



IN PARTNERSHIP WITH:
CNRS

**Université Nice - Sophia
Antipolis**

Activity Report 2015

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:

- 3.4. - Machine learning and statistics
 - 3.4.1. - Supervised learning
 - 3.4.2. - Unsupervised learning
 - 3.4.4. - Optimization and learning
 - 3.4.6. - Neural networks
 - 3.4.7. - Kernel methods
 - 3.4.8. - Deep learning
- 5.3. - Image processing and analysis
 - 5.3.4. - Registration
- 5.4.1. - Object recognition
- 5.4.3. - Content retrieval
- 5.4.4. - 3D and spatio-temporal reconstruction
- 5.4.5. - Object tracking and motion analysis
- 5.4.6. - Object localization
- 5.9. - Signal processing
 - 5.9.3. - Reconstruction, enhancement
 - 5.9.6. - Optimization tools
- 6.1. - Mathematical Modeling
 - 6.1.2. - Stochastic Modeling (SPDE, SDE)
- 6.3.1. - Inverse problems

Other Research Topics and Application Domains:

- 1.1. - Biology
 - 1.1.3. - Cellular biology
 - 1.1.4. - Developmental biology
- 2.6. - Biological and medical imaging

1. Members

Research Scientists

Xavier Descombes [Team leader, Inria, Senior Researcher, HdR]
Laure Blanc-Féraud [CNRS, Senior Researcher, HdR]
Eric Debreuve [CNRS, Researcher, HdR]
Grégoire Malandain [Inria, Senior Researcher, HdR]
Florence Besse [CNRS, Researcher, 50%]
Caroline Medioni [CNRS, Researcher, 20%]
Sébastien Schaub [CNRS, IR, 20%]

PhD Students

Lola-Xiomara Bautista Rozo [Univ. Nice]

Thomas Benseghir [Inria, until Jul 2015]
Gaël Michelin [Inria]
Emmanuelle Poulain [Inria, from december]
Agustina Razetti [Univ. Nice]
Emmanuel Soubies [Univ. Nice]
Alexis Zubiolo [Univ. Nice]

Visiting Scientist

Simone Rebegoldi [Univ. Modena and Reggio Emilia, from May 2015 until Aug 2015]

Administrative Assistants

Jane Desplanques [Inria, 40%, from May]
Nadezda Lacroix-Coste [Inria, 40%, until April]
Micheline Hagnere [CNRS, Assistant of pole SIS at I3S, until August]
Frédéric Fontaine [CNRS, Assistant of pole SIS at I3S, from September]

Others

Nicolas Cedilnik [Univ. Nice, intern, from May 2015]
Yaqun Liu [CNRS, intern, from Jun 2015 until Sep 2015]
Sen Wang [Inria, intern]
Wei Shen [CNRS, intern, from May 2015 until Nov 2015]
Gilles Aubert [Univ. Nice, Professor, HdR]
Marine Breuilly [Univ. Nice]

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 genetical 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 experiments 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

Prizes and distinctions

L. Blanc-Féraud has been declared Knight of the Legion of Honor september the 25th.

Awards

T. Benseghir and G. Malandain have received a best paper award at the IPCAI conference.

X. Descombes has co-authored of a paper that received the best student paper award at the Workshop on Diff - CV.

BEST PAPERS AWARDS:

[3]

T. BENSEGHIR, G. MALANDAIN, R. VAILLANT. *A tree-topology preserving pairing for 3D/2D registration*, in "International Conference on Information Processing in Computer-Assisted Interventions, IPCAI 2015", Barcelona, Spain, International Journal of Computer Assisted Radiology and Surgery, Springer Berlin Heidelberg, June 2015, vol. 10, n^o 6, pp. 913-923 [DOI : 10.1007/s11548-015-1207-0], <https://hal.inria.fr/hal-01183573>

[5]

A. DUNCAN, E. KLASSEN, X. DESCOMBES, S. ANUJ. *Geometric Analysis of Axonal Tree Structures*, in "1st International Workshop on Diff - CV: Differential Geometry in Computer Vision for Analysis of Shapes, Images and Trajectories (in conjunction with BMVC)", Swansea, United Kingdom, October 2015, <https://hal.inria.fr/hal-01247192>

5. New Software and Platforms

5.1. BioLib

KEYWORD: Biomedical imaging

FUNCTIONAL DESCRIPTION

Library of image analysis for biology: object detection, tracking. This year some new developments for embedding attractive interactions in the Multiple Births and Cut algorithm have been included.

- Participants: Sylvain Prigent, Xavier Descombes, Grégoire Malandain, Étienne Delclaux, Emmanuel Soubies and Sen Wang.
- Contact: Xavier Descombes

5.2. PIB

Biological imaging platform

FUNCTIONAL DESCRIPTION

This platform, based on the DTK meta-platform, aims at gathering the team software development, and at providing a visual development tool.

- Participants: Étienne Delclaux, Grégoire Malandain and Xavier Descombes
- Contact: Xavier Descombes

5.3. Stracking

KEYWORDS: Bioinformatics - Biology - Biomedical imaging

SCIENTIFIC DESCRIPTION

Head Tracking and Flagellum Tracing for Sperm Motility Analysis : Sperm quality assessment plays an essential role in human fertility and animal breeding. Manual analysis is time-consuming and subject to intra- and inter-observer variability. To automate the analysis process, as well as to offer a means of statistical analysis that may not be achieved by visual inspection, we present a computational framework that tracks the heads and traces the tails for analyzing sperm motility, one of the most important attributes in semen quality evaluation. Our framework consists of 3 modules: head detection, head tracking, and flagellum tracing. The head detection module detects the sperm heads from the image data, and the detected heads are the inputs to the head tracking module for obtaining the head trajectories. Finally, a flagellum tracing algorithm is proposed to obtain the flagellar beat patterns.

FUNCTIONAL DESCRIPTION

This software is developed within the ANR project MOTIMO. It allows to segment and track spermatozoons from confocal microscopy image sequences.

- Participants: Huei Fang Yang, Xavier Descombes, Sylvain Prigent and Grégoire Malandain
- Contact: Xavier Descombes

6. New Results

6.1. Exact continuous penalties for ℓ_2 - ℓ_0 minimization

Participants: Emmanuel Soubies, Laure Blanc-Féraud, Gilles Aubert.

We consider the following ℓ_0 -regularized least squares problem

$$\hat{x} \in \arg \min_{x \in \mathbb{R}^N} G_{\ell_0}(x) := \frac{1}{2} \|Ax - d\|^2 + \lambda \|x\|_0, \quad (1)$$

where $A \in \mathbb{R}^{M \times N}$, $d \in \mathbb{R}^M$ represents the data and $\lambda > 0$ is an hyperparameter characterizing the trade-off between data fidelity and sparsity. This problem finds a wide range of applications in signal/image processing, learning and coding areas among many others. We proposed a unified framework for exact continuous penalties approximating the ℓ_0 -norm. In other words, we are concerned by the design of a class of continuous relaxations of G_{ℓ_0} , preserving all its global minimizers, and for which any local minimal point is also one of the initial functional. Hence, we highlight five *necessary and sufficient* conditions on the continuous penalty approximating the ℓ_0 -norm ensuring that the minimizers of the underlying continuous relaxation of G_{ℓ_0} are consistent with those of G_{ℓ_0} . However, some local minimizer of the relaxed functional are not minimizer of G_{ℓ_0} which is an interesting point for such highly non-convex functional. This work offers a new way to compare penalties approximating the ℓ_0 -norm. Finally, it is worth noting that the CEL0 penalty [1], [14], [17] is the inferior limit of the obtained class of penalties and seems to be the best choice to do in order to obtained an equivalent continuous reformulation of (1).

6.2. Application of the Continuous Exact ℓ_0 relaxation to Channel and DOA sparse estimation problems

Participants: Emmanuel Soubies, Laure Blanc-Féraud.

This work is made in collaboration with Adilson Chinatto, Cynthia Junqueira, João M. T. Romano (University of Campinas, Brazil) and Pascal Larzabal, Jean-Pierre Barbot (ENS Cachan, SATIE Lab).

This work is devoted to two classical sparse problems in array processing: Channel estimation and DOA (Direction Of Arrivals) estimation. We show how our results on ℓ_0 optimization [1], [14], [17] can be used, at the same computational cost, in order to obtain improvement in comparison with ℓ_1 optimization (usually used) for sparse estimation. Moreover, for the DOA case, we show that our analysis conducted in the Single Measurement Vector (SMV) case [1] can be generalized to the Multiple Measurement Vectors (MMV) case. In that case, the variable x is not a vector of \mathbb{R}^N but a matrix of $\mathbb{R}^{N \times K}$ where N is the signal length and K the number of snapshots. Hence, one wants to apply sparsity to the rows of x , i.e. x must have a small number of nonzero rows, instead of applying the sparsity on all the components of x . This results in a row-structured sparsity penalty which is modelled using a mixed ℓ_2 - ℓ_0 norm.

Finally, numerical experiments demonstrate the efficiency of the proposed approach compared to classical methods as ℓ_1 relaxation, Iterative Hard Thresholding or MUSIC algorithms and that it can reach the Cramer Rao Bound in some cases [4].

6.3. From TIRF microscope calibration to 3D biological reconstructions

Participants: Emmanuel Soubies, Laure Blanc-Féraud, Sébastien Schaub, Gilles Aubert.

This work is made in collaboration with Agata Radwanska, Ellen Van Obberghen-Schilling (iBV).

Total Internal Reflection Fluorescence microscopy (TIRF) is a method of choice to visualize membrane-substrate interactions. The principle of this device relies on the total internal reflection phenomenon generating an evanescent wave capable of producing a selective excitation of the dye molecules within a single layer of 100 to 500nm. The fast decay of the evanescent wave varies with respect to the incident angle of the light beam. Hence, intensity variations on TIRF images, occurring when changing the incident angle, are, in part, due to the axial positions of the observed structures. While a direct interpretation of Multi-Angle TIRF (MA-TIRF) images in terms of axial structure positions is not an easy task, reconstruction algorithms can be dedicated to compute a quantitative depth map with high axial resolution. However, the success of such reconstruction methods strongly depends on the system calibration.

We have proposed a pipeline for MA-TIRF calibration. Considering back focal plane (BFP) images of several solutions differing by their refractive indices, we validate the theoretical relation linking the tension applied to the galvanometric mirror (which controls the laser beam orientation) and the incident angle of the beam on the specimen. Then it is crucial to verify if the simple exponential decaying model of the evanescent wave is sufficient to describe our setup. To this end we propose to build a phantom sample (for which the geometry is known) using a large lens placed into a homogeneous fluorescent solution (Fig. 1 top). Based on a least square estimation, we showed a good agreement between the estimated slope of the lens (we assume the lens to be linear near the border) and the expected one up to 400nm depth (Fig. 1 bottom-left). To complete the validation procedure, we use a sample for which the structures of interest are labeled using two different fluorescent proteins sensitive to different wavelengths and emitting respectively green and red fluorescence. Then, using standard variational approaches, we obtain a co-localization of the reconstructed structures with a precision around 30-40nm (Fig. 1 bottom-middle) over at least 170nm depth showing the precision of the method. Finally, once this calibration step is achieved, we perform color-coded depth representation of 3D biological structures living in the vicinity of the cell membrane (Fig. 1 bottom-right). All these experiments have been made on an experimental TIRF system developed at iBV lab in Valrose.

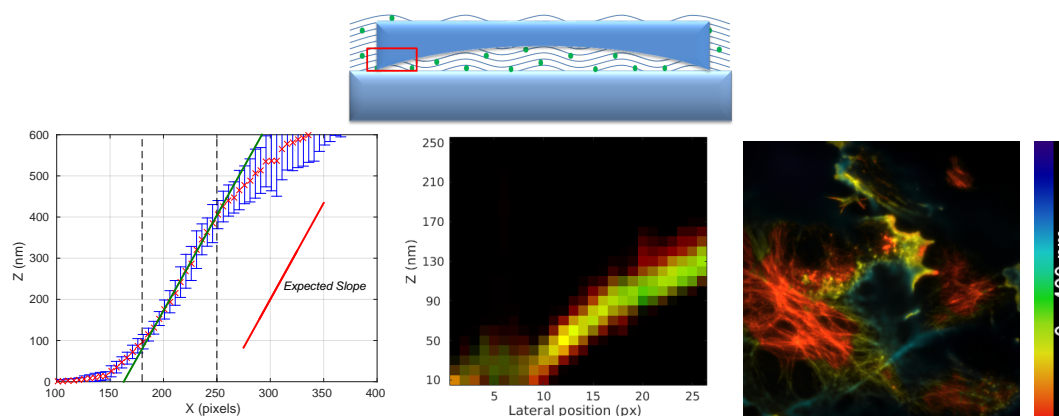


Figure 1. Top: Phantom sample constructed from a large lens and an homogeneous fluorescent solution. The red rectangle represents the observed region through the MA-TIRF setup. Bottom: estimated (green) and expected (red) slope of the lens within the red zone of the top figure (left), results of the co-localization experiment along a XY-line (middle) and a color-coded depth representation of a 3D biological reconstruction (right).

6.4. Phase estimation in Differential Interference Contrast (DIC) microscopy

Participants: Lola-Xiomara Bautista Rozo, Laure Blanc-Féraud.

We present a gradient-based optimization method for the estimation of a specimen phase function from polychromatic DIC images. The method minimizes the sum of a nonlinear least-squares discrepancy measure and a smooth approximation of the total variation. A new formulation of the gradient and a recent updating rule for the choice of the step size are both exploited to reduce computational time. Numerical simulations on two computer-generated objects show significant improvements, both in efficiency and accuracy, with respect to a more standard choice of the step size.

6.5. Spatio-temporal registration of 3D microscopy image sequences of Arabidopsis floral meristems

Participants: Gaël Michelin, Grégoire Malandain.

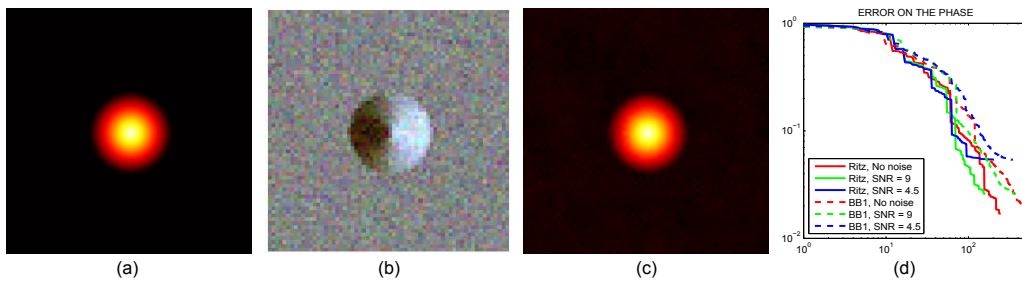


Figure 2. Data and results for the cone object. From left to right: true object, noisy DIC color image taken at angle $\tau_0 = 0^\circ$ and $SNR = 4.5$, reconstructed phase and the relative error versus the number of iterations.

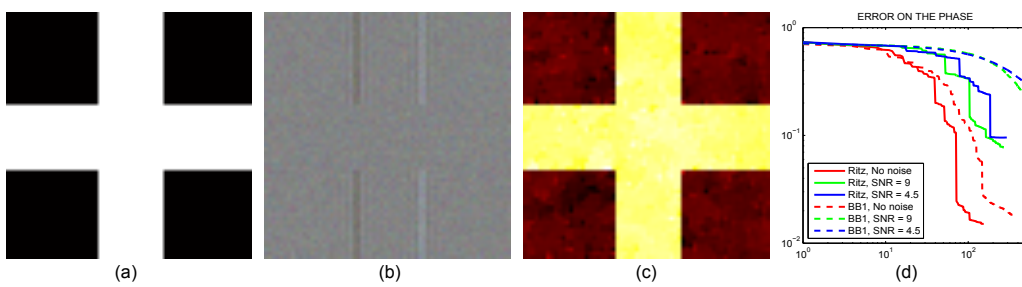


Figure 3. Data and results for the cross object. From left to right: true object, noisy DIC color image taken at angle $\tau_0 = 0^\circ$ and $SNR = 4.5$, reconstructed phase with and the relative error versus the number of iterations.

This work is made in collaboration with Léo Guignard and Christophe Godin (Virtual Plants), within the Morphogenetics Inria Project Lab.

The shoot apical meristem (SAM) is at the origin of all the plant above-ground organs (including stems, leaves and flowers) and is a biological object of interest for the understanding of plant morphogenesis. The quantification of tissue growth at a cellular level requires the analysis of 3D microscopic image sequences of developing meristems. To address inter-individual variability, it is also required to compare individuals. This obviously implies the ability to process inter-individual registration, i.e. to compute spatial and temporal correspondences between sequences from different meristems.

In [8], we propose a spatial registration method dedicated to microscopy floral meristem (FM) images, based on the registration of both the outer and the inner surfaces of the L1 layer (the epidermal cell layer). A given meristem (one timepoint) can be compared to a sequence (several timepoints) of another meristem: the goodness-of-fit criterion allows to identify the best corresponding time-point in this sequence of another individual, achieving the temporal registration (see figure 4). Since the morphological deformations remain important between successive images of a sequence, images interpolation between time-points is also performed in order to refine the sequence temporal resolution and thus to ensure a precise temporal registration.

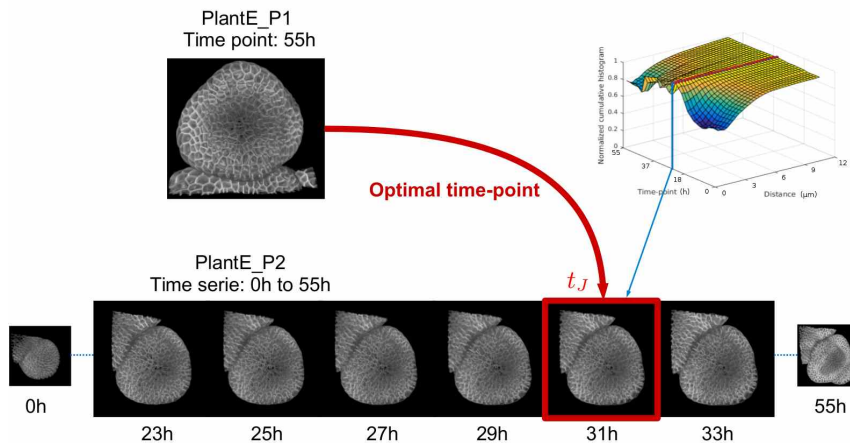


Figure 4. Inter-individual temporal registration result with 3D views of the registered meristem and the interpolated movie at several time-points.

6.6. Epidermal cell layer thickness variability in *Arabidopsis* floral meristems

Participants: Gaël Michelin, Grégoire Malandain.

This work is made in collaboration with Yassin Refahi (Sainsbury Lab., University of Cambridge) and Jan Traas (ENS Lyon), within the Morphogenetics Inria Project Lab.

Flowers from the same species display a great robustness in their global shape and their developing stage can be theoretically identifiable to their size. The cells in epidermal (L1) and sub-epidermal (L2) layers of the floral meristem divide anticlinally, i.e. in a sideways fashion that ensures that L1 and L2 remain distinct. Thus a goodness-of-fit criterion on L1 and L2 layers is considered as an adequate registration quality measure in the inter-individual spatio-temporal registration framework developed in [8].

The aim of the present work is to investigate the variability of L1 layer thickness over development stages of an individual and between individuals. The study results may impact the way we process the inter-individual spatial registration. Therefore we measured the thickness distribution (histogram) of the L1 cells and we plotted the distribution of cells thickness (see figure 5) on images provided from three distinct floral meristems at acquisition time-points. Our results tend towards showing that L1 thickness increases over time non-uniformly, with a higher L1 thickness on sepals for advanced developing stages. We also observed an inter-individual thickness variability of about 15% for developing floral meristems at close developing stages. Future investigations will consist in taking a larger set of data to assess our first observations, in providing a biological interpretation of these observations and in using this knowledge to propose a refined spatial registration method.

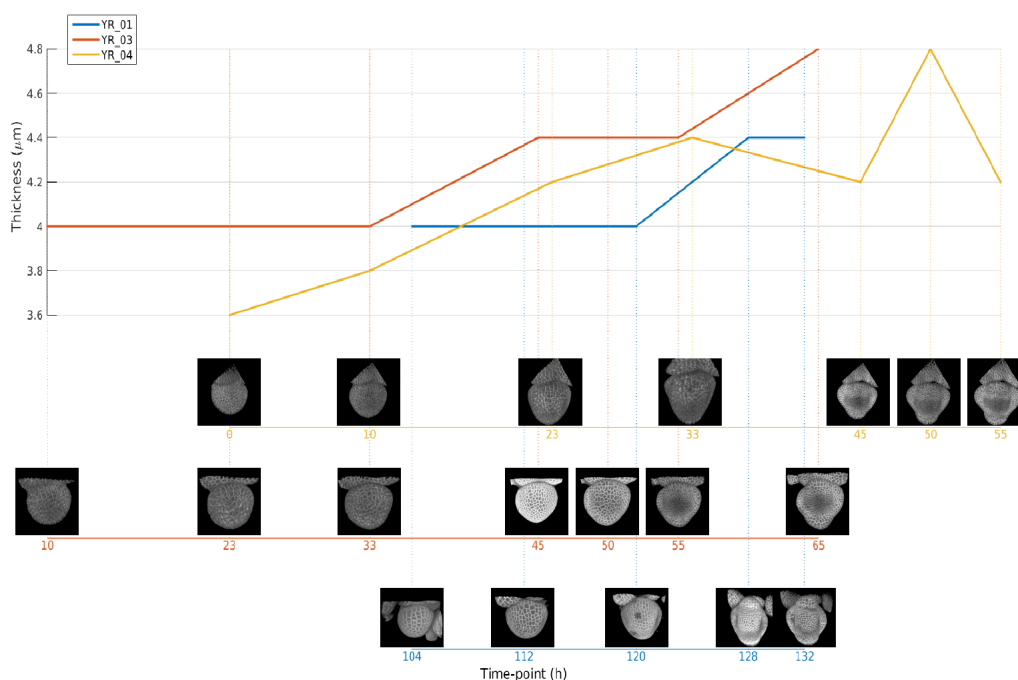


Figure 5. Epidermal cell layer thickness distribution over floral meristem development. Each row relates the measures at different developing times of a floral meristem.

6.7. Statistical Characterization, Modelling and Classification of Morphological Changes in *imp* Mutant *Drosophila* Gamma Neurons

Participants: Agustina Razetti, Caroline Medioni, Florence Besse, Xavier Descombes.

In *Drosophila* brain, gamma neurons in the mushroom body are involved in higher functions such as olfactory learning and memory. During metamorphosis, they undergo remodelling after which they adopt their adult shape. Some mutations alter remodelling and therefore neuronal final morphology, causing behavioural dysfunctions. The RNA binding protein *Imp*, for example, was shown to control this remodelling process at least partly by regulating profilin expression. This work aims at precisely characterizing the morphological changes observed upon *imp* knockdown in order to further understand the role of this protein. We developed a methodological framework that consists in the selection of relevant morphological features (axon length and shape and branch length distribution and density), their modelling and parameter estimation. We thus perform

a statistical comparison and a likelihood analysis to quantify similarities and differences between wild type and mutated neurons. The data was a set of 3D images showing a single neuron taken with a confocal microscope and provided by F. Besse group, IBV. The workflow from raw data to the likelihood analysis is summarized on figure 6. We show that imp mutant neurons can be classified into two phenotypic groups (called Imp L and Imp Sh) that differ in several morphological aspects. We also demonstrate that, although Imp L and wild-type neurons show similarities, branch length distribution is discriminant between these populations. Finally, we study biological samples in which Profilin was reintroduced in imp mutant neurons, and show that defects in main axon and branch lengths are partially suppressed.

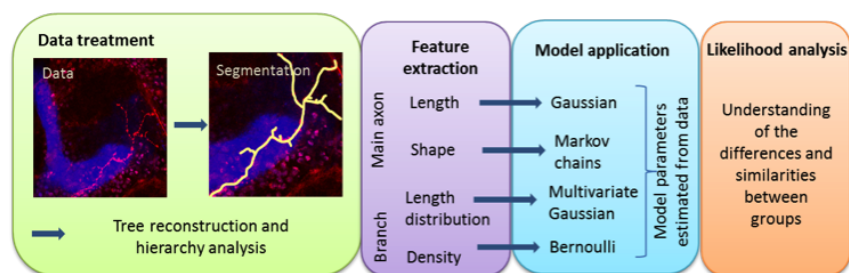


Figure 6. Summary of the workflow from raw data to the likelihood analysis.

6.8. Genome-wide search for factors that control the assembly of RNA granules

Participants: Wei Shen, Nicolas Cedilnik, Florence Besse, Xavier Descombes.

This work has been done in collaboration with Fabienne De Graeve from iBV

In vivo, mRNAs are packaged together with regulatory proteins into ribonucleoprotein particles (RNP) that control their fate and undergo extensive remodeling in response to developmental cues or environmental stresses. Cytoplasmic RNPs of different sizes, composition and regulatory properties have been described, including large macromolecular complexes such as P-bodies, stress granules, or germ cell granules. We aim at studying the different RNA granules distribution within the cytoplasm depending on genomic factors.

Before considering a spatial statistics analysis of the granules, it is necessary to detect them on confocal microscopy images of the cells. Therefore, we have studied a first pipeline for detecting these granules in confocal microscopy images. We have marked cells with DAPI for detecting nuclei. These nuclei are then classified into "dead" or "alive" by a support vector machine (SVM) using intensity and shape criteria. In the second step we consider GFP marked images to segment the cytoplasm and detect the granules within the cytoplasm. The cytoplasm segmentation is performed using an active contour whereas the granule detection is based on a marked point process model optimized by the multiple births and cut algorithm.

The full pipeline has been validated on a few samples from a pilot study. The next step will consist of a validation on the full study before considering a genome-wide screening.

6.9. Cells detection using segmentation competition

Participants: Sen Wang, Emmanuel Soubies, Xavier Descombes.

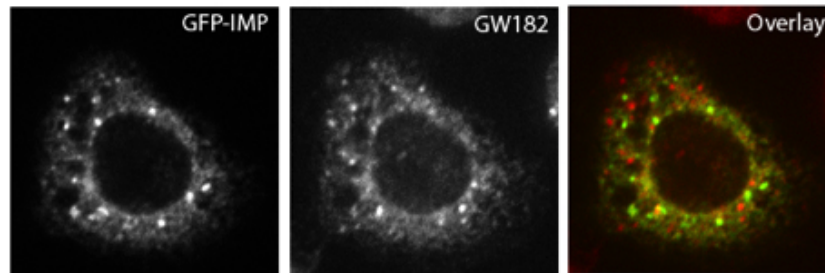


Figure 7. GFP-IMP particles are distinct from P-bodies. S2R+ cells expressing GFP-IMP fusions (left: green in the overlay) and stained with α -GW182 antibodies (middle: red in the overlay). GW182 is a well-described marker of P-bodies. Experiment performed in F. Besse lab at iBV (unpublished).

Marked point processes have proved to be very efficient for segmenting a collection of objects from digital images. The multiple birth and death algorithm provides an optimization framework that allows reasonable time computation. This algorithm has to be embedded in a simulated annealing framework which involves parameters tuning (initial temperature and cooling scheme). This tedious task can be overcome considering a graph cut algorithm instead of the probabilistic death step. The algorithm then consists in successively adding new random objects in the configuration and selecting the most relevant using the graph cut algorithm. In the graph construction a node is associated to each object. In the original algorithm proposed by [21] the regularity condition imposed by the graph cut prevents to consider attractive interactions such as clustering or alignment constraints, which restricts the model to repulsive properties such as non overlap between objects. To overcome this restriction we have investigated new graph constructions by considering nodes defined by clusters of interacting objects. Different strategies have been compared to avoid being trapped in local minima defined by clusters while minimizing the number of required iterations. We have applied this new algorithm on different bioimaging problems such as axon extraction or cells detection (see figure 8).



Figure 8. Axon detection on a synthetic image without (left) and with (middle left) attractive interactions and on real image (middle right) with attractive interactions (right).

6.10. Vesicles trajectory detection and analysis

Participant: Xavier Descombes.

This work has been done in collaboration with Maximilian Furthauer and Thomas Juan from iBV.

In many species, the left right asymetry of organs location is initiated in a ciliated cavity called Kupffer's vesicle in zebrafish. The cills beating induce a non symetrical flow in the cavity that can be studied by following the trajectory of exovesicles in the Kupffer's vesicle. The goal of this project is to automatically track these exovesicles and to perform a statistical analysis of theses trajectories in different conditions.

We consider 2D time sequences of images. To extract the vesicles from the time sequence we first remove the background by substracting a local time mean. We then detect the cell border using an active contour computed on the spatial derivative of the images. The vesicles are then simply detected using a threshold followed by a morphological opening to remove the noise. The trajectory are finally obtained using a morphological closing in time. We aim at statistically comparing populations. In order to aggregate trajectories from several samples, we project the datasets into the same space using a continuous transformation of each cell into a reference disk. We thus project all the obtained trajectories from a given population into this disk. We compute the speed vector on each time point of each detected trajectory. To obtain a dense representation of the norm and the orientation of the vector speed in the reference disk, we extrapolate the obtained vector speed to a regular lattice with a Gaussian Markov random field. Finally, we obtain two spatial maps of respectively the norm and the orientation of the speed [9](#).

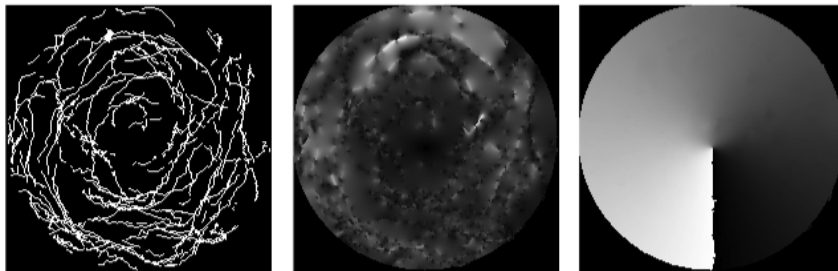


Figure 9. Exovesicles trajectories detected on the control population (left), the speed norm map (middle) and the angle map (left) showing an anticlockwise movement (black=0, white= 2π).

6.11. Extraction and Analysis of the Vascular Network to Classify and Grade Kidney Tumors in Histological Imaging

Participants: Alexis Zubiolo, Eric Debreuve, Xavier Descombes.

This work is made in collaboration with Philippe Pognonec (Team TIRO, CEA/UNS), Damien Ambrosetti (Histopathology department, CHU Pasteur, Nice).

The renal carcinoma is the most frequent type of kidney cancer (between 90% and 95% of all cases). Twelve classes of carcinoma can be distinguished, among which the clear cell carcinoma (CCRCC) and the papillary carcinoma (PRCC) are the two most common (75% and 10% of the cases, respectively). After the carcinoma has been diagnosed, the tumor is ablated and prepared for histological examination (fixation, staining, slicing, observation with a microscope). Along with genetic tests and protein reactions, the histological study allows to classify and grade the tumor in order to make a prognosis and to take decisions for the subsequent patient treatment. Digital histology is a recent domain (routinely, histological slices are studied by MDs directly on the microscope). The pioneer works deal with the automatic analysis of cells. However, one crucial factor for carcinoma classification is the structure of the vascular network. Coarsely, CCRCC is characterized by a "fishnet" structure while the PRCC has a tree-like structure.

In this context, our goal was to extract the vascular network from a given histological slice, compute features of the underlying graph structure, and classify the tumor into CCRCC or PRCC based on these features. The histological images being huge (typically, 100k x 100k pixels), they must be split into tiles (with some overlap to ease the combination of results) and processed tile-wise. The first step is to combine the color channels so that the vessels are as highlighted as possible. Then, the vascular network is detected by a processing pipeline including tailored, Gabor-like filtering, thresholding, and extraction of the skeleton. Small gaps in the skeleton are filled and some pruning is performed. Finally, the skeleton is converted to a graph representation. Based on the medical interpretation procedure, we focused our analysis of the graph on the following elements: the number of terminal and junction nodes, and the terminal branches. We proposed to compute the ratio between the number of terminal nodes and the number of junctions (T/J ratio), and the average length of terminal branches. Both features seem to be adapted to classification, especially the T/J ratio which, on the fairly small database of cases we currently have, exhibits an average value 65% higher for PRCC.

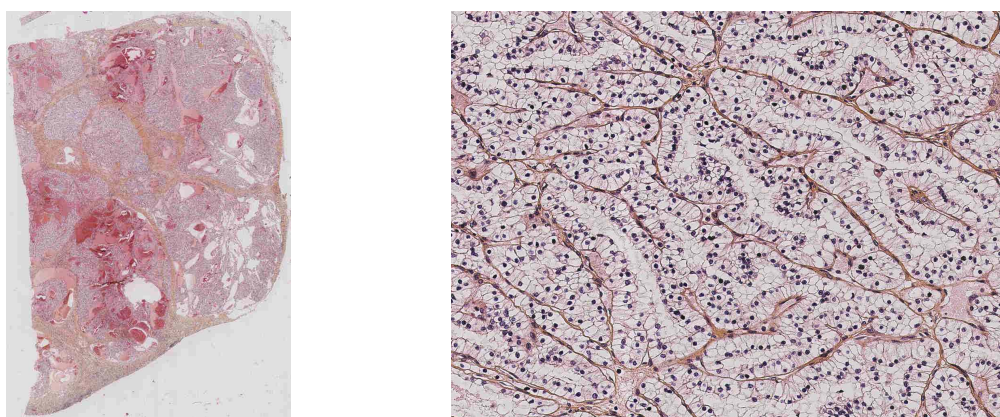


Figure 10. A histological slice through a kidney tumor: the whole slice (left) and a close-up (right).

7. Bilateral Contracts and Grants with Industry

7.1. Bilateral Contracts with Industry

General Electric Healthcare: a 6 months (from february to july) contract to finalize the PhD work of T. Benseghir.

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Renal tumor classification

Participants: Alexis Zubiolo, Eric Debreuve, Xavier Descombes.

Informal collaboration with the team TIRO, CEA/UNS (Philippe Pognonec), and the histopathology department of the CHU Pasteur (Damien Ambrosetti), Nice.

8.2. National Initiatives

8.2.1. LABEX SIGNALIFE

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

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

Florence Besse and Grégoire Malandain participated in the selection committee for LabeX PhD programme students.

8.2.2. ANR MOTIMO

Participants: Laure Blanc-Féraud, Xavier Descombes, Eric Debreuve, Huei Fang Yang, Ana Rita Lopes Simoes.

In collaboration with Institut de Mathématiques de Toulouse, INRA, Institut de Mécanique des Fluides de Toulouse, Laboratoire J-A Dieudonné, et IMV Technologies (PME). Details on the ([website](#))

8.2.3. ANR POXADRONO

Participants: Florence Besse [PI], Xavier Descombes, Laure Blanc-Féraud.

The young researcher ANR project POXADRONO is in collaboration with Caroline Medioni, Hélène Bruckert, Giovanni Marchetti, Charlène Perrois and Lucile Palin from iBV. It aims at studying ARN regulation in the control of growth and axonal guidance by using a combination of live-imaging, quantitative analysis of images, bio-informatic analysis and genetic screening.

8.2.4. ANR DIG-EM

Participants: Grégoire Malandain, Xavier Descombes.

Morphogenesis controls the proper spatial organization of the various cell types. While the comparatively simple process of patterning and cell differentiation has received considerable attention, the genetic and evolutionary drivers of morphogenesis are much less understood. In particular, we very poorly understand why some morphogenetic processes evolve very rapidly, while others show remarkable evolutionary stability.

This research program aims at developing a high-throughput computational framework to analyze and formalize high-throughput 4D imaging data, in order to quantify and formally represent with cellular resolution the average development of an organism and its variations within and between species. In addition to its biological interest, a major output of the project will thus be the development of robust general computational methods for the analysis, visualization and representation of massive high-throughput light-sheet data sets.

This 4-years project started october the 1st, 2014 and is leaded by P. Lemaire (CRBM, Montpellier). Participants are the CRBM, and two Inria project-team, Morpheme and Virtual Plants.

8.2.5. ANR PhaseQuant

Participants: Grégoire Malandain, Eric Debreuve.

The PhaseQuantHD project aims at developing a high-content imaging system using quadriwave lateral shearing interferometry as a quantitative phase imaging modality. Automated analysis methods will be developed and optimized for this modality. Finally an open biological study question will be treated with the system.

This 3-years project started october the 1st, 2014 and is leaded by B. Wattelier (Phasics, Palaiseau). Participants are Phasics, and three academic teams TIRO (UNS/CEA/CAL), Nice, Mediacoding (I3S, Sophia-Antipolis), and Morpheme.

8.2.6. Inria Large-scale initiative Morphogenetics

Participants: Grégoire Malandain, Xavier Descombes, Gaël Michelin.

This action gathers the expertise of three Inria research teams (Virtual Plants, Morpheme, and Evasion) and other groups (RDP (ENS-CNRS-INRA, Lyon), RFD (CEA-INRA-CNRS, Grenoble)) and aimed at understanding how shape and architecture in plants are controlled by genes during development. To do so, we will study the spatio-temporal relationship between genetic regulation and plant shape utilizing recently developed imaging techniques together with molecular genetics and computational modelling. Rather than concentrating on the molecular networks, the project will study plant development across scales. In this context we will focus on the Arabidopsis flower, currently one of the best-characterised plant systems.

8.2.7. Octopus Project

Participant: Eric Debreuve.

The Octopus project deals with automatic classification of images of zooplankton. It is conducted in collaboration with the Laboratoire d'Océanographie de Villefranche-sur-mer (LOV) et l'ENSTA Paris. The kickoff meeting took place in May 2015 and a 3-day *brainstorming* meeting on Deep Learning took place in December 2015. Participants are I3S (Frédéric Precioso and Mélanie Ducoffe), LOV (Marc Picheral and Jean-Olivier Irisson), and ENSTA Paris (Antoine Manzanera).

8.3. International Initiatives

8.3.1. Participation In other International Programs

ECOS-NORD PROJECT C15M01. In 2015 was the beginning of the execution of this project. The main work on this year was concentrated to understand clearly the DIC system located at UIS, its image formation model and phase recovery by simulations (joint paper accepted at ISBI 2016), and to acquire real data from it to be able to validate the simulated models.

Xavier Descombes was PI of a collaboration with the IITP in Moscow within a CNRS/RAS Grant (EDC26091) on the subject "Statistical Analysis of Images: mathematical modeling and applications".

8.4. International Research Visitors

8.4.1. Visits of International Scientists

Elena Zhizhina, Evgueny Pechersky and Serguei Komech from IITP Moscow (Russian Academy of Science) were invited one week respectively in october and in november.

Arturo Plata-Gomez, professor at the University Industrial of Santander (UIS) in Bucaramanga (Colombia) has visiting Morpheme from April 6 to April 24.

Simone Rebegoldi, Ph.D. student of the Department of Mathematics and Computer Science in University of Ferrara (Italy) spent 3 months in Morpheme group from may 1st to July 31.

8.4.2. Visits to International Teams

Laure Blanc-Feraud visited Universidad Industrial de Santander (UIS) in Colombia from December 3-11.

8.4.2.1. Research stays abroad

Laure en Colombie

9. Dissemination

9.1. Promoting Scientific Activities

9.1.1. Scientific events organisation

9.1.1.1. Member of the organizing committees

Xavier Descombes was member of the organization board for the "OPTITECH Event 2015".

9.1.2. Scientific events selection

9.1.2.1. Member of the conference program committees

Laure Blanc-Féraud was associate editor of the workshop on New Computational Methods in Inverse Problems - NCMIP 2015 (NCMIP) in ENS Cachan.

Eric Debreuve was the Area Chair of the topic "Image and video processing" for the conference European Signal Processing Conference (EUSIPCO).

9.1.2.2. Reviewer

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

Eric Debreuve was a reviewer for the conferences ISBI, ICIP, and ACIVS.

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

Grégoire Malandain was reviewer for the conferences ISBI, MICCAI, EMBC and TAIMA.

9.1.3. Journal

9.1.3.1. Member of the editorial boards

Laure Blanc-Féraud is Associate Editor of SIAM Journal Imaging Sciences and Traitement du Signal Journal.

Xavier Descombes is associated editor of DSP (Digital Signal Processing).

9.1.3.2. Reviewer - Reviewing activities

Eric Debreuve was reviewer for the journals Journal of Computational Physics (Elsevier), Pattern Recognition (Elsevier) and Revue de Traitement du Signal.

Xavier Descombes was reviewer for the journals IEEE TMI, IEEE IP, and IEEE SP.

Grégoire Malandain was reviewer for the journals MedIA, NeuroImage, IEEE TMI, and Medical Physics.

9.1.4. Invited talks

Grégoire Malandain was invited to give a talk at the *journées* "Bioimage-informatics", organized by the GDR 2588, and at "OPTITECH Event 2015".

9.1.5. Leadership within the scientific community

Laure Blanc-Féraud is director of GdR 720 ISIS of CNRS, a group for the animation of research at national french level on the thematic Signal Image and Vision. This group includes around 160 academic laboratories and twenty industrial partners totaling almost 3,000 members. She is member of the IEEE BISP (Biomedical Imaging Signal Processing) Technical Committee.

Xavier Descombes is member of the Scientific Committee of the competitiveness pole Optitech, member of IEEE BISP (Biomedical Imaging Signal Processing) Technical Committee and member of the Scientific Committee of Labex SIGNALIFE.

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

9.1.6. Scientific expertise

Laure Blanc-Féraud is part of the scientific committee of laboratory GreyC (UMR CNRS 6072) and of "Institut des Technologies Avancées en sciences du Vivant" (ITAV, USR CNRS 3505). She was part of the AERES expert committee of LJK Lab in Grenoble and part of the recruitment panel of a MCF at ISAE Toulouse and a "Comité de sélection" of a professor at the institute of Mathematics in Toulouse (IMT). She was external expert for the CPER Région Poitou-Charentes, and expert for PES applications for Région Franche-Comté. She was member of the jury of the price "La Recherche" She was member of the CNRS admission for chargé de recherche at INS2I of CNRS. She is expert member of the MIUR: Italian Ministry for Education, University and Research (Italie).

Eric Debreuve was a reviewer of a "Jeune chercheur" ANR proposal.

Xavier Descombes is expert for the MESR within the CIR program, and reviewer for three ANR proposals.

9.1.7. Research administration

Xavier Descombes is member of the "comité des projets" and the "comité de centre" of Inria CRI-SAM.

Grégoire Malandain is the head of the committee "Comité de suivi doctoral" of the Inria CRI-SAM.

9.2. Teaching - Supervision - Juries

9.2.1. Teaching

Master : Xavier Descombes, Traitement d'images, Analyse de données, Techniques avancées de traitement d'images, 30h Eq. TD, Niveau M2, ISAE, France.

Master : Xavier Descombes, Traitement d'images, master ISAB, 12h Eq. TD, Niveau M2, Université de Nice Sophia Antipolis, France.

Master : Xavier Descombes, Traitement d'images, master VIM, 12h Eq. TD, Niveau M2, Université de Nice Sophia Antipolis, France.

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

Master : Xavier Descombes, Bio-imageire, 9h Eq. TD, Niveau M2, Université de Nice Sophia Antipolis, France.

Master : Agustina Razetti, Traitement d'images, master ISAB, 6h Eq. TD, Niveau M2, Université de Nice Sophia Antipolis, France.

IUT : Agustina Razetti, Initiation à la mesure du signal, 18h Eq. TD, IUT Nice Côte d'Azur, Université de Nice Sophia Antipolis, France.

Master : Laure Blanc-Féraud, Fluorescence image restoration, 18h Eq. TD, M2 Computational Biology, University Nice Sophia Antipolis, France

Master : Laure Blanc-Féraud, Image restoration, 12h Eq. TD, M2 ISAB, University Nice Sophia Antipolis, France

Master : Laure Blanc-Féraud, Traitement numérique des images, 12h Eq. TD, M2 VIM, EPU University Nice Sophia Antipolis, France

Master 2: Eric Debreuve, Introduction to Inverse Problems in Image Processing, 28h Eq. TD, International Master "Computational Biology and Biomedicine", University Nice Sophia Antipolis.

Engineer 5th year: Eric Debreuve, 3D Computer Vision with the Kinect sensor, 32h Eq. TD, Polytech'Nice Sophia, University Nice Sophia Antipolis.

Master: Emmanuel Soubies, Traitement Numérique des Images, 10h Eq. TD, Niveau M2, EPU, Université de Nice Sophia Antipolis, France.

Licence: Emmanuel Soubies, Images et Filtres, 54h Eq. TD, Niveau L3, EPU, Université de Nice Sophia Antipolis, France.

9.2.2. Supervision

PhD: Alexis Zubiolo, Statistical Machine Learning for Automatic Cell Classification, Nice Sophia Antipolis university, defended december the 11th., Eric Debreuve (advisor).

PhD in progress: Lola Baustista, DIC microscopy image reconstruction, 1st november 2013, Laure Blanc-Féraud.

PhD in progress: Gaël Michelin, Quantitative tools for morphogenesis study, 1st october 2013, Grégoire Malandain (advisor).

PhD in progress: Agustina Razetti, Modelling and characterizing axon growth from in vivo data, 1st november 2014, Xavier Descombes (advisor), Florence Besse (co-supervisor).

PhD in progress: Emmanuel Soubies, MA-TIRF reconstruction and sparse l2-l0 optimization problem, 1st october 2013, Laure Blanc- Féraud and Sébastien Schaub.

9.2.3. Internships

Nicolas Cedilnik: L3 UNS. Detection and Classification of Cells Nuclei. Supervisors: X. Descombes, F. Besse.

Yaqun Liu: LM1 UNS. Tracking Growing Axons in 3D+t Microscopy Images. Supervisors: G. Malandain and C. Medioni.

Wei Shen: M2 Univ. Caen, RNA complex detection from confocal microscopy images. Supervisors: F. Besse, X. Descombes

Sen Wang: M2 Univ. Caen, Multiple Births and Cut algorithm including attractive interactions. Supervisors: E. Soubies, X. Descombes.

9.2.4. Juries

Laure Blanc-Féraud participated as chair to the PhD thesis committee of G. Tartavel (LTCI, Télécom ParisTech), as reviewer of the HDR of Anne Keonig (CEA LETI Grenoble) and reviewer of the 4 PhD theses: L. Gharsalli (Supelec, L2S, Gif sur Yvette), P. Irrera (LTCI, Télécom ParisTech), C. Soutour (IMB Bordeaux), O. Chabiron (IRIT Toulouse).

Xavier Descombes was examiner in the jury of A. Zubiolo and P. Cracium PhD defenses at University of Nice Sophia Antipolis and in the jury of Y. Quéau PhD defense at Paul Sabatier University (Toulouse) . He was reviewer for two PhD dissertations (M. Alsheh Ali at Paris V and R. Ben Salah, university of Poitiers) and one HdR (S. Chafik, university of Clermont Ferrand). He was president of three PdH juries (C. Meillier, university of Grenoble, S.G. Yeong, university of Nice Sophia Antipolis and R. Ben Salah, university of Poitiers).

Grégoire Malandain participated as chair to the PhD thesis committee of L. Guignard (Montpellier univ.), as reviewer to the PhD thesis of I. Melki (Paris Est univ.), H. Mi (Rouen univ.), M. Mustafa (Nottingham univ.), M. Vandenberghe (UPMC), W. Zhu (Strasbourg univ.), and as reviewer to the HdR of T. Delzescaux (UPMC).

9.3. Popularization

Gaël Michelin, Emmanuel Soubies, and Alexis Zubiolo participated as exhibitors to the "Fête de la science 2015" manifestation in Juan-les-Pins (palais des congrès).

10. Bibliography

Publications of the year

Articles in International Peer-Reviewed Journals

- [1] E. SOUBIES, L. BLANC-FÉRAUD, G. AUBERT. *A Continuous Exact l0 penalty (CELO) for least squares regularized problem*, in "SIAM J. on Imaging Science (SIIMS)", July 2015, vol. 8, n^o 3, pp. pp. 1607–1639 (33 pages) [DOI : 10.1137/151003714], <https://hal.inria.fr/hal-01102492>
- [2] A. VAN DER GUCHT, A. VERGER, E. GUEJ, G. MALANDAIN, G. HOSSU, Y. YAGDIGUL, V. ROCH, S. POUSSIER, L. MAILLARD, G. KARCHER, P.-Y. MARIE. *Age-related changes in FDG brain uptake are more accurately assessed when applying an adaptive template to the SPM method of voxel-based quantitative analysis*, in "Annals of Nuclear Medicine", December 2015, vol. 29, n^o 10, pp. 921-928, <https://hal.archives-ouvertes.fr/hal-01245045>

International Conferences with Proceedings

- [3] *Best Paper*
T. BENSEGHIR, G. MALANDAIN, R. VAILLANT. *A tree-topology preserving pairing for 3D/2D registration*, in "International Conference on Information Processing in Computer-Assisted Interventions, IPCAI 2015", Barcelona, Spain, International Journal of Computer Assisted Radiology and Surgery, Springer Berlin Heidelberg, June 2015, vol. 10, n^o 6, pp. 913-923 [DOI : 10.1007/s11548-015-1207-0], <https://hal.inria.fr/hal-01183573>.
- [4] A. CHINATTO, E. SOUBIES, C. JUNQUEIRA, J. M. T. ROMANO, P. LARZABAL, J.-P. BARBOT, L. BLANC-FÉRAUD. *L0-Optimization for Channel and DOA Sparse Estimation*, in "International Workshop on Computational Advances in Multi-Sensor Adaptive Processing (CAMSAP)", Cancun, Mexico, IEEE, December 2015, 4 p. , <https://hal.inria.fr/hal-01212042>
- [5] *Best Paper*
A. DUNCAN, E. KLASSEN, X. DESCOMBES, S. ANUJ. *Geometric Analysis of Axonal Tree Structures*, in "1st International Workshop on Diff - CV: Differential Geometry in Computer Vision for Analysis of Shapes, Images and Trajectories (in conjunction with BMVC)", Swansea, United Kingdom, October 2015, <https://hal.inria.fr/hal-01247192>.
- [6] M. LINDER, C. DUPLAA, T. COUFFINHAL, G. MALANDAIN. *Quantitative comparison of micro-vasculatures*, in "ISBI 2015 - International Symposium on Biomedical Imaging", Brooklyn, United States, April 2015, <https://hal.inria.fr/hal-01145908>
- [7] G. MICHELIN, L. GUIGNARD, U.-M. FIUZA, P. LEMAIRE, C. GODIN, G. MALANDAIN. *Cell Pairings for Ascidian Embryo Registration*, in "ISBI - International Symposium on Biomedical Imaging", New York, United States, April 2015 [DOI : 10.1109/ISBI.2015.7163872], <https://hal.inria.fr/hal-01113166>
- [8] G. MICHELIN, Y. REFAHI, R. WIGHTMAN, H. JÖNSSON, J. J. TRAAS, C. GODIN, G. MALANDAIN. *Spatio-temporal registration of 3D microscopy image sequences of Arabidopsis floral meristems*, in "ISBI - International Symposium on Biomedical Imaging", Prague, Czech Republic, April 2016 [DOI : 10.1109/ISBI.2015.7163872], <https://hal.inria.fr/hal-01251151>
- [9] E. POULAIN, S. PRIGENT, E. SOUBIES, X. DESCOMBES. *Cells Detection Using Segmentation Competition*, in "ISBI - International Symposium on Biomedical Imaging", Brooklyn, United States, IEEE, April 2015 [DOI : 10.1109/ISBI.2015.7164090], <https://hal.inria.fr/hal-01113167>
- [10] E. SOUBIES, S. SCHAUB, A. RADWANSKA, E. VAN OBERGHEN-SCHILLING, L. BLANC-FÉRAUD, G. AUBERT. *A Framework for Multi-angle TIRF Microscope Calibration*, in "ISBI - International Symposium on Biomedical Imaging", Prague, Czech Republic, IEEE, April 2016, 4 p. , <https://hal.inria.fr/hal-01257736>
- [11] H.-F. YANG, C.-S. CHEN, X. DESCOMBES. *Detection and Tracking of Golgi Outposts in Microscopy Data*, in "ISBI - International Symposium on Biomedical Imaging", Brooklyn, New York, United States, April 2015, <https://hal.inria.fr/hal-01113626>

- [12] A. ZUBIOLO, K. HARB, M. STUDER, E. DEBREUVE, X. DESCOMBES. *Morphological Analysis and Feature Extraction of Neurons from Mouse Cortices Multiscale 3D Microscopic Images*, in "37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC 2015)", Milan, Italy, IEEE Engineering in Medicine and Biology Society (EMBS), August 2015, <https://hal.inria.fr/hal-01176966>

National Conferences with Proceedings

- [13] Y. QUEAU, J.-D. DUROU, X. DESCOMBES. *Que peut-on apprendre d'une scène vue par une webcam à partir d'images prises au cours d'une journée ensoleillée ?*, in "Journées francophones des jeunes chercheurs en vision par ordinateur", Amiens, France, June 2015, 8 p. , <https://hal.archives-ouvertes.fr/hal-01161843>
- [14] E. SOUBIES, L. BLANC-FÉRAUD, G. AUBERT. *Seuillage CEL0 pour la minimisation l2- l0 : comparaisons avec IHT*, in "Colloque Gretsi", Lyon, France, September 2015, 4 p. , <https://hal.inria.fr/hal-01169557>

- [15] A. ZUBIOLO, K. HARB, M. STUDER, E. DEBREUVE, X. DESCOMBES. *Comment retrouver une constellation dans la galaxie ?*, in "Colloque Gretsi", Lyon, France, September 2015, 4 p. , <https://hal.inria.fr/hal-01176960>

Conferences without Proceedings

- [16] L. BAUTISTA, S. REBEGOLDI, L. BLANC-FÉRAUD, M. PRATO, L. ZANNI, A. PLATA. *Phase Estimation in Differential-Interference-Contrast (DIC) Microscopy*, in "ISBI 2016", Prague, Czech Republic, April 2016, <https://hal.inria.fr/hal-01255004>
- [17] E. SOUBIES, L. BLANC-FÉRAUD, G. AUBERT. *CEL0: a continuous alternative to l0 penalty*, in "Signal Processing with Adaptive Sparse Structured Representations (SPARS)", Cambridge, United Kingdom, July 2015, <https://hal.inria.fr/hal-01167192>

Scientific Books (or Scientific Book chapters)

- [18] E. SOUBIES, P. WEISS, X. DESCOMBES. *Graph Cut Based Segmentation of Predefined Shapes: Applications to Biological Imaging*, in "Pattern Recognition Applications and Methods", Advances in Intelligent Systems and Computing, Springer-Verlag, 2015, vol. 318, pp. 153-170 [DOI : 10.1007/978-3-319-12610-4_10], <https://hal.inria.fr/hal-01088384>

Research Reports

- [19] M. BREUILLY, K. CHATTI, J. DARCOURT, P. FRANKEN, J. GUGLIELMI, G. MALANDAIN, T. POURCHER. *From extraction of physiological features with dynamic μ -SPECT imaging to modelling of iodide biodistribution in stomach*, Inria Sophia Antipolis, August 2015, <https://hal.inria.fr/hal-01186222>
- [20] S. PRIGENT, X. DESCOMBES, D. ZUGAJ, L. PETIT, A.-S. DUGARET, P. MARTEL, J. ZERUBIA. *Assessing skin lesion evolution from multispectral image sequences*, Inria Sophia Antipolis ; Inria, June 2015, n^o RR-8745, <https://hal.inria.fr/hal-01164502>

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- [21] A. GAMAL ELDIN, X. DESCOMBES, G. CHARPIAT, J. ZERUBIA. *Multiple Birth and Cut for Multiple Object Detection*, in "Journal of Multimedia Processing and Technologies", 2012