Uppsala University, Uppsala, Sweden; Christina Runow Stark - Public Dental Service, Södersjukhuset, Stockholm, Sweden
Funding: Swedish Research Council; VINNOVA through MedTech4Health, AIDA; TN-faculty, UU;
Period: 20181001–
Abstract: Oral cancer is one of the most common malignancies in the world. It is noteworthy that the oral cavity can be relatively easily accessed for routine noninvasive screening tests that could potentially decrease the incidence of this type of cancer. Automated deep learning computer aided methods show promising ability for detection of subtle precancerous changes at a very early stage, also when visual examination

is less effective. Although the biological nature of subtle malignancy associated changes (MAC) is not fully understood, the consistency of morphology and textural changes within a cell dataset could shed light on the premalignant state. The aim of this project is twofold: On one hand, to increase understanding of this phenomenon by exploring and visualizing what parts of cell images are considered as most important when trained deep convolutional neural networks are used to differentiate cytological images into normal and abnormal classes. On the other hand, to increase understanding of the deep learning classification properties and to enable interpretation of classification behaviour. See Figure 23.

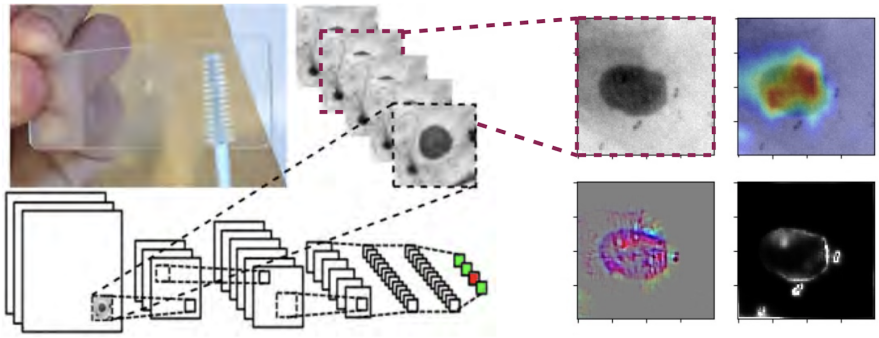

Figure 23: Visualization of convolutional neural network class activations in automated oral cancer detection for interpretation of malignancy associated changes

5.3 Microscopy, cell biology

31. **Automated quantification of axonal growth**
Petter Ranefall, Carolina Wählby
Partner: Sarah Pan, Alexander Ossinger, Andrej Bajic, Nils Hailer, Nikos Schizas - Dept. of Surgical Sciences, Uppsala University.
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 201610–
Abstract: The aim of this project is to establish a standardised method for measuring cell and axonal growth from spinal cord slice cultures. To measure the area of axons outside the explant body, pictures of spinal cord slice cultures are captured through a light microscope and then analysed in ImageJ and CellProfiler. Our plan is to use this method in future experiments on axonal regeneration and growth from the spinal cord. See Figure 24.

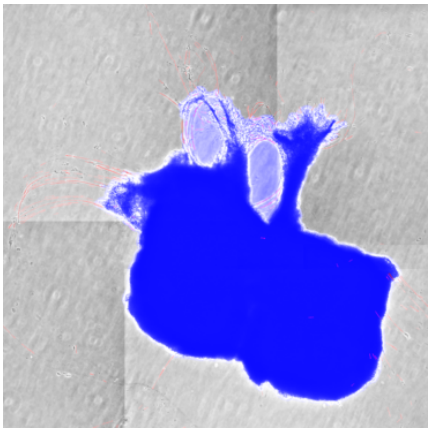

Figure 24: Automated quantification of axonal growth

32. **Assessing bacterial growth kinetics and morphology using time-lapse microscopy data**
Petter Ranefall, Carolina Wählby
Partner: Elisabet Nielsen - Dept. of Pharm. Biosci., UU, Chenyan Zhao, Pikkei Yuen, Pernilla Lagerbäck, Margreke Brill, Thomas Tängdén, Otto Cars - Dept. of Med. Sci., UU
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 201606–
Abstract: In vitro methods are often used to study the concentration-effect relationship for antimicrobial agents. Time-kill curve experiments have long been the standard methodology, with bacterial counts followed over time using viable count assessments on agar plates. This method is labor-intensive and recently digital time-lapse microscopy methods have become available which might allow a more rapid assessment of antibiotic activity. Additionally, these methods could add information related to drug-induced morphological changes. The aim of this project is to integrate information obtained from time-lapse microscopy in the characterization of antibiotic effect on bacterial growth and morphology. See Figure 25.

33. **SciLifeLab cancer stem cell program**
Damian Matuszewski, Petter Ranefall, Carolina Wählby, Ida-Maria Sintorn
Partner: Sven Nelander, Ingrid Lönnstedt, Cecilia Krona, Linnéa Schmidt, Karin Forsberg-Nilsson, Irina Alafuzoff, Ulf Landegren, Anna Segerman, Tobias Sjöblom, Lene Urborn, and Bengt Westermark - Dept. of Immunology, Genetics and Pathology and SciLifeLab, UU; Bo Lundgres - the Karolinska Institute and SciLifeLab, Stockholm; Rebecka Jörnsten - Chalmers, Gothenburg; and Göran Hesselager - UU Hospital, Uppsala
Funding: AstraZeneca-Science for Life Laboratory Joint Research Program
Period: 201303–
Abstract: The SciLifeLab Cancer Stem Cell Program is a cross-platform initiative to characterize cancer stem cells (CSCs). Previously, the development of drugs targeting the CSC population in solid tumors has been curbed by the lack of valid cell model systems, and the complex genetic heterogeneity across

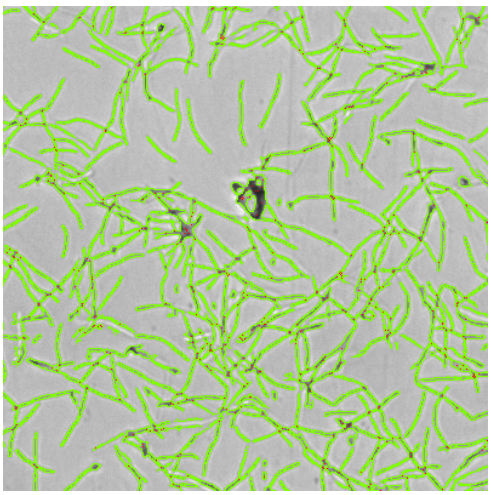

Figure 25: Assessing Bacterial Growth Kinetics and Morphology Using Time-lapse Microscopy Data

tumors, factors that make it hard to assess new targets or predict drug responses in the individual patient. To solve these problems, our aim is to develop a biobank of highly characterized CSC cultures as a valid model of cancer heterogeneity. We will combine mathematical and experimental approaches, including image-based high-throughput cell screening, to define the spectrum of therapeutically relevant regulatory differences between patients. This will help elucidate mechanisms of action and enable accurate targeting of disease subgroups. Patient data is continously collected, and close to one hundred primary cell lines have been established. The cultured cells are exposed to known and novel drug compounds at varying doses, and imaged by fluorescence as well as bright-field microscopy. Algorithms for cell cycle analysis and automatic selection of potentially effective treatments have been developed, and were published in a paper entitled: Image-Based Detection of Patient-Specific Drug-Induced Cell-Cycle Effects in Glioblastoma, in SLAS DISCOVERY 2018, `https://doi.org/10.1177/2472555218791414`. See Figure 26.

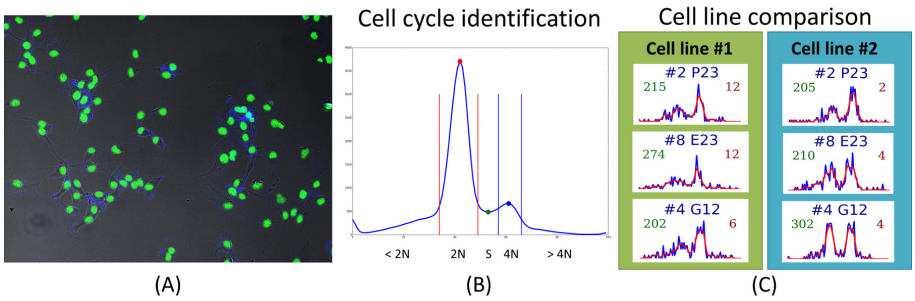

Figure 26: SciLifeLab Cancer Stem Cell Program

34. **A smart and easy platform to facilitate ultrastructural pathologic diagnoses**
Amit Suveer, Nataša Sladoje, Joakim Lindblad, Ida-Maria Sintorn
Partner: Vironova AB; Anca Dragomir - Uppsala Academic Hospital; Kjell Hultenby - Karolinska Institutet
Funding: MedTech4Health, Vinnova; TN-faculty, UU
Period: 201601–
Abstract: TEM is an essential diagnostic tool for screening human tissues at the nanometer scale. It is the only option in some cases and considered as gold standard for diagnosing several disorders, e.g. cilia and renal diseases, rare cancers to name a few. The high resolution of TEM provides unique morphological information, significant for diagnosis and personalized care management. However, the microscope is expensive, technically complex, bulky, needs a high level of expertise to operate, and still diagnosis is subjective and time-consuming. In this project we are collaborating with microscope manufacturers, pathologists,

and microscopists, to develop the next generation smart software and easy platform that will significantly simplify and enhance the TEM imaging and analysis experience. The work includes automated steering of a TEM microscope for the search for regions of interest, followed by automatic multiscale imaging and processing of the images of acquired regions. During 2018 we have continued development of the analysis methods in close collaboration with UAS and KS. Results have been presented at: IEEE International Symposium on Biomedical Imaging, USA; Swedish Symposium on Image Analysis, Stockholm, Sweden; Summer School on Image Processing, Graz, Austria; Swedish Symposium on Deep Learning, Göteborg; European Conference on Computer Vision, Munich, Germany. See Figure 27.

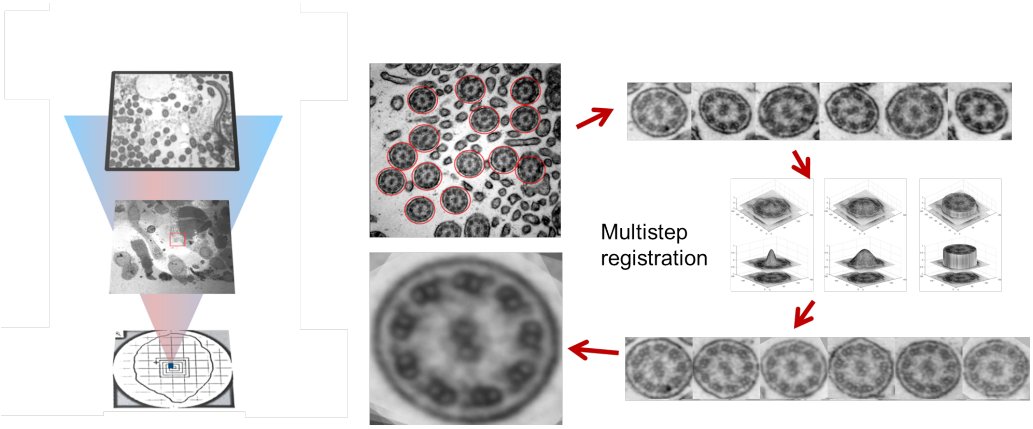

Figure 27: A smart and easy platform to facilitate ultrastructural pathologic diagnoses

35. **Advanced methods for reliable and cost efficient image processing in life sciences**
Nataša Sladoje, Joakim Lindblad, Ewert Bengtsson, Ida-Maria Sintorn
Partner: Marija Delić, Buda Bajić, Faculty of Technical Sciences, University of Novi Sad, Serbia
Funding: VINNOVA; UU TN-faculty; Swedish Research Council
Period: 201308–
Abstract: Within this project our goal is to increase reliability, efficiency, and robustness against variations in sample quality, of computer assisted image analysis in two particular research tracks, related to two applications: (1) Chromatin distribution analysis for cervical cancer diagnostics, and (2) Virus detection and recognition in TEM images. Efficient utilization of available image data to characterize barely resolved structures, is crucial in both the considered applications. We rely on theoretical work in discrete mathematics, which provides methods which enable preservation and efficient usage of information, aggregate information of different types, improve robustness of the developed methods and increase precision of the analysis results. During 2018, we have developed, applied and evaluated (quantitatively and qualitatively) several denoising methods on TEM images. This study is summarized in a paper accepted for the IEEE International Symposium on Biomedical Imaging (ISBI) 2018. We have presented our developed distance measures between multi-channel representations of image objects at two international conferences (ISMM and IWCIA). We have presented our results on developing a pipeline for automated detection and analysis of TEM images of cilia at SCIA 2018. We have continued with developing texture descriptors suitable for TEM images, which offer a good balance between simplicity and performance. See Figure 28.

36. **Protein inheritance in asymmetric cell division**
Petter Ranefall, Carolina Wählby
Partner: Alexander Julner-Dunn(1), Zhijian Li(2), Charles Boone(2) and Victoria Menendez-Benito(1), (1) Dept. of Biosciences and Nutrition, Karolinska Institute, Sweden; (2)The Donelly Center, University of Toronto, Canada
Funding: SciLifeLab
Period: 20170428–
Abstract: In some cells, such as yeast and stem cells, proteins are asymmetrically inherited during cell division. By doing this, cells can control cell fate and protect specific progeny from aging. Examples of age-dependent symmetric inheritance include centrosomes, histones, oxidized proteins and old mitochondria. Yet, we do not have a global view on which proteins in the cell are asymmetrically inherited. In this

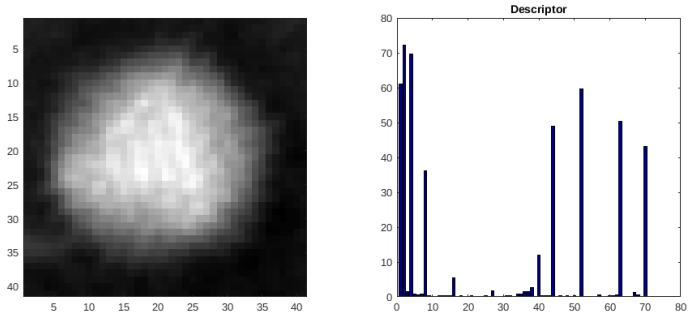

Figure 28: Advanced Methods for Reliable and Cost Efficient Image Processing in Life Sciences

project, we address this question by developing a systems-based approach to explore protein inheritance in yeasts. We use a technique, named recombination induced epitope tag (RITE), which is a living pulse-chase that allows tracking old (maternal) and new proteins by genetic switching between two fluorescent protein fusions. Our specific goals are: 1. To create the first yeast library for single-cell analysis of protein inheritance, by tagging each gene with RITE at its chromosomal location. 2. To generate a map of the proteome inheritance in budding yeast, by measuring the abundance and localization of old/new proteins in the yeast RITE library, using high-content microscopy and automated image analyses. We will generate resources, data and novel information that will facilitate the discovery of new asymmetries in protein inheritance that control cell fate, epigenetic memory and/or cellular ageing. See Figure 29 .

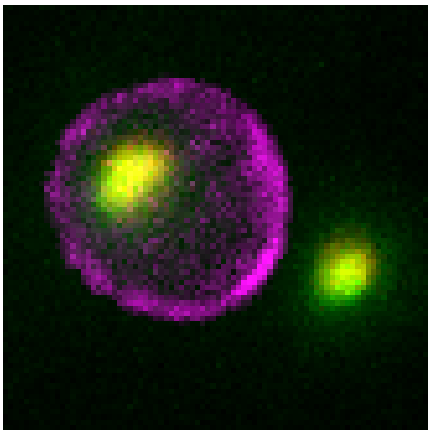

Figure 29: Protein inheritance in asymmetric cell division

37. **qUTI - A point-of care test for fast diagnosis of urinary tract infections**
Petter Ranefall
Partner: Özden Baltekin, Johan Elf, Ove Öhman, Astrego Diagnostics AB
Funding: Astrego Diagnostics AB
Period: 20170404–
Abstract: The emergence and spread of antibiotic-resistant bacteria are aggravated by incorrect prescription and use of antibiotics. A core problem is that there is no sufficiently fast diagnostic test to guide correct antibiotic prescription at the point of care. Here, we investigate if it is possible to develop a point-of-care susceptibility test for urinary tract infection, a disease that 100 million women suffer from annually and that exhibits widespread antibiotic resistance. We capture bacterial cells directly from samples with low bacterial counts (104 cfu/mL) using a custom-designed microfluidic chip and monitor their individual growth rates using microscopy. By averaging the growth rate response to an antibiotic over many individual cells, we can push the detection time to the biological response time of the bacteria. We find that it is possible to detect changes in growth rate in response to each of nine antibiotics that are used to treat urinary tract infections in

minutes. In a test of 49 clinical uropathogenic Escherichia coli (UPEC) isolates, all were correctly classified as susceptible or resistant to ciprofloxacin in less than 10 min. The total time for antibiotic susceptibility testing, from loading of sample to diagnostic readout, is less than 30 min, which allows the development of a point-of-care test that can guide correct treatment of urinary tract infection. See Figure 30 .

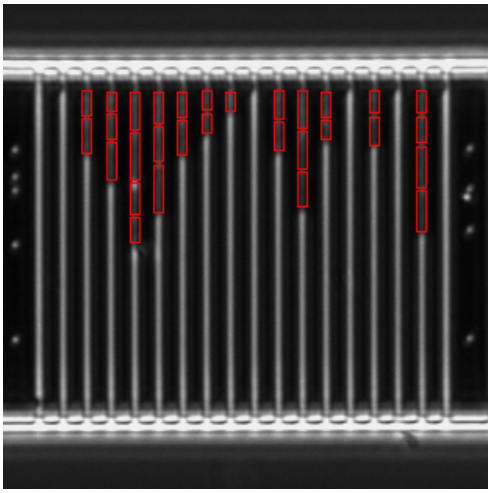

Figure 30: qUTI - A point-of care test for fast diagnosis of urinary tract infections

38. **Applying semi-automated histology-to-radiology co-registration in en bloc resected gliomas**
Petter Ranefall
Partner: Kenney Roodakker, Anja Smits, Dept. of Neurology, Uppsala University
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20171130–
Abstract: Gliomas are heterogeneous tumors in terms of imaging appearances, and a deeper understanding of the histopathological tumor characteristics that underlie the signal abnormalities on PET and MRI is needed. Here we used histology-to-radiology co-registration of gliomas with the aim to correlate local changes in tumor perfusion and 11C-methionine uptake with cell density, vascularity and proliferation in these areas. See Figure 31.

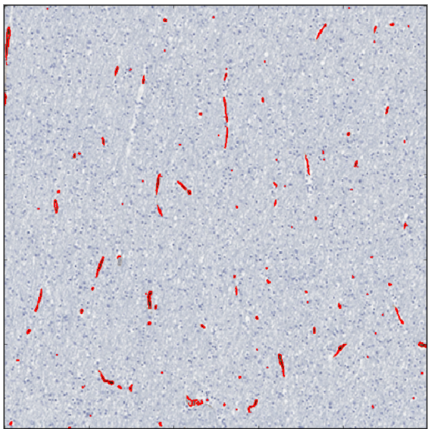

Figure 31: Applying semi-automated histology-to-radiology co-registration in en bloc resected gliomas

39. **Intracellular trafficking pathways of PDGFRb**
Petter Ranefall, Carolina Wählby
Partner: Natalia Papadopoulos, Carl-Henrik Heldin, Dept. of Medical Biochemistry and Microbiology, UU
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)

Period: 20171204–
Abstract: This project investigates trafficking pathways of PDGFRb from the cell surface upon activation with PDGF-BB ligand. PDGFRb is known to form dot-like clusters upon activation that only partially co-localize with the known markers of intracellular organelles. This project is designed to identify novel markers and trafficking pathways of PGDFRb. In order to distinguish between the PDGFRb localized at the cell surface and the intracellular pools, the cell surfice PDGFRb is labelled with biotin. Thus, confocal microscopy with triple staining is used to estimate the co-localization of signals between the three types of molecules: biotin, PDGFRb and organelle marker. The pipeline is used to analyze the images and estimate the presence of biotinylated PDGFRb within a given organelle. See Figure 32.

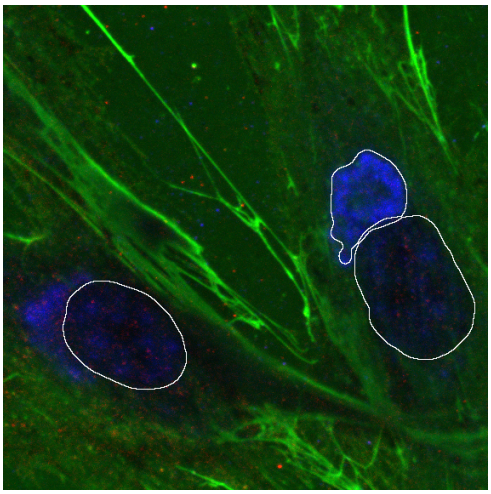

Figure 32: Intracellular trafficking pathways of PDGFRb

40. **Imaging protein synthesis in primary cortical neuronal culture using Click-iT textregistered Plus OPP Protein Synthesis Assay Kits**
Petter Ranefall
Partner: Rekha Tripathi, Pharmaceutical Biosciences, UU
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20171201–
Abstract: The goal of this project is to analyze protein translation rate in mouse primary cortical neurons and astrocytes. The aim is to assess the protein synthesis by using the OPP Kit in primary cortical cultures of wild type and SLC38A10-/- Knockout mice. To understand role of SLC38A10 in protein regulation in neurons and astrocytes. We are using Cell Profiler to measure fluorescence intensity. See Figure 33.

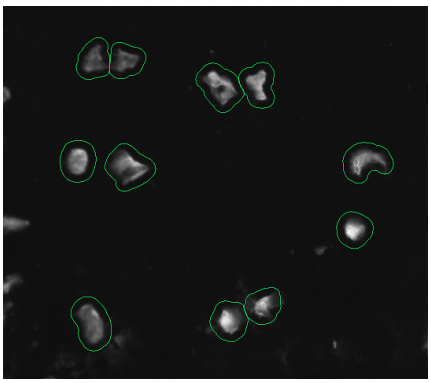

Figure 33: Imaging protein synthesis in primary cortical neuronal culture using Click-iT ®Plus OPP Protein Synthesis Assay Kits

41. **HASTE: Hierarchical Analysis of Spatial and Temporal Data**
Carolina Wählby, Håkan Wieslander
Partner: Andreas Hellander, Salman Toor, Ben Blamey, Dept. of Information Technology, Uppsala University, Ola Spjuth, Niharika Gauraha and Phil Harrison, Dept. of Pharmaceutical Biosciences, Uppsala University, Markus M. Hilscher, SciLifeLab, Dept. of Biochemistry and Biophysics, Stockholm University, Ida-Maria Sintorn, Vironova AB, Lars Carlsson, Johan Karlsson, Alan Sabirsh and Ola Engkvist, AstraZeneca AB, Mats Nilsson, Stockholm University
Funding: Swedish Foundation for Strategic Research (SSF)
Period: 20170103–
Abstract: Images contain very rich information, and digital cameras combined with image processing and analysis can detect and quantify a range of patterns and processes. The valuable information is however often sparse, and the ever increasing speed at which data is collected results in data-volumes that exceed the computational resources available. The HASTE project takes a hierarchical approach to acquisition, analysis, and interpretation of image data. We develop computationally efficient measurements for data description, confidence-driven machine learning for determination of interestingness, and a theory and framework to apply intelligent spatial and temporal information hierarchies, distributing data to computational resources and storage options based on low-level image features. At Vi2 we focus on developing the efficient measurements that will identify non-informative data early on in the analysis process; either online at data collection, or off-line prior to full data analysis. The challenge is to use minimal computational time and power to extract a broad range of informative measurements from spatial-, temporal-, and multi-parametric image data, useful as input for conformal predictions and efficient enough to work well in a streaming setting. Examples include drug localization in lung tissue, time lapse experiment outcome prediction and learning from few training examples. See Figure 34.

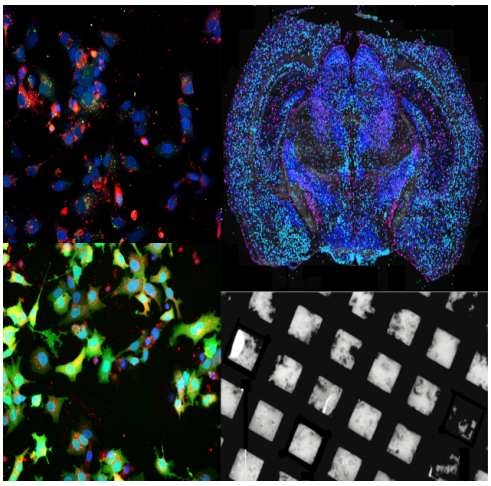

Figure 34: HASTE: Hierarchical Analysis of Spatial and Temporal Data

42. **Multi-layer object representations for integrated shape and texture analysis with applications in biomedical image processing**
Elisabeth Wetzer, Nataša Sladoje, Joakim Lindblad
Partner: Ida-Maria Sintorn - Vironova AB; Kjell Hultenby - Karolinska Institute
Funding: Centre for Interdisciplinary Mathematics, TN-Faculty, UU, Vinnova through MedTech4Health
Period: 20171001–
Abstract: The aim of the project is to develop the theoretical foundation for a class of methods applicable to multi-layered heterogeneous object representations and to apply and evaluate these methods in clinical biomedical applications. In 2018 focus has been on texture descriptors applied to multi-scale data to allow for a search of candidate areas that are likely to hold objects of interest in low resolution images. Convolutional neural networks are, in a number of different ways, combined with information extracted from Local Binary Pattern features, to provide a powerful tool for texture-based classification of biomedical data. Methods are evaluated on automatic detection and classification of diagnostically relevant regions - glomerulus

and foot processes - in TEM images of kidney tissue. The project is carried out in close collaboration with Vironova AB and Karolinska Institutet; they have provided samples, images, expertise in pathology, and an environment to implement and evaluate the developed methods. This work has resulted in a paper 'Towards Automated Multiscale Imaging and Analysis in TEM: Glomerulus Detection by Fusion of CNN and LBP Maps' presented at the BioImage Computing workshop at ECCV conference in Munich (published by Springer, LNCS) and at the SSDL symposium in Göteborg. See Figure 35.

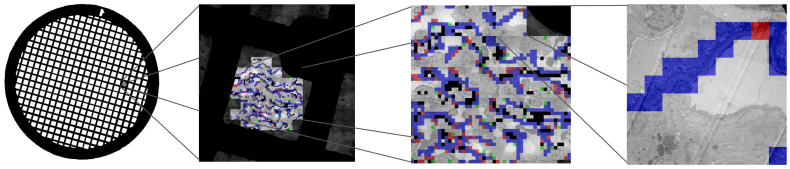

Figure 35: Multi-layer object representations for integrated shape and texture analysis with applications in biomedical image processing

43. **Human induced pluripotent cells derived neuroepithelial-like cells differentiation potential in the presence of the mouse auditory brainstem milieu**
Petter Ranefall, Carolina Wählby
Partner: Andreas Kaiser, Ekaterina Novozhilova, Petri Olivius, Dept. of Surgical Sciences, Uppsala University
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20170120–
Abstract: Stem cell therapy has been proposed as an option to treat sensorineural hearing loss since auditory system as well as the most of the central nervous system has a limited regenerative potential. The treatment of neurodegenerative diseases has been studied through the cell-based approach over the past years. Replacement of the damaged spiral ganglion neurons in the inner ear, the first-order neurons of the auditory pathway, with precursor cells would be a way to improve hearing function in patients with malfunctions of the auditory system including patients in need of a cochlear implant. In our project we use mouse organotypic auditory brainstem slice culture as a screening platform for donor cells differentiation potential to further proceed with in vivostudies. See Figure 36.

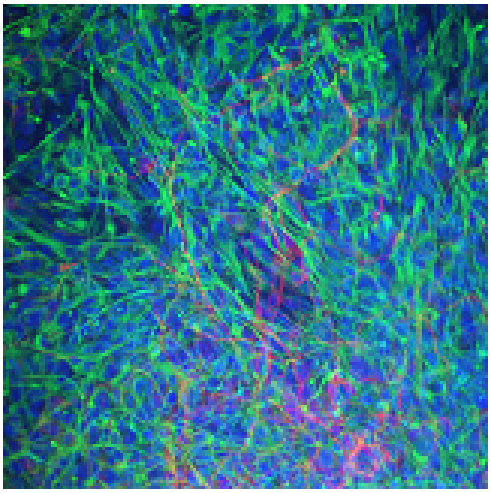

Figure 36: Human induced pluripotent cells derived neuroepithelial-like cells differentiation potential in the presence of the mouse auditory brainstem milieu

44. **Image- and AI-based cytological cancer screening**
Joakim Lindblad, Ewert Bengtsson, Carolina Wählby
Partner: Dr Christina Runow Stark - Medicinsk Tandvård, Folktandvården AB, Stockholm; Dr Eva Ramquist

- Karolinska University Hospital; Prof. Jan-Michaél Hirsch - Medicinsk Tandvård, Södersjukhuset; Dr. Kunjuraman Sujathan - Regional Cancer Centre, Kerala, India
Funding: VINNOVA through MedTech4Health, AIDA
Period: 20171001–
Abstract: Oral cancer incidence is rapidly increasing worldwide, with over 450,000 new cases found each year. The most effective way of decreasing cancer mortality is early detection, which makes routine screening of patient risk groups highly desired. Within this project, we aim to develop a system that uses artificial intelligence (AI) to automatically detect oral cancer in microscopy images of brush samples, which can quickly and without pain be routinely taken at ordinary dental clinics. We expect that the proposed approach will be crucial for introducing a screening program for oral cancer at dental clinics, in Sweden and the world. The project, which involves researchers from Uppsala University, Karolinska University Hospital, Folktandvården Stockholms län AB, and the Regional Cancer Center in Kerala, India, is further benefiting from AIDA to turn developed methods into clinically useful tools. During 2018 we presented posters at Congress of the European Association of Oral Medicine (EAOM), in Göteborg and Congress of the International Society for Advancement of Cytometry (CYTO), in Prague. We also acquired GPU resources for the project. We carried out a course project together with Master students Jo Gay and Hugo Harlin on use of texture in combination with CNNs for improved classification performance. See Figure 37.

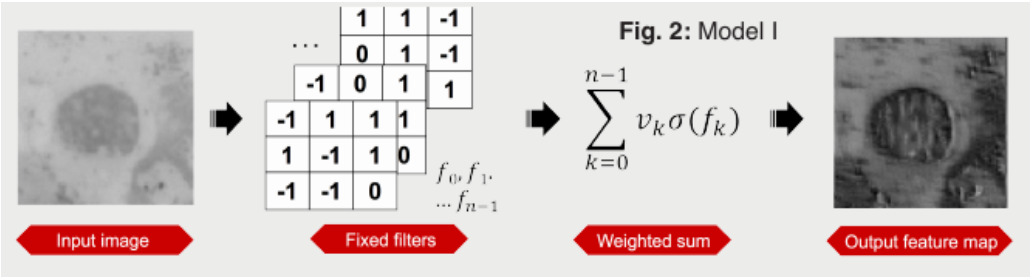

Figure 37: Image- and AI-based cytological cancer screening

45. **NEUBIAS (Network of EUropean BioImage AnalystS) - COST Action 15124**
Nataša Sladoje, Joakim Lindblad, Carolina Wählby, Petter Ranefall, Anna Klemm
Partner: NEUBIAS network with more than 240 members from more than 40 countries
Funding: EU Framework Programme Horizon 2020
Period: 20160503–
Abstract: This COST Action aims to provide a stronger identity to BioImage Analysts by organising different types of interactions between Life scientists, BioImage analysts, microscopists, developers and private sector. It collaborates with European Imaging research infrastructures to set up best practice guidelines for Image Analysis (IA). The Action successfully works on creating an interactive database for BioImage analysis tools and workflows with annotated image sample datasets, to help matching practical needs in biological problems with software solutions. It implements a benchmarking platform for these tools. To increase the overall level of IA expertise in the LSc, the Action proposes a novel training programme with three levels of courses, releasing of open textbooks, and offering of a short term scientific missions programme to foster collaborations, IA-technology access, and knowledge transfer for scientists and specialists lacking these means. We have been actively participating in different activities organized within NEUBIAS network. We were engaged as work group leaders, teachers, taggers, invited speakers at NEUBIAS workshops and symposia, and as Management Committee members. We have strengthen our collaboration with bioimage analysts from more than 40 NEUBIAS member-countries. See Figure 38.

46. **Sysmic: Development and application of systems microscopy for cancer cell migration**
Nicolas Pielawski, Anindya Gupta, Carolina Wählby
Partner: Staffan Strömplad and Carsten Daub, Dept. of Biosciences and Nutrition, KI, and SciLifeLab, Ulf Landegren, Dept. of Immunology, Genetics and Pathology, UU and SciLifeLab, Pontus Nordenfelt Dept. of Clinical Sciences, LU, Olink Bioscience and Sprint Bioscience
Funding: Swedish Foundation for Strategic Research (SSF)

Figure 38: NEUBIAS (Network of EUropean BioImage AnalystS) - COST Action 15124

Period: 20180122–
Abstract: The core biological theme of this project is cell migration; a basic but complex cellular process that is highly relevant to human cancer. This complexity is, in part, explained by plasticity in the possible cell migration strategies that cells adopt and by the fine-tuned spatiotemporal coordination of migratory forces. However, the molecular mechanisms and genetic regulation that give rise to cell migration plasticity and dynamic force control constitutes knowledge gaps that this project proposes to fill. We develop learning-based image analysis methods to identify different modes of cell migration an model traction force microscopy; measurements that will later be combined with single cell proteomics, and multiplex in situ protein detection. We will thus combine in a novel manner dynamic and quantitative microscopy observations of migrating cells with single cell RNA-seq and proteomics. All this is tailored to add to the understanding of cellular dynamics. Finally, we will explore developed migration and traction force models and profiling methods on 25 cancer cell lines. See Figure 39.

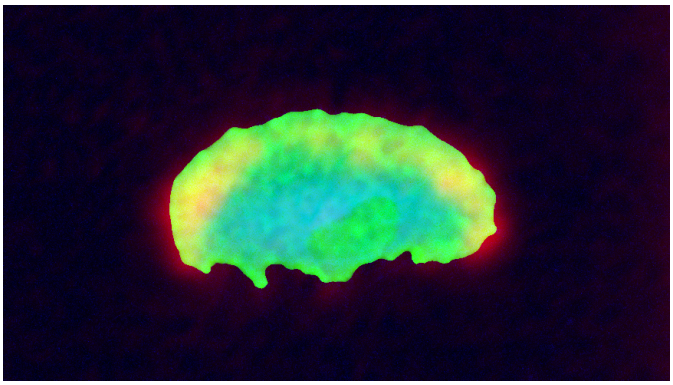

Figure 39: Sysmic: Development and application of systems microscopy for cancer cell migration

47. **Probing the role of Atox1 in breast cancer cell migration**
Anna Klemm
Partner: Stéphanie Blockhuys, Pernilla Wittung Stafshede, Chalmers University of Technology, Göteborg
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20181023–
Abstract: We study the role of Atox1 in breast cancer cell migration. Atox1 is a cytoplasmic Cu transporter and is overexpressed in breast cancer tissue. Previously, we observed using wound healing studies that upon Atox1 silencing the cell migration potential was reduced. Now, using the single cell approach, we want to define in details the role of Atox1 in the cancer cell migration. So far, we used manual cell tracking analysis, but now we look forward to have an automatic cell tracking analysis approach to make the evaluation less

laborious and more consistent. With this study, we hope to determine in more details the role of Atox1 in cancer cell migration. See Figure 40.

Figure 40: Probing the role of Atox1 in breast cancer cell migration

48. **Linking cell cycle with protein expression**
Anna Klemm, Carolina Wählby
Partner: Caroline Gallant, Dept. of Immunology, Genetics and Pathology, Uppsala University
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20180827–
Abstract: Pilot studies to characterize protein expression changes in human embryonic stem cells during the different cell cycle stages is led by Gallant group. They observed highly differential regulation of core pluripotency transcription factors in comparison to other stem cells factors, transcription factors or metabolic proteins, with a total of 92 proteins measured. They measure proteins using multiplex protein extension assays in lysates prepared from cells sorted by cell cycle phase. Together, we now aim to apply an orthogonal in situ method to confirm the relation of specific protein expression changes and cell cycle phase, where the image analysis part of the work is done at CBA. Together, we are applying a CellProfiler analysis pipeline that enables the assignment of cell cycle phase via measurement of the integrated intensity of a DNA stain in fixed cells. For every cell analyzed, we measure protein expression intensity and assign cell cycle phase. Subsequently, we will evaluate whether we can reproduce the differential cell cycle phase specific expression data obtained by multiplex protein analysis of cell lysates. See Figure 41.

49. **Searching for genetic targets for nonalcoholic fatty liver disease (NAFLD) and related diseases**
Anna Klemm
Partner: Casimiro Castillejo-López, Claes Wadelius, Uppsala University
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20181205–
Abstract: Obesity is rising worldwide due to an increase in total energy consumption and changes in life stiles. This pandemic growth has resulted in an increased incidence of obesity-associated nonalcoholic fatty liver disease (NAFLD) that is now recognized as the most common liver disease worldwide. The NAFLD disease spectrum extends from simple hepatic steatosis to inflammation and ballooning that can leads to cirrhosis and hepatocellular carcinoma. NAFLD is a complex disease in which genetic and environmental factors contribute to its development. The genetic component is importantly strong. It has been estimated an heritability of 52% in the general population which it is in accordance with the 35
textendash61% heritability reported in twin studies. The identified NAFLD risk genetic factors will provide new insights in the disease and will improved patient strati?cation and management. In this project we are using CRISPR-Cas9 for genetic modification of genes and regulatory elements that are associated with triglyceride metabolism in the hepatocyte derived cell line HepG2. The mutated cell lines are examined for anomalous accumulation of lipids using fluorescence microscopy. Except of lipids in the modified

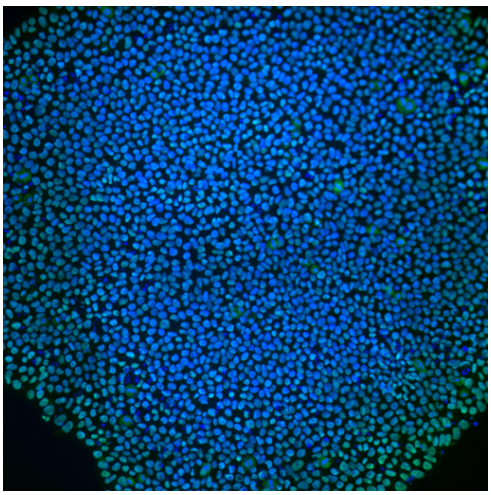

Figure 41: Linking cell cycle with protein expression

hepatocytes indicates that the mutation could had a direct role in the development of the disease. Contrary, mutations that decrease the cellular accumulation See Figure 42.

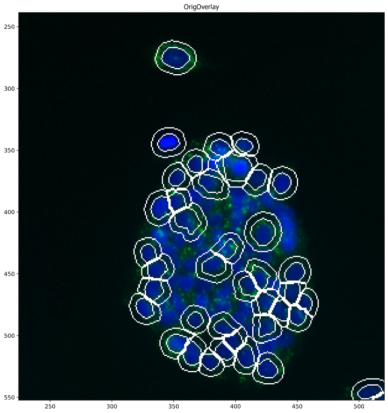

Figure 42: Searching for genetic targets for nonalcoholic fatty liver disease (NAFLD) and related diseases

50. **Identifying novel small molecule drugs for CCM treatment**
Anna Klemm, Petter Ranefall, Carolina Wählby
Partner: Joppe Oldenburg, Johan Brännström, Peetra Magnusson, Elisabetta Dejana, Uppsala University
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20180915–
Abstract: We are identifying modulators of VE-cadherin formation in images generated in a small molecule drug screen. We use CellProfiler to detect and quantify changes, and KNIME for automated classification of the images and hit-detection. See Figure 43.

51. **Analysis of fluorescent intensity in brain slices**
Anna Klemm, Petter Ranefall
Partner: Marta Ramos, Roberta Battistella, Iben Lundgaard, Lund University
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20180701–

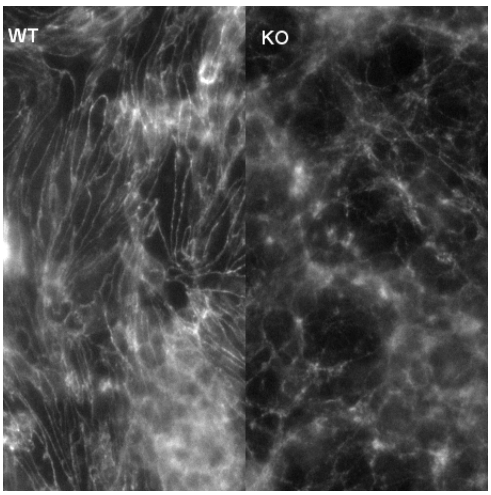

Figure 43: Identifying novel small molecule drugs for CCM treatment

Abstract: We automatically segment brain slices in large tile scans. In the brain area we measure the fluorescent intensity of different markers using automatic thresholding. See Figure 44.

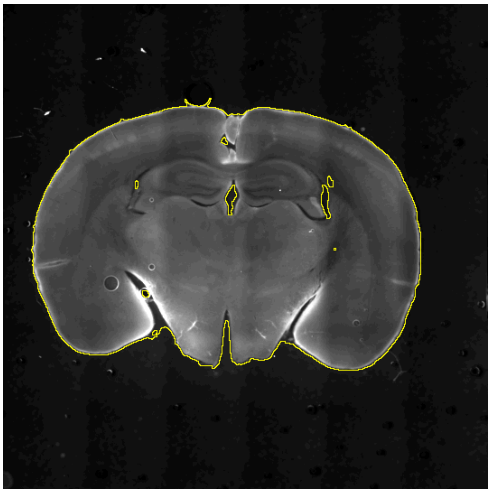

Figure 44: Analysis of fluorescent intensity in brain slices

52. **Efficient virus segmentation and classification in TEM images with minimal labeling**
Damian J. Matuszewski, Ida-Maria Sintorn
Funding: Science for Life Laboratory, VR
Period: 20180101–
Abstract: Convolutional neural networks (CNNs) offer human experts-like performance and in the same time they are faster and more consistent in their judgment. However, their successful training and use in many biomedical and clinical applications is often restricted by an insufficient amount of annotated images, the quality of the annotations and the cost of the state-of-the-art hardware required for analyzing the images. In this project, we develop methods for training efficient CNNs from images with minimal annotation. We also investigate the possibility of making CNNs lighter by parametrizing and modifying the popular U-Net architecture and decreasing the number of its trainable weights. We use a challenging application of a pixel-wise virus classi?cation in Transmission Electron Microscopy images to demonstrate our methods. During 2018 a paper entitled “Minimal annotation training for segmentation of microscopy images” was presented at the IEEE 15th International Symposium on Biomedical Imaging (ISBI 2018) and published in the conference proceedings. `https://doi.org/10.1109/ISBI.2018.8363599`. See Figure 45.

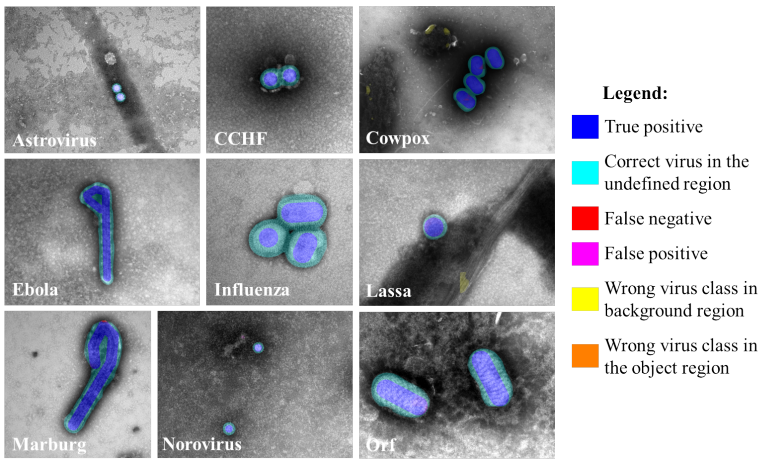

Figure 45: Efficient virus segmentation and classification in TEM images with minimal labeling

5.4 Microscopy, model organisms and tissues

53. **Cell distribution and protein expression in the ectocervix**
Petter Ranefall, Carolina Wählby
Partner: Anna Gibbs, Gabriella Edfeldt, Maria Röhl, Annelie Tjernlund - Dept. of Medicine, KI
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20150401–
Abstract: The female genital mucosa presents a comprehensive natural immune defense against HIV infection, although during exposure to a high dose of virus this is not enough to protect the individual against viral transmission. Some individuals have a stronger resistance against HIV than others and therefore it is highly important to investigate which factors that contribute to an effective local protection against sexual infection. The aim of this study is to quantify gene expression in the target cells of HIV in ectocervix, and measure the distance to the vaginal lumen, as well as epithelial thickness. These parameters will be compared in women involved in sex work between the groups of HIV-infected, highly HIV exposed HIV-uninfected that seems to be resistant, and HIV-uninfected women who have been involved in sex work for a short period. The project led to a joint publication: A. Gibbs, M. Buggert, G. Edfeldt, P. Ranefall, A. Introini, S. Cheuk, E. Martini, L. Eidsmo, T.B. Ball, J. Kimani, R. Kaul, A. Karlsson, C. Wählby, K. Broliden, and A. Tjernlund. HIV-infected women have high numbers of CD103-CD8+ T cells residing close to the basal membrane of the ectocervical epithelium. Journal of Infectious Diseases 2018 Jul 2;218(3):453-465. doi: 10.1093/infdis/jix661 See Figure 46.

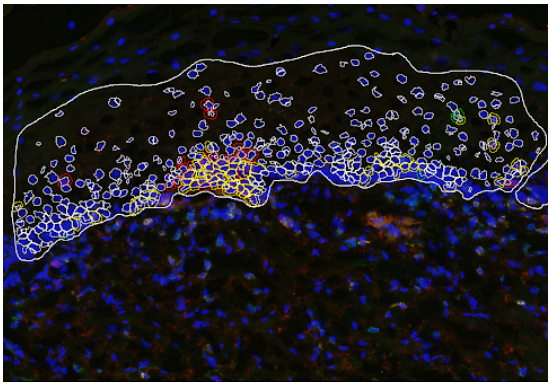

Figure 46: Cell Distribution and Protein Expression in the Ectocervix

54. **Quantification of zebrafish lipid droplets**

Petter Ranefall, Carolina Wählby
Partner: Marcel den Hoed, Manoj Bandaru, Benedikt von der Heyde, Anastasia Emmanouilidou - Dept. of Medical Sciences and SciLifeLab, UU
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20130801–
Abstract: The aim of this project is to identify novel targets for the therapeutic intervention of coronary artery disease. This is done by following-up results from genome-wide association studies in epidemiological studies using a zebrafish model system. Using image analysis we try to identify and characterize causal genes within loci that have so far been identified as associated with coronary heart disease by (high-throughput) screening of atherogenic processes in wildtype and mutant zebrafish, both before and after feeding on a control diet or a diet high in cholesterol. Using confocal microscopy we can image fat accumulation in the zebrafish. We have also developed methods for length and volume measurements as well as quantification of macrophages, neutrophils, IK17 and the overlap with these expressions and stationary lipids. Our results confirm that zebrafish larvae represent a promising model system for early-stage atherosclerosis. See Figure 47.

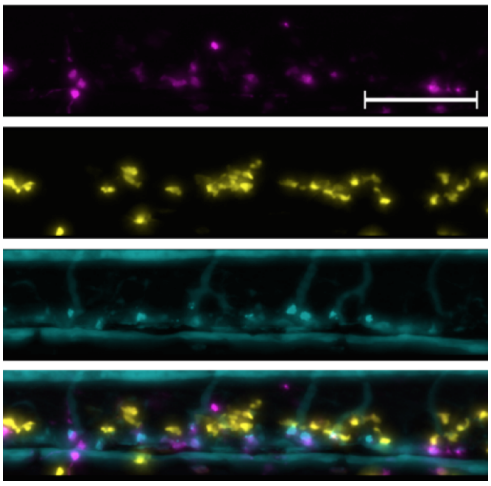

Figure 47: Quantification of Zebrafish Lipid Droplets

55. **Pigment gene expression in the early developing crow feather**
Petter Ranefall, Carolina Wählby
Partner: Chi-Chih Wu, Axel Klaesson, Ola Söderberg, Jochen Wolf - Dept. of Immunology, Genetics and Pathology, UU
Funding: SciLifeLab
Period: 20161108–
Abstract: The project is to quantify and compare pigment-associated gene expressions between two closest related crow species that carrion crow has black feathers and hooded crow has gray feathers in the belly. The cooperators have adapted in situ PLA with padlock probes to label targeted mRNAs across varied developmental stages of melanocytes in feathers. We are developing a CellProfiler pipeline and scripts to recognize and quantify signals across complex tissues with strong autofluorescence. See Figure 48.

56. **Effect of perfluorononanoic acid (PFNA) on early embryo development in vitro**
Petter Ranefall, Carolina Wählby
Partner: Ida Hallberg, Ylva Sjunnesson, Clinical Sciences, SLU
Funding: SciLifeLab
Period: 20170119–
Abstract: For the last decades a concern has been raised that female fertility is declining more than could be explained by the fact that we choose to have children later in life and possible genetic effects. Subfertility and infertility is a devastating experience for those who are affected and as the subject is also somewhat of a taboo the numbers affected are most likely higher than perceived among the general public. In our

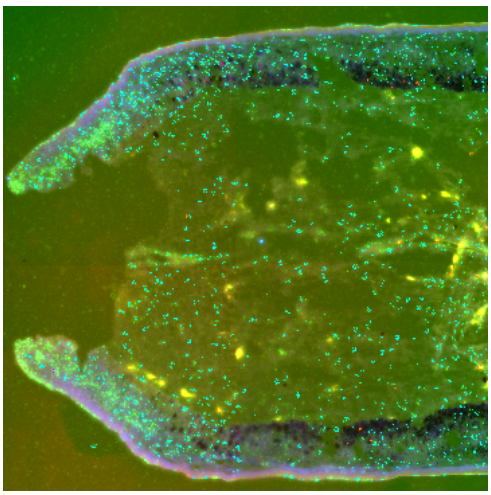

Figure 48: Pigment gene expression in the early developing crow feather

environment, we are continuously exposed to a number of exogenous chemicals, originating from industries, agriculture and other. As many of these chemicals show persistence and are very bio-accumulative, they will concentrate higher up in the food-chain, in both wildlife and humans. Many of the chemicals are new and have yet not been investigated regarding their full toxicological potential.Perfluorononanoic acid (PFNA) This project aim to further investigate perfluorononanoic acid (PFNA) and its effect on the early embryo development. This chemical is closely related to know toxic substances such as PFOS and PFOA, but is in contrary to those little research has yet been done regarding PFNAs potential toxicological effects. We have used a bovine model, where we collect material from the slaughter-house. See Figure 49.

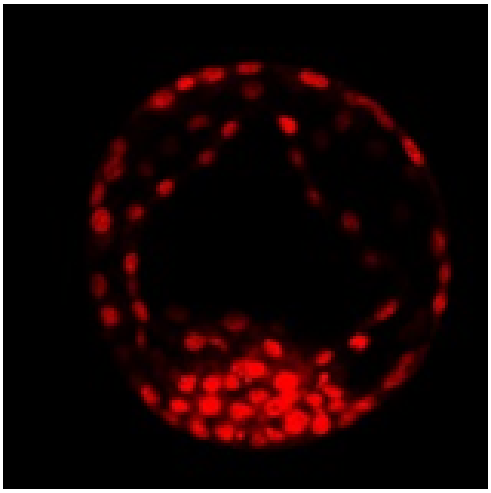

Figure 49: Effect of perfluorononanoic acid (PFNA) on early embryo development in vitro

57. **A model system for analysis of spinal cord injury**
Carolina Wählby
Partner: Nils Hailer and Nikos Schizas, Dept. of Surgical Sciences, UU
Funding: Science for Life Laboratory
Period: 20150101–
Abstract: Following spinal cord injury neurons die due to neurotoxicity and inflammation. We study these effects in a model system with spinal cord slice cultures, aiming to find methods to reduce neurotoxicity. Our focus is quantitative image analysis methods that delineate activated cells and quantify protein expression as a response to injury and treatment. See Figure 50.

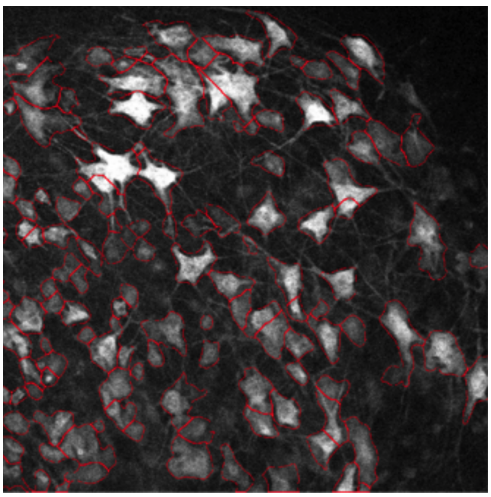

Figure 50: A Model System for Analysis of Spinal Cord Injury

58. **CerviScan**
Ewert Bengtsson, Joakim Lindblad
Partner: Rajesh Kumar, Centre for Development of Advanced Computing (CDAC), Thiruvananthapuram, Kerala, India; K. Sujathan, Regional Cancer Centre, Thiruvananthapuram, Kerala
Funding: Swedish Governmental Agency for Innovation Systems (VINNOVA); Swedish Research Council; SIDA
Period: 20080101–
Abstract: Cervical cancer is a disease that annually kills over a quarter of a million women world-wide. This number could be reduced by screening for signs of cancer precursors using the well-established Pap-test. However, visual screening requires highly trained cytotechnologists and is time consuming. For over 50 years attempts to automate this process have been made but still no cost effective systems are available. The CerviScan project is an initiative from the Indian government, run by CDAC and RCC in Kerala and CBA in Sweden, aimed at creating a low cost, automated screening system. A prototype system has been created and used to screen over 1000 specimen. Initial classification results are promising but screening times are still about 10 times longer than what is realistic in a real screening setting. During 2018 the application for funding of the next phase of the project, focusing on dedicated hardware and a more streamlined, high-throughput system, was finally approved in India. In Sweden the funding for our collaboration from the Swedish Research Links Programme has its last year 2019 and will be used for a joint workshop in Thiruvananthapuram in May 2019. See Figure 51.

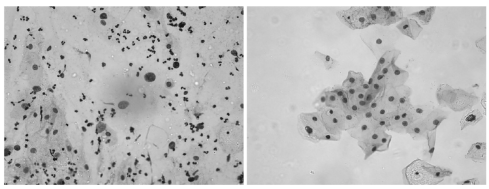

Figure 51: CerviScan

59. **Zebrafish as a model for cerebral palsy and intellectual disability**
Amin Allalou, Carolina Wählby
Partner: Marcel den Hoed, Marta Martín Martínez, Aida Hoshiar, Dept. of Immunology, Genetics and Pathology and SciLifeLab, UU
Funding: Science for Life Laboratory
Period: 20161001–
Abstract: The zebrafish (Danio rerio) is a good model organism for vertebrate development. The orga-

nization of the embryo is simple and the body is transparent, making it easy to study with many different microscopy techniques. In this project we are using the VAST (Vertebrate Automated Screening Technology) and fluorescent imaging with OPT (Optical Tomography) to do a preliminary screen to investigate if we can detect any phenotypes for a number of candidate genes for cerebral palsy and intellectual disability. We are also performing behavioral screening to see if there are any behavioral phenotypes that can associated with the genes of interest. See Figure 52.

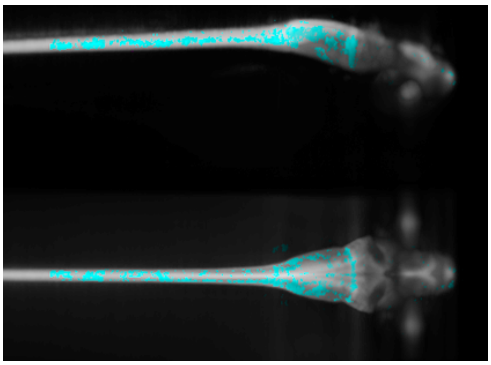

Figure 52: Zebrafish as a Model for Cerebral Palsy and Intellectual disability

60. **Heart rate analysis in zebrafish**
Amin Allalou, Carolina Wählby
Partner: Marcel den Hoed, Benedikt von der Heyde, Dept. of Medical Sciences and SciLifeLab, UU
Funding: Science for Life Laboratory
Period: 20161001–
Abstract: Due to the transparency of the young zebrafish the heart is easily accessible for optical analysis without any invasive procedures. Video-based quantification of heart rate and rhythm is a non-invasive method that can give important information on many phenotypic changes in heart. We have developed an analysis method to quantify the heart rate and rhythm based on video recordings of zebrafish from the VAST (Vertebrate Automated Screening Technology) system. Preprint at www.biorxiv.org. Translating GWAS-identified loci for cardiac rhythm and rate using an in vivo, image-based, large-scale genetic screen in zebrafish. Benedikt von der Heyde, Anastasia Emmanouilidou, Tiffany Klingström, Eugenia Mazzaferro, Silvia Vicenzi, Sitaf Jumaa, Olga Dethlefsen, Harold Snieder, Eco de Geus, Erik Ingelsson, Amin Allalou, Hannah L Brooke, Marcel den Hoed

61. **TissUUmaps - Integrating spatial and genetic information via automated image analysis and interactive visualization of tissue data**
Carolina Wählby, Gabriele Partel, Leslie Solorzano
Partner: Mats Nilsson, Markus Hilscher, Jessica Svedlund and Xiaoyan Qian - Stockholm University/SciLifeLab
Funding: ERC consolidator grant to Carolina Wählby
Period: 201109–
Abstract: Digital imaging of tissue samples and genetic analysis by next generation sequencing are two rapidly emerging fields in pathology. Digital pathology will soon be as common as digital images in radiology, and genetic analysis is rapidly evolving thanks to the impressive development of next generation sequencing technologies. However, most of today's available technologies result in a genetic analysis that is decoupled from the morphological and spatial information of the original tissue sample, while many important questions in tumor- and developmental biology require single cell spatial resolution to understand tissue heterogeneity. In this project, we develop computational methods that bridge these two emerging fields. We combine spatially resolved high-throughput genomics analysis of tissue sections with digital image analysis of tissue morphology. Together with collaborators from the biomedical field, we work with advanced digital image processing methods for spatially resolved genomics (Ke et al, Nature Methods 2013). The project has been enriched by decoding gene expression in 3D, and a novel image analysis pipeline that combines a learning approach and a graphical model that has increased recall, and a visualization tool at https://tissuumaps.research.it.uu.se/ See Figure 53.

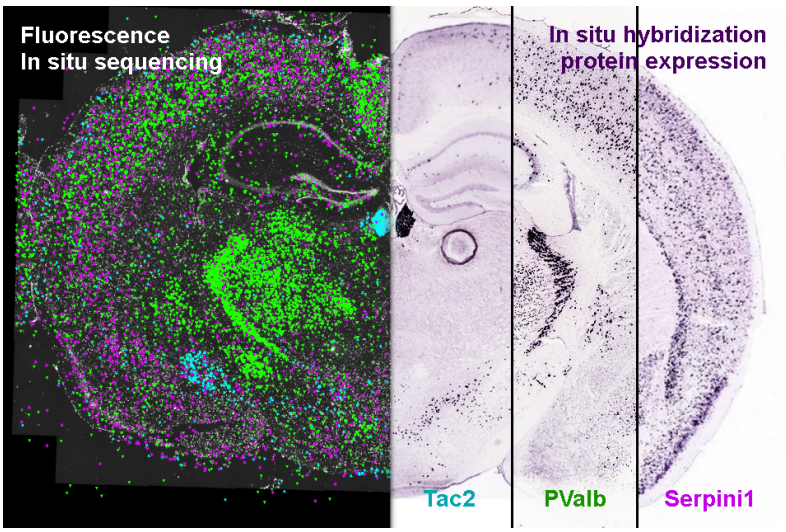

Figure 53: TissUUmaps - Integrating spatial and genetic information via automated image analysis and interactive visualization of tissue data

62. **Effects of repeated islet transplantation on islet engraftment in a mouse model**
Petter Ranefall, Anna Klemm
Partner: Hanna Liljebäck, Per-Ola Carlsson, Dept. of Medical Cell Biology, Uppsala Universitet
Funding: Science for Life Laboratory
Period: 20171016–
Abstract: The outcome of islet transplantation has improved progressively. However, the lack of organ donors makes islet transplantation available only to type I diabetes patients with the most severe glycemic lability. In the clinic, a second transplantation is often required to boost graft function and extend the time until recurrence of insulin dependence. Often, the second graft proves to work better than the initial islet transplant. In this study, we aimed to, in a mouse model with GFP positive islets, investigate whether this reflected differences in engraftment is caused by the repeated islet infusion procedure. See Figure 54.

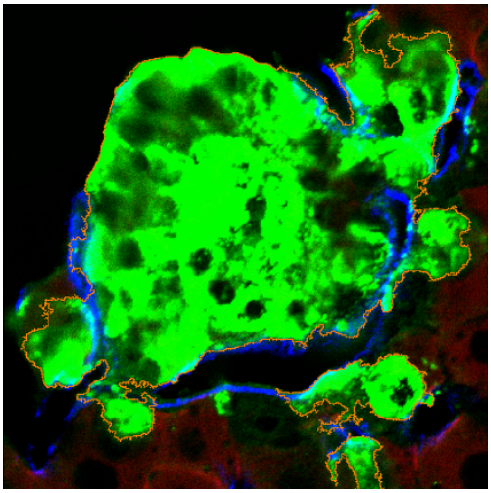

Figure 54: Effects of repeated islet transplantation on islet engraftment in a mouse model

63. **Effects of a mixture of endocrine disrupting compounds on growth and metabolism in a chicken embryo model**
Petter Ranefall, Carolina Wählby
Partner: Björn Brunström, Anna Mattsson, Anna Mentor, Environmental toxicology, EBC, Uppsala Uni-

versity
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20180118–
Abstract: The project is part of an EU project called EDC-MixRisk which aims to improve our understanding of health effects of endocrine disrupting chemicals. In EDC-MixRisk, a mixture of common chemicals have been identified in blood from pregnant women in Sweden and associated with risk for altered growth in their children. In this part of the project we use chicken embryos as a model to investigate how this mixture affects end points related to growth and metabolism in the developing embryo. The exposed chicken embryos will be examined for instance regarding body weight, amount of fat tissue, accumulation of fat in the liver and metabolic changes. The amount of fat in the liver is determined using a histological fat staining technique followed by quantitative analysis of microscopic images. See Figure 55.

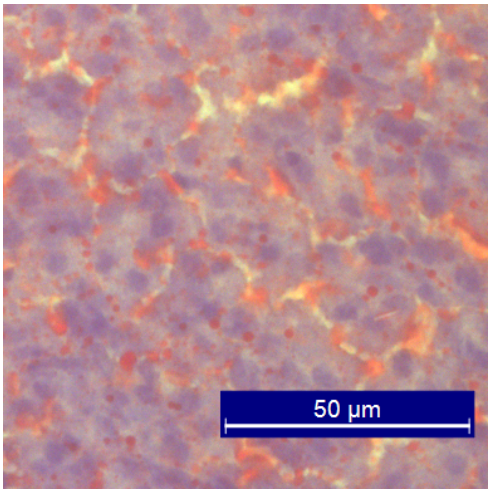

Figure 55: Effects of a mixture of endocrine disrupting compounds on growth and metabolism in a chicken embryo model

64. **Vgluts, alcohol and nicotine**
Petter Ranefall
Partner: Erika Comasco, Maria Vrettou, SciLifeLab, Dept. of Neuroscience, Uppsala University; Ingrid Nylander, Dept. of Pharmaceutical Biosciences, Uppsala University
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20180216–
Abstract: Initiation of alcohol and nicotine use in early age is a well-known risk factor for the development of addiction. The glutamatergic system plays an important role in mediating the reinforcing effects of addictive drugs and its dysfunction has been associated with addiction. The glutamatergic phenotype can be identified by the expression of the Vesicular Glutamate Transporters (Vgluts) 1, 2, and 3, which are the focus of our research [1, 2]. The present study aims to localize and quantify the effect of alcohol and/or nicotine exposure on Vgluts in the mesocorticolimbic brain of adolescents. Regions of interest are the ventral tegmental area, nucleus accumbens, prefrontal cortex, dorsal striatum, hippocampus, and amygdala; all key regions in the addiction neurocircuitry. Expression of Vglut1-3 in the brain of adolescent male rodents is assessed using in situ hybridization with DIG-labelled RNA probes on cryosections and visualized using a brightfield microscope. Cell counting and localization are performed using CellProfiler. Adolescence is a period during which the initial contact with alcohol and nicotine commonly occurs, while the brain is developing. Prevention and treatment of alcohol and nicotine use disorders can be improved by identifying early neuromolecular signatures of alcohol and nicotine on the brain. References 1. Comasco, E., J. Hallman, See Figure 56.

65. **Biomaterials for bone defects-image analysis of cell cultures**
Petter Ranefall, Carolina Wählby
Partner: Nils Hailer, Andreas Westermark, Erik Engberg, Dept. of Surgical Sciences, Uppsala University

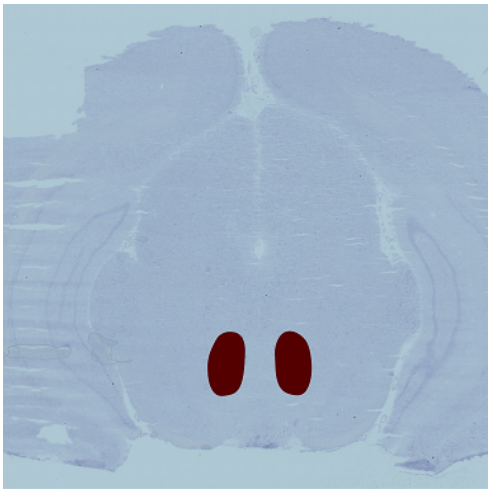

Figure 56: Vgluts, alcohol and nicotine

Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20180919–
Abstract: Bone defects are a common and sometimes very difficult problem in the patient population. If the body cańt heal the defect by itself, the gold standard treatment is bone grafting. This type of transplantation is the second most common worldwide, only surpassed by blood transfusion. There are several drawbacks with bone grafting: lack of availability, pain from the donor site and some immunological aspects when it comes to allografting. Biomaterials is a promising field for replacing bone and the current project is evaluating different types of 3D-printed scaffolds for bone regeneration. Bone cells (osteoblasts) derived from mouse are seeded onto these scaffolds and the cells are left to grow and produce bone matrix for four weeks. Cytoplasm and cell nucleus is then stained with Phalloidin/DAPI. Newly made bone is stained with Tetracycline that is incorporated already in the bone forming process. The image analysis will provide useful data for the quantification of cell establishment and growth. See Figure 57.

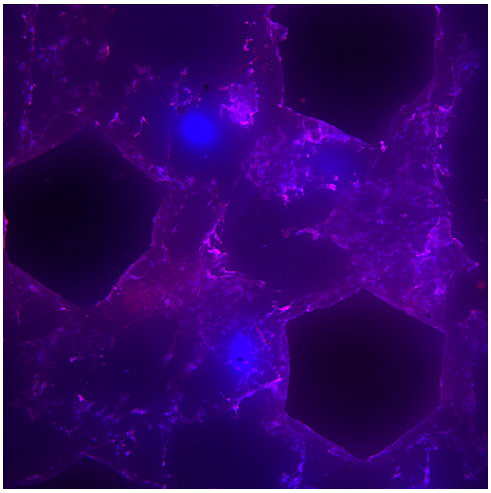

Figure 57: Biomaterials for bone defects-image analysis of cell cultures

66. **Development of a fat phantom**
Petter Ranefall, Carolina Wählby
Partner: Hana Dobsicek Trefna, Tiina Nydelö, Dept. of Electrical Engineering, Chalmers University of Technology
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)

Period: 20180813–

Abstract: Phantoms that closely mimic the dielectric properties of human tissues play an important role in testing and evaluating devices and various treatment and diagnostic schemes. A phantom is a physical model made from tissue equivalent materials to imitate the characteristics of biological tissue and of wave propagation inside the human body. The phantoms can be generalized into two groups: to mimic high-water-content tissues (muscle, brain) and low-water-content tissues (fat, bone). Finding a good composition of the latter is still challenging. In this project we investigate phantoms comprising discontinuous or percolating oil phase in hydrogel continuous matrix manufactured from oil-in-water emulsion precursors. Focusing on the influence of the composition on their dielectric properties at the microwave frequencies. The particular interest is to correlate the size of oil domains (and later percolation) with the permittivity of the phantom. The images taken by CLSM microscope are segmented to estimate the diameter of the droplets and their distribution in the focal plane of the microscope. See Figure 58.

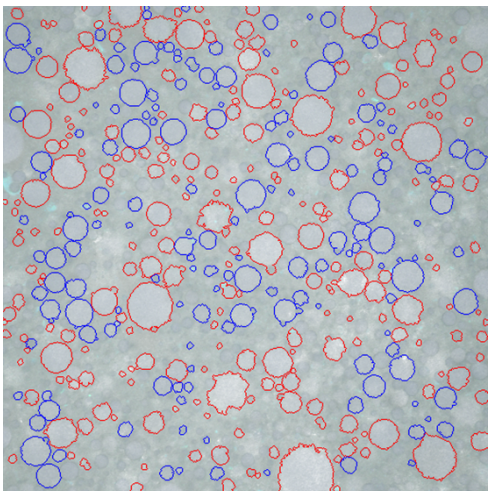

Figure 58: Development of a fat phantom

67. **Quantitative gene expression screening of in situ stained zebrafish**
Amin Allalou, Carolina Wählby
Partner: Johan Ledin - Genome Engineering Zebrafish, SciLifeLab. Maria Tenje - Customized Microfluidics, SciLifeLab.
Funding: Science for Life Laboratory TDP
Period: 20180101–
Abstract: Researchers using the Genome Engineering Zebrafish (GEZ) to generate mutant lines are often in need of subsequent phenotyping of the mutant line. This requires careful characterization of mutant lines using panels of well-established cell- and tissue-specific markers and whole mount in situ hybridization (WISH). However, many researchers are only left with in situ stained fish and no good tools or knowledge of how to extract unbiased statistical information regarding the gene expression. Results are often based on manual counting and region estimation from 2D projection images of a small number of samples. Each mutant line generated at the GEZ carries an abundance of information in their expression, using low throughput and visual quantification will miss the more subtle, yet important, phenotypes. In this project we will developed a state-of-the-art analysis pipeline consisting of a 3D imaging technique (Optical projection tomography) for chromogenic WISH stain and subsequent image analysis methods. The analysis will provide unbiased quantification and localization of expression patterns and detect statistical significant differences in any mutant line. This project is a collaboration between BioImage Informatics facility, Genome Engineering Zebrafish and Customized Microfluidics at SciLifeLab. See Figure 59.

68. **High-throughput screening in live zebrafish**
Amin Allalou, Hanqing Zhang
Partner: Johan Ledin - Genome Engineering Zebrafish, SciLifeLab. Tatjana Haitina - Dept. of Organismal Biology, Evolution and Development, UU.

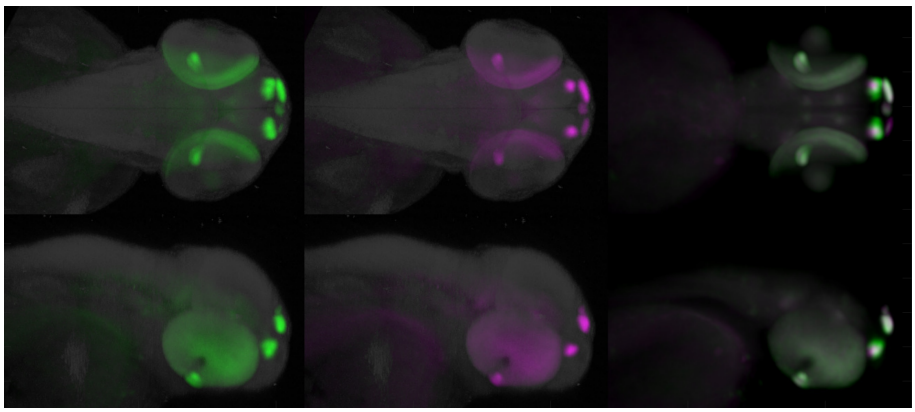

Figure 59: Quantitative gene expression screening of in situ stained zebrafish

Funding: Science for Life Laboratory TDP
Period: 20181201–
Abstract: In this project we aim to develop and implement a high-throughput phenotypic screening platform capable of functionally screening thousands of human disease-associated gene variants in vivo. By developing novel computation tools for automated image analysis and combining them with high-throughput 3D fluorescence imaging of live zebrafish using the VAST (Vertebrate Automated Screening Technology) system, we will quantify gene expression and extract morphological features with high precision. We will be able to detect subtle features that can often not be detected and statistically validated by visual inspection of a small number of samples. In addition, by extracting as much information as possible per fish and experiment we can learn and understand multiple effects and hopefully improve the starting point for experiments done on more advanced animals and clinical trials. By implementing this new technology and providing state-of-the art 3D imaging and quantitative analysis as a joint GEZ (Genome Engineering Zebrafish) - BIIF (BioImage Informatics facility) SciLifeLab service we will be able to offer users an analysis currently not available anywhere else. See Figure 60.

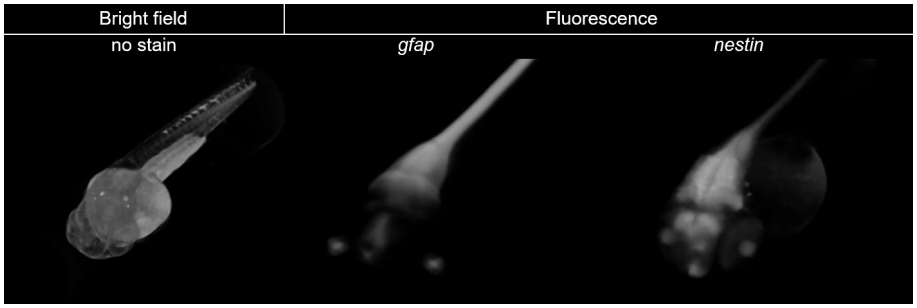

Figure 60: High-throughput screening in live zebrafish

69. **Effects of repeated intraportal islet transplantation on islet engraftment in a GFP mouse model**
Anna Klemm
Partner: Hanna Liljebäck, Per-Ola Carlsson
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20181129–
Abstract: The outcome of islet transplantation has improved progressively. However, the lack of organ donors makes islet transplantation available only to patients with type I diabetes with the most severe glycemic lability. In the clinic, a second transplantation is often required to boost graft function and extend the time until recurrence of insulin dependence. In this study, we aimed to, in a mouse model with GFP positive islets, investigate if the repeated islet infusion procedure itself has a positive effect on islet engraftment in the liver. See Figure 61.

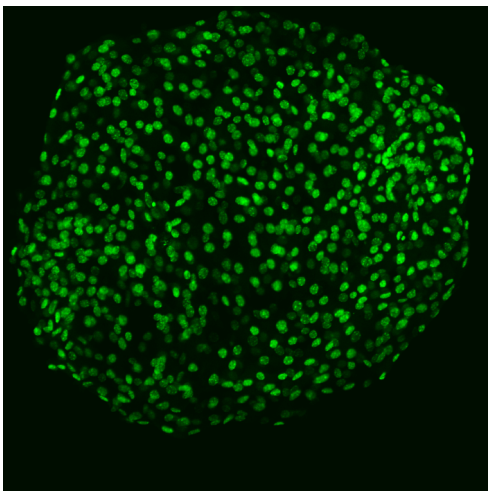

Figure 61: Effects of repeated intraportal islet transplantation on islet engraftment in a GFP mouse model

70. **Imaging mass spectrometry of mouse implantation sites**
Anna Klemm, Carolina Wählby
Partner: Ingela Lanekoff, UU
Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20180628–
Abstract: Mass spectrometry imaging enables visualization of the chemical microenvironment in regional features within thin tissue sections. In this project, thin tissue sections of mouse embryo implantation sites on day 8 of pregnancy were imaged with nanospray desorption electrospray ionization (nano-DESI) mass spectrometry to reveal molecular signatures during embryonic development. Nano-DESI is a recently established non-commerially availabe technique for mass spectrometry imaging that yields chemical information from localizations on the tissue without the need for sample preparation. The acquired data contains a full mass spectrum, with thousands of peaks, in each pixel of the image in a format that is currently not readable by commerial softwares. The aim of the project is to streamline data processing and analysis to find co-localizing and anti-localizing molecules to further our understanding of the importance of molecular localization in successful pregnancy. In particular, tissue sections from wild type and knock out mice, that deliver pups prematurely, will be evaluated. A successful project is anticipated to provide novel image analysis tools for data collected by nano-DESI mass spectrometry imaging of biological systems. See Figure 62.

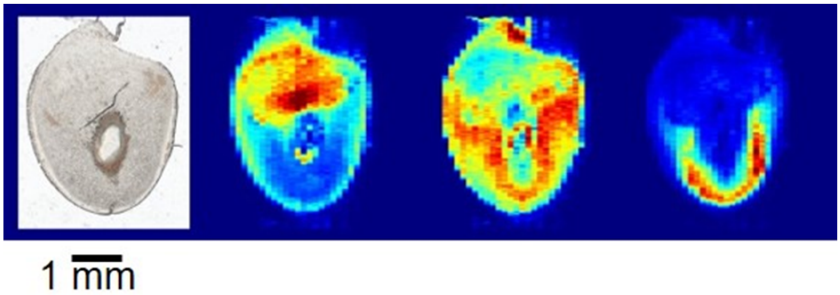

Figure 62: Imaging mass spectrometry of mouse implantation sites

71. **Automated Detection and Counting of Cells in Zebrafish**
Anna Klemm, Petter Ranefall
Partner: Ci Song, Marcel den Hoed, Uppsala University

Funding: SciLifeLab BioImage Informatics Facility (www.scilifelab.se/facilities/bioimage-informatics)
Period: 20180409–
Abstract: Large-scale genome-wide association studies have identified numerous loci that are robustly associated with blood cell count. Identifying and characterizing causal genes in these loci using in vivo model systems is anticipated to shed light on the biological regulation of red blood cell biogenesis and regulation. The zebrafish (Danio rerio) is an attractive vertebrate animal model to study erythrocytes, thanks to recent developments in automated handling. This allows high-throughput, image-based genetic screens. A transgenic zebrafish line has been obtained with fluorescently labeled erythrocytes (gata1:dsRed). The current project aims to quantify red blood cell count using videos acquired in the dorsal artery and caudal vein. See Figure 63.

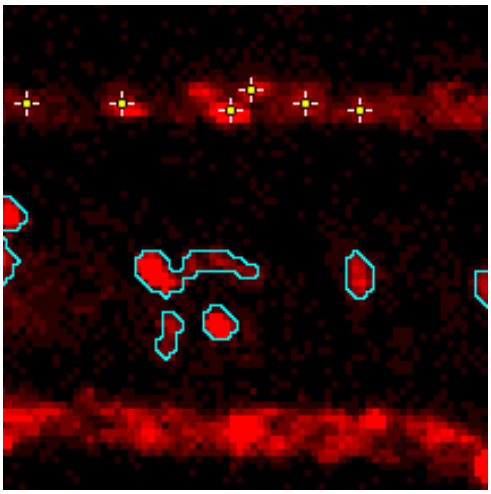

Figure 63: Automated Detection and Counting of Cells in Zebrafish

5.5 Humanities

72. **Recognition and datamining for handwritten text collections**
Anders Brun, Ewert Bengtsson, Fredrik Wahlberg, Tomas Wilkinson, Kalyan Ram, Anders Hast, Ekta Vats
Partner: Carl Nettelblad, Dept. of Information Technology, Lasse Martensson, Dept. of Business and Economics Studies, Högskolan i Gävle; Mats Dahllöf, Dept. of Linguistics and Philology, UU; Alicia Fornés, Universitat Autonoma de Barcelona, Spain; Jonas Lindström, Dept. of History, UU
Funding: UU; Swedish Research Council; Riksbankens Jubileumsfond; eSSENCE
Period: 20120101–
Abstract: This cross disciplinary initiative takes its point of departure in the analysis of handwritten text manuscripts using computational methods from image analysis and linguistics. It sets out to develop a manuscript analysis technology providing automatic tools for large-scale transcription, linguistic analysis, digital paleography and generic data mining of historical manuscripts. The mission is to develop technology that will push the digital horizon back in time, by enabling digital analysis of handwritten historical materials for both researchers and the public. One postdoc started and several new results were presented. See Figure 64.

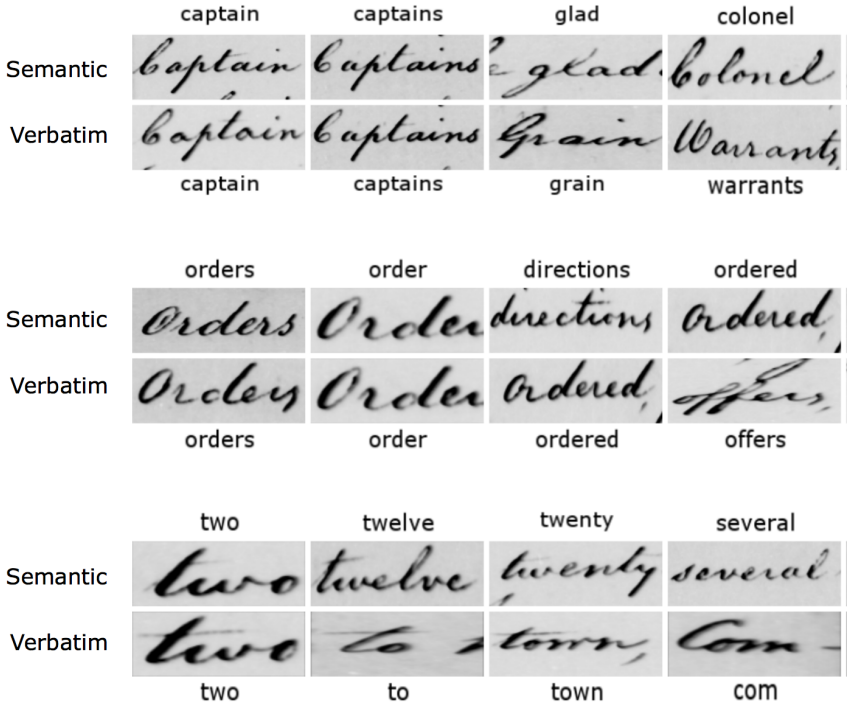

Figure 64: Recognition and Datamining for Handwritten Text Collections

73. **Writer identification and dating**
Anders Brun, Fredrik Wahlberg, Anders Hast, Ekta Vats
Partner: Lasse Martensson, Dept. of Business and Economics Studies, Högskolan i Gävle; Mats Dahllöf, Dept. of Linguistics and Philology, UU; Alicia Fornés, Universitat Autonoma de Barcelona, Spain
Funding: UU; Swedish Research Council; Riksbankens Jubileumsfond; eSSENCE
Period: 201401—-
Abstract: The problem of identifying the writer of some handwritten text is of great interest in both forensic and historical research. Sadly the magical CSI machine for identifying a scribal hand does not exist. Using image analysis, statistical models of how a scribe used the quill pen on a parchment can be collected. These measurements are treated as a statistical distribution over writing practices. We are using this information to identify single writers and perform style based dating of historical manuscripts. During 2016 we continuted to analyze over 10000 manuscript pages form the collection Svenskt Diplomatarium, from Riksarkivet. Using our newest methods, based on recent trends in deep learning, we are able to estimate the production

date of a manuscript in this collection with a median error of less than 12 years. See Figure 65.

Figure 65: Writer Identification and Dating

74. **Image analysis for landscape analysis**
Anders Brun
Partner: Bo Malmberg, Michael Nielsen, Dept. of Human Geography, Stockholm University; Anders Wästfelt, Dept. of Economics, SLU
Funding: SLU; Stockholm University
Period: 200901—-
Abstract: This project is a collaboration with researchers at SU and SLU. It aims to derive information about rural and city landscapes from satellite images. The project focuses on using texture analysis of images, rather than only pixelwise spectral analysis, to segment the image into different meaningful regions. This is an ongoing collaboration, which has so far resulted in one patent and one journal publication on the detection of damaged forest from aerial photographies. See Figure 66.

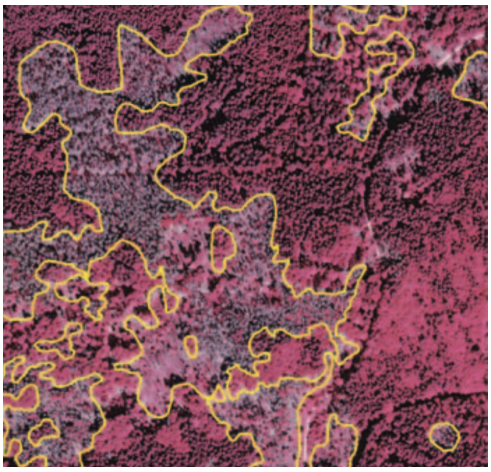

Figure 66: Image Analysis for Landscape Analysis

75. **Color names**
Gunilla Borgefors
Funding: UU
Period: 20160701–
Abstract: Recently, there is a trend in machine and deep learning applications to use many different, rather random, colour names for image annotation, retrieval, and training. Therefore, naming colours is also important. But what is cerulean to an artist may be just blue to you and the same colour as grass to a Zulu! In fact, there are many languages that do not have a term for ”blue”, while Russian has two: light blue and dark blue. And these two ”blues” are as different to them as blue and green is to us. The five ”blue” patches in the Figure are taken from an often used set in deep learning applications. One is called just ”blue”, while the others have - according to the authors - self-explanatory names. Can you name them? In this project I investigate results from colour semantics and colour perception experiments to get a better understanding on how different people understand colour names and what the consequences for how you should name colours in various applications. The paper ”The Scarcity of Universal Colour Names” was published in the proceedings of ICPRAM 2018. See Figure 67.

Figure 67: Color names

76. **Computerised image processing in handwritten text recognition**
Raphaela Heil, Anders Hast, Ekta Vats, Anders Brun
Partner: Lasse Mårtensson, Dept. of Swedish Language and Multilingualism, Stockholm University.
Funding: TN-Faculty
Period: 20180115–
Abstract: This project is concerned with handwritten text recognition with a special focus on the handling of historical documents. It encompasses the development and implementation of new computational methods for the recognition, transcription and analysis of manuscripts. The long-term strategic goal is to develop a user-friendly tool to support historians, palaeographers and other researchers from the digital humanities in the transcription and analysis of historical material.

77. **Historical handwritten text recognition**

Ekta Vats, Anders Hast

Partner: Per Cullhed - University Library, UU, Lasse Mårtensson - Dept. of Swedish Language and Multilingualism, Stockholm University, Alicia Fornés - Universitat Autonoma de Barcelona, Spain, Prashant Singh - Dept. of Information Technology, UU

Funding: Swedish e-Science Academy (eSSENCE)

Period: 20170501–

Abstract: Automatic recognition of poorly degraded handwritten text is challenging due to complex layouts and paper degradations over time. Typically, an old manuscript suffers from degradations such as paper stains, faded ink and ink bleed-through. There is variability in writing style, and the presence of text and symbols written in an unknown language. This hampers the document readability, and renders the task of transcription and word spotting in a set of non-indexed documents, to be more difficult. The aim of this project is to facilitate basic research on handwritten text recognition by developing efficient methods for recognition of complex handwritten text using advanced HTR technology. The present investigation belongs to a set of methods known as word spotting, that accelerate the word recognition process by finding multiple instances of a word on-the-fly in a set of unedited material. PI Anders Hast, along with postdoc Ekta Vats, have achieved significant advances in HTR research with scientific peer-reviewed publications that are highly relevant to this project. See Figure 68.

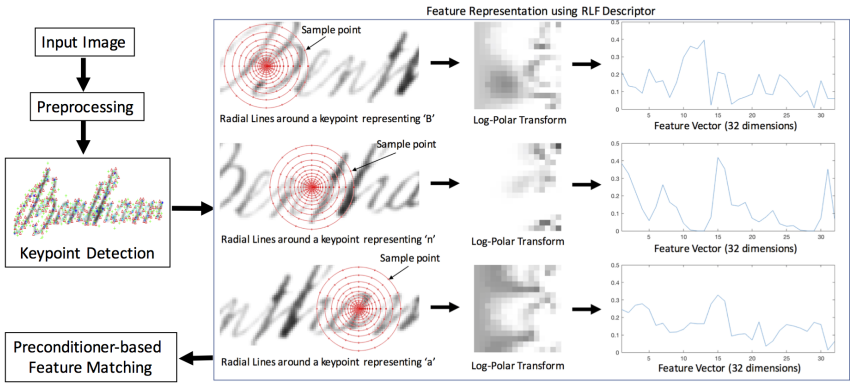

Figure 68: Historical Handwritten Text Recognition

5.6 Cooperation partners

International

Université des Sciences, des Techniques et des Technologies de Bamako, USTTB, Bamako

Dept. of Medicine and Immunology, University of Toronto, Canada

Dept. of Medical Microbiology, University of Manitoba, Winnipeg, Canada

National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, Canada

The Donelly Center, University of Toronto, Canada

Dept. of Oral and Maxillofacial Surgery, Aalborg University Hospital, Denmark

Thomas Johann Seebeck Dept. of Electronics, Tallinn University of Technology, Estonia

Eliko Tehnoloogia Arenduskeskus OÜ , Tallinn, Estonia

IRCCyN, University of Nantes, France

Service de Chirurgie Maxillofaciale et Stomatologie, Centre Hospitalier Universitaire Hôtel-Dieu, Université de Nantes, France

Département Homme et Environnement, CNRS, UMR 7206, Muséum national d'Histoire naturelle, Musée de l'Homme, Paris, France

Assistance Publique - Hôpitaux de Paris, Service de Chirurgie Maxillofaciale et Plastique, Hôpital Necker - Enfants Malades, Université Paris Descartes, Université Sorbonne Paris Cité, France

Immune Dynamics, Charité - Universitätsmedizin, Berlin, Germany.

Deutsches Rheumaforschungszentrum, a Leibniz Institute, Berlin, Germany

Institute of Molecular and Clinical Immunology, Medical Faculty, Otto von Guericke University, Magdeburg, Germany

Dept. of Computer Science, Faculty of Informatics, University of Debrecen, Hungary

Centre for Development of Advanced Computing (CDAC), Thiruvananthapuram, Kerala, India

Regional Cancer Centre, Thiruvananthapuram, Kerala, India

Faculty of Geodesy and Geomatics Engineering, K.N. Toosi University of Technology, Tehran, Iran

Politecnico di Torino, Italy

Dept. of Medical Microbiology, Kenyatta National Hospital, University of Nairobi, Kenya

Institute of Artificial Intelligence and Cognitive Engineering, University of Groningen, The Netherlands

i3S, Instituto de Investigação e Inovação em Saúde, University of Porto, Portugal

Institute of Molecular Pathology and Immunology, University of Porto, Portugal

Faculty of Medicine, University of Porto, Portugal

Center for Microscopy-Microanalysis and Information Processing, Politehnica University of Bucharest, Romania

Dept. of Pathology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Dept. of Electronic Computers RSREU, Ryazan, Russia

Faculty of Technical Sciences, University of Novi Sad, Novi Sad, Serbia

Universitat Autonoma de Barcelona, Spain

Eastern Mediterranean University, North Cyprus, Turkey

Adobe Research, San Jose, USA

Dept. of Computer Science, Boston University, USA

Broad Institute of Harvard and MIT, Boston, USA

Dept. of Electrical and Computer Engineering, University of Iowa, USA

Dept. of Radiology, University of Iowa, USA

Mt Sinai-Beth Israel Hospital, New York, USA

Perelman School of Medicine, University of Pennsylvania, Philadelphia.

Dept. of Radiology, MIPG, University of Pennsylvania, USA

Dept. of Mathematics, West Virginia University, USA

National

Dept. of Cell and Molecular Biology, UU

Dept. of History, UU

Dept. of Immunology, Genetics and Pathology, UU

Dept. of Linguistics and Philology, UU

Dept. of Mathematics, UU

Dept. of Medical Biochemistry and Microbiology, UU

Dept. of Medical Cell Biology, UU

Dept. of Medical Sciences, UU

Dept. of Neuroscience, UU

Dept. of Organismal Biology, UU

Dept. of Pharmaceutical Biosciences, UU

Dept. of Surgical Sciences, UU

Science for Life Laboratory, UU

University Library, UU

Dept. Of Mathematical Sciences, Chalmers University of Technology, Gothenburg

Dept. Of Electrical Engineering, Chalmers University of Technology, Gothenburg

Dept. of Clinical Neuroscience, Sahlgrenska Academy, University of Gothenburg, Gothenburg

Dept. of Business and Economics Studies, University of Gävle, Gävle

Dept. of Ophthalmology, Gävle Hospital, Gävle

Centre for Research and Development, UU/Region Gävleborg, Gävle

Dept. of Industrial Development, IT and Land Management, University of Gävle, Gävle

Halmstad University, Halmstad

Luleå University of Technology, Luleå, Sweden

Dept. of Clinical Sciences, Lund university, Lund

Dept. of Experimental Medical Science , Lund university, Lund

Dept. of Biosciences and Nutrition, Karolinska Institute, Stockholm

Clinical research centre, Karolinska Institute, Stockholm

Dept. of Laboratory Medicine, Karolinska Institute, Stockholm

Dept. of Medical Biochemistry and Biophysics, Karolinska Institute, Stockholm

Dept. of Medicine, Karolinska Institute, Stockholm

Dept. of Pathology and Cytology, Karolinska Institute, Stockholm

Dept. of Real Estate and Construction Management, KTH Royal Institute of Technology, Stockholm

Science for Life Laboratory, Stockholm

Dept. of Biochemistry and Biophysics, Stockholm University, Stockholm

Dept. of Human Geography, Stockholm University, Stockholm

Dept. of Swedish Language and Multilingualism, Stockholm University, Stockholm

Dept. of Psychology, Stockholm University, Stockholm

Dept. of Biomedical Engineering, Umeå University, Umeå

Dept. of Radiation Sciences, Umeå University, Umeå

Dept. of Clinical Sciences, SLU, Uppsala

Dept. of Economics, SLU, Uppsala

Alten Sweden AB, Gothenburg

Antaros Medical AB, BioVenture Hub, Mölndal

AstraZeneca AB, Stockholm

Public Dental Service, Södersjukhuset, Stockholm, Sweden

Vironova AB, Stockholm

Astrego Diagnostics AB, Uppsala

Imint Image Intelligence AB, Uppsala

Precisit AB, Uppsala

Unibap AB, Uppsala

The Swedish mapping, cadastral and land registration authority

6 Publications

Our second most important products are our publications; the most important products are our examined students, at all levels. In 2018, we published 20 articles in scientific journals and 15 in fully reviewed proceedings. Someone from CBA was first authors in only 7 of the 20 journal articles, but of 11 of the 15 proceedings articles. This is easily explainable, as our co-operation partners, especially in medicine, are not used to publish in proceedings, while for us that is often a better choice than a journal. Of the 35 papers, 11 were published in general in-subject journals and proceedings, while 24 are found in application publications. All journal articles were published in different journals and all but one proceedings article were also at different conferences. This diversity is explained by the fact that we work in a wide area, from pure mathematics to many different applications. We also wrote a number of partially or non-reviewed articles, but sadly produced no popular publications this year.

As a curiousity, we have collected the abstracts of this year's journal publications and made a so called word-cloud from them, to see which words emerge as most used, see Figure 70. One conclusion studying the word-cloud is that we publish our traditional medical application oriented papers in journals, while newer approaches, such as deep learning methods, are mainly found in the proceedings papers.

Note that Authors affiliated with CBA are in bold.

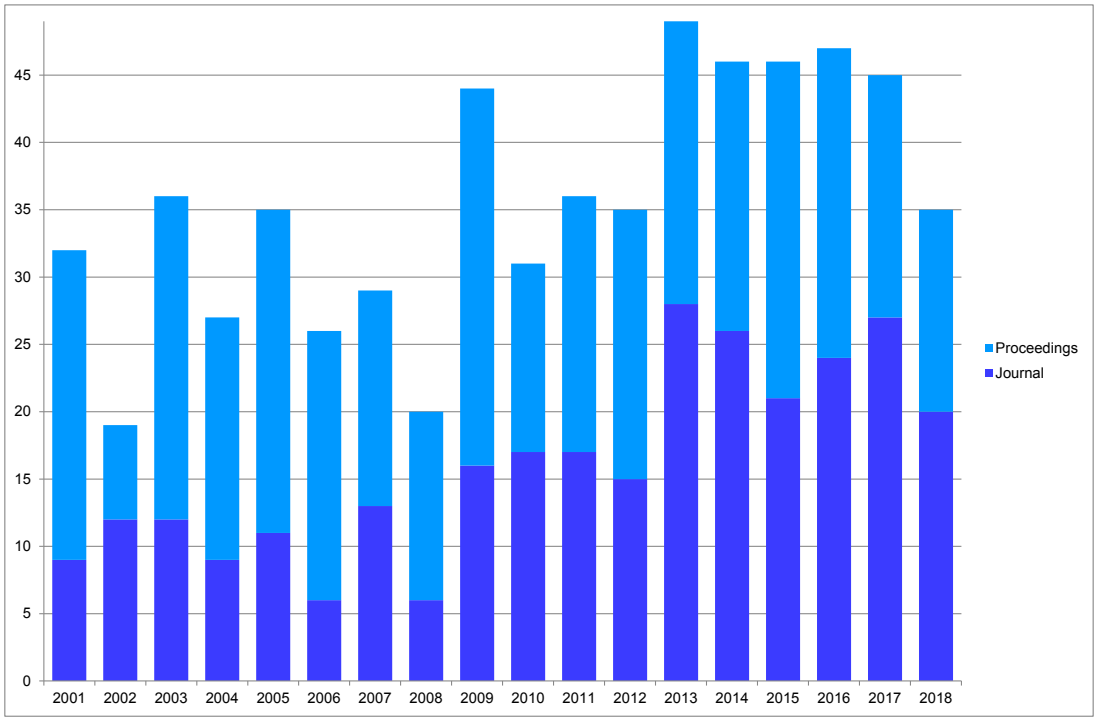

Figure 69: The number of publications from CBA 2001–2018.

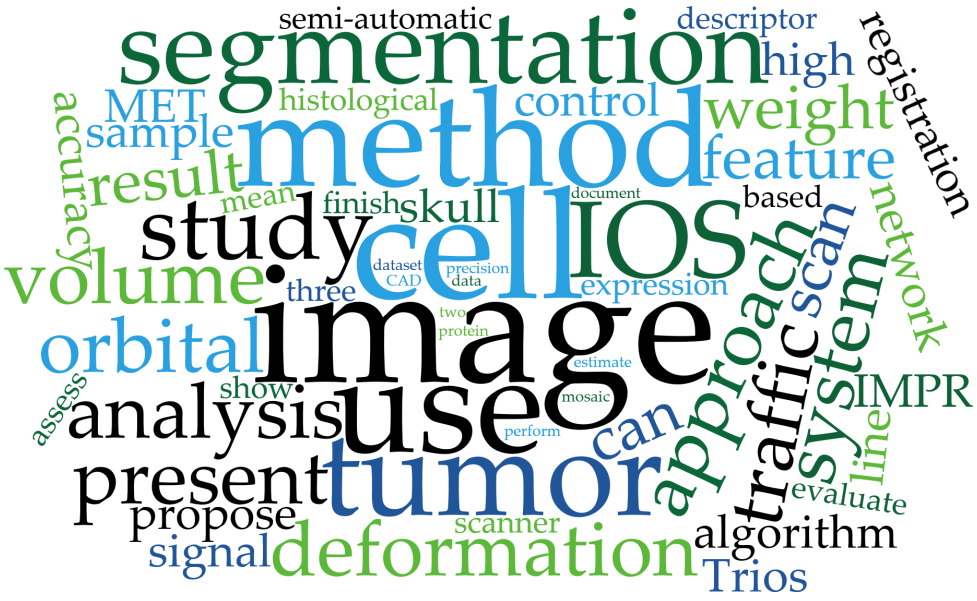

Figure 70: Word-cloud of abstracts of all journal publications from CBA during 2018.

6.1 Journal articles

1. **GISwaps : A new method for decision making in continuous choice models based on even swaps**
   Authors: Milutinovic, Goran(1); Ahonen-Jonnarth, Ulla(1); **Seipel, Stefan**(1)
   (1) Dept. of Industrial Development, IT and Land Management, University of Gävle
   Journal: International Journal of Decision Support System Technology, Vol. 10, No. 3, pp. 57-78 *Abstract:* This article describes how continuous GIS-MCDM problems are commonly managed by combining some weighting method based on pairwise comparisons of criteria with an aggregation method. The reliability of this approach may be questioned, though. First, assigning weights to criteria, without taking into consideration the actual consequences or values of the alternatives, is in itself controversial. Second, the value functions obtained by this approach are in most cases linear, which is seldom the case in reality. The authors present a new method for GIS-MCDM in continuous choice models based on Even Swaps. The method is intuitive and easy to use, based on value trade-offs, and thus not relying on criteria weighting. Value functions obtained when using the method may be linear or non-linear, and thereby are more sensitive to the characteristics of the decision space. The performed case study showed promising results regarding the reliability of the method in GIS-MCDM context.

2. **PDNet : Semantic segmentation integrated with a primal-dual network for document binarization**
   Authors: **Ayyalasomayajula, Kalyan Ram; Malmberg, Filip; Brun, Anders**
   Journal: Pattern Recognition Letters, Vol. 121, pp. 52-60
   Abstract: Binarization of digital documents is the task of classifying each pixel in an image of the document as belonging to the background (parchment/paper) or foreground (text/ink). Historical documents are often subjected to degradations, that make the task challenging. In the current work a deep neural network architecture is proposed that combines a fully convolutional network with an unrolled primal-dual network that can be trained end-to-end to achieve state of the art binarization on four out of seven datasets. Document binarization is formulated as an energy minimization problem. A fully convolutional neural network is trained for semantic segmentation of pixels that provides labeling cost associated with each pixel. This cost estimate is refined along the edges to compensate for any over or under estimation of the foreground class using a primal-dual approach. We provide necessary overview on proximal operator that facilitates theoretical underpinning required to train a primal-dual network using a gradient descent algorithm. Numerical instabilities encountered due to the recurrent nature of primal-dual approach are handled. We provide experimental results on document binarization competition dataset along with network changes and hyper-parameter tuning required for stability and performance of the network. The network when pre-trained on synthetic dataset performs better as per the competition metrics.

3. **Human Immunodeficiency Virus-Infected Women Have High Numbers of CD103-CD8+ T Cells Residing Close to the Basal Membrane of the Ectocervical Epithelium**
Authors: Gibbs, Anna(1); Buggert, Marcus(2,3,4,); Edfeldt, Gabriella(1); **Ranefall, Petter(5)**; Introini, Andrea(1); Cheuk, Stanley(1); Martini, Elisa(1); Eidsmo, Liv(1); Ball, Terry B.(6,7); Kimani, Joshua(8); Kaul, Rupert(9); Karlsson, Annika C.(4); **Wählby, Carolina(5)**; Broliden, Kristina(1); Tjernlund, Annelie(1)
(1) Dept. of Medicine Solna, Center for Molecular Medicine, Karolinska Institutet, Karolinska University Hospital Solna, Stockholm, Sweden.
(2) Dept. of Microbiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia.
(3) Institute for Immunology, Perelman School of Medicine, University of Pennsylvania, Philadelphia.
(4) Dept. of Medicine Huddinge, Karolinska Institutet, Stockholm, Sweden.
(5) Science for Life Laboratory, Uppsala, Sweden.
(6) Dept. of Medical Microbiology, University of Manitoba, Winnipeg, Canada.
(7) National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg.
(8) Dept. of Medical Microbiology, Kenyatta National Hospital, University of Nairobi, Kenya.
(9) Dept. of Medicine and Immunology, University of Toronto, Canada.
Journal: Journal of Infectious Diseases, Vol. 2018, No. 3, pp. 453–665,
Abstract:
BACKGROUND: Genital mucosa is the main portal of entry for various incoming pathogens, including human immunodeficiency virus (HIV), hence it is an important site for host immune defenses. Tissue-resident memory T (TRM) cells defend tissue barriers against infections and are characterized by expression of CD103 and CD69. In this study, we describe the composition of CD8+ TRM cells in the ectocervix of healthy and HIV-infected women.

METHODS: Study samples were collected from healthy Swedish and Kenyan HIV-infected and uninfected women. Customized computerized image-based in situ analysis was developed to assess the ectocervical biopsies. Genital mucosa and blood samples were assessed by flow cytometry.

RESULTS: Although the ectocervical epithelium of healthy women was populated with bona fide CD8+ TRM cells (CD103+CD69+), women infected with HIV displayed a high frequency of CD103-CD8+ cells residing close to their epithelial basal membrane. Accumulation of CD103-CD8+ cells was associated with chemokine expression in the ectocervix and HIV viral load. CD103+CD8+ and CD103-CD8+ T cells expressed cytotoxic effector molecules in the ectocervical epithelium of healthy and HIV-infected women. In addition, women infected with HIV had decreased frequencies of circulating CD103+CD8+ T cells.

CONCLUSIONS: Our data provide insight into the distribution of CD8+ TRM cells in human genital mucosa, a critically important location for immune defense against pathogens, including HIV.

4. **Automatic detection of multisize pulmonary nodules in CT images : Large-scale validation of the false-positive reduction step**
Authors: **Gupta, Anindya**(1); Saar, Tonis(2); Martens, Olev(1); Le Moullec, Yannick(1)
(1) Thomas Johann Seebeck Dept. of Electronics, Tallinn University of Technology, Tallinn, 19086, Estonia.
(2) Eliko Tehnoloogia Arenduskeskus OÜ, Tallinn 12618 and OÜ, Tallinn, 10143, Estonia.
Journal: Medical physics (Lancaster), Vol. 45, No. 3, pp- 1135–1149
Abstract:
PURPOSE: Currently reported computer-aided detection (CAD) approaches face difficulties in identifying the diverse pulmonary nodules in thoracic computed tomography (CT) images, especially in heterogeneous datasets. We present a novel CAD system specifically designed to identify multisize nodule candidates in multiple heterogeneous datasets.

METHODS: The proposed CAD scheme is divided into two phases: primary phase and final phase. The primary phase started with the lung segmentation algorithm and the segmented lungs were further refined using morphological closing process to include the pleural nodules. Next, we empirically formulated three subalgorithms modules to detect different sizes of nodule candidates ($\geq$ 3 and $<$ 6 mm; $\geq$ 6 and $<$ 10 mm; and $\geq$ 10 mm). Each subalgorithm module included a multistage flow of rule-based thresholding and morphological processes. In the final phase, the nodule candidates were augmented to boost the performance of the classifier. The CAD system was trained using a total number of nodule candidates = 201,654 (after augmentation) and nonnodule candidates = 731,486. A rich set of 515 features based on cluster, texture, and voxel-based intensity features were utilized to train a neural network classifier. The proposed method was trained on 899 scans from the Lung Image Database Consortium/Image Database Resource Initiative

(LIDC-IDRI). The CAD system was also independently tested on 153 CT scans taken from the AAPM-SPIE-LungX Dataset and two subsets from the Early Lung Cancer Action Project (ELCAP and PCF).

RESULTS: For the LIDC-IDRI training set, the proposed CAD scheme yielded an overall sensitivity of 85.6% (1189/1390) and 83.5% (1161/1390) at 8 FP/scan and 1 FP/scan, respectively. For the three independent test sets, the CAD system achieved an average sensitivity of 68.4% at 8 FP/scan.

CONCLUSION: The authors conclude that the proposed CAD system can identify dissimilar nodule candidates in the multiple heterogeneous datasets. It could be considered as a useful tool to support radiologists during screening trials

5. **A fast Fourier based feature descriptor and a cascade nearest neighbour search with an efficient matching pipeline for mosaicing of microscopy images**
   Authors: **Hast, Anders**; Sablina, Victoria A.(1); **Sintorn, Ida-Maria**(2); Kylberg, Gustaf(2)
   (1) Dept. of Electronic Computers, Ryazan State Radio Engineering University Ryazan, Russia
   (2) Vironova AB, Stockholm, Sweden
   Journal: Pattern Recognition and Image Analysis, Vol. 28, No. 2, pp. 261–272
   Abstract: Automatic mosaicing is an important image processing application and we propose several improvements and simplifications to the image registration pipeline used in microscopy to automatically construct large images of whole specimen samples from a series of images. First of all we propose a feature descriptor based on the amplitude of a few elements of the Fourier transform, which makes it fast to compute and that can be used for any image matching and registration applications where scale and rotation invariance is not needed. Secondly, we propose a cascade matching approach that will reduce the time for the nearest neighbour search considerably, making it almost independent on feature vector length. Moreover, several improvements are proposed that will speed up the whole matching process. These are: faster interest point detection, a regular sampling strategy and a deterministic false positive removal procedure that finds the transformation. All steps of the improved pipeline are explained and the results comparative experiments are presented.

6. **Radial line Fourier descriptor for historical handwritten text representation**
   Authors: **Hast, Anders; Vats, Ekta**
   Journal: Journal of WSCG, Vol. 26, No. 1, pp. 31–40
   Abstract: Automatic recognition of historical handwritten manuscripts is a daunting task due to paper degradation over time. Recognition-free retrieval or word spotting is popularly used for information retrieval and digitization of the historical handwritten documents. However, the performance of word spotting algorithms depends heavily on feature detection and representation methods. Although there exist popular feature descriptors such as Scale Invariant Feature Transform (SIFT) and Speeded Up Robust Features (SURF), the invariant properties of these descriptors amplify the noise in the degraded document images, rendering them more sensitive to noise and complex characteristics of historical manuscripts. Therefore, an efficient and relaxed feature descriptor is required as handwritten words across different documents are indeed similar, but not identical. This paper introduces a Radial Line Fourier (RLF) descriptor for handwritten word representation, with a short feature vector of 32 dimensions. A segmentation-free and training-free handwritten word spotting method is studied herein that relies on the proposed RLF descriptor, takes into account different keypoint representations and uses a simple preconditioner-based feature matching algorithm. The effectiveness of the RLF descriptor for segmentation-free handwritten word spotting is empirically evaluated on well-known historical handwritten datasets using standard evaluation measures.

7. **Multiplexed fluorescence microscopy reveals heterogeneity among stromal cells in mouse bone marrow sections**
   Authors: Holzwarth, Karolin(1); Köhler, Ralf(2); Philipsen, Lars(3); Tokoyoda, Koji(2); **Ladyhina, Valeriia; Wählby, Carolina**; Niesner, Raluca A.(2); Hauser, Anja E.(1,2)
   (1) Immune Dynamics, Charité - Universitätsmedizin, Berlin, Germany.
   (2)Deutsches Rheumaforschungszentrum, a Leibniz Institute, Berlin, Germany.
   (3) Institute of Molecular and Clinical Immunology, Medical Faculty, Otto von Guericke University, Magdeburg, Germany.
   Journal: Cytometry Part A, Vol. 93, No. 9, pp. 876–888
   Abstract: The bone marrow (BM) consists of multiple, structured micro-environmental entities-the so called niches, which contain hematopoietic cells as well as stromal cells. These niches fulfill a variety of functions, such as control of the hematopoietic stem cell pool, differentiation of hematopoietic cells, and maintenance

of immunological memory. However, due to the molecular and cellular complexity and a lack of suitable histological multiplexing methods, the composition of the various BM niches is still elusive. In this study, we apply multiepitope-ligand-cartography (MELC) on bone sections from mice. We combine multiplexed immunofluorescence histology data with various object-based segmentation approaches in order to define irregularly shaped, net-like structures of stromal cells. We confirm MELC as a robust histological method and validate our automated segmentation algorithms using flow cytometry and manual evaluation. By means of MELC multiplexing, we reveal heterogeneous expression of leptin receptor (LpR), BP-1, and VCAM-1 in the stromal network. Moreover, we demonstrate by quantification a preferential contact of B cell subsets as well as of plasma cells to processes of CXCL12-expressing stromal cells, compared with stromal somata. In summary, our approach is suitable for spatial analysis of complex tissue structures.

8. **Image-Based Detection of Patient-Specific Drug-Induced Cell-Cycle Effects in Glioblastoma**
   Authors: **Matuszewski, Damian J.; Wählby, Carolina**(1); Krona, Cecilia(2); Nelander, Sven(2); **Sintorn, Ida-Maria**
   (1) Science for Life Laboratory, UU
   (2) Dept. of Immunology, Genetics and Pathology, UU
   Journal: SLAS Discovery: Advancing Life Sciences R&D, Vol. 23, No. 10, pp. 1030–1039
   Abstract: Image-based analysis is an increasingly important tool to characterize the effect of drugs in large-scale chemical screens. Herein, we present image and data analysis methods to investigate population cell-cycle dynamics in patient-derived brain tumor cells. Images of glioblastoma cells grown in multiwell plates were used to extract per-cell descriptors, including nuclear DNA content. We reduced the DNA content data from per-cell descriptors to per-well frequency distributions, which were used to identify compounds affecting cell-cycle phase distribution. We analyzed cells from 15 patient cases representing multiple subtypes of glioblastoma and searched for clusters of cell-cycle phase distributions characterizing similarities in response to 249 compounds at 11 doses. We show that this approach applied in a blind analysis with unlabeled substances identified drugs that are commonly used for treating solid tumors as well as other compounds that are well known for inducing cell-cycle arrest. Redistribution of nuclear DNA content signals is thus a robust metric of cell-cycle arrest in patient-derived glioblastoma cells.

9. **Finish line distinctness and accuracy in 7 intraoral scanners versus conventional impression: an in vitro descriptive comparison**
   Authors: Nedelcu, Robert(1); Olsson, Pontus; **Nyström, Ingela**; Thor, Andreas (1)
   (1) Dept. of Surgical Sciences, Plastic & Oral and Maxillofacial Surgery, UU
   Journal: BMC Oral Health, Vol. 18, eid. 27
   Abstract: Several studies have evaluated accuracy of intraoral scanners (IOS), but data is lacking regarding variations between IOS systems in the depiction of the critical finish line and the finish line accuracy. The aim of this study was to analyze the level of finish line distinctness (FLD), and finish line accuracy (FLA), in 7 intraoral scanners (IOS) and one conventional impression (IMPR). Furthermore, to assess parameters of resolution, tessellation, topography, and color.

   METHODS: A dental model with a crown preparation including supra and subgingival finish line was reference-scanned with an industrial scanner (ATOS), and scanned with seven IOS: 3M, CS3500 and CS3600, DWIO, Omnicam, Planscan and Trios. An IMPR was taken and poured, and the model was scanned with a laboratory scanner. The ATOS scan was cropped at finish line and best-fit aligned for 3D Compare Analysis (Geomagic). Accuracy was visualized, and descriptive analysis was performed.

   RESULTS: All IOS, except Planscan, had comparable overall accuracy, however, FLD and FLA varied substantially. Trios presented the highest FLD, and with CS3600, the highest FLA. 3M, and DWIO had low overall FLD and low FLA in subgingival areas, whilst Planscan had overall low FLD and FLA, as well as lower general accuracy. IMPR presented high FLD, except in subgingival areas, and high FLA. Trios had the highest resolution by factor 1.6 to 3.1 among IOS, followed by IMPR, DWIO, Omnicam, CS3500, 3M, CS3600 and Planscan. Tessellation was found to be non-uniform except in 3M and DWIO. Topographic variation was found for 3M and Trios, with deviations below $\pm$ 25 μm for Trios. Inclusion of color enhanced the identification of the finish line in Trios, Omnicam and CS3600, but not in Planscan.

   CONCLUSIONS: There were sizeable variations between IOS with both higher and lower FLD and FLA than IMPR. High FLD was more related to high localized finish line resolution and non-uniform tessellation, than to high overall resolution. Topography variations were low. Color improved finish line identification in

some IOS. It is imperative that clinicians critically evaluate the digital impression, being aware of varying technical limitations among IOS, in particular when challenging subgingival conditions apply.

10. **Comparison analysis of orbital shape and volume in unilateral fractured orbits**
Authors: Nilsson, Johanna(1,2); **Nysjö, Johan**; Carlsson, Anders-Petter(1,2) ; Thor, Andreas(1)
(1) Plastic and Oral & Maxillofacial Surgery, Dept. of Surgical Sciences, UU
(2) Dept. of Oral & Maxillofacial Surgery, Zealand University Hospital, Køge, Denmark
Journal: Journal of Cranio-Maxillofacial Surgery, Vol. 46, No. 3, pp. 381–387
Abstract: Facial fractures often result in changes of the orbital volume. These changes can be measured in three-dimensional (3D) computed tomography (CT) scans for preoperative planning and postoperative evaluation. The aim of this study was to analyze the orbital volume and shape before and after surgical treatment of unilateral orbital fractures using semi-automatic image segmentation and registration techniques. The orbital volume in 21 patients was assessed by a semi-automatic model-based segmentation method. The fractured orbit was compared relative to the contralateral orbit. The same procedure was performed for the postoperative evaluation. Two observers performed the segmentation procedure, and the inter- and intraobserver variability was evaluated. The interobserver variability (mean volume difference $\pm$ 1.96 SD) was -0.6 $\pm$ 1.0 ml in the first trial and 0.7 $\pm$ 0.8 ml in the second trial. The intra-observer variability was -0.2 $\pm$ 0.7 ml for the first observer and 1.1 $\pm$ 0.9 ml for the second observer. The average volume overlap (Dice similarity coefficient) between the fractured and contralateral side increased after surgery, while the mean and maximum surface distance decreased, indicating that the surgery contributed to a re-establishment of size and shape. In conclusion, our study shows that the semi-automatic segmentation method has precision for detecting volume differences down to 1.0 ml. The combination of semi-automatic segmentation and 3D shape analysis provides a powerful tool for planning and evaluating treatment of orbital fractures.

11. **Region-by-region analysis of PET, MRI and histology in en bloc-resected oligodendrogliomas reveals intra-tumoral heterogeneity**
Authors: Roodakker, Kenney Roy(1); Alhuseinalkhudhur, Ali(1,2); **Al-Jaff, Mohammed**; Georganaki, Maria(3); Zetterling, Maria(4); Berntsson, Shala G.(1); Danfors, Torsten(2); **Strand, Robin**(2); Edqvist, Per-Henrik(5); Dimberg, Anna(3); Larsson, Elna-Marie(3,6); Smits, Anja(1,7)
(1) Dept. of Neuroscience, Neurology, UU
(2) Dept. of Surgical Sciences, Radiology, UU
(3) Dept. of Immunology, Genetics and Pathology, Rudbeck Laboratory, UU
(4) Dept. of Neuroscience, Section of Neurosurgery, UU
(5) Dept. of Immunology, Genetics and Pathology and Science for Life Laboratory, UU
(6) Dept. of Radiology, Uppsala University Hospital
(7) Institute of Neuroscience and Physiology, Dept. of Clinical Neuroscience, Sahlgrenska Academy, University of Gothenburg, Sweden
Journal: European Journal of Nuclear Medicine and Molecular Imaging
Abstract:
PURPOSE: Oligodendrogliomas are heterogeneous tumors in terms of imaging appearance, and a deeper understanding of the histopathological tumor characteristics in correlation to imaging parameters is needed. We used PET-to-MRI-to-histology co-registration with the aim of studying intra-tumoral 11C-methionine (MET) uptake in relation to tumor perfusion and the protein expression of histological cell markers in corresponding areas.

METHODS: Consecutive histological sections of four tumors covering the entire en bloc-removed tumor were immunostained with antibodies against IDH1-mutated protein (tumor cells), Ki67 (proliferating cells), and CD34 (blood vessels). Software was developed for anatomical landmarks-based co-registration of subsequent histological images, which were overlaid on corresponding MET PET scans and MRI perfusion maps. Regions of interest (ROIs) on PET were selected throughout the entire tumor volume, covering hot spot areas, areas adjacent to hot spots, and tumor borders with infiltrating zone. Tumor-to-normal tissue (T/N) ratios of MET uptake and mean relative cerebral blood volume (rCBV) were measured in the ROIs and protein expression of histological cell markers was quantified in corresponding regions. Statistical correlations were calculated between MET uptake, rCBV, and quantified protein expression.

RESULTS: A total of 84 ROIs were selected in four oligodendrogliomas. A significant correlation ($p < 0.05$) between MET uptake and tumor cell density was demonstrated in all tumors separately. In two tumors, MET correlated with the density of proliferating cells and vessel cell density. There were no significant

correlations between MET uptake and rCBV, and between rCBV and histological cell markers.

CONCLUSIONS: The MET uptake in hot spots, outside hotspots, and in infiltrating tumor edges unanimously reflects tumor cell density. The correlation between MET uptake and vessel density and density of proliferating cells is less stringent in infiltrating tumor edges and is probably more susceptible to artifacts caused by larger blood vessels surrounding the tumor. Although based on a limited number of samples, this study provides histological proof for MET as an indicator of tumor cell density and for the lack of statistically significant correlations between rCBV and histological cell markers in oligodendrogliomas.

12. **A strategy for OCT estimation of the optic nerve head pigment epithelium central limit-inner limit of the retina minimal distance, PIMD-2Π**
Authors: Sandberg Melin, Camilla(1,2); **Malmberg, Filip**; Söderberg, Per G.(1)
(1) Gullstrand lab, Ophthalmology, Dept. of Neuroscience, UU
(2) Centre for Research and Development, UU/Region Gävleborg, Gävle, Sweden.
Journal: Acta Ophthalmologica Scandinavica, Vol. 96
Abstract:
PURPOSE: To develop a semi-automatic algorithm for estimation of pigment epithelium central limit-inner limit of the retina minimal distance averaged over 2Π radians (PIMD-2Π) and to estimate the precision of the algorithm. Further, the variances in estimates of PIMD-2Π were to be estimated in a pilot sample of glaucomatous eyes.

METHODS: Three-dimensional cubes of the optic nerve head (ONH) were captured with a commercial SD-OCT device. Raw cube data were exported for semi-automatic segmentation. The inner limit of the retina was automatically detected. Custom software aided the delineation of the ONH pigment epithelium central limit resolved in 500 evenly distributed radii. Sources of variation in PIMD estimates were analysed with an analysis of variance.

RESULTS: The estimated variance for segmentations and angles was 130 μm^2 and 1280 μm^2 , respectively. Considering averaging eight segmentations, a 95 % confidence interval for mean PIMD-2Π was estimated to 212 $\pm$ 10 μm (df = 7). The coefficient of variation for segmentation was estimated at 0.05. In the glaucomatous eyes, the within-subject variance for captured volumes and for segmentations within volumes was 10 μm^2 and 50μm^2 , respectively.

CONCLUSION: The developed semi-automatic algorithm enables estimation of PIMD-2Π in glaucomatous eyes with relevant precision using few segmentations of each captured volume.

13. **An Objective Scoring Framework for Histology Slide Image Mosaics Applicable for the Reliable Benchmarking of Image Quality Assessment Algorithms**
Authors: Totu, Tiberiu(1); Buga, Roxana(1); Dumitru, Adrian(2); Costache, Mariana(2); **Sladoje, Nataša**; Stanciu, Stefan(1)
(1) Center for Microscopy-Microanalysis and Information Processing, Politehnica University of Bucharest, Bucharest, Romania
(2) Dept. of Pathology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
Journal: IEEE Access, Vol. 6, pp. 53080–53091
Abstract: The conversion of histology slides into electronic format represents a key element in modern histopathology workflows. The most common way of converting physical histology slides into digital versions consists of tile-based scanning. In such approaches, the entire image of the slide is generated by consecutively scanning adjacent sample regions with a degree of overlap and then stitching these together to constitute an image mosaic. To achieve a high-quality result, the image acquisition protocol for collecting the mosaic tiles requires a recalibration of the microscope when moving from one sample region to another. This recalibration procedure typically involves focus and illumination adjustments, aimed at rendering a homogeneous image mosaic in terms of brightness, contrast, and other important image properties. The accurate evaluation of the digital slide's quality factor is, therefore, an important matter, as it can lead to designing efficient (and automated) mosaic generation protocols. We introduce here a new methodology for the evaluation of image mosaics collected with brightfield microscopy on histology slides, coined Objective Quantifiable Scoring System (OQSS). It relies on objective scoring criteria that take into consideration fundamental characteristics of image mosaics, and on histology specific aspects. We present the theoretical principles of this methodology and discuss the potential utility of this framework as a quality ground-truth tagging mechanism of histology slide image mosaics applicable for the reliable benchmarking of image quality assessment algorithms.

14. **Quantitative image analysis of protein expression and colocalisation in skin sections**
Authors: Zhang, Hanqian(1); Ericsson, Maja(1); Virtanen, Marie(1); Weström, Simone(1); **Wählby, Carolina**(2); Vahlquist, Anders(1); Törmä, Hans(1)
(1) Dept. of Medical Sciences, Dermatology and Venereology, UU
(2) SciLifeLab, UU
Journal: Experimental dermatology, Vol. 27, No. 2, pp. 196–199
Abstract: Immunofluorescence (IF) and in situ proximity ligation assay (isPLA) are techniques that are used for in situ protein expression and colocalisation analysis, respectively. However, an efficient quantitative method to analyse both IF and isPLA staining on skin sections is lacking. Therefore, we developed a new method for semi-automatic quantitative layer-by-layer measurement of protein expression and colocalisation in skin sections using the free open-source software CellProfiler. As a proof of principle, IF and isPLA of ichthyosis-related proteins TGm-1 and SDR9C7 were examined. The results indicate that this new method can be used for protein expression and colocalisation analysis in skin sections.

15. **Accuracy and precision of 3 intraoral scanners and accuracy of conventional impressions : A novel in vivo analysis method**
Authors: Nedelcu, Robert(1); **Olsson, Pontus**; **Nyström, Ingela**; Rydén, Jesper(2); Thor, Andreas(1)
(1) Dept. of Surgical Sciences, Plastic & Oral and Maxillofacial Surgery, UU
(2) Dept. of Mathematics, UU
Journal: Journal of Dentistry, Vol. 69, pp. 110-118
Abstract: Objective: To evaluate a novel methodology using industrial scanners as a reference, and assess in vivo accuracy of 3 intraoral scanners (IOS) and conventional impressions. Further, to evaluate IOS precision in vivo. Methods: Four reference-bodies were bonded to the buccal surfaces of upper premolars and incisors in five subjects. After three reference-scans, ATOS Core 80 (ATOS), subjects were scanned three times with three IOS systems: 3M True Definition (3M), CEREC Omnicam (OMNI) and Trios 3 (TRIOS). One conventional impression (IMPR) was taken, 3M Impregum Penta Soft, and poured models were digitized with laboratory scanner 3shape D1000 (D1000). Best-fit alignment of reference-bodies and 3D Compare Analysis was performed. Precision of ATOS and D1000 was assessed for quantitative evaluation and comparison. Accuracy of IOS and IMPR were analyzed using ATOS as reference. Precision of IOS was evaluated through intra-system comparison. Results: Precision of ATOS reference scanner (mean 0.6 mu m) and D1000 (mean 0.5 mu m) was high. Pairwise multiple comparisons of reference-bodies located in different tooth positions displayed a statistically significant difference of accuracy between two scanner-groups: 3M and TRIOS, over OMNI (p value range 0.0001 to 0.0006). IMPR did not show any statistically significant difference to IOS. However, deviations of IOS and IMPR were within a similar magnitude. No statistical difference was found for IOS precision. Conclusion: The methodology can be used for assessing accuracy of IOS and IMPR in vivo in up to five units bilaterally from midline. 3M and TRIOS had a higher accuracy than OMNI. IMPR overlapped both groups. Clinical significance: Intraoral scanners can be used as a replacement for conventional impressions when restoring up to ten units without extended edentulous spans.

16. **Orbital shape in intentional skull deformations and adult sagittal craniosynostoses**
Authors: Sandy, Ronak(1);Hennocq, Quentin(2); **Nysjö, Johan**; Giran, Guillaume(3); Friess, Martin(4); Khonsari, Roman Hossein(2)
(1) Dept. of Oral and Maxillofacial Surgery, Aalborg University Hospital, Denmark.
(2) Assistance Publique - Hôpitaux de Paris, Service de Chirurgie Maxillofaciale et Plastique, Hôpital Necker - Enfants Malades, Université Paris Descartes, Université Sorbonne Paris Cité, France.
(3) Service de Chirurgie Maxillofaciale et Stomatologie, Centre Hospitalier Universitaire Hôtel-Dieu, Université de Nantes, France.
(4) Département Homme et Environnement, CNRS, UMR 7206, Muséum national d'Histoire naturelle, Musée de l'Homme, Paris, France.
Journal: Journal of Anatomy, Vol. 233, No. 3, pp. 302-310
Abstract: Intentional cranial deformations are the result of external mechanical forces exerted on the skull vault that modify the morphology of various craniofacial structures such as the skull base, the orbits and the zygoma. In this controlled study, we investigated the 3D shape of the orbital inner mould and the orbital volume in various types of intentional deformations and in adult non-operated scaphocephaly - the most common type of craniosynostosis - using dedicated morphometric methods. CT scans were performed on 32 adult skulls with intentional deformations, 21 adult skull with scaphocephaly and 17 non-deformed adult

skulls from the collections of the Museum national d'Histoire naturelle in Paris, France. The intentional deformations group included six skulls with Toulouse deformations, eight skulls with circumferential deformations and 18 skulls with antero-posterior deformations. Mean shape models were generated based on a semi-automatic segmentation technique. Orbits were then aligned and compared qualitatively and quantitatively using colour-coded distance maps and by computing the mean absolute distance, the Hausdorff distance, and the Dice similarity coefficient. Orbital symmetry was assessed after mirroring, superimposition and Dice similarity coefficient computation. We showed that orbital shapes were significantly and symmetrically modified in intentional deformations and scaphocephaly compared with non-deformed control skulls. Antero-posterior and circumferential deformations demonstrated a similar and severe orbital deformation pattern resulting in significant smaller orbital volumes. Scaphocephaly and Toulouse deformations had similar deformation patterns but had no effect on orbital volumes. This study showed that intentional deformations and scaphocephaly significantly interact with orbital growth. Our approach was nevertheless not sufficient to identify specific modifications caused by the different types of skull deformations or by scaphocephaly.

17. **Traffic signal optimization through discrete and continuous reinforcement learning with robustness analysis in downtown Tehran**
Authors: Aslani, Mohammad(1); **Seipel, Stefan**(1); Mesgari, Mohammad Saadi(3); Wiering, Marco(4)
(1) Dept. of Industrial Development, IT and Land Management, University of Gavle, Gavle, Sweden
(2) Faculty of Geodesy and Geomatics Engineering, K.N. Toosi University of Technology, Tehran, Iran
(3) Institute of Artificial Intelligence and Cognitive Engineering, University of Groningen, Groningen, The Netherlands
Journal: Advanced Engineering Informatics, Vol. 38, pp. 639-655
Abstract: Traffic signal control plays a pivotal role in reducing traffic congestion. Traffic signals cannot be adequately controlled with conventional methods due to the high variations and complexity in traffic environments. In recent years, reinforcement learning (RL) has shown great potential for traffic signal control because of its high adaptability, flexibility, and scalability. However, designing RL-embedded traffic signal controllers (RLTSCs) for traffic systems with a high degree of realism is faced with several challenges, among others system disturbances and large state-action spaces are considered in this research.

The contribution of the present work is founded on three features: (a) evaluating the robustness of different RLTSCs against system disturbances including incidents, jaywalking, and sensor noise, (b) handling a high-dimensional state-action space by both employing different continuous state RL algorithms and reducing the state-action space in order to improve the performance and learning speed of the system, and (c) presenting a detailed empirical study of traffic signals control of downtown Tehran through seven RL algorithms: discrete state Q-learning(λ), SARSA(λ), actor-critic(λ), continuous state Q-learning(λ), SARSA(λ), actor-critic(λ), and residual actor-critic(λ).

In this research, first a real-world microscopic traffic simulation of downtown Tehran is carried out, then four experiments are performed in order to find the best RLTSC with convincing robustness and strong performance. The results reveal that the RLTSC based on continuous state actor-critic(λ) has the best performance. In addition, it is found that the best RLTSC leads to saving average travel time by 22% (at the presence of high system disturbances) when it is compared with an optimized fixed-time controller.

18. **Continuous residual reinforcement learning for traffic signal control optimization**
Authors: Aslani, Mohammad(1); **Seipel, Stefan**(1); Wiering, Marco(2)
(1) Dept. of Industrial Development, IT and Land Management, University of Gävle, Sweden.
(2) Institute of Artificial Intelligence and Cognitive Engineering, University of Groningen, Groningen, the Netherlands.
Journal: Canadian journal of civil engineering (Print), Vol. 45, No. 8, pp. 690-702
Abstract: Traffic signal control can be naturally regarded as a reinforcement learning problem. Unfortunately, it is one of the most difficult classes of reinforcement learning problems owing to its large state space. A straightforward approach to address this challenge is to control traffic signals based on continuous reinforcement learning. Although they have been successful in traffic signal control, they may become unstable and fail to converge to near-optimal solutions. We develop adaptive traffic signal controllers based on continuous residual reinforcement learning (CRL-TSC) that is more stable. The effect of three feature functions is empirically investigated in a microscopic traffic simulation. Furthermore, the effects of departing streets, more actions, and the use of the spatial distribution of the vehicles on the performance of CRL-TSCs

are assessed. The results show that the best setup of the CRL-TSC leads to saving average travel time by 15% in comparison to an optimized fixed-time controller.

19. **Image Processing using Color Space Models for Forensic Fiber Detection**
Authors: **Wetzer, Elisabeth**; Lohninger, Hans(1)
(1) Vienna University of Technology
Journal: IFAC PapersOnLine, Vol. 51, pp. 445–450
Comment: Special issue from 9th Vienna International Conference on Mathematical Modelling
Abstract: The purpose of this study is to investigate the feasibility of automating fiber analysis in forensic science applications. In order to make self-directed collection of spectral data possible the number of measuring locations needs to be restricted to fibers only. Full scans of the samples would result in very large amounts of data of which only a small part carries actual information about the objects of interest.

    Images obtained by optical microscopes are used for preprocessing to find suitable candidates for measuring locations that subsequently may be used to control the microscope stage for spectroscopic measurements. This paper presents a method based on a nonlinear transform known to enhance the contrast in a way that makes segmentation on grayscale images possible. It further introduces an approach using the differences between the color channels of RGB images combined with common morphological operators to segment color images. A third application is presented that enables the search for fibers matching a query object in color based attributes, for which it is necessary to consider multiple color models. This approach reduces time and efforts significantly when trying to match one specific fiber to other samples.

20. **Distance functions based on multiple types of weighted steps combined with neighborhood sequences**
Authors: Nagy, Benedek(1); **Strand, Robin**; Normand, Nicolas(2)
(1) Eastern Mediterranean University, North Cyprus, Mersin-10, Turkey
(2) LS2N UMR CNRS 6004, Université de Nantes, France
Journal: Journal of Mathematical Imaging and Vision, Vol. 60, Issue 8, pp. 1209-1219
Abstract: In this paper, we present a general framework for digital distance functions, defined as minimal cost paths, on the square grid. Each path is a sequence of pixels, where any two consecutive pixels are adjacent and associated with a weight. The allowed weights between any two adjacent pixels along a path are given by a weight sequence, which can hold an arbitrary number of weights. We build on our previous results, where only two or three unique weights are considered, and present a framework that allows any number of weights. We show that the rotational dependency can be very low when as few as three or four unique weights are used. Moreover, by using n weights, the Euclidean distance can be perfectly obtained on the perimeter of a square with side length 2n. A sufficient condition for weight sequences to provide metrics is proven.

6.2 Refereed conference proceedings

1. **Segmentation of Post-operative Glioblastoma in MRI by U-Net with Patient-specific Interactive Refinement**
Authors: **Dhara, Ashis Kumar; Ayyalasomayajula, Kalyan Ram**; Arvids, Erik(1); Fahlström, Markus(1); Wikström, Johan(1); Larsson, Elna-Marie(1); **Strand, Robin**
(1) Dept. of Surgical Sciences, Radiology, UU
In Proceedings: 4th International Brain Lesion (BrainLes) workshop, a MICCAI 2018 satellite event, LNCS Vol. 11383 (revised selected papers) pages 115-122
Abstract: Accurate volumetric change estimation of glioblastoma is very important for post-surgical treatment follow-up. In this paper, an interactive segmentation method was developed and evaluated with the aim to guide volumetric estimation of glioblastoma. U-Net based fully convolutional network is used for initial segmentation of glioblastoma from post contrast MR images. The max flow algorithm is applied on the probability map of U-Net to update the initial segmentation and the result is displayed to the user for interactive refinement. Network update is performed based on the corrected contour by considering patient specific learning to deal with large context variations among different images. The proposed method is evaluated on a clinical MR image database of 15 glioblastoma patients with longitudinal scan data. The experimental results depict an improvement of segmentation performance due to patient specific fine-tuning. The proposed method is computationally fast and efficient as compared to state-of-the-art interactive segmentation tools. This tool could be useful for post-surgical treatment follow-up with minimal user intervention.

2. **Interactive Segmentation of Glioblastoma for Post-surgical Treatment Follow-up**
Authors: **Dhara, Ashis Kumar**; Arvids, Erik(1); Fahlström, Markus(1); Wikström, Johan(1); Larsson, Elna-Marie(1); **Strand, Robin**
(1) Dept. of Surgical Sciences, Radiology, UU
In Proceedings: International Conference on Pattern Recognition ICPR 2018, pp. 1199-1204
Abstract: In this paper, we present a novel framework for interactive segmentation of glioblastoma in contrast-enhanced T1-weighted magnetic resonance images. U-net based-fully convolutional network is combined with an interactive refinement technique. Initial segmentation of brain tumor is performed using U-net, and the result is further improved by including complex foreground regions or removing background regions in an iterative manner. The method is evaluated on a research database containing post-operative glioblastoma of 15 patients. Radiologists can refine initial segmentation results in about 90 seconds, which is well below the time of interactive segmentation from scratch using state-of-the-art interactive segmentation tools. The experiments revealed that the segmentation results (Dice score) before and after the interaction step (performed by expert users) are similar. This is most likely due to the limited information in the contrast-enhanced T1-weighted magnetic resonance images used for evaluation. The proposed method is computationally fast and efficient, and could be useful for post-surgical treatment follow-up.
Comment: Best paper award (Track 5 - biomedical imaging and bioinformatics).

3. **Denoising of short exposure transmission electron microscopy images for ultrastructural enhancement**
Authors: Bajić, Buda(1); **Suveer, Amit**; **Gupta, Anindya**(2); Pepić, Ivana(1); **Lindblad, Joakim; Sladoje, Nataša; Sintorn, Ida-Maria**(3)
(1) Faculty of Technical Sciences, University of Novi Sad, Serbia
(2) T. J. Seebeck Dept. of Electronics, Tallinn University of Technology, Estonia (3) Vironova AB, Stockholm, Sweden
In Proceedings: International Symposium on Biomedical Imaging (ISBI 2018), pp. 921–925
Abstract: Transmission Electron Microscopy (TEM) is commonly used for structural analysis at the nm scale in material and biological sciences. Fast acquisition and low dose are desired to minimize the influence of external factors on the acquisition as well as the interaction of electrons with the sample. However, the resulting images are very noisy, which affects both manual and automated analysis. We present a comparative study of block matching, wavelet domain, energy minimization, and deep convolutional neural network based approaches to de-noise short exposure high-resolution TEM images of cilia. In addition, we evaluate the effect of denoising before or after registering multiple short exposure images of the same imaging field to further enhance fine details.

4. **SoftCut: A Virtual Planning Tool for Soft Tissue Resection on CT Images**
   Authors: **Blache, Ludovic**; **Nysjö, Fredrik**; **Malmberg, Filip**; Thor, Andreas(1); Rodríguez-Lorenzo, Andrés(1); **Nyström, Ingela**
   (1) Plastic & Oral and Maxillofacial surgery, Dept. of Surgical Sciences, UU
   In Proceedings: Medical Image Understanding and Analysis (MIUA), Communications in Computer and Information Science, Vol. 894, pp. 299–310
   Abstract: With the increasing use of three-dimensional (3D) models and Computer Aided Design (CAD) in the medical domain, virtual surgical planning is now frequently used. Most of the current solutions focus on bone surgical operations. However, for head and neck oncologic resection, soft tissue ablation and reconstruction are common operations. In this paper, we propose a method to provide a fast and efficient estimation of shape and dimensions of soft tissue resections. Our approach takes advantage of a simple sketch-based interface which allows the user to paint the contour of the resection on a patient specific 3D model reconstructed from a computed tomography (CT) scan. The volume is then virtually cut and carved following this pattern. From the outline of the resection defined on the skin surface as a closed curve, we can identify which areas of the skin are inside or outside this shape. We then use distance transforms to identify the soft tissue voxels which are closer from the inside of this shape. Thus, we can propagate the shape of the resection inside the soft tissue layers of the volume. We demonstrate the usefulness of the method on patient specific CT data.

5. **The Scarcity of Universal Colour Names**
   Author: **Borgefors, Gunilla**
   In Proceedings: Proceedings of 7th International Conference on Pattern Recognition Applications and Methods (ICPRAM 2018), pp. 496–502
   Abstract: There is a trend in Computer Vision to use over twenty colour names for image annotation, retrieval and to train deep learning networks to name unknown colours for human use. This paper will show that there is little consistency of colour naming between languages and even between individuals speaking the same language. Experiments will be cited that show that your mother tongue influences how your brain processes colour. It will also be pointed out that the eleven so called basic colours in English are not universal and cannot be applied to other languages. The conclusion is that only the six Hering primary colours, possibly with simple qualifications, are the only ones you should use if you aim for universal usage of your systems. That is: black, white, red, green, blue, and yellow.

6. **TexT - Text extractor tool for handwritten document transcription and annotation**
   Authors: **Hast, Anders**; Cullhed, Per(1); **Vats, Ekta**
   (1) University Library, UU
   In Proceedings: Italian Research Conference on Digital Libraries IRCDL 2018: Digital Libraries and Multimedia Archives, Communications in Computer and Information Science, No. 806, pp. 81–92
   Abstract: This paper presents a framework for semi-automatic transcription of large-scale historical handwritten documents and proposes a simple user-friendly text extractor tool, TexT for transcription. The proposed approach provides a quick and easy transcription of text using computer assisted interactive technique. The algorithm finds multiple occurrences of the marked text on-the-fly using a word spotting system. TexT is also capable of performing on-the-fly annotation of handwritten text with automatic generation of ground truth labels, and dynamic adjustment and correction of user generated bounding box annotations with the word being perfectly encapsulated. The user can view the document and the found words in the original form or with background noise removed for easier visualization of transcription results. The effectiveness of TexT is demonstrated on an archival manuscript collection from well-known publicly available dataset.

7. **When Can l_p-norm Objective Functions Be Minimized via Graph Cuts?**
   Authors: **Malmberg, Filip(1); Strand, Robin(1)**
   (1) Dept. of Radiology. UU
   In Proceedings: International Workshop on Combinatorial Image Analysis, Lecture Notes in Computer Science, pp. 112–117
   Abstract: Techniques based on minimal graph cuts have become a standard tool for solving combinatorial optimization problems arising in image processing and computer vision applications. These techniques can be used to minimize objective functions written as the sum of a set of unary and pairwise terms, provided that the objective function is sub-modular. This can be interpreted as minimizing the l_1-norm of the vec-

tor containing all pairwise and unary terms. By raising each term to a power p, the same technique can also be used to minimize the lp-norm of the vector. Unfortunately, the submodularity of an l_1-norm objective function does not guarantee the submodularity of the corresponding lp-norm objective function. The contribution of this paper is to provide useful conditions under which an l_p-norm objective function is submodular for all $p \geq 1$, thereby identifying a large class of l_p-norm objective functions that can be minimized via minimal graph cuts.

8. **Minimal Annotation Training for Segmentation of Microscopy Images**
   Authors: **Matuszewski, Damian J.(1); Sintorn, Ida-Maria(1)**
   (1) Science for Life Laboratory, UU
   In Proceedings: IEEE Symposium on Biomedical Images, pp. 387–390
   Abstract: In many biomedical applications, successful training of Convolutional Neural Networks (CNNs) is restricted by an insufficient amount of annotated images. Although image augmentation can help training CNNs from a relatively small image set, in many applications, the objects of interest cannot be accurately delineated due to their fuzzy shape, image quality or a limitation in time, experience or knowledge of the expert performing the annotation. We propose an approach for training a CNN for segmentation of images with minimal annotation. The annotation consists of center points or lines of target objects of approximately known size. We demonstrate this approach in the application of Rift Valley virus segmentation in a challenging transmission electron microscopy image dataset. Our method achieves a Dice score of 0.900 and intersection over union of 0.831. Using the suggested minimal annotation training is particularly useful for applications in which full object annotations are not available or feasible.

9. **An intelligent user interface for efficient semi-automatic transcription of historical handwritten documents**
   Authors: **Hast, Anders; Vats, Ekta**
   In Proceedings: 23rd International Conference on Intelligent User Interfaces Companion, eid. 48
   Abstract: Transcription of large-scale historical handwritten document images is a tedious task. Machine learning techniques, such as deep learning, are popularly used for quick transcription, but often require a substantial amount of pre-transcribed word examples for training. Instead of line-by-line word transcription, this paper proposes a simple training-free gamification strategy where all occurrences of each arbitrarily selected word is transcribed once, using an intelligent user interface implemented in this work. The proposed approach offers a fast and user-friendly semi-automatic transcription that allows multiple users to work on the same document collection simultaneously.

10. **Learning surrogate models of document image quality metrics for automated document image processing**
    Authors: Singh, Prashant(1); **Vats, Ekta; Hast, Anders**
    (1) Division of Scientific Computing, UU
    In Proceedings: 13th IAPR Workshop on Document Analysis Systems, pp. 67–72
    Abstract: Computation of document image quality metrics often depends upon the availability of a ground truth image corresponding to the document. This limits the applicability of quality metrics in applications such as hyperparameter optimization of image processing algorithms that operate on-the-fly on unseen documents. This work proposes the use of surrogate models to learn the behavior of a given document quality metric on existing datasets where ground truth images are available. The trained surrogate model can later be used to predict the metric value on previously unseen document images without requiring access to ground truth images. The surrogate model is empirically evaluated on the Document Image Binarization Competition (DIBCO) and the Handwritten Document Image Binarization Competition (H-DIBCO) datasets.

11. **Whole Slide Image Registration for the Study of Tumor Heterogeneity**
    Authors: **Solorzano, Leslie**(1); Almeida, Gabriela(2,3,4); Mesquita, Bárbara(2,3); Martins, Diana(2,3); Oliveira, Carla(2,3,4); **Wählby, Carolina**(1)
    (1) Science for Life Laboratory, Uppsala
    (2) i3S, Instituto de Investigação e Inovação em Saúde Universidade do Porto, Portugal
    (3) Ipatimup, Institute of Molecular Pathology and Immunology, University of Porto,Portugal
    (4) Faculty of Medicine of the University of Porto, Porto, Portugal
    In Proceedings: MICCAI 2018 - International Workshop on Ophthalmic Medical Image Analysis : OMIA 2018, COMPAY 2018: Computational Pathology and Ophthalmic Medical Image Analysis, Lecture Notes in Computer Science (LNCS) 11039, pp. 95–102

Abstract: Consecutive thin sections of tissue samples make it possible to study local variation in e.g. protein expression and tumor heterogeneity by staining for a new protein in each section. In order to compare and correlate patterns of different proteins, the images have to be registered with high accuracy. The problem we want to solve is registration of gigapixel whole slide images (WSI). This presents 3 challenges: (i) Images are very large; (ii) Thin sections result in artifacts that make global affine registration prone to very large local errors; (iii) Local affine registration is required to preserve correct tissue morphology (local size, shape and texture). In our approach we compare WSI registration based on automatic and manual feature selection on either the full image or natural sub-regions (as opposed to square tiles). Working with natural sub-regions, in an interactive tool makes it possible to exclude regions containing scientifically irrelevant information. We also present a new way to visualize local registration quality by a Registration Confidence Map (RCM). With this method, intra-tumor heterogeneity and characteristics of the tumor microenvironment can be observed and quantified.

12. **Towards automated multiscale imaging and analysis in TEM: Glomerulus detection by fusion of CNN and LBP maps**
Authors: **Wetzer, Elisabeth; Lindblad, Joakim; Sintorn, Ida-Maria**; Hultenby, Kjell(1); **Sladoje, Nataša**
(1) Clinical Research Centre, Karolinska Insitutet, Huddinge
In Proceedings: Workshop on BioImage Computing, European Conference on Computer Vision (ECCV)
Abstract: Glomerulal structures in kidney tissue have to be analysed at a nanometer scale for several medical diagnoses. They are therefore commonly imaged using Transmission Electron Microscopy. The high resolution produces large amounts of data and requires long acquisition time, which makes automated imaging and glomerulus detection a desired option. This paper presents a deep learning approach for Glomerulus detection, using two architectures, VGG16 (with batch normalization) and ResNet50. To enhance the performance over training based only on intensity images, multiple approaches to fuse the input with texture information encoded in local binary patterns of different scales have been evaluated. The results show a consistent improvement in Glomerulus detection when fusing texture-based trained networks with intensity-based ones at a late classification stage.

13. **Mapping of roof types in orthophotos using feature descriptors**
Authors: Åhlén, Julia(1); **Seipel, Stefan**
(1) University of Gävle
In Proceedings: International Multidisciplinary Scientific GeoConference : SGEM 2018, pp. 285–291
Abstract: In the context of urban planning, it is very important to estimate the nature of the roof of every building and, in particular, to make the difference between flat roofs and gable ones. This analysis is necessary in seismically active areas. Also in the assessment of renewable energy projects such solar energy, the shape of roofs must be accurately retrieved. In order to perform this task automatically on a large scale, aerial photos provide a useful solution. The goal of this research project is the development of algorithm for accurate mapping of two different roof types in digital aerial images. The algorithm proposed in this paper includes several components: pre-processing step to reduce illumination differences of individual roof surfaces, statistical moments calculation and color indexing. Roof models are created and saved as masks with feature specific descriptors. Masks are then used to mark areas that contain elements of the different roof types (e.g. gable and hip). The final orthophoto visualize an accurate position of each of the roof types. The result is evaluated using precision recall method.

14. **Visual GISwaps : an interactive visualization framework for geospatial decision making**
Authors: Milutinovic, Goran(1); **Seipel, Stefan**(1)
(1) Faculty of Engineering and Sustainable Development, University of Gävle, Sweden
In Proceedings: 13th International Joint Conference on Computer Vision, Imaging and Computer Graphics Theory and Applications (VISIGRAPP), Vol. 3, pp. 236-243
Abstract: Different visualization techniques are frequently used in geospatial information systems (GIS) to support geospatial decision making. However, visualization in GIS context is usually limited to the initial phase of the decision-making process, i.e. situation analysis and problem recognition. This is partly due to the choice of methods used in GIS multi-criteria decision-making (GIS-MCDM) that usually deploy some non-interactive approach, leaving the decision maker little or no control over the calculation of overall values for the considered alternatives; the role of visualization is thus reduced to presenting the final results of the computations.

The contributions of this paper are twofold. First, we introduce GISwaps, a novel, intuitive interactive

method for decision making in geospatial context. The second and main contribution is an interactive visualization of the choice phase of the decision making process. The visualization allows the decision maker to explore the consequences of trade-offs and costs accepted during the iterative decision process, both in terms of the abstract relation between different decision variables and in spatial context

15. **HarmonicIO : Scalable data stream processing for scientific datasets**
    Authors: Torruangwatthana, Preechakorn; **Wieslander, Håkan**; Blamey, Ben; Hellander, Andreas; Toor, Salman
    (1) Division of Scientific Computing, UU
    (2) Computational Science, UU
    In Proceedings: IEEE 11th International Conference on Cloud Computing (CLOUD 2018), pp. 879-882
    Abstract: Many streaming frameworks have been introduced to deal with the needs for online analysis of massive datasets. Scientific applications often require significant changes to make them compatible with these frameworks. Other issues include tight coupling with the underlying infrastructure, shared computing environment, static topology settings, and complex configuration. In this article we present HarmonicIO, a lightweight streaming framework specialized for scientific datasets. It boasts a smart dynamic architecture, is highly elastic, and enforces a clear separation between framework components and application execution environment using container technology.

6.3 Other

Authors affiliated with CBA are in bold.

1. **BIM and 3D property visualisation**
   Authors: Andrée, Martin(1); Paasch, Jesper(2,3); Paulsson, Jenny(4); **Seipel, Stefan**(2)
   (1) Swedish Land Survey
   (2) University of Gävle
   (3) The Swedish mapping, cadastral and land registration authority
   (4) Dept. of Real Estate and Construction Management of the KTH Royal Institute of Technology, Stockholm
   Event: FIG Congress 2018
   Comment: Abstract review

2. **Localization of lung fields in HRCT images using a deep convolution neural network**
   Authors: Kumar, Abhishek(1); Agarwala, Sunita(2); **Dhara, Ashis Kumar**; Mukhopadhyay, Sudipta(3); Nandi, Debashis(2); Garg, Mandeep(4); Khandelwal, Niranjan(4); Kalra, Naveen(4)
   (1) Univ. of Hyderabad, India
   (2) National Institute of Technology, Durgapur, India
   (3) Indian Institute of Technology Kharagpur, India
   (4) Postgraduate Institute of Medical Education and Research, India
   Event: SPIE Medical Imaging 2018 : Computer-Aided Diagnosis, No. 10575, pp. 1057535:1–8, eid. 1057535
   Comment: Abstract review

3. **Brush Biopsy For HR-HPV Detection With FTA Card And AI For Cytology Analysis - A Viable Non-invasive Alternative**
   Authors: Runow Stark, Christina(1); Gustavsson, Inger(2); Gyllensten, Ulf(2); Darai Ramqvist, Eva(3); **Lindblad, Joakim; Wählby, Carolina; Bengtsson, Ewert**; Hirsch, Jan-Michael(5)
   (1) Public Dental Health Center of Stockholm County Council, Medicinsk Tandvård, Södersjukhuset Stockholm.
   (2) Dept. of Immunologi, Genetics och Pathology
   (3) Departmen of Pathology and Cytology, Karolinska Institute, Stockholm.
   (4) Science for Life Laboratory, UU
   (5) Oral and Maxillofacial Surgery, UU
   Event: 14th Biennial Congress of the European Association of Oral Medicine (EAOM2918), Göteborg
   Comment: Abstract review

4. **Detection of Malignancy-Associated Changes Due to Precancerous and Oral Cancer Lesions: A Pilot Study Using Deep Learning**
   Authors: **Bengtsson, Ewert; Wieslander, Håkan; Forslid, Gustav; Wählby, Carolina**(1); Hirsch, Jan-Michael(2); Runow Stark, Christina(3); **Kecheril Sadanandan, Sajith(1); Lindblad, Joakim**
   (1) Science for Life Laboratory, UU
   (2) Oral and Maxillofacial Surgery, UU
   (3) Public Dental Health Center of Stockholm County Council, Medicinsk Tandvård, Södersjukhuset Stockholm.
   Event: CYTO conference 2018
   Comment: Abstract review

5. **Extracting script features from a large corpus of handwritten documents**
   Authors: **Vats, Ekta; Hast, Anders**; Mårtensson, Lasse(1)
   (1) Dept. of Business and Economics Studies, University of Gävle
   Event: Digital Humanities in the Nordic Countries, Helsinki, Finland
   Comment: Extended abstract review

6. **Towards automated multiscale imaging and analysis in TEM: Glomeruli detection by fusion of CNN and LBP maps**
   Authors: **Wetzer, Elisabeth; Lindblad, Joakim; Sintorn, Ida-Maria**; Hultenby, Kjell(1); **Sladoje, Nataša**
   (1) Electron Microscopy Core Facility, Karolinska Institute, Huddinge
   Event: Swedish Symposium on Deep Learning 2018, Gothenburg

7. **Word Spotting in Historical Handwritten Manuscripts using Capsule Networks**
   Authors: **Heil, Raphaela; Vats, Ekta; Hast, Anders**
   Event: Bibliotheca Baltica Symposium

8. **The Effect of DMPA Use on the Human Cervical Epithelium : Mechanisms Revealed by Image Analysis**
   Authors: Edfeldt, Gabriella(1); Lajoie, Julie(2); Röhl, Maria(1); Omollo, Kenneth(3); **Wählby, Carolina**; Boily-Larouche(2), Genevieve; Kimani, Joshua(3); Fowke, Keith(2,3); Broliden, Kristina(1); Tjernlund, Annelie
   (1) Karolinska Institute, Stockholm, Sweden
   (2) Univ Manitoba, Winnipeg, MB, Canada
   (3) Univ Nairobi, Nairobi, Kenya
   Journal: AIDS Research and Human Retroviruses, Vol. 34, No. s1, pp. 310
   Comment: meeting abstract

9. **Aliroj al esperanto**
   Editors: **Christer O. Kiselman**, Renato Corsetti, Probal Dasgupta
   Publisher: Dobřichovice: KAVEA-PECH
   Comment: **Christer O. Kiselman also wrote the introduction to this book, pages 5-8**

10. **CBA Annual Report 2017**
    Editors: **Gunilla Borgefors, Filip Malmberg, Ingela Nyström, Ida-Maria Sintorn, Leslie Solorzano, Robin Strand**
    Publisher: **Centre for Image Analysis, 108 pages**

7 Activities

This year, we where part of organizing six different events, four small Swedish ones and two large ones. We held 18 seminars at various places, 7 in Uppsala, 5 in the rest of Sweden, and 6 in the rest of Europe. No less than 13 different persons from CBA held these seminars. We are really proud of our long-standing well attended seminar series, with a CBA seminar almost all Monday afternoons. In 2018, we had 40 seminars, of which 14 were held by external scientists. The average number of attendees were 22, ranging from 14 to 35. As usual, we attended many international and national meetings, where we presented our work as invited speaker or giving oral or poster presentations of reviewed papers: we had 10 invited speakers and 16 reviewed conference presentations. We also presented our work at 17 non-reviewed conferences, where 8 were at the Swedish Symposium for Image Analysis and 4 at the sister meeting Swedish Symposium on Deep Learning that was held for the second time this year. We also attended 21 conferences just to listen and learn. In 2018, we had 9 visiting scientists that stayed for shorter or longer times. They were from France, Germany, Madagascar, Serbia, The Netherlands, and USA. The most distinguished visitor was Professor Douglas Hofstadter from Indiana University. PhD student Teo Asplund spent three months at Center for Mathematical Morphology in Fontainebleau, France and other made short visits in France, Germany, New Zealand, and Serbia. A rewarding and necessary part of being an international scientist is serving the scientific community by working for professional organizations, being Editors of scientific journals, serving in program committees for international and national conferences, reviewing for international journals (which often goes undocumented), being members of dissertation committees, and functioning as evaluators of projects and positions. Nowadays, many of the CBA seniors have many such engagements, which are listed in Section 7.9.

7.1 Conference organization

1. **Fest Seminar in Honour of Professor Gunilla Borgefors**
   Organisers: Filip Malmberg, Ingela Nyström, Ida-Maria Sintorn, Nataša Sladoje, Robin Strand
   Address: ITC Aula and Eklundshof
   Date: 20180223
   Comment: CBA arranged a fest seminar to honour Gunilla as she was awarded the title Professor Emerita. More than 50 participants celebrated her eventful career. Invited speakers were Ewert Bengtsson, Punam K. Saha, Stina Svensson, Christer O. Kiselman, Fredrik Walter, and Gabriella Sanniti di Baja.

2. **AIMday Machine Learning in Life Science and Medicine**
   Organisers: Robin Strand, Carl Nettelblad, Dept. of IT
   Address: Navet, Uppsala Biomedical Center
   Date: 20180531
   Comment: Organized by the biomed-IT arena

3. **Uppsala Health Summit on Cancer Care**
   Organisers: Carolina Wählby
   Address: Uppsala Castle, Uppsala
   Date: 20180614–20180615
   Comment: Organized a workshop on Precision medicine in Cancer Care.

4. **Analysis Day in Memory of Mikael Passare**
   Organisers: Pavel Kurasov, Mats Andersson, Christer O. Kiselman
   Address: Stockholm University
   Date: 20180919
   Comment: An annual conference devoted to the memory of Mikael Passare (1959–2011). Five lectures.

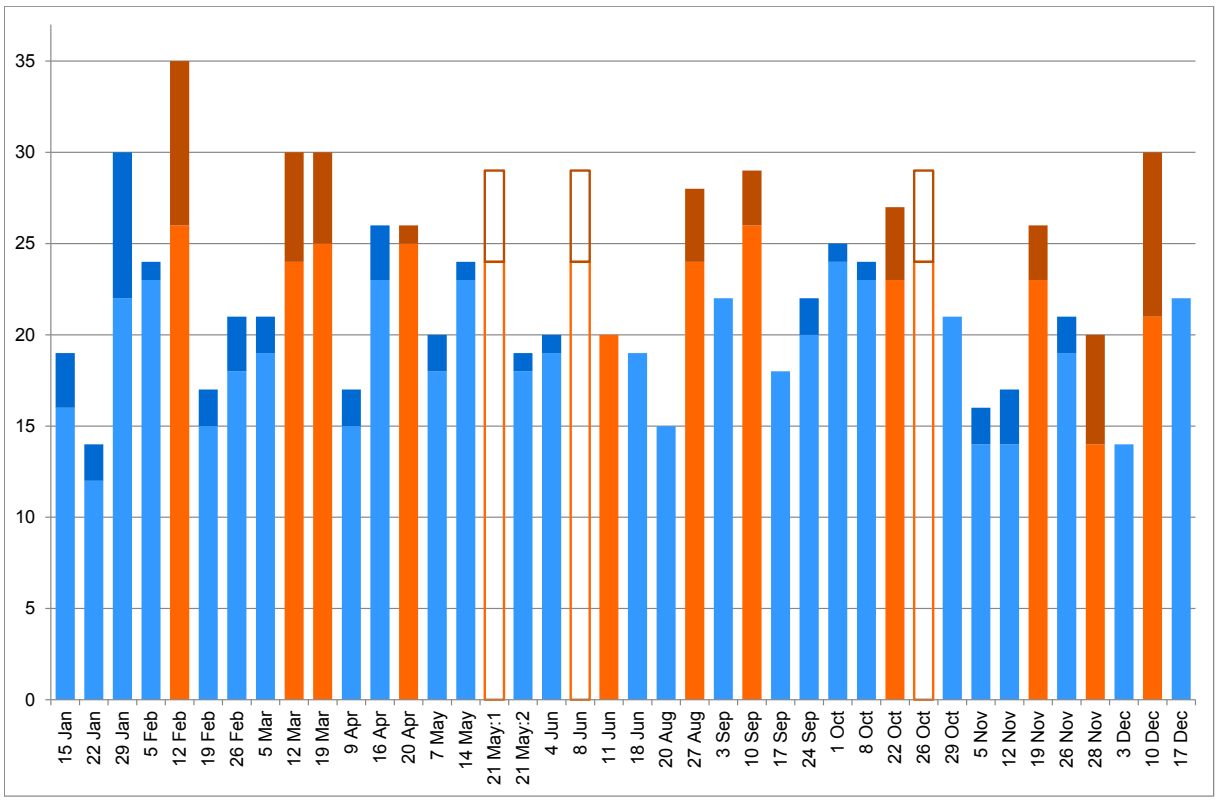

Figure 71: Our own seminar series. Blue represents seminars given by CBA people, while red represents guest lecturers. The saturated color on top represents guest attendants. For three seminars data is missing, these are shown as blank bars and represented by the median value.

5. **Shape Analysis: Euclidean, Discrete, and Algebraic Geometric Methods**
   Organisers: Michael Breuss (Cottbus), Alfred M. Bruckstein (Haifa), Christer O. Kiselman (Uppsala), Petros Maragos (Athens)
   Address: Sloss Dagstuhl, Saarland
   Date: 20181014–20181019
   Comment: 26 lectures and 24 very short presentations.

6. **NEUBIAS, Training School for Early Career Investigators (TS8)**
   Organisers: Anna Klemm
   Address: Edinburgh, UK
   Date: 20181016–20181019

7.2 Seminars held outside CBA

1. **Stefan Seipel**
   Date: 20180215
   Address: Presentation for USA:s ambassador at Gävle Innovation Arena
   Title: GIS – Research and Challenges

2. **Amin Allalou**
   Date: 20180309
   Address: Evolutionary Biology Centre, EBC
   Title: Quantitative gene expression screening of in-situ stained zebrafish
   Comment: Presentation at Uppsala Zebrafish Forum Seminar.

3. **Ingela Nyström**
   Date: 20180321
   Address: Chalmers University of Technology, Göteborg
   Title: Medical Image Analysis at CBA and Gender Diversity at CBA
   Comment: Invited to give a lunch seminar in the project Women in SciencE (WiSE) at Chalmers and MedTech West.

4. **Teo Asplund**
   Date: 20180426
   Address: Centre de Morphologie Mathématique, MINES Paristech, Paris, France
   Title: Towards a Better Approximation of Continuous Morphology through Irregular Sampling

5. **Carolina Wählby**
   Date: 20180426
   Address: Karolinska Institutet, Stockholm
   Title: Workshop on Phenotypic screening – how to query biology in high content and high throughput analysis?

6. **Ida-Maria Sintorn**
   Date: 20180426
   Address: Dept. IT, UU
   Title: A flavor of image analysis and related areas
   Comment: Ida-Maria represented Vi2 in the GE- Dept. IT workshop

7. **Stefan Seipel**
   Date: 20180517
   Address: UU Innovation Seminar – "Building a Sustainable City", UU
   Title: Sustainable Cities with 3D Interactive Techniques

8. **Carolina Wählby**
   Date: 20180523
   Address: University of Tartu, Tartu, Estonia
   Title: ERC grant preparation workshop for researchers in Computer Science and Informatics
   Comment: An event supported by Informatics Europe, an association of CS departments in Europe. The workshop was focus on preparation of ERC starting and consolidator grants.

9. **Nicolas Pielawski, Leslie Solorzano**
   Data: 20180618
   Address: BMC, UU
   Title: Simple Artificial Intelligence for helping Cell Migration Research (Pielawski), Image analysis for digital histopathology for personalized cancer treatment (Solorzano)
   Comment: (Presentations in the context of a summer school for medical students (SOFOSKO).)

10. **Anna Klemm**
    Date: 20180911
    Address: SciLifeLab, Uppsala
    Title: Visit of the Royal Swedish Society, SciLifeLab

11. *Conference:* RIKEN-K-SciLifeLab conference: Artificial Intelligence meets Life Sciences
    Carolina Wählby
    Date: 20180920–20180921
    Address: SciLifeLab, Stockholm
    Title: Deep learning as a tool in microscopy data analysis and digital pathology

12. *Conference:* AI in medicine
    Carolina Wählby
    Date: 20181002
    Address: Swedish Pharmaceutical Society, Stockholm
    Title: AI for image-based screening (Orig in Swedish: AI för bildbaserad 'screening')

13. **Christer O. Kiselman**
Date: 20181016
Address: Schloss Dagstuhl, Saarland
Title: Shape Analysis: Euclidean, Discrete, and Algebraic Geometric Methods
Comment: Duality of convolution operators: A tool for shape analysis?

14. **Gunilla Borgefors**
Date: 20181026
Address: Missionskyrkan, Uppsala
Title: Färgseende & Färgnamn (Colour Vision and Colour Names)

15. *Conference:* Franco-Swedish Workshop
Joakim Lindblad
Date: 20181116
Address: Institute Pascal laboratory, Campus Le-Puy-en-Velay, France
Title: Automated imaging and analysis of Glomuerli in TEM by fusion of CNN and LBP

16. *Conference:* Franco-Swedish Workshop
Nataša Sladoje
Date: 20181116
Address: Institute Pascal laboratory, Campus Le-Puy-en-Velay, France
Title: Fast and robust symmetric image registration based on intensity and spatial information

17. **Ida-Maria Sintorn**
Date: 20181119
Address: Tampere Technical University, Finland
Title: Image analysis for automated screening and analysis of biological samples using MiniTEM
Comment: Invited to give a presentation about my research to their department and to discuss/explore joint research interests

18. *Conference:* SciLifeLab Price winners
Anna Klemm, Nicolas Pielawski
Date: 20181223
Address: SciLifeLab, Uppsala
Title: SciLifeLab BioImage Informatics Facility
Comment: Presentation
Moderation of a Q&A session with high school students

7.3 Seminars at CBA

1. **Lovisa Lugnegård**
Date: 20180115
Title: Microscope simulator for the HASTE project

2. **Petter Ranefall**
Date: 20180122
Title: Image analysis of bacteria growth for a fast point-of-care test of antibiotic resistance

3. **Anindya Gupta**
Date: 20180129
Title: Deep neural networks for the classification and denoising of medical and biomedical images

4. **Raphaela Heil**
Date: 20180205
Title: A brief overview of previous projects

5. **Douglas Hofstadter**
Date: 20180212
Title: Self-Driving Cars and Mechanical Translation: Just Around the Corner, or in Never-Never-Land?

6. **Ludovic Blache**
   Date: 20180219
   Title: Interactive cutting tool for resection planning on volumetric data
7. **Kalyan Ram Ayyalasomayajula**
   Date: 20180226
   Title: Generating quill based handwriting using RNNs
8. **Gunilla Borgefors**
   Date: 20180305
   Title: Language complexity, spatial reasoning and thinking in genders
9. **Jennifer Alvén**
   Date: 20180305
   Title: Medical image analysis at Chalmers and anatomy-aware CNNs
10. **Fred Hamprecht**
    Date: 20180319
    Title: Signed graph partitioning in (bio-) image analysis
11. **Giorgia Milli**
    Date: 20180409
    Title: New methods for image-based sequencing of mRNA
12. **Anna Klemm**
    Date: 20180416
    Title: BioImage Analysis of Light-Microscopy Data
13. **Boguslaw Obara**
    Date: 20180420
    Title: BioImage Informatics: Where BioImaging Meets Computer Science
14. **Fredrik Nysjö**
    Date: 20180507
    Title: Evaluation of HASP for Virtual Planning for Complex Mandible Fractures
15. **Filip Malmberg**
    Date: 20180514
    Title: Boolean maps – connectivity with respect to random thresholds
16. **Patrik Källback and Per Andrén**
    Date: 20180521
    Title: Mass spectrometry imaging – from drug discovery to neuroscience
17. **Ekta Vats**
    Date: 20180521
    Title: Recent advances in historical handwritten text recognition
18. **Damian Matuszewski**
    Date: 20180604
    Title: Deep learning segmentation of biomedical images with minimal labelling
19. **Anne Carpenter**
    Date: 20180608
    Title: A picture is worth a million data points: Tackling world health problems via cell morphology
20. **Atsushi Imiya**
    Date: 20180611
    Title: Tensor PCA: Theory, Theory, Computation and Applications
21. **Amit Suveer**
    Date: 20180618
    Title: Denoising of Cilia Cross-section Images in Transmission Electron Microscopy

22. **Sukalpa Chanda**
Date: 20180820
Title: Text Line Segmentation and Background In-painting in Historical Document Images

23. **Mariëlle Jansen**
Date: 20180827
Title: MRI-based image analysis of liver lesions

24. **Tomas Wilkinson**
Date: 20180903
Title: Segmentation-free Word Image Retrieval in Historical Manuscripts using Deep Learning

25. **Chris Ciesielski**
Date: 20180910
Title: Hierarchical segmentation in a directed graph setting which optimizes a graph cut energy

26. **Teo Asplund**
Date: 20180917
Title: Adaptive morphology on irregularly sampled images and point clouds

27. **Håkan Wieslander**
Date: 20180924
Title: Analysis of image stream data from Transmission electron microscopy

28. **Karl Bengtsson Bernander**
Date: 20181001
Title: A Method for Detecting Resident Space Objects and Orbit Determination Based on Star Trackers and Image Analysis

29. **Nicolas Pielawski**
Date: 20181008
Title: Cutting the legs of the crab

30. **Antoine Vacavant**
Date: 20181022
Title: Robust image processing algorithms, involving tools from digital geometry and mathematical morphology

31. **Elisabeth Wetzer**
Date: 20181029
Title: Automated imaging and analysis of Glomuerli in TEM by fusion of CNN and LBP

32. **Nadezhda Koriakina**
Date: 20181105
Title: Evaluation of coherence-based beamforming for B-mode and speckle tracking echocardiography

33. **Gabriele Partel**
Date: 20181112
Title: Improving recall of image-based 'in-situ' sequencing

34. **Saikat Chatterjee**
Date: 20181119
Title: Excitement and frustration in today's machine learning area

35. **Leslie Solorzano**
Date: 20181126
Title: Integrating spatial and genetic information using image analysis and interactive visualization of tissue data

36. **Alexandru Telea**
Date: 20181128
Title: Image-Based Graph Visualization: Advances and Challenges

37. **Filip Malmberg**
Date: 20181203
Title: Optimization of Max-Norm Objective Functions in Image Processing and Computer Vision

38. **Martin Danelljan**
Date: 20181210
Title: Efficient Online Learning for Video Object Tracking and Segmentation

39. **Johan Öfverstedt**
Date: 20181217
Title: Stochastic Distance Transform

7.4 Conference participation

7.4.1 Special invited speakers

1. *Conference:* 2nd NEUBIAS Bioimage Analysis Community Conference 2018
Nataša Sladoje
Date: 20180131–20180202
Address: Szeged, Hungary
Title: Improved distance measures between images and their performance in biomedical applications

2. *Conference:* CYTO 2018
Carolina Wählby
Date: 20180428–20180602
Address: Prague, Czech Republic
Title: Artificial Intelligence as a Tool in Image Cytometry: Potentials and Pitfalls

3. *Conference:* Annual Conference of the Nordic Microscopy Society (SCANDEM)
Ida-Maria Sintorn
Date: 20180627–20180628
Address: Copenhagen, Denmark
Title: Image analysis for automated screening and analysis of biological samples using MiniTEM

4. *Conference:* 26th Summer School on Image Processing (SSIP)
Joakim Lindblad, Nataša Sladoje
Date: 20180712–20180718
Address: Medical University of Graz, Austria
Title: (Lindblad) Diving Deeper Into Deep Learning. (Sladoje) Image distance measures with application to object detection, classification, and registration

5. *Conference:* AIMed Europe
Carolina Wählby
Date: 20180912–20180913
Address: London, United Kingdom
Title: AI in Digital Pathology - where are we now?

6. *Conference:* British Science Festival
Carolina Wählby
Date: 20180913–20180914
Address: University of Hull, Hull, United Kingdom
Title: You may see the robot now

7. *Conference:* Life meets Light - Second Scientific Conference of the Leibniz Science Campus InfectoOptics
Ida-Maria Sintorn
Date: 20180905–20180906
Address: Jena, Germany
Title: Towards self searching TEM for virus diagnostics

8. *Conference:* Advances in Biomedical Imaging
   Anna Klemm
   Date: 20181009
   Address: Berlin, Germany
   Title: Digital Image Processing and Analysis as a Tool in Life Science

9. *Conference:* NII Shonan Meeting meeting: Patient Similitude: Combining Histopathological Images & Multiple-Scale Molecular Phenotypes
   Carolina Wählby
   Date: 20181110–20181115
   Address: Shonan Village, Zushi, Japan
   Title: Combining image-based in situ RNA sequencing with quantitative analysis of cell and tissue morphology

10. *Conference:* Forska! Sverige dagen 2018: AI som verktyg för hälsa (Research! Sweden day 2018: AI as a tool for health)
    Carolina Wählby
    Date: 20181128
    Address: Kungliga Myntkabinettet, Slottsbacken 6, Stockholm
    Title: AI som verktyg för hälsa -Var står vi idag? (AI as a tool for health - Where are we today?)
    Comment: This was an event for Swedish politicians and decision-makers.

7.4.2 Refereed conference presentations

1. *Conference:* 7th International Conference on Pattern Recognition Applications and Methods (ICPRAM 2018)
   Gunilla Borgefors
   Date: 20180116–20180118
   Address: Madeira, Portugal
   Title: The Scarcity of Universal Colour Names

2. *Conference:* 9th Vienna International Conference on Mathematical Modelling
   Elisabeth Wetzer
   Date: 20180220–20180223
   Address: MATHMOD 2018 Office, Automation and Control Institute, TU Wien, Austria
   Title: Image Processing Using Color Space Models for Forensic Fiber Detection

3. *Conference:* Human Cell Atlas meeting
   Carolina Wählby
   Date: 20180308–20180309
   Address: Cambridge, UK
   Title: Improving recall of in situ sequencing by self-learned features and a graphical model

4. *Conference:* SciLifeLab-WCMM Fellows
   Anna Klemm
   Date: 20180314
   Address: Stockholm
   Title: SciLifeLab BioImage Informatics Facility

5. *Conference:* The IEEE International Symposium on Biomedical Imaging (ISBI)
   Damian Matuszewski
   Date: 20180404–20180407
   Address: Omni Shoreham Hotel, Washington, D.C, USA
   Title: Minimal annotation training for segmentation of microscopy images

6. *Conference:* The IEEE International Symposium on Biomedical Imaging (ISBI)
   Amit Suveer
   Date: 20180404–20180407
   Address: Omni Shoreham Hotel, Washington, D.C, USA

Title: Denoising of Short Exposure Transmission Electron Microscopy Images for Ultrastructural Enhancement

7. *Conference:* The IEEE International Symposium on Biomedical Imaging (ISBI)
   Nataša Sladoje, Joakim Lindblad
   Date: 20180404–20180407
   Address: Omni Shoreham Hotel, Washington, D.C, USA
   Title: Denoising of Short Exposure Transmission Electron Microscopy Images for Ultrastructural Enhancement

8. *Conference:* 13th IAPR International Workshop on Document Analysis Systems (DAS)
   Ekta Vats
   Date: 20180424–20180427
   Address: Vienna, Austria
   Title: Learning Surrogate Models of Document Image Quality Metrics for Automated Document Image Processing

9. *Conference:* SciLifeLab Science Summit
   Anna Klemm, Petter Ranefall
   Date: 20180425
   Address: Aula Medica, Karolinska Institutet, Stockholm
   Title: SciLifeLab BioImage Informatics Facility

10. *Conference:* CYTO 2018
    Ewert Bengtsson
    Date: 20180428–20180502
    Address: Prague, Czech Republic
    Title: Detection of Malignancy-Associated Changes Due to Precancerous and Oral Cancer Lesions: A Pilot Study using Deep Learning

11. *Conference:* European Conference on Digital Pathology
    Ida-Maria Sintorn
    Date: 20180530–20180601
    Address: Helsinki, Finland
    Title: Facilitating ultrastructural pathology through automated imaging and analysis

12. *Conference:* 22nd Medical Image Understanding and Analysis (MIUA 2018)
    Ingela Nyström, Ludovic Blache
    Date: 20180709–20180711
    Address: University of Southampton, UK
    Title: SoftCut: A Virtual Planning Tool for Soft Tissue Resection on CT Images
    Comment: Nyström chaired the first session - "Deep Learning in Medical Imaging". Blache presented the manuscript.

13. *Conference:* 24th International Conference on Pattern Recognition (ICPR) 2018
    Robin Strand
    Date: 20180820–20180824
    Address: China National Convention Center, Beijing, China
    Title: Interactive Segmentation of Glioblastoma for Post-surgical Treatment Follow-up
    Comment: Best paper award (Track 5 - Biomedical imaging and bioinformatics)

14. *Conference:* 15th European Conference on Computer Vision (ECCV)
    Joakim Lindblad, Nataša Sladoje, Elisabeth Wetzer
    Date: 20180908–20180914
    Address: GASTEIG Cultural Center, Munich, Germany
    Title: Towards automated multiscale imaging and analysis in TEM: Glomerulus detection by fusion of CNN and LBP maps
    Comment: Presented at the Workshop on BioImage Computing

15. *Conference:* Medical Image Computing and Computer Assisted Intervention (MICCAI)
Ashis Kumar Dhara
Date: 20180916–20180920
Address: Grenada, Spain
Title: Segmentation of Post-operative Glioblastoma in MRI by U-Net with Patient-specific Interactive Refinement
Comment: The presentation was at the satellite event BRaTS.

16. *Conference:* International workshop on combinatorial image analysis, IWCIA
Filip Malmberg
Date: 20181122–20181124
Address: Axis Vermar Conference & Beach Hotel, Porto, Portugal
Title: When can l_p-norm objective functions be minimized via graph cuts?

7.5 Non-refereed conference presentations

1. *Conference:* 2nd NEUBIAS Bioimage Analysis Community Conference 2018
Joakim Lindblad, Nataša Sladoje
Date: 20180131–20180202
Address: Szeged, Hungary
Title: EDAM-bioimaging: the ontology of bioimage informatics operations, topics, data, and formats

2. *Conference:* Swedish Symposium of Image Analysis (SSBA)
Kalyan R. Ayyalasomayajula
Date: 20180307–20180309
Address: KTH, Stockholm
Comment: Title: Document Binarization Combining with Graph Cuts and Deep Neural Networks

3. *Conference:* Swedish Symposium on Image Analysis (SSBA)
Gunilla Borgefors
Date: 20180307–20180309
Address: KTH, Stockholm
Title: Problems with Colour Names

4. *Conference:* Swedish Symposium on Image Analysis (SSBA)
Damian Matuszewski
Date: 20180307–20180309
Address: KTH, Stockholm
Title: Deep learning segmentation of biomedical images with minimal labelling

5. *Conference:* Swedish Symposium on Image Analysis (SSBA)
Fredrik Nysjö
Date: 20180307–20180309
Address: KTH, Stockholm
Title: RayCaching: Point-Based Isosurface Visualisation in Large Volume Datasets

6. *Conference:* Swedish Symposium on Image Analysis (SSBA)
Gabriele Partel
Date: 20180307–20180309
Address: KTH, Stockholm
Title: Improving Recall of In Situ Sequencing by Self-Learned Features and a Graphical Model

7. *Conference:* Swedish Symposium on Image Analysis (SSBA)
Leslie Solorzano
Date: 20180307–20180309
Address: KTH, Stockholm
Title: Region-based Registration of Whole Slide Images

8. *Conference:* Swedish Symposium on Image Analysis (SSBA)
   Amit Suveer
   Date: 20180307–20180309
   Address: KTH, Stockholm
   Title: Denoising of Short Exposure Transmission Electron Microscopy Images using CNN

9. *Conference:* Swedish Symposium of Image Analysis (SSBA)
   Johan Öfverstedt
   Date: 20180307–20180309
   Address: KTH, Stockholm
   Title: Distance Between Vector-Valued Images Based on Intersection Decomposition with Applications in Object Detection

10. *Conference:* European Congress on Digital Pathology (ECDP)
    Leslie Solorzano
    Date: 20180529–20180601
    Address: Helsinki, Finland
    Title: Quality assurance and local regions for WSI registration

11. *Conference:* Bibliotheca Baltica
    Raphaela Heil
    Date: 20181004–20181005
    Address: Rostock, Germany
    Title: Word Spotting in Historical Handwritten Manuscripts using Capsule Networks

12. *Conference:* Swedish e-Science Academy (eSSENCE)
    Ekta Vats
    Date: 20181016–20181017
    Address: Uppsala, Sweden
    Title: Interactive historical manuscript transcription

13. *Conference:* Swedish Symposium on Deep learning (SSDL)
    Kalyan Ram Ayyalasomayajula
    Date: 20180905–20180906
    Address: Wallenberg Conference Center, Göteborg
    Title: Realistic handwritten document generation using an RNN with style transfer based pre- and post-processing

14. *Conference:* Swedish Symposium on Deep Learning (SSDL)
    Eva Breznik
    Date: 20180905–20180906
    Address: Wallenberg Conference Center, Göteborg
    Title: Using deep learning with anatomical information for segmentation of abdominal organs in whole-body MRI

15. *Conference:* Swedish Symposium on Deep Learning (SSDL)
    Raphaela Heil
    Date: 20180905–20180906
    Address: Wallenberg Conference Center, Göteborg
    Title: Exploring the Applicability of Capsule Networks for Word Spotting in Historical Handwritten Manuscripts

16. *Conference:* Swedish Symposium on Deep Learning (SSDL)
    Elisabeth Wetzer
    Date: 20180905–20180906
    Address: Wallenberg Conference Center, Göteborg
    Title: Towards automated multiscale imaging and analysis in TEM: Glomeruli detection by fusion of CNN and LBP maps

17. *Conference:* SciLifeLab Satellite Symposium NLSDays
Anna Klemm, Petter Ranefall
Date: 20180910
Address: Aula Medica, Karolinska Institutet, Stockholm
Title: SciLifeLab BioImage Informatics Facility

7.6 Attended conferences

1. *Conference:* NEUBIAS
Petter Ranefall
Date: 20180130–20180202
Address: Szeged, Hungary

2. *Conference:* Second Network Meeting for Sida- and ISP-funded PhD Students in Mathematics
Christer O. Kiselman
Date: 20180226–20180227
Address: Sida Headquarters in Stockholm

3. *Conference:* Swedish Symposium of Image Analysis (SSBA)
Ewert Bengtsson, Ludovic Blache, Eva Breznik, Anders Brun, Ashis K. Dhara, Anindya Gupta, Raphaela Heil, Anna Klemm, Joakim Lindblad, Giorgia Milli, Ingela Nyström, Nicolas Pielawski, Martino Pilia, Ida-Maria Sintorn, Nataša Sladoje, Robin Strand, Elisabeth Wetzer, Håkan Wieslander
Date: 20180307–20180309
Address: KTH, Stockholm
Comment: CBA had 26 participants at the Swedish Symposium on Image Analysis (SSBA) this year. Sintorn and Brun on the SSBA board 2016-2018. Sintorn elected as new SSBA Chair and Strand as Vice-Chair. Several CBA presentations and PhD students as session chairs. There were some 140 participants from academia and industry who gathered for a PhD student day and two symposium days. The interest from non-academic organisations continues.

4. *Conference:* NEUBIAS workshop
Nataša Sladoje
Date: 20180412–20180413
Address: Univ. of Nantes, France

5. *Conference:* Phenotypic screening
Anna Klemm
Date: 20180426
Address: SciLifeLab, Solna

6. *Conference:* Cytometry editorial board meeting
Ewert Bengtsson
Date: 20180428
Address: Prague, Czech Republic
Comment: The meeting took place during the CYTO 2018 congress

7. *Conference:* SIAM Conference on Imaging Science
Elisabeth Wetzer
Date: 20180605–20180608

8. *Conference:* 24th International Conference on Pattern Recognition (ICPR) 2018
Ingela Nyström
Date: 20180820–20180824
Address: China National Convention Center, Beijing, China
Comment: Participated in IAPR Executive Committee meetings. After ten years as member of the ExCo, Nyström concluded her terms as 2nd Vice-President 2008-2010, Secretary 2010-2014, President 2014-2016, and Past President 2016-2018.

9. *Conference:* 24th International Conference on Pattern Recognition (ICPR) 2018
Ida-Maria Sintorn
Date: 20180821–20180824
Address: China National Convention Center, Beijing, China
Comment: Represented Sweden (SSBA) at the IAPR Governing Board meeting.

10. *Conference:* Royal Society of Sciences in Uppsala Day
Ewert Bengtsson, Gunilla Borgefors
Date: 20180904
Address: Gustavianum, Uppsala

11. *Conference:* Swedish Symposium on Deep Learning (SSDL)
Petter Ranefall, Robin Strand
Date: 20180905–20180906
Address: Wallenberg Conference Center, Göteborg

12. *Conference:* Medical Image Computing and Computer Assisted Intervention (MICCAI)
Eva Breznik
Date: 20180916–20180920
Address: Granada, Spain

13. *Conference:* KNIME Workshop
Anna Klemm
Date: 20180917
Address: SciLifeLab, Solna

14. *Conference:* KNIME Workshop
Petter Ranefall
Date: 20180917
Address: SciLifeLab, Solna

15. *Conference:* Artificial Intelligence Meets Life Sciences – 5th RIKEN-KI/SciLifeLab Symposium
Petter Ranefall
Date: 20180920
Address: SciLifeLab, Solna

16. *Conference:* Workshop on prostate cancer grading
Ewert Bengtsson
Date: 20181011
Address: Martini Klinik, Hamburg, Germany
Comment: Discussion on a possible joint project

17. *Conference:* MC meeting - Correlated Multimodal Imaging in Life Sciences
Joakim Lindblad, Nataša Sladoje
Date: 20181012
Address: COST office Brussels
Comment: COST action CA17121

18. *Conference:* 6th NEUBIAS workshop
Nataša Sladoje, Joakim Lindblad
Date: 20181016–20181019
Address: Mrc Centre For Regenerative Medicine (univ. Edinburgh), Edinburgh, United Kingdom

19. *Conference:* Euro-Bioimaging
Anna Klemm, Petter Ranefall
Date: 20181129
Address: Stockholm

20. *Conference:* Workshop: Sweden in Euro-Bioimaging
Ewert Bengtsson, Petter Ranefall
Date: 20181207
Address: Hotel C, Stockholm

21. *Conference:* AI and Machine Learning
Petter Ranefall
Date: 20181212
Address: ÅF, Solna

7.7 Visiting scientists

1. **Douglas Hofstadter**
Address: Center for Research on Concepts and Cognition, Indiana University, Bloomington, Indiana, USA
Host: Gunilla Borgefors
Data: 20171201–20180223
Topic: Sabbatical

2. **Fanja Rakotondrajao**
Address: Université d'Antanarivo, Madagascar
Host: Christer Oscar Kiselman
Date: 20180214–20180228
Topic: Mathematical concepts and their linguistic expression in a multicultural setting. Principles of mathematical terminology.
Comments: Fanja is professor of Mathematics at Université d'Antanarivo, President of the Mathematical Society of Madagascar, Member of the Malagasy Academy. The visit was supported by the Royal Academy of Arts and Sciences. Fanja was also invited to the Second Network Meeting for Sida- and ISP-funded PhD Students in Mathematics held in Stockholm February 26 and 27. The title of her presentation was "What we learn, what we get to know."

3. **Fred Hamprecht**
Address: Interdisciplinary Center for Scientific Computing (IWR) and
Dept. of Physics and Astronomy
Heidelberg Collaboratory for Image Processing (HCI), University of Heidelberg, Heidelberg, Germany
Host: Carolina Wählby
Date: 20180318–20180322
Topic: Seminars and planning for sabbatical during 2019

4. **Anne Carpenter**
Address: Imaging Platform, Broad Institute of Harvard and MIT, Boston, MA, USA
Host: Carolina Wählby
Date: 20180602–20180608
Topic: Seminars and discussions on equal opportunities in academia

5. **Mariëlle Jansen**
Address: Image Sciences Institute
University Medical Center Utrecht, The Netherlands
Host: Robin Strand
Date: 20180813–20181117
Topic: Guest PhD student

6. **Chris Ciesielski**
Address: Dept. of Mathematics, West Virginia University, USA
Medical Image Processing Group, Dept. of Radiology, Univ. of Pennsylvania
Host: Robin Strand, Filip Malmberg
Date: 20180910–20180912
Topic: Research collaboration

7. **Antoine Vacavant**
Address: Université d'Auvergne Clermont, Clermont-Ferrand, France
Host: Nataša Sladoje
Date: 20181018–20181024

Topic: Robust image processing algorithms, involving tools from digital geometry and mathematical morphology; Image-guided liver cancer modeling for computer-aided diagnosis and treatment
Comments: Visit supported by the TOR program of Institut Français de Suède

8. **Ljiljana Teofanov**
Address: University of Novi Sad, Serbia
Host: Nataša Sladoje
Date: 20181208–20181211
Topic: Numerical methods for diffeomorphic image regisitration
Comments: Visit supported by VR-SRL grant (Sweden-Serbia collaboration)

9. **Nenad Teofanov**
Address: University of Novi Sad, Serbia
Host: Nataša Sladoje
Date: 20181208–20181211
Topic: A wavelet approach to image compression
Comments: Visit supported by VR-SRL grant (Sweden-Serbia collaboration)

7.8 Visits to other research groups

1. **Teo Asplund**
Host: Jesús Angulo
Address: CMM-Centre de Morphologie Mathématique, MINES Paristech, PSL Research University, Fontainebleau
Date: 20180201–20180430
Topic: Research collaboration.
Comments: A three month visit to the Centre for Mathematical Morphology.

2. **Stefan Seipel**
Host: Prof. Simon Kingham
Address: Geospatial Research Group at Canterbury University, New Zealand
Date: 20180205–20180210
Topic: Collaboration in GeoHealth.

3. **Nataša Sladoje, Joakim Lindblad**
Address: Univ. of Novi Sad, Serbia
Date: 20180531–20180609
Topic: PhD supervision and research visit
Comments: Supported by VR-SRL Sweden-Serbia grant.

4. **Carolina Wählby and Gabriella Edfeldt**
Host: Anja Hauser and Raluka Nieser
Address: Group of Anja Hauser and Raluka Nieser, Charité, Berlin, Germany,
Date: 20181028–20181031
Topic: Imaging and image analysis for MELC
Comments: The visit was sponsored by the ISAC Scholars program.

5. **Nataša Sladoje, Joakim Lindblad**
Host: Antoine Vacavant
Address: Université Clermont Auvergne,Institute Pascal laboratory, Campus Le-Puy-en-Velay, France
Date: 20181106–20181117
Topic: Guest professor
Comments: Joakim was awarded a visiting professor grant from the Université Clermont Auvergne, France.

7.9 Committees

Ewert Bengtsson
International:

- Lifetime Fellow of the Institute of Electrical and Electronics Engineers (IEEE), 2015–
  Comment: Member since 1974.
- Member of the International Society for Optical Engineering (SPIE), 2004–
- Member of the International Society for Analytical Cytology (ISAC), 2000–
- Editorial Board member of *Computer Methods and Programs in Biomedicine,* 1995–
  Comment: Published by Elsevier.
- Editorial Board member of *Cytometry,* 2017–
  Comment: Published by Wiley.
- Editorial Board member of *Machine Graphics & Vision,* 1994–
  Comment: Published by the Polish Academy of Sciences.
- Editorial Board Member of *Journal of Multimedia Information System*, 2014–
  Comment: Published by Korea Multimedia Society.
- Expert for evaluating application for promotion to professor position by Dr. Hazem Hiary at The University of Jordan, Amman, Jordan.
- Expert member of the Labex project review jury for the ANR, French Research Council.
- Programme committee, International Conference of Mass Data Analysis of Images and Signals (MDA).

National:

- Member of the Royal Swedish Academy of Engineering Sciences (IVA), 2006–
  Comment: Division VII: Basic and Interdisciplinary Engineering Sciences.
- Member of the Royal Society of Sciences in Uppsala (Kungliga Vetenskaps-Societeten), 1998–
  Comment: Elected member of the oldest scientific society in Sweden (founded 1710).
- Scientific board of Swedish Association for Medical Engineering and Physics, "Svensk förening för medicinsk teknik och fysik" 2013-
- Scientific board of Hillevi Fries Research Scholarship Foundation, 2006–
  Comment: A Swedish foundation that accepts applications and gives out research grants for urology research.
- Chair of UU steering group for the ALLVIS project implementing centralized storage of research data for Uppsala University, 2015-20180630
- Expert for evaluating application for docent position at Linköping University by Evren Özarslan

Gunilla Borgefors
International:

- Fellow of the International Association for Pattern Recognition (IAPR), 1998–
  Comment: 1st Vice President 1994–96, Secretary 1990–94, etc., etc.
- Chair of the Fellow committee of the International Association for Pattern Recognition (IAPR), 2016-2018
  Comment: Member 2014-2016.
- Member of the King Sun Fu Prize committee of the International Association for Pattern Recognition (IAPR), 2016-2022
- Fellow of the Institute of Electrical and Electronics Engineers, Inc. (IEEE), 2007
  Comment: Senior member 1998.

- Editor-in-Chief of *Pattern Recognition Letters,* 2011-2018
  Comment: Published by Elsevier. PRL is an official journal of the International Association of Pattern Recognition. Borgefors was Associate/Area Editor 2004–2010.

- Editorial Board member of *Image Processing and Communications,* 1994–
  Comment: Published by the Institute of Telecommunications, Bydgoszcz, Poland.

- Editorial Board member of *Pattern Recognition and Image Analysis: Advances in Mathematical Theory and Applications,* 1993–
  Comment: Published by Interperiodica Publishing in cooperation with the Russian Academy of Sciences.

- Editorial Board of the book series Computational Imaging and Vision, 2003–
  Comment: Published by Springer.

- Steering committee for Discrete Geometry for Computer Imagery (DGCI) conferences, 2000–

- Steering committee for International Symposium on Mathematical Morphology (ISMM), 2011–

- International liaison Chair, 24st International Conference Pattern Recognition (ICPR 2018) Beijing, China, August 2018.

- Technical committee, 22th Medical Image Understanding and Analysis (MIUA 2018), Southampton, England, July 2018

- Programme committee, 3rd International Workshop on AI aspects of Reasoning, Information, and Memory (AIRIM 18),Poznań, Poland, September 2018.

- Programme committee, 22st International Conference on Computer Vision and Graphics(ICCVG 2018,) Warsaw, Poland, September 2018.

- Programme committee, 23rd Iberoamerican Congress on Pattern Recognition (CIARP 2018), Madrid, Spain, November 2018.

- Election committee for the appointment of Loizos Michael to Associate Professor at the Open University of Cyprus in Nicosia, January 2018.

- Examiner of the Thesis of Sahar Zafari, School of Engineering Science, Lappeenranta University of Technology, Finland, October 2018.
  Comment: Title: Segmentation of partially overlapping convex objects in silhouette images.

National:

- Member of the Royal Swedish Academy of Engineering Sciences (IVA), 2011–
  Comment: Division VII: Basic and Interdisciplinary Engineering Sciences.

- Member No. 19 of the Royal Society of Sciences in Uppsala (Kungliga Vetenskaps–Societeten), 2000–
  Comment: Elected member of the oldest scientific society in Sweden (founded 1710).

- Member of Swedish Parliamentarians and Scientists, 1987–
  Comment: Members are elected. Only one scientist per field admitted.

- Member of the Board/Steering Committee for Onsala Space Observatory, 2011–

- Dissertation committee for Hamid Behjat, Dept. of Biomedical Engineering, Lund University, 2018-04-26
  Comment: Title: Domain-Informed Signal Processing with Application to Analysis of Human Brain Functional MRI Data.

- Dissertation committee for Sofie Liljegren, Dept. of Physics and Astronomy, UU, 2018-05-30
  Comment: Title: Stellar Winds of Cool Giants: Investigating the Mass-Loss Mechanism of AGB Stars.

Christer O. Kiselman
International:

- American Mathematical Society (life member)
- Société Mathématique de France
- International Academy of Sciences, San Marino
- Internacia Scienca Akademio Comenius
- European Mathematical Society
- Polska Akademia Umiejetności (Polish Academy of Arts and Sciences)
- Associate Member, Scandinavian Society for Iranian Studies

National:

- Royal Academy of Arts and Sciences, Uppsala, 1983– .
- Royal Society of Sciences (Kungliga Vetenskaps-Societeten), Uppsala, 1984– .
- Royal Swedish Academy of Sciences, 1990– .
- Swedish Astronomical Society (life member)
- Swedish Mathematical Society (life member)

Joakim Lindblad
International:

- Management committe member substitute, NEUBIAS – A new Network of European BioImage Analysts to advance life science imaging, 20160503–20200502
  Comment: EU COST Action CA 15124
- Program committee member, CTIC Workshop on Computational Topology in Image Context.
- Program committee member, IWCIA - International Workshop on Combinatorial Image Analysis.
- Management committe member substitute, COMULIS - Correlated Multimodal Imaging in Life Sciences.
  Comment: EU COST Action CA 17121 - European Cooperation in Science and Technology

National:

- Steering board member - International Master program in Image Analysis and Machine Learning.

Filip Malmberg
International:

- Deputy editor of *Pattern Recognition Letters,* 2015–
  Comment: Published by Elsevier. PRL is an official journal of the International Association of Pattern Recognition.
- Program commitee member, 23rd Iberoamerican Conference on Pattern Recognition (CIARP 2018), Madrid, Spain, November 2018.
- Program commitee member, Medical Image Understanding and Analysis - MIUA 2018

National

- Steering board member - International Master program in Image Analysis and Machine Learning.
- Ph.D. thesis committee for Viktor Larsson, 20180601
  Comment: Thesis title: ”Computational Methods for Computer Vision, Minimal Solvers and Convex Relaxations”
- Ph.D. thesis committee for Saeed Gholami Shahbandi, 20180614
  Comment: Thesis title: Interpretation and Alignment of 2D Indoor Maps : Towards a Heterogeneous Map Representation

Ingela Nyström
International:

- Member of the Executive Committee of International Association for Pattern Recognition (IAPR) 2008–2018
  Comment: 2nd Vice President 2008–2010, Secretary 2010–2014, President 2014–2016, Past President 2016–2018
- Chair of the IAPR Nominating Committee 2016–2018
- Chair of the IAPR Constitutions and Bylaws Committee 2018–
- Invited Speakers Chair, 24th International Conference on Pattern Recognition (ICPR 2018), Beijing, China, Aug 2018
- Program Committee, 22nd Medical Image Understanding and Analysis (MIUA 2018), Southampton, UK, July 2018
- Program Committee, 14th International Conference on Signal Image Technology and Internet-based Systems (SITIS 2018), Las Palmas de Gran Canaria, Spain, Nov 2018

National:

- Member of the Royal Society of Arts and Sciences of Uppsala (Kungliga Vetenskapssamhället i Uppsala), 2012–
  Comment: Board member 2016–, 4 meetings per year
- Member of the Council for Research Infrastructure (RFI), the Swedish Research Council, 2014–
  Comment: Vice-Chair 2015–, meetings approximately 10 days per year
- Deputy Member of the Board of Misconduct in Research ("Nämnden för utredning av oredlighet i forskning") at UU, 2017–, 8 meetings per year
- Member of the Programme Board for the Bachelor Programme in Biomedical Engineering at UU, 2018, 4 meetings per year
- Member of the Steering Group for the Digital Humanities Uppsala research network, 2018–, 6 meetings per year
- Member of Advisory Committee forming WoMHeR - Uppsala Center for Women's Mental Health during the Reproductive Lifespan, 2018–, 6 meetings per year
- Mentor in the TekNat Mentorship Programmes: 2014–2015, 2016–2017, 2018–2019
- Auscultation for participants in the course "Supervising PhD students", 2015–, approximately 4 times per year
- External evaluator of position as Researcher in 3D Image Analysis at DTU Compute, Technical University of Denmark, 2018
- External evaluator of position as Senior Lecturer in Biomedical Image Sciences at Linköping University, 2018
- External evaluator of position as Professor in Computer Graphics at Linköping University, 2018

Stefan Seipel
National:

- Board of UpGIS, the network of Geographical Information Systems at UU, 2013–
- Dissertation committee of Fernando Bevilacquas, Skövde University, 20181119
  Comment: Title: Game-calibrated and user-tailored remote detection of emotions: A non-intrusive, multifactorial camera-based approach for detecting stress and boredom of players in games

Ida-Maria Sintorn
National:

- Chair of the Swedish Society for Automated Analysis (SSBA), 2018-.
  Comment: Board member since 2008
- Steering board member - International Master program in Image Analysis and Machine Learning.
- Vi2 division representative in the Collaborations Group at Dept. IT, UU, 20180101–20180831.
- Group member, Vi2 Head of Division candidate suggestion
  Comment: other group members appointed by Head of Department were Åsa Cajander, Maike Paetzel, and Camilla Pajunen.
- PhD thesis evaluation committee, 20180420
  Comment: Erik Bylow, Centre for Mathematical Sciences, Lund University
  title:Optimization Methods for 3D Reconstruction: Depth Sensors, Distance Functions and Low-Rank Models

Nataša Sladoje
International:

- Associate Editor for Pattern Recognition Letters
  Comment: Published by Elsevier. PRL is an official journal of the International Association of Pattern Recognition.
- Management committe member, NEUBIAS - A new Network of European BioImage Analysts to advance life science imaging, 20160503–20200502
  Comment: COST Action CA 15124
- Management committe member, COMULIS - Correlated Multimodal Imaging in Life Sciences, 20181012–20221011
  Comment: EU COST Action CA 17121 - European Cooperation in Science and Technology
- PhD thesis commitee member, 20180302
  Comment: PhD for Monica Jane Emerson ”Statistical Image Analysis of Tomograms with Application to Fibre Geometry Characterisation” , The Technical University of Denmark

National:

- Steering board member - International Master program in Image Analysis and Machine Learning.
- Steering board member - Civilingenjörsprogrammet Industriell ekonomi, 20180101–20181231
- Steering board member - International Master program in Data Science, 20180101–20181231

Robin Strand
International:

- Program Committee, 21st International Conference on Discrete Geometry for Computer Imagery (DGCI 2018), Paris, France
- Program Committee, 2nd Workshop on Reproducible Research in Pattern Recognition (RRPR 2018), Beijing, China.
- Program Committee, 24nd International Conference on Pattern Recognition (ICPR 2018), Beijing, China
- Program Committee, Medical Image Understanding and Analysis (MIUA 2018), Southampton, UK

National:

- Member and reviewer of the review panel NT-19 (Biomedical Engineering) at the Swedish Research Council, 2018
- Vice Chair, Swedish Society for Automated Image Analysis, 2018–

- Steering committee deputy board member, Analytic Imaging Diagnostic Arena, AIDA, 2017–
- Steering committee member of the AstraZeneca funded project Imiomics, metabolomics, proteomics, and genomics of Type-2-Diabetes Mellitus development and regression
- Member of the board for Centre for Image Analysis, Uppsala University, 2017–20181231
- Dissertation committee for Thobias Romu, Linköping University, Linköping, 2018-03-21
  Comment: Title: Fat-Referenced MRI – Auto-Calibrated Quantitative MRI for Tissue Characterization and Volume Measurement
- Election committee, Dept. of IT. Deputy member
- Coordinator of biomedical information technology (biomed-IT) at the Dept. of IT –20181231

Carolina Wählby
International:

- Management Committee for NEUBIAS
  Comment: A Network of European BioImage Analysts to advance life science imaging (NEUBIAS), fully funded by COST, a European cooperation in Science and Technology.

National:

- Member of the Royal Swedish Academy of Engineering Sciences (IVA),
  Comment: Division VII; Basic and Interdisciplinary Engineering Sciences
- Member of the Electorial Board ("elektorsförsamlingen") of the Faculty of Science and Technology, UU, 2014-
- Board of National Microscopy Infrastructure
  Comment: A Swedish infrastructure for advanced microscopy.
- Board of Swedish Bioimaging
  Comment: A Swedish network for research infrastructures in biomedical imaging and image analysis, 2015-2018
- Board of Upptech, 20160906
  Comment: Upptech (Uppsala University School of Technology) has been established by the Faculty of Science and Technology at Uppsala University for raising visibility of, profiling, and enhancing the university's research and teaching within technology.
- Scientific Advisory Board of BioVis, 20160101
  Comment: BioVis is a part of Uppsala University and associated with SciLifeLab, it is a core facility belonging to the Faculty of Medicine.
- Board of Science for Life Laboratory Uppsala, 20160401
  Comment: Science for Life Laboratory, or SciLifeLab, is a national center for molecular biosciences with focus on health and environmental research.
- Thesis opponent, 20180907
  Comment: Hanqing Zhang, Umeå University, Umeå , Sweden, title; Digital holography and image processing methods for applications in biophysics.
- Licentiate thesis committee, 20180619
  Comment: Hamidur Rahman, Malardalen University, Sweden, Thesis title: An Intelligent Non-Contact based Approach for Driver's Cognitive Load Monitoring

Teo Asplund, Fredrik Nysjö, Elisabeth Wetzer, and Tomas Wilkinson

- Editors, SSBAktuellt, the newsletter of the Swedish Society for Automated Image Analysis