IN PARTNERSHIP WITH:
CNRS

Université Nice - Sophia Antipolis

Activity Report 2019

Project-Team MORPHEME

Morphologie et Images

IN COLLABORATION WITH: Institut de Biologie de Valrose, Laboratoire informatique, signaux systèmes de Sophia Antipolis (I3S)

RESEARCH CENTER
Sophia Antipolis - Méditerranée

THEME
Computational Biology

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Project-Team MORPHEME

Creation of the Team: 2011 September 01, updated into Project-Team: 2013 July 01

Keywords:

Computer Science and Digital Science:

A3.4. - Machine learning and statistics
A3.4.1. - Supervised learning
A3.4.2. - Unsupervised learning
A3.4.4. - Optimization and learning
A3.4.6. - Neural networks
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A3.4.8. - Deep learning
A5.3. - Image processing and analysis
A5.3.2. - Sparse modeling and image representation
A5.3.4. - Registration
A5.4.1. - Object recognition
A5.4.3. - Content retrieval
A5.4.4. - 3D and spatio-temporal reconstruction
A5.4.5. - Object tracking and motion analysis
A5.4.6. - Object localization
A5.9. - Signal processing
A5.9.3. - Reconstruction, enhancement
A5.9.5. - Sparsity-aware processing
A5.9.6. - Optimization tools
A6.1. - Methods in mathematical modeling
A6.1.1. - Continuous Modeling (PDE, ODE)
A6.1.2. - Stochastic Modeling
A6.3.1. - Inverse problems

Other Research Topics and Application Domains:

B1.1. - Biology
B1.1.3. - Developmental biology
B2.6. - Biological and medical imaging

1. Team, Visitors, External Collaborators

Research Scientists

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Xavier Descombes [Team leader, Inria, Senior Researcher, HDR]
Grégoire Malandain [Inria, Senior Researcher, HDR]
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Sarah Laroui [Bayer (cifre)]
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Technical staff
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Interns and Apprentices
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Ghosh Avrajit [CNRS, from May 2019 until Jul 2019]
Deborah Cottais [CNRS, from Mar 2019 until Aug 2019]
Cédric Dubois [Univ Côte d'Azur, from Mar 2019 until Sep 2019]
Angie Moullet [Inria, from Dec 2019 until May 2020]
Paul Emmanuel Ponsenard [Inria, from Jun 2019 until Sep 2019]
Zhankeng Zhang [Inria, from Apr 2019 until Sep 2019]

Visiting Scientists
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External Collaborators
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Sébastien Schaub [CNRS]

2. Overall Objectives

2.1. Overall Objectives

Morpheme is a joint project between Inria, CNRS and the University of Nice-Sophia Antipolis, involving the Computer Science, Signals and Systems Laboratory (I3S) (UMR 6070) and the Institute for Biology of Valrose (iBV) (CNRS/INSERM).

The scientific objectives of MORPHEME are to characterize and model the development and the morphological properties of biological structures from the cell to the supra-cellular scale. Being at the interface between computational science and biology, we plan to understand the morphological changes that occur during development combining in vivo imaging, image processing and computational modeling.

The morphology and topology of mesoscopic structures, indeed, do have a key influence on the functional behavior of organs. Our goal is to characterize different populations or development conditions based on the shape of cellular and supra-cellular structures, including micro-vascular networks and dendrite/axon networks. Using microscopy or tomography images, we plan to extract quantitative parameters to characterize morphometry over time and in different samples. We will then statistically analyze shapes and complex structures to identify relevant markers and define classification tools. Finally, we will propose models explaining the temporal evolution of the observed samples. With this, we hope to better understand the development of normal tissues, but also characterize at the supra-cellular level different pathologies such as the Fragile X Syndrome, Alzheimer or diabetes.

3. Research Program

3.1. Research program

The recent advent of an increasing number of new microscopy techniques giving access to high throughput screenings and micro or nano-metric resolutions provides a means for quantitative imaging of biological structures and phenomena. To conduct quantitative biological studies based on these new data, it is necessary to develop non-standard specific tools. This requires using a multi-disciplinary approach. We need biologists to define experiment protocols and interpret the results, but also physicists to model the sensors, computer scientists to develop algorithms and mathematicians to model the resulting information. These different expertises are combined within the Morpheme team. This generates a fecund frame for exchanging expertise, knowledge, leading to an optimal framework for the different tasks (imaging, image analysis, classification, modeling). We thus aim at providing adapted and robust tools required to describe, explain and model fundamental phenomena underlying the morphogenesis of cellular and supra-cellular biological structures. Combining experimental manipulations, in vivo imaging, image processing and computational modeling, we plan to provide methods for the quantitative analysis of the morphological changes that occur during development. This is of key importance as the morphology and topology of mesoscopic structures govern organ and cell function. Alterations in the genetic programs underlying cellular morphogenesis have been linked to a range of pathologies.
Biological questions we will focus on include:

1. what are the parameters and the factors controlling the establishment of ramified structures? (Are they really organize to ensure maximal coverage? How are genetic and physical constraints limiting their morphology?),
2. how are newly generated cells incorporated into reorganizing tissues during development? (is the relative position of cells governed by the lineage they belong to?)

Our goal is to characterize different populations or development conditions based on the shape of cellular and supra-cellular structures, e.g. micro-vascular networks, dendrite/axon networks, tissues from 2D, 2D+t, 3D or 3D+t images (obtained with confocal microscopy, video-microscopy, photon-microscopy or micro-tomography). We plan to extract shapes or quantitative parameters to characterize the morphometric properties of different samples. On the one hand, we will propose numerical and biological models explaining the temporal evolution of the sample, and on the other hand, we will statistically analyze shapes and complex structures to identify relevant markers for classification purposes. This should contribute to a better understanding of the development of normal tissues but also to a characterization at the supra-cellular scale of different pathologies such as Alzheimer, cancer, diabetes, or the Fragile X Syndrome. In this multidisciplinary context, several challenges have to be faced. The expertise of biologists concerning sample generation, as well as optimization of experimental protocols and imaging conditions, is of course crucial. However, the imaging protocols optimized for a qualitative analysis may be sub-optimal for quantitative biology. Second, sample imaging is only a first step, as we need to extract quantitative information. Achieving quantitative imaging remains an open issue in biology, and requires close interactions between biologists, computer scientists and applied mathematicians. On the one hand, experimental and imaging protocols should integrate constraints from the downstream computer-assisted analysis, yielding to a trade-off between qualitative optimized and quantitative optimized protocols. On the other hand, computer analysis should integrate constraints specific to the biological problem, from acquisition to quantitative information extraction. There is therefore a need of specificity for embedding precise biological information for a given task. Besides, a level of generality is also desirable for addressing data from different teams acquired with different protocols and/or sensors. The mathematical modeling of the physics of the acquisition system will yield higher performance reconstruction/restoration algorithms in terms of accuracy. Therefore, physicists and computer scientists have to work together. Quantitative information extraction also has to deal with both the complexity of the structures of interest (e.g., very dense network, small structure detection in a volume, multiscale behavior, ...) and the unavoidable defects of in vivo imaging (artifacts, missing data, ...). Incorporating biological expertise in model-based segmentation methods provides the required specificity while robustness gained from a methodological analysis increases

the generality. Finally, beyond image processing, we aim at quantifying and then statistically analyzing shapes and complex structures (e.g., neuronal or vascular networks), static or in evolution, taking into account variability. In this context, learning methods will be developed for determining (dis)similarity measures between two samples or for determining directly a classification rule using discriminative models, generative models, or hybrid models. Besides, some metrics for comparing, classifying and characterizing objects under study are necessary. We will construct such metrics for biological structures such as neuronal or vascular networks. Attention will be paid to computational cost and scalability of the developed algorithms: biological experimentations generally yield huge data sets resulting from high throughput screenings. The research of Morpheme will be developed along the following axes:

- **Imaging:** this includes i) definition of the studied populations (experimental conditions) and preparation of samples, ii) definition of relevant quantitative characteristics and optimized acquisition protocol (staining, imaging, ...) for the specific biological question, and iii) reconstruction/restoration of native data to improve the image readability and interpretation.
- **Feature extraction:** this consists in detecting and delineating the biological structures of interest from images. Embedding biological properties in the algorithms and models is a key issue. Two main challenges are the variability, both in shape and scale, of biological structures and the huge size of data sets. Following features along time will allow to address morphogenesis and structure development.
- **Classification/Interpretation:** considering a database of images containing different populations, we can infer the parameters associated with a given model on each dataset from which the biological structure under study has been extracted. We plan to define classification schemes for characterizing the different populations based either on the model parameters, or on some specific metric between the extracted structures.
- **Modeling:** two aspects will be considered. This first one consists in modeling biological phenomena such as axon growing or network topology in different contexts. One main advantage of our team is the possibility to use the image information for calibrating and/or validating the biological models. Calibration induces parameter inference as a main challenge. The second aspect consists in using a prior based on biological properties for extracting relevant information from images. Here again, combining biology and computer science expertise is a key point.

4. Highlights of the Year

4.1. Highlights of the Year

Luca Calatroni get a CNRS position as scientist and joined the team in october 2019.

5. New Software and Platforms

5.1. Obj.MPP

KEYWORDS: Object detection - Marked Point Process - Parametric model

FUNCTIONAL DESCRIPTION: Obj.MPP implements the detection of parametric objects using a Marked Point Process (MPP). A parametric object is an n-dimensional piece of signal defined by a finite set of parameters. Detecting an object in a signal amounts to finding a position at which the signal can be described well enough by a specific set of parameters (unknowns of the detection problem). The detection task amounts to finding all such objects. Typically, the signal is a 2-dimensional grayscale image and the parametric objects are bright disks on a dark background. In this case, each object is defined by a single parameter: the disk radius. Note however that the core function of Obj.MPP is not tied to a particular context (2-dimensional imaging is just an example).

- Author: Eric Debreuve
- Contact: Eric Debreuve
- Publications: Stochastic geometry for image analysis - Multiple objects detection in biological images using a marked point process framework - An efficient optimizer for simple point process models - Multiple Birth and Cut Algorithm for Multiple Object Detection
- URL: https://team.inria.fr/morpheme/obj-mpp-object-detection-using-a-marked-point-process/

5.2. ATOLS

Adaptative Threshold Operator based on Level Sets

KEYWORDS: Object detection - Level Set

FUNCTIONAL DESCRIPTION: Atols is a Python script allowing to detect features on images using a contrast scoring. Thus, it's possible to detect features at different levels of intensity unlike a simple threshold which would only keep features above its value.

- Authors: Kevin Giulietti and Guillaume Lavisse
- Contact: Xavier Descombes
- URL: https://team.inria.fr/morpheme/software/

5.3. Small particle detection

KEYWORDS: Image processing - Image segmentation - Object detection - Computational biology - Fluorescence microscopy - Biomedical imaging

FUNCTIONAL DESCRIPTION: An algorithm primarily design to detect objects whose sizes aren't larger a few pixels (particles) on fluorescence microscopy images.

It is an simplified version of marked point process.

- Contact: Nicolas Cedilnik
- Publications: SPADE: A Small Particle Detection Method Using A Dictionary Of Shapes Within The Marked Point Process Framework - SPADE: A Small Particle Detection Method Using A Dictionary Of Shapes Within The Marked Point Process Framework
- URL: https://gitlab.inria.fr/ncedilni/spade

6. New Results

6.1. Exact biconvex reformulation of the $\ell_2 - \ell_0$ minimization problem

Participants: Gilles Aubert, Arne Henrik Bechensteen, Laure Blanc-Féraud.

We focus on the problem of minimizing the least-squares loss function under the constraint that the reconstructed signal is at maximum k-sparse. This is called the ℓ_2-ℓ_0 constrained problem. The ℓ_0 pseudo-norm counts the number of non-zero elements in a vector. The minimization problem is of interest in signal processing, with a wide range of applications as compressed sensing, source separation, and super-resolution imaging, for example.

Based on the results of [31], we reformulate the ℓ_0 pseudo-norm exactly as a convex minimization problem by introducing an auxiliary variable. We then propose an exact biconvex reformulation of the $\ell_2 - \ell_0$ constrained and penalized problems. We give correspondence results between minimizer of the initial function and the reformulated ones. The reformulation is biconvex. This property is used to derive two minimization algorithm, CoBic (Constrained Biconvex) and PeBic (Penalized Biconvex).

We apply the algorithms to the problem of Single-Molecule Localization Microscopy and compare the results with the well-known IHT algorithm [22]. Both visually and numerically the biconvex reformulations perform better. Furthermore, the algorithm has been compared to the IRL1-CEL0 [23] and Deep-STORM [25]. The IRL1-CEL0 minimizes an exact relaxation [29] of the $\ell_2 - \ell_0$ penalized form and Deep-STORM is an algorithm that uses deep-learning and convolutional network to localize the molecules. This work has been presented at the ISBI 2019 conference [6], as well as a more mathematical article was presented as a poster at GRETSI 2019 [12]. A full journal article has been submitted to the Biomedical Optics Express for a feature issue: Superresolution Microscopy on the 25th Anniversary of STED Microscopy and the 20th Anniversary of SIM.

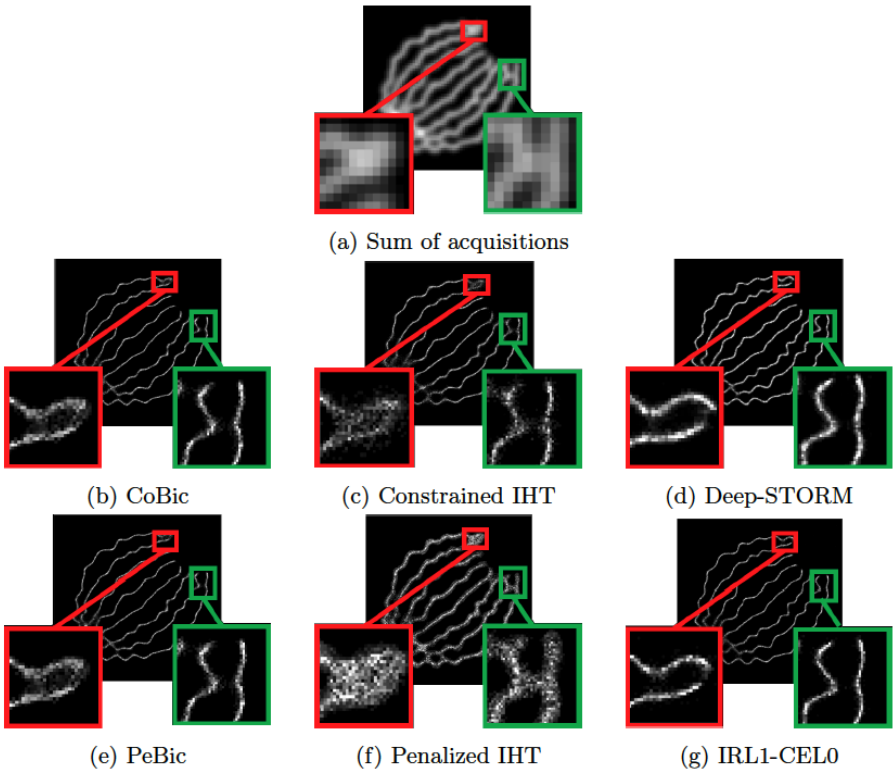

Figure 1. Reconstructed images from the simulated ISBI dataset [28], 99 non-zero pixels on average. Top: Sum of the acquisitions. Middle: From left to right: CoBic, Constrained IHT and Deep-STROM. Bottom: From left to right: PeBic, Penalized IHT and IRL1-CEL0.

6.2. Biological Image Super-resolution Enhanced with Tensor

Participants: Jose Henrique de Morais Goulart, Laure Blanc-Féraud, Eric Debreuve, Sébastien Schaub.

This work is part of the BISET project, funded by the académie 1 RISE (Réseaux, Information et Société numErique) of Idex UCA JEDI.

Fluorescence microscopy imaging has numerous applications in biological sciences, but has limited resolution due to light diffraction. Recently proposed super-resolution techniques acquire an image time series at a high frame rate and exploit independent random fluorophore blinking for reconstruction. This approach holds great potential for observing live-cell sub-cellular phenomena, which is a challenging scenario with strict constraints over the deployed excitation levels and the acquisition time.

The BISET project aimed to develop tensor-based super-resolution fluorescence microscopy algorithms based on this approach. Assuming a known separable PSF $h(x, y) = g(x)g(y)$, a third-order tensor model with two spatial diversities and one temporal diversity was proposed. The model unknowns are high-dimensional fluorophore spatial profiles along x and y directions and temporal fluorophore profiles modeling blinking. Our formulation employs a least-squares loss term and penalty functions promoting spatial profile sparsity (necessary for fluorophore locality) and temporal profile group sparsity (which controls the number of fluorophores).

The formulation is nonconvex but block-convex in the unknown profiles and thus can be solved by alternating minimization. It has a significantly smaller number of unknowns in comparison with a matrix-based convex one (with frames as columns), in consonance with the current trend of employing nonconvex formulations rather than overparameterized convex ones which are often too costly. However, its resolution is numerically challenging for high-density acquisitions. Indeed, even though the proposed algorithm is able to reveal the overall target structure in our simulations, it produces a "dotted" reconstruction. For comparison, we developed a matrix-based formulation with nonconvex group-sparsity regularization, which is more costly to solve but achieves better results. These findings were published in the IEEE CAMSAP 2019 conference [11], and were also presented on October 2019 in a GdR ISIS (Information, Signal, Image et Vision)/MIA (Mathématiques de l'Imagerie et de ses Applications)/ONDES meeting [1] held in Paris and entitled "Co-conception: hybrid sensors and algorithms for innovative systems". An illustration of the results produced by the developed tensor and matrix methods is given in Figure 2, along with outcomes of other state-of-art methods. In conclusion, though our tensor approach is innovative and was shown to be promising, further research is needed to overcome the model estimation difficulties.

6.3. Classification and Modeling of the Fibronectin Networks in Extracellular Matrices

Participants: Anca-Ioana Grapa, Laure Blanc-Féraud, Xavier Descombes.

This work is done in collaboration with Ellen Van Obberghen-Schilling and Georgios Efthymiou (iBV).

We are interested in the numerical analysis and modeling of the Fibronectin (FN) networks, a major extracellular matrix (ECM) molecule, expressed in pathological states (fibrosis, cancer, etc). Our goal is to develop numerical quantitative biomarkers that describe the geometrical organization of the different four variants of the FN fiber networks, from 2D confocal microscopy images. Since the functions of these variants are not well defined in the context of their role within the tumour microenvironment, we hope that a computational model might be able to provide a meaningful description that incorporates the structural differences among the variants.

In a previous work, we have derived a pipeline to classify a given tissue among the four FN variants (cell-derived matrices), based on a decomposition into discrete fast curvelet transform coefficients. We ensured the invariance to rotation of the coefficients and then fed them to a DAG-SVM multiclassifier, in order to prove their discriminative ability in the context of classification of the four FN variants. The results were published in [24] and show that the curvelet coefficients are capable of discerning among the four FN variants with similar performances to those of a human annotator.

[1] Meeting webpage: `http://www.gdr-isis.fr/index.php?page=reunion&idreunion=401`.

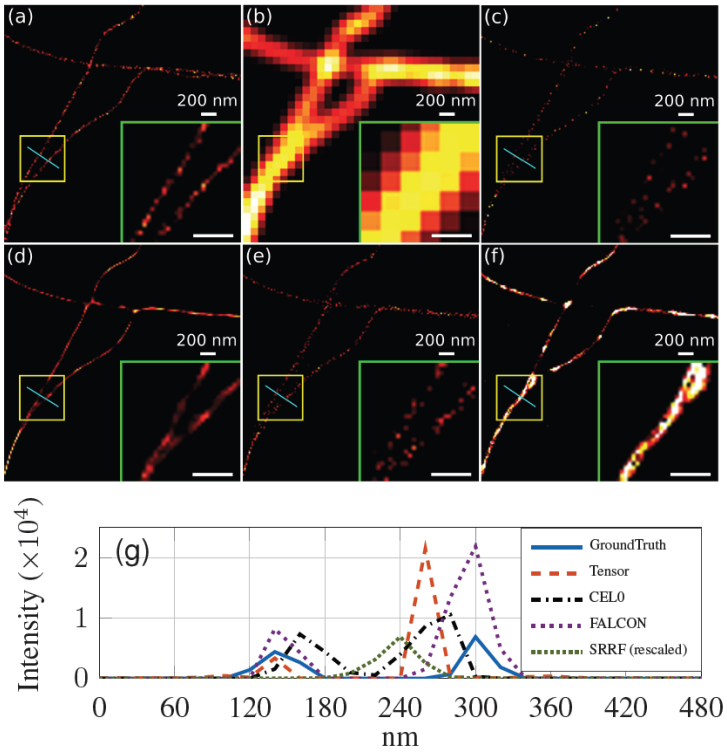

Figure 2. Results for reconstruction of simulated microtubules: (a) integrated ground truth; (b) integrated observed stack (5× zoom); (c) proposed tensor approach; (d) proposed matrix approach; (e) FALCON; (f) SRRF; (g) intensity profiles along the shown blue line. The frame in the bottom right corner shows a $2.66\times$ *zoom of the smaller yellow frame.*

The second step of our work consisted in setting up the modeling of the FN networks starting from a graph-based representation, built on top of Gabor features (fiber scale, orientation, etc). The graph parameters corresponding to the geometrical and topological features of the improved skeletonizations (i.e. median pore circularity, ratio of fiber thinness, fiber thickness kurtosis, fiber connectivity) of the four FN variants, are then classified by a DAG-SVM. It is thus shown through the analysis of the feature distribution over the four variants, features PCA analysis and SVM-based classification, that graph features can discriminate among the FN variants almost as well as our first work. This proves that the graph representation embeds the most relevant information provided by the image.

The next step focused on the development of a metric between graphs that takes into account their topology and geometry. This distance is bound to provide a quantitative but also a qualitative comparison of the four FN variants as well as a differentiation between normal and tumour-like FN fibers. In order to evaluate the distance among graphs, we have referred to graph-matching techniques, which are considered standard problems that deal with graph comparison. The main idea is to obtain an evaluation of the similarity between two graphs, by finding the optimal correspondence between their nodes, such as to align their structure, i.e their adjacency matrices. We expect to obtain invariance with respect to translation, rotation and scale.

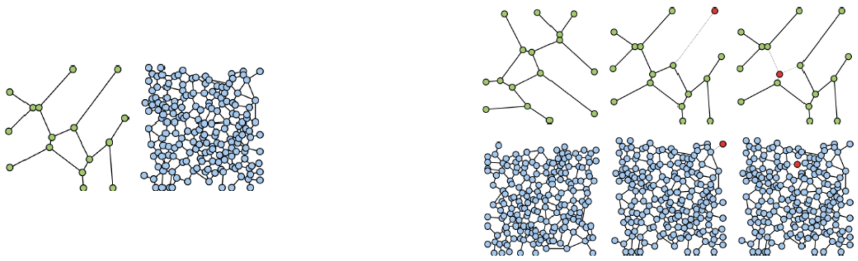

Figure 3. Generated toy-graphs with different dimensions: $16, 181$ *nodes (left side). Right side illustrates the database of toy-graphs derived from the initial ones, but having small modifications in terms of node order (first column) and different number of nodes (second and third column). The purpose is to match the nodes of every pair of graph (initial-modified) using the graph-matching and optimal assignment framework and compare the performances of the two methods.*

More specifically, we are interested in one of the various techniques to perform many-to-many graph matching [32], where the merging of multiple nodes to match another one is allowed, especially in the case of graphs with different dimensions (i.e. different number of total vertices). Alternatively, we considered a different line of work, based on optimal transport for the comparison of structured objects (e.g. graphs) with associated probability distributions. We focus on the work of Peyré et al. [26] that have considered a metric called Gromov-Wasserstein, capable of comparing objects that lie in spaces with different dimensions, by minimizing the cost of mass transport from one discrete distribution to the other. In the context of graph matching techniques, this can be regarded as a probabilistic assignment problem.

In [13], we have compared the two aforementioned approaches from a graph-matching perspective, on randomly generated graphs (Figure 3), in the context of a preliminary study for the future modeling of FN graph-based representations. We have tested different graph scenarios, with various information captured by the adjacency matrix (binary adjacency matrix, shortest path between nodes). Moreover, we have slightly modified the second method by optimal transport, to make it feasible for direct one-to-one matching, by adding dummy masses. We have concluded that the graph matching by many-to-many assignment, captures a meaningful distance between two given graphs with good performances, while the Gromov-Wasserstein discrepancy is computed faster but with lower performances.

One advantage of using graph-matching techniques for comparing fiber networks, comes from the possibility of defining a median graph that will be representative of a FN class. Currently, we are developing methodologies for deriving the representative graph for FN variants, using the metric provided by the many-to-many graph assignment problem. The challenges range from deciding a good technique to perform a meaningful matching among the graphs, to determining the adjacency of the median graph and the corresponding physical localization of the nodes.

A second advantage is given by the possibility of computing various deformation maps between FN fiber networks: the matching serves as a registration between the graphs, and once after having obtained an assignment between the corresponding graph edges, we can compute the differences in terms of fiber length, orientation, etc (see Figure 4 for a example of a deformation map in terms of fiber length - which can be regarded as a local stretching of the fibers that should be applied to first graph in order to obtain the second one)).

The deformation maps can subsequently be analyzed in a test hypothesis framework that decides whether the variation of a certain parameter (e.g. length) is due to the the variance within the same class or not.

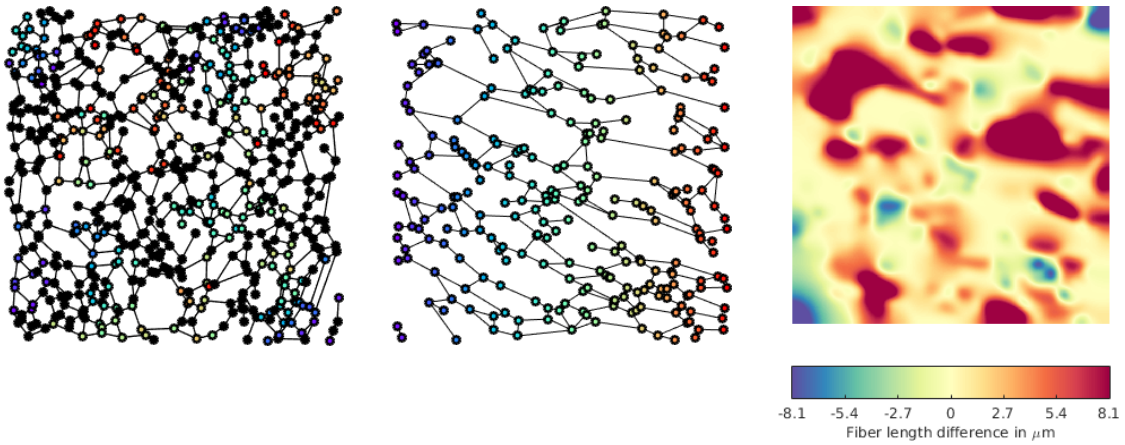

Figure 4. From left to right: graph network FN A+; graph network FN A+ ("tumour-like"); Deformation map between FN A+ and FN A+ (tumour-like)

Once we have derived a meaningful median graph based on graph-matching distances, we might be able to perform classification of the graph networks. Additionally, the fiber properties statistics inferred from the graph local properties, as well as Gabor filters parameters, can be of use to interpret the local differences within a specific class and among FN variants.

Anca Grapa's work is supported by the French Government (National Research Agency, ANR) through the "Investments for the Future" LABEX SIGNALIFE: program reference ANR-11-LABX-0028-01.

6.4. Classification of the Fibronectin Networks in Extracellular Matrices using CNN and DAG-SVM of confocal and coverslip scanner images

Participants: Ghosh Avrajit, Anca-Ioana Grapa, Laure Blanc-Féraud, Xavier Descombes.

This work is done in collaboration with Ellen Van Obberghen-Schilling and Georgios Efthymiou (iBV).

We are interested in the numerical analysis and modeling of the Fibronectin (FN) networks, a major extracellular matrix (ECM) molecule, expressed in pathological states (fibrosis, cancer, etc).

Firstly, during one experiment, confocal images 3128×3128 pixels with a lateral resolution of 0.27μm/pixel were acquired with a Zeiss LSM710 confocal system $10X/0.45$ with the pinhole diameter set to its maximal value. Subsequently, images of FN variants in a different experiment were acquired using a coverslip scanner (Vectra Polaris Automated Quantitative Pathology Imaging System) based on fluorescence whole-slide scanning on a similar resolution to that of the confocal system.

For each of the experiments, 70 images (for every FN variant) corresponding to a representative region of 512×512 pixels were selected for feature extraction and classification.The set of 280 gray-scale images was classified with a DAG-SVM classifier using curvelet features using the parametrization from [24]. Additionally, it was classified with the GoogLeNet [30] pretrained Convolutional Neural Net (CNN) architecture using the MATLAB Deep Learning Toolbox and a 22-layer deep network trained on more than 1 million images for classification into 1000 object categories. A set of 196 images was used for the training of the algorithm, and the remaining 84 for testing it. The training image set was presented to the algorithm 25 times (epochs), in order to improve classification accuracy.

The results (Figures 5, 7, 6, and 8) show that the information in the FN images is relevant enough in a CNN-based classification to distinguish FN variants better than curvelet-based features. Additionally, the coverslip scanner acquired samples are classified with a higher accuracy, underlining the potential benefit of using the scanner for future experiments.

Actual / Predicted	FN B-A+	FN B-A-	FN B+A-	FN B+A+
FN B-A+	85.7	0	28.5	14.3
FN B-A-	0	80.9	14.3	4.8
FN B+A-	0	9.5	90.5	0
FN B+A+	9.5	14.3	0	76.2

Figure 5. Confusion matrix in percentage form of the CNN classification of FN variant confocal images. General mean accuracy of classification is 83.3%.

Actual/ Predicted	FN B-A+	FN B-A-	FB B+A-	FN B+A+
FN B-A+	64.3	2.9	25.7	7.1
FN B-A-	0	90	0	10
FN B+A-	25.7	4.3	45.7	24.3
FN B+A+	0	15.7	8.6	75.7

Figure 6. Confusion matrix in percentage form of the DAG-SVM classification of FN variants, using curvelets features. General mean accuracy of classification is 68.9%.

6.5. Tumor cell tracking for automatic detection of cell death time, and classification of its type

Participants: Deborah Cottais, Eric Debreuve.

This work was made in collaboration with Jérémie Roux (IRCAN, Nice, France).

Actual/ Predicted	FN B-A+	FN B-A-	FB B+A-	FN B+A+
FN B-A+	95.2	0	0	4.7
FN B-A-	0	100	0	0
FN B+A-	0	4.7	62	33
FN B+A+	0	0	0	100

Figure 7. Confusion matrix in percentage form of the CNN classification of FN variant coverslip scanner images. General mean accuracy of classification is 89.3%.

Actual/ Predicted	FN B-A+	FN B-A-	FB B+A-	FN B+A+
FN B-A+	72.8	0	0	27.1
FN B-A-	0	85.7	8.5	5.7
FN B+A-	0	10	65.7	24.2
FN B+A+	15.7	0	11.43	72.8

Figure 8. Confusion matrix in percentage form of the DAG-SVM classification of FN variant coverslip scanner images (curvelet features).General mean accuracy of classification is 74.2%.

The available data were multi-channel videos acquired in fluorescence microscopy. We first performed cell segmentation on the channel in which the geometrical information was predominant. Then we performed tracking of the segmented cells. More precisely, we refer to tracking as the construction of cell trajectories along the video (see Fig. 9). By *transferring* this cell tracking onto the channel in which the radiometric information of the cells is the richest (mean intensity, variance, texture), we were able to extract characteristics for each cell, and study their temporal evolution to deduce the moment of cell death. Next, we are planning to develop a method of classification of the cell deaths into predefined types.

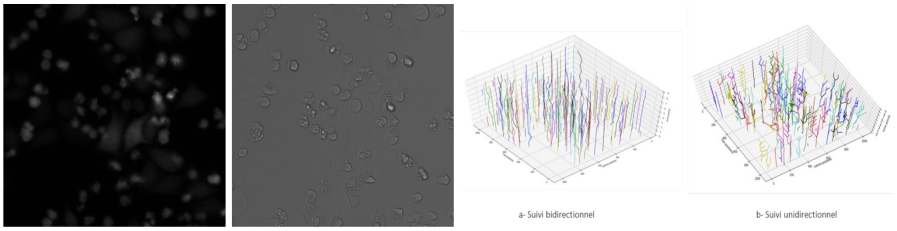

Figure 9. From left to right: two channels of a video frame and tracking trajectories of the segmented cells.

6.6. Cytoplasm segmentation from cells confocal microscopy images

Participants: Somia Rahmoun, Eric Debreuve, Xavier Descombes, Fabienne de Graeve.

As part of the ANR project RNAGRIMP, two series of images have been acquired using fluorescence microscopy: one where the cell cytoplasm has been stained with GFP (Green Fluorescent Protein), the second where the nuclei have been stained with DAPI (4',6-diamidino-2-phenylindole). The first steps are detecting the nuclei on the DAPI images and learning a classification procedure into living cell or dead cell based on morphological and radiometric nuclei properties (average intensity, area, granularity, circularity, ...).

The next step is to segment (i.e., extract automatically the region of) the cell cytoplasms on the GFP images. Indeed, the target RNP-IMP granules appear in that compartment of the cell and are visible through their GFP response. This segmentation problem is particularly difficult due the heterogeneity of the cells intensity. This heterogeneity even appears within a given cell. Besides, cells sometimes form cluster in which there is no clear separation between adjacent cells.

In this context, we have considered a two steps algorithm to segment the cytoplasm. The first step consists of the image segmentation in small areas called superpixels that represent adjacent pixels with similar intensity. An automatic algorithm based on the watershed transform has been chosen after evaluating and comparing different strategies (based on iterative clustering, minimum spanning tree, persistent edge selection ...).

The second step of the proposed approach performs superpixels merging to obtain the final segmentation. Starting from the previously detected nuclei to define cell seeds, the neighboring superpixels are merged iteratively if a radiometric similarity is detected. Ambiguities between neighboring cells are solved by combining radiometric and shape criteria. This cell growth process is considered layer by layer and performed in parallel.

6.7. Adaptative thresholding using persistent diagrams

Participants: Paul Emmanuel Ponsenard, Xavier Descombes.

In this project we have proposed a new algorithm for adaptative thresholding based on persistence diagrams. A common difficulty in binarizing biological images lies in the heterogeneity of the signal. This heterogeneity can be due to the sensor itself but also to variability in the cell response to a given marker. Therefore the binarization can not be adequately performed by using the same threshold on the whole image. In this context, adaptative approaches that estimate a local or regional proper threshold are needed. Last year, we have proposed a solution that embedded both a contrast term and a shape criterion to select the most relevant connected components among the different level sets of the image. In this work we focus on the connected component trajectories along the grey values defining the levels sets. More precisely, the persistent diagram studies the evolution of the different connected components of a binarized image for successive thresholds. The life time of a connected component is thus defined as the timelapse between its birth (gray level for which the component appears) and its death (gray level for which the component is merged with a neighboring one). As a final result for the binarization, we propose to keep the connected components with the longest lifetimes. A result on mitochondrial network binarization is shown on figure 10.

6.8. Graph matching and median graph through simulating annealing

Participants: Zhankeng Zhang, Xavier Descombes.

Graph matching when the number of nodes and edges differs is known as an NP-hard problem. Therefore, sub-optimal optimization algorithms have been proposed to solve this problem. In this work, we evaluate the possibility to reach, at least theoretically, the global optimum by using simulated annealing. We have developed an improved version of the simulating annealing scheme based on a Metropolis sampler. To solve the problem of dimension matching (different number of nodes) we have classically added dummy nodes in the smaller graph. Besides, we have shown that adding dummy nodes in both graphs provides more flexibility in the matching, thus improving the matching result. Finally, within this framework we were able to define and compute "median" graph as shown on figure 11. The algorithm consists in aligning all the graphs in a first step. The median graph is then obtained by considering two types of move in the simulated annealing: adding/removing an edge and switching two nodes. To validate this work we have considered a classification scheme between graphs. The obtained results overcome those obtained with state of the art graph matching algorithms while the computational time remains reasonable.

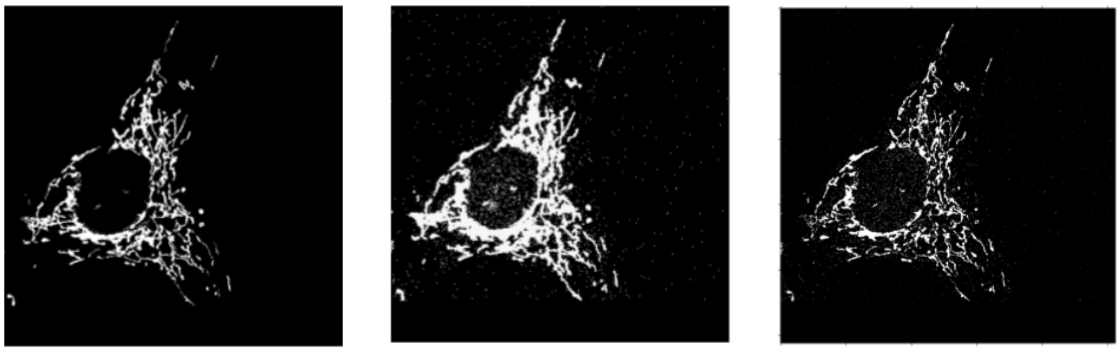

Figure 10. Image of Mitochondria from Bost team at C3M (left), Binarization obtained with a global threshold (middle) and with the persistence diagram approach. (right).

6.9. Botrytis cinerea phenotype recognition and classification: toward the establishment of links between phenotypes and antifungal molecules

Participants: Sarah Laroui, Eric Debreuve, Xavier Descombes.

This work is made in collaboration with Aurelia Vernay and Florent Villiers (Bayer).

Botrytis cinerea is a reference model of filamentous phytopathogen fungi. Some chemical treatments can lead to characteristic morphological changes, or phenotypic signatures. These phenotypes could be associated with the treatment Mode of Action (Figure 12). In order to recognise and characterise different phenotypes and associate them with the different modes of action of the molecules (Figure 13), 24-hour images are taken by transmitted light microscopy. Because of the different dose-response effects, each given molecule is tested at ten concentrations.

We compared the results of classification of these images using two methods: random forests and convolutional neural networks (Deep Learning).

To learn the Random Forest classifier, we developed a robust image analysis and classification framework relying on morphometric and topological characteristics. A number of 16 features are extracted from three representations of the objects (binary mask, skeleton and graph). Some are calculated globally over all the objects of an image (ex: the skeleton length variance) while others are calculated on each object of an image (ex: the number of nodes of the graph). The second method uses a convolutional neural network. It has been implemented using Tensorflow, an open source library for Machine Learning, created by Google to develop applications in Deep Learning.

This method achieves better results than Random Forests, and it proved to be very robust to inter-experiment variations with an average classification accuracy of 88%. In addition, it does not require data pre-processing for feature extraction. However the explanatory aspect that exists with random forests is lost.

6.10. Estimating the volume of a copepod from a single image with Deep Learning

Participants: Cédric Dubois, Eric Debreuve.

This work was made in collaboration with Jean-Olivier Irisson (Laboratoire d'Océanographie de Villefranche).

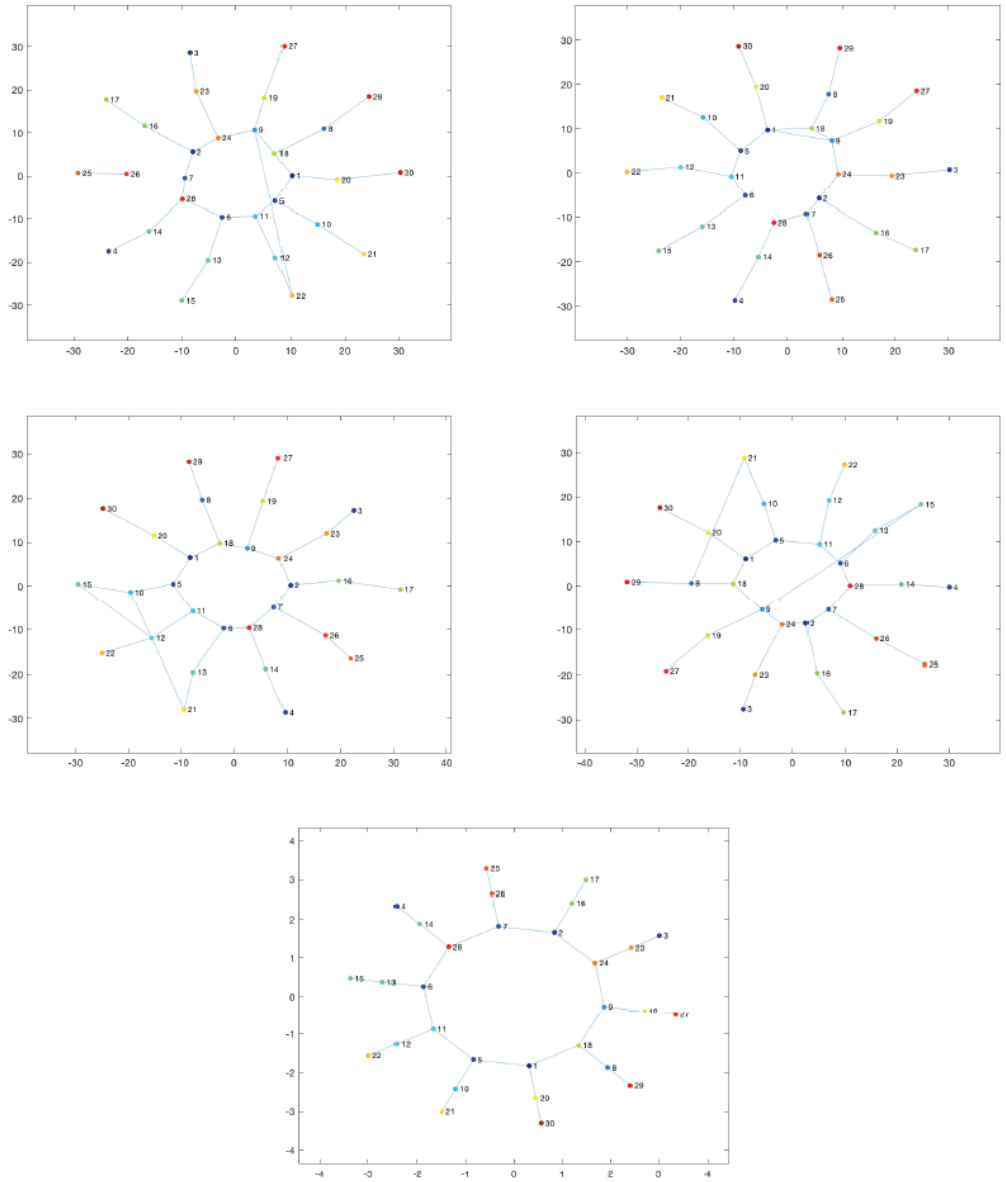

Figure 11. Four samples of noisy SUN graph and computed median graph

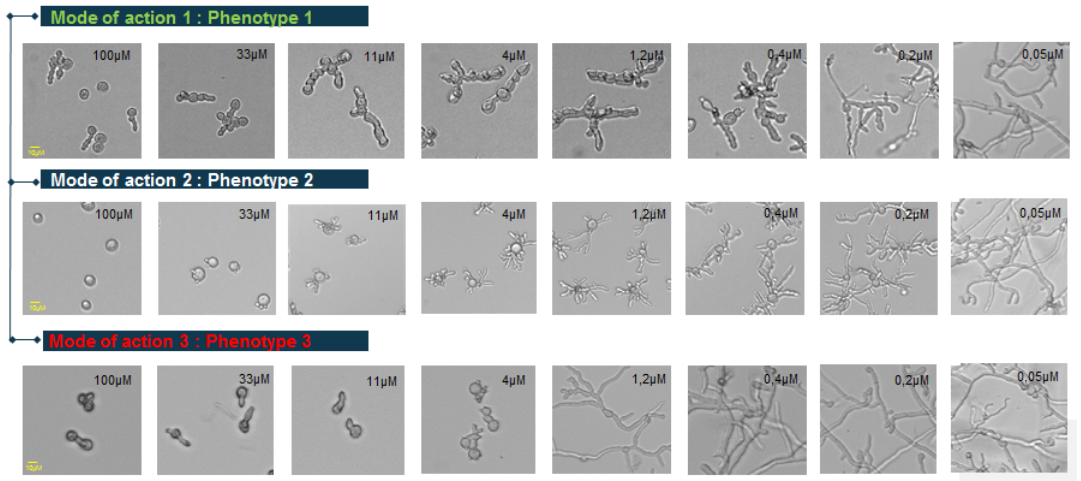

Figure 12. Characteristic phenotypic signatures for different chemical treatments at different concentrations (transmitted light microscopy, ImageXpress microscope, 10x lens).

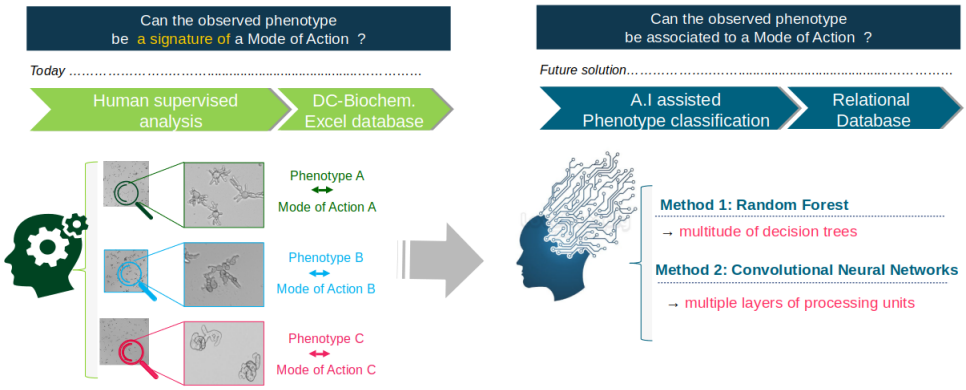

Figure 13. Example of phenotypic signatures obtained with molecules with three different mode of action. Strategy of automatic recognition and characterisation of different phenotypes and associate them with the different modes of action of the molecules.

Ecologists and biogeochemists are interested in estimating the volume of copepods (to then convert it into a biomass), a subclass of zooplankton, in order to estimate how much carbon it can store and how much it will store in the future. Those studies are made thanks to the online database EcoTaxa, which gives access to a large number of plankton images. The standard method used in ecology produces partially incorrect results due to geometric approximations and projection issues (from 3D to the 2D image plane). We first proposed a study of the error made by this method on the volume estimation of copepods. Then we proposed a new method based on the deep learning framework. Its performances have been analyzed on simulated data (Fig. 14) and preliminary tests have been made on a subset of the data of the *UVP5hd GreenEdge 2016* acquisition campaign available on EcoTaxa. Our work pointed out the limitations of both methods, indicating that a broader study is needed to improve the computation of copepod volumes.

This work formed the basis for Cédric Dubois's PhD which began on October 1st 2019 with a Ministère de la Recherche funding.

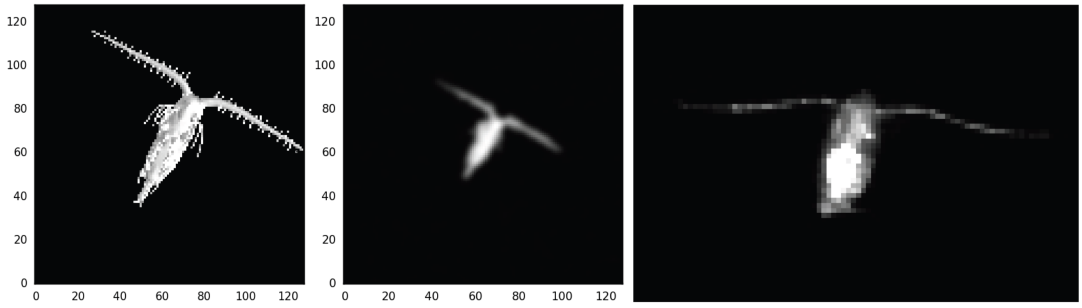

Figure 14. Left: synthetic 3D model of a typical copepod. Middle: a simulated 2D observation of the model. Right: a real observation.

6.11. Cell lineage calculation

Participants: Manuel Petit [Mosaic, Lyon], Christophe Godin [Mosaic, Lyon], Grégoire Malandain.

This work is made within the IPL Naviscope.

In recent years, techniques to image the development of biological organisms have made spectacular progresses. Researchers are now able to observe the trajectories corresponding to the development of 3D- plant tissues or animal embryo with cellular resolution. However, such observations yield a large amount of data, which, in turn, require fast and robust analysis tools to extract information while minimizing user interaction. The goal of M. Petit, which PhD thesis has begun november the 1st, is first to propose new lineage extraction schemes, and then analysis tools over a population of lineages.

6.12. Morphogenesis of the sea urchin embryo

Participants: Angie Moullet, Grégoire Malandain.

This work is made in collaboration with Barthélmy Delorme and Matteo Rauzi (iBV, Nice).

The goal of the project is to understand how biophysical forces are generated and how they work to produce exquisitely precise and controlled tissue shape changes in embryo development. Tissue morphogenesis is a process by which the embryo is reshaped into the final form of a developed animal. Tissues are constituted by cells that are interconnected one another: local changes of cell mechanical properties and shape drive consequent tissue shape change. Nevertheless, the knowledge per se of the mechanisms and mechanics at the

cell level which drive cell shape changes is insufficient to explain how tissues change their shape. Emerging properties arise at higher scales resulting from the interaction of cells within tissues and of tissues coordinating and interacting with one another.

To study the embryo evolution at a cellular scale, temporal series will be acquired by a multi-view light-sheet microscope. We will use the Mediterranean sea urchin embryo species Paracentrotus lividus as a model system and focus on the process of tissue folding, that will process that is vital since folding defects can impair neurulation in vertebrates and gastrulation in all animals which are organized into the three germ layers. From the technological perspective, new tools are needed to be able to visualize cells and to provide quantifiable data at high temporal and spatial resolution over large regions and across the entire embryo.

The goal of A. Moullet's internship (that begins dec. the 1st) is to measure and study the archenteron length evolution over a population of sea urchin embryos.

6.13. 3D Coronary vessel tracking in x-ray projections

Participants: Emmanuelle Poulain, Grégoire Malandain.

This work is made in collaboration with Régis Vaillant (GE-Healthcare, Buc, France) and Nicholas Ayache (Inria Epione team).

Percutaneous Coronary Intervention (PCI) is a minimally procedure which is used to treat coronary artery narrowing. The physician intervenes on the patient under the guidance of an x-ray imaging system. This system is not able to display a visual assessment of the coronary wall, contrary to the pre-operative Computed Tomography Angiography (CTA). To help physician to exploit this information during the course of the procedure, registering these two modalities would be useful. To this aim, we first proposed in a previous work a method of 3D coronary tracking of the main vessel in x-ray projections [27]. This approach is only applicable when the operator has avoided vessel superimposition over the vessel of interest. To further extend the concept, we explore the benefit of doing the deformable registration over the whole coronary tree. This benefit is illustrated in Fig. 15 and through tracking videos presented in https://3dvttracking.github.io/.

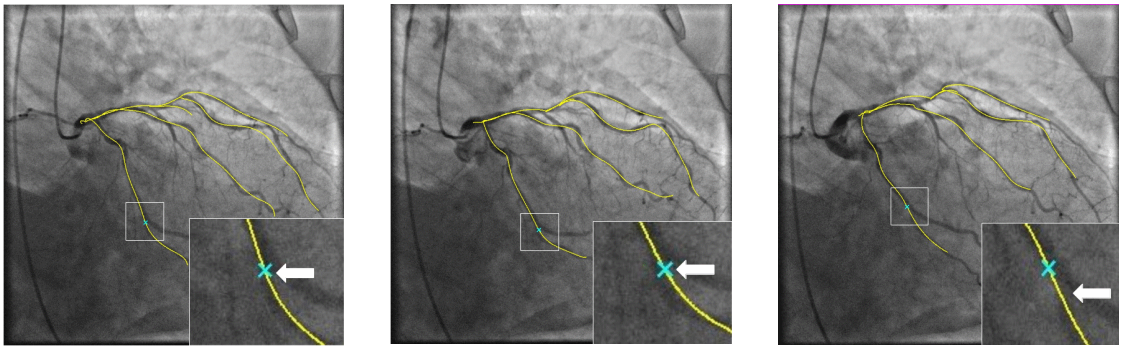

Figure 15. Tracking results for one patient over one cardiac cycle. The yellow curve represents the projected 3D vessel, the blue cross represents the point tracked as the bifurcation, and the white arrow points to the bifurcation. Those images come from a 15 frames sequence. This figure shows the frames 1, 6, 15, from left to right.

The proposed approach involves several algorithmic steps: a rigid registration of the tree to an iso-cardiac phase projection followed by a deformation of the tree represented as a tree-spline.

Indeed, a tree-spline i.e. a tree with a spline attached to each edge and shared control points between these points describes a 3D coronary tree and is able to represent its deformation along the time. We combine this description with a registration algorithm operating between the tree-spline and the angiographic projection of the coronary tree. It starts by the estimation of a rigid transformation for the iso cardiac phase time followed by a non-rigid deformation of the tree driven by the pairings formed between the projection of the edges of the tree-spline and the observed x-ray projection of the coronary arteries. The pairings are built taking into account the tree topology consistency. Anatomical constraints of length preservation is enforced when deforming the arteries.

This work has been published in FIMH [9].

7. Bilateral Contracts and Grants with Industry

7.1. Bilateral Contracts with Industry

General Electric Healthcare: a 2 months (from feb. 2019 to mar. 2019) for the end of the thesis of E. Poulain.

Bayer, Lyon: a 36 months (from aug. 2018 to jul. 2021) companion contract for the Cifre thesis of S. Laroui.

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Labex Signalife

The MORPHEME team is member of the SIGNALIFE Laboratory of Excellence.

Florence Besse and Xavier Descombes are members of the Scientific Committee.

8.1.2. Idex UCA Jedi

Luca Calatroni is responsible of the project "Action 2, DEP attractivité du territoire du IDEX JEDI, Académie 2 'Systemes complexes'".

Xavier Descombes is co-PI of the MOORPHEUS project funded by the Academy 4 of IDEX-JEDI ("Modélisation computationnelle de la croissance et de l'organisation spatiale dynamique des organoides/tumoroides de prostate"), in collaboration with C3M.

Biological Image Super-resolution Enhanced with Tensor (Biset) supported by Académie 1 RISE. Participants : E. Debreuve, L. Blanc-Féraud, S. Schaub.

Multiscale Tomography : imaging and modelling ancient materials, technical traditions and transfers, (ToMaT), supported by Idex UCA JEDI structuring Project, Participants: L. Blanc-Féraud, Vanna-Lisa Coli, Juliette Leblond, Didier Binder, Louise Gomart, Serge Cohen.

The PhD grant of Clara Sanchez is funded by the IDEX EUR DS4H. Participants: E. Debreuve, C. Rovère (IPMC).

8.1.3. 3AI Côte d'Azur

Laure Blanc-Féraud and Grégoire Malandain are chair holders of the 3AI Côte d'Azur, in the "Computational Biology and Bio-Inspired AI" axis.

The PhD grant of Vasiliki Stergiopoulou is funded by the 3AI Côte d'Azur.

8.2. National Initiatives

8.2.1. ANR RNAGRIMP

Participants: Florence Besse [PI], Fabienne de Graeve, Xavier Descombes, Eric Debreuve, Somia Rahmoun.

Here, we propose to study the molecular bases underlying the assembly and regulation of RNA granules, using the highly conserved IMP-containing granules as a paradigm. Specifically, we propose to perform an unbiased genome-wide RNAi screen on Drosophila cultured cells to identify mutant conditions in which the organization and/or distribution of IMP-containing granules is altered. To quantitatively and statistically analyze mutant conditions, and to define precise and coherent classes of mutants, we will combine high throughput microscopy with the development of a computational pipeline optimized for automatic analysis and classification of images. The function of positive hits isolated in the screen will then be validated in vivo in Drosophila neurons using fly genetics and imaging techniques, and characterized at the molecular and cellular levels using biochemical assays, in vitro phase transition experiments and live-imaging. Finally, the functional conservation of identified regulators will be tested in zebrafish embryos combining gene inactivation and live-imaging techniques. This integrative study will provide the first comprehensive analysis of the functional network that regulates the properties of the conserved IMP RNA granules. Our characterization of the identified regulators in vivo in neuronal cells will be of particular significance in the light of recent evidence linking the progression of several degenerative human diseases to the accumulation of non-functional RNA/protein aggregates.

This 4-years project started january, 2016 and is leaded by F. Besse (iBV, Nice). Participants are iBV, institut de biologie Paris Seine (IBPS, Paris), and Morpheme.

8.2.2. ANR HMOVE

Participants: Xavier Descombes, Eric Debreuve, Somia Rahmoun.

Among the signaling molecules involved in animal morphogenesis are the Hedgehog (Hh) family proteins which act at distance to direct cell fate decisions in invertebrate and vertebrate tissues. To study the underlying process we will develop accurate tracking algorithm to compare trajectories of different Hh pools transportation in live animals. This will allow us to analyze the contribution of the different carriers in the establishment of the Hh gradient. Moreover, we will develop new methods to modify the spatio-temporal and dynamical properties of the extra-cellular Hh gradient and separate the contribution of the apical versus basal Hh pools. We will complete this study with a genome-wide screen to identify genes and related cellular processes responsible for Hh release. The particular interest of this collaboration lies in the combination of development of tracking algorithm to analyze Hh distribution and trajectories with extremely powerful genetics, ease of in vivo manipulation and lack of genetic redundancy of Drosophila.

This 4-years project started january, 2016 and is leaded by P. Thérond (iBV, Nice). Participants are iBV and Morpheme.

8.2.3. ANR Cell Whisper

Participant: Grégoire Malandain.

Successful embryogenesis requires the differentiation of the correct cell types, in defined numbers and in appropriate positions. In most cases, decisions taken by individual cells are instructed by signals emitted by their neighbours. A surprisingly small set of signalling pathways is used for this purpose. The FGF/Ras/ERK pathway is one of these and mutations in some of its individual components cause a class of human developmental syndromes, the RASopathies. Our current knowledge of this pathway is, however, mostly static. We lack an integrated understanding of its spatio-temporal dynamics and we can imperfectly explain its highly non-linear response to a graded increase in input stimulus.

This systems biology project combines advanced quantitative live imaging, pharmacological/optogenetics perturbations and computational modelling to address 3 major unanswered questions, each corresponding to a specific aim:

- Aim 1: What is the spatio-temporal dynamic of intracellular signal transduction in response to FGF?
- Aim 2: What is the molecular basis of the switch-like response to graded extracellular signals?
- Aim 3: Can the results be integrated into a predictive computational model of the pathway?

Through this approach, in a simplified model system, we hope to gain an integrated view of the pathway's dynamics.

This 4-years project started october the 1st, 2019 and is leaded by P. Lemaire (CRBM, Montpellier). Participants are CRBM (Montpellier), LIRMM (Montpellier), MOSAIC (Inria Grenoble) and Morpheme.

8.2.4. Inria Large-scale initiative Naviscope

Participant: Grégoire Malandain.

This action gathers the expertise of seven Inria research teams (Aviz, Beagle, Hybrid, Morpheme, Parietal, Serpico and Mosaic) and other groups (MaIAGE, INRA, Jouy-en-Josas and UMR 144, Institut Curie Paris) and aimed at developing original and cutting-edge visualization and navigation methods to assist scientists, enabling semi-automatic analysis, manipulation, and investigation of temporal series of multi-valued volumetric images, with a strong focus on live cell imaging and microscopy application domains. More precisely, the three following challenges will be addressed:

- Novel machine learning methods able to detect the main regions of interest, and automatic quantification of sparse sets of molecular interactions and cell processes during navigation to save memory and computational resources.
- Novel visualization methods able to encode 3D motion/deformation vectors and dynamics features with color/texture-based and non-sub-resolved representations, abstractions, and discretization, as used to show 2D motion and deformation vectors and patterns.
- Effective machine learning-driven navigation and interaction techniques for complex functional 3D+Time data enabling the analysis of sparse sets of localized intra-cellular events and cell processes (migration, division, etc.).

8.3. International Research Visitors

8.3.1. Visits of International Scientists

Alin Achim, professor at Bristol university, is an invited professor in Morpheme since september 2019 for a ten months period (Leverhulme grant).

9. Dissemination

9.1. Promoting Scientific Activities

9.1.1. Scientific Events: Selection

9.1.1.1. Member of the Conference Program Committees

Laure Blanc-Féraud was member of the Conference Program Committees of NCMIP (New Computational methods for Inverse Problems), OSA Applied Optics Congress Mathematics in imaging, Workshop SPARS (Signal processing with Adaptive Sparse Structured Representation).

Luca Calatroni was the co-organiser of the workshop Regularisation methods for inverse problems and machine learning (Jussieu, Paris), 19 November 2019.

9.1.1.2. Reviewer

Laure Blanc-Féraud was a reviewer for the conferences IEEE ISBI, ICIP and ICASSP.

Xavier Descombes was a reviewer for for the conferences ISBI, ICIP, ICASSP.

Grégoire Malandain was a reviewer for the conference ISBI.

9.1.2. Journal

9.1.2.1. Member of the Editorial Boards

Laure Blanc-Féraud was Associated Editor for the journals SIAM Imaging Sciences. She was also responsible of the editorial field "Image" of the SCIENCES new editorial project of ISTE/WILEY Group which concerns the publication of collections of multi-authored titles in the fields of pure and applied sciences, health and humanities.

Luca Calatroni is a guest-editor of the Journal of Mathematical Neuroscience for the special issue on Colour representation and Cortical-inspired image processing

Xavier Descombes is Associated Editor for the journal Digital Signal Processing.

9.1.2.2. Reviewer - Reviewing Activities

Florence Besse was a reviewer for the journals Nature, Development, RNA, LifeStarAlliance, Front.mol.biol.

Luca Calatroni was a reviewer for the Journal of Mathematical Imaging and Vision, Applied Mathematics and Computation and SIAM Journal of Imaging Sciences.

Xavier Descombes was a reviewer for the Journal of the American Statistical Association.

9.1.3. Invited Talks

Laure Blanc-Féraud was invited to give a talk at to give a talk during the Sparsity4PSL International Summer School.

Luca Calatroni was invited to give a talk at the GdR Vision 2019 (Marseille), 10 October 2019, at the Statistical and Computational Learning seminars (Università di Genova, IIT, LCSL), 29 November 2019, and a BaD seminar (University of Bologna), December 3 2019.

Xavier Descombes was invited to give a talk at the Institut Henro Poincaré (Paris) for the workshop "Statistical Modeling for Shapes and Imaging", march 11-15.

9.1.4. Leadership within the Scientific Community

Laure Blanc-Féraud is member of IEEE BISP (Biomedical Imaging Signal Processing) Technical Committee.

Xavier Descombes is member of IEEE BISP (Biomedical Imaging Signal Processing) Technical Committee.

Grégoire Malandain is member of the IEEE/EMB Technical Committee on Biomedical Imaging and Image Processing (BIIP). He is an member of the Scientific Committee of the MIA department of INRA.

9.1.5. Scientific Expertise

Laure Blanc-Féraud is a member of the ANR scientific evaluation committee ASTRID.

Luca Calatroni was in the committee for the evaluation of PhD allocation for the Region Normandie.

Xavier Descombes is a member of the ANR scientific evaluation committee CE45.

Xavier Descombes is an expert of the French Research Ministry for evaluating companies CIR and JEI.

9.1.6. Research Administration

Laure Blanc-Féraud is a member of the "Commission Administrative Paritaire" for "chargé de recherche" of CNRS. She is a member of the Conseil Scientifique et Pédagogique de l'EUR DS4H, and of the Academic Council of the 3IA Côte d'Azur project, in charge of the biological axis.

Eric Debreuve is member of the Comité Permanent des Ressources Humaines (CPRH), UNS, section 61.

Xavier Descombes is member of the "comité des projets" of Inria CRISAM, of the Comité Permanent des Ressources Humaines (CPRH), UNS, section 61, of the ANR evaluation committee CE45, of the Labex Signalife Scientific Council.

9.2. Teaching - Supervision - Juries

9.2.1. Teaching

Licence : Arne Bechensteen, Outils pour la physique, 42h, L1, Polytech Nice Sophia, France

Licence : Arne Bechensteen, Programmation impérative PeiP1, 13h30, L1, Polytech Nice Sophia, France

Master : Arne Bechensteen, Traitement Numérique des Images, 8h, M2, Polytech Nice Sophia, France

Master : Arne Bechensteen, Compression, analyse et visualisation de contenus multimédia, 2h, M2, Polytech Nice Sophia, France

Licence: Florence Besse, RNA localization, 3h, L3, ENS Ulm, France

Master: Florence Besse, Neuron cell biology and circuits, 6h, M1/2, Université Côte d'Azur, France

Master: Florence Besse, RNA localization and neuron morphology, 4h, M1/2, Université Côte d'Azur, France

Master: Laure Blanc-Féraud, Traitement avancé des images, master STIMM, 8h Eq. TD, Niveau M2, Université Côte d'Azur, France.

Master: Eric Debreuve, scientific image processing, 9h EqTD, M1 + M2, Université Côte d'Azur, France

Master: Xavier Descombes, Traitement d'images, Analyse de données, Techniques avancées de traitement d'images, 10h Eq. TD, Niveau M2, ISAE, France.

Master: Xavier Descombes, Traitement d'images, master, 9h Eq. TD, Niveau M2, Université Côte d'Azur, France.

Master: Xavier Descombes, Bio-imagerie, master IRIV, 6h Eq. TD, Niveau M2, Université de Strasbourg, France

Master: Xavier Descombes, Analyse d'images, master GBM, 9h Eq. TD, Niveau M2, Université Côte d'Azur, France.

Master: Xavier Descombes, Traitement d'images scientifiques, master SVS, 15h Eq. TD Niveau M2, Université Côte d'Azur.

Licence: Henrique Goulart, Automatique, 30h, niveau L3, École Polytechnique Universitaire de Nice Sophia-Antipolis, France

Licence: Henrique Goulart, Traitement Numérique du Signal, 48h, niveau L3, École Polytechnique Universitaire de Nice Sophia-Antipolis, France

Master: Sarah Laroui, Analyse d'images, master GBM, 10h Eq. TD, Niveau M2, Université Côte d'Azur, France.

Master/Ingénieur: Sarah Laroui, Data Science, M2/Ingénieur 5, Niveau 5eme année ingénieur, 4h Eq. TD, Polytech Nice Sophia, France.

IUT 1ere année: Sarah Laroui, Acquisition et codage de l'information, niveau 1ère Année DUT RT, 13h30 Eq. TD, Institut Universitaire de Technologie (IUT) Sophia, France.

DUT: Somia Rahmoun, Acquisition et Codage de l'Information, 8h Eq.TD, Bac+1, IUT Réseaux et Télécommunications de Nice Côte d'Azur, France

9.2.2. Supervision

PhD: Emmanuelle Poulain, Recalage déformable entre angioscanner cardiaque 3D statique et angiographie coronaire dynamique 2D+t, université Côte d'Azur, october 10th, 2019, Grégoire Malandain.

PhD in progress: Arne Bechensteen, TIRF-MA and super-resolution by sparse estimation method, october 2nd, 2017, Laure Blanc-Féraud, Gilles Aubert, Sébastien Schaub.

PhD in progress: Cédric Dubois, Classification du plancton conjointe en espèce et traits morphologiques et fonctionnels avec contrainte de relations espèces-traits et de hiérarchie des espèces en taxonomie génétique, october 1st, 2019, Eric Debreuve, Jean-Olivier Irisson (LOV, Villefranche-sur-mer).

PhD in progress: Anca-Ioana Grapa, Characterization of the organization of the Extracellular Matrix (ECM) by Image Processing, 19 September 2016, Laure Blanc-Féraud, Xavier Descombes, E. van Obberghen, (iBV).

PhD in progress: Sarah Laroui, Classification and modelling of botrytis cinerea fungi growth from microscope images: toward the establishment of links between phenotypes and antifongic molecules, 1st August 2018, Eric Debreuve, Xavier Descombes

PhD in progress: Manuel Petit, Quantifying and modeling trajectories of living form development, 1st November 2019, Grégoire Malandain, Christophe Godin (EPI Mosaic, Inria, Lyon).

PhD in progress: Clara Sanchez, Lipides nutritionnels et neuroinflammation : dévelopement d'outil de morphométrie cellulaire, 1st october 2019, Carole Rovère (IPMC), Eric Debreuve.

PhD in progress: Vasiliki Stergiopoulou, Learning and optimization for 3D+T super-resolution in fluorescent microscopy, January 1st 2020, Laure Blanc-Féraud, Luca Calatroni, Sébastien Schaub.

PhD in progress: Rudan Xiao, Analysis and classification of cellular and vascular markers in histological images: application to kidney cancer, 1st october 2019, Xavier Descombes, Eric Debreuve.

9.2.3. Post-doctorates

Post-doc: Vanna Lisa Coli, Image processing for ancient pottery, co-supervised by Laure Blanc-Féraud and Juliette Leblond EPI Factas.

Post-doc: Henrique Goulart, Superresolution microscopy by blinking molecules, supervised by Laure Blanc-Féraud, Eric Debreuve and Sébastien Schaub.

9.2.4. Internships

Amina Achaibou, Détection, caractérisation et clustering de cellules gliales dans le cadre d'une étude des lipides nutritionnels, Eric Debreuve

Ghosh Avrajit, Deep Learning for ExtraCellular Matrix classification, Laure Blanc-Féraud, Xavier Descombes

Deborah Cottais, Tumor cell tracking for automatic detection of cell death time, and classification of its type, Eric Debreuve

Paul-Emmanuel Ponsenard, Image binarization using persistence diagram, Xavier Descombes

Pat Vatiwutipong, Master of mathematics, "Properties of the d-Radon transform and application to imaging issues in archeology , co-supervised by Juliette Leblond EPI FACTAS and Laure Blanc-Féraud.

Zhankeng Zhang, Graph matching and classification using simulated annealing, Xavier Descombes

9.2.5. Juries

Florence Besse particpated to 4 PhD defense committees (UCA (2) and University of Montpellier (2)) and 2 HDR defense committees (UCA and Paris Descartes)

Laure Blanc-Féraud was part of 3 PhD defense committees (Megane Boudineau IRIT Toulouse, Aleix Boquet Pasteur Institute Paris as reviewer, Jabrane Karkouri CReatis Lyon) and one HDR committee (Mathieu Aucejo CNAM Paris). She was part of 2 "comités de suivi de thèse".

Xavier Descombes participated as a reviewer to the PhD thesis committee of Lamees Nasser (Paris Sorbonne University) and Kim Jonkhoon (Paul Sabatier University, Toulouse).

Grégoire Malandain participated as reviewer to the PhD thesis committee of Carlos Tor Diez (COMUE Bretagne Loire) and as supervisor to the PhD thesis committee of Emmanuelle Poulain (université Côte d'Azur)

9.3. Popularization

9.3.1. Education

Luca Calatroni participates to the Italian project “Penne amiche della scienza” to promote scientific research in Primary Schools.

9.3.2. Interventions

Laure Blanc-Féraud gave a conference in high school CIV during "la fête de la science".

National events: Village des Sciences et de l’Innovation d’Antibes Juan les Pins 2019.

The Morpheme team took part in "La fête de la Science” during the "Village de la Science” in Juan-Les-Pins. Somia Rahnmoun, Cedric Dubois and Arne Bechensteen were present at the Inria stand for this event.

10. Bibliography

Publications of the year

Articles in International Peer-Reviewed Journals

[1] V. L. COLI, P.-H. TOURNIER, V. DOLEAN, I. EL KANFOUD, C. PICHOT, C. MIGLIACCIO, L. BLANC-FÉRAUD. *Detection of Simulated Brain Strokes Using Microwave Tomography*, in "IEEE Journal of Electromagnetics, RF and Microwaves in Medicine and Biology", June 2019, vol. 1, 1 p. [*DOI :* 10.1109/JERM.2019.2921076], https://hal.archives-ouvertes.fr/hal-02149100

[2] F. DE GRAEVE, E. DEBREUVE, S. RAHMOUN, S. ECSEDI, A. BAHRI, A. HUBSTENBERGER, X. DESCOMBES, F. BESSE. *Detecting and quantifying stress granules in tissues of multicellular organisms with the Obj.MPP analysis tool*, in "Traffic", July 2019 [*DOI :* 10.1111/TRA.12678], https://hal.archives-ouvertes.fr/hal-02193101

[3] J. DICHAMP, C. BARREAU, C. GUISSARD, A. CARRIÈRE, Y. MARTINEZ, X. DESCOMBES, L. PENICAUD, J. ROUQUETTE, L. CASTEILLA, F. PLOURABOUÉ, A. LORSIGNOL. *3D analysis of the whole subcutaneous adipose tissue reveals a complex spatial network of interconnected lobules with heterogeneous browning ability*, in "Scientific Reports", December 2019, vol. 9, n^{o} 1 [*DOI :* 10.1038/s41598-019-43130-9], https://hal.archives-ouvertes.fr/hal-02136531

[4] E. SOUBIES, L. BLANC-FÉRAUD, G. AUBERT. *New Insights on the Optimality Conditions of the l2-l0 Minimization Problem*, in "Journal of Mathematical Imaging and Vision", 2019, forthcoming [*DOI :* 10.1007/s10851-019-00917-9], https://hal.inria.fr/hal-02144528

[5] E. SOUBIES, A. RADWANSKA, D. GRALL, L. BLANC-FÉRAUD, E. VAN OBBERGHEN-SCHILLING, S. SCHAUB. *Nanometric axial resolution of fibronectin assembly units achieved with an efficient reconstruction approach for multi-angle-TIRF microscopy*, in "Scientific Reports", December 2019, vol. 9, n^{o} 1 [*DOI :* 10.1038/s41598-018-36119-3], https://hal.inria.fr/hal-02017844

International Conferences with Proceedings

[6] A. BECHENSTEEN, L. BLANC-FÉRAUD, G. AUBERT. *New methods for $\ell_2 - \ell_0$ minimization and their applications to 2D Single-Molecule Localization Microscopy*, in "IEEE International Symposium on Biomedical Imaging", Venice, Italy, July 2019 [*DOI :* 10.1109/ISBI.2019.8759567], https://hal.inria.fr/hal-02107577

[7] V. L. COLI, P.-H. TOURNIER, V. DOLEAN, I. EL KANFOUD, C. PICHOT, C. MIGLIACCIO, L. BLANC-FÉRAUD. *Detection of Brain Strokes Using Microwave Tomography*, in "IEEE 2018 - International Symposium on Antennas and Propagation and USNC-URSI Radio Science Meeting", Boston, United States, IEEE, January 2019, pp. 223-224 [*DOI :* 10.1109/APUSNCURSINRSM.2018.8609404], https://hal.archives-ouvertes.fr/hal-01824526

[8] K. GIULIETTI, L. GUILLAUME, A. CHARAZAC, C. STÉPHAN, F. BOST, X. DESCOMBES. *An Adaptative Threshold Operator Taking Shape into Account: Application to Mitochondrial Network Segmentation*, in "IEEE International Symposium on Biomedical Imaging", Venise, Italy, April 2019 [*DOI :* 10.1109/ISBI.2019.8759501], https://hal.archives-ouvertes.fr/hal-02389038

[9] E. POULAIN, G. MALANDAIN, R. VAILLANT. *3D Coronary Vessel Tree Tracking in X-Ray Projections*, in "FIMH 2019 - 10th Functional Imaging and Modeling of the Heart", Bordeaux, France, Functional Imaging and Modelling of the Heart, Springer, May 2019, vol. Lecture Notes in Computer Science, n^{o} 10263, pp. 388-396 [*DOI :* 10.1007/978-3-319-59448-4_20], https://hal.inria.fr/hal-02153710

[10] E. SOUBIES, L. BLANC-FÉRAUD, S. SCHAUB, E. VAN OBBERGHEN-SCHILLING. *Improving 3D MA-TIRF Reconstruction with Deconvolution and Background Estimation*, in "IEEE International Symposium on Biomedical Imaging", Venise, Italy, April 2019 [*DOI :* 10.1109/ISBI.2019.8759103], https://hal.inria.fr/hal-02017862

[11] J. H. DE MORAIS GOULART, L. BLANC-FÉRAUD, E. DEBREUVE, S. SCHAUB. *A study on tensor and matrix models for super-resolution fluorescence microscopy*, in "CAMSAP 2019 - IEEE International Workshop on Computational Advances in Multi-Sensor Adaptive Processing", Le Gosier, Guadeloupe, Proceedings of the IEEE International Workshop on Computational Advances in Multi-Sensor Adaptive Processing, December 2019, https://hal.archives-ouvertes.fr/hal-02309659

National Conferences with Proceedings

[12] A. BECHENSTEEN, L. BLANC-FÉRAUD, G. AUBERT. *Exact biconvex reformulation of the $L2-L0$ minimization problem*, in "GRETSI 2019", Lille, France, August 2019, https://hal.inria.fr/hal-02382369

[13] A.-I. GRAPA, L. BLANC-FÉRAUD, E. VAN OBBERGHEN-SCHILLING, X. DESCOMBES. *Optimal Transport vs Many-to-many assignment for Graph Matching*, in "GRETSI 2019 - XXVIIème Colloque francophone de traitement du signal et des images", Lille, France, August 2019, https://hal.archives-ouvertes.fr/hal-02279634

Conferences without Proceedings

[14] V. L. COLI, D. BINDER, L. BLANC-FÉRAUD, S. COHEN, L. GOMART, J. LEBLOND. *Modélisation 3D des fabriques et identification des techniques : nouvelles méthodes de segmentation et de reconnaissance de formes*, in "Céramiques imprimées de Méditerranée occidentale. Matières premières, productions, usages", Nice, France, Didier Binder and Stéphane Azoulay and Alain Burr and Claire Manen and Martine Regert and Chrystèle Vérati, 2019, https://hal.archives-ouvertes.fr/hal-02398835

[15] L. GOMART, D. BINDER, L. BLANC-FÉRAUD, S. COHEN, V. L. COLI, L. DRIEU, M. GABRIELE, J. LEBLOND, D. PISANI, S. SORIN. *Des macro-traces au synchrotron : premiers résultats et enjeux relatifs aux méthodes de montage des céramiques*, in "Céramiques imprimées de Méditerranée occidentale. Matières premières, productions, usages", Nice, France, Didier Binder and Stéphane Azoulay and Alain Burr and Claire Manen and Martine Regert and Chrystèle Vérati, 2019, https://hal.archives-ouvertes.fr/hal-02398865

[16] S. LAROUI, E. DEBREUVE, X. DESCOMBES, F. VILLALBA, F. VILLIERS, A. VERNAY. *Machine-learning assisted phenotyping: From fungal morphology to mode of action hypothesis*, in "IUPAC - 14th International Congress of Crop Protection Chemistry", Ghent, Belgium, May 2019, https://hal.archives-ouvertes.fr/hal-02403936

[17] E. SOUBIES, L. BLANC-FÉRAUD, G. AUBERT. *On the Local Minimizers of the CEL0 Relaxation*, in "SPARS 2019 - Signal Processing with Adaptive Sparse Structured Representations - Workshop", Toulouse, France, July 2019, https://hal.inria.fr/hal-02263782

Other Publications

[18] M. BERTALMIO, L. CALATRONI, V. FRANCESCHI, B. FRANCESCHIELLO, D. PRANDI. *Cortical-inspired Wilson-Cowan-type equations for orientation-dependent contrast perception modelling*, October 2019, working paper or preprint, https://hal.archives-ouvertes.fr/hal-02316989

[19] L. CALATRONI, G. GARRIGOS, L. ROSASCO, S. VILLA. *Accelerated iterative regularization via dual diagonal descent*, December 2019, working paper or preprint, https://hal.archives-ouvertes.fr/hal-02423682

[20] M. LAMINE BENOMAR, A. M. CHIKH, X. DESCOMBES, M. BENAZZOUZ. *Multi Features Based Approach for White Blood Cells Segmentation and Classification in Peripheral Blood and Bone Marrow Images*, September 2019, working paper or preprint, https://hal.archives-ouvertes.fr/hal-02279352

[21] S. PARISOTTO, L. CALATRONI, A. BUGEAU, N. PAPADAKIS, C.-B. SCHÖNLIEB. *Variational Osmosis for Non-linear Image Fusion*, October 2019, https://arxiv.org/abs/1910.02012 - 10 pages, 7 figures [*DOI :* 10.02012], https://hal.archives-ouvertes.fr/hal-02314972

References in notes

[22] A. BECK, Y. C. ELDAR. *Sparsity constrained nonlinear optimization: Optimality conditions and algorithms*, in "SIAM Journal on Optimization", 2013, vol. 23, n^{o} 3, pp. 1480–1509

[23] S. GAZAGNES, E. SOUBIES, L. BLANC-FÉRAUD. *High density molecule localization for super-resolution microscopy using CEL0 based sparse approximation*, in "Biomedical Imaging (ISBI 2017), 2017 IEEE 14th International Symposium on", IEEE, 2017, pp. 28–31

[24] A.-I. GRAPA, R. MEUNIER, L. BLANC-FÉRAUD, G. EFTHYMIOU, S. SCHAUB, A. RADWANSKA, E. VAN OBBERGHEN-SCHILLING, X. DESCOMBES. *Classification of the fibronectin variants with curvelets*, in "ISBI 2018 - IEEE 15th International Symposium on Biomedical Imaging", Washington, DC, United States, April 2018, pp. 930-933 [*DOI :* 10.1109/ISBI.2018.8363723], https://hal.archives-ouvertes.fr/hal-01868726

[25] E. NEHME, L. E. WEISS, T. MICHAELI, Y. SHECHTMAN. *Deep-STORM: super-resolution single-molecule microscopy by deep learning*, in "Optica", 2018, vol. 5, n^{o} 4, pp. 458–464

[26] G. PEYRÉ, M. CUTURI, J. SOLOMON. *Gromov-Wasserstein Averaging of Kernel and Distance Matrices*, in "ICML 2016", New-York, United States, Proc. 33rd International Conference on Machine Learning, June 2016, https://hal.archives-ouvertes.fr/hal-01322992

[27] E. POULAIN, G. MALANDAIN, R. VAILLANT. *3D Coronary vessel tracking in x-ray projections*, in "International Conference on Functional Imaging and Modeling of the Heart (FIMH)", Toronto, Canada, LNCS, June 2017, vol. 10263, pp. 204-215 [*DOI :* 10.1007/978-3-319-59448-4_20], https://hal.inria.fr/hal-01502128

[28] D. SAGE, H. KIRSHNER, T. PENGO, N. STUURMAN, J. MIN, S. MANLEY, M. UNSER. *Quantitative evaluation of software packages for single-molecule localization microscopy*, in "Nature methods", 2015, vol. 12, n^{o} 8, pp. 717–24

[29] E. SOUBIES, L. BLANC-FÉRAUD, G. AUBERT. *A Unified View of Exact Continuous Penalties for $\ell_2 - \ell_0$ Minimization*, in "SIAM Journal on Optimization", 2017, vol. 27, n^{o} 3, pp. 2034–2060

[30] C. SZEGEDY, W. LIU, Y. JIA, P. SERMANET, S. REED, D. ANGUELOV, D. ERHAN, V. VANHOUCKE, A. RABINOVICH. *Going Deeper with Convolutions*, 2014

[31] G. YUAN, B. GHANEM. *Sparsity Constrained Minimization via Mathematical Programming with Equilibrium Constraints*, in "arXiv:1608.04430", August 2016

[32] M. ZASLAVSKIY, F. BACH, J.-P. VERT. *Many-to-Many Graph Matching: A Continuous Relaxation Approach*, in "Machine Learning and Knowledge Discovery in Databases", Berlin, Heidelberg, Springer Berlin Heidelberg, 2010, pp. 515–530