Vetenskapsrådet

Application

2015-03-31

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Descriptive data

Project info

Project title (Swedish)*

Automatisk målföljning av cellmigration och förökning i time-lapse-mikroskopi

Project title (English)*

Automated tracking of cell migration and proliferation in time-lapse microscopy

Abstract (English)*

Biological cells migrate and change morphology. This plays a crucial role in many biological processes such as embryonic development, inflammatory immune response, wound repair, and tumor metastasis. Therefore, numerous biomedical studies have been conducted to understand the behavior of different cell-types. Large-scale studies of cell migration and proliferation could yield insights on tumor development and metastasis, and thus improve the current understanding of cancer. These studies could also provide knowledge on how to artificially grow tissue-specific stem cells and potentially cure painful degenerative diseases such as muscular dystrophies; or provide knowledge on the complex pathways from genes to phenotypes, through embryonic development studies in model organisms.

Time-lapse microscopy is the most important tool to study morphological changes and cell behaviors, such as migration, proliferation, mitosis (cell division), and apoptosis (cell death). Advances in microscopy hardware with new imaging modalities and motorized stages, along with the rapid development of high-resolution digital image sensors now allow for the fully automated acquisition of massive amounts of digital image data, both in 2D and 3D. Manual interpretation of this data is however very time consuming. Therefore, the use of time-lapse microscopy in large-scale studies of cell migration and proliferation is hindered by both the lack of robust and generally applicable methodologies and the lack of software tools for automatically tracking cell migration and proliferation.

Motivated by the above, we propose to, from a signal processing perspective, develop the theory and methods required to automatically track migrating cells and create linage trees that describe their proliferation through mother-daughter relations. The cell-tracking problem can be viewed as an application-specific multiple-target tracking problem. While multiple-target tracking is a well-established research area, the cell-tracking problem has several distinct challenges that are not resolved by current approaches. Apart from migrating, cells frequently adhere to each other and are then typically detected (segmented) jointly. Cells also significantly change their morphologies, divide, and die. These challenges call for substantial research efforts and new results. Therefore, we outline an ambitious research program aimed at studying fundamental aspects of the cell-tracking problem. These will include: (i) combinatorial optimization techniques to solve global data association and cell track-linking problems; (ii) data cleansing and processing methods such as state-space based multiple-hypothesis density smoothers that can harness spatial correlations in cell migration introduced by tissue-movement; and (iii) probability density estimation techniques and their use in soft output classifiers to detect relevant cell events, including migration, mitosis, and apoptosis.

The proposed research will be conducted within the department of Signal Processing at KTH, and will rely on probability theory, estimation and detection theory, statistical learning, and continuous and discrete optimization. The biomedical relevance of the results obtained, and access to new image data, is secured through established collaborations with biomedical labs. These collaborations are based on mutual benefits rather than shared funding. We have also already constructed a highly capable software platform for cell tracking which will allow us to pursue the above-mentioned topics in parallel throughout the four-year span of the project. The platform supports the processing of both 2D and 3D image data. Results from each topic, in themselves motivated by theoretical arguments and modeling assumptions, can thus also be tested and evaluated in the context of a full cell tracking solution. The platform also makes it possible to immediately make our results available in a form that is usable for biomedical researchers without engineering backgrounds.

Popular scientific description (Swedish)*

Många typer av biologiska celler, de små enheter som alla levande organismer består av, har förmågan att förflytta sig och ändra form. Denna förmåga har en stor inverkan på ett flertal viktiga biologiska processer och system, som till exempel fosterutveckling, det inflammatoriska immunförsvaret, sårläkning och tumörspridning. Som ett specifikt exempel kan vi nämna muskelstamceller. Dessa celler är en typ av stamceller som ligger i ett tunt lager utanpå muskelfibrer, och som då en muskel skadas söker upp och reparerar skadan. Om det skulle vara möjligt att artificiellt odla sådana celler i större mängder, vilket det tyvärr inte är idag, så skulle dessa kunna användas i nya behandlingar för patienter med muskelnedbrytande sjukdomar så som muskeldystrofier av olika slag. För att göra detta möjligt behöver dock cellbiologer studera och förstå cellers rörelser och tillväxtförmågor under olika odlingsförhållanden.

Det vanligaste sättet att studera cellrörelse idag är med hjälp av mikroskopi. Moderna digitala mikroskop kan automatiskt producera stora mängder av högupplösta bilder och videosekvenser, men det är tyvärr fortfarande inte möjlig att utnyttja dessa tekniker fullt ut i storskaliga cellbiologisk studier då det helt enkelt är för tidsödande och svårt at gå igenom och tolka all data som genereras. Det finns därför ett stort behov av att automatisera dataanalysen genom att skapa innovativa datorprogram, så att dessa studier kan genomföras. Resultaten kan förutom att leda till botemedel mot muskeldystrofier också leda till en bättre förståelse kring tumörspridning och hur gener tillsammans påverkar en individs egenskaper.

I detta projekt vill vi utnyttja metoder från ett forskningsområde kallat signalbehandling för att lösta dataanalys och automatiseringsproblemet. Signalbehandling kan beskrivas som en del av den tillämpade matematiken som studerar hur man utvinner information ur signaler, där begreppet signal inkluderar de ovan nämnda digitala mikroskopbilderna. Signalbehandling tillämpas idag överallt i samhället, även om vi inte alltid tänker på det. Exempel på signalbehandling i vardagen är: då elektromagnetiska vågor omvandlas till tal av en mobiltelefon; då de mycket små mönstren på en CD-skiva omvandlas till musik; och då en dator känner igen personer i ett digitalfoto. Till exemplen på medicinsk signalbehandling hör de datorprogram som omvandlar elektromagnetiska signaler till bilder av vårt inre i till exempel MR (magnetresonanstomografi), eller de datorprogram som inom kort i smarta klockor kommer att ta reda på hur vi mår genom att mäta biologiska signaler genom huden.

Vi ämnar använda signalbehandling som ett verktyg för att skapa datorprogram som automatiskt extraherar cellrörelser och celltillväxt genom delning, ur en videosekvens fångad av ett mikroskop. Dessa program kan sedan användas för snabba och pålitliga analyser av cellbiologiska och biomedicinska experiment. Detta kommer i slutändan att öka vår förståelse av biologiska processer, och underlätta utvecklandet av nya mediska behandlingar som minskar onödigt lidande.

Project period

Number of project years*

4

Calculated project time*

2016-01-01 - 2019-12-31

Classifications

Select a minimum of one and a maximum of three SCB-codes in order of priority.

Select the SCB-code in three levels and then click the lower plus-button to save your selection.

SCB-codes*

2. Teknik > 202. Elektroteknik och elektronik > 20205. Signalbehandling

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Enter a minimum of three, and up to five, short keywords that describe your project.

Keyword 1*

Cell Tracking

Keyword 2*

Data Analytics

Keyword 3*

Multiple Target Tracking

Keyword 4

Biomedical Imaging

Keyword 5

Signal Processing

Research plan

Ethical considerations

Specify any ethical issues that the project (or equivalent) raises, and describe how they will be addressed in your research. Also indicate the specific considerations that might be relevant to your application.

Reporting of ethical considerations*

The proposed project will develop the theory of, and methods for, application-specific multiple-target tracking, following established research practices in signal processing, electrical engineering, computer science, and applied mathematics. We do not ourselves directly conduct any biomedical research and no funding is sought by us to fund such research. However, digital image data that we may obtain from our collaborators is typically obtained from experiments that involve animals.

We have so far collaborated with labs in Europe (Labs connected to SciLifeLab in Sweden), the US (the Blau Lab), and Canada (the Gilbert Lab), and have no current plans to expand our collaborative network outside of these countries. The specific research projects conducted in these labs, from which we have received image data, are subject to separate ethical approvals in the respective countries where they are taking place.

Relating specifically to projects in the US: The animal protocols adopted within the Blau Lab are subject to approval by the Stanford University Administrative Panel on Laboratory Animal Care (APLAC) and experiments are performed in compliance with the institutional guidelines of Stanford University. APLAC is accredited by the Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC), see labanimals.stanford.edu for additional details.

Relating specifically to projects in Canada: The animal protocols adopted by the Gilbert Lab are subject to approval by the Toronto Animal Care Committee and the University of Toronto Office of Research Ethics in accordance with guidelines established by the Canadian Council on Animal Care, see www.medresearch.utoronto.ca/dcm_animal_protocol.html for additional details.

We also wish to stress that much of the proposed research can in principle be conducted without obtaining further image data from collaborating labs, albeit with a negative impact on the biomedical relevance of the methods developed. The proposed research could (and will partially) be advanced through the use of publically available image data sets, such as those published as supplemental material in the cell tracking challenges described in the research proposal. We are therefore not forced to enter into any ethically questionable collaboration in order to advance our own scientific work. We have also made this clear to potential collaborators in the past.

Dual Use: Given that a project goal is to publish open source software to aid biomedical researchers, there is a potential that the same software will be misused in order to aid ethically questionable medical research outside of our established collaborations, by simplifying the data analysis of these experiments. Further, given the methodological similarities of cell tracking with other target tracking applications, including the tracking of individual humans and crowds in video images, there is a potential that the methods developed will be used in military applications related to surveillance and radar. We do however not ourselves judge these potential misuses of the specific technologies developed in the project to be significantly more probable than the misuse of any other similar technologies developed in the field of physical sciences and engineering.

Finally, we will not store any form of patient data as part of the project.

The project includes handling of personal data

No

The project includes animal experiments

No

Account of experiments on humans

No

Research plan

1 Purpose and aims

Biological cells migrate and change morphology [A1]. This plays a crucial role in many biological processes such as embryonic development, inflammatory immune response, wound repair, and tumor metastasis [A2]. Numerous biomedical studies have been conducted to understand the behavior of different cell-types, and time-lapse microscopy is the most important tool to study cell behaviors such as migration, proliferation, mitosis (cell division), apoptosis (cell death), and morphological changes.

Early works on cell behavior involved the observation of cells using transmission microscopy, and the sketching of cells by hand at appropriate time intervals [A3]. Advances in microscopy hardware with new imaging modalities and motorized stages, along with the rapid development of high-resolution digital image sensors now allow for the fully automated acquisition of massive amounts of digital image data, both in 2D and 3D. A modern automated microscope is able to capture high-resolution images at regular intervals from hundreds of parallel fields of view. However, most of the analysis of such microscopy time-lapse image data is, unfortunately, still performed manually, albeit aided by software tools for annotation such as the commonly adopted ImageJ [A4]. This analysis is often a very demanding and time-consuming process [A5]. Moreover, manual processing of the time-lapse image sequences can make the obtained results hard to reproduce, and biased by the expectations of the person performing the data analysis.

The development of robust and generally applicable methodologies and software tools for automatically tracking cell migration and proliferation is the only remaining hurdle that prevents the routine application of fully automated, and therefore truly large scale, biomedical studies of cell behavior [A6, A7]. The fundamental importance of large scale cell studies has been recognized by the National Institute of Health (NIH) in the US, which financially supports developments in the area through the "Follow that Cell Challenge" [A8]. Large scale studies of cell migration and proliferation could yield the insights on tumor metastasis required to cure cancers, provide knowledge of how to artificially grow tissue-specific stem cells and cure painful degenerative diseases such as muscular dystrophies [A9], or to understand the complex pathways from genes to phenotypes through embryonic development studies in model organisms [A10]. Motivated by such potential breakthroughs, we aim to, from a *signal processing* perspective, develop the theory and methods required to automatically track migrating cells and create linage trees that describe their proliferation through mother daughter relations.

The cell-tracking problem can be viewed as an application-specific multiple-target tracking problem. While multiple-target tracking is a well established research area [A11], the cell-tracking problem has several distinct challenges that are not resolved by current approaches to track for example humans, vehicles, and aircraft. These challenges call for substantial research efforts and new results. Cells typically divide, through a process called mitosis, and die, through a process called apoptosis, during the span of an experiment. This calls for tracking methods that are able to handle dividing tagets and detect dead targets, even when the dead targets remain in the image sequence as debris among live targets. Cells are also prone to adhere to each other, which frequently leads to them being segmented (detected) jointly. Thus, a functional cell-tracking algorithm should ideally be able to handle the case where several tracked objects are at times segmented as a single object [A12]. Cells that are part of tissue move in unison and utilizing their shared movement is then often a key to obtaining satisfactory tracking results [A10]. Cells also change morphology during migration, mitosis, and apoptosis, and classifiers trained to detect these morphological changes can be used to guide the

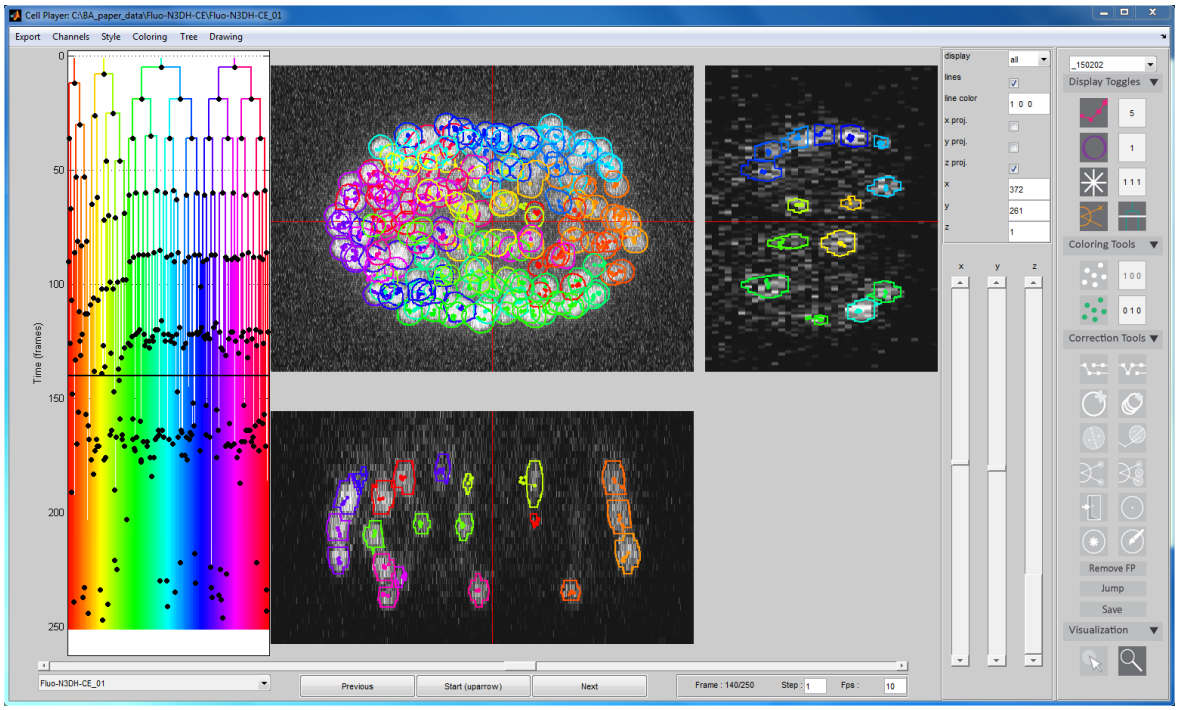

Figure 1: Screenshot of the software for cell tracking developed by the PI's team. The picture illustrates the software applied to fluorescent 3D image data obtained from a developing *C. elegans* embryo, starting at 4 cells, and ending with 290 cells. The image data used for the illustration was obtained using confocal microscopy at the Waterson Lab, George Washington University, DC, USA, and was one of the data sets in the second cell tracking challenge [A13]. Video examples of tracking results are also available at `tinyurl.com/kth-autocell`

tracking algorithm. However, the potentially most important aspect of the cell-tracking problem, and a key difference to many of the applications for which multiple-target trackers have been developed in the past, is that the cell-tracking problem is inherently a non-causal data analytics problem rather than a causal tracking problem. The algorithms developed should therefore ideally through batch processing use information from the entire data set to make reliable decisions regarding migration and proliferation at any one time-instance.

In this proposal we outline an ambitious research program aimed at solving fundamental aspects of the cell-tracking problem by developing methods and theory for: combinatorial optimization to solve global data association and track linking problems; data cleansing and state-space processing using multiple-hypothesis smoothers to extract tissue dynamics; and probability density estimation for use in advanced soft-output classifiers for cell event detection. Access to relevant biomedical time-lapse image data, as well as feedback on the biomedical utility of the methods developed, is secured through existing cross-disciplinary collaborations with biomedical labs, see Section 7, and active participation in international collaborative efforts, see Section 5. Dissemination of our research results will be through theory publications in the engineering literature, through methods publications aimed at researchers in biomedicine, and though open access cell tracking software developed by the PI's team, see Figure 1 and Section 3.2.4.

2 Survey of the field

There are a number of overview publications outlining systems for automated cell tracking, e.g., [A6, A14]. See also the introduction of [JJ9][1] for an up-to-date overview of the state of the art, and [JJ10] for a related survey on (sub-cellular) particle tracking. Semi-complete proof-of-concept systems for cell tracking include [A14], and the open source software recently used for tracking cells in a *Drosophila* embryo [A10]. There are also some available software packages such as: ImageJ [A4]; CellProfiler [A15]; Icy [A16]; and the commercial Imaris by Bitplane [A17] . This said, the capabilities of existing software are still rather rudimentary. The PI's team at KTH has also developed a user friendly software platform, partially described in [JJ7, JJ10, JJ9, JJ30, JJ38] and illustrated in Figure 1, that will be used within the proposed project. Section 5 further describes the world leading performance of this platform.

Existing approaches to cell tracking are often divided into two categories: tracking by detection, and tracking by model evolution [A18, JJ10]. Some authors classify approaches that utilize state-space processing as a separate category [A10], but we will discuss such methodologies in the context of tracking by detection. In tracking by detection, each image is separately segmented to separate the cells from the background, and the so obtained segmented areas are then linked temporally between images in a process typically referred to as data association or track linking. In tracking by model evolution, cells are simultaneously segmented and tracked, for example by evolving the contours of cells from one image to the next. We primarily focus on tracking by detection as this methodology is more amendable to global data association, as it allows for advanced classifiers that operate on visual cues to aid the tracking, and as it can easily be combined with application-specific segmentation for greater flexibility. We believe that this leads to superior overall performance when the segmentation problem can be solved with reasonable accuracy for each single image.

2.1 Segmentation

Many different segmentation algorithms have been applied to the problem of segmenting live cells [A7], and we can only cover a fraction here. The problem of segmenting cells can be made easier by marking the cells or their nuclei with fluorescent proteins or dyes, but in many applications this approach is unsuitable due to photo-toxicity (whereby cells are killed or alter behavior due to the excitation energy) by or photo-bleaching (whereby cells loose their fluorescence over time). However, in 3D experiments, fluorescent labelling may be the only viable option. In the proposed project we consider both images from fluorescence microscopy including confocal microscopy and selective plane illumination microscopy, as well as from transmitted light microscopy including bright field microscopy, phase contrast microscopy, and differential interference contrast (DIC) microscopy.

The simplest, and still predominant [A7], way of segmenting cells in an image is to threshold the image intensity or some other parameter computed from the image, such as the local intensity variance [A19, A20]. A more refined method is to use classifiers trained on spatial features to classify pixels as either cell or background pixels [A21]. Phase contrast microscopy and DIC microscopy create images with characteristic intensity patterns around object boundaries. These imaging artifacts cause problems for many segmentation algorithms, but preconditioning algorithms that utilize convex optimization and sparsity, and model the optical systems used to produce the images, have been reported to segment such images with high accuracy [A22]. In some cases, such as in [A23] which deals with with hematopoietic stem

[1] Citations labelled JJ refer to research papers listed in the PI's publication list.

cells (HSCs), similarity in cell morphology can be exploited to improve segmentation through template matching. However, most cell types significantly change their morphology, making template matching inappropriate [A6]. Other algorithms include active contour methods, such as level sets, that operate on region boundaries instead of the regions themselves [A24].

2.2 Data association

Data association is often done frame by frame in a sequential manner, starting with a number of cells in the first frame and then matching detections in consecutive frames to the cells in the previous frame. Data association problems can be posed as a number of integer linear programming problems or min-cost flow problems, and solved using combinatorial optimization techniques. Frame by frame matching is used, e.g., in [A19, A24, A25]. This produces a result which is locally optimal at every step, but since there is no way of changing matchings at a later point in time, an ambiguity present in only one frame can cause error propagation. Most algorithms that use frame by frame matching have heuristics to process the trajectories after the matching is finished, but this can typically only resolve some of the errors. In [A26] the data association was instead done by first connecting detections that belong to the same track with high probability into so called tracklets, and then connecting tracklets through integer linear programming with results superior to those presented in [A25]. However, the integer linear programming is computationally expensive and that limits the number of tracklets that can be simultaneously merged into tracks. Moreover, errors in the tracklets can not be corrected.

In [JJ7, JJ38], we developed a novel tracking algorithm that makes use of information from all frames simultaneously to form tracks, and that has very low computational complexity, even for large problem instances. It uses dynamic programming to find an optimal way of adding one additional cell to a tentative cell lineage tree with a number of already present cells. We also allow for swapping of matchings in the trajectories of old and new cells, to minimize the risk of an existing cell conflicting with the correct matchings in subsequent steps of the algorithm. The algorithm also has the advantage of not relying on any hard decisions about events like cell death and cell division, prior to the tracking process. An example cell lineage tree extracted by this tracking algorithm is shown in Figure 1. Dynamic programming has previously been used to track people in computer vision applications [A27], but these algorithms use other methods to avoid conflicts among tracks and handle fewer targets. There are also examples of dynamic-programming-based multiple-target trackers in the aerospace and electronics systems (radar) literature [A28], and although these elegantly combine dynamic motion models with data ambiguities and false detections (clutter), they scale poorly with the number of targets and do not straightforwardly extend to cover joint segmentation and dividing targets.

2.3 State-space processing

Cells typically do not display any observable inertia due to their size relative to the viscosity of the surrounding media [A1]. State-space based filters and smoothers have for this reason not been as widely used in cell tracking as in general for multiple target tracking [A11]. Most cell tracking solutions have either relied purely on tracking by detection, as outlined above, or tracking by model evolution, where a model is evolved for the purpose of segmentation rather than leveraging the target's dynamic behavior.

This said, when cells move in chemotactic gradients [A1] or are attached to semi-rigid structures such as tissue, they can display predictable migratory behavior. Applying state-space processing as a data cleansing step, following segmentation and preceding data associ-

ation, can also help alleviate problems with missed detections in sequences of frames, something which can cause problems in global data association algorithms. A state-space filter that propagates a target hypothesis density distribution modeled by a Gaussian mixture model (GMM), without first resolving the data association problem, was proposed in [A29] and extended to a state-space smoother in [A30]. We recently applied the method of [A29] in [JJ30] to resolve target ambiguities in a particle tracking problem. The algorithm of [JJ30] was also used to harness predictable motion caused by tissue movement in a *Drosophila* embryo as part of our solutions to the third cell tracking challenge, see Section 5. GMMs where also used in [A10] although without the global data association applied in [JJ30], and without the use of a dynamic motion model.

2.4 Classification

Statistical learning techniques allow for the automated extraction of relevant information from data and are extremely useful for automated analysis. Examples in the cell tracking literature include the naïve Bayes classifier used in [A25] for segmentation, the logistic regression classifiers used in [JJ7, JJ38] to feed the data association algorithm with information on the likelihood of cell events, and the gradient boosted tree classifiers used in [A12] to resolve joint segmentation. Nonetheless, the automated cell tracking literature largely lacks deep explorations on how to fully exploit statistical learning techniques.

Classification methods are typically divided into soft and hard classifiers. Soft classifiers provide information in terms of probabilities of events or classes, while hard classifiers provide only a decision upon which event or class is more probable. The most common approaches to hard classification are Neural Networks (NNs) and Support Vector Machines (SVMs), the latter used to detection mitotic events in [A14]. Soft classification has been somewhat less explored in the literature, and in spite of the wide variety of approaches that have been investigated, none have become prevalent. However, methods that approach both classification and probability density estimation (PDE), such as [A31], do hold a theoretical advantage. The classification problem can always be solved optimally by using the conditional probability density functions of the features. Therefore, accurate conditional PDEs yield good soft classification performances, and we intend to explore this in the cell tracking context. In fact, it is known that even simple hard classifiers based on PDEs are optimal under widely-satisfied assumptions [A32].

3 Project description

3.1 Theory and methods

The project is methodologically based in the field of signal processing, and will rely on probability theory, estimation and detection theory, statistical learning, and continuous and discrete optimization. Planned contributions to the field are listed below.

3.2 Work- and time-plan

The project will address all parts of the tracking-by-detection pipeline as outlined in Section 2, except segmentation. The omission of segmentation is due to the fact that, although it is a key step of any cell tracking solution, it is also the most explored step [A7]. Thus, we intend to simply apply the latest state-of-the-art in segmentation, and focus on tracking that works with less than perfect segmentation results. The planned work is divided into three work packages (WPs) centered on distinct phases of the pipeline, and one evaluation and dissemination package (DP) centered on the continued development of our software platform. While the

results obtained in each WP will naturally contribute to the improvement of our overall cell tracking solution, no WP is critically dependent on the outcome of any other WP, and the WPs will thus be pursued in parallel during the full duration of the proposed project.

3.2.1 WP1: Data association

The data association method presented in [JJ7, JJ38] applies the Viterbi algorithm to resolve dynamic programming problems that occur when adding a cell track to a current lineage tree. The method is at its core a greedy iterative algorithm and is thus, as any greedy algorithm, subject to local optima and error propagation. A swapping operation, whereby previously laid tracks can be modified is included in [JJ7] as a partial remedy to this. However, we believe that it is possible to improve the capabilities of this swapping operation by replacing the shortest path problem that we currently solve on a trellis graph by a shortest path problem on a more general graph. This will allow more sophisticated edits to preexisting tracks, while still maintaining the global data association properties of the method in [JJ7]. However, this requires non-trivial modifications of our global data fidelity metric in order to avoid graph cycles of negative cost, and this is a topic we wish to pursue further. We will also work on more rigorously placing our data fidelity metric in a Bayesian framework. This is challenging as the resulting metrics still need to admit computationally feasible optimization algorithms for the data association.

3.2.2 WP2: State-space processing

As noted, in [JJ30] we combined the state-space density filter of [A29] with the data association method of [JJ7]. A natural next step is to use the state-space density smoother of [A30] instead. However, due to the computational complexity of [A30] we will have to develop suitable gating and model order reduction methods to realize this goal. Further, although [A30] formally allows for target birth and death processes, it is still challenging to properly incorporate cell mitosis and apoptosis events, in particular with classifier input, and this is something that we aim to address in this WP. Another task that we intend to address is how to extend [A30] to incorporate spatial and structural information. In, for example, later stages of embryonic development, cells may form part of tissue which implies that nearby cells should have similar velocity and acceleration. Similar effects have been observed in dense cell cultures where cells, although not bound to neighbors, exert forces on their surrounding cells. One idea to capture such physical constraints is to adapt principles from Kalman filtering with state constrains [A33], and extend these to target hypothesis density estimation.

3.2.3 WP3: Classification

The data association algorithm in [JJ7] uses event probabilities generated by soft classification techniques for the track linking decisions, but we have so far only used off-the-shelf methods for this purpose. The logistic regression used in [JJ7] represents the simplest of generalized linear models, and although it has been proven to work reasonably well in practice, PDE based methods should be able to better model the complex feature space of the heterogeneous cell population. Therefore, we intend to adapt existing and develop novel PDE methods using optimization theory on function spaces [A34], and apply these to soft classification in the data association stage. This way, we will be able to create tailored classifiers that use spatial features from the segmented areas and temporal features from the state-space pre-processing to assess the likelihood of relevant cell events, e.g., mitosis and apoptosis. We believe these classifiers will decisively improve both the accuracy and the reliability of our tracking results.

3.2.4 DP1: Dissemination and software platform

Dissemination of research results will primarily be through the signal processing, medical imaging, and machine learning literature, although some publications in the biomedical literature as a result of cross-disciplinary collaborations are expected. In order to make the research results immediately available to researchers in biomedicine we will parallel to the scientific WPs continue to maintain and develop our full cell tracking software platform partially described in [JJ7, JJ38, JJ30] and [JJ10, JJ9]. This will allow us to validate the work performed in WP1 – WP3 in the context of a fully functional cell tracking software. In the past, we have made this platform available to the biomedical labs with whom we have collaborated, and we are working towards an open source release of the entire platform during 2015 to further benefit the community at large. This effort to develop usable software is extremely important for the societal benefits of our research since, as noted in [A35], the traditional sole focus on algorithmic novelty "yields hundreds of publicly funded proof-of-principle papers describing algorithms that do not make their way out of the literature and into the biology laboratory".

3.3 Project participants and roles

The primary research work within the project will be conducted by PhD students, who will work across the three WPs and DP1. Klas Magnusson, who has previously been the single PhD student in the team working on the topic of cell tracking, will be part of the project until his graduation in 2016. Pol del Aguila Pla, a recently hired PhD student with past expertise in image processing and classification, will continue to work on the project, initially with emphasis on WP3. A yet unidentified third PhD student will be recruited in 2018 in order to ensure continuity of this line of research. The PI will supervise the PhD students work throughout the project, and make first person contributions to each WP.

4 Significance

The primary purpose of the project is to advance the theory and methods within the areas of signal processing that apply to the cell tracking problem. Significant and fundamental contributions are expected within the areas of multiple target tracking by dynamic programming, state-space based probability hypothesis density filtering and smoothing, classifier design and theory, and to some extent, possibly, image processing for segmentation. The work is also indirectly expected to contribute to other research areas – primarily biomedicine – by making novel tools and technologies available, both through research publications on methodology and through open source software tools. The end results are thus expected to have high significance also for the understanding of biological systems, as indicated in the introduction.

5 Preliminary Results

The PI and his team have actively studied automated data analytics for cell migration and morphology since 2009, primarily through the work of a single PhD student (Klas Magnusson) and with funding from the Swedish Research Council (VR) since 2012. Our development of signal processing methods for global data association through dynamic programming was published in [JJ7, JJ38]. Preliminary results on the use of Gaussian mixture probability hypothesis density (GM-PHD) filtering in conjuncture with global data association was published in [JJ30]. Software developed by members at KTH has also been applied in biomedical studies as reported in, e.g., [A9].

We have also taken an active role in a set of international particle and cell tracking challenges, arranged parallel to the IEEE International Symposium on Biomedical Imaging and

with the purpose of assessing and improving current state-of-the-art in the field, and will continue to do so. We contributed to the paper in Nature Methods [JJ10] that reported the results from the particle tracking challenge, and the paper in Bioinformatics [JJ9] that reported the results of the first cell tracking challenge[2]. The results of, in particular, the cell tracking challenges have been very encouraging. As noted in [JJ9] regarding the first cell tracking challenge: "When we look at the number of appearances of each method among the top three best performing methods, both [the method of the PI's team from KTH, Sweden] and [the method of the team from the German Cancer Research Institute, Heidelberg, Germany] appeared in all eight data sets", and "It is remarkable that [the method of the PI's team from KTH, Sweden] was, at worst, second fastest among the top three best performers in terms of [segmentation] and [tracking]". In the second cell tracking challenge our team scored *highest* in terms of the final rank on *all* 14 datasets included [A13]. Individual results from the third cell tracking challenge are not yet publicly available. We were in both the second the third cell tracking challenge awarded the Bitplane award. We are naturally immensely proud of having, with the funding of a single previous VR grant and starting as novices in the field, developed the world leading solution in terms of tracking performance and applicability for different cell types and microscopy techniques.

6 Equipment and Infrastructure Needs

No specialized equipment or infrastructure, other than desktop computers with somewhat larger than usual storage capabilities, are needed for the project. Access to relevant biomedical image data is primarily secured through collaborations as outlined in Section 7, and through open sources such as in the cell tracking challenges described in Section 5.

7 International and National Collaboration

Collaborations with biomedical research labs are crucial for ensuring the relevance and applicability of the proposed research. We have, since the start of our work in this area, collaborated closely with the Blau Lab at Stanford University, CA, USA, and have also collaborated with the Gilbert Lab at the University of Toronto, in collaborations driven by mutual benefit. We intend to continue these collaborations, and thus have access to relevant data and biomedical expertise. These collaborations have resulted in joint publications in the past [JJ7]. Klas Magnusson, a member of our team, also contributed to the NIH application from the Blau Lab that made it to the final round in the still ongoing "Follow That Cell Challenge" [A8], and has also spent significant amounts of time in the Blau Lab. In order to broaden our national collaborations we have also initiated collaborations with researchers at SciLifeLab at KTH and Uppsala University (UU), and recently contributed to the submission of a joint paper with Carolina Wählby's lab at CBA (Centrum för Bildanalays) and UU. These early collaborations have however not yet led to any (published) joint work, although the PI was invited to speak on the state-of-the-art in automated cell tracking at the "Frontiers in Cell Migration" workshop organized by SciLifeLab and UU. Although the research output of the proposed project is expected to contribute to ongoing biomedical research, the grant will not be used to co-fund any other project.

[2]The number of participating teams have grown from 6 to 8 to 11 from the first to the second to third cell tracking challenge. This further supports the relevance of these events.

8 Other grants

The PI was awarded a VR grant (Projectbidrag Unga Forskare) for 2012 – 2015 with a total amount of funding of 3564 kSEK. It targets the same application area (cell tracking), but is non-overlapping in time with the currently proposed project. The PI is also a co-applicant on an application submitted to the SSF call "Framework Grants for Research on Generic Methods and Tools for Future Production" in 2015, with no scientific overlap with the present proposal. The PI has no other current external grants or pending grant applications, and the continued research efforts outlined herein are critically dependent on the approval of this application.

9 Independent Research Profile

The PI is employed by the department of signal processing at KTH, which is the same department that granted his PhD. The PI's research independence is however supported: by a majority of the PI's publication being without the inclusion of his former PhD advisor; by a large set of independent international collaborations; an international Post Doc; and by international research visits. The PI is the only faculty who conducts research on cell tracking within the department, and the PI did not perform any such research during his PhD.

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Interdisciplinarity

My application is interdisciplinary

☐

An interdisciplinary research project is defined in this call for proposals as a project that can not be completed without knowledge, methods, terminology, data and researchers from more than one of the Swedish Research Councils subject areas; Medicine and health, Natural and engineering sciences, Humanities and social sciences and Educational sciences. If your research project is interdisciplinary according to this definition, you indicate and explain this here.

Click here for more information

Scientific report

Scientific report/Account for scientific activities of previous project

The PI has an ongoing project grant from VR (Projektbidrag Unga Forskare) entitled "Real Time Automated Cell Tracking in Time-Lapse Microscopy" (Automatisk realitidsmålföljning av celler i timelapsemikroskopi), grant no. 621-2011-5884, with a total funding of 3561 kSEK. Grant no. 621-2011-5884 overlaps scientifically with the currently submitted proposal, but did not include now proposed parts on state-space processing and classification. It will also end in 2015. The PI was awarded the SSF project grant "Ingvar Carlsson Award" of 3000 kSEK in total, for the period 2009-2012, but this project had no scientific overlap with the VR grant, or with the current proposal. The PI has applied for other grants during the grant period of 2011-2015 (an ERC StG, an SSF grant, and VR framework grants as a co-applicant), but no such grants have been awarded and no other external research funding has been available for the project.

VR grant no. 621-2011-5884 has generated several publications in the engineering literature, including:

- K. E. G. Magnusson, J. Jaldén, P. M. Gilbert, and H. M. Blau, "Global linking of cell tracks using the Viterbi algorithm," IEEE Transactions on Medical Imaging, Nov. 2014, Accepted for publication, published online.
- K. E. G. Magnusson and J. Jaldén, "A batch algorithm using iterative application of the Viterbi algorithm to track cells and construct cell lineages," in Proc. International Symposium on Biomedical Imaging (ISBI), Apr. 2012. (Received a student best paper award).
- K. E. G. Magnusson and J. Jaldén, "Tracking of non-Brownian particles using the Viterbi algorithm," in Proc. International Symposium on Biomedical Imaging (ISBI), Apr. 2015.

The first two publications outline our dynamic programming algorithm used for track linking through global data association, and the first publication also includes more thorough evaluations on biomedical image data. The last publication outlines the use of the probability hypothesis density filters to capture predictable motion in a sub-cellular particle tracking application. Open access to these publications is secured though KTHs DiVA-database.

We have also actively contributed to a set of international collaborative efforts arranged in the form of challenges where competing teams applied their cell (and particle) tracking methods to common data sets. We also co-authored articles that describe the challenge outcomes and current state of the art in the field, including:

- M. Maška, *et al.*, "A benchmark for comparison of cell tracking algorithms," Bioinformatics, vol. 30, no. 11, pp. 1609–1617, 2014. (open access)
- N. Chenouard, *et al.*, "Objective comparison of particle tracking methods: Results and lessons from the first particle tracking challenge," Nature Methods, vol. 11, no. 3, pp. 281–289, Mar. 2014. (open access)

These publications describe several aspects of our tracking system, including parts such as segmentation and post-processing, and provide thorough comparisons with the current state of the art.

The challenges are perhaps the best illustration of the world-class performance of the methods developed by the PI's team. Citing from the report of the first cell tracking challenge (Maška, 2014): "When we look at the number of appearances of each method among the top three best performing methods, both [the method of the PI's team from KTH, Sweden] and [the method of the team from the German Cancer Research Institute, Heidelberg, Germany] appeared in all eight data sets", and "It is remarkable that [the method of the PI's team from KTH, Sweden] was, at worst, second fastest among the top three best performers in terms of [segmentation] and [tracking]". In the second cell tracking challenge our team scored *highest* in terms of the final rank on *all* 14 datasets included in the challenge, and we were awarded the Bitplane award as one of the top three teams. The final results of the third cell tracking challenge have not yet been released, but we have been notified that we will again receive a Bitplane award as one of the top four teams.

Finally, we are currently working towards the open source release of the software platform that has been developed during the project. The open source release requires some additional documentation, but we have during the ongoing project already made the software available to biomedical collaborators and to some other biology labs that have contacted us directly.

Budget and research resources

Project staff

Describe the staff that will be working in the project and the salary that is applied for in the project budget. Enter the full amount, not in thousands SEK.

Participating researchers that accept an invitation to participate in the application will be displayed automatically under Dedicated time for this project. Note that it will take a few minutes before the information is updated, and that it might be necessary for the project leader to close and reopen the form.

Dedicated time for this project

	Role in the project	Name	Percent of full time
1	Applicant	Joakim Jaldén	20

Salaries including social fees

	Role in the project	Name	Percent of salary	2016	2017	2018	2019	Total
1	Applicant	Joakim Jaldén	20	198,200	204,100	210,200	216,500	829,000
2	PhD Student	Klas Magnusson	50	151,600				151,600
3	PhD Student	Pol del Aguila Pla	80	423,300	472,400	508,000	171,500	1,575,200
4	PhD Student	NN	50			275,700	292,200	567,900
	Total			773,100	676,500	993,900	680,200	3,123,700

Other costs

Describe the other project costs for which you apply from the Swedish Research Council. Enter the full amount, not in thousands SEK.

Premises

	Type of premises	2016	2017	2018	2019	Total
1	Kontor	80,000	70,000	102,000	70,000	322,000
	Total	80,000	70,000	102,000	70,000	322,000

Running Costs

	Running Cost	Description	2016	2017	2018	2019	Total
1	Resor och Traktamenten	Konferensresor	77,000	68,000	99,000	68,000	312,000
2	IT utrustning	Stat. Datorer och Lagring	40,000	20,000	40,000	20,000	120,000
	Total		117,000	88,000	139,000	88,000	432,000

Depreciation costs

Depreciation cost	Description	2016	2017	2018	2019

Total project cost

Below you can see a summary of the costs in your budget, which are the costs that you apply for from the Swedish Research Council. Indirect costs are entered separately into the table.

Under Other costs you can enter which costs, aside from the ones you apply for from the Swedish Research Council, that the project includes. Add the full amounts, not in thousands of SEK.

The subtotal plus indirect costs are the total per year that you apply for.

Total budget

Specified costs	2016	2017	2018	2019	Total, applied	Other costs	Total cost
Salaries including social fees	773,100	676,500	993,900	680,200	3,123,700		3,123,700
Running costs	117,000	88,000	139,000	88,000	432,000		432,000
Depreciation costs					0		0
Premises	80,000	70,000	102,000	70,000	322,000		322,000
Subtotal	970,100	834,500	1,234,900	838,200	3,877,700	0	3,877,700
Indirect costs	289,000	253,000	371,000	254,000	1,167,000		1,167,000
Total project cost	1,259,100	1,087,500	1,605,900	1,092,200	5,044,700	0	5,044,700

Explanation of the proposed budget

Briefly justify each proposed cost in the stated budget.

Explanation of the proposed budget*

The VR budget is intended to cover the salary one PhD student (Pol del Aguila Pla) at 80% activity throughout the project, apart from the final project year (2019) when he is expected to graduate. The budget initially also partially (50%) covers the salary of a senior PhD student (Klas Magnusson) who is expected to graduate during the first project year. Klas will spend time to publish ongoing work on cell tracking, and handover to Pol. They are both employed (doktorandtjänst) by the Department of Signal Processing at KTH. The budget also includes partial (50%) funding for the salary of a third, not yet identified, PhD student, starting in 2018, in order to ensure continuity of the departments' research efforts in the area of cell tracking. All PhD salaries are calculated according to the doctoral salary ladder in use at KTH, and include social costs.

The budget includes funding for the PI (20%), intended to cover his own direct research contributions to the project, as well as the supervision of the PhD students. Salary costs are based on the current salary of the PI including social costs, and assume a 3% annual increase in salary.

Travel costs are calculated as one travel per participant per year, based on the department's budget key. A similar budget has been prepared for the rent. IT costs are intended to cover required laptops and stationary computers, along with additional storage solutions for shared data (primarily hard-drives for biomedical images obtained from labs that we collaborate with).

No funding is sought to fund research at other labs. No other fuding is available for the project during 2016-2019, and the PI has no other current application for the cell-tracking project.

Indirect costs are specified below:

- Summa högskolegemensamma: 23,76%
- Summa skolgemensamma: 6,33%
- Summa avdelningsgemensamma: 7,26%
- Summa indirekta kostnader: 37,4%

Other funding

Describe your other project funding for the project period (applied for or granted) aside from that which you apply for from the Swedish Research Council. Write the whole sum, not thousands of SEK.

Other funding for this project

Funder	Applicant/project leader	Type of grant	Reg no or equiv.	2016	2017	2018	2019

CV

Curriculum Vitae – Joakim Jaldén (born: 1976)

1. Higher education qualifications

- M.Sc. (Civilingenjör) in Electrical Engineering,
  KTH Royal Institute of Technology, Stockholm, Sweden, Sept. 23, 2002

2. Doctoral degree

- Ph.D. in Telecommunications (main supervisor, B. Ottersten),
  KTH Royal Institute of Technology, Stockholm, Sweden, Jan. 11, 2007

3. Postdoctoral positions

- Institute of telecommunications, Vienna University of Technology, Vienna, Austria,
  July 2007 – June 2009
- Signal Processing Lab, School of Electrical Engineering, KTH, Stockholm, Sweden
  Jan. 2007 – June 2007

4. Qualification required for appointment as a docent

- Docent degree in Signal Processing,
  KTH Royal Institute of Technology, Stockholm, Sweden, March 1, 2012

5. Current position

- Associate Professor (Universitetslektor) in Signal Processing,
  Signal Processing Lab, KTH Royal Institute of Technology, Oct. 2012 –
  (Percent research in position is not specified)

6. Previous positions and periods of appointment

- Assistant Professor (bitr. Lektor) in Signal Processing,
  Signal Processing Lab, KTH Royal Institute of Technology,
  July 2009 – Sep. 2012
- Visiting researcher (post-doc level),
  ETH Zürich, Switzerland, Austria,
  Aug. 2008 – Sept. 2008
- Visiting researcher (master thesis work),
  Stanford University, CA, USA,
  Oct. 2001 – Apr. 2002

7. Interruptions in research

- Parental leave, Sept. 2012 – Nov. 2012

8. Supervision (as main advisor / huvudhandledare)

- Klas Magnusson, admitted to Ph.D. studies 2011-02-28 (main advisor since 2012-12-13)
- Alla Tarighati, admitted to Ph.D. studies 2011-12-06 (main advisor since 2013-01-30)
- Pol del Aguila Pla, admitted to Ph.D. studies 2014-08-12
- Marie Maros, admitted to Ph.D. studies 2014-08-12

Note: No Ph.D. students have yet graduated with me as a main advisor, due to a KTH requirement of a docent degree for the main advisor.

9. Other information of relevance for the application

Scientific awards

2012 *Best student paper (as co-author)*, International Symposium on Biomedical Imaging (ISBI), for paper "A batch algorithm using iterative application of the Viterbi algorithm to track cells and construct cell lineages" co-authored with K. E. G. Magnusson.

2011 *NEWCOM++ Distinguished Achievement Award*, for a "particularly relevant scientific results during the network life". NEWCOM++ (Network of Excellence in Wireless Communications) was an FP7 project funded by the European Union (EU) joining 17 academic and industrial partners.

2009 *Ingvar Carlsson Award*, Swedish Foundation for Strategic Research (SSF), given to 12 out of 52 applicants from all natural and technical sciences and included a project grant of 3.000 kSEK over 3 years.

2007 *Best student paper (as first author)*, International conference on Acoustics, Speech and Signal Processing (ICASSP), for paper "Full diversity detection in MIMO systems with a fixed-complexity sphere decoder" co-authored with L. G. Barbero, B. Ottersten, and J. S. Thompson.

2006 *Young Author Best Paper Award*, IEEE Signal Signal Processing Society, for paper "On the complexity of sphere decoding in digital communications" co-autored with B. Ottersten and published in the IEEE Transactions on Signal Processing.

Academic appointments and meritation

- *General chair* for the 16th IEEE International Workshop on Signal Processing Advances in Wireless Communications, SPAWC 2015, July 2015.
- *Invited speaker* at the "Frontiers in Cell Migration" workshop, SciLifeLab, Uppsala University, Dec. 2014
- *Tutorial Organizer and Speaker* at the ICASSP 2014 conference, Florence, Italy. The 3 hour tutorial was entitled "Bits and flops in modern communcation: Analyzing complexity as the missing piece of the wireless-communications puzzle" and held in cooperation with Petros Elia, EURECOM, France.
- *Elected member* of IEEE Signal Processing Society's Signal Processing for Communications and Networking Technical Committee (SPCOM-TC), Jan. 2013 –
- *Associate Editor* for IEEE Transactions on Signal Processing, Jan. 2012 –
- *Associate Editor* for IEEE Communication Letters, Dec. 2009 – Dec. 2011.
- *Reviewer* for most IEEE journals in the area of Signal Processing, Communications and Information Theory as well as most major international conferences in these areas.
- *Tutorial Organizer and Speaker* at the CrownCom 2010 conference, Cannes, France. The 3 hour tutorial was entitled "Performance vs. Algorithmic Complexity in MIMO and Cooperative Communications" and held in cooperation with Petros Elia, EURECOM, France.
- *Area Chair* for the 2011 European Signal Processing Conference (EUSIPCO-2011), Barcelona, Spain.

Total publication output in brief

- 28 journal publications
- 43 international conference papers
- 2 book chapters
- A Google Scholar h-index of 20

Publication list

Joakim Jaldén — Publications

Database for citation count: Google Scholar, per March 29, 2015.

Five most highly cited publications (all years)

[JJ1] Joakim Jaldén and Björn Ottersten, "On the complexity of sphere decoding in digital communications," *IEEE Transactions on Signal Processing*, vol. 53, no. 4, pp. 1474–1484, Apr. 2005. Number of citations: **532**

[JJ2] Dirk Wübben, Dominik Seethaler, Joakim Jaldén, and Gerald Matz, "Lattice reduction: A survey with applications in wireless communications," *IEEE Signal Processing Magazine*, vol. 28, no. 3, pp. 70–91, May 2011. Number of citations: **117**

[JJ3] Marcus Isaksson, Joakim Jaldén, and Martin J. Murphy, "On using an adaptive neural network to predict lung tumor motion during respiration for radiotherapy applications," *Medical Physics*, vol. 32, no. 12, pp. 3801–3809, Dec. 2005. Number of citations: **77**

[JJ4] Joakim Jaldén, Dominik Seethaler, and Gerald Matz, "Worst- and average-case complexity of LLL lattice reduction in MIMO wireless systems," in *Proc. IEEE International Conference on Acoustics, Speech, and Signal Processing (ICASSP)*, Apr. 2008. Number of citations: **74**

[JJ5] Joakim Jaldén and Björn Ottersten, "An exponential lower bound on the expected complexity of sphere decoding," in *Proc. IEEE International Conference on Acoustics, Speech, and Signal Processing (ICASSP)*, May 2004. Number of citations: **74**

1. Peer-reviewed journal articles (since March 2007)

[JJ6] Alla Tarighati and Joakim Jaldén, "Bayesian design of tandem networks for distributed detection with multi-bit sensor decisions," *IEEE Transactions on Signal Processing*, vol. 63, no. 7, pp. 1821–1831, Apr. 2015. Number of citations: **0**

[JJ7] Klas E. G. Magnusson, Joakim Jaldén, Penney M. Gilbert, and Helen M. Blau, "Global linking of cell tracks using the Viterbi algorithm," *IEEE Transactions on Medical Imaging*, Nov. 2014, Accepted for publication, published online. Number of citations: **1**

[JJ8] Efthymios Tsakonas, Joakim Jaldén, Nicholas Sidiropoulos, and Björn Ottersten, "Convergence of the Huber regression M-estimate in the presence of dense outliers," *IEEE Signal Processing Letters*, vol. 21, no. 10, pp. 1211 – 1214, Oct. 2014. Number of citations: **0**

[JJ9] Martin Maška, VladimÌr Ulman, David Svoboda, Pavel Matula, Petr Matula, Cristina Ederra, Ainhoa Urbiola, Tomás España, Subramanian Venkatesan, Deepak M.W. Balak, Tereza Bolcková, Markéta Štreitová, Craig Carthel, Stefano Coraluppi, Nathalie Harder, Karl Rohr, Klas E.G. Magnusson, Joakim Jaldén, Helen M. Blau, Oleh Dzyubachyk, Pavel Křížek, Guy M. Hagen, David Pastor-Escuredo, Daniel Jimenez-Carretero, Maria J. Ledesma-Carbayo, Arrate Muñoz-Barrutia, Erik Meijering, Michal Kozubek, and Carlos Ortiz de Solorzano, "A benchmark for comparison of cell tracking algorithms," *Bioinformatics*, vol. 30, no. 11, pp. 1609–1617, 2014. Number of citations: **15**

[JJ10] Nicolas Chenouard, Ihor Smal, Fabrice de Chaumont, Martin Maška, Ivo F. Sbalzarini, Yuanhao Gong, Janick Cardinale, Craig Carthel, Stefano Coraluppi, Mark Winter, Andrew R. Cohen, William J. Godinez, Karl Rohr abd Yannis Kalaidzidis, Liang Liang, James Duncan, Hongying Shen, Yingke Xu, Klas Magnusson, Joakim Jaldén, Helen M. Blau, Perrine Paul-Gilloteaux, Philippe Roudot, Charles Kervrann, FranÁois Waharte, Jean-Yves Tinevez, Spencer L. Shorte, Joost Willemse, Katherine Celler, Gilles P. van Wezel, Han-Wei Dan, Yuh-Show Tsai, Carlos Ortiz de SolÛrzano, Jean-Christophe Olivo-Marin, and Erik Meijering, "Objective comparison of particle tracking methods:

Results and lessons from the first particle tracking challenge," *Nature Methods*, vol. 11, no. 3, pp. 281–289, Mar. 2014. Number of citations: **43**

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2. Peer-reviewed conference contributions (since March 2007)

[JJ30] Klas E. G. Magnusson and Joakim Jaldén, "Tracking of non-Brownian particles using the Viterbi algorithm," in *Proc. International Symposium on Biomedical Imaging (ISBI)*, Apr. 2015. Number of citations: **0**

[JJ31] Alla Tarighati and Joakim Jaldén, "A general method for the design of tree networks under communication constraints," in *Proc. IEEE International Conference on Information Fusion*, 2014. Number of citations: **0**

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[JJ33] Alla Tarighati and Joakim Jaldén, "Bayesian design of decentralized hypothesis testing under communication constraints," in *Proc. IEEE International Conference on Acoustics, Speech, and Signal Processing (ICASSP)*, May 2014. Number of citations: **2**

[JJ34] Joakim Jaldén and Tobias Oechtering, "Distributed Bayesian detection for the butterfly network," in *Proc. IEEE Workshop on Signal Processing Advances in Wireless Communications (SPAWC)*, 2013. Number of citations: **1**

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[JJ43] John Flåm, Joakim Jaldén, and Saikat Chatterjee, "Gaussian mixture modeling for source localization," in *Proc. IEEE International Conference on Acoustics, Speech, and Signal Processing (ICASSP)*, May 2011. Number of citations: **5**

[JJ44] Siamak Yousefi and Joakim Jaldén, "On the predictability of phase noise modeled as flicker FM plus white FM," in *Proc. Asilomar Conference on Signals, Systems & Computers*, Nov. 2010. Number of citations: **1**

[JJ45] Petros Elia and Joakim Jaldén, "Fundamental rate-reliability-complexity limits in outage limited MIMO communications," in *Proc. IEEE International Symposium on Information Theory (ISIT)*, June 2010. Number of citations: **0**

[JJ46] Joakim Jaldén, Peter Fertl, and Gerald Matz, "On the generalized mutual information of BICM systems with approximate demodulation," in *Proc. IEEE Information Theory Workshop (ITW)*, Jan. 2010. Number of citations: **20**

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[JJ49] Dominik Seethaler, Joakim Jaldén, Christoph Studer, and Helmut Bölcskei, "Tail behavior of sphere-decoding complexity in random lattices," in *Proc. IEEE International Symposium on Information Theory (ISIT)*, June 2009. Number of citations: **10**

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[JJ51] Johannes Maurer, Joakim Jaldén, and Gerald Matz, "Multi-threshold TOP — full-diversity vector perturbation precoding with finite-rate feedforward," in *Proc. Asilomar Conference on Signals, Systems & Computers*, Oct. 2008. Number of citations: **9**

[JJ52] Petros Elia and Joakim Jaldén, "Construction criteria and existence results for approximately universal linear space-time codes with reduced decoding complexity," in *Proc. Allerton Conference on Communication, Control, and Computing*, Sept. 2008. Number of citations: **3**

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[JJ54] Peter Fertl, Joakim Jaldén, and Gerald Matz, "Capacity-based performance comparison of MIMO-BICM demodulators," in *Proc. IEEE Workshop on Signal Processing Advances in Wireless Communications (SPAWC)*, July 2008. Number of citations: **30**

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[JJ56] Joakim Jaldén, Johannes Maurer, and Gerald Matz, "On the diversity order of vector perturbation precoding with imperfect channel state information," in *Proc. IEEE Workshop on Signal Processing Advances in Wireless Communications (SPAWC)*, July 2008. Number of citations: **10**

[JJ57] David Wisell, Joakim Jaldén, and Peter Händel, "Behavioral power amplifier modeling using the LASSO," in *Proc. IEEE International Instrumentation & Measurement Technology Conference (I2MTC)*, May 2008. Number of citations: **7**

[JJ58] Wing-Kin Ma, Chao-Cheng Su, Joakim Jaldén, and Chong-Yung Chi, "Some results on 16-QAM MIMO detection using semidefinite relaxation," in *Proc. IEEE International Conference on Acoustics, Speech, and Signal Processing (ICASSP)*, Apr. 2008. Number of citations: **16**

[JJ59] Joakim Jaldén and Gerald Matz, "MIMO receiver diversity in general fading," in *Proc. IEEE International Conference on Acoustics, Speech, and Signal Processing (ICASSP)*, Apr. 2008. Number of citations: **11**

[JJ60] Joakim Jaldén, Dominik Seethaler, and Gerald Matz, "Worst- and average-case complexity of LLL lattice reduction in MIMO wireless systems," in *Proc. IEEE International Conference on Acoustics, Speech, and Signal Processing (ICASSP)*, Apr. 2008. Number of citations: **74**

[JJ61] Erik G. Larsson and Joakim Jaldén, "Soft MIMO detection at fixed complexity," in *Proc. of IEEE Global Telecommunications Conference (GLOBECOM)*, Nov. 2007. Number of citations: **2**

[JJ62] Joakim Jaldén, Luis G. Barbero, Björn Ottersten, and John S. Thompson, "Full diversity detection in MIMO systems with a fixed-complexity sphere decoder," in *Proc. IEEE International Conference on Acoustics, Speech, and Signal Processing (ICASSP)*, Apr. 2007. Number of citations: **45**

3. Monographs (since March 2007)

None

4. Research review articles (since March 2007)

[JJ63] Dirk Wübben, Dominik Seethaler, Joakim Jaldén, and Gerald Matz, "Lattice reduction: A survey with applications in wireless communications," *IEEE Signal Processing Magazine*, vol. 28, no. 3, pp. 70–91, May 2011. Number of citations: **117**

5. Books and book chapters (since March 2007)

[JJ64] Charlotte Dumard, Joakim Jaldén, and Thomas Zemen, "Multi-user MIMO receiver processing for time-varying channels," in *Wireless Communications Over Rapidly Time-Varying Channels*, Franz Hlawatsch and Gerald Matz, Eds. Elsevier: Academic Press, Mar. 2011. Number of citations: **0**

[JJ65] Joakim Jaldén and Björn Ottersten, "Detection based on relaxation in MIMO systems," in *Handbook on Advancements in Smart Antenna Technologies for Wireless Networks*, Chen Sun, Jun Cheng, and Takashi Ohira, Eds. IGI Publishing Company: Premier Reference Source, 2008. Number of citations: **0**

6. Patents (since March 2007)

[JJ66] Erik G. Larsson and Joakim Jaldén, "Method and arrangement relating to telecommunications," U.S. Patent no. 8,369,461 (granted on Feb. 5, 2013). Number of citations: **0**

7. Open access computer programs or data bases (since March 2007)

None

8. Popular science articles/presentations (since March 2007)

None

CV

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Research education

Dissertation title (swe)
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Dissertation title (en)
Detection for Multiple Input Multiple Output Channels

Organisation	Unit	Supervisor
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Subject doctors degree	ISSN/ISBN-number	Date doctoral exam
20204. Telekommunikation	1653-5146/91-7178-519-1	2007-01-11

Publications

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Jaldén, Joakim has not added any publications to the application.

Register

Terms and conditions

The application must be signed by the applicant as well as the authorised representative of the administrating organisation. The representative is normally the department head of the institution where the research is to be conducted, but may in some instances be e.g. the vice-chancellor. This is specified in the call for proposals.

The signature *from the applicant* confirms that:

- the information in the application is correct and according to the instructions form the Swedish Research Council
- any additional professional activities or commercial ties have been reported to the administrating organisation, and that no conflicts have arisen that would conflict with good research practice
- that the necessary permits and approvals are in place at the start of the project e.g. regarding ethical review.

The signature *from the administrating organisation* confirms that:

- the research, employment and equipment indicated will be accommodated in the institution during the time, and to the extent, described in the application
- the institution approves the cost-estimate in the application
- the research is conducted according to Swedish legislation.

The above-mentioned points must have been discussed between the parties before the representative of the administrating organisation approves and signs the application.

Project out lines are not signed by the administrating organisation. The administrating organisation only sign the application if the project outline is accepted for step two.

Applications with an organisation as applicant is automatically signed when the application is registered.